Neuromuscular Control and Ankle Instability

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Lateral ankle sprains (LAS) are common injuries in athletics and daily activity. Although most are resolved with conservative treatment, others develop chronic ankle instability (AI)—a condition associated with persistent pain, weakness, and instability—both mechanical (such as ligamentous laxity) and functional (neuromuscular impairment with or without mechanical laxity). The predominant theory in AI is one of articular deafferentation from the injury, affecting closed-loop (feedback/reflexive) neuromuscular control, but recent research has called that theory into question. A considerable amount of attention has been directed toward understanding the underlying causes of this pathology; however, little is known concerning the neuromuscular mechanisms behind the development of AI. The purpose of this review is to summarize the available literature on neuromuscular control in uninjured individuals and individuals with AI. Based on available research and reasonable speculation, it seems that open-loop (feedforward/anticipatory) neuromuscular control may be more important for the maintenance of dynamic joint stability than closed-loop control systems that rely primarily on proprioception. Therefore, incorporating perturbation activities into patient rehabilitation schemes may be of some benefit in enhancing these open-loop control mechanisms. Despite the amount of research conducted in this area, analysis of individuals with AI during dynamic conditions is limited. Future work should aim to evaluate dynamic perturbations in individuals with AI, as well as subjects who have a history of at least one LAS and never experienced recurrent symptoms. These potential findings may help elucidate some compensatory mechanisms, or more appropriate neuromuscular control strategies after an LAS event, thus laying the groundwork for future intervention studies that can attempt to reduce the incidence and severity of acute and chronic lateral ankle injury.

INTRODUCTION

The ankle is the most commonly injured joint during athletic participation [1] and 85% of those injuries are lateral ankle sprains (LAS), making the lateral ligament complex the most often injured structure in sports and recreation [2]. LAS involve a hypersupination/inversion of the foot, which may damage the anatomical structures in the lateral ankle, including: muscles, nerves, ligaments, and tendons. The primary injury to the lateral ligament complex may lead to mechanical instability; however, concomitant injury to the peroneal muscles/tendons, superficial peroneal nerve, and ankle joint proprioceptors may also lead to functional instability characterized by neuromuscular dysfunction, increasing the susceptibility of the ankle to further injury [3].

Freeman et al [4] presented the first work aimed at characterizing functional ankle instability (AI) after LAS and categorized it as a condition where the ankle and foot tend to "give way." Patients with AI typically present with pain, swelling, or repetitive injury [5]. Several terms have been used to describe this phenomenon of repetitive ankle sprains and instability, including mechanical instability, functional instability, chronic instability, residual instability/disability, and sprained ankle syndrome. It is relevant to distinguish between functional instability and mechanical instability. *Mechanical instability* refers to measurable laxity (either by clinical examination or dynamic imaging) of the joint, as well as arthrokinematic restrictions and degenerative and synovial changes [6]; but not all cases of AI can be explained by laxity [3]. Many individuals who have LAS experience a lingering feeling of instability combined with episodes of the ankle "giving way" under normal circumstances

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without the existence of mechanical laxity [3]. This is often termed *functional instability* and has been linked to impaired proprioception, neuromuscular control, postural sway, and strength [6]. Although functional and mechanical instability are linked [7], it is important to note that they can exist independently of each other [8]. Regardless of the presence or absence of mechanical laxity, the condition of repeated episodes of the ankle "giving way" is generally attributed to neuromuscular and proprioceptive deficits [3].

It has been reported that 55% of individuals who experience an ankle sprain do not receive any medical attention; yet, residual symptoms are as common in individuals who received medical attention as those who did not [8]. The literature suggests that individuals often trivialize LAS and that contemporary treatment paradigms are insufficient in preventing recurrent injuries or symptoms [6], leading to a circumstance in which more than 70% of individuals who have an ankle sprain report residual symptoms 6 weeks to 18 months after injury [9,10]. This is a significant long-term concern, because articular degeneration and osteoarthritis have been linked to recurrent symptoms and repetitive sprains [11-13]. Clinicians should be aware of the neuromuscular control patterns exhibited by individuals with AI, such that they can be properly equipped to manage and rehabilitate individuals who suffer LAS. Therefore, the purpose of this focused review is to summarize the literature available on neuromuscular control strategies in persons with AI; specifically focusing on chronic AI, regardless of the presence or absence of mechanical instability from ligamentous or other intra-articular pathology.

MECHANISM OF ANKLE JOINT STABILITY AND CONTROL

Neuromuscular control can be defined as the interaction between the nervous and musculoskeletal systems to produce a desired effect or response to a stimulus [14]. During activity, dynamic and static restraints work together, via open-loop (preparatory), closed-loop (reactive), and voluntary mechanisms, to maintain correct joint alignment and stability in response to forces imposed on the joint [15].

