Aging of the Somatosensory System: A Translational Perspective

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Balance in the elderly population is a major concern given the often catastrophic and disabling consequences of fall-related injuries. Structural and functional declines of the somatosensory system occur with aging and potentially contribute to postural instability in older adults. The objectives of this article are: (1) to discuss the evidence regarding age-related anatomical and physiological changes that occur in the peripheral proprioceptive and cutaneous systems, (2) to relate the basic science research to the current evidence regarding clinical changes associated with normal aging, and (3) to review the evidence regarding age-related proprioceptive and cutaneous clinical changes and relate it to research examining balance performance in older adults. The article is organized by an examination of the receptors responsible for activating afferent pathways (muscle spindle, golgi tendon organ, and articular and cutaneous receptors) and the corresponding sensory afferent fibers and neurons. It integrates basic science laboratory findings with clinical evidence suggesting that advanced aging results in a decline in cutaneous sensation and proprioception. The potential relationship between postural instability and sensory impairments in older adults also is discussed. Current laboratory and clinical evidence suggests that aging results in: (1) diverse and nonuniform declines in the morphology and physiological function of the various sensory structures examined, (2) preferential loss of distal large myelinated sensory fibers and receptors, and (3) impaired distal lower-extremity proprioception, vibration and discriminative touch, and balance. These findings provide foundational knowledge that emphasizes the importance of using reliable and valid sensory testing protocols for older adults and the need for further research that clarifies the relationship between sensory impairment and balance.

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Balance is a fundamental skill that is often compromised with advancing age.[1] Balance impairment in older adults increases the risk for falls,[2] which ultimately can lead to increased morbidity,[3] mortality,[3,4] and health care costs.[5] One third of adults over the age of 65 years fall each year, and fall-related costs are expected to exceed $32 billion by the year 2020.[5] Falls in older adults also are associated with decreased confidence in movement and balance.[6,7] Loss of confidence, or fear of falling, often results in decreased physical activity that, in turn, may perpetuate further decline in postural stability and quality of life.[8] Consequently, researchers and clinicians have an intense interest in identifying the components that contribute to postural instability and falls in older adults.

Postural control represents a complex interplay between the sensory and motor systems and involves perceiving environmental stimuli, responding to alterations in the body's orientation within the environment, and maintaining the body's center of gravity within the base of support.[9,10] Sensory information about the status of the body within the environment emanates primarily from the proprioceptive, cutaneous, visual, and vestibular systems. Researchers[11–13] have concluded that individuals rely primarily on proprioceptive and cutaneous input to maintain normal quiet stance and to safely accomplish the majority of activities of daily living, but must integrate information from multiple sensory systems as task complexity and challenge to postural stability increase.

Multimodal afferent input is integrated at various levels of the central nervous system, resulting in efferent processing for the coordinated firing of multiple alpha motoneurons and their corresponding muscle fibers. Specifically, processing occurs reflexively at the level of the spinal cord or is sent cranially to subcortical or cortical areas for more refined voluntary movements. The speed at which these events occur belies the complexity required for adequate functional outcomes. For example, research suggests that older adults who cannot recover from external environmental challenges (eg, a "trip") within 145 milliseconds are likely to fall, underscoring the cause for concern in the normal age-related declines noted in the functioning of the sensory or motor systems.[14]

Impairments in sensation, strength (force-generating capacity of a muscle), reaction time, vestibular function, and vision occur with aging and are believed to collectively contribute to the increased likelihood of falling.[15–17] Physical therapists are faced with the challenging task of examining older adults for the presence of sensorimotor impairments and then accurately relating these deficits to the patients' functional abilities in order to plan interventions that optimize function and reduce fall risk. The complexity of this evaluative task is increased by the heterogeneous characteristics within the older adult population and the reality that apparently healthy older adults may well have idiopathic changes and diverse impairments that potentially contribute to a decline in balance.

The reality of what is normal for elderly people underscores the importance of addressing subtle and not-so-subtle balance problems with all older adults. A 2003 meta-analysis provides evidence that multidisciplinary and multifactorial risk factor screening and intervention programs for community-dwelling older adults are likely to prevent falls.[18] Additionally, research suggests that balance and mobility measures may help distinguish between the effects of aging and disease states such as peripheral nerve disease,[19] thus helping clinicians identify patients who may be moving along a continuum toward further balance impairment and fall risk (Fig. 1).

When faced with a multidimensional problem such as balance impairment, the more knowledge that a person has about both the physiological and clinical foundations of the problem, the broader the potential avenues for developing effective assessments and interventions for all older adults. Translational research directly linking age-related physiological change in somatosensory systems with functional outcomes in humans is scant, no doubt due to the challenges inherent in examining physiological correlates in live human subjects. Currently, no reviews were identified that have addressed the collective body of knowledge surrounding cutaneous and proprioceptive declines that occur with aging, even though these

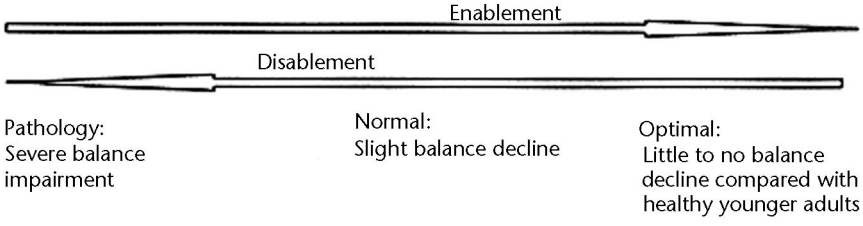

Figure 1.
Balance impairment in older adults. The goals of physical therapy are to enable a shift toward normal function for those with pathology and optimal function for those with normal age-related balance decline.

