PRESYNAPTIC INHIBITION: AGE-RELATED CHANGES IN A SPINAL REFLEX PATHWAY

by

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Abstract

Older adults use more muscle activity than younger adults when performing the same motor task. There is evidence to suggest that age alters the spinal and cortical pathways that control coordinated movements between agonist and antagonist muscles. The purpose of the current work was to investigate the changes in presynaptic inhibition across young and old adults at rest and during isometric plantar flexion. The results of the study indicate that young adults were able to modulate the presynaptic inhibition pathway to a greater extent than old adults. The young adults demonstrated a significant decrease in the D1 conditioned soleus H-reflex at rest and during a plantar flexion contraction at 10% of maximum (rest: 48.2% ± 16.0% of test H-reflex, P= 0.001; plantar flexion: 52.9 ± 25.0%; P= 0.001), whereas the old adults only displayed a significant decrease in the H-reflex at rest (rest: 88.0 ± 10.4% of test H-reflex, P= 0.022; plantar flexion: 102 ± 18.6%, P= 0.97). Additionally, there were greater levels of activity, although statistically insignificant, in the antagonist muscle (tibialis anterior) in old adults during plantar flexion (young plantar flexion: 4.9 ± 3.7% MVC; old plantar flexion: 7.8 ± 3.5% MVC), further supporting the notion that older adults rely more on descending commands than incoming sensory feedback when performing different physical tasks. This work provides further insight on the decline in neural function and can inform clinical work and future mechanistic studies.

Key Words: Hoffmann Reflex, Voluntary Movement, Presynaptic Inhibition, Coactivation, Age

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Introduction

Healthy aging of the human body is accompanied by a decrease in the ability to perform activities of daily living (Hortobágyi and DeVita, 2006). This includes the ability to complete simple, voluntary movements. Control of voluntary movement requires both sensory feedback from peripheral receptors, as well as descending commands from higher centers that converges onto interneurons in the spinal cord (Nielsen, 2004). These interneurons can selectively control the excitatory and inhibitory input received by spinal motor neurons (Barbeau et al., 2000). The strength of spinal and cortical pathways that control voluntary movement appears to change with aging (Hortobágyi and DeVita, 2006). Presynaptic inhibition of Ia afferent terminals is one spinal pathway that is altered with age (Baudry et al., 2010). Reduced function in this pathway may contribute to the greater levels of muscle activity used by older people to perform a desired action (Earles et al., 2001).

Concurrent activation of the agonist and antagonist muscles (coactivation) is a strategy used by the central nervous system to stabilize joints during unpredictable or unfamiliar movement, for example when trying to balance on an unstable platform (Nielsen and Kagamihara, 1993), or when trying to balance on a narrow beam (Llewellyn et al., 1990). Coactivation is also a strategy used when learning a new motor task (Smith, 1981). The heightened levels of coactivation exhibited by older adults may help them reduce movement by improving stability, but this reduces the maneuverability required for the control of posture and balance (Hasan, 2005; Koceja and Mynark, 2000). Nonetheless, older adults may need to rely more on coactivation to control their movements due to deterioration in spinal reflex pathways (Kojeca and Mynark, 2000).

The purpose of this study was to compare the changes that occur in presynaptic inhibition of the Ia afferent pathway in young and old adults at rest and during muscle contractions. The results provide insight on the decline in neural function and inform both clinical work and future mechanistic studies.

Background

This section describes the anatomy of a spinal reflex pathway, its modulation during voluntary actions, and a technique that is used to measure this modulation in humans.

Monosynaptic Pathway

The monosynaptic pathway refers to the neural circuit that comprises a single synapse between an afferent input signal and its output response onto a muscle (Enoka, 2008). Afferent fibers carry sensory information to the motor neuron pool. The motor axon, a type of efferent nerve fiber, conveys information from the motor neuron and the central nervous system to the muscles they innervate (Silverthorn, 2010).

A sensory receptor known as the muscle spindle is responsible for relaying messages (action potentials) via large sensory neurons called Ia afferents to the spinal cord where they synapse onto motor neurons innervating the same muscle (Crowe and Matthews, 1964). The muscle spindle is composed of small muscle fibers called intrafusal fibers that are innervated by gamma motor neurons (Kuffler, 1950). Ia afferent sensory nerves encircle the non-contractile center region of the intrafusal fibers and are activated by stretch of the intrafusal fiber (Kuffler, 1950). Any movement that increases muscle length stimulates the muscle spindle and causes the Ia afferents to discharge action potentials more rapidly (Matthews, 1981).

The signal conveyed along afferent pathways can be modulated before it reaches the motor neuron (Enoka, 2008). The mechanism by which the input can be modulated is called presynaptic inhibition and involves spinal interneurons (Pierrot-Deseilligny and Burke, 2005). Presynaptic inhibition is likely imposed on many different types of afferent fibers (Rudomin and Schmidt, 1999). Due to its size and accessibility, however, most is

known about the monosynaptic projection of Ia afferents onto homonymous motor neurons (Enoka, 2008).

Spinal Interneurons

It was initially thought that spinal reflexes, which are fast motor actions emitted by the central nervous system in response to a particular stimuli, occurred independently from voluntary movement (Nielsen, 2004). The current viewpoint is that reflexes and voluntary movements are inseparable, mainly because inputs from sensory afferents and descending supraspinal neurons converge onto the same interneurons (Nielsen, 2004). Interneurons make up a large percentage of all neurons and aside from the monosynaptic component of the stretch reflex pathway, all spinal reflexes comprise interposed interneurons between the input and the output (Burke, 1999).

The observation that interneurons serve as a convergence point for numerous inputs has been clearly demonstrated in the cat spinal cord by Baldissera (1981 cited in Nielsen, 2004) and Jankowska (2001). Their role during movement, however, is less certain due to technical difficulties associated with recording the action potentials discharged by interneurons (Pierrot-Deseilligny and Burke, 2005). Furthermore, the interneurons responsible for presynaptic inhibition have not been specifically identified in humans (Rudomin and Schmidt, 1999), and their presumed function can only be estimated with indirect methods, such as the Hoffmann reflex (Nielsen, 2004).

Hoffmann Reflex

The Hoffmann reflex (H-reflex) is a method of indirectly observing the strength of the monosynaptic connection between Ia afferents and homonymous motor neurons by

measuring the electrical response recorded in a muscle after stimulating a nerve (Enoka, 2008).

The H-reflex was discovered by Hoffmann (1918, 1922, cited in Schieppati, 1987) when he elicited a contraction in the calf muscles by stimulating the posterior tibial nerve in the popliteal fossa. Hoffmann (1918, 1922 cited in Schieppati, 1987) also observed that the response to the stimulation comprised two components (Figure 1): (1) M-wave – due to direct stimulation of the motor axons; and (2) H-reflex – due to the generation of action potentials in the Ia afferent that travel into the spinal cord and back out to the muscle (Magladery and McDougal, 1950 cited in Schieppati, 1987). Directly stimulating a peripheral nerve allows the investigator to bypass the muscle spindle, removing any influence it has on the signal sent from the Ia afferent to the motor neuron pool (Enoka, 2008). This provides the investigator with a tool to infer what is happening at the spinal level to the monosynaptic pathway (Enoka, 2008).