There are 2 plausible theories to help explain the development of AI: altered closed-loop vs. altered open-loop neuromuscular control. In general, open-loop control consists of anticipatory (ie, before stimulus onset) muscle activation to prepare oneself for the stimulus [16]. In the ankle, this consists of activating the musculature surrounding the joint before stimulus onset (landing) to control dynamic stability. Conversely, closed-loop control in the ankle joint is based on a reflex arc initiated after the mechanoreceptor-rich lateral ligamentous complex [3,17,18] registers a stretch as the foot is forced into inversion, sending an afferent signal to the spinal cord, followed by an efferent signal to the γ-motor neuron of the muscle spindles in the peroneal muscles, sensitizing the muscle spindles to stretch and finally resulting in a contraction in the muscle to oppose the stretch [19]. Many researchers have studied this reflex as a function of reflex latency [17,20-31], reflex amplitude [17,20], and electromechanical delay [15,25], yet there is a great deal of uncertainty in the literature as to the exact role that this reflex plays in preventing ankle sprains.

Closed-Loop Control of Ankle Stability

Articular deafferentation was first proposed as the mechanism behind AI by Freeman et al [4] in 1965 when they described functional AI (as opposed to mechanical instability/laxity). They proposed that damage to the proprioceptive ligamentous structures after LAS created a void in the proprioceptive feedback to the central nervous system and predisposed those individuals to episodes of the ankle "giving way" [4]. One could infer that reflex responses (closed-loop control) would be negatively affected in those individuals with proprioceptive impairment. Specifically, delayed reaction time of the evertor muscles of the ankle to unexpected inversion perturbations may be an important clinical manifestation of this disrupted closed-loop neuromuscular control system.

Konradsen and Ravn [32] published one of the first studies evaluating peroneal reaction time (PRT) in subjects with AI; defined as the time difference between the onset of the perturbation and the onset of peroneal muscle activity. Their findings supported the theory of articular deafferentation in that they found individuals with AI had delayed PRT compared with healthy, noninjured controls (ie, peroneus longus/brevis reaction time: AI 82/84 ms vs. normal 65/69 ms). Karlsson and Andreasson [33] and Lofvenberg et al [34] performed similar studies, and both groups found that individuals with AI had significantly delayed PRT. However, other researchers have failed to reproduce these findings. Ebig et al [24] tested unilateral AI patients for PRT in response to an inversion perturbation, using the contralateral limb as a control, and found no significant differences between limbs. Fernandes et al [23] tested the hypothesis that there would be a difference in PRT at varying degrees of frontal plane movement (thus evaluating both open and closed packed positions of the ankle) in subjects with AI as compared with noninjured controls, and found no statistical evidence to support those hypotheses. To further demonstrate the contradictory findings in the literature concerning PRT in subjects with AI, Vaes et al [30,31] found a delayed PRT in AI subjects as compared with noninjured controls in one study [30], but found no differences between the groups in a second study published only a year later [31]. Vaes et al suggested that the inconsistent findings in the literature may be due to a lack of standardization in: 1) inclusion criteria for AI and control subjects between studies, 2) the inversion perturbation, and 3) the quantity/severity of the initial ankle injuries of the AI subjects [31]. Although it is accepted that the measurement of reflex response time is a reliable measure [35], there is an obvious lack of a consensus on whether PRT is in fact delayed in individuals with AI. The reasons for these inconsistent findings are unclear; however, it is possible that these differences may be due to a lack of homogenous criteria

used to identify individuals with AI, as well as methodological inconsistencies.

Further, the external validity of this type of testing can be questioned, in that it is limited to a description of a reflex response to a highly controlled perturbation during static stance conditions. This is not the condition in which ankle injuries typically occur, nor is it considered a position of vulnerability for the ankle joint, as the ankle is usually in a closed-packed configuration during this type of testing. Because the clinical relevance of the static measure of PRT is questionable, more dynamic testing conditions must be evaluated. Although there is a dearth of literature evaluating dynamic ankle stability, recent research has begun to focus on reflex responses during dynamic activities such as gait and landing. Hopkins et al [36] compared the reflex responses with sudden ankle inversion during static stance and gait, and found a decreased (ie, quicker) response time during walking than during quiet stance. These authors speculated that increased muscle preactivation and muscle spindle sensitivity changes during gait [36]. Gruneberg et al [20] evaluated landings on inverting and noninverting surfaces and found an increase in response intensity (ie, amplitude) in the peroneal musculature during the inverting condition. This indicates that the stretch reflex response does contribute to the electromyographic response after landing, suggesting that reflex mechanisms superimpose themselves over preprogrammed muscle activation after foot contact [20]. However, it is extremely difficult to separate the 2 sources of activation [37]. Although these studies add to the understanding of dynamic neuromuscular control in healthy, uninjured ankles, they do not contribute to understanding the pathoetiology of AI.