Table 1.
Axon Classification, Axon Diameter, Receptor Types, and Function[a]

Sensory and Motor Fibers[b]	Sensory Fibers[c]	Diameter (nm)	End Organ/Receptor	Function
A-alpha	Ia	10–20	M: extrafusal fibers	Muscle contraction
			S: nuclear bag and chain intrasfusal fibers	Detect changes in the length and velocity of muscle stretch
	Ib	10–20	S: GTO	Detect muscle tension
			S: GTO ligament receptors	Detect tension in ligaments
A-beta	II	4–12	S: nuclear bag 2 and chain fibers	Detect changes in length of muscle stretch
			S: Meissner's corpuscle (skin)	Vibration and discriminative touch
			S: pacinian corpuscle (skin)	Vibration and discriminative touch
			S: Merkel disk (skin)	Pressure on the skin
			S: Ruffini's endings (skin)	Skin stretch
			S: Ruffini's joint receptor	Extremes of range of motion and more to passive than active motion
			S: pacinian joint receptor	Joint range of motion
A-gamma		2–8	M: dynamic-nuclear bag 1 fibers	Muscle spindle alignment
			M: static-nuclear bag 2 and chain fibers	Muscle spindle alignment
A-delta	III	1–5	S: free nerve endings (skin and joints)	Crude touch, pain, temperature
C	IV	<1	S: free nerve endings (skin and joints)	Detect pain, temperature

[a] M=motor branch, S=sensory branch, GTO=golgi tendon organs.
[b] Erlanger J, Gasser HS. *Electrical Signs of Nervous Activity*. Philadelphia, Pa: University of Pennsylvania Press; 1937.
[c] Lloyd D. Neuro patterns controlling transmission of ipsilateral hindlimb reflexes in cat. *J Neurophysiol*. 1943;6:293–315.

systems appear to play regulatory roles in postural stability.[13]

Therefore, the objectives of this article are: (1) to review the evidence regarding normal age-related physiological and anatomical changes that occur in the peripheral proprioceptive and cutaneous systems, (2) to relate the basic science research to the current evidence regarding clinical changes associated with normal aging, and (3) to review the evidence regarding age-related proprioceptive and cutaneous clinical changes and relate it to research examining balance performance in older adults. The article is organized by an examination of the receptors responsible for activating afferent pathways (muscle spindle, golgi tendon organ, and articular and cutaneous receptors), as well as by an examination of the peripheral pathways themselves.

Muscle Spindle

Structure and Function

Muscle spindles are stretch-sensitive mechanoreceptors that provide the nervous system with information about the muscle's length and velocity of contraction, thus contributing to an individual's ability to discern joint movement (kinesthesia) and joint position sense (JPS). Collectively, these functions are referred to as "proprioception," and it appears that muscle spindles play an important role in providing afferent feedback that translates to appropriate reflexive and voluntary movements.[20,21]

Muscle spindles are composed of a connective tissue capsule and intrafusal fibers, which are juxtaposed and parallel to extrafusal or ordinary muscle fibers (Tab. 1, Fig. 2). Intrafusal fibers are contractile on the end and noncontractile centrally and are composed of the nuclear bag and the nuclear chain fibers. The bag and chain fibers transmit afferent information regarding dynamic and static muscle states to the central nervous system via type Ia and II myelinated fibers.[22] The gamma (γ) motoneurons synapse on the contractile region of the intrafusal fibers and maintain sensitivity by initiating increased tension

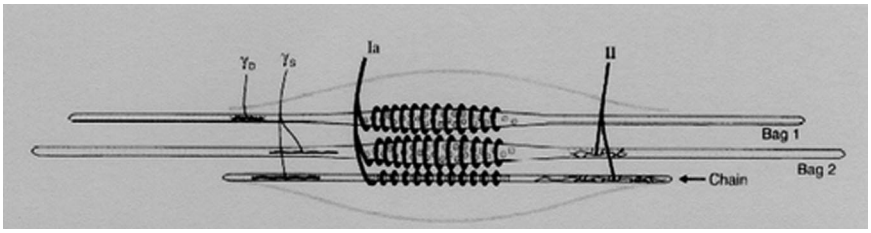

Figure 2.
The structural components of the mammalian muscle spindle. The intrafusal fibers include the nuclei bag 1 and bag 2 fibers together with the smaller chain fibers. Ends of the bag fibers extend beyond the capsule while chain fibers are within the limits of the capsule. Large Ia afferent fibers wrap around the nucleated portion of all 3 intrafusal fiber types. Smaller type II afferent fibers terminate to side and predominantly supply bag 2 and chain fibers. Gamma dynamic (γ_D) efferent fibers innervate bag 1 fibers, whereas gamma static (γs) efferent fibers innervate bag 2 and chain fibers. Reprinted from Proske U. The mammalian muscle spindle. *New Physiol Sci.* 1997;12:37–42, with permission from the American Physiological Society.

in the intrafusal fibers when the muscle is actively shortened.[22]

The interdependent relationship among the intrafusal fibers, Ia and II afferent fibers, and alpha-gamma motor units requires precise and integrated action by the central nervous system. Specifically, "alpha-gamma coactivation" is dependent upon sensory information from the muscle spindle correctly synapsing on the appropriate alpha-gamma motoneurons and spinal cord interneurons.[23] The direct synapse on alpha motoneurons results in the classic monosynaptic stretch reflex, while synapses on spinal cord interneurons result in facilitating or inhibiting multiple muscles to ensure uninterrupted and coordinated movements.[24] Alpha and gamma motoneurons also receive converging information from articular receptors, cutaneous receptors, spinal interneurons, and higher centers to ensure accurate feedback regarding muscle length and velocity of contraction and thus appropriate force development throughout the length of the muscle.[23]

Muscle Spindle: Anatomical and Physiological Age-Related Changes

Various investigators[25–27] have suggested that aging results in morphologic changes to the muscle spindle. In 1972, Swash and Fox[25] reported that aged human muscle spindles exhibited increased spindle capsule thickness and a loss of total intrafusal fibers per spindle. The authors also observed spherical axonal swellings and expanded motor end plates and postulated that spindle modifications may be the result of dennervation.[25]