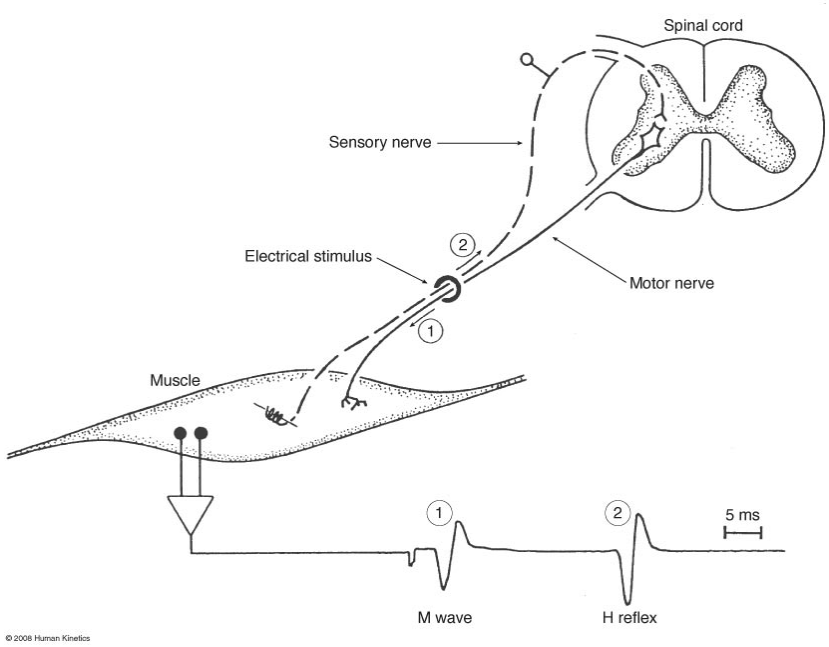


Figure 1. H-reflex pathway. From the electrical stimulus applied to the peripheral nerve, evoked action potential travels (2) along the sensory nerve to the spinal cord where it synapses with a motor nerve that carries the signal to the muscle, and (1) along the motor nerve to the muscle (Figure adopted from Enoka, 2008).

H-reflexes are most often studied in the soleus muscle because the posterior tibial nerve is easily accessible for external stimulation (Capaday, 1997). The significant difference in Ia afferent and alpha motor neuron diameters in the soleus make it easy to selectively activate Ia afferents at low stimulus intensities (Capaday, 1997). Its monosynaptic character also makes it an ideal pathway to study because the investigator does not have to be concerned with polysynaptic influences, those connections comprising more than a single synapse, making it harder to identify the origin of any change seen in the amplitude of the H-reflex (Enoka, 2008).

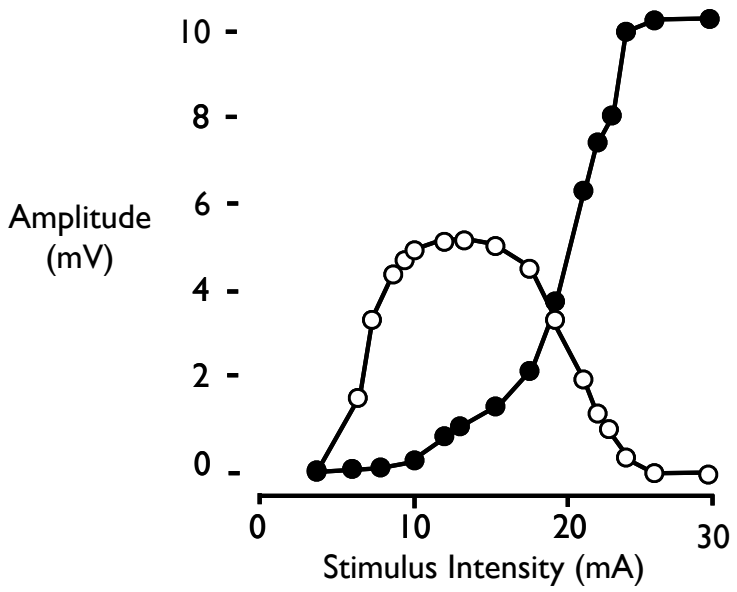


Figure 2. Recruitment curve demonstrating changes in the H-reflex amplitude (open circles) and M-wave amplitude (filled circles) with increasing stimulus intensity (Duchateau cited in Enoka, 2008).

Systematically increasing the stimulus intensity allows the investigator to identify the current at which the H-reflex reaches its maximum amplitude (H_{max}) and the point at which the M-wave reaches its maximum amplitude (M_{max}). The resulting graph is known as a recruitment curve (Figure 2). M_{max} represents the point at which all the motor neurons are activated and provides an index of the maximal response of all the motor units (Pierrot-Deselligny and Burke, 2005). H_{max} is often expressed relative to M_{max} because it provides the investigator with an index of how many motor units are activated by the H-reflex stimulus (Tucker and Turker, 2004). Because the amplitude of the M-wave provides an index of the relative stimulus intensity, any change in the H-reflex amplitude given a constant M-wave amplitude indicates that other factors besides stimulus intensity caused the change in the H-reflex amplitude (Enoka, 2008).

As indicated by the recruitment curve (Figure 2), the H-reflex amplitude increases before the M-wave amplitude with an increase in stimulus intensity. This difference is explained by the axial resistance of the Ia afferents being less than that of the motor axons (Enoka, 2008). The progressive increase in the H-reflex amplitude as the stimulus intensity first begins to increase is due to the activation of more motor neurons by the Ia afferents. The Ia afferent input activates motor neurons in the order of smallest to largest due to the greater input resistance of the small motor neurons. Eventually the stimulus becomes strong enough, however, to activate the motor axons, despite their smaller size, resulting in the appearance of the M-wave (Pierrot-Deseilligny and Burke, 2005). The motor axons are activated in the order of low-to-high axial resistance and axon diameter, which means that the largest motor units are activated first to produce the M-wave (Pierrot-Deseilligny and Burke, 2005). M-wave amplitude increases monotonically with an increase in stimulus intensity, whereas the H-reflex amplitude reaches a peak at intermediate intensities (Pierrot-Deseilligny and Burke, 2005; Stein and Thompson, 2006). The decrease in the H-reflex amplitude is due to the antidromic volley in the motor axon, the action potentials traveling toward the muscle, colliding with the action potentials discharged by the motor neuron in response to the Ia afferent input (Knikou, 2008).

To minimize the influence of the action potential collisions on estimating the responsiveness of the reflex pathway, Knikou (2008) suggested that a reflex be tested on the ascending limb of the recruitment curve. Crone et al. (1990) found that testing should occur at a minimum of 10% of the M-wave maximum with the stimulus intensity adjusted to produce a small M-wave and an H-reflex at an acceptable percentage of M_{max}. At 50% of the H-reflex maximum, the reflex is sensitive to both excitation and inhibition, which makes

it difficult to determine what causes any changes in the H-reflex amplitude (Zehr and Stein, 1999).

