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Research Article

Knee Joint Neural Pathways and their Osteoarthritis Pathogenic Linkage Implications

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Abstract

Knee joint osteoarthritis, a widespread disabling disease with no known cause continues to produce considerable bouts of intractable pain as a result of multiple disease associated problems despite years of research. This paper examines some probable neural influences that may be involved or implicated in inducing and perpetuating knee joint osteoarthritis, a major chronically painful, disabling and debilitating health condition. Presented are data retrieved from several sources that discuss the nature of the knee joint nerves and their ramifications in various knee joint tissue, their proposed functional importance, and connections with the spinal cord, central nervous system and motor control pathways, as this affects joint biomechanics, pain production, joint instability at the knee, and possible knee joint pathology. As such, it is concluded that to reduce the risk of joint injury, as well as to improve the effectiveness of treatments designed to avert knee joint damage and ensuing osteoarthritis pain, a better understanding of the probable neural origin[s] of knee joint pathology and pain may permit the development of more precise as well as targeted noninvasive nerve sparing preventive and intervention strategies for mitigating disabling knee osteoarthritis.

Keywords: Cartilage Degeneration; Neural Pathways; Knee Joint; Osteoarthritis; Pain

Introduction

Osteoarthritis, a widespread oftentimes progressive albeit non-fatal disabling joint disease affecting many older as well as younger adults commonly produces high levels of intractable pain, stiffness, and movement dysfunction. A disease now acknowledged to not only involve the cartilage tissues lining the joint, but also its surrounding and intrinsic tissues, including the synovial membrane lining the joint capsule, the muscles surrounding the joint, the joint ligaments, tendons, menisci, and bone as well as the nerves and their diverse joint capsule, ligament, bone, menisci, and muscles sensory endings, its treatment remains highly challenging and commonly induces limited functional results. As well, the limited ability to mitigate the disease, plus metabolic factors that foster obesity, frequently induce varying degrees of knee joint instability, lower leg mal-alignment, muscle weakness and inflammation of the surrounding knee joint tissues, and muscles plus possible damage to their embedded nerve endings that transmit or relay sensory and motor information to and from the spinal cord and central nervous system, thus often inducing a further cycle of joint destruction, neuro inflammation and pain provoking central sensitization mechanisms [1-3].

At the same time, and despite a host of pharmacologic related research efforts and various resultant efforts developed to mitigate the pain induced by this disease, most fail to impact the disease process and extent to any permanent degree, and some may well exacerbate the disease and/or worsen the individual's health status, as well as impacting important sensory messages that are designed to help avert excess injurious joint movements. Moreover, even when attempted, the disease is not uniformly remediated by surgery or similar invasive strategies and pain once localized initially and intermittently to the knee area can spread to other sites and become persistent if the pain fibers in the joint remain hyper excitable in response to noxious internal as well as non-noxious external stimuli.

It is possible however, that concerted efforts to more clearly examine, uncover or clarify those key sources of knee joint osteoarthritis pain, especially those of mechanical origin that can initiate or perpetuate an unrelenting inflammatory state that stimulates multiple pain receptor pathways as well as possible progressive nerve damage, and increases in peri vascular nerve density in damaged knee tissues, along with abnormal centrally located as well as muscle based neural responses [4,5], can yet be mitigated or prevented to some degree. Moreover, rather than blocking or cutting pain provoking nerves, efforts to protect the nerve tissues that provide the damaged knee joint with sensory as well as motor control sources of information, may be more helpful than not in efforts to relieve pain and restore function to affected joint tissues, as well as the nervous pathways serving the knee that project neuro segmentally to muscles in multiple respects, including but not limited to, multiple social and economic realms, plus lower levels of undue suffering and dysfunction [6].

By contrast, because factors that stem from an impairment of any component of the nervous pathways supplying the knee, along with age associated nervous system alterations, including direct damage to the sensory receptors embedded in the joint tissues of the knee that may be significantly damaged and induce neuropathic pain [7], along with various neuropathies [8] or other neural conditions [9] one or more of these structures if damaged in some way may yet render some key contributions to the disease due to their influence on pain, limb position sense, limb movement patterns and responsiveness to perturbations, thus possibly failing to protect against excessive bouts of joint impact loading sufficient to cause damage to cartilage and its matrix, plus joint instability [10,11]. As well, persistent pain that extends to multiple sites and induces a state of pain sensitization to even the slightest movement may be expected to impact mental health status, as well as the ability of the affected adult to function physically quite markedly [9-11].