The findings of a recent study by Kararizou et al[26] provide further clarification and suggest that morphologic changes within the muscle spindle may be specific to certain muscles and only evident during advanced aging. The investigators studied the morphometric characteristics of 72 muscle spindles obtained from individuals (26–93 years of age) postmortem, with samples taken from the deltoid (n=23), biceps (n=22), quadriceps femoris (n=22), and extensor digitorum brevis (n=5) muscles. Statistical analysis combining data from all 4 muscles failed to exhibit significant changes for any of the outcome variables. However, individual muscle analysis revealed that spindles from the deltoid muscle (P=.03) and the extensor digitorum brevis muscle (P=.04) had a significant reduction in spindle diameter as a function of age. In addition, the smallest muscle spindle diameter was identified in a subject who was 93 years of age. A significant decline in the number of intrafusal fibers (P=.04) also was observed in the deltoid muscle with the smallest quantity of fibers seen in an individual who was 82 years of age. No significant shifts were observed in any of the outcome variables for the quadriceps femoris or biceps muscle, implying that age may have a regional effect on specific muscles.

Some authors[28,29] have theorized that muscle-specific spindle alterations may be the result of local denervation, as research has demonstrated an increased proportion of type I extrafusal muscle fibers observed within the deltoid and extensor digitorum brevis muscles with age. The transition of type II to type I extrafusal fibers may be partially explained by the loss of type II axons and reinnervation of these muscle fibers by surviving type I axons.[26,29] Further study is needed to confirm whether the loss of innervation is the causative factor leading to morphological changes within the aging muscle spindle and what level and region (distal versus proximal lower-extremity muscles) of anatomical loss is associated with impaired proprioception and ultimately balance dysfunction.

Liu et al[27] have expanded on previous research by demonstrating that microstructural and biochemical age-related modifications occur within the postmortem human muscle spindle. They reported that the total number of biceps brachii muscle intrafusal fibers (P=.0004) and nuclear chain fibers (P<.0001) per spindle were significantly decreased for older adults (n=21 total samples; n=5 subjects, age=69–83 years) as compared with younger adults (n=36 total samples; n=10 subjects, age=19–48 years).[27] In contrast, there was no significant group dif-

Table 2.
Proprioceptive Somatosensation: Age-Related Anatomical, Physiological, and Clinical Changes[a]

Model	Muscle Spindle Changes	Articular Receptor Changes	Clinical Proprioception
Human	Increased capsular thickness[25] ↓ number of intrafusal fibers[25] ↓ spindle diameter in deltoid and extensor digitorum brevis muscles; no changes in quadriceps femoris or biceps muscles[26] ↓ number of total intrafusal fibers and chain fibers in biceps muscle; no changes in the number of bag fibers[27] Modifications in myosin heavy chain content[27] Alterations in distal sensory axons[25]	↓ in all joint receptor types in coracoacromioclavicular ligaments in patients undergoing shoulder arthroscopy[49]	↓ JPS in the great toe[60] ↓ JPS ankle in weight bearing[56] and non–weight bearing[52,53] ↓ JPS in the knee in partial weight bearing but not full weight bearing[55] ↓ JPS in older adults with knee osteoarthritis[65,70] No changes in hip JPS[58]
Animal	Impaired spindle sensitivity with aging[21]	↓ in pacinian, Ruffini's, and golgi tendon–like receptors in older rabbits' anterior cruciate ligments[50] ↓ joint receptors and afferent input in mice with osteoarthritis[66–68]	

[a] JPS=joint position sense.

ference in nuclear bag fibers. The authors suggested that the loss of nuclear chain fibers may impair the static sensitivity of the spindle and ultimately the ability to correctly interpret muscle length and JPS.[27] Interestingly, previous physiological studies[30,31] have revealed a decline in static ankle JPS in older adults.

Liu and colleagues[27] also examined myosin heavy chain (MyHC) protein content of the spindle fibers. Myosin heavy chain isoforms were used because they have been shown to be key contractile muscle proteins and major determinants of maximum shortening velocity of muscle cells.[32] The investigators identified that 3 types of MyHC isoforms had modified expression in aged muscle spindles when compared with those from young subjects.[27] Specifically, α cardiac MyHC expression was decreased in all 3 intrafusal fiber types in older spindles, whereas fetal MyHC isoform expression was decreased only in bag 2 intrafusal fibers. Additionally, slow MyHC expression was increased in bag 1 fibers, but not in bag 2 or chain fibers, suggesting that modifications seen with aging are not necessarily symmetrical across all intrafusal fiber types. It also is intriguing that similar MyHC adaptations occur in rats in response to hind-limb unloading[33] and denervation.[34,35]

The potential link between pathological spindle modifications and aging, decreased weight bearing, and peripheral neuropathy are intriguing considering that various investigators have identified that sensory impairments and postural instability occur with advanced aging,[16,36] osteoarthritis (OA),[37–39] and peripheral nerve disease.[40–42] More importantly, collaborative bench and clinical research may assist in determining the influence that exercise has on the aging muscle spindle and whether modifications, such as those in MyHC isoforms, translate to improved proprioception and postural stability in older adults.

Aged muscle spindles also appear to exhibit impaired sensitivity. Miwa et al[21] examined the afferent response of muscle spindles to varying levels of stretch applied to the medial gastrocnemius muscle of middle-aged (n=10, 10–14 months of age) and old (n=14, 28–30 months of age) rats. Older rats had significantly ($P<.001$) lower discharge rates than middle-aged rats when compared at the same muscle length, implying a decline in spindle static sensitivity. The dynamic index, a measure of spindle dynamic sensitivity, also was significantly ($P<.005$) lower for aged rats. Morphological changes such as increased capsular thickness and a decreased number of intrafusal fibers may account for the dampening of static and dynamic muscle spindle sensitivity that is seen with aging.[21]

These studies provide initial evidence that selective morphological and functional changes do occur in human muscle spindles during aging (Tab. 2). The findings are important to rehabilitation professionals because they imply that the muscle spindle is a plastic structure and that modifications

are not uniform across all muscles or intrafusal fiber types. Future translational research that investigates the influence of rehabilitation strategies on functional adaptations of the aging muscle spindle is warranted and may assist in defining the mechanisms associated with improved proprioception, function, and balance in older adults.