Another challenge associated with using the H-reflex technique to study spinal pathways is that the H-reflex amplitude is depressed shortly after a preceding activation of the reflex pathway (Hultborn et al., 1996). This depression, termed post-activation depression, has been observed in several conditions: stimulating the nerve used to elicit the H-reflex response (Magladery et al., 1952 cited in Hutlborn et al., 1996); during passive lengthening of the muscle (Mark et al., 1968; Romano and Schieppati, 1987 cited in Hultborn et al., 1996); and following a voluntary contraction of the test muscle (Schieppati and Cernna, 1984; Schieppati et al., 1995, Crone and Nielsen, 1989 cited in Hultborn et al., 1996). Post-activation depression interferes with determining whether any change in the amplitude of the H-reflex is due to inhibition or facilitation (Crone and Nielsen, 1989; Hultborn et al., 1996). The depression is likely caused by a reduction in the amount of neurotransmitter released from active Ia afferents (Crone and Nielsen, 1989; Hultborn et al., 1996).

To minimize the influence of post-activation depression on test H-reflexes, there needs to be a suitable amount of time between successive H-reflexes (Pierrot-Deseilligny and Burke, 2005), the involved joints should be stabilized to reduce any stretch of the tested muscle (Brooke et al., 1997), and the muscle should be activated (Pierrot-Deseilligny and Burke, 2005). Despite the limitations with the H-reflex technique, including the complexity of the spinal cord pathways, the H-reflex provides a useful non-invasive tool for studying specific spinal pathways.

Presynaptic Inhibition

Presynaptic inhibition of Ia afferents involves pathways that modulate the release of neurotransmitter at the synapse between Ia afferents and motor neurons (Rudomin and Schmidt, 1999). Frank and Fuortes (1957, cited in Hultborn et al., 1987) were the first to demonstrate presynaptic mechanism by observing a reduction in the signal sent from Ia afferents to a motor neuron pool without detecting any change in the excitability of the motor neurons. Interneurons acting on Ia afferents seem to mediate the depression observed in the amplitude of the H-reflex (Eccles, 1964 cited in Knikou, 2008).

One pathway that produces presynaptic inhibition involves two primary afferent depolarization (PAD) interneurons known as first order and last order PAD interneurons (Rudomin and Schmidt, 1999). These interneurons receive inputs from the muscle, Ia and Ib afferents, and descending tracts (Pierrot-Deseilligny and Burke, 2005). The last order interneuron, which synapses directly onto the Ia terminal, receives excitatory input from the first order interneuron and inhibitory input from descending tracts (Pierrot-Deseilligny and Burke, 2005). The first order interneuron receives excitatory input from descending tracts and Ia afferents (Pierrot-Deseilligny and Burke, 2005). Hence, descending tracts can both facilitate and depress interneurons that mediate presynaptic inhibition via various pathways (Enoka, 2008).

The mechanism of action that reduces neurotransmitter release is for the PAD interneurons to allow an efflux of Cl^- from the Ia afferent terminal that depolarizes the cell and causes the presynaptic terminal to become less sensitive to incoming action potentials (Rudomin and Schmidt, 1999). Consequently, the influx of Ca^{++} into the cell as a result of arriving action potentials is decreased, which reduces the amount of neurotransmitter released, resulting in a smaller post-synaptic potential (Rudomin and Schmidt, 1999).

Therefore, the purpose of presynaptic inhibition is to modulate the amount of neurotransmitter released from the Ia afferents terminals onto motor neurons during a task (Knikou, 2008; Misiaszek, 2003).

Measuring Presynaptic Inhibition

The H-reflex can be used to study presynaptic inhibition via a conditioning stimulus. There are two methods (Figure 3) of activating the PAD interneurons assumed to be responsible for presynaptic inhibition of the soleus. One method is known as heteronymous facilitation and involves activating the monosynaptic connection between the quadriceps Ia afferents and the soleus motor neuron pool (Hultborn et al., 1987). The Ia afferents from the quadriceps facilitate the H-reflex of the soleus, but also receive input from the same PAD interneurons presumed to produce presynaptic inhibition of the soleus motor neurons (Meunier and Pierrot-Deseilligny, 1998). The size of the reflex facilitation reflects the amount of presynaptic inhibition imposed on the Ia fibers (Hutlborn et al., 1987).

The other method is known as D1 inhibition and is achieved by activating the Ia afferents from the tibialis anterior by stimulating the peroneal nerve (Mizuno et al., 1971). Because PAD interneurons for an agonist receive input from the afferents of the antagonist muscle, stimulating the peroneal nerve shortly before evoking an H-reflex in the soleus will depress the H-reflex amplitude. This technique was first used in humans by Mizuno et al. (1971) and is the technique that will be used in the current study. To be certain that depression of the H-reflex is due to presynaptic inhibition, the test H-reflex amplitude must be kept constant between tasks.

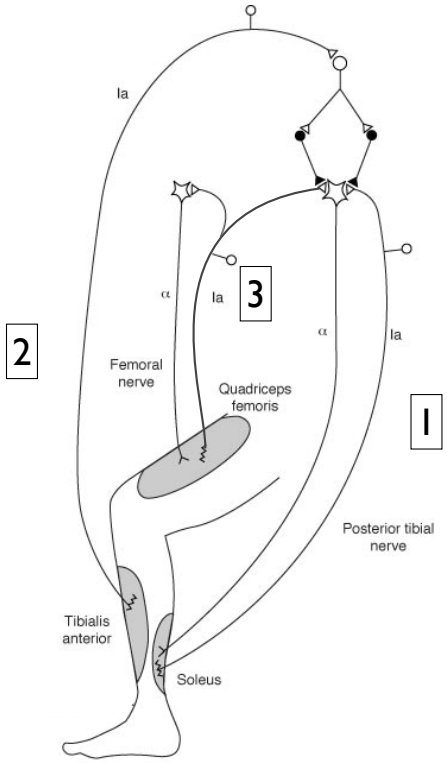


Figure 3. Pathway 1 follows the H-reflex pathway in the soleus, pathway 2 follows the D1 inhibition pathway for the soleus and pathway 3 follows the heteronymous facilitation pathway for the soleus (Cited in Enoka, 2008).

Presynaptic Inhibition During Voluntary Movement

Presynaptic inhibition modulates the amount of neurotransmitter released from the Ia afferent onto the motor neuron during voluntary actions (Rudomin and Schmidt, 1999). The amount of H-reflex depression caused by Ia presynaptic inhibition varies with the demands of the motor task (Capaday and Stein, 1986; Edamura et al., 1991; Llewellyn et al., 1990; Morin et al., 1982). For example, Tanaka (1974) found inhibition of the soleus H-reflex from stimulating the peroneal nerve became larger when subjects voluntarily activated their tibilalis anterior, the antagonist to the soleus. Similarly, stimulating the ipsilateral sural nerve, located in the foot, causes a decrease in the inhibition during plantar

flexion as a result of less presynaptic inhibition being send to the soleus, the active muscle during plantar flexion (Iles, 1996).

