MOTOR FUNCTION IN AGING ADULTS: REHABILITATIVE STRATEGIES THROUGH PRACTICE AND ELECTRICAL STIMULATION

by

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Abstract

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Motor function in aging adults: Rehabilitative strategies
through practice and electrical stimulation

Thesis directed by Professor Roger M. Enoka

This dissertation explores the effects of aging on motor function with a specific focus on manual dexterity and walking endurance. The first two studies focus on manual dexterity in older adults, examining how practice can influence motor performance, particularly through improvements in the grooved pegboard task times. These studies revealed that initial performance significantly explains the extent of improvement in manual dexterity, suggesting the idea of stratifying older adults based on their initial performance rather than their chronological age. Moreover, this stratification can provide more insightful details about their improvement in force steadiness, the ability to sustain an isometric contraction at a submaximal target force. The performance of grooved pegboard test in both fast and slow groups of older adults can be explained by force steadiness and this explanation is unchanged for the slow older adults from before to after a practice intervention.

The subsequent studies shift focus to the application of Transcutaneous Electrical Nerve Stimulation (TENS) in enhancing walking endurance and balance in older adults. These studies investigate the biomechanical outcomes of TENS application during the 6-minute walk test, providing insights into the potential of TENS to change walking endurance of older adults. The results found a significantly reduced 6-min walking distance under the application of TENS compared with the control condition. However, re-examination of the data from middle-aged and older adults with machine learning techniques can explain the common kinematic changes

induced by TENS in walking speed and walking balance, providing a detailed characterization of stride variability, and walking patterns under different stimulation conditions in middle-aged and older adults.

Together, these studies explore a comprehensive view of how targeted interventions, both in the form of physical practice and electrical stimulation can minimize the decline in motor function associated with aging. Moreover, new analytical approaches of clustering and machine learning can augment our understanding of age-related declines in motor function.

DEDICATION

This dissertation is dedicated to those who have been my pillars during the past six years of effort and research:

To my beloved partner, Mélanie, who has supported, encouraged, and loved me through the challenges of life, being my comfort during both the highs and the lows.

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INTRODUCTION

Motor control is an essential ability of the human body, facilitating movement production, object manipulation, and limb coordination. It relies on the adequate interaction between the sensory and motor systems. Factors such as aging and neurological diseases can compromise these systems, thereby impairing motor control and increasing mortality risk (Metz, 2000; Vestergaard, Patel, et al., 2009). The NIH toolbox for Assessment of Neurological and Behavioral Function provides a comprehensive view of these interactions across four primary domains: cognitive, motor, emotional, and sensory (Gershon et al., 2013; Reuben et al., 2013). This dissertation evaluates the impact of aging on three categories of the motor domain: locomotion, balance, and dexterity. It also evaluates the rehabilitative potential of practical and therapeutic interventions in minimizing the decline in performance among middle-aged and older adults. As the global population of individuals aged 60 and older continues to rise significantly, it is becoming increasingly important to understand how aging affects motor control. Developing tools to minimize the decline of motor skills is now a crucial public health concern. Additionally, enhancing our scientific understanding of these processes can help in the early detection and prevention of aging-related comorbidities.

MOTOR FUNCTION AND AGING

As the human body ages, the neuromuscular system undergoes numerous physiological changes (Hunter et al., 2016), such as the stiffening of muscle fibers and loss of motor neurons, that contribute significantly to the decline in motor function. This decline affects several motor control areas including, but not limited to, maximal muscle force (Frontera et al., 1991), force steadiness (Galganski et al., 1993), manual dexterity (Marmon, Pascoe, et al., 2011), and standing balance (Abrahamová & Hlavacka, 2008) in older adults. These physiological changes not only affect the physical capacity to perform tasks of daily living but also impact their speed and accuracy. Among others, muscle atrophy, increased stiffness of connective tissues, and reduced neuronal conductivity are all important factors that compound the effects of aging, leading to a significant decrease in motor control and consequently quality of life.

Motor units are fundamental elements of motor function and were described by Sherrington (Sherrington, 1925) as the "final common pathway". They translate synaptic input from the brain or other neurons to the musculoskeletal system. Each motor unit consists of a motor neuron and its innervated muscle fibers, which contributes to muscle contractions and mobility through twitch responses (Heckman & Enoka, 2012; Liddell & Sherrington, 1925). From around the age of 65, motor function begins to decline, becoming significantly noticeable by age 75 (Hortobágyi et al., 2015; Shiffman, 1992). This decline often involves a reduction in the number of motor neurons (Grounds, 2002; Hepple & Rice, 2016; McNeil et al., 2005; Tomlinson & Irving, 1977), causing muscle fibers that lose their innervating neurons to either die or become reinnervated by adjacent motor neurons (Purves-Smith et al., 2014). This increase in the innervation number of the remaining motor neurons (Fling et al., 2009) enhances the twitch force of each motor unit, resulting in less precise movements compared to those in younger individuals (Clark et al., 2014; Galganski et al., 1993; Poston et al., 2013; Roos et al., 1997; Sleimen-Malkoun et al., 2013).

Sarcopenia is a progressive and generalized skeletal muscle disorder that occurs with aging and is associated with an increased likelihood of adverse outcomes, including falls and physical disability (Cruz-Jentoft et al., 2019). This disease, leading to muscle atrophy and motor neuron loss, further exacerbates the decline in motor function, particularly affecting muscle mass and strength (Narici et al., 1991). It is to note that this condition not only affects muscle mass, but also significantly impacts muscle metabolism and hormonal setting (Priego et al., 2021), which are crucial for maintaining muscle health. Sarcopenia was suggested to occur at a higher rate in lower limbs than upper limbs (Janssen et al., 2000), indicating that muscles are not necessarily experiencing the same changes over the lifespan. Such a greater loss of muscle mass and muscle strength in the lower limb with aging may lead to greater motor impairment in the lower limb relative to the upper limb. Therefore, it is necessary to conduct precise and separate examinations of motor control in upper limbs and lower limbs, which will be explored in the subsequent chapters.

HAND FUNCTION

Independence in daily activities heavily relies on hand function (Rantanen, 2003). However, daily activities involving the effective control of the hands and upper limbs, such as handwriting, reaching, grasping, and executing precise movements diminish in quality with age, negatively affecting quality of life (Bennett & Castiello, 1994; Carnahan et al., 1998; Cooke et al., 1989; Goggin & Meeuwsen, 1992; Ketcham et al., 2002).

Manual dexterity

Manual dexterity, essential for effectively performing daily tasks, worsens with age, further affecting living situation (Ostwald et al., 1989; Seidel et al., 2009). Defined by the NIH Toolbox for the Assessment of Neurological and Behavioral Function, it is a key aspect for the motor domain. It involves the hand's ability to manipulate objects through a quick and accurate set of movements, integral for activities such as holding a pen, buttoning a shirt, grooming, and cooking (Gershon et al., 2013). In addition to good motor control, these tasks require the ability to correctly integrate sensory inputs from the various sensory systems to adequately plan and correct the expected movement. The ability to perform manual dexterity is quantified by NIH-approved toolbox tests such as the Roylan 9-hole pegboard test and the 25-hole Lafayette grooved pegboard test. These tests provide sensible measures of dexterity, with the pegboard tests challenging individuals to demonstrate their visuomotor coordination and movement speed (Gershon et al., 2013).

The differentiation between these tests becomes evident in their design and what they measure. The 9-hole pegboard test, for instance, assesses the time required to insert and remove nine cylindrical pegs from a board as efficiently as possible. It is a straightforward measure of dexterity, with average performance times varying significantly with age: 49 ± 13 s for age 3, 19 ± 3 s for ages 18-29, and 24 ± 6 s for ages 70-85 (Kallen et al., 2012). The outcome of this test reveals changes in dexterity across different ages, but its specificity in distinguishing performance between middle-aged and older healthy adults is limited (Yancosek & Howell, 2009).

In contrast, the Lafayette Grooved Pegboard Test (GPT) is a more complex assessment of manual dexterity, as it requires the insertion of 25 key-shaped pegs into randomly oriented matching holes. This test requires greater visuomotor coordination, tactile acuity, and cognitive demand. This design makes the GPT a more sensitive tool for capturing more details of manual dexterity across various age groups (Ashendorf et al., 2009; Bowden & McNulty, 2013; Bryden & Roy, 2005; Wang et al., 2011). For example, Almuklass, Feeney, Mani et al. (2018) explored this test in more details by splitting the GPT time into peg-manipulation cycles contain four phases: 1) selecting a peg from the well, 2) transporting the peg toward the hole, 3) inserting the peg into the hole 4) returning the hand for the next cycle. Based on the regression models from this study, the pegboard times in young and middle-aged adults can be explained by the third and fourth phases, whereas the predictors of older adults were the first and second phases of the peg-manipulation cycle. This phase separation is a key solution to understand the speed and precision portion of the GPT separately.

The hand dexterity not only assesses dexterity but also cognition, attention, and executive functioning (Schwalbe et al., 2023; Tolle et al., 2020). This cognitive component reveals the connection between the motor and cognitive domains, especially in aging populations where cognitive decline may parallel motor skill deterioration (Abe et al., 2017; Heintz Walters et al., 2021; Kobayashi-Cuya et al., 2018). Thus, enhancing manual dexterity can have broader benefits, potentially aiding cognitive function.

Age-related variability in manual dexterity

Performance on these pegboard tests shows the variability of manual dexterity with age. For example, the average completion time for the GPT ranges widely: 59 ± 6 s for young adults, 66 ± 9 s for middle-aged adults, and 89 ± 16 s for older adults (Marmon, Pascoe et al., 2011). Based on another study performed on 305 participants ranging from 3 to 85 years old, the 9-hole pegboard and GPT had their fastest completion time by the age of 30 and then increased steadily with advancing age, particularly after the age of 75 years (Wang et al., 2011). However, the variability in GPT among different age groups remains important. For instance, Wang et al. (2011) reported that the performance of the older group was more variable compared to middle-aged and young adults, with some older adults being more impacted by the aging process than others. The use of various strategies for executing the pegboard trials, along with high variability in motor performance, perception, and cognitive function, could explain the high variability in the older group. Accordingly, some studies found that age alone is not the best feature explaining the variability in the young, middle-aged, and older adults in manual dexterity (Hamilton et al., 2017), postural control (Davis, Allen et al., 2020; Muir et al., 2013), or gait speed (Hortobágyi et al., 2015; Shkuratova et al., 2004). These findings suggest adopting a new method to investigate the inherent variability within this large spectrum by stratifying older adults based on their performance rather than their chronological age, to explore differences within each performance group.

Association between manual dexterity and force steadiness

Manual dexterity tasks require not only coordination of hand muscles but also precise control over the force exerted by these muscles. The variability in the force produced by the muscles involved in the task, reflecting the underlying behavior of motor units and neural control mechanisms, and is closely linked to manual dexterity. When a person tries to maintain an isometric contraction at a submaximal target, the force produced is not perfectly steady, but fluctuates around the targeted force level (Laidlaw et al., 2000; Tracy & Enoka, 2002). The magnitude of fluctuations in the force produced, referred to as force steadiness, is closely linked with manual dexterity (Almuklass et al., 2016; Enoka & Farina, 2021; Marmon, Pascoe et al., 2011).

Neurological diseases or changes in the function of the motor units can impact the variability of the force fluctuations. Among several parameters to measure the variability of force steadiness, the coefficient of variation (CV) for force is one of the popular metrics. It assesses the variation of the force fluctuation normalized to the average force value. Studies have shown that older adults exhibit greater coefficient of variation for force, more so for low force levels, suggesting age-related changes in neural control that impact both force steadiness and manual dexterity (Christou, 2011; Enoka & Farina, 2021; Galganski et al., 1993). Due to the loss of motor neurons or muscle fibers in older adults, the central nervous system is required to recruit more motor units to compensate for the required force (Pascoe et al., 2013). In addition to the decline in discharge rate modulation in this age group, this alteration diminishes the functionality of the muscles in hand and, consequently, impacts the quality of life.

Further confirming the link between force steadiness and manual dexterity, recent studies showed how controlling command signals from the central nervous system influences both force steadiness and manual dexterity. First, the CV for force at lower target forces is significantly correlated with time to complete the GPT (Almuklass et al., 2016; Feeney et al., 2018; Hamilton et al., 2017). In a study by Marmon, Pascoe et al. (2011), 36% of variance in GPT for 75 adults (age 19-89) was explained by maximal grip strength and CV for force during index finger abduction at 5% maximal voluntary contraction. Moreover, there is a direct correlation between CV for force and common input signal to the motor neuron pool (Castronovo et al., 2015; Enoka & Farina, 2021; Farina & Negro, 2015; Negro et al., 2009; Thompson et al., 2018). The ability to perform a precise task such as GPT, requires fine control in the level of hand muscles. This fine control can be examined by the inspection of regularity in the action potentials during a steady force task. The main purpose during the force steadiness task is to increase the force to the target level and maintain it steady rather than matching the target force. This strategy helps the motor cortex to adjust the rate coding in activated motor units rather than recruiting and derecruiting extra new units.

Exploring this adjustment in consistently activated units is the link between fine muscle controls and descending inputs. The regularity of the descending input coming from brain and spinal cord can adjust the regularity in twitch timing and steadiness of the force fluctuation, whereas a high variance in descending input or presence of independent inputs on motor units can generate irregular spike trains and fluctuates the force trace generated by the active motor units. For example, Negro et al. (2009) decomposed the discharge time of over 200 motor units recorded from high density surface grid electrodes in a hand muscle using the Convolution Kernel Compensation (CKC) decomposing algorithm (Holobar & Zazula, 2007). All the discharge times were combined in the form of binary spike trains and filtered with a 400 ms Hanning window to estimate the smoothed cumulative spike train of the motor neuron pool. A principal component analysis could extract the first common component of all motor units and explained 74% of the force fluctuation during a steady isometric contraction with a hand muscle at 10% of maximal force. In a different study, Feeney et al. (2018) found a significant association between low-frequency common drive and force steadiness on a wrist extension task in young ($R^2 = 0.31$) and older ($R^2 = 0.39$) adults. The common finding in these studies is that the variability of force during an isometric steady task is the translation of the variability in the common synaptic input to the motor neuron pool (Del Vecchio, Germer, et al., 2019; Farina et al., 2016; Farina & Negro, 2015; Mazzo et al., 2022). The correlation between force steadiness and variability in neural drive follows the total number of muscles contributed to the task and proportion of the net force each muscle is exerting.

By knowing this link between common synaptic input, force steadiness, and manual dexterity, recent studies have been focusing on increasing the complexity of force steadiness tasks to better replicate real-life hand functions. This can be done by asking participants to do two concurrent force steadiness tasks (Almuklass et al., 2016; Feeney et al., 2018; Hamilton et al., 2019), performing two non-synergistic digit actions (Del Vecchio, Falla, et al., 2019), performing the task after an intense exercise causing damage to the muscle (Dartnall et al., 2009; Turner et al., 2008; Vila-Chã et al., 2012), or when individuals are confronted with a cognitive challenge (Pereira et al., 2015, 2019). As a result of increasing the complexity of the task, the CV for force increases compared to a single-action task. For example, Almuklass et al. (2016) found that the CV for force is greater when steadiness tasks performed with pinch grip, wrist extension and index finger abduction at 5% and 10% of the maximal strength were performed concurrently. Also, using multiple regression analyses, this study found that 70% of the variance in the GPT time for young adults can be explained by two variables: the time to match 10% MVC force during the double-action pinch task and the CV for force during the single-action wrist extension task at 10% MVC force. In general, double-action tasks are better replicates to the manual dexterity, and examining the variance in common synaptic input to these tasks or explaining the performance in manual dexterity with variety of single- or double- action tasks can help us examining the effect of aging on manual dexterity.

