

Short Paper

Pain and OA

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Osteoarthritis (OA), in which joint degeneration leads to a loss of mobility and function, is one of the most common causes of disability. The most prominent feature but least studied aspect of OA is joint pain. The World Health Organisation recently estimated that about 10% of the world's population over the age of 60 years suffers from OA pain¹ which equates to an enormous socioeconomic concern. Currently, arthritic pain is generally not treated efficiently and the side-effects of commonly used analgesic agents are often hazardous. Clearly there is a pressing need to better understand the causes and mechanisms of OA pain so that more efficacious targets can be identified to help alleviate these debilitating symptoms.

Experimental assessment of joint pain is extremely complex due to the subjective nature of pain and the cognitive interpretation of this sensory information. We and others have used behavioural studies to measure knee pain in animal models of OA²⁻⁴. In these studies, pain was assessed by joint incapacitance and von Frey hair algesimetry. Joint incapacitance gives a measure of hindlimb weight-bearing by using a dual channel weight averager, while von Frey hair algesimetry determines an animal's response threshold to a tactile mechanical stimulus applied to the hindpaw. Following induction of OA in rats by intra-articular injection of sodium monoiodoacetate, a significant weight-bearing deficit was observed in the ipsilateral hindlimb as well as the occurrence of referred pain in regions remote from the original osteoarthritic lesion. We have recently shown that a neurochemical called vasoactive intestinal peptide (VIP) induced pain in rat knees and that blockade of this peptide with the selective antagonist VIP₆₋₂₈ reduced joint pain in OA joints⁴.

The neurobiological processes responsible for the generation of OA pain are also not clearly defined. Noxious mechanical stimuli are detected by a specific group of sensory nerves (type III and type IV afferents) located throughout the joint in the capsule, ligaments, menisci, periosteum and subchondral bone⁵⁻¹⁰. These pain sensing nerve fibres, which typically have a high threshold of activation, are called noci-

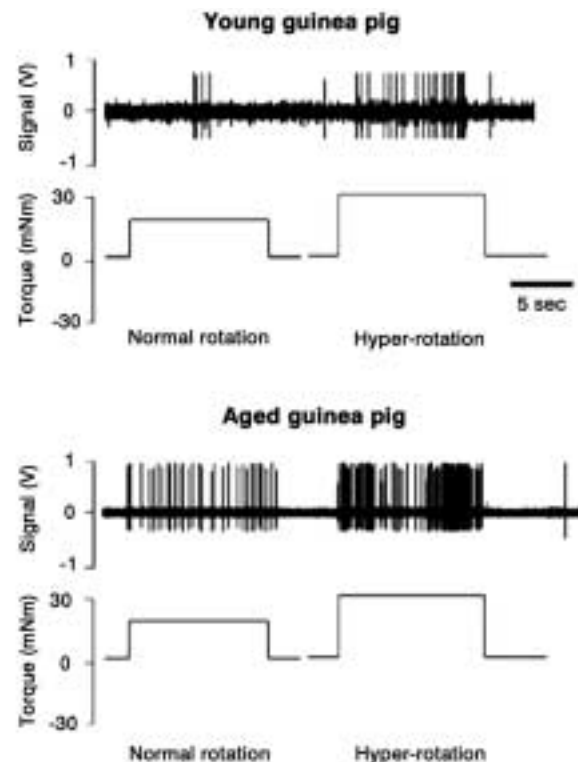


Figure 1. Electrophysiological recordings from young (top) and old (bottom) guinea pig knee joint afferents. Recordings were made in response to normal (innocuous) and hyper-rotation (noxious stimulus) of the knee joint. Afferent firing rate was significantly elevated in old versus young animals suggesting that joint mechanosensitivity and nociception is age-dependent.

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ceptors. Joint movement causes the opening of mechanogated ion channels located on the terminals of sensory nerves resulting in depolarization and nerve firing¹¹. The resulting action potentials are propagated towards the central nervous system, which translates this electrical activity into mechanosensation. If joint movement becomes painful, then nerve firing rate dramatically increases and the central nervous system interprets these signals as pain. We have recently shown that mechanosensory nerves become sensitized during OA causing an increase in afferent firing rate even in response to normal joint movements¹². In this same study we also found that local administration of VIP sensitizes joint nerves while the antagonist VIP₆₋₂₈ inhibited afferent activity. These findings provided the first electrophysiological evidence regarding the origin of OA pain and corroborated our behavioural studies described above.

Age has been highlighted as a potential risk factor for OA. Indeed one report has gone as far as proposing that almost everybody over the age of 70 years has some degree of joint deterioration¹. A question we were interested in answering was what effect does age have on the perception of joint pain? We carried out a series of experiments using young and old Dunkin Hartley guinea pigs, which are known to develop idiopathic OA with advancing age. Electrophysiological recordings were made from knee joint primary afferents in response to innocuous (normal working range) and noxious joint rotation. For a given level of torque, afferent firing rate was found to be significantly enhanced in older guinea pigs compared to young animals (Figure 1). Thus, joint mechanosensation is augmented in older guinea pigs indicating that nociception is age-dependent. Whether this is due to plasticity changes in the peripheral nervous system or whether this is correlated to severity of OA degeneration is currently under investigation.

In summary, OA causes a sensitization of joint nociceptors leading to increased pain perception. These nociceptive signals can be attenuated by local administration of a neuropeptide antagonist, VIP₆₋₂₈. Furthermore, mechanosensitivity and joint nociception is enhanced in old guinea pigs compared to younger animals. Future studies are required to gain a better understanding of the neurophysiological processes and the mediators responsible for the generation and maintenance of OA pain.

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