Additional research has been performed to evaluate the importance of articular deafferentation in ankle stability by taking advantage of the fact that the lateral ankle ligaments do not have any motor properties. Anesthesia placed into the ligaments would affect only sensory neural information, thereby providing a means to study the influence of ligament-based proprioception on motor coordination of the ankle joint. DeCarlo and Talbot [38] found that overall proprioceptive function, assessed via measurement of postural sway, was not negatively affected with deafferentation of the lateral ankle ligaments; in fact, subjects significantly improved in their ability to control postural sway in the injected ankle. Konradsen et al [39] found that introduction of anesthesia into the entire ankle and foot did not alter active position sense, indicating that this sense was subserved by muscle and tendon receptors above the anesthetized ankle joint. PRT was also found to be unaffected by anesthetic blockade of the ankle ligament mechanoreceptors, suggesting that this reflex is controlled primarily by the muscle and tendon receptors in the absence of proprioceptive information from the lateral ankle ligaments. These findings were subsequently confirmed [40-42] and collectively they indicate that the redundancy in the neuromuscular system, specifically afferently, should be able to compensate for a loss of information from the ligaments.

Finally, a study by Konradsen et al [43] evaluating the role of the dynamic defense mechanism of the ankle has led to the postulate that the reflex response alone (when electromechanical delay and time required to reach peak torque are taken into account) is too slow to prevent an ankle sprain. Specifically, those authors found that the first evidence of active eversion occurred 176 ms after onset of platform movement, yet the degree of motion that may result in damage to the lateral ligamentous structures (ie, ~40° of inversion) could occur as early as 100 ms after the onset of movement. Therefore, the relatively minor delays in PRT in subjects with AI may be irrelevant, as reflex responses alone are likely too slow to protect the ankle from a sudden inversion load, again implying that preparatory activity (ie, open-loop control) must be present to protect from an ankle sprain [43]. Therefore, before any clinical conclusions can be made, much more work is needed to truly understand the role closed-loop control plays in dynamic stability about the ankle joint, especially in persons with AI. It appears that closed-loop control may *not* be the most important factor responsible for the maintenance of joint stability.

Open-Loop Control of Ankle Stability

Impact attenuation in gait and landing situations has received considerable attention in the literature [16]. This area of research has important clinical relevance as it has been hypothesized that failure to appropriately plan and implement neuromuscular strategies to attenuate impacts may lead to musculoskeletal injuries [16]. During gait, the ankle musculature is active before and during the early portion of the stance phase to help stabilize the foot and ankle [44]. It has been suggested that spindle sensitivity may be increased during the early stance phase of gait, which may result in increased joint stiffness from alpha-gamma coactivation [44]. Muscle activation is crucial to maintain appropriate joint stiffness. An insufficient level of joint stiffness may not provide the appropriate amount of deceleration of the joint to allow for a safe landing, whereas an excessive amount of joint stiffness may be detrimental to muscle, tendon, and bony structures, because these structures absorb more of the load [16]. Proper neuromuscular control during jump landings involves modulation of temporal and amplitude characteristics of muscle activations to appropriately modulate joint stiffness to the constraints imposed by the task, including jump height and landing surface material properties [16]. After touchdown, stretch reflex mechanisms become active to adjust the preprogrammed movement pattern based on the proprioceptive feedback gained after the kinetic chain is closed. As stated previously, stretch reflex mechanisms alone are ineffective in controlling joint rotation due to the delay in their implementation. The interaction between preparatory and reactive muscle activation patterns is important, but not well understood [16].

During the airborne phase of a jump/drop landing, there is a cascade of neuromuscular events that occur to prepare for impact. This includes a buildup of muscle activity before foot

contact, often termed *preactivation*. Anticipatory modulation of these neuromuscular events is dependent on alpha-gamma coactivation and its effects on muscle spindle sensitivity. Several studies have evaluated this anticipatory modulation and found that preactivation is altered with changes in jump height [45-48], landing surface compliance [49,50], and landing technique [51,52]. All of these factors influence ground reaction force; therefore, different amplitudes of muscle force are needed to control joint rotations. This modulation of anticipatory activations is based on the information available to the central nervous system during the preparatory phase, including visual and vestibular feedback, which is integrated with knowledge from previous experience dealing with similar stimuli. Specifically, there appears to be a linear increase in electromyographic activity in both flexors and extensors in the lower extremity with increasing drop height [45,53], which points to a general strategy used to modulate muscle force regardless of the mechanical action and anatomical characteristics of each particular muscle [16]. This central strategy is supported by research evaluating modulation in the preparatory activity of the forearm muscles prior to a catching task in response to a change in the momentum of the ball (as dictated by a change in the ball drop height), which found that upper limb muscle preparatory activity is modulated in a similar manner to lower limb musculature [54,55].