Golgi Tendon Organ and Articular Receptors

Structure and Function

The golgi tendon organ (GTO) and articular receptors provide additional proprioceptive information that is important for accurate assessment of joint movement. The GTO is located at the muscle-tendon interface and relays afferent information about tensile forces within the tendon. Golgi tendon organs are sensitive to very slight changes (<1 g) in tension and are responsive to tension that occurs either by active contraction or by passive stretch.[43] The activation of the GTO results in Ib afferent neuron activation (Tab. 1). This afferent information synapses in the spinal cord on interneurons which are inhibitory to the alpha motoneuron of the associated muscle, resulting in decreased tension within the muscle and tendon.

Articular or joint proprioceptors respond to mechanical deformation of the joint capsule and ligaments. Joint receptors include the rapidly adapting pacinian corpuscles (PCs), slower-adapting Ruffini's endings, ligament receptors, and free nerve endings. The Ruffini's endings are activated at the extremes of joint movement and respond more to passive motion. Pacinian corpuscles respond to mechanical stimulation during movement, but not when the joint is held in a constant position. Ligament receptors are structurally and functionally similar to GTOs and respond to tension. Free nerve endings respond to extreme mechanical deformation and inflammation. The overall contribution of joint receptors to proprioception continues to be debated as some reports have demonstrated that anesthetically blocking or removing articular receptors does not significantly impair the ability to detect motion.[44–46] It is accepted that joint receptors are primarily activated at the end range of motion,[46] but may have a larger influence on proprioception through interneuronal connections to gamma motoneurons, thus biasing spindle sensitivity.[47,48]

Articular Receptors: Anatomical and Physiological Age-Related Change

Only 2 studies were found that have critically analyzed the relationship between the aging process and structural modifications within articular receptors, and none were found that examined age-related changes in the GTO. Morisawa[49] examined the mechanoreceptors (Ruffini's, pacinian, golgi tendon-like ligament receptors, and free nerve endings) from the coracoacromial ligaments of 23 patients pending shoulder surgery. The author reported a general decline in the numbers of all receptor types as subjects increased in age from 20 to 78 years of age. Aydog and colleagues[50] recently conducted similar histological analysis of anterior cruciate ligaments (ACLs) from young (2 months, n=5), adult (12 months, n=4), and old (60 months, n=5) rabbits. They identified a significant ($P<.05$) stepwise decrease in the numbers of Ruffini's, pacinian, and golgi tendon-like ligament receptors across age groups. Pacinian and Ruffini's receptors that were visualized in older rabbits also demonstrated irregular and flattened margins.

Proprioception: Clinical Age-Related Change

Proprioception can be assessed clinically through examination of awareness of JPS and joint kinesthesia (motion). Joint kinesthesia is determined by establishing a threshold at which motion is detected during various velocities and ranges of movement. Joint position sense is evaluated by having the individual experience a specific joint position (angle) and then reproduce the position actively or react during passive movement.[51] Table 2 provides a summary of anatomical, physiological, and clinical changes to proprioceptive somatosensation.

Verschueren et al[52] examined dynamic JPS for passive ankle plantar flexion tested at various velocities (15°, 20°, 25°, 30°/s). A total of 102 older (mean age=62.5 years, SD=5.0) and 24 young (mean age=21.7 years, SD=2.0) men completed the proprioceptively controlled task, which included having subjects open their hand when the ipsilateral ankle reached the prescribed target angle. The oldest category of adults (70 years of age) exhibited significantly greater ($P<.05$) deviation from the specific target angle and variability in performance when compared with younger adults. Adults aged 60 to 70 years also demonstrated increased variance in performance, but were no different from younger adults in their ability to reach the prescribed target angle. Sixty-five of the older adults and 15 of the younger adults were retested while also having vibration (60 Hz) applied to the tibialis anterior tendon. Vibration resulted in a marked increase in positioning errors for older adults, but not young adults, suggesting that the age-related decline in dynamic JPS was a combination of reduced cutaneous and spindle function. Finally, the authors analyzed the

effects of knowledge of results practice and determined that both younger and older adults significantly improved ($P < .05$) following practice trials. These findings demonstrate that dynamic JPS may improve in older adults who undergo focused practice.

Madhavan and Shields[53] expanded on this testing protocol by testing velocities from 10° to 90°/s. The investigators also included measures of balance (single-leg stance time), electromyographic (EMG) muscle activity, and self-report of function (36-Item Short-Form Health Survey questionnaire [SF-36]). Older adults had decreased dynamic ankle JPS, and proprioceptive decline was strongly associated ($R^2 = .92$) with single-leg stance time (eyes closed). Furthermore, elderly participants had co-contraction of the plantar flexors and dorsiflexors throughout the passive proprioceptive positioning task. Increased EMG activity was not seen in younger adults, and the authors hypothesized that older adults' inability to relax may have been a mechanism to increase sensitivity or "gain" in the muscle spindle.

These findings are consistent with previous research showing that co-contractions about the ankle serve as a compensatory strategy for elderly people to maintain postural control.[54] Older adults also demonstrated improved performance with practice, providing additional evidence that short-term training may enhance test performance. The next logical step in this research would be to examine whether proprioceptive training actually influences functional measures and carries over to reduce the risk of falls in older adults.