Furthermore, Capaday and Stein (1987) found that the amplitude of the soleus H-reflex is strongly modulated during walking. The amplitude increases linearly during the stance phase, in parallel with the soleus EMG (suggesting heightened activity in the muscle), and then is suppressed completely during the swing phase when the ankle flexor (tibialis anterior, the antagonist to the soleus) is active (Schneider et al., 2000). At matching levels of EMG activity, the H-reflex amplitude is much greater during standing than in the early part of the stance phase of walking (Capaday and Stein 1987; Morin et al., 1982).

Baudry et al. (2010) were further able to demonstrate that presynaptic inhibition depends not only on the muscles in use during a task, but also on the type of load the muscle encounters. They found that presynaptic inhibition of Ia afferents in the extensor carpi radialis muscle was reduced during position control compared with an equivalent torque during force control in young subjects. Furthermore, it has been shown that presynaptic inhibition can be modulated through practicing an activity (Perez et al., 2007). After having subjects practice a cocontraction task, Perez et al. (2007) found that the H_{max}/M_{max} ratio was significantly decreased, indicating an increase in presynaptic inhibition. The last two examples, from Baudry et al. (2010) and Perez et al. (2007), illustrate that presynaptic inhibition is dependent on the actions of the agonist and antagonist muscles, and can be altered with practice. Aging, however, appears to make individuals less reliant on presynaptic inhibition and more reliant on coactivation.

Changes in Presynaptic Inhibition with Age

The human body's ability to control and fine-tune voluntary movement declines with advancing age (Hortobágyi and DeVita, 2006). Changes in the neuromuscular system include a decrease in the number of motor neurons, which results in a decline in the ability to perform motor tasks (Campbell et al., 1973; Doherty et al., 1994; Masakado et al., 1994 cited in Burnett et al., 2000). One way in which this decline in function manifests in older adults is their apparent decreased ability to modulate presynaptic inhibition.

The amount of presynaptic inhibition evident in a soleus H-reflex of young adults is inversely related to the plantar flexion torque produced during isometric contraction of the calf muscles (Butchart et al., 1993). Older adults exhibit only a slight reduction in presynaptic inhibition with increases in torque, demonstrating that the control of transmission in spinal pathways changes with advancing age (Butchart et al., 1993). To compensate for this adaptation, older adults use greater amounts of coactivation of the agonist and antagonist muscles when performing a given task (Spiegel et al., 1996). For example, Baudry et al. (2010) found that young adults rely more on afferent feedback to motor neurons across position and force tasks, whereas old adults instead modulated coactivation across the two tasks. The difference in control strategies was associated with less steady contraction for the old adults at low target forces (Baudry et al., 2010).

The current study examined the changes that occur in presynaptic inhibition between young and old subjects during different muscle contractions in the lower leg. The H-reflex method was used to study the monosynaptic connection between the Ia afferent and motor neurons of the soleus muscle and the influence of activating the PAD interneurons on the amplitude of the soleus H-reflex. The expectation was that young subjects would be able to modulate presynaptic inhibition between rest and the contraction task, which would be

observed as a greater depression in the amplitude of the H-reflex at rest compared with a plantar-flexion contraction. Conversely, older adults would be less able to modulate presynaptic inhibition and would display increased coactivation between the soleus and tibialis anterior instead of a significant depression of the H-reflex amplitude.

Methods

Nineteen adult volunteers, 10 young (24.6±3.2 yrs) and 9 old adults (78.2±4.4 yrs) participated in the study after written informed consent had been obtained. The University of Colorado institution review board approved the protocol. Exclusion criteria included individuals with known neurological disorders, hip or knee replacements in the right leg, or use of a pacemaker. Each subject attended a single 3-hr session.

Experimental Set-Up

Subjects were seated in a chair with the right foot strapped to a pedal attached to a tri-axial force transducer (JR3, Woodland, CA). The subjects were seated with joint angles of 120-degree angle at the hip, 160-degree angle at the knee, and 110-degree angle at the ankle (Figure 4). The plantar flexion force signal was sampled at 2000 Hz and stored on a computer for offline analysis

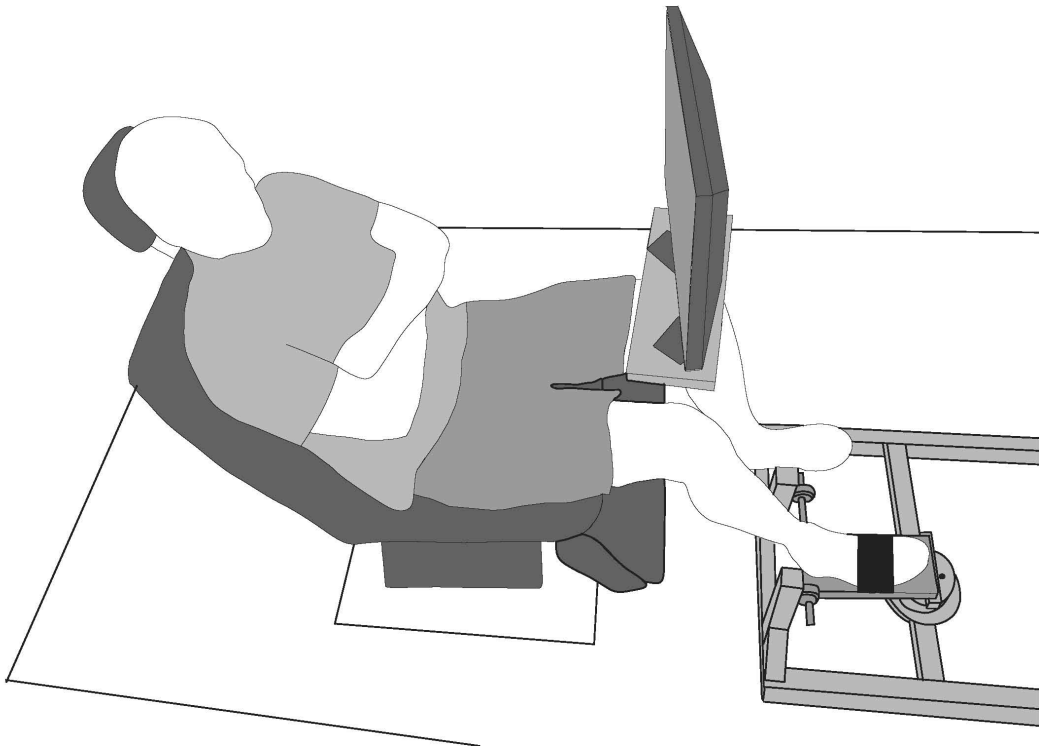


Figure 4. Subject was seated in a chair with the right foot strapped to a force transducer. The monitor provided force and EMG feedback to the subject.