BALANCE AND GAIT

Age-related changes in neuromuscular system significantly impact mobility, particularly walking and balance (Maki & McIlroy, 1996). This reduction in balance and walking performance in older adults contributes to the risk of fall and consequently the decline in mobility, quality of life, fatigue, and risk of accidents (Hortobágyi et al., 2015; Rubenstein & Josephson, 2002; Schmid et al., 2007). Among various mobility tests, walking assessments provide valuable insights into an individual's mobility levels and independence (Vestergaard, Nayfield, et al., 2009). The two most common measures of walking tests are speed and distance. These two measures can be combined with wearable sensors, such as Inertial Measurement Units (IMU) or with more complex tasks such as Timed up-to-go (TUG) test to provide more insight about joint kinematics and balance abilities, respectively. Recent advancements in technology have impacted how mobility is assessed in older adults.

Standing balance

One form of motor function in humans is balance. Balance represents a state where the center of mass stays within the limits of the base of support. In humans, upright standing can be modelled as an inverted pendulum rotating around the ankle joint. The intended equilibrium position is a slight forward vertical of the body, generating gravity-driven instability. The central nervous system must maintain the position of body segments in daily activities to avoid instability and falls. Balance requires integrating information from several sensory systems, including the proprioceptive, visual, and vestibular systems (Peterka, 2002), to maintain stability during standing and walking (Forbes et al., 2018; Henry & Baudry, 2019; Sturnieks et al., 2008). The effective integration of sensory inputs contributes to the elaboration of the motor command associated with the maintenance of upright standing (Lephart et al., 1997; Peterka, 2002) and the adjustments to internal and external perturbations (Jacobs & Horak, 2007). However, the physiological changes within the sensory and motor systems lead to a progressive reduction in balance abilities with aging (Henry & Baudry, 2019) and neurological diseases (Soyuer et al., 2006).

Balance is commonly assessed during quiet standing in various conditions, such as different standing surfaces or visual conditions. Based on the NIH Toolbox test of standing balance, these conditions can vary between rigid and soft surfaces and eyes open or closed (Rine et al., 2013). Postural stability during quiet standing can be measured using postural sway, or the fluctuations in the position of the body within the base of support provided by the feet (Winter, 1995). Postural sway is solely related to the necessary mechanics to maintain upright posture over a relatively small base of support (Baudry, 2016). The outcome variables for the postural sway can be obtained while participants are standing on a balance force plate, by measuring the maximal displacement of the center of pressure in coronal and sagittal coordination (Baudry & Duchateau, 2012) or rate of sway area (Davis, Allen, et al., 2020), which is defined as the area enclosed by the center-of-pressure trajectory per unit time (Hufschmidt et al., 1980; Prieto et al., 1996).

Different mechanisms contribute to maintaining standing balance, such as regulating the stiffness in ankle muscles through tonic muscle activity (Kearney & Hunter, 1982) and proprioceptive reflexes (Fitzpatrick et al., 1994). In addition to these mechanisms of action, Davis et al. (Davis, Allen, et al., 2020) found that coefficient of variation for force during submaximal isometric contractions in hip abductors and ankle dorsiflexors are consistent explanatory variables for sway-are rate in healthy young and older adults, suggesting the presence of variability in common descending inputs as an important factor controlling motor function through standing balance.

By looking at the specific age groups, it has been thought that the decline in postural sway and risk of fall follows the chronological age (Abrahamová & Hlavacka, 2008; Hytönen et al., 1993; Johansson et al., 2017; Kang et al., 2013; Pajala et al., 2008; Sturnieks et al., 2008), but it is important to note that similar to motor function in upper limbs, the variability in motor function performance in lower limb increases by aging. Accordingly, some studies found that age alone could not distinguish young and older adults' postural control (Davis, Allen, et al., 2020; Muir et al., 2013) or gait speed (Hortobágyi et al., 2015; Shkuratova et al., 2004). Thus, standing balance performance can be quite different among older adults. For example, Qiu and Xiong (2015), examined test-retest reliability of 18 postural sway measures in young and older adults and found no significant risk of fall predictor among any of these tests. In another study by Davis, Allen, et al. (2020), both young and old participants could be stratified into low- or high-sway groups, which is in contrast with the casual thought of direct association between age and decline in standing balance. Consistent with manual dexterity, this stratification on standing balance suggests a novel evaluation method on older adults based on their performance rather than their chronological age.

In general, motor function closely ties to neurological health, with both central and peripheral nervous systems playing important roles. Neurodegenerative diseases such as Parkinson's and Alzheimer's disease as well as the factor of aging, directly affect motor skills by diminishing the neural pathways involved in motor control. Understanding these connections is crucial for developing targeted interventions that address not only the physical but also the neurological aspects of motor decline.

Walking and gait control

Walking is not just a basic means of mobility but a complex activity that demands coordination and co-contraction of muscles across both legs. The performance in walking tests, which can be measured through endurance or fast walking tasks, reflects functional mobility of a person (Baert et al., 2014; Goldman et al., 2008; Hyngstrom et al., 2014; Perera et al., 2014). For instance, in a study by Vestergaard, Patel, et al. (2009), 948 older men and women performed a 400-m endurance walking test. The authors ran multiple regression analysis to explain the rate of mortality using physical performance in older adults by including time to complete the test, coefficient of variation of the 20-m lap time, the need to rest during the test, and the ability to complete the walk as well as the mortality over the next 6 years as the outcome variables. In age- and sex- adjusted analyses, after accounting mental health, social status, physical activity level, and lower extremity of performance of the participants, both time to complete the 400-m walk and lap time coefficient of variation were among the significant predictors of mortality. Other forms of endurance walking such as 2-, 6-, and 12-min walk tests, assess how far participants can walk in the specified amount of time (Goldman et al., 2008; Motl et al., 2013; Sandroff et al., 2013, 2015). Butland et al. (1982) suggested that the duration of the walking endurance test was not critical to adequately evaluate a person's mobility. However, recent use of time-series analysis to investigate the parameters of walking abilities require a significant amount of data. Thus, a moderate time, such as six minutes, would be a good balance to perform walking endurance without exhausting participants.

Although, basic time and distance measurement in walking tests can reveal general informative insights of human, the variability and characteristics of walking patterns are more detailed into human walking analysis but require more biomechanical assessments. Walking patterns can be defined by strides and each stride consists of stance and swing phases. Each stride starts from an event on one leg to its next subsequent occurrence in the same leg. Looking at only one leg, the stance event starts with the heel strike, when the heel of one foot touches the ground, and ends with the toe-off, when the foot leaves the ground. Following the stance phase, the swing event, comes after the toe-off moment, by an increase in hip flexion and ends right before the heel strike. By looking at both feet in the walking pattern, there is a time when the stance phase of each leg overlaps and both feet are concurrently on the ground. This phase is called double-support, and its' duration reduces by increasing the walking speed.

Walking speed is an important factor associated with activities of daily living, cognitive function, and mortality (Potter et al., 1995; Rosano et al., 2008; Shinkai et al., 2000; White et al., 2013). Older adults experience slower walking speeds with higher variability compared to younger adults (Vestergaard, Patel, et al., 2009). Although both the maximal and preferred walking speed start to decline with advancing age, the maximal walking speed begins to decline earlier than the preferred walking speed (Bohannon & Williams Andrews, 2011; Himann et al., 1988; Oberg et al., 1993). In two studies (Elble et al., 1991; Winter et al., 1990), walking abilities of older adults were characterized by their kinematics, with reduction in gait velocities, stride length, arm-swing angle, and rotation of hip and knees compared to young adults. Part of these adaptations occur to limit the decline in walking speed. For example, the decrease in stride length in older adults is compensated by an increase in cadence or step frequency. Also, double-support time is increased to maintain the walking balance due to high balance confidence in this age group. A different view of these changes in walking pattern reveals the alteration in muscle activation in older adults. The distribution of muscle activation shifts with age, as most of the muscle activation is transferred from the distal lower limb to the more proximal hip and knee muscles. This shift provides many of the joint powers at hip and knee joints rather than ankle joints and alters the balance strategies to proximal muscles or "hip strategy" than distal muscles or "ankle strategy" (Cofré et al., 2011; DeVita & Hortobagyi, 2000; Franz, 2016; Judge et al., 1996; Kerrigan et al., 1998; Nashner & McCollum, 1985; Savelberg et al., 2007; Silder et al., 2008).

Wearable sensors and advanced gait analysis systems now allow for real-time, high-precision monitoring of walking patterns, providing insights into the subtle changes that might not be evident in traditional tests. These technologies can detect early signs of mobility decline, allowing for timely interventions that can drastically improve the quality of life. The integration of wearable sensors with machine learning can transform gait analysis into more precise pattern recognition. These techniques can detect subtle gait abnormalities that precede obvious motor dysfunction symptoms, such as those associated with multiple sclerosis or other neurological diseases. By analyzing data from accelerometers and gyroscopes, machine learning models predict fall risks and monitor gait changes over time, facilitating earlier and personalized interventions. This integration between wearable sensors and machine learning not only enhances the accuracy of gait assessments but also selects rehabilitation strategies for individual needs, improving outcomes in the aging population.

TREATMENT AND INTERVENTION

Not all age-related declines in motor performance are permanent. As individuals age, the integration of sensory feedback into motor control becomes less efficient. This inefficiency can lead to an increased risk of falls and a general decline in motor coordination. Sensory inputs from visual, auditory, and proprioceptive systems are essential for the precise execution of movements. With aging, sensory degradation, such as in vision and proprioception, directly impacts motor output, leading to compensatory strategies that may not always be effective. Although some changes relative to the structure of muscles or neurons, such as muscle fiber or motor unit loss are inevitable, lifestyle and daily activities can delay their onset. Interventions that improve the processing of sensory feedback, such as proprioceptive neuromuscular facilitation through electrical stimulation, as well as motor training, are essential in maintaining motor function in older adults.

Physical practice

Several studies have suggested that changes in neural strategies (Feeney et al., 2018), increased endpoint variability (Christou & Enoka, 2011), and decreased force steadiness (Marmon, Pascoe, et al., 2011) all contribute to the decrease in manual dexterity with age. In a study by Marmon, Gould, et al. (2011), six practice sessions (5 blocks of 5 GPT trials on each session) decreased the pegboard time in older adults (75 ± 4 yr) from initial value of 93 ± 12 s to 67 ± 5 s. This improvement in the GPT performance was accompanied by a reduction in CV for force (~30%) during index finger abduction. Similarly, Kobayashi et al. (2014) found that training steady movements for eight weeks (3 times per week) with light loads (30% of maximum) increased MVC force for the knee extensors and decrease CV for force at 10%, 30%, and 65% MVC for the knee extensors and elbow flexors. It is important to note that these muscle groups were not targeted in the prescribed exercises, but they helped increase the time of maintaining standing balance on one leg. As mentioned before, reduction in low-oscillation variability of neural drive can be a potential reason for all these improvements in force steadiness and consequently balance and manual dexterity.

The age-related decline in balance performance can also be reduced with exercise (Gillespie et al., 2012). Sarcopenia, or muscle loss, can cause a decline in power, strength, and endurance, resulting in a decrease in the level of physical activity and increase in the level of disability in older adults. The loss of muscle fiber can be due to biological aging and chronic low levels of physical activity. Several studies have found that muscle hypertrophy due to resistance or strength training can regain part of the strength and former functionality of the aged muscle (Keen et al., 1994a; Kobayashi et al., 2014; Laidlaw et al., 1999; Pyka et al., 1994; Singh et al., 1999). For example, Pyka et al. (1994) did a resistance training study on eight older adults (61-78 yr) and found that a 15-week knee extensor resistance training program (3 days / week) on knee extensors can increase the size of fiber types I and II by 48 and 62%, respectively, as well as 61% increase in knee extension maximal strength. In addition to motor functions, other domains of the NIH toolbox can be improved by strength training in older adults. For example, Özkaya et al. (2005) conducted a study on 36 older adults (60 – 85 yr) that received one of the three interventions: control, strength training, or endurance training. They found that nine weeks of strength training improved various motor function tasks (i.e. chair stand, 6-min walking test, TUG), and facilitated early sensory processing and cognitive functioning in older adults. Most of the age-related practice studies focused on the chronological age. However, evidence suggests that the effect of aging on motor function the analysis of practice effects should be examined more through performance-based stratifications rather than chronological age. In the motor function of upper limbs, for example, Hamilton et al. (2019) performed a k-medoid stratification on GPT times in middle-age (48 ± 6 yr) and older adults (73 ± 4 yr) and found two groups of fast (53 ± 5 s) and slow (77 ± 7 s) which each contained participants from both age groups. Interestingly, the GPT in each group could be explained by different variables. The GPT in fast group was correlated with force steadiness during wrist extension at 10% MVC and two measures of motor variability, whereas the GPT in slow group was correlated with two different measures of motor variability and a decision-making metric, but not force steadiness. Looking at the lower body motor function, Alenazy, Al-Jaafari, Folkesson-Dey, et al. (2023), did a similar stratification method on 6-min walking test on older adults (72 ± 5 yr) and found high discriminatory logistic regressions models on force-plate and kinematic data obtained during the balance tasks between slow and fast walkers. The importance of performance stratification rather than chronological stratification urges the future implications on motor function and practice to be examined with this new perspective.

Electrical stimulation

Electrical stimulation, which is commonly used in clinical settings for rehabilitation, has been used since the 18th century. Electrical stimulation is a non-invasive technique that involves applying currents between two electrodes placed on the skin above the muscles or nerves (Miller et al., 2017; Schuhfried et al., 2012). The parameters of the stimulus (frequency, intensity, pulse width, and pulse shape) can evoke action potentials in peripheral nerve or intramuscular axons. This form of treatment in healthy adults can be used to restore muscle mass after immobilization to improve function of healthy muscles (Maffiuletti, 2010). Three main forms of electrical stimulations are functional electrical stimulation (FES), neuromuscular electrical stimulation (NMES), and transcutaneous electrical nerve stimulation (TENS), which vary in terms of their stimuli parameters, such as pulse duration, frequency, and phase shape (Collins, 2007; Maffiuletti, 2010; Osiri et al., 2000; Vanderthommen & Duchateau, 2007).

FES uses electrical pulses to elicit functional contractions in muscles. This intervention assists the subject to perform a missed action or correct an on-going action. For example, FES can be used to correct the footdrop by evoking muscular contractions that dorsiflex the ankle of the subject during the swing phase of walking test (Hausmann et al., 2015). It is also shown that the FES engages sensory axons that are spread throughout the entire nervous system, with FES-related adaptations of the nervous system that improve motor function even in the absence of stimulation (Prochazka, 2018; Shin et al., 2008).

Unlike FES, NMES does not generate functional movements in limbs. This form of stimulation is used for rehabilitative or training purposes to recover muscle mass and function by eliciting action potentials in terminal motor axons (Maffiuletti, 2010). Time-series rehabilitation sessions of NMES can improve motor function in older adults and people with neurological diseases (Duchateau & Hainaut, 1988; Gondin et al., 2011; Truong et al., 2017). For example, Almuklass, Davis, Hamilton, Hebert, et al., (2018) found that 6 weeks of NMES applied to the dorsiflexors and plantar flexors of people with MS improves gait speed (time to walk 25 ft), walking endurance (6-min walking test), and self-reported measures of fatigue, time to complete the GPT, and walking disability with washout period of 4 weeks after the intervention. Similarly, Mani, Almuklass, Amiridis, et al. (2018) found a decrease in time and increase in distance in 400-m walking test in thirty healthy old adults (74 ± 5 yr) after 3 weeks of treatment with

NMES. In another approach, Banerjee et al. (2005), tested the performance of NMES in multi-muscles along with 30 session of training exercises in six weeks (five session per week) and found an increase in peak oxygen consumption during a treadmill test, 6-min walking distance, and strength of the quadriceps muscles in sedentary adults (48 ± 12 yr).