There is evidence that the amount of weight bearing may influence the level of age-related proprioceptive decline for the knee. In a study by Bullock-Saxton et al,[55] for example, errors in knee JPS during full weight bearing did not differ between young (20–35 years), middle-aged (40–55 years), and older (60–75 years) participants with normal lower-extremity function. The lack of a change with age may reflect that weight bearing maximizes afferent input from multiple joints and all types of proprioceptors (joint receptors, muscle spindle, GTO, and cutaneous input). When subjects were tested in partial weight bearing (30% of full weight bearing), there were differences ($P < .05$) between older adults and participants in the middle-aged and young groups, implying that accuracy of knee JPS is weight dependent.[55] Interestingly, multiplanar weight-bearing JPS at the ankle in older adults (n=46, mean age=73.12 years) exhibited a significant reduction from young control subjects (n=10, mean age=22.20 years). However, JPS at the ankle was not able to discriminate between older adults who had not fallen and those with a history of a fall within the past year (n=22, mean age=73.12 years),[56] possibly due to the complexity of issues contributing to falls risk.[57]

The current literature involving aging and lower-extremity proprioception also provides evidence that proximal joints may not be affected to the same extent as distal joints. Pickard et al[58] compared hip JPS in 30 healthy young control subjects (mean age=21.7 years) and 29 healthy elderly subjects (mean age=75 years). Both active and passive hip abduction and adduction JPS were tested, and the results demonstrated that there were no significant group differences. Total hip replacement (with capsulectomy) also has been shown to have a minimal effect on overall hip proprioception.[59] The hypothesis of a distal-to-proximal loss of proprioception also is supported by these studies involving knee and ankle JPS, in addition to research showing that perception of joint motion at the first metatarsophalangeal joint was significantly different between young and old adults.[60]

Further clinical research that defines reliable and valid assessment measures for distal (great toe and ankle) JPS is needed, as predominant proprioceptive changes seen in aging and peripheral nerve disease often occur from distal to proximal. One of the leading mechanisms for the age-related progression of sensory and motor impairments from distal to proximal appears to be the reduction in the rate of axonal transport.[61–63] For example, fast axonal transport was slowed from a mean of 453 mm/d (SD=16) in 3-month-old rats to 406 mm/d (SD=16) in 38-month-old rats.[63] The rate of distal neurofilament protein transport also is delayed in distal axons with aging.[61] The interdependency of the cell body, neurotrophic signaling, myelin, distal receptors, and axonal transport reinforces that most likely all of these areas play a role in the distal-to-proximal decline of sensation that is seen in aging.

No studies were found that have specifically examined or directly linked age-related articular receptor physiological change and function. Studies involving orthopedic pathologies such as ACL sprains and lower-extremity OA provide some information about the function of articular receptors.[64–71] For example, Adachi et al[64] reported a modest, but significant, correlation ($r = -.41$, $P = .03$) between a decline in JPS and the total number of ACL mechanoreceptors located in patients who underwent knee arthroscopy (n=29, age=14–47 years).

Previous studies involving older adults with knee OA have shown

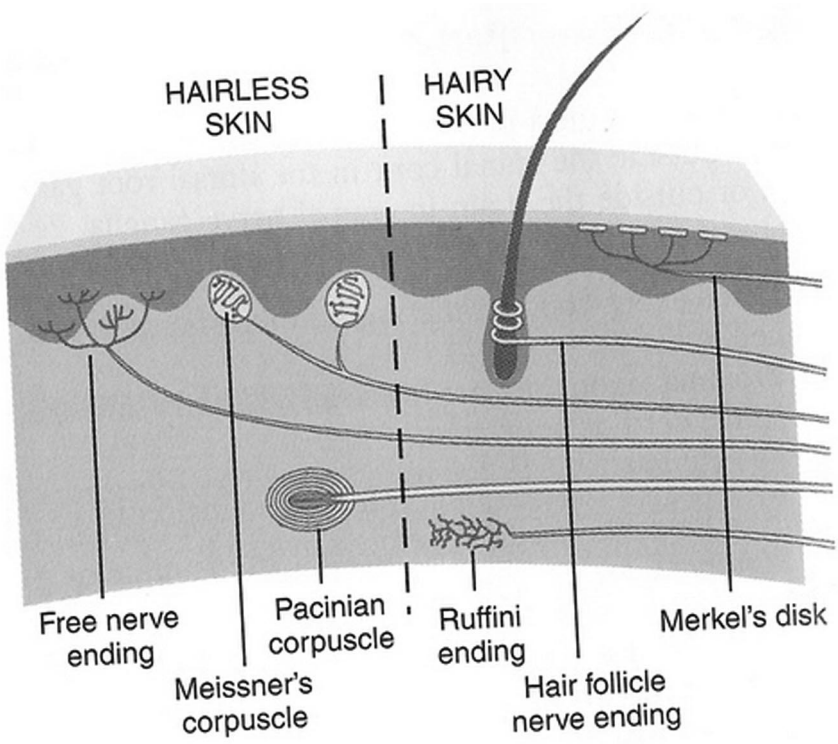

Figure 3.
The cutaneous receptors. The superficial fine touch receptors have small receptor fields and include the Meissner's corpuscles, Merkel disks, and hair follicle receptors. The subcutaneous fine touch receptors have larger receptor fields and include the pacinian corpuscles and Ruffini's endings. All of the fine touch receptors transmit information via medium myelinated Aβ or type II fibers. Free nerve endings are located throughout the skin and provide information about coarse touch, pain, and temperature. The information from free nerve endings is transmitted by thinly (Aδ) or nonmyelinated (C) fibers. Reprinted from Lundy-Eckman L. *Neuroscience: Fundamentals of Rehabilitation*. 2nd ed. Philadelphia, Pa: WB Saunders Co; 2002:99–122, with permission of Elsevier.

decreased numbers of articular receptors and neuronal degeneration.[66–68] Animal studies[66,67] suggest that denervation and mechanoreceptor loss actually precede joint degeneration and may potentially be a causative factor in knee OA. Patients with unilateral knee OA also exhibited decreased JPS when compared against healthy controls,[65] and knee OA in humans is associated with impaired proprioception,[69–71] postural instability,[38,72] and increased risk for falls.[73] Radiographic evidence of knee OA has been demonstrated in more than 30% of the population over 60 years of age, and it has been suggested that radiography may underestimate the actual rate of occurrence.[74] This high prevalence underscores the importance of conducting clinical trials with older adults with lower-extremity OA, proprioceptive decline, and postural instability in order to better identify patient subgroups who are likely to respond to balance training.[75]