Recent research has evaluated this open-loop (preparatory) activity in the ankle musculature of individuals with AI [56-58]. Caulfield et al [56] presented the first attempt to monitor preparatory muscle activity in subjects with AI and found that in 2 different jumping conditions (drop jump and forward jump), individuals with AI displayed a reduced amount of activation of the peroneal musculature before foot contact compared with uninjured controls. The authors speculated that because both of these jumping conditions have different stiffness (landing) requirements, the reduced peroneal activation represents a robust feature of the motor program in individuals with AI [56]. They postulated that articular deafferentation may cause prolonged inhibitory effects because of the proprioceptive deficit, but also suggested that the changes in peroneal activation may instead be from local damage to the muscle or nerve as a result of the initial injury [56]. Regardless of the cause of this improper neuromuscular activation, a reduction or disorganization of preactivation of the peroneal muscles would place individuals with AI at an increased risk for injury. Further, Delahunt et al evaluated the kinetics and 3-dimensional kinematics, along with muscle activations, during single-leg landings [57]. Those authors also found that this reduced peroneal activation resulted in a more inverted position of the ankle at touchdown, furthering the conclusions of a predisposition to ankle injury from improper positioning of the joint [57].

Although an abundance of literature exists evaluating landing biomechanics in a variety of populations, only 2 studies have evaluated landing kinematics in individuals with AI. Caulfield and Garrett [59] evaluated 2-dimensional kinematics (sagittal plane) in single-leg landings in individuals with AI and found they had similar sagittal plane kinematic patterns as uninjured controls; however, those patterns were shifted toward greater dorsiflexion and knee flexion throughout the maneuver. Those authors speculated that the increased dorsiflexion was a protective mechanism that functioned by placing the ankle in a more stable configuration, described as a more close-packed ankle mortise, and concluded that these findings arose from preprogrammed motor plans, as opposed to reflexively mediated peripheral events [59]. Conversely, Delahunt et al also measured kinematics during landing in individuals with AI and found a decreased amount of dorsiflexion during the loading phase of the landing. Specifically, those authors found an earlier peak ground reaction force in AI subjects than in healthy controls (60 ms vs. 75 ms postcontact), indicating an inability to appropriately control weight acceptance during landings and placing AI subjects in a vulnerable position in which reduced ankle dorsiflexion did not allow for a close-packed position of the ankle mortise within the time frame of peak impact [57]. The timing of peak ground reaction force and the simultaneous vulnerability of the ankle joint is relevant because LAS would most likely occur shortly after this time frame. Furthermore, inappropriate weight acceptance combined with altered kinematics may also result in increased stress on the articular structures of the ankle joint [60]. To the authors' knowledge, no studies have evaluated kinematics during landing on an inverting/supinating surface in individuals with and without AI.

Arthrogenic Muscle Inhibition

It has been postulated that altered neuromuscular control patterns may be due to residual arthrogenic muscle inhibition, which is described as a continuing inhibition of the musculature surrounding a joint after swelling or damage to the structures of that joint [61]. Myers et al [17] studied the effects of both lidocaine and saline injections directly into the lateral ankle ligaments on the protective response of the peroneal muscles in response to stretch and found a decreased response amplitude after both injections. Because both injections caused a decreased response, the authors inferred that edema caused by the injections altered the sensorimotor influence of the lateral ankle stabilizers thus inhibiting dynamic stabilization of the ankle joint [17]. A more recent study by Hopkins and Palmieri [62] found similar adverse effects on peroneus longus activation after an intra-articular injection of a saline.

Arthrogenic muscle inhibition is often quantified through evaluation of the Hoffman-reflex (H-reflex), which is a measure of motor neuron pool excitability and reflex arc delay. The functional significance of arthrogenic muscle inhibition as a mediating factor in the development of residual symptoms following LAS is evident in a study by McVey et al [63], who found that individuals with AI demonstrated arthrogenic muscle inhibition as evidenced by a decreased H-reflex: M-wave ratio. These authors found that despite aggressive rehabilitation aimed at restoring strength and function after

LAS, the post-injury inhibition persisted possibly contributing to the residual dysfunction. They also proposed that some patients who suffer LAS may not recover full muscle activation, which could prevent the ability to "cope" with the injury, resulting in recurrent instability.