Transcutaneous electrical nerve stimulation (TENS) is another electrostimulation tool that has been used in rehabilitation settings. TENS formerly has been used as a pain relief intervention (Neto et al., 2017; Osiri et al., 2000; Resende et al., 2018), but recent studies have shown changes in sensory improvement and motor function tests under the influence of TENS. TENS can be used to augment sensory feedback during the performance of an action or as a treatment to modify neural pathways engaged during a task (Cuypers et al., 2010). For example, previous studies found that applying TENS during the 6-minute walking test in a group of control healthy middle-aged adults increases walking distance in the 6-minutes walking test (Almuklass et al., 2020; Carzoli et al., 2022). Similarly, applying TENS during performance of gait speed, walking endurance, and dynamic balance in MS patients with mild to moderate levels of disability improves their performance. It is important to note that the intensity of TENS in this test were set just above the motor threshold and was applied continuously during each test.

Although the aid of TENS on demyelinated sensory neurons in patients with MS is clearer, this mechanism in healthy adults requires more systemic studies. Presumably enhancing the activation of motor neurons during voluntary contractions can facilitate sensory feedback and integration throughout the nervous system (Mang et al., 2011, 2012; Trimble & Enoka, 1991). Along with understanding the mechanism of TENS through more systemic studies on different muscles, manipulation of parameters of TENS revealed more insightful information regarding muscle activation and motor function. Some studies found that the continuous application of

TENS during an action has beneficial outcomes (Bisio et al., 2015; Shimodozono et al., 2014; Walker et al., 2014), whereas some other studies found this benefit at low frequency burst of pulses mode in TENS (Dickstein & Kafri, 2008; Veldman et al., 2018; Wu et al., 2006). In a recent study, Carzoli et al. (2022), found that applying fast bursts of TENS pulses during the 6-minute walking test increases the walking distance in middle-aged adults compared to the continuous form of TENS or the control intervention (when the electrodes are placed over the muscle but off). The idea of desensitization of sensory neurons to continuous impulses could address the effectiveness of burst TENS over continuous TENS, but other factors such as age and location of TENS electrodes can impact results in a different way. For example, applying synchronous application of TENS over two nerves of median and ulnar has shown to have more effectiveness than similar application but only in one nerve (Celnik et al., 2007).

SUMMARY AND OBJECTIVES

Motor function declines with aging. The NIH toolbox for Neurological and Behavioral function comprises tests which can be used to assess motor function domain across the lifespan. Three of these tests, dexterity, endurance, and balance are points of interest in this review. Dexterity in the form of manual dexterity is closely associated to the quality of life and rate of mortality and can be measured by the Lafayette Grooved Pegboard Test (GPT). The significant correlations between performance of this test, ability of the hand muscles to sustain a force at submaximal isometric threshold and neural drive controlling the target muscles suggest more detailed exploration by including the factor of manual dexterity based on performance rather than age to explore these neuromuscular correlations before and after practice in older adults. Therefore, the first two studies of this dissertation will focus on evaluating the effect of the practice on performance of manual dexterity, specifically by stratifying older adults based on their performance.

Two other categories in the motor domain, balance and endurance can also provide a better quality of life and decrease mortality during the lifespan. Several studies presented the application of electrical stimulation as a rehabilitation tool to improve the performance of these categories in the form of standing balance and six-minute walking test, respectively. Among the electrical stimulation applications, transcutaneous electrical nerve stimulation (TENS) has a proven improvement on patients with neurological diseases. However, it requires more investigation on healthy adults. The second part of this review will emphasize on the treatment of TENS during walking and standing balance on older adults and analytic applications on assessing biomechanical features in these tests for better understanding the application of TENS in older adults.

Chapter II

Practice-Induced Changes in Manual Dexterity of Older Adults Depend on Initial Pegboard Time

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ABSTRACT

Purpose: The purpose of our study was to determine the influence of practice on the pegboard times and peg-manipulation phases of older adults who were classified as having either slow or fast initial pegboard times. ***Methods***: Participants (n = 26, 70 ± 6.6 years) completed two evaluation sessions and six practice sessions in which they performed 25 trials (5 blocks of 5 trials) of the grooved pegboard test. All practice sessions were supervised and the time to complete each trial was recorded. In each evaluation session, the pegboard was mounted on a force transducer so that the downward force applied to the board could be measured. ***Results***: Participants were stratified into two groups based on the initial time to complete the grooved pegboard test: a fast group (68.1 ± 6.0 s) and a slow group (89.6 ± 9.2 s). Both groups exhibited the classic two-phase profile (acquisition + consolidation) for learning a de novo motor skill. Despite the similar learning profile for the two groups, there were differences between groups in the phases of the peg-manipulation cycle that became faster with practice. The fast group appeared to reduce trajectory variability when transporting the peg, whereas the slow group seemed to exhibit both a decrease in trajectory variability and greater precision when inserting pegs into the holes. ***Conclusion***: The changes underlying practice-induced decreases in grooved pegboard time differed for older adults who initially had either a fast or a slow pegboard time.

INTRODUCTION

Manual dexterity refers to an individual's ability to coordinate the fingers and manipulate objects in a timely manner. It has been identified as one the NIH Toolbox biomarkers of neurological health and motor function across the lifespan (Gershon et al., 2013; Reuben et al., 2013). The NIH Toolbox instrument to assess manual dexterity is a pegboard test, either the Lafayette Grooved Pegboard Test or the Rolyan 9-hole Peg Test (Wang et al., 2011). Manual dexterity is required for numerous activities of daily living and becomes compromised with advancing age (Carey et al., 2002, 2008; Ostwald et al., 1989; Seidel et al., 2009).

Fundamentally, the time it takes to complete a pegboard test as quickly as possible depends on the speed and accuracy with which each of the pegs can be manipulated (Almuklass, Feeney, et al., 2018). In young adults (n = 30), for example, 70% of the variance in the time to complete the grooved pegboard test was explained by two factors: 1. the speed at which a submaximal target force (10% of maximum) could be matched during an isometric contraction with a hand muscle (pinch grip); and 2. the magnitude of the force fluctuations during a steady submaximal contraction (force steadiness) with the wrist extensor muscles (Almuklass et al., 2016). The regression model indicated that young adults with faster pegboard times matched the target force more quickly but were less accurate during the steady contraction; that is, they maximized speed at the expense of accuracy.

Furthermore, in a group of older adults (n = 25), 59% of the variance in the time to complete the grooved pegboard test was explained by age, force steadiness during a submaximal isometric contraction with a hand muscle, and pinch-grip strength (Marmon, Pascoe, et al., 2011). However, previous studies have shown that motor performance measures increase in variability among subjects as age increases (Bohannon et al., 2014; Davis, Alenazy, et al., 2020; Narici et al., 1991; Suetta et al., 2019a; Wang et al., 2011). Indeed, Hamilton et al. found the grooved pegboard times for adults (40-79 yrs) could be clustered with a k-medoid analysis into two groups (faster and slower) that were independent of chronological age (Hamilton et al., 2019). Each group included both middle-aged (40-59 yrs) and older (65-79 yrs) adults. Although the specific explanatory variables differed for the two groups of participants, they comprised measures of movement variability (accuracy) with greater variability being associated with longer pegboard times.

The consistent finding that measures of accuracy, such as force steadiness, can explain significant amounts of variance in the pegboard times of older adults has been validated with the improvements observed after practicing the pegboard test. For example, Marmon et al. examined the association between changes in grooved pegboard times and force steadiness after older adults completed six practice sessions in which the pegboard test was performed 25 times (Marmon, Gould, et al., 2011). Pegboard times decreased significantly across the first five practice sessions and was significantly correlated with improvements in force steadiness during both index finger abduction and an index finger-thumb pinch grip. Similarly, Kornatz et al. found that a 6-week training program performed by older adults reduced movement variability and improved performance on the Purdue pegboard test (Kornatz et al., 2005). The training program involved lifting and lowering submaximal loads with the index finger during which movement variability was quantified as the standard deviation of acceleration. The improvement in the pegboard score was strongly correlated ($r^2 = 0.56$) with the reduction in the standard deviation of acceleration.

The aim of our study was to determine the influence of practice on the pegboard times and peg-manipulation phases of older adults who were classified as having either slow or fast initial pegboard times. We hypothesized that the reduction in grooved pegboard times would not be associated with chronological age and that the rate of improvement would be greater for participants with slower pegboard times.

METHODS

Participants

Twenty-eight healthy, right-handed individuals (71 ± 8 years, mean ± standard deviation), as determined by the Edinburgh Handedness Inventory (Oldfield, 1971), participated in our study. All participants were free of neurological disease and were not taking any medications known to influence neuromuscular function. After removal of outliers, data from 26 participants (70 ± 6.6 years, range: 60 - 83 years) were included in the final analysis. All participants were given a verbal and written description of study protocols and provided written informed consent prior to participating. The protocols were approved by the Institutional Review Board at the University of Colorado Boulder.

Grooved Pegboard Test

The grooved pegboard test required participants to use their right hands to place keyhole-shaped metal pegs into 25 holes on a board as quickly as possible. The holes were arranged in a 5×5 matrix and the keyholes had different orientations across the board. Participants first practiced the task by inserting pegs into the first row of holes. Subsequently, participants were verbally cued to perform the test and the time taken to insert all 25 pegs was recorded.

Testing Procedures

The study comprised a familiarization session and an evaluation session performed before and after six practice sessions. The practice sessions and final evaluation session were completed with a maximum of three days between consecutive sessions. The primary outcome variables were time to complete the grooved pegboard test in all sessions, time to complete each phase of the grooved pegboard test, and standard deviation of the pegboard time. Each evaluation session involved one grooved pegboard test during which the downward force applied to the pegboard was measured with a force transducer (Model SBO-200-311062; TT, Temecula, CA) attached beneath it.

The force was sampled at 100 Hz with an analog-to-digital converter (Power 1401, Cambridge Electronic Design, Cambridge, UK) and low-pass filtered at 12 Hz (second-order bidirectional Butterworth filter, cutoff 12 Hz). The force signal was used to identify the timings of the 4 peg-manipulation phases: selection, transport, insertion, and return (Almuklass et al., 2017). Force signals and phase times were obtained with Spike2 data acquisition software (version 9.08).

Each of the 6 practice sessions comprised 5 blocks of 5 trials of the grooved pegboard test. Each block was separated by 2-5 minutes of rest, and the time between trials in each block were separated by 30-60 s. Time to complete the pegboard test was recorded for all 150 practice trials performed by each participant.

Data Analysis

Pegboard time corresponded to the duration from the moment the participant lifted their right hand off the table to begin the test until the insertion of the last peg. The times for the four phases of the peg-manipulation cycle were determined from synchronized event makers that indicated the beginning of the retrieval of a peg from the well. We used the first derivative of the force signal to identify the starting point of each phase by analyzing the regular pattern of each peg cycle (Almuklass et al., 2017). Phase calculations were derived from the average of pegs 1-3 at the start of the test and pegs 22-24 at the end of the test. Peg 25 was excluded, as there was no event marker for the end of phase four (return phase).

To assess the variability in pegboard times, the standard deviation was calculated for each practice session. A Gaussian filter with $\sigma = 3$ was used to smooth the performance trace of the 150 practice trials of pegboard times for each participant. To examine the trend of the changes in pegboard time across all trials, two linear functions were fitted to the smoothed pegboard times. Bilinear cutoff points from trial 3 to 149 were examined, and the resulting lines with the lowest average root mean square deviations were selected.

To emphasize differences between subjects at both ends of the performance spectrum, subjects were stratified into two groups based on the initial grooved pegboard time (Figure 1). Two different cluster analysis methods (k-medoid, hierarchical) were used to stratify participants (Avrillon et al., 2023; Hamilton et al., 2019) with similar groupings and statistical significance for all variables. All data presented are from the k-medoid clustering method. Unpaired t-tests were performed to identify changes between groups, Pearson correlation coefficients were calculated to examine the predictive power of age and time to complete the first pegboard on all other performance metrics, and repeated measure ANOVAs and pairwise t-tests were used to examine changes across multiple or two sessions, respectively. The level of significancy (α) in all tests was set to 0.05. All statistical analysis was performed using Python (version 3.9.13) and R (version 4.2.3).

RESULTS

We obtained results from 26 participants after eliminating two outliers due to their extremely long pegboard times (158 s and 138 s). The participants were stratified into slow (14 participants, 89.6 ± 9.2 s mean ± standard deviation) and fast (12 participants, 68.1 ± 6.0 s) groups (Figure 1).

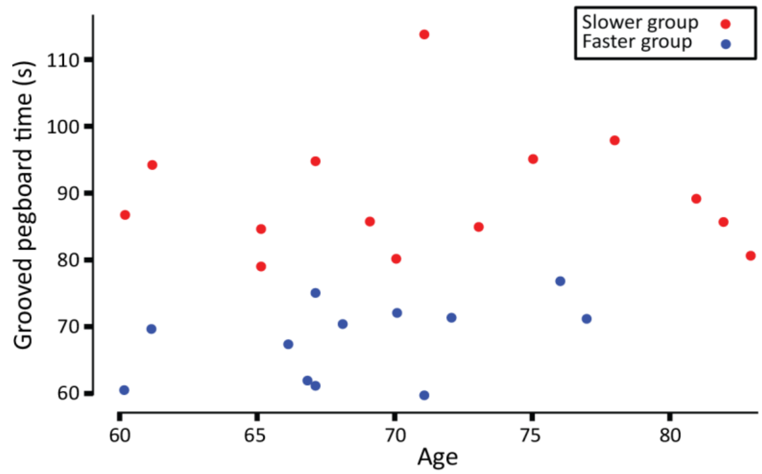

Figure 1. Time to complete the grooved pegboard test (s) during the first evaluation session. Each data point shows the pegboard time for one participant, who ranged in age from 60 to 83 yrs. K-medoid cluster analysis identified two groups of individuals: the times for one group were faster (blue) than those for the other group (red).

Participants completed six pegboard practice sessions (25 trials in each session), and the average pegboard time in the last evaluation session was significantly less than that in the first evaluation session for all participants (p-value < 0.0005) (Figure 2A and 2B). We also observed a significantly greater decrease in pegboard time for the slow group than the fast group (p-value < 0.0005) (Figure 2C).