In addition, among the results of this possible scenario is the induction of an undesirable state of knee muscle atrophy and possible excess weakness, ligament degeneration and laxity, plus poor muscle endurance, essential for adequate joint protection [9]. At the same time, several other centrally derived sensory-motor factors that appear to sub-serve movement and joint sense, plus overall motor control and co-ordination may have a further bearing on seriously exacerbating osteoarthritis joint damage if these are rendered suboptimal or distorted, especially as far as their ability to activate one or more muscle, ligament or tendon based sensory receptors in a timely and protective way during locomotion and other weight bearing activities [9].

However, due to the reliance of radiographs alone for diagnosing osteoarthritis and a predominant focus on the impacts of the disease on cartilage tissue, but rarely on its surrounding supportive tissues, and possible upstream pathological determinants [12], including the possible involvement of the intricate neural network of the knee, which is determined by L2-S2 nerve branches [13], as well as the state of health of these neural connections, efforts focused solely on pain relief may foster joint attrition inadvertently, .and a continued cycle of pain and joint destruction. Indeed, rather than efforts to consider whether there is a breakdown in the protective role of the intricate neural network at the knee joint that is impacting optimal functional performance in some way in substantive numbers of osteoarthritis cases, many current articles that do describe targeted efforts to prioritize relieving knee joint pain do this by examining the influence of selective and invasive nerve cutting, or nerve blocking strategies via anesthetic injections [14] in an effort to provide an alternative for total knee replacement surgery in cases suffering from refractory knee osteoarthritis pain [15] even though intuitively, this may yet expose the joint to more damage, and hasten the processes of joint destruction via its pain averting impact on joint proprioception and the 'absence' of painful sensory cues to limit weight bearing, while inducing some form of neuropathy [8], thus furthering rather than containing any abnormal joint biomechanics and their oftentimes dire consequences [9,16].

As argued by Dye., *et al*. [17] the entire degree to which the richly innervated knee and its intraarticular components are maintained optimally at a high structural and functional level is probably crucial in all likelihood for fostering tissue homeostasis and integrity, and mediating the prevailing kinematics and kinetic properties of the lower leg, knee joint contact forces and contact areas, ligamentous strains, cartilage stresses, fibril strains, and fluid pressures [16] and thus should be evaluated and assessed at the outset of any knee joint pain complaint. On the other hand, the failure of current intraarticular soft tissue reconstructions of the knee as well as the failure of interventions that target nerve transmission, may be due, in part, to both faulty assumptions, as well as their limited ability to effectively restore joint neurosensation attributable to excess joint damage, persistent nerve entrapment or stretching, focal swelling,

changes in its integrity and signal intensity where this exists [8]. As well there may signs of denervation edema and muscle fat infiltration in association with motor nerves that are challenging to detect and prevent pain resolution if undetected [8]. A possible associated slower than desirable isometric time rate of tension development and reduced peak torque for the knee extensors of such as patient is also compatible with a reduction of facilitatory afferent inputs from these muscles that can provoke poor muscle endurance [18], and/or the perpetuation of central motor control abnormalities that compound any damage at the knee joint.

Review aims

Since osteoarthritis remains the most common form of arthritis and is a disease that affects many older adults highly negatively, this report elected to gain insight into the possibility that disturbances in neuromotor control may be one contributing factor to the alterations in motor function found in knee osteoarthritis that can arguably impact joint biomechanics and physiology and explain its progressive nature. That is, this narrative summary report examines if there is probable association between the knee joint neural circuitry and exposure to trauma that can lead to biomechanical disturbances and consequent joint damage, but whether this is often overlooked in the more immediate desire to alleviate the ensuing knee joint pain and patient distress [9], as well as by possible patient centered 'demands' for rapid pain relief.

Accordingly, the specific review aim was to examine what we currently know about the anatomy and function of the sensory receptors that serve the knee joint and their central connections and to thereby provide a basis for evaluating whether more attention to the contribution of the knee afferents and their role in averting pathology plus, whether their failure that may serve as a source of osteoarthritis pain, as well as possible joint destruction are indicated.

Significance

An improved ability to conceptualize the causes of knee joint pathology, and select the best possible methods of intervention for ameliorating the knee osteoarthritis symptoms that does not induce excess anesthesia or surgically destroy the nerves that supply the knee may help avert unwanted side effects such experiencing altered joint sensation, bruising, crusting, hyper pigmentation, itching, local pain, numbness, redness, swelling, tenderness on palpation, and tingling and possible increases in joint damage due to excess loading that may ensue [19].