Cutaneous Receptors

Structure and Function

The cutaneous mechanoreceptors that innervate glabrous or hairless skin are the rapidly adapting Meissner's corpuscle (MC), the slowly adapting Merkel disk, rapidly adapting PC, and the slowly adapting Ruffini's ending (Fig. 3). These 4 receptors, in combination with hair cells, deliver important feedback about the environment (Tab. 1).[43] Cutaneous receptors are not typically thought of as proprioceptors, but the information they provide supplements the JPS and movement.[43] For example, the cutaneous receptors on the plantar surface of the foot deliver information about the site and force of weight-bearing activities,[31,76,77] and research by Burke et al[78] has demonstrated that cutaneous receptors influence muscle activity in the lower extremities. The investigators demonstrated that cutaneous stimulation of the ipsilateral or contralateral lower extremity increased the quadriceps femoris muscle excitability and the reflex response. This finding implies that communication occurs among the cutaneous receptors, the muscle-spindle gamma efferent system, and alpha motoneuron activity.[78]

Cutaneous Receptors: Anatomical and Physiological Age-Related Change

Research involving large myelin-related mechanoreceptors appears to be warranted because previous research suggests that aging affects these fibers and receptors to a greater extent than unmyelinated nerve fibers that transmit nociception.[79] In addition, due to their relatively large size, the majority of studies involving the effects of age on cutaneous receptor decline have involved PCs and MCs.

As early as 1958, Cauna and Mannan[80] presented initial evidence that human PCs decrease in number with advanced age. Structural adaptations with aging are supported by physiologic studies, such as that of Verrillo,[81] which have shown that vibrotactile sensitivity involving PC pathways becomes impaired with age. More recent work has shown that, at a vibration frequency of 250

Table 3.
Cutaneous Somatosensation: Age-Related Anatomical, Physiological, and Clinical Changes

Model	Pacinian Corpuscle	Meissner's Corpuscle	Clinical Cutaneous Testing
Human	↓ number with increasing age[80]	↓ concentration with increasing age[83]	Diminished vibration perception threshold testing[77,86–88]
	↓ vibration perception thresholds and perceived magnitude of vibration at frequencies that activate pacinian channels[81,82]	↓ size and number with increasing age[84]	Diminished monofilament testing[77]
		↓ number in the finger and impaired touch thresholds[85]	Diminished 2-point discrimination testing[89–92]

Hz (resulting in preferential activation of PCs), older adults who were healthy (n=5, mean age=68.6 years) required significantly greater amplitudes of vibration (mean increase= 19.2 dB) to achieve the same sensation-perceived magnitude as younger subjects (n=5, mean age= 23.5 years).[82]

Meissner's corpuscles also exhibit structural modifications and an overall decline in number and cross-sectional area with aging.[83–85] Bolton et al[83] studied punch skin biopsies from the little finger and plantar aspect of the great toe in 91 individuals ranging in age from 11 to 89 years. Analysis revealed a progressive age-related decrease in both the great toe and little finger MC mean concentrations (number of MCs/mm^2). Iwasaki et al[84] analyzed tissue specimens from the right index finger of 10 male subjects (mean age=71.7 years, SD=10.3) and found a significant correlation between MC concentration ($r = -.674$, $P < .05$) and age. Findings from this study also demonstrated a significant weak-to-moderate correlation between MC cross-sectional area ($r = -.43$, $P < .01$) and age.[84] Bruce[85] combined histological and sensation testing and determined that older adults not only had decreased MCs in the index finger, but also exhibited impaired touch thresholds that were elevated 2½ times over those of young control subjects.

The current body of knowledge indicates that both pacinian and Meissner's receptors are reduced in number with aging. In addition, both have been associated clinically with declines in vibration perception or touch thresholds. With the exception of Bolton et al,[83] the vast majority of physiological research involving MCs and PCs has been conducted on the fingers. One study was found that examined the distribution and composition of cutaneous receptors in the plantar surface of the feet.[76] This 2002 report by Kennedy and Inglis[76] was conducted on 13 volunteers, aged 22 to 50 years (mean age=29.6 years), who were healthy. Microneurographic recordings of the tibial nerve at the popliteal fossa were used to classify receptor types and fields. The investigators found that 70% of the skin receptors in the plantar foot were fast adapting. They suggested that the high percentage of fast-adapting receptors may reflect the large degree of dynamic sensitivity that is needed for proper weight bearing and balance control. Additional study is needed to validate this theory and the degree of lower-extremity cutaneous receptor decline that is associated with impaired balance.

Cutaneous Somatosensation: Clinical Age-Related Change

Consistent with the anatomical findings of declining cutaneous receptors with age, multiple studies[77,81,82,86–88] have demonstrated that older adults have impaired abilities to detect vibration (Tab. 3). Perry[77] compared the level of plantar surface vibration and monofilament sensitivity in young adults (n=7, age=23–26 years) and older adults (n=95, age=65–73 years) at 4 test sites (great toe, first metatarsal head, fifth metatarsal head, and heel). Older adults had insensitivity to quantitative vibration stimulation (25 and 100 Hz) and monofilament testing (2.83–6.85, or 0.07–300 g of force) across all sites in comparison with the young adults. When analyzing results only from older adults (≥65 years of age), Perry observed a clear demarcation point in the early seventies (72–73 years of age) where vibration perception thresholds doubled. However, monofilament testing did not allow for the same level of discrimination in older adults. Perry concluded that vibration perception threshold testing may provide a more sensitive measure to detect the onset of age-related plantar insensitivity.[77] These findings,[77] combined with previous research,[81,82] support the view that older adults lose vibratory sensation with age and that vibratory testing should be considered when screening

for distal sensory impairments in older adults. Questions concerning the effect that the loss of vibratory sense has on balance and fall risk also remain unanswered and merit further investigation.