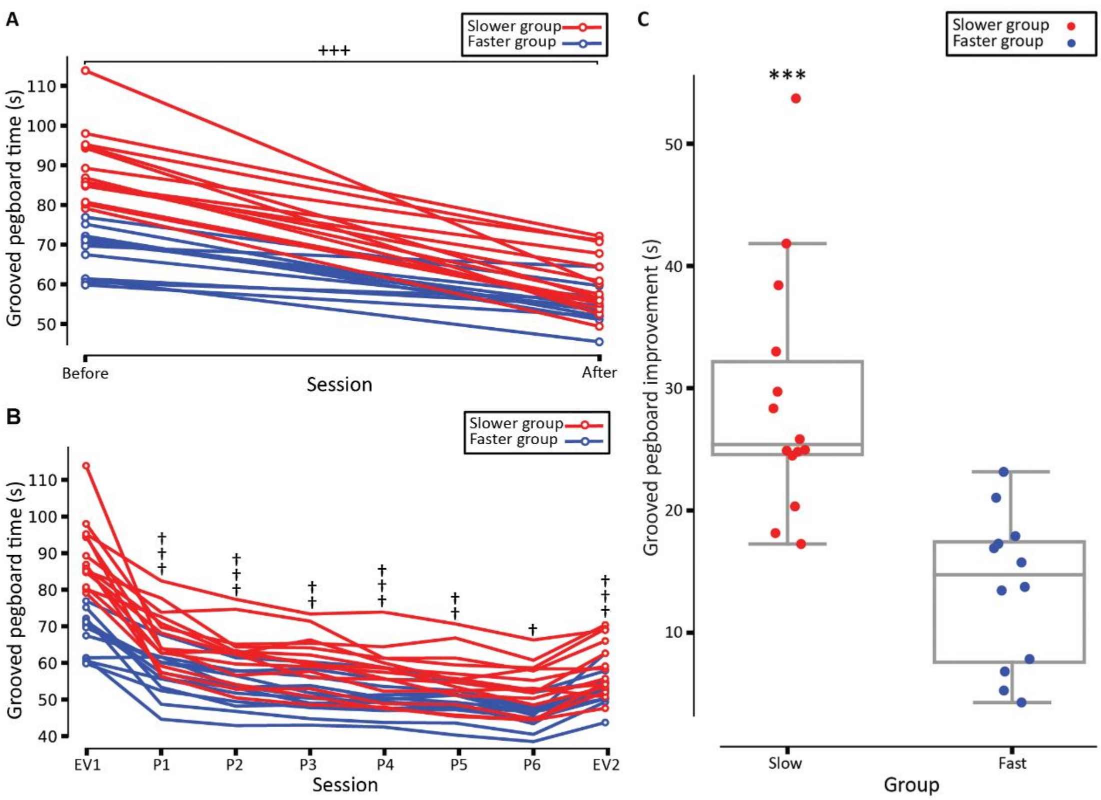

Figure 2. Changes in the grooved pegboard time from the first to the second evaluation session (A) and across the six practice sessions (B) for the fast (blue) and slow (red) groups. Each line indicates the data for one participant. (A) shows that there was a significant decrease in pegboard time from before to after (+++, $p < 0.0005$). (B) shows the average time to complete the pegboard test for each practice session (P1 to P6), as well as the single pegboard times for evaluation (EV) sessions 1 and 2. Each session showed significant difference as compared to the previous session (†, $p < 0.05$; ††, $p < 0.005$; †††, $p < 0.0005$), and each practice session average was significantly lower than EV1 ($p < 0.05$). The percent decline in pegboard time from the first to the second evaluation session is shown in (C) for the participants in each group, with the slow group improving more than the fast group (***, $p < 0.0005$). Each box represents the first quartile, median, and last quartile of each group along with two bars showing minimal and maximal times.

To test our hypothesis that performance on the first pegboard would be a better predictor of improvement than age, we performed correlation analyses for each variable and found that the first pegboard time was significantly correlated with the decrease in pegboard time ($r = 0.85$, p-value < 0.0005) (Figure 3A), whereas age was not ($r = 0.04$, p-value $= 0.84$) (Figure 3B). Additional correlation analyses found multiple moderate-to-strong ($r > 0.4$, $p < 0.05$) results

(Figure 3C) between pegboard-related metrics and the decrease in pegboard time. Age did not outperform the first pegboard time for any single metric.

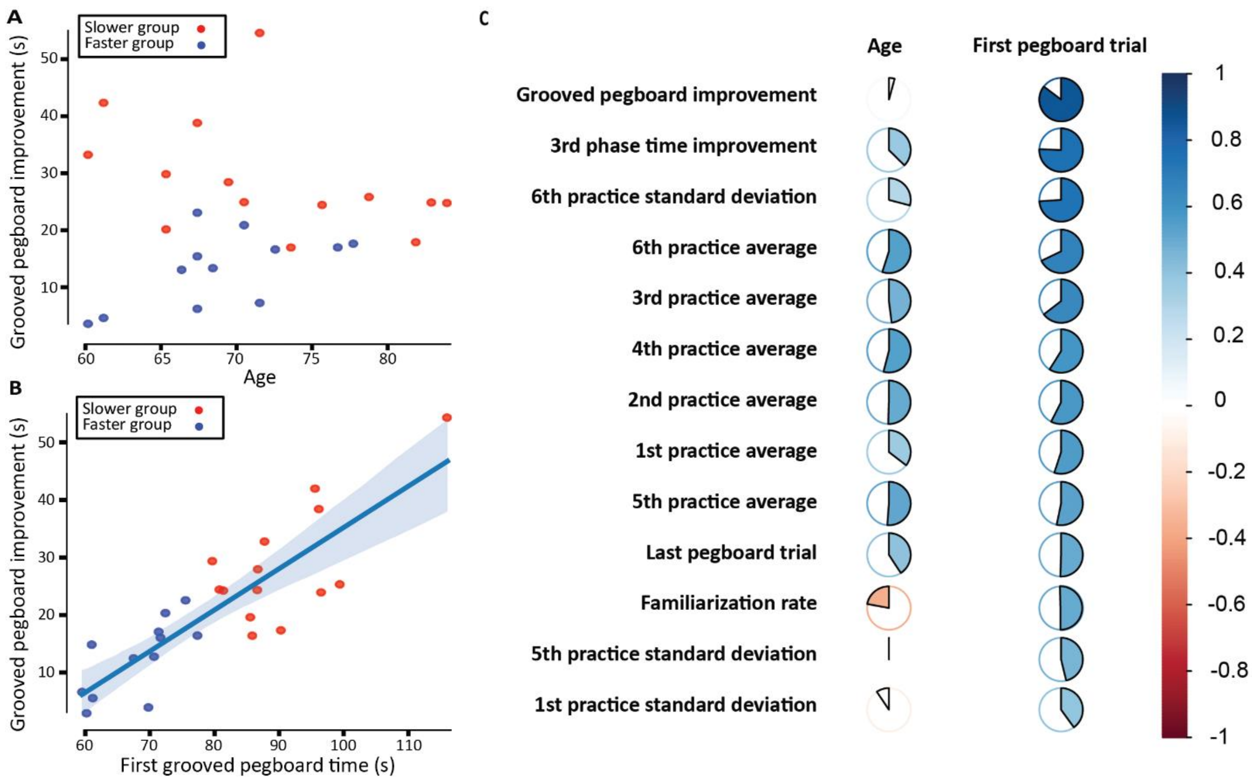

Figure 3. Correlation of the grooved pegboard time. The decrease in time to complete the grooved pegboard from the first to the second evaluation session was not related to chronological age (A) but was strongly correlated with pegboard time during the first evaluation session (B; $p < 0.00005$). Each data point indicates the pegboard time for one participant. All statistically significant correlations (range: 1 to –1) with age and first pegboard trial are shown in (C; $r > 0.4$, $p < 0.05$). The blue-filled area in each circle indicates the strength of the correlation with a filled circle denoting a correlation of 1.0.

Both groups of participants exhibited a large initial decrease in pegboard time (task acquisition) followed by a gradual improvement across subsequent trials (consolidation). After fitting bilinear functions for each subject, we eliminated one outlier due to the extremely high cutoff trial (trial 77). Looking at the pegboard times for each subject, there was no significant difference (p-value = 0.83) in the cutoff trial that distinguished the acquisition and consolidation phases for the slow (12.3 ± 8.7 trials) and fast (11.7 ± 6.5 trials) groups (Figure 4). However, there were significant differences between the slopes during the acquisition phase (Slow group = -1.43 ± 0.88 s/trial, Fast group = -0.77 ± 0.42 s/trial; $p = 0.027$) and the consolidation phase (Slow group = -0.07 ± 0.03 s/trial, Fast group = -0.05 ± 0.2 s/trial; $p = 0.043$) within each group. These slopes indicate that both groups show two different rates of improvement in the pegboard. (Figure 4).

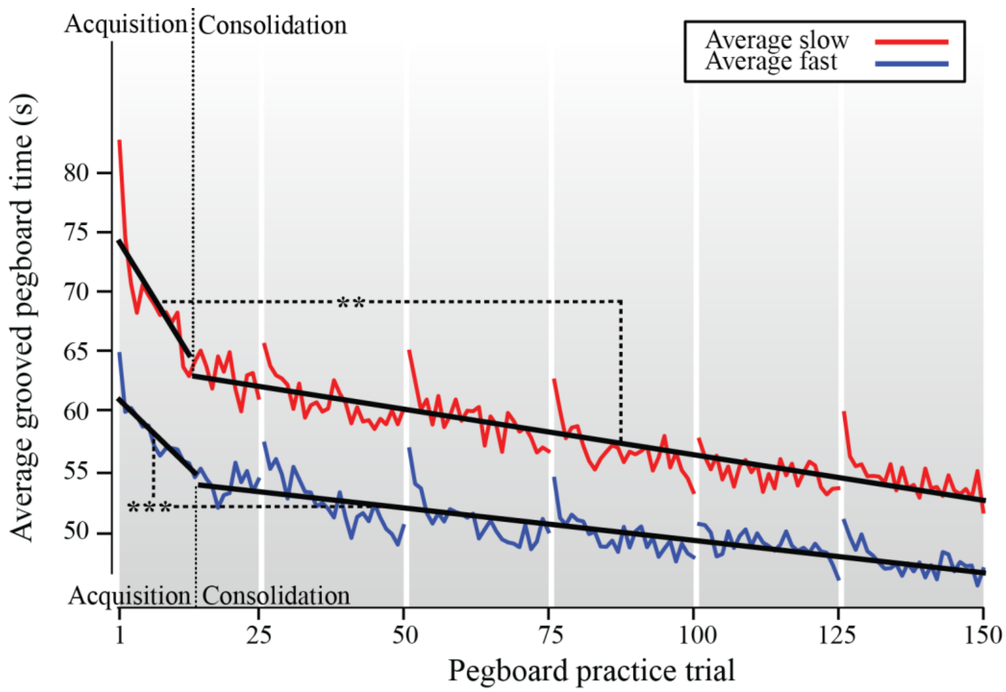

Figure 4. Practice-induced change rate in grooved pegboard time. The decrease in average time (s) to complete the grooved pegboard test across all sessions (152 trials per person) for the slow (red) and fast (blue) groups of participants. Gaussian-smoothed times ($\sigma = 3$) for each group were fitted with bilinear functions (black), and the two phases were interpreted as changes attributable to task acquisition and consolidation of the task. The rates of change in the pegboard times during the acquisition and consolidation phases were significantly ($p < 0.05$) greater for the slow group.

The variability in pegboard times across the practice sessions (5 trials x 5 blocks) was calculated as the standard deviation of the 25 trials performed in each session. Statistical analysis of the data for all participants indicated a significant decrease ($p < 0.005$) in the average standard deviation in the second (3.78 ± 1.11 s) and sixth (3.31 ± 0.99 s) practice session relative to the first one (5.56 ± 1.87 s). Also, there were between-group differences between the first (fast: 4.61 ± 0.62 s; slow, 6.37 ± 2.2 s, p = 0.013), fifth (fast: 3.39 ± 0.71 s; slow, 2.67 ± 0.57 s, p = 0.009), and sixth (fast: 2.75 ± 0.6 s; slow, 3.80 ± 1.01 s, p = 0.004) (Figure 5).

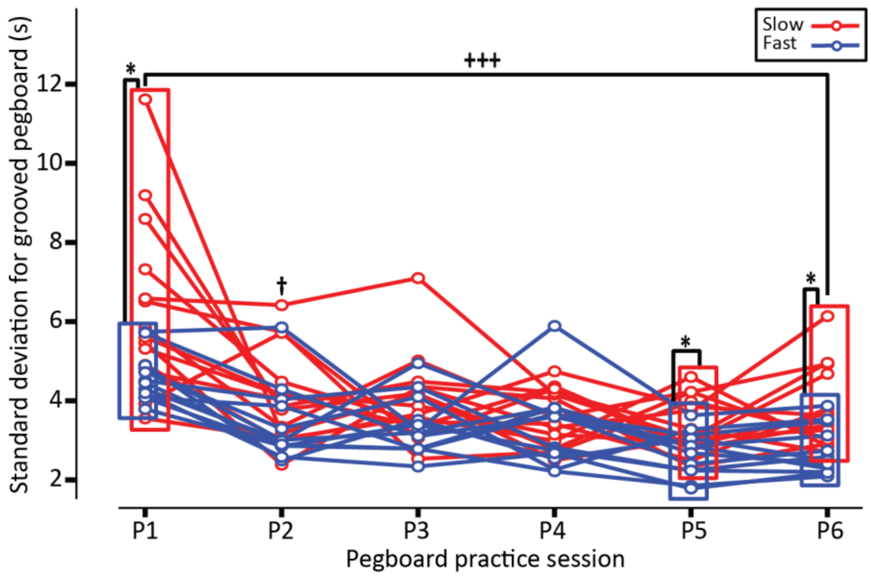

Figure 5. Variability in the grooved pegboard time. Average standard deviation for the pegboard times within each of the six practice sessions. Each data point represents the standard deviation for the times of all 25 trials performed in each practice (P) session. Significance markers have the following representations: *, p < 0.05 between groups; +++, p < 0.0005 all subjects; †, p < 0.05 all subjects.

When participants were considered as a single group, there was a significant decrease in time for the last three of the four peg-manipulation phases from Before (phase 2 = 0.65 ± 0.27 s, phase 3 = 1.30 ± 0.34 s, phase 4 = 0.28 ± 0.14 s) to After the six practice sessions (phase 2 = 0.44 ± 0.16 s, p-value = 0.0003; phase 3 = 1.05 ± 0.16 s, p-value = 0.0007; phase 4 = 0.18 ± 0.09 s, p-value = 0.002) (Figure 6A). When the groups were considered separately, there was a significant difference only in phase 2 from Before (0.62 ± 0.22 s) to After the six practice sessions (0.44 ± 0.16 s; p-value = 0.005) for the fast group (Figure 6B). In contrast, the slow group exhibited significant differences for three phases from Before (phase 2 = 0.68 ± 0.31 s, phase 3 = 1.51 ±

0.32 s, phase 4 = 0.33 ± 0.17 s) to After the six practice sessions (phase 2 = 0.45 ± 0.16 s, p-value = 0.01; phase 3 = 1.08 ± 0.15 s, p-value = 0.0002; phase 4 = 0.19 ± 0.09 s, p-value = 0.009) (Figure 6C).

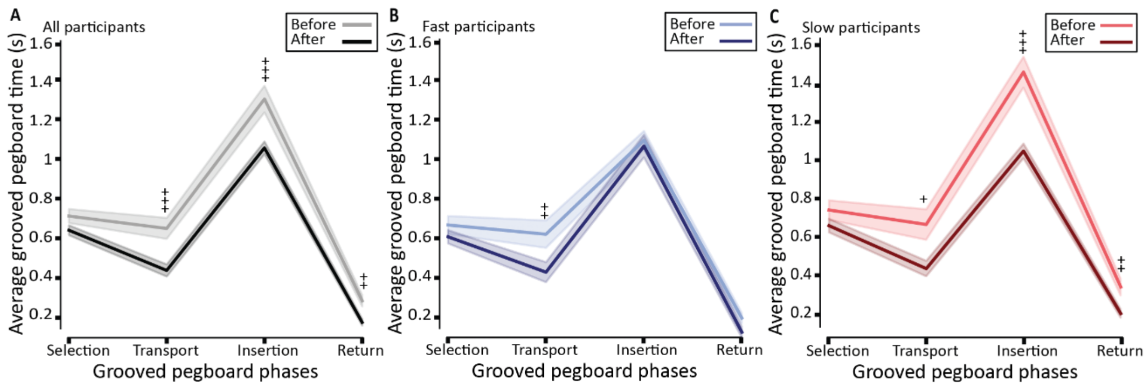

Figure 6. Peg-manipulation phase times. Time to complete the four phases of each peg-manipulation cycle averaged across all participants (A), fast group (B), and slow group (C). The values indicate the mean ± SE for time (s) to complete each of the four phases in the first evaluation session (Before practice, lighter color) and in the second evaluation session (After practice, darker color). The four phases are based on those defined by Almuklass et al. (2017). *, $p < 0.05$; **, $p < 0.005$; ***, $p < 0.0005$).