Hypotheses

It was hypothesized that the knee joint sensory-motor pathways are clearly important probable determinants of knee joint health and stability.

Conversely, where nerve damage or dysfunction of the knee sensory-motor systems exists and is not identified or is treated by invasive attempts to alter or block knee nerve transmission processes artificially, more knee pain and joint damage can possibly be anticipated in the long term.

To this end, this paper is a narrative one divided into three major components, including the implications of this information for research and practice. It houses articles extracted largely from PUBMED published between January 01, 1980-October 31, 2022, using the key words: *innervation of the knee joint, mechanoreceptors, muscle spindles, osteoarthritis.* The focus was placed on the neuronal pathways underpinning motor control and pain sites located in the periphery rather than any psychosocial factors. The discussion centers on how this information might be employed to foster conservative forms of joint protection and intervention, rather than surgical and invasive approaches for ameliorating knee osteoarthritis pain.

Methods

To obtain the desired data to fulfill the study aims, an extensive scan of available documents housed in the PUBMED data base and published in English over the time January 01, 1980-October 31, 2022, using the key words: *innervation, knee joint, mechanoreceptors, muscle spindles, osteoarthritis.* The focus was placed on the neuronal pathways underpinning motor control and pain sites located in the periphery rather than any psychosocial factors. A narrative overview is provided and the discussion centers on how this information might be employed to foster conservative forms of joint protection and intervention, rather than surgical and invasive approaches for ameliorating knee osteoarthritis pain. Excluded were surgical studies, studies of osteoarthritis in general, and preprints.

Results

Studied since the 1940s there are currently 1547 articles listed on PUBMED that focus on some aspect of the knee joint neurological system and its extrinsic origin in the lumbar spine, as well as its intra articular ramifications, and central connections. Often reviewed or studied separately, all three major components of this complex neural network that extends beyond the knee joint to the central nervous system are involved in controlling its motion and stability, as well as pain [8,20-24]. Supplying different tissue structures and knee joint, the extensive array of nerve branches to the knee that originate from variable regions of the lumbar spinal cord and include 6 key nerves including: the superolateral branch from the vastus lateralis, the superomedial branch from the vastus medialis, the middle branch from the vastus intermedius, the inferolateral (recurrent) branch from the common peroneal nerve, the inferomedial branch from the saphenous nerve, and a lateral articular nerve branch from the common peroneal nerve are vital because collectively they convey important information to and from multiple knee joint sites as well as various components of the knee joint, including the joint capsule [25] and those muscles that move and stabilize the knee [24], especially the muscle spindle sensory organs, that in turn receive top-down as well as peripheral input, including those from surrounding from cutaneous afferents that mediate knee joint control and protection [26].

As well as the key knee joint tissues, the tissues covering the bones that make up the knee joint as well as the bone regions located at the top of the tibia and fibula of the knee joint, plus the walls of their associated blood vessels to the knee are supplied by a wide network of joint as well as accessory nerves which carry information to the brain via the L2-S2 dorsal nerve roots of the spinal cord.

Hence, even though the precise anatomical arrangement of this extensive sensory network in both the capsular and ligamentous tissues as well as in the periosteum, joint capsule and epiphyseal bone bloodvessel walls of the knee joint may not be the focal point of osteoarthritis research, research suggests that the network probably serves both a proprioceptive protective role as well as a nutritive role. Moreover, even though there are many discrepancies as far as the anatomical description and terminology of the articular nerves supplying the human knee capsule and other structures [25], their association with a functional role in the processes of joint loading and possible joint degradation processes and pain if impaired, cannot be ruled out with any degree of accuracy.

Indeed, even if the pattern of distribution of sensitive nerves supplying the knee joint capsule may allow for accurate and safe movements at the knee when intact [25], if they are injured, compressed, or traumatized in some way, some degree of subnormal joint function appears possible. In particular, if prolonged, and especially if the muscle spindle receptors of any key knee muscle are compromised in some way and for any reason, one can expect the independent preparatory control of reflex muscle stiffness, the selective extraction of information during implicit motor adaptation, and ensuing segmental stretch reflexes to prove inefficient or suboptimal at best [26].