Discriminative touch (ie, 2-point sensation) has been found to be compromised with aging.[89–92] Stevens et al[92] assessed 2-point gap discrimination in 5 body regions (volar forearm, upper and lower surfaces of the forefinger, and plantar and dorsal surfaces of the forefoot) in 60 healthy older adults (>65 years of age, mean and age range not reported) and 19 young adults (18–28 years of age). Older subjects exhibited an average decline in the foot, fingertip, and forearm of 91%, 70%, and 22%, respectively. These findings agree with previous findings that the loss of tactile acuity occurs in older adults and is greater in the distal extremities.[89,90] Additionally, there was no significant difference between the dorsal and ventral surfaces of the foot or finger, providing evidence against the hypothesis that sensory differences result more from physical wear and tear to the skin of the plantar surface of the foot and palmar aspect of the finger.[92]

A degradation of tactile acuity in aging may be clinically meaningful in that a recent study identified that the loss of 2-point sensation in the plantar aspect of the toe was significantly greater in "fallers" than in "nonfallers."[91] The researchers conducted balance and 2-point sensation tests on 19 participants (mean age=78.4 years, SD=1.3) who had sustained at least 2 falls in a 6-month period and 124 nonfallers (mean age=77.8 years, SD=0.53). Subjects who had sustained multiple falls had a significant ($P<.05$) increase in mediolateral sway (28% more sway) and impaired 2-point sensation ($\overline{X}$=14.9 mm, SD=1.1 versus $\overline{X}$=12.98 mm, SD=0.3) versus controls. Further prospective research will assist in determining whether 2-point sensation of the feet has a clinically relevant role as an assessment measure in older adults.

Peripheral Sensory Innervation: Anatomical, Physiological, and Clinical Age-Related Change

Mechanoreceptors that summate to a critical level result in peripheral afferent neural signals that travel within peripheral axons to cell bodies located within the dorsal root ganglion (DRG). Sensory information then travels along the proximal axons of the DRG into the spinal cord. These steps require healthy axons that can transmit information, as well as dorsal root ganglion cells that process and pass information to the spinal cord.

A reduction in the number and density of myelinated peripheral nerve fibers and a decrease in thickness of the myelin in the remaining fibers have consistently been reported with aging in several animal species (for a review, see Verdu et al[62]). There is also a large body of literature demonstrating age-related changes in large fiber structure and nerve conduction velocity (NCV).[62,86,93–95] Specifically, studies involving mice have shown that myelin thickness, the number of large myelinated fibers, and sensory NCV actually increase in young mice up to 12 months of age. In mice 12 to 20 months of age (middle to early old age), there are only mild age-related declines. Past 20 months (old age), sensory nerves show a steady decline in the numbers of axons, myelin and fiber thickness, and sensory NCV.[62,93,95]

An age-related decline in sensory NCV and sensory nerve action potentials (SNAPs) have been identified in humans.[86,94] Taylor[94] found that adult sensory nerve conduction parameters (NCVs, SNAPs, and waveform durations) peaked at age 40 years and subsequently declined. Further study by Bouche et al[86] revealed that marked motor and sensory nerve conduction changes consistently occurred in the lower extremities of subjects over 80 years of age. As compared with young adults (21–29 years of age), older adults (63–80 years of age) showed significant ($P<.05$) reductions only in sural (−73%) and median (−38%) SNAP amplitudes, suggesting that sensory fibers are affected prior to motor fibers with aging. In contrast, the oldest group of adults (>80 years of age) demonstrated significant ($P<.01$) global declines in both motor and sensory nerve conduction velocities and response amplitudes. There also was a progressive and significant increase in the tibial H-reflex latency time among the 3 age groups. The age-related increase in the H-reflex latency implies that the spinal reflex loop was delayed,[96] and other authors[97] have postulated that this potentially contributes to postural instability.

The aging-associated decline in sensory nerve conduction and clinical sensory testing was once thought to be due to the loss of sensory neurons.[98] However, contemporary research that has utilized improved laboratory techniques for counting neurons challenges this idea.[99,100] Recent experiments that analyzed the total number of neurons from the cervical and lumbar DRGs of 3- and 30-month-old rats discovered only a small (≈12%) decrease for older rats. There was no significant relationship between the degree of sensory neuron loss and behavioral deficits (eg, von Frey tactile testing and hotplate testing). Myelin-related DRG neurons in older rats exhibited significantly smaller cross-sectional area (≈16% in lumbar DRGs, $P<.001$), suggesting that neurons may atrophy with age.

However, there was no significant difference between young and old rats with respect to unmyelinated DRG neurons.[99] These findings provide some evidence to suggest that aging predominately results in atrophy of myelinated primary sensory neurons.

Kishi et al[101] found similar bias toward myelinated neurons in their analysis of rats with diabetic peripheral neuropathy (DPN). In general, there was no difference in the total number of L5 DRG neurons between rats with DPN and healthy age-matched controls, but once cells were grouped based on size, large myelinated DRG neurons in diabetic rats exhibited a 43% decrease ($P=.01$) compared with healthy controls. The results suggest that large myelinated sensory neurons may be preferentially affected by pathology and that the structural response of sensory neurons to pathology is progressively worse (cell loss or necrosis) than normal aging (cell atrophy, but limited numbers of cell death).

These findings support the view that testing large myelinated pathways (eg, reflex, vibration, proprioception, discriminative touch) may provide the most sensitive measures for identifying and discriminating sensory impairments due to aging versus those due to peripheral nerve disease. Research by Richardson[102] supports this concept, as deficits in sensory testing domains (Achilles reflex testing, 128-Hz vibration tuning fork testing at the great toe, or JPS at the great toe) accurately separated older adults with and without electrodiagnostically confirmed peripheral nerve disease. The presence of abnormal testing in 2 out of 3 of these domains identified distal peripheral neuropathy with a sensitivity of 94.1% and a specificity of 88.4%.[102]

The knowledge that sensory neurons in older adults may be atrophied as opposed to lost also provides foundational justification for examining the influence of therapeutic interventions (eg, exercise, sensory re-education, modality application) on the physiological function of these cells and the resulting effect on sensation and physical performance. Interventions such as monochromatic infrared photo energy[103–105] and electrical stimulation therapy,[106,107] which are aimed at improving distal sensation, have shown some promise in the treatment of people with diabetic peripheral neuropathy. Future research may focus on identifying characteristics of older adults capable of recovering from sensory dysfunction and those for whom compensation rather than recovery is the key to intervention.

