Emerging evidence suggests that the central nervous system (CNS) is a key contributor to the problem of painful peripheral nerve disease in people with diabetes, according to a special article in the February issue of *Pain*, the official publication of the International Association for the Study of Pain (IASP).

Studies using advanced imaging techniques are providing new insights into the role of the CNS (brain and spinal cord) in the development of diabetic peripheral neuropathy (DPN) as well as its symptoms. According to a report by Dr. Solomon Tesfaye of Sheffield (UK) Teaching Hospitals NHS Foundation Trust and colleagues, "Although DPN has been considered a disease of the peripheral nerve, from numerous studies it is becoming apparent that there are indeed changes within the CNS that...appear to be concomitant with the evolution of painful and painless DPN."

Diabetic Peripheral Neuropathy—Not Just 'Peripheral'?

Diabetic peripheral neuropathy occurs in about one-half of all patients with diabetes. About half of these—that is, one-fourth of all people with diabetes—have pain and other symptoms of DNP. In addition to progressive and severe pain, patients with DNP have insensitivity to trauma, placing them at risk of foot ulcerations, infections, and amputations.

Several general risk factors for DPN have been identified, including poor control of blood glucose levels, high cholesterol, and obesity. But there is little information on factors leading to the development of painful DPN.

Previous studies have focused on the peripheral mechanisms of DPN—including "dying back" of nerve cells (from the furthest point upward) and loss of the myelin "insulation" of nerve cells. There is now strong evidence that small blood vessel disease leading to reduced oxygen supply (hypoxia) to the peripheral nerves contributes to the development of DPN. But there are still no "consistently unique" tests or indicators associated with painful DPN.

Researchers are now looking beyond the peripheral nerves to CNS factors that might explain the development of painful DNP. Those studies—using sophisticated MRI and magnetic resonance spectroscopy techniques—have led to a number of findings suggesting a role of the CNS, including:

- Differences in the cross-sectional area (width) of the spinal cord, particularly before symptoms of DPN have appeared.
- Loss of volume (atrophy) in the primary sensory cortex—the main brain area involved in sense of touch.
- Differences in blood supply in a part of the brain called the thalamus—oversupply (hyperperfusion) in painful DPN, compared with undersupply (hypoperfusion) in painless DPN.

- Changes in higher brain areas, specifically the "pain processing matrix"—thought to be involved not only in detecting the location and intensity of pain but also the emotional (affective) responses.
- Reductions in the brain gray matter, particularly in areas where "somatosensory perceptions" are processed.

Dr. Tesfaye and colleagues believe that further studies using advanced imaging techniques have the potential to further clarify the nature of CNS involvement in DPN. "Imaging may help us to unravel one of the fundamental unanswered questions—where can the primary pathophysiology of the painful symptomatology of DPN be found?" the researchers write. They hope that further detailed MRI studies "may lead to development of more rational therapies to help reduce the burden of DPN."

More information: Solomon Tesfaye et al. Diabetic peripheral neuropathy may not be as its name suggests, *PAIN* (2016). DOI: 10.1097/j.pain.0000000000000465

This topic, among others, will be discussed at **the first Middle East Practical Diabetes Meeting which will be held at Hotel Marriott Al Jaddaf, Dubai on April 13-14, 2016.**