Arthrogenic muscle inhibition may not only have an effect on the evertors of the ankle joint, but may also inhibit the ankle joint invertors through a process of selective inhibition. The process of selective inhibition was described by Swearingen and Dehne [64], who found the decreased stress tolerance of an injured joint triggers a reflexive inhibition which affects muscles that are capable of increasing tensile stress on the damaged ligaments. It follows that the ankle invertors would be inhibited after lateral ankle joint injury because they can initiate movement in the same direction as the initial injury. It has been shown that a strength deficit exists in the invertors of the ankle in subjects with AI [65-67]. Wilkerson et al [65] postulated that in the closed kinetic chain (foot fixed to the ground), the ankle invertors become very important to the maintenance of postural stability over the foot. This is evident when the center of mass moves laterally past the lateral border of the foot. In these situations, the eccentric action of the invertor muscles keeps the medial edge of the foot firmly planted, which would prevent the lateral border from becoming a fulcrum about which the ankle turns.

CLINICAL IMPLICATIONS

During dynamic activity, open-loop mechanisms enable the neuromuscular system to act faster than closed-loop mechanisms with regard to one's ability to make adjustments to expected or unexpected perturbations [68]. Preactivating a muscle group in anticipation of a movement is thought to reduce the phase lag (delay between the input and output of a system), thereby increasing the efficiency between the central nervous system and effector organ [68]. Therefore, the adage that "practice makes perfect" regarding the refinement of open-loop mechanisms affords patients with AI the ability to tolerate the changes/perturbations that occur during dynamic activities (running, cutting, jumping). Therefore, from a clinical perspective, it is important to not only concentrate on activities that emphasize strength and power, but the fine tuning of preprogrammed motor responses (coordination) as well. Although the exact neuromuscular mechanisms behind AI remain unclear, traditional rehabilitation paradigms aimed at improving both open- and closed-loop neuromuscular control can be employed.

The initial phases of rehabilitation after LAS include reduction in pain and swelling, which is important in maintaining/restoring proper neuromuscular control of dynamic joint stability because of the effects of arthrogenic muscle inhibition described earlier. Pain/edema management should be followed by exercises to regain function such as passive and active range of motion, and isometric, isotonic, and eccentric strengthening exercises. After a functional base is established, it is imperative that rehabilitation exercises concentrate on both anticipatory and reactive responses to perturbations; specifically, focus on restoring motor patterns that control vulnerable ankle positions (ie, inversion, plantar flexion). Sample activities may include: open-chain manual resistance exercises, resistive tubing exercises where the patient is instructed to resist sudden motions in a specific direction, and seated and standing multiplanar wobble board activities [69]. As the patient advances, static and dynamic balance activities should be added. Examples of these may include: eyes open/eyes closed standing activities involving single, double, and tandem stances on firm and unstable surfaces (eg, foam pads, balance platforms, mini-trampoline), Star Excursion Balance Test [70], and the Functional Hop Test [71]. More advanced rehabilitation exercises should incorporate jump landing patterns in all 4 directions, and include a variety of heights and landing surfaces (eg, stable, foam, mini-trampoline). For all of these activities, it is important that emphasis be placed on jump direction and timing. As the patient approaches pre-injury status, activity-specific exercises should be incorporated such as agility and speed drills, emphasizing change of direction while minimizing time to completion. Last, perturbation training exercises should be employed to further fine tune open-loop mechanisms during dynamic activities. Although there is little evidence to support the efficacy of perturbation training programs in patients with AI, Fitzgerald et al [72] conclude that perturbation training programs for the anterior cruciate ligament reconstructed knee, allowed patients to return to a high level of function without continued risk for episodes of "giving way."

FUTURE RESEARCH

It is evident that the knowledge base about the neuromuscular control paradigms in individuals with AI is limited and that further research is needed. Most important, a generally accepted tool/criteria for selecting and categorizing individuals with AI must be created and implemented to allow comparisons of all research. Furthermore, no research studies to date have evaluated neuromuscular control in individuals who have experienced LAS but did not develop AI. Evaluating these individuals may help elucidate some compensatory mechanisms or more appropriate neuromuscular control strategies following a LAS event. Based on these potential findings, future intervention studies can be performed to reduce the incidence and severity of acute and chronic lateral ankle injury. It is known that episodes of the ankle "giving way" occur most often in dynamic conditions. Therefore, evaluating muscle activation and kinematics during dynamic activities, such as landings, may help elucidate the mechanism of disorder. There is evidence to suggest that preprogrammed motor plans may be altered in individuals with AI, predisposing them to ankle inversion moments. Furthermore, the effect of these altered open-loop control strategies should be evaluated when dealing with perturbations to the joint, as a perturbation of some magnitude is often present during an episode of "giving way." Finally, prospective studies evaluating neuromuscular control pat-

terns before an initial injury may help elucidate whether individuals are predisposed to the initial injury or if the injury alters their motor programs, predisposing them to subsequent reinjury (manifested as AI). For example, the hypothesis of neuromuscular inhibition as a predominant factor in AI could best be evaluated via a prospective study measuring the H-reflex:M-wave ratio in athletes and monitoring who gets injured, how and if the ratio is affected, and which individuals develop instability.