DISCUSSION

The main finding of our study was that the initial pegboard time of older adults has greater explanatory power than chronological age to predict metrics of manual dexterity and the improvement elicited by a practice intervention. When considering typical age groups (i.e., young, middle-aged, and older individuals), most measures of manual dexterity decline as age increases (Bowden & McNulty, 2013; Hamilton et al., 2017; Marmon, Pascoe, et al., 2011; Ruff & Parker, 1993; Wang et al., 2011). However, variability in most measures of manual dexterity also increases with age (Wang et al., 2011, 2015). As a result, chronological age is often a poor discriminator of performance capabilities within cohorts of older adults. When attempting to explain differences in pegboard times of older adults, therefore, a more appropriate approach is to stratify participants based on pegboard time instead of age. Hamilton et al., for example, used such an approach to classify participants into groups of fast and slow times and found that the variance in pegboard times could be explained by different statistical models (Hamilton et al., 2019). Variance in the pegboard times of the faster group was partially explained by variability in motor function during a whole-body leaning task, whereas the variance for the slow group was more related to decision-making strategies.

Decreases in Grooved Pegboard Times with Practice

As reported previously by Marmon et al., the pegboard times of older adults can be improved with practice (Marmon, Gould, et al., 2011). In that study, 23 older adults (75.0 ± 4.4 yr) completed an evaluation session before and after six practice sessions in which they performed five blocks of five trials of the grooved pegboard test. Average time to complete the grooved pegboard test before the practice intervention was 93 ± 12 s and this declined progressively by 38% to 67 ± 5 s across the first five of the six practice sessions. The average initial grooved pegboard time of our participants was faster (80 ± 13 s) but declined by relatively similar amounts after the practice intervention (26 ± 11%). Marmon et al. found that the six practice sessions did not alter the strength of hand muscles (index finger abduction and pinch grip), but it did improve the ability to perform steady contractions (coefficient of variation for force) at submaximal target forces (5, 15, and 25% of maximal force) (Marmon, Gould, et al., 2011). Consistent with other results (Davis, Alenazy, et al., 2020; Kornatz et al., 2005), this finding was interpreted as indicating that measures of force steadiness provide insight on the neural control of muscle function (Enoka & Farina, 2021).

Our current study probed more deeply into the details of the practice-induced decreases in the grooved pegboard times of older adults. This was accomplished by stratifying participants into two groups based on grooved pegboard times before the practice intervention and comparing the improvements elicited by the six practice sessions. Two statistical methods (k-medoid, hierarchical) were used to categorize participants and they produced similar results; all significant variables presented within the paper remained significant regardless of stratification method. Although both groups exhibited a decrease in pegboard time from before to after the intervention, the percent decline in pegboard time (fast: 19.2 ± 8.3%; slow: 29.0 ± 10.0%), improvement in pegboard phases, and the changes in within-session SD across practice sessions differed between the two groups. These findings underscore the utility of distinguishing between the two groups of older participants (Davis, Alenazy, et al., 2020; Hamilton et al., 2019).

Based on standardized instructions, the NIH Toolbox measure of manual dexterity corresponds to the time taken to complete a pegboard test on the first trial after being given the opportunity to insert pegs into the first row of the board (Hamilton et al., 2017; Marmon, Pascoe, et al., 2011). Due to the lack of familiarity with this task, the time it takes older adults to complete the test decreases quite rapidly on subsequent trials. Consistent with the literature on motor-skill learning (Dayan & Cohen, 2011; Haith & Krakauer, 2018; Spampinato & Celnik, 2021), the rate of improvement in pegboard time exhibited two phases for both groups of participants: an initial fast rate and a subsequent slower rate. When learning a de novo motor skill, such as the grooved pegboard test, the initial fast decline in pegboard time across sessions is attributed to the time it takes to assemble a new skill (Krakauer et al., 2019). This phase imposes a relatively high cognitive load and seems to involve the hippocampus, premotor cortex, and parietal cortex (Wise & Murray, 2000). Once acquired, the new skill can be further improved with practice during the consolidation phase (Yamada et al., 2019). These subsequent improvements likely evolve by individuals exploring strategies that accrue savings in time by manipulating the speed-accuracy tradeoff (Dayan & Cohen, 2011; Krakauer et al., 2019). According to this scheme, participants would search for a combination of speed and accuracy with which the pegs could be manipulated to minimize the time to complete the task, which appears to differ across individuals (Almuklass et al., 2016).

Although the developers of the Toolbox used the average of two trials as the measure of pegboard time (Wang et al., 2011), our results suggest that it takes many more trials for older adults to become familiar enough with the task to provide a baseline measure. Our data suggest approximately 12 pegboard trials are required to attain the basic features of the motor skill. Subsequent practice-induced decreases in pegboard time presumably involved a reduction in the attentional demand and an improvement in the quality of the motor execution (Krakauer et al., 2019). Based on the findings of Marmon et al. in which six practice sessions of the grooved pegboard test did not alter the strength of hand muscles in older adults (Marmon, Gould, et al., 2011), it is likely that the decreases in pegboard time were caused by changes that took place in the nervous system (Keen et al., 1994b; Kornatz et al., 2005; Poston et al., 2008). One possibility is a reduction in the noisiness of the motor signal (Krakauer et al., 2019). For example, Marmon et al. found that decrease in pegboard time after six practice sessions was associated with an improvement in force steadiness (accuracy) during submaximal isometric contractions (Marmon, Gould, et al., 2011).

Another feature of the improvements observed during the consolidation phase was the transition between practice sessions. In addition to showing the progressive declines in pegboard time across the sessions, the shading in Figure 4 indicates the values that were obtained from each of the six practice sessions. Note that there was a transient increase in pegboard time at the beginning of each practice session for both groups of participants. Such effects are typically attributed to a decay in the gains achieved in the preceding practice session (Krakauer et al., 2019). Within a few trials of the 25 performed in each practice session, however, the pegboard times resumed the progressive decline evident in the consolidation phase, which is evidence for the savings retained for the motor skill.

Although both groups of participants exhibited the two classic phases of motor-skill learning, the pegboard times of the slow groups were longer than those of the fast group at all time points during the intervention. Such differences are typically attributed to differences in the formation of habits between individuals, where habitual behavior is insensitive to changes in the goals of a task (Haith & Krakauer, 2018). Moreover, habits are most evident when actions must be performed rapidly. Within this scheme, practice elicits three distinct changes in behavior: it improves skill level by enabling rapid actions, it reduces cognitive effort, and it promotes the translation of the action into habitual activity. In the context of our study, anecdotally, our fastest subject revealed they have been a piano player throughout their life, which could form dexterity-related habits that lead to quicker pegboard performance. Pre-existing habits such as this may point to the notion that perhaps not all subjects were performing a strictly de novo motor skill, but rather improving on an existing motor plan. We did not have any form of questionnaire to test for these kinds of connections for all subjects, but this could be an interesting topic for future studies.

Performance Variability

One of the major challenges in learning a new motor skill is to reduce variability in the performance of the task by changing the quality of the action execution (Krakauer et al., 2019). In terms of the pegboard task, such adaptations could increase the speed of each action, improve the accuracy (mean error) and precision (variable error) of peg manipulation, and enable the development of smooth, stereotypical trajectories.

In our study, we assessed the influence of practice on motor acuity by measuring the variability in pegboard times across practice sessions (Figure 5) and the times to complete the four peg-manipulation phases before and after the practice intervention (Figure 6). The variability in pegboard times was quantified as the standard deviation of the times for the 25 trials performed in each practice session. There was a statistically significant decrease across all participants in the standard deviation during the second practice session relative to the first, which presumably reflected the learning that occurred during the acquisition phase. Comparing the variability between groups shows consistently lower variability for the fast group relative to the slow group. This difference between groups is significantly different in the first, fifth and sixth practice sessions. The difference between group standard deviations in the first practice session can be explained by the differing capabilities of slow and fast people in the acquisition phase to become familiar with the de novo task. The differences in the fifth and sixth practice sessions may be attributed to an increase in variability as a result of the speed-accuracy tradeoff for the slow group over the consolidation phase, despite their overall improvement in this phase; if the slow group was nearing their performance ceiling, they may have begun altering their motor plan to perform the task quicker at the expense of accuracy.

To assess the influence of practice on the motor-execution components of skill learning, we compared the duration of the four peg-manipulation phases (Almuklass et al., 2017; Almuklass, Feeney, et al., 2018) before and after practice. In contrast to studies on the learning of arbitrary visuomotor associations in which individual movements within a sequence of practiced tasks do not improve (Krakauer et al., 2019), we found significant reductions in some of the peg-manipulation phases. However, there were differences between the two groups of participants. The fast group experienced a reduction in the time to complete the transport phase, which involves moving each peg from the well to the next hole on the board. A likely explanation for this improvement is that the trajectories for the reaching action became less variable across pegs. For example, Shmuelof et al. found that improvements in the performance of an arc-pointing task after five days of practice were attributed to reductions in trial-to-trial trajectory variability (Shmuelof et al., 2012).

The slow group also reduced the time to perform the peg-transport phase, but in addition exhibited faster peg-insertion and hand-return phases. The faster hand-return phase might also be explained by a reduction in trajectory variability across pegs. The faster peg-insertion phase, which displayed the greatest improvement, indicates that participants in the slow group needed less time to insert each peg into the hole once contact had been made with the board. The improvement cannot be explained by accuracy in placing a peg at the hole, but rather the more precise application of the downward force on the peg. Such learning likely involves a reduction in the variability of the applied force (Feeney et al., 2018; Hamilton et al., 2017; Lodha & Christou, 2017), which has been shown to be associated with decreases in pegboard times (Kornatz et al., 2005; Marmon, Gould, et al., 2011).

CONCLUSION

Consistent with the literature on de novo motor-skill learning, six sessions of practice reduced the pegboard times of all older adults by engaging first a relatively rapid acquisition phase and then a slower consolidation phase. Nonetheless, the changes observed in the four phases of the peg-manipulation cycle observed after the practice intervention differed for the participants who were stratified into groups of fast and slow performers based on initial grooved pegboard time.

Chapter III

Explaining the Influence of Practice on the Grooved Pegboard Times of Older Adults: Role of Force Steadiness

Experimental Brain Research Under review

ABSTRACT

The purpose was to identify the variables that can explain the variance in the grooved pegboard times of older adults who were categorized as having either fast or slow pegboard times. Participants (*n* = 28; 60-83 yrs) completed two experimental sessions, one before and one after, six sessions in which they practiced the grooved pegboard test. The two groups were distinguished with a cluster analysis of the average pegboard time in each practice session. The explanatory variables for the pegboard times before and after practice were the durations of 4 peg-manipulation phases and 8 measures of force steadiness (coefficient of variation [CV] for force) during isometric contractions with the index finger abductor and wrist extensor muscles. Average pegboard time during practice was 73 ± 11 s for the fast group and 85 ± 13 s for the slow group. Time to complete the grooved pegboard test after practice decreased by 25 ± 11% for the fast group and by 28 ± 10% for the slow group. The peg-manipulation times and CV for force explained more of the variance in the pegboard times before practice for the fast group (Adjusted R^2 = 0.85) than for the slow group (Adjusted R^2 = 0.67) but less after practice for the fast group (R^2 = 0.51) than the slow group (Adjusted R^2 = 0.64). The explanatory variables for the variance in the pegboard times differed between before and after practice for the fast group but not the slow group.

INTRODUCTION

Manual dexterity is considered such an important attribute that it is included in the National Institute of Health (NIH) Toolbox as one of the biomarkers of neurological health and motor function across the lifespan (Gershon et al., 2013; Reuben et al., 2013). One of the recommended instruments to quantify manual dexterity is the grooved pegboard test (Thompson-Butel et al., 2014; Wang et al., 2011), with time to complete the test providing a quantitative measure of manual dexterity. The functional significance of the pegboard test is underscored by slower times being associated with declines in motor performance of healthy adults 20-88 yrs (Bowden & McNulty, 2013), reductions in activities of daily living in adults >65 yrs (Seidel et al., 2009), and increases in dependency among adults >63 yrs (Ostwald et al., 1989; Williams et al., 1982).

On average, older adults take longer to complete the grooved pegboard test than middle-aged and young adults (Almuklass, Feeney, et al., 2018; Ashendorf et al., 2009; Feeney et al., 2018; Marmon, Pascoe, et al., 2011). As with many tests of motor function, however, there is substantial variability among older adults in pegboard times, with chronological age often being a poor predictor of performance times (Bohannon et al., 2014; Davis, Allen, et al., 2020; Narici et al., 1991; Suetta et al., 2019b; Wang et al., 2011). An alternative approach to identifying the adaptations underlying declines in motor function with advancing age is to categorize participants by performance scores and to compare differences between groups (Daneshgar et al., 2023; Davis, Allen, et al., 2020; Hamilton et al., 2019).

Older adults respond positively to various practice and training interventions, including the practice of a manual dexterity task. For example, Marmon, Gould, et al. (2011) found that six practice sessions of the grooved pegboard test (5 sets of 5 trials in each session) reduced the time it took older adults (75.0 ± 4.4 yrs) to complete the grooved pegboard test from an initial time of 93 ± 12 s to a final time of 67 ± 5 s. Although the secondary outcomes of this study were significantly correlated with the decrease in pegboard time, the explanatory power of the regression model was modest ($R^2 = 0.59$). One factor that likely contributed to this result was the selection of participants based on chronological age instead of performance capacity. When the latter approach was used, Daneshgar et al. (2023) found that practice-induced decreases in pegboard times of older adults differed for those initially classified as fast performers relative to those with slower pegboard times. The older adults with faster times reduced the time taken to transport each peg from the well to the next hole, whereas those with slower time mainly reduced the time taken to insert each peg into a hole. Presumably, the baseline attributes differed for these two groups of older adults.

One metric of precision in motor performance is the amplitude of the force fluctuations during steady submaximal contractions, which is known as force steadiness (Enoka & Farina, 2021). When normalized as the coefficient of variation (CV) for force, the amplitude of the force fluctuations decreases as the target force level increases (Galganski et al., 1993). The CV for force at low target forces is correlated with time to complete the grooved pegboard test (Almuklass et al., 2016; Feeney et al., 2018; Hamilton et al., 2017). For example, Almuklass et al. (2016) found that 70% of the variance in the pegboard times of young adults could be explained by two variables: the time to match a submaximal target force set at 10% of maximum during a double-action task involving wrist extension and a pinch grip task and the CV for force during single-action wrist extension task.

In contrast, Marmon, Pascoe et al. (2011) found that only 36% of the variance in grooved pegboard times for 75 adults (19-89 yrs) could be explained by the CV for force during index finger abduction at a target force set at 5% of maximum (partial $r = 0.57$) and maximal grip strength (partial $r = -0.34$). However, a subsequent analysis of the data for older adults (65-89 yrs) found that 59% of the variance in grooved pegboard times was explained by three variables: age (partial $r = 0.66$), index finger force steadiness (partial $r = -0.31$), and pinch grip strength (partial $r = 0.26$). Moreover, Marmon, Gould, et al. (2011) reported that decreases in pegboard times after six practice sessions were correlated with improvements in force steadiness measured during finger abduction and precision pinch.