Moreover, while receptors of the knee joint that stem from its major nerves are able to produce a discriminating afferent inflow to the central nervous system under normal conditions and thereby to contributing to the protection and function of the joint via its muscles [27], there is a positive correlation between the number of mechanoreceptors per standardized area unit and the clinical presentation of certain knee disorders [28]. Thus, the presence of some form of permanent neural damage, often seen in osteoarthritis, may help explain why the disease continues to produce increasingly aberrant movements and oftentimes evidence of knee instability and excess pain and excess stimulation of the joint pain receptors. Moreover, instead of providing optimal loading responses to various tensile, compressive, and shear deformities placed on knee joint tissues, the resultant deficiencies in mechanical transduction processes and that might ensue may fail to stimulate appropriate stress adaptors and the capacity of multiple knee tissues to withstand collectively and successfully to avert knee joint injury and pain [29]. Physical therapies, including bracing, taping, electrical muscle stimulation and other modes of noninvasive intervention designed to promote propriocepive sensibility may in contrast provide for safe and temporary relief of knee osteoarthritis pain that is therapeutic and safe [30].

In sum, this system of knee joint control that involves multiple nerve pathways is very complex while designed to protect the joint, may fail to do so a) if their ability to transmit desirable afferent information to the spinal cord and central nervous system is disrupted or the nerves themselves are compromised in some way, for

example by prevailing abnormal disease associated static and dynamic tensile stresses in the tissues containing these. Indeed, considerable evidence has pointed to the idea that mechanoreceptors at the knee joint may have an effect on its neuromuscular function including proprioception, muscle reflexes muscle stiffness, muscle-force deficits, gait, and muscle coordination and timing changes [31,32].

There may also be excess activation of pain carrying nerve fibers if joint inflammation prevails, as well as if those who are overweight produce inflammatory substances within the knee joint extra and intra-articular fat pads, and blood vessels passing between the tibial and femoral periosteum and are compounded by various degrees of reactive muscle spasm and subchondral bone fractures. As well nervous transmission at the knee may be impaired in the face of any persistent or progressive damage to the knee joint capsule, the medial meniscus, the cruciate, collateral and meniscofemoral ligaments, and sheaths of tendons related to the knee joint. More joint damage than desirable might be expected to readily prevail thereafter, especially if knee joint effusion occurs and these nerve sources designed to protect the joint fail to respond to dynamic movements that place excess stress on the joint in a timely manner.

Diego Ariel de Lima., *et al*. [33] who studied the human knee anterolateral ligament innervation pattern concluded that it is thus highly important to understand the nature of the knee neural innervation and their differing functional attributes as their failure to function optimally might raise the risk of an injury that could further compromise the proprioceptive role of those receptors designed to secure joint stability. We also note and concur that despite the central involvement of hyaline cartilage in osteoarthritis pathogenesis, the source of this damage, and ensuing pain can undoubtedly stem from damage or trauma to the richly innervated synovium, subchondral bone and periosteum components of the joint as well as the nerve endings and their central connections. Tissue damage during joint degeneration also generates enormous bouts of nociceptive stimuli in the presence of inflammatory mediators, including bradykinin, prostaglandins and leukotrienes that both lowers the threshold of the Aδ and C pain fibers, but may reduce inputs to other afferents that could counter this, resulting in a heightened response to painful stimuli [34]. Related alterations in proprioceptive inputs and responses may further impact postural control and its impact on stability when the individual is in an upright position [35].

Consequently, although not the only cause of osteoarthritis knee pain, it is conceivable that any deficient or abnormal neural input from the knee joint nerves in the periphery may clearly foster a cycle of pain and dysfunction due to their importance in subserving and regulating central nervous system sensory functions, plus segmental and intersegmental sensory motor neural processes that underpin knee joint sensibility, motion and stability, plus muscle tone and various motor reflexes [36]. Since a majority of knee afferents are indeed unmyelinated [35], and respond to strong mechanical stimulation or noxious forced movement [36], even under conditions of nerve blocks, a majority of these fibers can yet be expected to relay noxious stimuli [35] that in time may override any invasive forms of intervention designed to ablate or impact nerve conduction at the knee. As well, since there are multiple nerves and projections involved in knee motor control, the choice of which nerve to ablate and how precise the ablation process is and for how long, must remain uncertain at best.

Wotjys., *et al*. [37] for example identified that substance-P containing nerve fibers associated with pain production in the retinaculum, fat pad, periosteum, and subchondral plate of patellae that can all be affected with degenerative disease and their widespread and possibly non uniform distribution may explain why denervation at the knee may still produce pain or non-permanent results especially if these procedures damage the joint capsule and its sensory innervation [20] and thereby the ability to withstand or respond to strong force or deep pressure [38]. Moreover, if osteoarthritis pathology is not reduced, a recent study conducted in an animal model showed that as regards pain receptors at the knee joint, one might expect these to increase in the bone, synovial tissues and meniscus of the knee medial compartment in the presence of osteoarthritis damage [39], for example if one or more reflexive protective mechanisms are suboptimally activated and fail to trigger muscle responses that would prevent the joint from excessive stretch stimuli. On the other hand according to the gate theory of pain deficient sensory inputs might well exacerbate the influence of any persistent pain inputs due to presence of osteoarthritis damage or inflammation.