CONCLUSION

AI is a complex neuromuscular disorder, which affects a large percentage of individuals who have a LAS. The neuromuscular mechanism behind the pathology of AI remains unclear. Although this is a relatively new area of research, several theories exist and have been explored, yet there is no consensus in the literature. However, it is likely that a combination of factors leads to the development of AI including impairments in open- and closed-loop control mechanisms. More research is needed regarding neuromuscular control strategies in AI. Then clinicians can design more suitable treatment and rehabilitation paradigms, specifically geared toward reducing the incidence and severity of AI.

REFERENCES

1. Nelson AJ, Collins CL, Yard EE, Fields SK, Comstock RD. Ankle injuries among United States high school sports athletes, 2005-2006. J Athl Train 2007;42:381-387.
2. Garrick JG. The frequency of injury, mechanism of injury, and epidemiology of ankle sprains. Am J Sports Med 1977;5:241-242.
3. Hertel J. Functional instability following lateral ankle sprain. Sports Med 2000;29:361-371.
4. Freeman MA, Dean MR, Hanham IW. The etiology and prevention of functional instability of the foot. J Bone Joint Surg Br 1965;47:678-685.
5. Gerber JP, Williams GN, Scoville CR, Arciero RA, Taylor DC. Persistent disability associated with ankle sprains: a prospective examination of an athletic population. Foot Ankle Int 1998;19:653-660.
6. Hertel J. Functional anatomy, pathomechanics, and pathophysiology of lateral ankle instability. J Athl Train 2002;37:364-375.
7. Hubbard TJ, Kramer LC, Denegar CR, Hertel J. Correlations among multiple measures of functional and mechanical instability in subjects with chronic ankle instability. J Athl Train 2007;42:361-366.
8. Smith RW, Reischl SF. Treatment of ankle sprains in young athletes. Am J Sports Med 1986;14:465-471.
9. Braun BL. Effects of ankle sprain in a general clinic population 6 to 18 months after medical evaluation. Arch Fam Med 1999;8:143-148.
10. Yeung MS, Chan KM, So CH, Yuan WY. An epidemiological survey on ankle sprain. Br J Sports Med 1994;28:112-116.
11. Buckwalter JA, Saltzman C, Brown T. The impact of osteoarthritis: implications for research. Clin Orthop Relat Res 2004;427:S6-S15.
12. Gross P, Marti B. Risk of degenerative ankle joint disease in volleyball players: study of former elite athletes. Int J Sports Med 1999;20:58-63.
13. Harrington KD. Degenerative arthritis of the ankle secondary to long-standing lateral ligament instability. J Bone Joint Surg Am 1979;61: 354-361.
14. Enoka RM. Neuromechanics of Human Movement. 3rd ed. Boulder, CO: Human Kinetics; 2002.
15. Moore BD, Drouin J, Gansneder BM, Shultz SJ. The differential effects of fatigue on reflex response timing and amplitude in males and females. J Electromyogr Kinesiol 2002;12:351-360.
16. Santello M. Review of motor control mechanisms underlying impact absorption from falls. Gait Posture 2005;21:85-94.
17. Myers JB, Riemann BL, Hwang JH, Fu FH, Lephart SM. Effect of peripheral afferent alteration of the lateral ankle ligaments on dynamic stability. Am J Sports Med 2003;31:498-506.
18. Michelson JD, Hutchins C. Mechanoreceptors in human ankle ligaments. J Bone Joint Surg Br 1995;77:219-224.
19. Johansson H, Sjolander P, Sojka P. A sensory role for the cruciate ligaments. Clin Orthop Relat Res 1991;268:161-178.
20. Gruneberg C, Nieuwenhuijzen PH, Duysens J. Reflex responses in the lower leg following landing impact on an inverting and non-inverting platform. J Physiol 2003;550:985-993.
21. Johnson MB, Johnson CL. Electromyographic response of peroneal muscles in surgical and nonsurgical injured ankles during sudden inversion. J Orthop Sports Phys Ther 1993;18:497-501.
22. Beckman SM, Buchanan TS. Ankle inversion injury and hypermobility: effect on hip and ankle muscle electromyography onset latency. Arch Phys Med Rehabil 1995;76:1138-1143.
23. Fernandes N, Allison GT, Hopper D. Peroneal latency in normal and injured ankles at varying angles of perturbation. Clin Orthop Relat Res 2000;375:193-201.
24. Ebig M, Lephart SM, Burdett RG, Miller MC, Pincivero DM. The effect of sudden inversion stress on EMG activity of the peroneal and tibialis anterior muscles in the chronically unstable ankle. J Orthop Sports Phys Ther 1997;26:73-77.
25. Mora I, Quinteiro-Blondin S, Perot C. Electromechanical assessment of ankle stability. Eur J Appl Physiol 2003;88:558-564.
26. Konradsen L, Ravn JB. Prolonged peroneal reaction time in ankle instability. Int J Sports Med 1991;12:290-292.
27. Konradsen L, Olesen S, Hansen HM. Ankle sensorimotor control and eversion strength after acute ankle inversion injuries. Am J Sports Med 1998;26:72-77.
28. Shima N, Maeda A, Hirohashi K. Delayed latency of peroneal reflex to sudden inversion with ankle taping or bracing. Int J Sports Med 2005;26:476-480.
29. Larsen E, Lund PM. Peroneal muscle function in chronically unstable ankles. A prospective preoperative and postoperative electromyographic study. Clin Orthop Relat Res 1991;272:219-226.
30. Vaes P, Van Gheluwe B, Duquet W. Control of acceleration during sudden ankle supination in people with unstable ankles. J Orthop Sports Phys Ther 2001;31:741-752.
31. Vaes P, Duquet W, Van Gheluwe B. Peroneal reaction times and eversion motor response in healthy and unstable ankles. J Athl Train 2002;37:475-480.
32. Konradsen L, Ravn JB. Ankle instability caused by prolonged peroneal reaction time. Acta Orthop Scand 1990;61:388-390.
33. Karlsson J, Andreasson GO. The effect of external ankle support in chronic lateral ankle joint instability. An electromyographic study. Am J Sports Med 1992;20:257-261.
34. Lofvenberg R, Karrholm J, Sundelin G, Ahlgren O. Prolonged reaction time in patients with chronic lateral instability of the ankle. Am J Sports Med 1995;23:414-417.
35. Benesch S, Putz W, Rosenbaum D, Becker H. Reliability of peroneal reaction time measurements. Clin Biomech 2000;15:21-28.
36. Ty Hopkins J, McLoda T, McCaw S. Muscle activation following sudden ankle inversion during standing and walking. Eur J Appl Physiol 2007;99:371-378.
37. Duncan A, McDonagh MJ. Stretch reflex distinguished from pre-programmed muscle activations following landing impacts in man. J Physiol 2000;526 Pt 2:457-468.
38. DeCarlo MS, Talbot RW. Evaluation of ankle joint proprioception following injection of the anterior talofibular ligament. J Ortho Sport Phys Ther 1986;8:70-76.
39. Konradsen L, Ravn JB, Sorensen AI. Proprioception at the ankle: the effect of anaesthetic blockade of ligament receptors. J Bone Joint Surg Br 1993;75:433-436.