The current report extends the analysis to data not included in our previous paper on the effects of practice on the grooved pegboard times of older adults (Daneshgar et al., 2023). The purpose of this report was to identify the variables that can explain the variance in the grooved pegboard times of older adults who were categorized as having either fast or slow pegboard times. The analysis focused on the pegboard times recorded before and after a 6-session practice intervention. The explanatory variables were the durations of the four peg-manipulation phases and force steadiness (CV for force) during eight tasks involving index finger abduction and wrist extension. We hypothesized that the faster pegboard times after practice would be explained by different outcome variables for the two groups of participants.

METHODS

Participants

Twenty-eight healthy individuals (mean ± SD: 71 ± 8 years, 22 women) participated in the study. They were all right-handed as assessed by the 10-item Edinburgh handedness inventory (Oldfield, 1971). All participants were free from neurological disease and musculoskeletal abnormalities that could influence upper limb function. None of the participants were currently taking any medication known to influence neuromuscular function. All participants received both verbal and written explanations of the study protocol and provided written informed consent before participating in the study. The protocol was approved by the Institutional Review Board at the University of Colorado Boulder.

This paper reports the analysis of data acquired in a project from which some of the data have been published previously (Daneshgar et al., 2023). The protocol for the project involved a familiarization session followed by two evaluation sessions, one before and another after, six practice sessions of the grooved pegboard test. The primary outcome variables were the time to complete the grooved pegboard test, the durations of the four peg-manipulation phases, and the CV for force during steady submaximal contractions. In each evaluation session, participants performed one grooved pegboard test during which the durations of the 4 peg-manipulation phases were measured and 8 steadiness tasks with the index finger abductor (first dorsal interosseous) and the wrist extensor muscles. Between the two evaluation sessions, participants completed six sessions in which they practiced the grooved pegboard test. The practice sessions were separated by 2-3 days. Each practice session comprised 25 trials performed in 5 blocks of 5 trials.

The outcomes of the current report comprise measurements obtained from the same participants as in our previous paper, but the participants were stratified into two groups based on the average pegboard times across the practice sessions instead of the pegboard time recorded during the first evaluation session. One additional participant was removed from the data set used in the current report due to the presence of several extremely high CV for force values.

Grooved pegboard test

The grooved pegboard test (Lafayette Instruments, Lafayette, IN) requires participants to place keyhole-shaped pegs into 25 holes on the board as quickly as possible. The holes are also keyhole-shaped with different orientations across the board and are arranged in a 5x5 matrix on the board. When performing this test, right-handed participants insert pegs from top to bottom and left to right. As in the standardized instructions, participants were introduced to the test by inserting pegs into the first row of the pegboard. Subsequently, participants were verbally cued to perform the test and the time taken to insert all 25 pegs was recorded manually. Additionally, the downward force applied by the peg to the grooved pegboard during each evaluation session was measured with a force transducer (Model SBO-200-311062; TT, Temecula, CA) attached beneath the pegboard. The force recordings were used to determine the duration (s) of the four peg-manipulation phases: selection, transport, insertion, and return (Almuklass, Feeney, et al., 2018).

Force steadiness

Force steadiness during index finger abduction involved aligning the proximal interphalangeal joint of the index finger with a force transducer (Model LBM-50-384800; TT, Temecula, CA) to record the applied force. The other fingers were used to grasp the platform (Fig 1). Force steadiness during wrist extension was measured with a second force transducer (0.0056 V/N, JR3 Model 45E15A-U760-A, Woodland, CA) placed above the back of the hand. The instruction to each participant was to move a cursor or trace displayed on the monitor by performing isometric contractions and applying a force in either of two directions: index finger abduction or wrist extension. In addition to these single-action tasks, participants performed concurrent index finger abduction and wrist extension as a double-action task (Almuklass et al., 2016; Feeney et al., 2018).

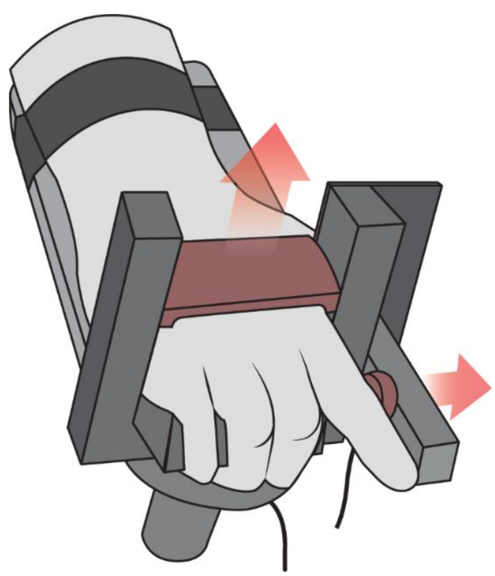

Figure 1. Position of the right hand in the apparatus for the force steadiness tasks. (a) The red elements show the placement of the force transducer and the direction of the force applied by the index finger and the back of the hand.

Before beginning the force steadiness tasks, participants performed maximal voluntary contractions (MVCs) with each test muscle. This task required the participant to increase force from rest to maximum gradually over three seconds and then to maintain the maximal force for another three seconds. Participants were provided with strong verbal encouragement during each MVC. A minimum of three MVC trials were recorded with at least one minute of rest between trials, and the percentage difference between the strongest two trials was determined. When the difference was greater than 5%, additional trials were performed (maximum of five trials) until this criterion was met. The peak force was used as the MVC force.

Steady contractions were performed at four target forces for both the single- and double-action tasks: 5%, 10%, 15%, and 25% MVC force with one minute of rest in between each trial. Each target force for the single-action tasks was displayed as a horizontal green line on a monitor that was placed 1.5 m in front of the seated participant. The single-action tasks involved participants increasing the applied force gradually up to the target line and then holding it steady for 20 s (Fig. 2a). They were asked to keep the applied force steady rather than matching the target force. The double-action tasks involved moving a single cursor from the bottom left corner of the screen to the target in the center of the screen. The abduction force applied by the index finger moved the cursor in the x-direction, and the wrist extension force moved it in the y-direction. Once the target was acquired, the participant held the force steady for 20 s (Fig.2c). The gain of the visual feedback was scaled to provide a constant excursion of the signal on the monitor in both tasks and all target forces. The single-action tasks were performed before the double-action tasks, but the order of the target forces was counterbalanced across participants.

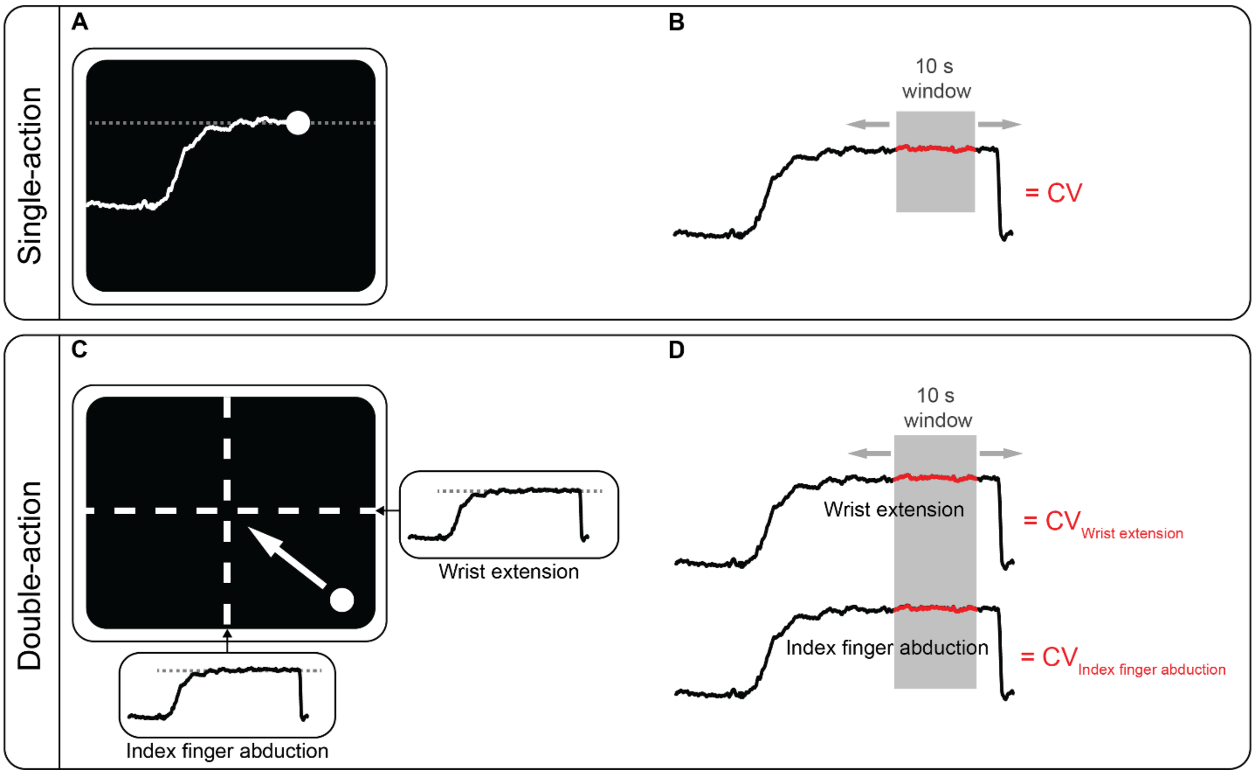

Figure 2. Schematic example of the applied forces during single-action (A & B) and double-action (C & D) steadiness tasks. Single-action tasks required participants to move the applied force up to the dotted target line and then keep the force steady (A). The steadiest 10 s of the trace was identified, and the amplitude of the force fluctuations is reported as the CV for force (B). Double-action tasks required participants to apply two forces: index finger abduction and wrist extension. This was accomplished by moving the cursor to the center of the screen (C) and then applying steady forces. A 10-s moving window identified the minimum sum of squares of the CV for the two forces and then the CV for force in each trace (index finger abduction and wrist extension) was measured and reported separately (D).

The force signals were low-pass filtered at 12 Hz (second-order bidirectional Butterworth filter) and sampled at 100 Hz with an analog-to-digital converter (Power 1401, Cambridge Electronic Design, Cambridge, UK). The force data was acquired with Spike2 data-acquisition software (Version 9.08, Cambridge Electronic Design, Cambridge, UK) and stored on a computer for offline analysis.

Data analysis

Pegboard time was defined as the duration from the moment the participant first lifted the right hand off the table to begin the test to the moment when the last peg was inserted into the board. Times for the 25 pegboard trials in each practice session were averaged and participants were clustered with a k-means analysis into fast and slow groups (Fig. 3) Although the optimal number of clusters suggested by silhouette analysis differed, the number of clusters was arbitrarily set at two based on the research question and our approach for implementing a binary classification of the participants. Differences in grooved pegboard times between baseline and after practice for both groups as well as the differences between fast and slow groups were evaluated with a linear mixed model. In this model, fixed effects were the pegboard time and sessions, and the crossed random effect was the variability within subjects. Also, the intercept was set to random.

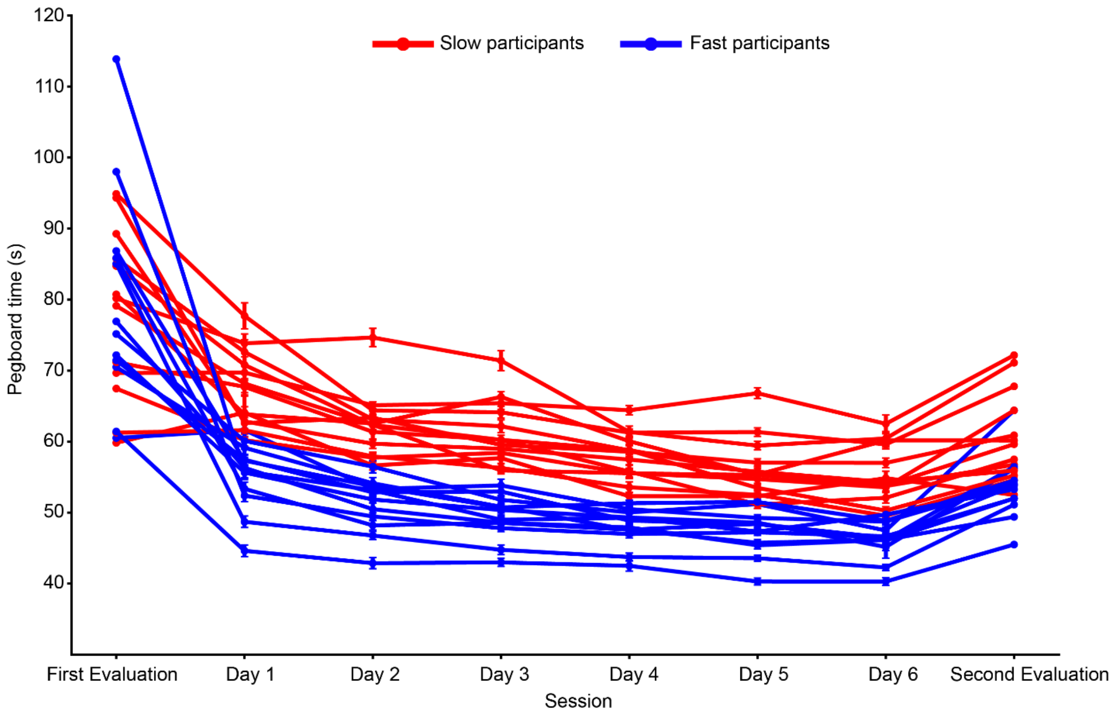

Figure 3. Time to complete the grooved pegboard test in the first and second evaluation sessions, and the average value for each of the six practice sessions. Each line represents one participant (n = 25). They were clustered into two groups based on the six average practice sessions: fast (blue) and slow (red) groups. The first and second evaluation sessions correspond to single pegboard times and practice days are represented as an average ± standard error of the 25 trials in each session.

The durations of the peg-manipulation phases were determined from the average of three pegs at the beginning of the test and pegs 22, 23, 24. The last peg was excluded due to absence of the hand return phase at the end of the test. Insertion of the first and last three pegs were indicated by event markers that were manually identified by the investigators. This was accomplished by using the first derivative of the force signal to indicate the onset and offset of the applied force. The offset and onset on the force signal correspond to the transitions between the peg-manipulation phases.

MVC forces from before and after the practice sessions were compared with a paired t-test. The amplitude of the force fluctuations during the single-action tasks was expressed as the CV for force during the steadiest 10 s interval in the force trace. This was identified by moving a 0.1 s window in non-overlapping increments along the entire 20 s recording. The minimal CV for force during 100 contiguous windows was used as the measure of force steadiness. A similar approach was used for the double-action trials, but the criterion was applied to both force traces concurrently (Figure 2). The steadiness criterion for the double-action tasks was the time when the summed square of the CVs ($CV_1^2 + CV_2^2$) was at a minimum. When this criterion was met, CV_1 and CV_2 were reported as independent CVs for the respective tasks. All CV for force values were obtained using MATLAB (version R2023b). All pegboard times and CVs for force were recorded, as well as the absolute and percent change of each variable from before to after the practice sessions.

To evaluate the differences in CV for force, four separate linear mixed models were developed, two for each group (fast and slow performers). Assumptions of normality and homoscedasticity were tested using Q-Q plots, Shapiro-Wilk test, and residual-fitted value plots. The models included the type of task (single-action and double-action), force level (5%, 10%, 15%, and 25%), session (before and after practice), and all interactions between these variables were set as fixed effects, whereas participants across all force levels, variables, and sessions represented a crossed random effect. All fixed effects were considered to have random intercepts. The goodness of fit for each model was evaluated with the Akaike Information Criterion (AIC) and Log-likelihood test. Subsequently, Bonferroni corrected post-hoc tests were performed to assess the differences within main or interaction effects.