EMG recordings

Electromyographic signals were recorded from the soleus, tibialis anterior, and medial gastrocnemius with surface electrodes (silver-silver chloride electrodes, 8 mm for the tibialis anterior and medial gastrocnemius, 4 mm for the soleus) placed in a bipolar configuration directly over the belly of the muscles in accordance with SENIAM recommendations (Hermens et al., 1999). The EMG signals were amplified (500-1500) times and band pass filtered (13-1000 Hz) prior to sampling at 2 Hz (Coulborn Instruments) and stored on a computer for offline analysis. The EMG signal of the soleus, gastrocnemius and tibialis anterior was recorded during a 50ms window immediately prior to the application of the electrical stimulus.

MVC Recording

The maximal voluntary contraction (MVC) of the soleus muscle was obtained before the force-matching task in order to set a target force. The MVC force was achieved by a gradual 3 s increase in force until the maximum was reached, and then the subject held the contraction for 3 s. At least 2 trials were performed to ensure a subject's maximum by having them achieve peak forces within 5% of each other. MVC values also allowed for the normalization of the soleus and medial gastrocnemius EMGs. A dorsiflexion MVC was obtained in order to normalize the tibialis anterior EMG during the force-matching task.

Electrical Stimulation

Electrical stimulation was used to elicit the test H-reflex and to provide the conditioning stimulus for D1 inhibition (Mizuno et al., 1971). The stimulation was elicited by electrical stimulation (Grass S88K, Astra-Med, West Warwick, RI, 1 ms rectangular pulse) of the target nerve through a constant current unit (Model CCUI, Astra-Med) that was connected to disposable adhesive surface electrodes (Conmed, Utica NY). The soleus-H reflex was achieved by stimulating the posterior tibial nerve in the popliteal fossa. The common peroneal nerve was stimulated just above the head of the fibula to provide D1 inhibition.

Motor threshold (the lowest stimulus required to see a response in the motor neurons) of the tibialis anterior was determined by making sure that there was both an M-wave and a twitch in the tibialis anterior with stimulation of the common peroneal nerve (Pierrot-Deseilligny and Burke, 2005). The intensity of the conditioning stimulus was expressed relative to the motor threshold for comparison across subjects.

Test H reflexes and conditioned H reflex

H REFLEX. A recruitment curve (Figure 2) for the H-reflex and M-wave of the soleus was recorded when the subject was at rest. An electrical stimulus was delivered to the posterior tibial nerve (10 pulses) with 5 s between each pulse. The EMG activity in response to each stimulus within a train was averaged and monitored on an oscilloscope and simultaneously stored on a computer for offline analysis. The initial intensity was set below the H-reflex threshold and was increased until a maximum value of the M-wave (M_{max}) was reached. The stimulus intensity was then adjusted to yield a test H-reflex amplitude between 10-25% of M_{max}.

D1 INHIBITION. The test H-reflex was conditioned by a stimulus applied to the common peroneal nerve to activate the PAD interneurons assumed to be responsible for presynaptic inhibition of soleus Ia afferents. The delay between the test stimulus and conditioned stimulus was ~20 ms, the test stimulus was elicited first. The amplitude of the test H-reflex and the conditioned H-reflex were averaged over 20 responses.

Experimental Procedure

The locations for the EMG electrodes were determined while the subject performed plantar flexion (for the soleus and medial gastrocnemius) and during dorsiflexion (for the tibialis anterior) contractions. With the recording electrodes in place, the location for the stimulating electrodes for the posterior tibial nerve (test H-reflex) and the common peroneal nerve (DI conditioning reflex) stimulating electrodes were determined.

Once both stimulating sites had been located, the recruitment curve for the H-reflex and M-wave in the soleus was established. The subject then performed dorsiflexion and plantar flexion MVCs. An average of 20 test H-reflexes were recorded as a baseline

measure. The conditioning stimulus was then applied to the common peroneal nerve ~20 ms before the H-reflex stimulation was evoked and averaged over 20 responses (Mizuno et al., 1971). Once the subject received both test and conditioned reflex stimuli at rest, the subject was required to match a target force set at 10% of the force measured during the plantar flexion MVC and the reflexes were tested again. The change in amplitude was compared between test and conditioned reflexes, in young and old adults, when at rest and during a light contraction as a measure of how the level of presynaptic inhibition changes with contraction and age.

Statistical analysis

MVC, M_{max} and H_{max} amplitudes were compared between age groups with unpaired t-tests. The latency and duration of the H-reflex between age groups were also compared with unpaired t-tests. The amplitude of the test H-reflex was compared to the amplitude of the conditioned H-reflex at rest and during the contraction task with paired t-tests within age groups and compared between age groups using unpaired t-tests. EMG activity in the soleus, gastrocnemius, and tibialis anterior was compared with unpaired t-tests between age groups.

Results

Data are expressed as means ± SD in text and means ± SE in figures. The level of statistical significance was set at $P < 0.05$ for both paired and unpaired t-tests.

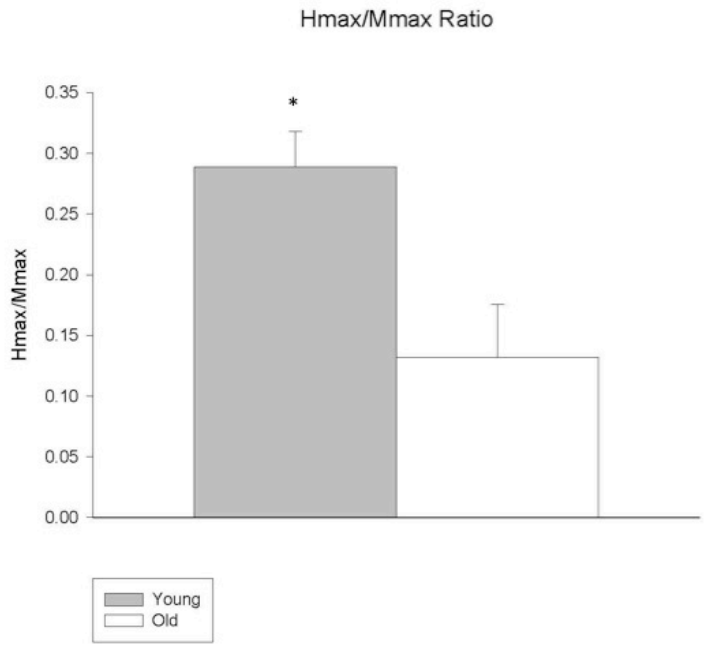
Maximal Voluntary Contraction (MVC)

The maximal voluntary force (MVC) exerted by the plantar flexors differed for young and old subjects. Young subjects produced 0.124 ± 0.036 V of force and the older subjects produced 0.082 ± 0.044 V of force (unpaired t-test, $P = 0.015$). Young subjects produced 33% more force than older subjects.