40. Hertel J, Guskiewicz KM, Kahler DM, Perrin D. Effect of lateral ankle joint anesthesia on center of balance, postural sway, and joint position sense. J Sport Rehabil 1996;5:111-119.

41. Riemann BL, Myers JB, Stone DA, Lephart SM. Effect of lateral ankle ligament anesthesia on single-leg stance stability. Med Sci Sports Exerc 2004;36:388-396.

42. Khin Myo H, Ishii T, Sakane M, Hayashi K. Effect of anesthesia of the sinus tarsi on peroneal reaction time in patients with functional instability of the ankle. Foot Ankle Int 1999;20:554-559.

43. Konradsen L, Voigt M, Hojsgaard C. Ankle inversion injuries. The role of the dynamic defense mechanism. Am J Sports Med 1997;25:54-58.

44. Nakazawa K, Kawashima N, Akai M, Yano H. On the reflex coactivation of ankle flexor and extensor muscles induced by a sudden drop of support surface during walking in humans. J Appl Physiol 2004;96: 604-611.

45. Santello M, McDonagh MJ. The control of timing and amplitude of EMG activity in landing movements in humans. Exp Physiol 1998;83: 857-874.

46. Dietz V, Noth J. Pre-innervation and stretch responses of triceps brachii in man falling with and without visual control. Brain Res 1978;142: 576-579.