Four separate linear regression models were developed to explain the pegboard times for the fast and slow groups. The explicit explanatory variables included in the four models were the CV for force and the four peg-manipulation phase times. To explain differences in the pegboard times in each evaluation session, only variables from the same session were included in the regression models. Assumptions of linearity, independence, normality, and homoscedasticity were tested using visual inspection of residual plots and the Shapiro-wilk normality test. Correlations between all variables in each model were evaluated to avoid collinearity and only variables with no correlation were added to the models.

Due to the large number of CV for force variables and to keep the models as simple as possible, the linear regression models were developed with the stepwise forward-and-backward method and were limited to a maximum of five variables. The significance of each model was assessed with R-squared and adjusted R-squared values for single linear regressions, as well as the AIC, coefficients, standard errors, and p-values of the selected variables. Within each model, the strength and collinearity of the explanatory variables were assessed with partial r and variance inflation factor (VIF) values. The level of significance (α) in all tests was set to 0.05. Statistical analyses were performed using Jamovi (version 2.3.26) and Python (version 3.11.5).

RESULTS

The 25 participants included in the statistical analysis were categorized into two groups based on average grooved pegboard times across the six practice sessions: fast ($n = 12$; 73 ± 11 s) and slow ($n = 13$; 85 ± 13 s) performers (Fig. 3). The pegboard times in the second evaluation session were 53.6 ± 4.5 s for the fast group and 60.7 ± 6.4 s for the slow group, which corresponded to reduction from the first evaluation session of 25 ± 11% for the fast group and 28 ± 10% for the slow group. The results of the linear mixed models satisfied assumptions of normality, homoscedasticity, and linearity, and indicated significant main effects for pegboard time ($p = 0.002$) and practice ($p < 0.001$). A paired t-test showed no statistically significant difference in MVC force when measured before and after practice for both index finger abduction (before =

25.3 ± 7.9 N, after = 24.2 ± 7.2 N, $p = 0.35$) and wrist extension (before = 41.1 ± 11.3 N, after = 45.2 ± 12.9 N, $p = 0.11$).

Force Steadiness

Assumptions of normality and homoscedasticity for the linear mixed models were satisfied. The results were similar for the two groups of participants with significant main effects for task and target force but with a significant interaction between practice and target force for the slow group of participants. The main effects of task and muscle on CV for force were significant for both groups ($p < 0.001$ for all). The post-hoc test for the main effect of the target force indicated that the CV for force at 10%, 15%, and 25% was significantly less than that at 5% for both groups across tasks, sessions, and muscles ($p < 0.001$ for all). However, the post-hoc tests indicated significant interactions between target force and practice session ($p = 0.027$) for the slow group with a significant decrease in CV for force from before to after practice at 5% target force ($p < 0.001$; Figs, 4 and 5). The results for the wrist extensors are also plotted in Figures 6 and 7, and the summary CV for force data for both groups and muscles is listed in Tables 1 to 4.

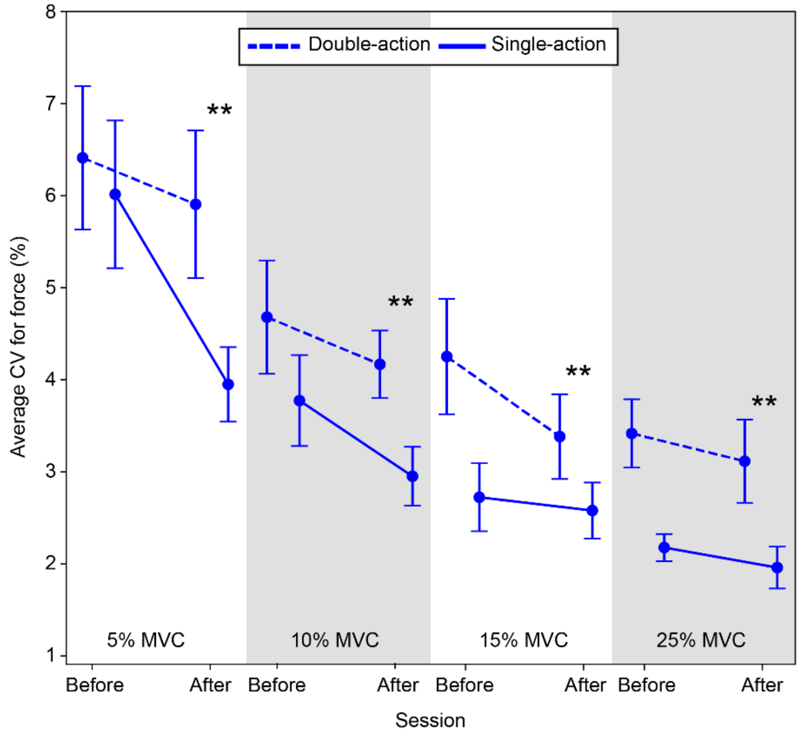

Figure 4. Changes in force steadiness in index finger abduction / fast group. Average CV for force ± standard error (%) at each of the target forces for the finger abduction task for the fast group from before to after practice sessions. Dashed lines represent the double-action tasks and solid lines indicate the single-action tasks. White and grey columns show the different target forces. ** $p < 0.001$ main effect for practice, which means the data were combined across tasks and muscles.

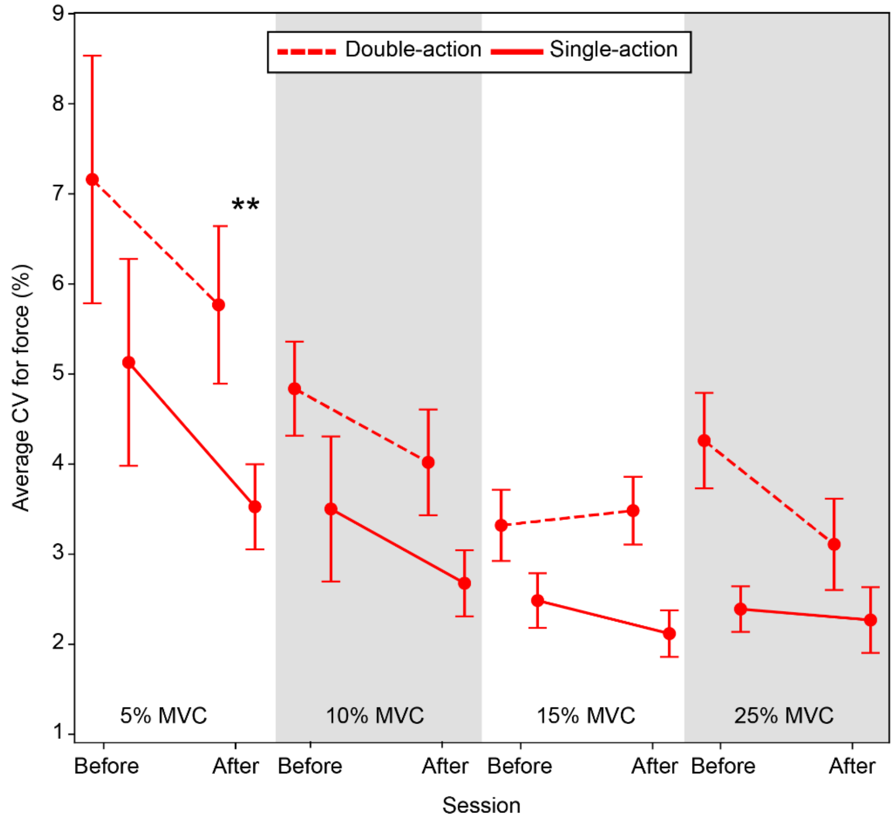

Figure 5. Changes in force steadiness in index finger abduction / slow group. Average CV for force ± standard error (%) at each of the target forces for the finger abduction task for the slow group from before to after practice sessions. Dashed lines represent the double-action task and solid lines indicate the single-action tasks. White and grey columns show the different target forces. ** $p < 0.001$ main effect for practice, which means the data were combined across tasks and muscles.

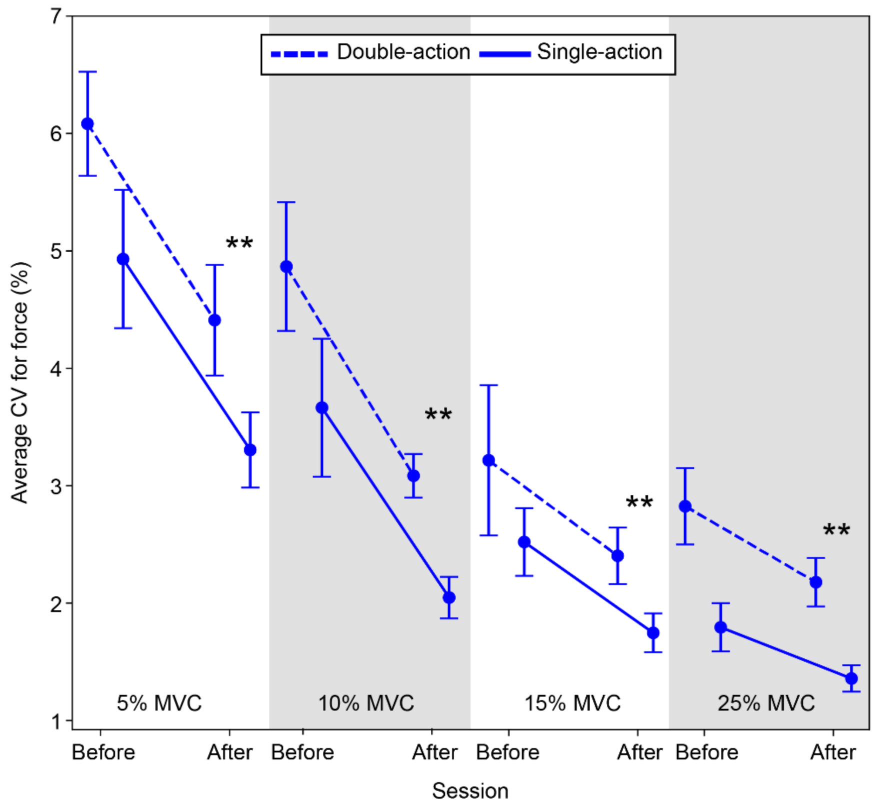

Figure 6. Changes in force steadiness in wrist extension / fast group. Average CV for force ± standard error (%) at each of the target forces for the wrist extension task for the fast group from before to after practice sessions. Dashed lines represent the double-action task and solid lines indicate the single-action tasks. White and grey columns show the different target forces. ** $p < 0.001$ main effect for practice, which means the data were combined across tasks and muscles.

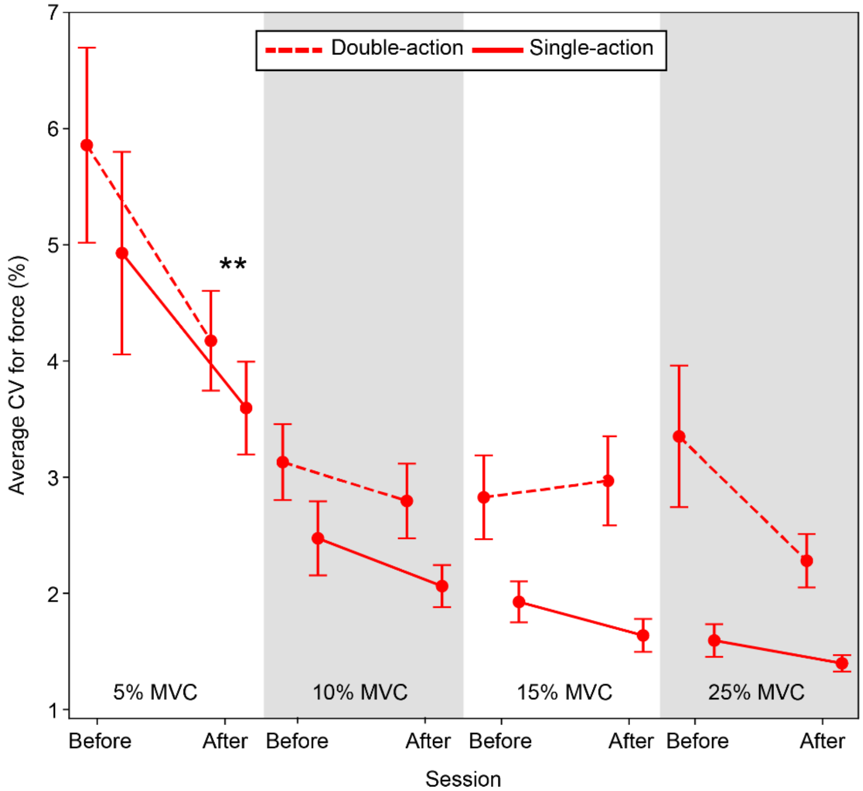

Figure 7. Changes in force steadiness in wrist extension / slow group. Average CV for force ± standard error (%) at each of the target forces for the wrist extension task for the slow group from before to after practice sessions. Dashed lines represent the double-action task and solid lines indicate the single-action tasks. White and grey columns show the different target forces. ** $p < 0.001$ main effect for practice, which means the data were combined across tasks and muscles.

Supplementary Table 1. Average CV for force (%) during index finger abduction for the fast group.

Target Force (% MVC)	Before		After	
	Single action	Double action	Single action	Double action
5	6.0 ± 2.8	6.4 ± 2.7	3.9 ± 1.4	5.9 ± 2.8
10	3.8 ± 1.7	4.7 ± 1.3	2.9 ± 1.1	4.2 ± 1.3
15	2.7 ± 1.3	4.2 ± 2.2	2.6 ± 1.0	3.4 ± 1.6
25	2.17 ± 0.51	3.4 ± 1.3	1.95 ± 0.79	3.1 ± 1.6

Data listed as mean ± SD

Supplementary Table 2. Average CV for force (%) during index finger abduction for the slow group.

Target Force (%MVC)	Before		After	
	Single action	Double action	Single action	Double action
5	5.1 ± 4.1	7.2 ± 4.9	3.5 ± 1.7	5.8 ± 3.1
10	3.5 ± 2.9	4.9 ± 1.9	2.7 ± 1.3	4.0 ± 2.1
15	2.5 ± 1.1	3.3 ± 1.4	2.09 ± 0.93	3.5 ± 1.4
25	2.38 ± 0.91	4.2 ± 1.9	2.3 ± 1.3	3.1 ± 1.8

Data listed as mean ± SD

Supplementary Table 3. Average CV for force (%) during wrist extension for the fast group.

Target Force (% MVC)	Before	After	Before	After
	Single action	Double action	Single action	Double action
5	4.9 ± 2.0	6.1 ± 1.5	3.3 ± 1.1	4.4 ± 1.6
10	3.7 ± 2.0	4.9 ± 1.9	2.05 ± 0.61	3.09 ± 0.64
15	2.5 ± 1.0	3.2 ± 2.2	1.74 ± 0.57	2.40 ± 0.84
25	1.79 ± 0.71	2.8 ± 1.1	1.36 ± 0.39	2.18 ± 0.71

Data listed as mean ± SD

Supplementary Table 4. Average CV for force (%) during wrist extension for the slow group.

Target Force (% MVC)	Before		After	
	Single action	Double action	Single action	Double action
5	4.9 ± 3.1	5.9 ± 3.0	3.6 ± 1.4	4.2 ± 1.5
10	2.5 ± 1.1	3.1 ± 1.2	2.06 ± 0.66	2.8 ± 1.2
15	1.93 ± 0.64	2.8 ± 1.3	1.64 ± 0.51	3.0 ± 1.4
25	1.59 ± 0.50	3.3 ± 2.2	1.40 ± 0.26	2.28 ± 0.83

Data listed as mean ± SD

Regression models for pegboard times

Multiple linear regression models were developed for both the pegboard times recorded during the two evaluation sessions and for the two groups of participants. All the basic assumptions for these regression models were met. Models for each session were derived from the variables measured in the same session only.