Recruitment Curve

M_{max} values did not differ between old and young subjects. Young subjects produced an average M_{max} of 5.32 ± 0.83 V and old subjects produced an average M_{max} of 5.43 ± 2.50 V (unpaired t-test, $P= 0.906$). The average H-reflex amplitude, however, did differ between age groups (Figure 5B). For a given stimulus intensity, young subjects produced H-reflexes with larger amplitudes. The average H-reflex amplitudes were 13.2 ± 10.0 V for the young subjects and 6.26 ± 5.7 V for the old subjects (unpaired t-test, $P= 0.05$). The H_{max}/M_{max} ratio was significantly larger in young subjects (young = .289 ± .093; old = .132 ± .131; unpaired t-test, $P= 0.042$; Figure 5A).

A.



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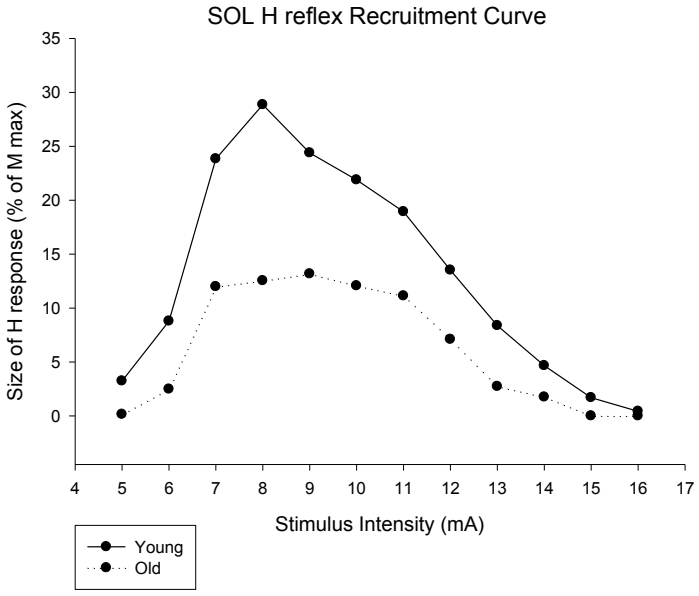


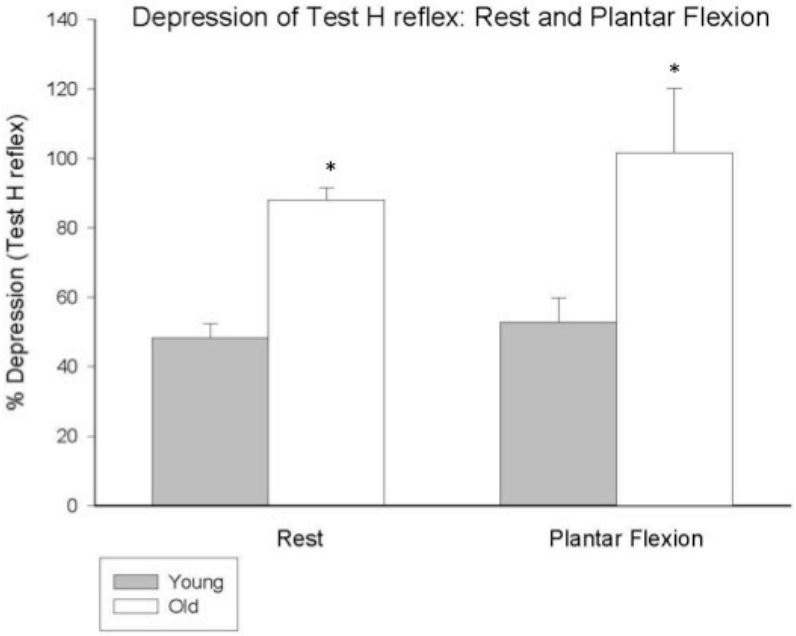
Figure 5. The normalized Hmax/Mmax ratio for young and old subjects (A), and the average recruitment curve for the soleus (SOL) H-reflex of young and old subjects (B).

Test H Reflex

The stimulus intensity for the test H reflex was adjusted across contraction intensities to keep the amplitude between 10-25% of M_{max} across an average of 20 reflexes. The H-reflex amplitude for the young subjects was 15.2± 5.9% of M_{max} at rest and 16.1± 7.06% of M_{max} during plantar flexion (paired t-test, P= 0.121) and for the old subjects it was 13.4± 3.9% of M_{max} at rest and 15.1± 4.87% M_{max} during plantar flexion (paired t-test, P= 0.059). The amplitude of the M-wave (rest: young, 6.31 ± 13.7 %M_{max}; old, 8.0± 6.9 %M_{max}; contraction: young, 7.8 ± 20.2 %M_{max}; old, 7.2 ± 7.1 %M_{max}) also remained constant across contraction intensities (paired t-test, young, P= 0.492; old, P= 0.544).

The latency of the H-reflex was longer for younger subjects than for old subjects (young: 49.0 ms; old: 44.3 ms; unpaired t -test P = 0.005), and the duration of the H-reflex was longer for young subjects (young: 17.3 ms; old: 14.2 ms; unpaired t-test P = 0.278). The conditioned H-reflex amplitude at rest was depressed for both the young subjects (48.2 ± 16.0%; paired t-test, P= 0.001) and the old subjects (88.0 ± 10.4%; paired t-test, P= 0.022). However, the conditioned H-reflex was depressed during the plantar flexion contraction only for the young subjects (52.9 ± 25.0%; paired t-test, P= 0.001) and not the old subjects (102 ± 18.6%; paired t-test, P= 0.97). The depression exhibited by young subjects was significantly greater (unpaired t-tests) than that for the old subjects at rest and during plantar flexion (Figure 6A; rest: P= 0.006; contraction: P= 0.026). Nonetheless, the amount of depression did not differ (unpaired t-tests) between rest and plantar flexion (Figure 6B) for either young subjects (P = 0.742) or old subjects (P = 0.109).

A.



B.

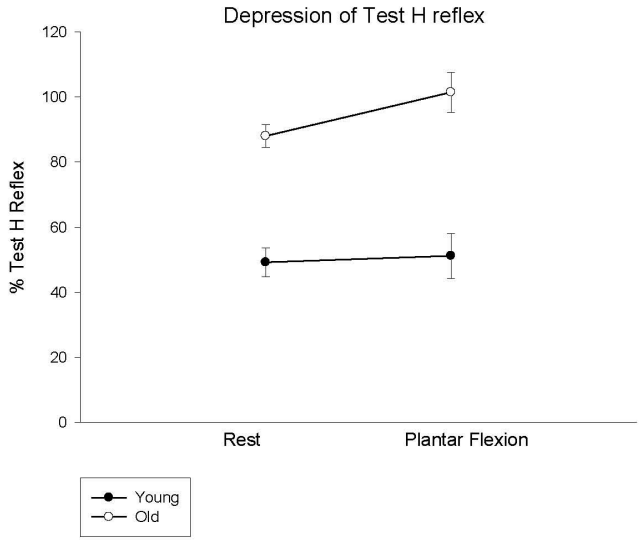
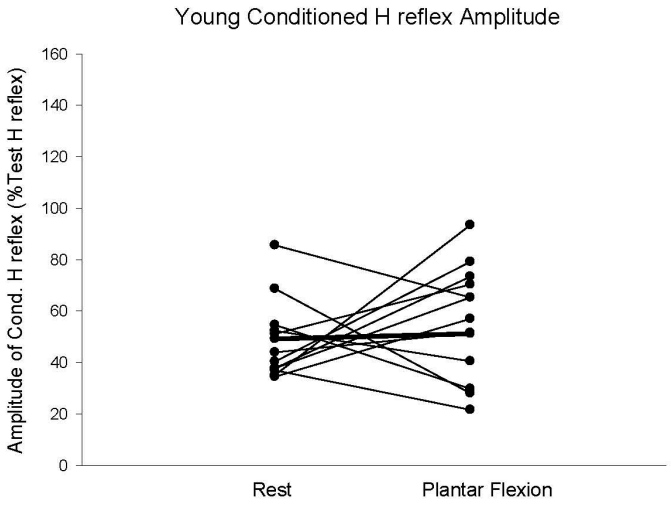