47. Dietz V, Noth J, Schmidtbleicher D. Interaction between pre-activity and stretch reflex in human triceps brachii during landing from forward falls. J Physiol 1981;311:113-125.

48. Dyhre-Poulsen P, Laursen AM. Programmed electromyographic activity and negative incremental muscle stiffness in monkeys jumping downward. J Physiol 1984;350:121-136.

49. Santello M, Miller J, McDonagh MJN. Activation pattern of human leg muscles during landing from a jump onto low and high compliance surfaces. J Physiol 1993;459:504P.

50. McKinley P, Pedotti A. Motor strategies in landing from a jump: the role of skill in task execution. Exp Brain Res 1992;90:427-440.

51. Dyhre-Poulsen P, Simonsen EB, Voigt M. Dynamic control of muscle stiffness and H reflex modulation during hopping and jumping in man. J Physiol 1991;437:287-304.

52. McNitt-Gray JL, Hester DM, Mathiyakom W, Munkasy BA. Mechanical demand and multijoint control during landing depend on orientation of the body segments relative to the reaction force. J Biomech 2001;34: 1471-1482.

53. Santello M, McDonagh MJ, Challis JH. Visual and non-visual control of landing movements in humans. J Physiol 2001;537:313-327.

54. Lacquaniti F, Maioli C. Adaptation to suppression of visual information during catching. J Neurosci 1989;9:149-159.

55. Lacquaniti F, Maioli C. The role of preparation in tuning anticipatory and reflex responses during catching. J Neurosci 1989;9:134-148.

56. Caulfield B, Crammond T, O'Sullivan A, Reynolds S, Ward T. Altered ankle-muscle activation during jump landing in participants with functional instability of the ankle joint. J Sport Rehabil 2004;13:189-200.

57. Delahunt E, Monaghan K, Caulfield B. Changes in lower limb kinematics, kinetics, and muscle activity in subjects with functional instability of the ankle joint during a single leg drop jump. J Orthop Res 2006;24: 1991-2000.

58. Fu SN, Hui-Chan CW. Modulation of prelanding lower-limb muscle responses in athletes with multiple ankle sprains. Med Sci Sports Exerc 2007;39:1774-1783.

59. Caulfield BM, Garrett M. Functional instability of the ankle: differences in patterns of ankle and knee movement prior to and post landing in a single leg jump. Int J Sports Med 2002;23:64-68.

60. Caulfield B, Garrett M. Changes in ground reaction force during jump landing in subjects with functional instability of the ankle joint. Clin Biomech (Bristol, Avon) 2004;19:617-621.

61. Hopkins JT, Ingersoll CD. Arthrogenic muscle inhibition: a limiting factor in joint rehabilitation. J Sport Rehabil 2000;9:877-883.

62. Hopkins JT, Palmieri R. Effects of ankle joint effusion on lower leg function. Clin J Sport Med 2004;14:1-7.

63. McVey ED, Palmieri RM, Docherty CL, Zinder SM, Ingersoll CD. Arthrogenic muscle inhibition in the leg muscles of subjects exhibiting functional ankle instability. Foot Ankle Int 2005;26:1055-1061.

64. Swearingen RL, Dehne E. A study of pathological muscle function following injury to a joint. J Bone Joint Surg Am 1964;46A:1364.

65. Wilkerson GB, Pinerola JJ, Caturano RW. Invertor vs. evertor peak torque and power deficiencies associated with lateral ankle ligament injury. J Orthop Sports Phys Ther 1997;26:78-86.

66. Munn J, Beard DJ, Refshauge KM, Lee RY. Eccentric muscle strength in functional ankle instability. Med Sci Sports Exerc 2003;35:245-250.

67. Ryan L. Mechanical stability, muscle strength, and proprioception in the functionally unstable ankle. Aus J Physiother 1994;40:41-47.

68. Kandel ER, Schwartz JH, Jessell TM. *Principles of Neuroscience.* 4th ed. New York: McGraw-Hill Publishing Co; 2000.

69. Houglum PA. Therapeutic Exercise for Athletic Injuries. Champaign, IL: Human Kinetics; 2001.

70. Kinzey SJ, Armstrong CW. The reliability of the star-excursion test in assessing dynamic balance. J Orthop Sports Phys Ther 1998;27:356-360.

71. Tibbetts NL, Weichel DW, Kaminski TW. Examining the test-retest reliability of a novel functional hop test. J Athl Train 2004;39:S-91A.

72. Fitzgerald GK, Axe MJ, Snyder-Mackler L. The efficacy of perturbation training in nonoperative anterior cruciate ligament rehabilitation programs for physical active individuals. Phys Ther 2000;80:128-140.