Findings by Elfvin., *et al*. [40] that emphasize the complex innervation of the synovial membrane, with nerve fibers containing a host of neuroactive substances further imply these fibers are probably involved in many functions such as vasoregulation and control of synovial secretion in addition to being a source of mediators in joint inflammation. The presence of optimally functional fine tuning of limb movement and coordination at the knee that impacts its weight bearing responses, and protective mechanisms against injury, may well stem from more distant neural sources such as the ankle [41] and lumbar spine, the source of knee joint innervation networks, as well as explaining pain origins that are not influenced by standard practices localized to the knee joint. The fact that repeat treatments are needed quite commonly, and post injection studies commonly do not mention the parallel importance of averting further injury to the joint in the absence or decrease of pain post injection, implies there is less chance of any true curative impact as documented [42,43]. As with most studies examining the use of injections with various substances and that are said to reduce pain, and have an acceptable safety profile uniformly, almost all fail to employ functional measures, or advanced diagnostic tools to examine joint structures and their responses over any extended period [44,45] and study cases are often younger than 60 years of age [44] and who show declining returns in pain perception within 6 months. However, why this form of intervention does not provide for any sustainable outcomes is unclear at best, although possible explanations include the persistence or exacerbation of joint mechanoreceptor abnormalities, declining sensory receptor numbers, plus heightened pain stimulation in the joint due to abnormal stimulation of intra articular bone and vascular sensory receptors [46]. In addition, damage to ligaments containing sensory receptors can foster a state of abnormal neuromuscular junction remodeling and atrophy in the quadriceps and other lower leg muscles, associated with inflammatory signs and changes in muscle gene and protein expression [47,48].

There can hence be little argument that more attention in this regard must be forthcoming in the context of any preventive effort against further joint injury whether injections are forthcoming or not [29,49,50]. Unfortunately, this remains a very poorly researched realm, and one not well studied in the older population. In this respect, the outcomes of injecting key knee nerves said to be somewhat superior to standard physical therapy may indeed be less beneficial in the long run and has not been tested thoroughly alongside standard therapy [49] to establish if it is possible much suffering that could be averted to some degree persists unabated [50] or returns once the anesthesia wears off, especially among the obese osteoarthritis population [51] and those cases with sustained or prolonged knee joint effusion and sinovitis [52].

Discussion and Conclusions

Osteoarthritis, the most common joint disease remains the single most important cause of disability in the older adult population and continues to pose significant challenges to health care professionals despite years of study In this respect. Often highly neglected in this realm are references to the role of the knee joint nerves and their widespread connections and functional importance.

Nonetheless, both past and current evidence continues to point to a possible role of some form of damage or disruption or slowing of one or more of the neural pathways subserving the knee joint and that commonly influence and control the normal timing and desired response magnitudes of various limb movements and their resultant impact on joint reactive forces in the absence of joint pathology. Indeed, the possibility of an impairment in some component of the intricate and complex knee joint nerve supply and its spinal segmental, intersegmental, as well as their central and motor control connections may well explain the clinical observation of oftentimes distinct postural changes in the lower leg in cases suffering from knee osteoarthritis during standing and walking, which could contribute to further joint derangement. There may also be an ensuing reduced ability to avert falling injuries that may lead to more extensive joint injury in those with poor joint sensation and delayed or suboptimal muscle responses.

However, a review of the literature shows almost all current 2022 medical and surgical approaches designed to mitigate knee osteoarthritis, appear to focus solely on pain relief, rather than uncovering any meaningful understanding of any pain origins and their possible reversal. This may be because both the patient and provider continue to believe the disease is a degenerative one, and that no improvement can be expected over time and rather than wait for possible healing states to emerge, desire immediate pain relief, regardless of the multiple possible sources of excessive pain that could be averted, and the impact of some intervention modes on possibly exacerbating this inadvertently in the long run.

For example, even if knee pain abates, ample research shows the muscles surrounding the osteoarthritis joint are commonly weaker, and thus may respond more slowly than healthy muscle to perturbations especially in the absence of pain cues, and no concurrent attempt to foster improvements in knee muscle strength or endurance. In addition, surgery does not always benefit the individual especially if important nerves are already damaged, and minimal attention is given to surgical impacts of cutting the skin and joint tissues on joint inflammatory and protective processes.