Figure 6. Depression of the test H-reflex in young and old subjects at rest and during 10% plantar flexion (A). There was no significant difference between the depression produced between conditions for either group of subjects (B)**.**

A.



B.

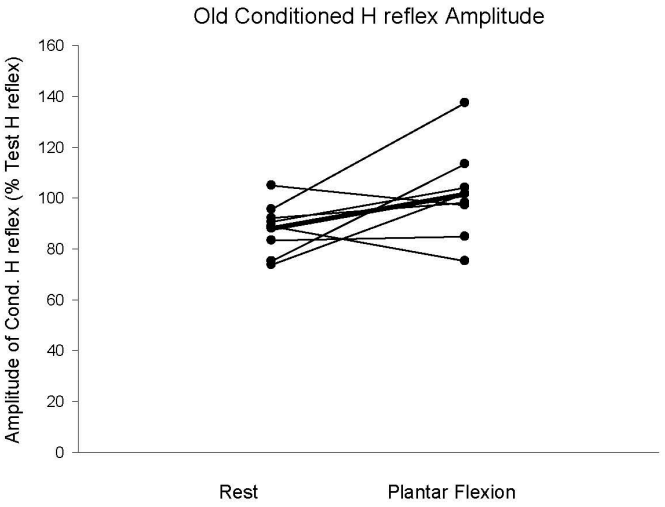


Figure 7. Amplitude of the conditioned H reflex for young (A) and old (B) subjects at rest and during plantar flexion. Each line indicates the response of a single subject. Thick line represents the average depression at rest and during plantar flexion.

EMG Amplitude

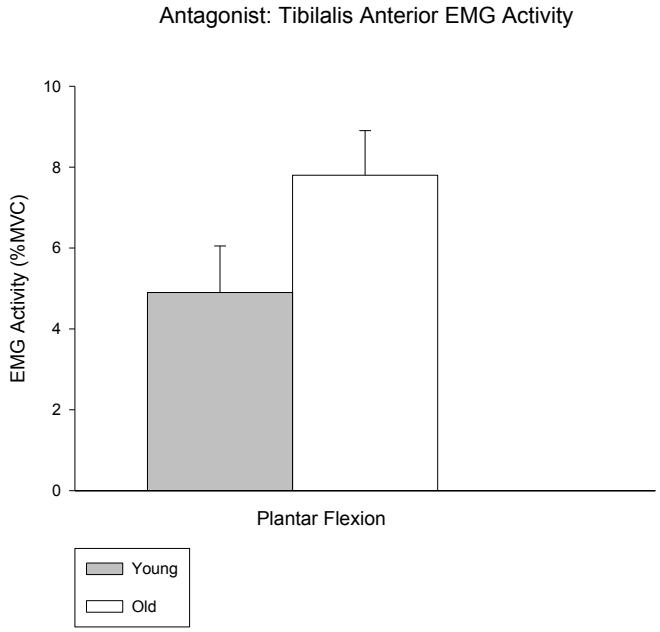
There was also no significant difference in EMG amplitude between young and old subjects (unpaired t-tests) during plantar flexion for the soleus (P= 0.598), gastrocnemius (P= 0.145), or tibialis anterior (P= 0.102) (Table 1). Old subjects displayed 33% more EMG activity in the tibialis anterior (antagonist coactivation) during plantar flexion than young subjects (Figure 8A). The coactivation ratio between the level of activity in the antagonist (tibialis anterior) and agonist muscle (soleus) was statistically insignificant, but larger in old subjects (young coactivation ratio= .644 ± .695; old coactivation ratio= .677 ± .562; unpaired t-test, P= .740) (Figure 8B).

Table 1. EMG amplitude in young and old subjects at 10% MVC Plantar Flexion.

	SOL PF	GM PF	TA PF
Young	12.2±11.0 %	13.3±9.9 %	4.9±3.7 %
Old	14.6±8.8 %	22.5±16.4 %	7.8±3.5 %

Soleus (SOL), gastrocnemius (GM) and tibialis anterior (TA) . Values are expressed as %MVC.

A.



B.

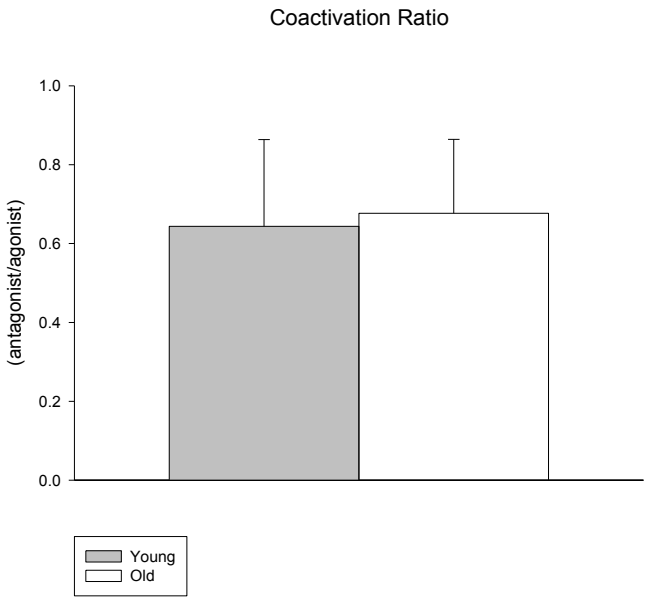


Figure 8. Amplitude of EMG acvtivity in the tibialis anterior during 10% plantar flexion (A). There was no significant difference in the coactivation ratio (tibilalis anterior/ soleus) between young and old subjects (B).

Discussion

The original finding of this study was that young subjects significantly depressed the amplitude of the soleus test H-reflex at both rest and during 10% plantar flexion. Old subjects also displayed a significant depression of the H-reflex at rest, but there was no presynaptic inhibition as indexed by a D1 conditioning stimulus during plantar flexion. The depression achieved by young subjects, at rest and during plantar flexion, was significantly greater than that produced by old subjects. There was also a statistically insignificant trend towards heightened activity in the antagonist muscle, the tibialis anterior, during the contraction task in old subjects.