One of the leading hypotheses regarding the physiological basis for the age-related changes discussed involves the influence of neurotrophin-signaling components. Neurotrophins are polypeptides that are essential in the development and survival of neurons in both the central and peripheral nervous systems. A reduction of neurotrophins within the skin and neurotrophin receptors in primary sensory neurons is associated with aging and may contribute to the distal sensory impairments that are seen with aging.[100,108] Neurotrophins also play an essential role in activity-dependent plasticity and are enlightening our understanding of how exercise influences the nervous system. For example, following a nerve crush injury, DRG neurons from adults rats that exercised for a 3- to 7-day period contained higher levels of neurotrophins and showed improved axonal regeneration ($P<.01$ at 3 days; $P<.0001$ at 7 days) when compared with sedentary animals.[109] The total distance of axonal regeneration was strongly correlated ($r=.626$, $P<.001$) to the distance that animals ran, implying that a potentially important relationship may exist between exercise duration and neuronal outgrowth.[109] Similar lines of research involving healthy aged animals and those with neuropathy may provide additional evidence of the benefits of exercise in promoting sensory neuronal health and function. Conducting further clinical trials also appears warranted as a Cochrane Review[110] recently concluded that there is inadequate evidence to evaluate the effects of exercise on functional ability in patients with polyneuropathy.

Somatosensory Integration: Age-Related Clinical Change

Computerized dynamic posturography (CDP) was designed to discriminate among the influences on postural stability provided by the visual, vestibular, and somatosensory systems.[111] Various authors have used CDP and other clinical examination approaches to investigate the influence of sensory impairments on postural instability in older adults. Judge et al[112] examined 110 older adults (mean age=80 years) with the CDP sensory organization test (SOT) and found that errors in proprioception had a greater effect on balance than did errors in vision, with the oldest participants demonstrating the greatest difficulty in conditions where proprioception was reduced.

Using CPD, Peterka and Black[113] found that balance equilibrium scores for older adults up to 80 years of age exhibited substantial changes only when both proprioceptive and visual cues were disrupted. Camicoli et al[114] examined 48 healthy older subjects (33 subjects ≥80 years of age [mean age=88 years, SD=5] and 15 subjects <80 years of age [mean age=72 years, SD=3]) who performed the CDP SOT and clinical measures of balance and perfor-

mance (Tinetti Balance Scale, single-leg stand, gait speed over 9 m). The investigators identified a significant difference in the adaptive ability of the "old-old" (80 years of age and older) participants when proprioceptive input was disrupted, confirming again that even with vision available, the oldest participants needed accurate proprioception to maintain balance while the young-old participants (<80 years of age) were better able to adapt to proprioceptive errors by using visual cues.

Sensory impairment in older adults is also associated with functional decline and fall risk. Kaye and colleagues[115] compared a variety of functional and neurologic screens between 17 young-old adults (mean age=70 years, SD=2.6) and 34 old-old adults (mean age=89 years, SD=4.3) and found that vibration sense (big toe), balance (Romberg test, one-leg standing), and function (gait speed) were significantly impaired in the oldest participant group. Similarly, Anacker and Di Fabio[116] found that time to fall while standing on a compliant surface (eyes open and eyes closed) discriminated fallers from nonfallers, suggesting that in a group of similarly aged older adults (n=47, mean age=80.5 years, SD=9), the reliance on accurate proprioception information was increased in fallers.

Finally, Lord and colleagues[15,17,36] have shown that lower-limb proprioception is significantly reduced in older adults with a history of falling. The delineation between abilities of young-old and old-old adults is consistent with clinical and bench research findings demonstrating an accelerated loss in JPS in old-old adults (>70 years of age),[52] reduced NCV of motor and sensory nerves in old-old adults (≥80 years of age),[86] and animal models demonstrating a reduction in myelin thickness, in the number of large myelinated fibers,[62] and in muscle spindle sensitivity in old-old rats.[21]

These findings suggest the need to provide some older adults (particularly the old-old) with compensatory strategies that increase sensory information during function, such as increased cutaneous and proprioceptive feedback through the use of orthoses or an assistive device, improved lighting in all domains of function, and visually demonstrative boundaries on steps and curbs. Alternately, these results combined with previously discussed information suggest that, for some older adults (particularly the young-old), interventions designed to enhance recovery of sensory and balance function may be more appropriate than those focusing on compensatory strategies. These findings also emphasize the importance of distinguishing between young-old and old-old adults when conducting research and when developing appropriate examination and intervention strategies.

Summary and Conclusions

The following provides a summary of the themes that consistently emerged in our review of the influence of age on peripheral somatosensory systems:

(1) A diverse and nonuniform decline of sensory structure and physiological function occurs across the life span, with evidence of accelerated declines with advanced aging.

(2) There exists a preferential loss in anatomical structure and physiological function of large myelinated fibers and associated receptors.

(3) Ample clinical studies demonstrate that older adults exhibit impaired proprioception, vibration, and discriminative touch, all of which rely upon large myelinated afferent fiber functioning.

(4) Age-related involvement of sensory fibers occurs earlier than motor fibers.

(5) Nominal evidence exists linking impaired proprioception and cutaneous sensation in the lower extremities with balance dysfunction in older adults.

These conclusions highlight the importance of using and refining sensory measures (vibration, monofilament, 2-point discrimination, and proprioception testing) that can reliably and accurately assess the function of large myelinated fibers within the lower extremities of older adults. They also emphasize the need for additional research examining the physiological changes that occur in sensory structures and function over time and the effect that such changes have on postural stability in older adults.

Both authors provided concept/idea/project design, writing, and consultation (including review of manuscript before submission).

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