Since there is increasing evidence that the rates of disability produced by osteoarthritis are not inevitable, but that lifestyles and behaviours have powerful influences as well, even palliative approaches such as weight loss, and joint protection may reduce the degree of harm that can stem from invasive efforts that attempt to disrupt nerve transmission. Moreover, injections that are used to a high degree and are reportedly safe, may not provide any greater benefit than placebo, and may yet be harmful if repeated or the joint is overused thereafter [53]. As well, whether any of these recommended approaches can assist in efforts to improve cartilage regeneration efforts and can minimize inflammation that can worsen structural damage, while improving the mechanical environment of *the* knee joint, also awaits further research. However, it is the present author's view that to correct or attenuate osteoarthritic symptomology safely, efforts to examine and accurately differentiate the possible key sources of preventable pain and dysfunction, followed at a minimum by carefully construed joint protection education and the provision of any desirable resources and prescriptive advice as far as the benefits and downside of nerve blocks, nerve ablation, joint injections, narcotic and excess pain medications are concerned. Stressed too, should be the ongoing need to maximize muscle function, regardless of any other desirable extrinsically applied or advocated strategies, and possibly in allaying nerve growth in bone cysts found in osteoarthritis subchondral bone [59]. It is also the author's view that even if such an approach does not prevent the progression of the disease or reverse it, health status as a whole is likely to be more positively impacted than not. Since for many older people with knee osteoarthritis, the ability to engage or not engage in meaningful social actions and functional activities is key to their well-being, helping to restore their ability to function physically and do no harm is seemingly imperative for many. The awareness that abnormally mediated cartilage cell-matrix interactions may be occurring inadvertently as a consequence of abnormal motor control mechanisms as a result of nerve damage or pathway disruptions also appears especially salient. On the other hand, a role for careful sensory stimulation approaches that parallel protective approaches against impact loading may arguably help to reduce intractable pain, while fostering a state of knee joint tissue reconstitution, rather than excess cartilage matrix damage, and poorly coordinated knee movements and heightened pain sensitivity responses [54,55]. As well, denervation strategies and others that may relieve pain should be carried out cautiously and mindfully, because these may yet foster a state of increasing susceptibility to joint destruction if parallel efforts are not made to protect the 'painfree' joint from excess loading due to an improved ability to function physically for extended periods, at least, temporarily [56,57].

In the interim, it can be deduced that even if only considering the knee joint ligaments alone, their compromise could induce an array of highly disordered movement and position messages as well fostering abnormal noxious stimuli. In turn, their effects on the muscle-spindle system surrounding the affected knee are so potent that even ligament stretches at very low loads may induce major loading aberrations [58]. These events may well have the added effect of inducing a differential array of abnormal biomechanical responses and a limited ability to adapt favorably to joint loads at the molecular and cellular level [29], while provoking long term adverse neuronal influences that mediate bone pathology and chronic pain states [59,60].

As such, it appears reasonable to assert that a failure to detect and intervene upon the presence of any suboptimal reflex control mechanisms at the knee joint may not only engender excesses of ligament laxity and joint instability, as well as injurious falls, but can undoubtedly induce greater degrees of cartilage and bone attrition and perpetual pain states than the osteoarthritis patient would otherwise experience if their nerves were intact and able to help stiffen the knee muscles optimally when exposed to perturbations. By analogy, to prove efficacious, osteoarthritis preventive intervention strategies that account for the prevailing status of the nervous system as this impacts the knee joint physiology and structure, especially muscle structure and function, may be expected to influence the molecular environment of the cartilage tissue more favorably than not.

In short, it is concluded that while more research is desirable, attention to the neural status of the knee osteoarthritis sufferer, especially its impact on muscle force production, and intervening insightfully using minimally invasive approaches may make the difference between a life of chronic pain, and an inability to engage in meaningful social actions and functional activities that are related to overall health, as well as health care needs and costs. Needed here in all likelihood are knowledge of basic knee joint control mechanism, neuropathic sources of pain, and cartilage and bone molecular responses to muscle contractile processes and their impact on movement quality. As well, the integration of careful holistic differential assessments, recognition or reframing the osteoarthritis problem as a possible neural network control abnormality as indicated, plus careful long-term planning, management and periodic neural based evaluations is strongly advocated.

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Conflict of Interest

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