H reflex Amplitude

The purpose of this study was to compare the changes that occur in presynaptic inhibition of the Ia afferent pathway in young and old adults at rest and during muscle contractions. The significantly larger depression in the H-reflex seen in young subjects, but not in old subjects, is consistent with previous findings (Buchart et al. 1993; Earles et al. 2001). Although these earlier studies also found significant differences in the magnitude of presynaptic inhibition elicited during different contraction intensities in the soleus, the current study found no significant difference in the depression when evoked at rest or during plantar flexion. Meunier and Pierrot-Deseilligny (1998) also found no significant difference in the level of presynaptic inhibition elicited at different contraction intensities in the soleus. These contradictory findings are probably due to the methods utilized to set the target torque for different contraction intensities. For example, Earles et al. (2001) used the amplitude of the EMG data to set the stimulus intensity, Buchart et al. (1993) used the same absolute torque for all subjects, and Meunier and Pierrot-Deseilligny (1998) set

target torques relative to the MVC torque of each subject. The current study used the latter approach and obtained the same findings.

Similar results were obtained when heteronymous facilitation (the pathway between the quadriceps Ia afferent and the soleus motor neuron pool) was used to study presynaptic inhibition. Koceja and Mynark (2000) use the heteronymous facilitation method to demonstrate that old subjects showed no change in the soleus H_{max}/M_{max} ratio, an index of how many motor units are active, when moving from supine to standing. In contrast, there was a significant decrease in the H_{max}/M_{max} ratio in young subjects when they went from supine to standing demonstrating a selective activation of muscles between tasks. Assuming that M_{max} does not change between tasks, a decrease in the ratio must be due to a depression in the size of the H-reflex, suggesting more presynaptic inhibition during standing in young subjects.

Hultborn and Pierrot-Deseilligny (1987) demonstrated that heteronymous facilitation from the quadriceps to the soleus caused a decrease in presynaptic inhibition of the soleus H-reflex, but an increase in presynaptic inhibition of the quadriceps H-reflex. These findings demonstrated that as one muscle contracted, presynaptic inhibition decreased in the contracting muscle, but increased in the muscle not involved in the contraction, allowing selective activation of the agonist muscle. Hutlborn and Pierrot-Deseilligny (1987) called this effect motor contrast, which is desired when trying to produce an isolated action. The results of the current study demonstrate no significant reduction in presynaptic inhibition in old subjects from rest to 10% plantar flexion, indicating a decreased ability to selectively activate muscles across tasks and suggesting the reliance on a different strategies to perform the requisite tasks.

EMG Amplitude

The effects of presynaptic inhibition can also be investigated by analyzing EMG activity across tasks. Schneider et al. (2000) studied the modulation of the soleus H-reflex during walking and found that the soleus H-reflex was strongly suppressed during the swing phase when the antagonist muscle (tibialis anterior) was active. They also demonstrated that the H_{max} amplitude was reached at the same time that the peak soleus EMG amplitude was reached. Furthermore, the minimal amplitude for the soleus H-reflex coincided with an EMG burst in the tibialis anterior. These data illustrate the importance of modulating presynaptic inhibition based on the demands of a task.

Koceja et al. (1993) similarly demonstrated a depression of the soleus H-reflex amplitude as the body position shifted from prone to standing, despite an increase in background EMG activity. Old subjects, in contrast, exhibited no change in the soleus H-reflex amplitude (Koceja and Mynark, 1995). In the current study, old subjects did not show any significant change in the H-reflex amplitude between rest and plantar flexion, but there was more EMG activity in the tibialis anterior during plantar flexion compared to young subjects. Conversely, young subjects displayed a significant depression in the H-reflex amplitude at rest and during plantar flexion. These data demonstrate that old subjects used more coactivation between the agonist and antagonist muscles across contraction intensities, instead of modulating presynaptic inhibition. These findings are consistent with previous studies.

Hortobágyi et al. (2003) examined the ability of old subjects to execute daily tasks and found that old subjects used more EMG activity in both the agonist and antagonist muscles, demonstrating that old subjects were working at a higher level of effort relative to their

maximal capability as compared with young subjects. Similarly, old women used greater coactivation and displayed greater leg stiffness than young women when stepping down from a raised platform (Hortobágyi and DeVita, 2000). Furthermore, Tracy and Enoka (2001) found that old subjects used greater coactivation of the antagonist muscle than young subjects during both submaximal isometric and anisometric contractions with leg muscles.

The connection between the modulation of the H-reflex amplitude and coactivation was clearly illustrated by Baudry et al. (2010) when subjects were required to perform submaximal, steady contractions. Young subjects modulated the H-reflex amplitude between force and position tasks, whereas the old subjects varied the level of coactivation between the agonist and antagonist muscle across tasks in old subjects instead of modulating the H-reflex amplitude.

The disproportionate increase in EMG activity in old subjects during activities of daily living is further explained by comparing the cortical activity between young and old subjects. Old subjects recruit more cortical and subcortical areas than young subjects to perform a simple task (Mattay et al., 2002), which is consistent with heightened reliance on descending commands by old adults over incoming sensory information, resulting in elevated coactivation instead of presynaptic inhibition.

Limitations

The H-reflex technique is an indirect method of studying spinal interneuronal circuits, which constrains the interpretation of the data. To keep the test H-reflex amplitude constant between contraction intensities, it was necessary to adjust the stimulus intensity, which likely changed the Ia afferents and motor units that contributed to the amplitude of

the H-reflex (Pierrot-Deseilligny and Mazevet, 2000). The study could have been strengthened by recruiting more participants, testing the heteronymous-facilitation pathway and measuring presynaptic inhibition in the antagonist muscle. However, although it is theoretically possible to elicit an H-reflex in any muscle during a voluntary contraction, it can be challenging in many subjects to elicit an H- reflex in the tibialis anterior at rest (Semmler and Turker, 1994 cited in Zehr, 2002).

Conclusion

The data from the current study illustrate that presynaptic inhibition of Ia afferent fibers is an important control mechanism during voluntary movement. It allows the selective activation of the active muscle while simultaneously reducing the activity in the antagonist muscle and muscles not involved in the contraction. This allows for more efficient, controlled movement. However, old subjects exhibited a reduced ability to modulate incoming sensory information and they instead had to rely more on descending commands, which cause the increased coactivation in the antagonist muscle. Although coactivation augments stability, it results in more muscle activity than is necessary to produce a given task and decreases the ability to control voluntary movements.

Nonetheless, presynaptic inhibition is just one spinal pathway that contributes to the control of voluntary actions. Future studies should investigate other spinal pathways, such as reciprocal Ia inhibition, recurrent inhibition, and Ib inhibition, to determine the extent to which the current findings generalize to changes in the management of all sensory feedback with advancing age.

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