The model for the pegboard times of the fast group in the first evaluation session (Fig. 8a) explained 85% of the variance (Adjusted $R^2 = 0.85$, $AIC = 70.97$, $p = 0.006$) with four predictor variables: CV for force during single-action wrist extension at 25% MVC (partial $r = 0.93$, $VIF = 1.33$, $p < 0.001$), CV for force during single-action index finger abduction at 25% MVC (partial $r = -0.84$, $VIF = 1.15$, $p = 0.002$), peg transport time (partial $r = -0.88$, $VIF = 1.15$, $p = 0.002$), and hand return time (partial $r = 0.71$, $VIF = 1.31$, $p = 0.033$). The model for the slow group (Fig, 8c) explained 67% of the variance in the pegboard time in the first evaluation session (Adjusted $R^2 = 0.67$, $AIC = 91.44$, $p = 0.001$) with two predictor variables: CV for force during double-action index finger abduction at 5% MVC (partial $r = 0.73$, $VIF = 1.11$, $p = 0.0007$) and peg insertion time (partial $r = 0.62$, $VIF = 1.11$, $p < 0.031$).

The model for the pegboard times for the fast group in the second evaluation session (Fig. 8b) explained 51% of the variance ($R^2 = 0.51$, $AIC = 64.86$, $p < 0.009$) with a single variable: CV for force during double-action index finger abduction at 15% MVC (partial $r = 0.61$, $p < 0.009$). The model for the pegboard times of the slow group in the second evaluation session (Fig. 8d) explained 64% of the variance (Adjusted $R^2 = 0.64$, $AIC = 74.58$, $p = 0.002$) with two predictors: peg insertion time (partial $r = 0.66$, $VIF = 1.008$, $p < 0.019$) and CV for force during single-action index finger abduction at 5% MVC (partial $r = 0.66$, $VIF = 1.008$, $p = 0.005$).

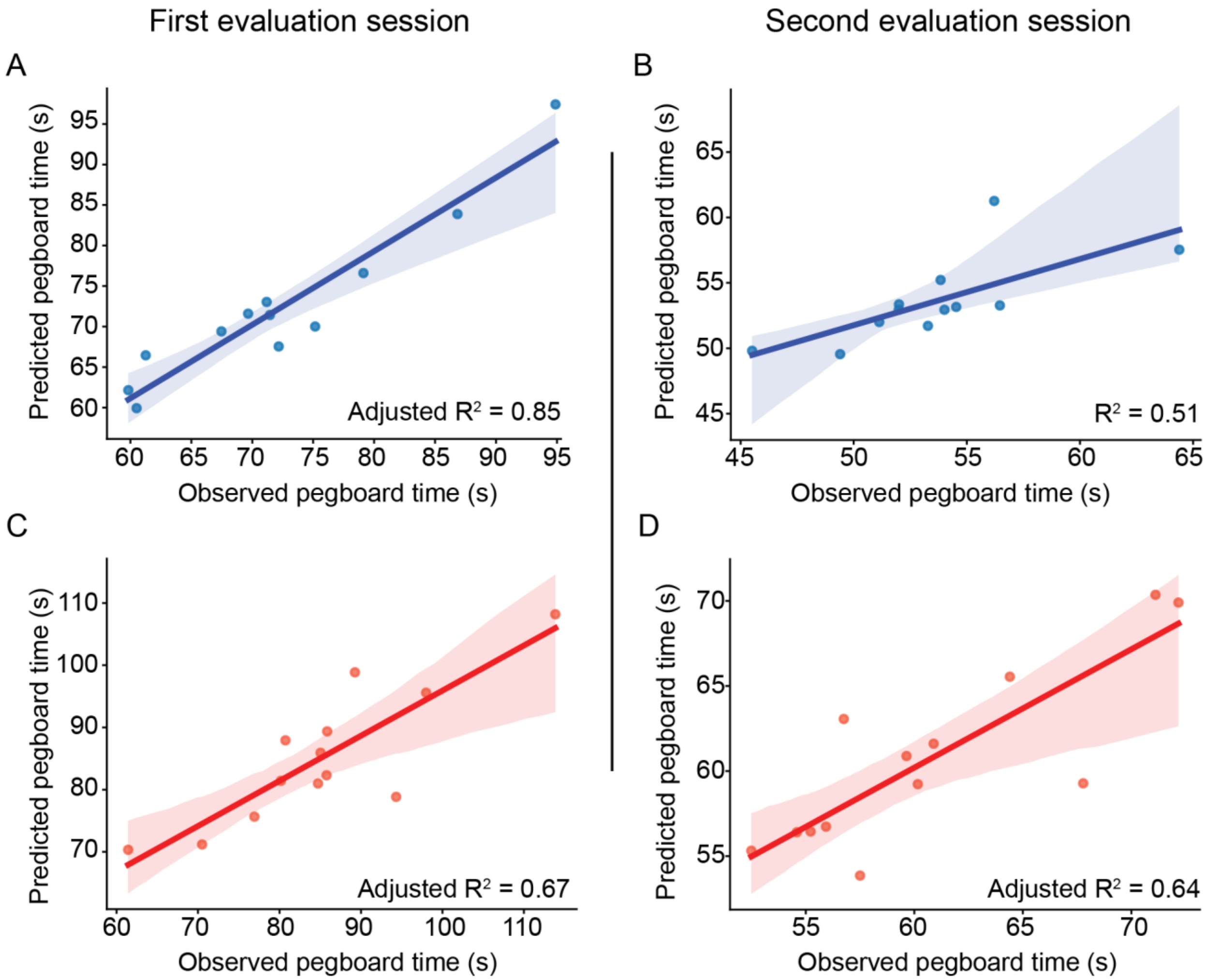

Figure 8. Association between observed and predicted pegboard times. (A) The regression model for the fast group (blue) for the pegboard times in the first evaluation session. (B) The regression model for the fast group for the pegboard times in the second evaluation session. (C) The regression model for the slow group (red) for the pegboard times in the second evaluation session. (D) The regression model for the slow group for the pegboard times in the second evaluation session. The explanatory variables, which are reported in the text, were identified with a forward-backward stepwise, multiple-regression analysis.

DISCUSSION

The main finding of the study was that the durations of peg-manipulation phases and measures of force steadiness were able to explain more than one half of the variance in time to complete the grooved pegboard test for the two groups of older adults. However, the percentage of variance explained declined after practice for the fast group, whereas it was relatively similar for the slow group. Moreover, measures of force steadiness emerged as explanatory variables in all four regression models (before and after practice for each group of participants), whereas phase durations were only included in three of the models. The findings indicate that the two groups of participants exhibited different force-control attributes during the grooved pegboard test both before and after the practice intervention.

Force steadiness

The fluctuations in force during steady contractions are a product of the cumulative activity of all the engaged motor units (Enoka & Farina, 2021). In a seminal study, Negro et al. (2009) demonstrated that 74% of the fluctuations in force during a steady contraction with a hand muscle at 10% of maximal force could be explained by low-frequency modulation of the summed discharge rates of motor unit action potentials. This result indicates that the effective neural drive to muscle depends on the summed activity of the activated individual motor units. As demonstrated in a series of studies by Farina and colleagues, modulation of the cumulative train of discharge times is attributable to the variance in the common synaptic input received by the involved motor neurons (Del Vecchio, Germer, et al., 2019; Farina et al., 2016; Farina & Negro, 2015; Mazzo et al., 2022; Negro et al., 2016; Thompson et al., 2018). Given the observed decrease in the CV for force with an increase in target force, the underlying variance in common synaptic input must decline as target force increases (Dideriksen et al., 2012) despite an increase in the proportion of common synaptic input (Castronovo et al., 2015).

When quantified as the CV for force during steady submaximal contractions, measures of force steadiness can explain significant amounts of the variance in the performance of various motor tasks (Enoka & Farina, 2021; Maillet et al., 2022; Pethick et al., 2022). For example, differences in force steadiness have been shown to be associated with time to complete a pegboard test of manual dexterity (Almuklass et al., 2016; Feeney et al., 2018; Hamilton et al., 2017; Marmon, Pascoe, et al., 2011), postural sway during standing balance (Carzoli et al., 2022; Davis, Allen, et al., 2020; Hirono et al., 2021; Kouzaki & Shinohara, 2010), walking performance (Almuklass, Davis, Hamilton, Vieira, et al., 2018; Davis, Alenazy, et al., 2020; Hyngstrom et al., 2014; Mani, Almuklass, Hamilton, et al., 2018), and fall risk in older adults (Carville et al., 2007). The results of our study contribute to this literature by demonstrating that the association between force steadiness and grooved pegboard time differed among older adults depending on the time it took them to complete the test. Moreover, the reductions in the CV for force during index finger abduction and wrist extension after practice were interpreted as indicating decreases in the variance in common synaptic input to the involved motor neurons during these tasks (Dideriksen et al., 2012; Feeney et al., 2018; Pereira et al., 2019).

As observed in our study, others have reported significant differences in the CV for force between single- and double-action tasks (Almuklass et al., 2016; Feeney et al., 2018; Hamilton et al., 2019). Moreover, the CV for force increases when a muscle applies a force at the same time as other muscles perform another action (Del Vecchio, Germer, et al., 2019), after intense exercise that causes muscle damage (Dartnall et al., 2009; Turner et al., 2008; Vila-Chã et al., 2012), when individuals are confronted with a cognitive challenge (Pereira et al., 2015, 2019), and it decreases after strength training (Keen et al., 1994a; Kobayashi et al., 2014; Laidlaw et al., 1999). These observations of a change in the CV for force when the same task was performed before and after an intervention indicate that the variance in the common synaptic input was changed by the demands of the protocol. In our study, the explanatory variables in the regression models for the fast group included the CV for force during a single-action task before practice, but the CV for force during a double-action task after practice. In contrast, the models for the slow group included the CV for force during a double-action task before practice, but the CV for force during a single-action task after practice. This suggests that the greater variance in the common synaptic input during double-action index finger abduction was more influential for the fast group before practice but the slow group after practice. Perhaps the difference reflected changes in the distribution of common synaptic input to the motor neuron pool as assessed by the identification of motor unit modes (Del Vecchio et al., 2023; Levine et al., 2023; Ricotta et al., 2023; Weinman et al., 2024).

Peg-manipulation phases

Based on the trajectory of the downward force applied to the pegboard during the grooved pegboard test, Almuklass et al. (Almuklass et al., 2017; Almuklass, Feeney, et al., 2018) identified four phases during the manipulation of each peg: (1) selection of the peg from the well; (2) transport the peg to the next hole; (3) insert the peg into the hole; and (4) return the hand to the well for the next peg. When comparing the times for these phases before and after the practice intervention, Daneshgar et al. (Daneshgar et al., 2023) found that the only significant decrease in time for the fast group was for phase 2 (peg transport). In contrast, times for phases 2, 3, and 4 all decreased for the slow group, but the greatest decrease was for phase 3 (peg insertion).

Three of the regression models in our current study included one or two of the peg-manipulation phases as an explanatory variable. These were the transport and return phases in the model for the first evaluation session (before practice) of the fast group, and the insertion phase in both models for the slow group. The findings for the fast group indicate that their faster pegboard times in the second evaluation session were not attributable to decreases in any of the peg-manipulation phases. In contrast, the fast pegboard times for the slow group in the second evaluation session were associated with a decrease in the average time to insert the pegs into the pegboard. Coupled with change in the steadiness task from a double action to a single action, which suggests a decrease in the variance in the common synaptic input, the faster pegboard times in the second evaluation session for the slow group likely involved an improvement in the precision of peg insertion into the board (Almuklass et al., 2016; Ambike et al., 2013; Elliott et al., 2020; Werremeyer & Cole, 1997).

LIMITATIONS

Although our study has provided valuable insights into the association between force steadiness and motor function in older adults, there are some limitations that must be acknowledged and addressed in future research. In particular, the set of outcome variables should be expanded to identify attributes that can explain more of the variance in the pegboard times for the fast group of older adults after a practice intervention. Potential additional variables could include measures of muscle strength, tactile sensation (Sobinov & Bensmaia, 2021), cognitive function (such as memory, attention, and executive function) (Hamilton et al., 2017; Pereira et al., 2019; Seol et al., 2023), and reports of daily physical and mental engagement. Moreover, additional steadiness tasks could be explored, such as those involving other muscle groups and different loading conditions. Nonetheless, the capacity of normalized force fluctuations (steadiness) during submaximal isometric contractions with a single hand muscle (first dorsal interosseus) to explain significant amounts of the variance in the grooved pegboard times of older adults remains remarkable.

CONCLUSION

The decrease in time to complete the grooved pegboard test after six practice sessions was related to the CV for force during steady, submaximal contractions performed with a single hand muscle for both groups of participants. However, the outcome variables explained less of the variance in the pegboard times for the fast group in the second relative to the first evaluation session, whereas the explanatory power of the regression models for the slow group was similar in both evaluation sessions. The arbitrary stratification of older adults into fast and slow performers yielded distinct characteristics for each group that would have been masked had they been assessed as a single homogeneous group.

Chapter IV

Influence of Transcutaneous Electrical Nerve Stimulation on the Distance Walked by Older Adults During the 6-min Test of Walking Endurance

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ABSTRACT

The purpose of our study was to compare the influence of two types of transcutaneous electrical nerve stimulation (TENS) on the performance of older adults on the 6-min test of walking endurance and on the ability to maintain balance during upright standing. Twenty-six healthy older adults (72 ± 5.4 yrs) performed tests of motor function while TENS was applied to the tibialis anterior and rectus femoris muscles of each leg. Linear mixed models were used to compare the influence of TENS on walking distance in a 6-min test of walking endurance and on sway-area rate in tests of standing balance. There was a significant decrease in the distances walked in each minute of the 6-min walk test for both the Continuous and Burst TENS modes compared with Baseline ($p < 0.01$ and $p < 0.001$, respectively). The influence of TENS on walking distance was associated with several significant effects on the mean and coefficient of variation for stride length and stride frequency between the first and last minute of the test and between the two TENS modes and the Baseline values. In contrast, there was no significant effect of TENS on sway-area rate in any balance test, which indicates that the supplementary sensory feedback compromised walking performance of older adults but not the ability to maintain balance during upright standing.

INTRODUCTION

Walking performance declines progressively during healthy aging and eventually compromises an individual's ability to maintain an independent lifestyle (Casanova et al., 2011; Cooper et al., 2011; Fritz & Lusardi, 2009; Vestergaard, Patel, et al., 2009; Warren et al., 2016). The progressive decline in walking performance was underscored in a cohort study involving participants from several countries. The study found that age was a significant determinant of performance on the 6-min test of walking endurance ($p < 0.001$) (Casanova et al., 2011). The decline in walking endurance among older adults reflects a decrease in the overall physical function of these individuals. For example, Rikli & Jones. (1998) found that a significant decrease in the distance walked during the 6-min test by older adults (60–87 years) was moderately associated with the decline in self-reported functional abilities.

Although performance on tests of walking endurance largely depends on the cardiorespiratory capabilities of the individual (Dalgas et al., 2014; Rasekaba et al., 2009; Reuben et al., 2013; T. Wu & Zhao, 2021), reductions in walking endurance observed in older adults over a 3-year period were significantly associated with declines in the strength and speed of leg muscles (Beauchamp et al., 2014). Moreover, the predictor variables that were able to explain the mobility loss over a 9-year period experienced by older women comprised several neuromuscular variables, including strength of the dorsiflexors, hip-flexion range of motion, the presence of primitive reflexes, and tremor (Stenholm et al., 2015). These findings are consistent with the conclusion that adaptations in multiple physiological systems contribute to declines in walking endurance among older adults, including declines in sensorimotor function (Lange-Maia et al., 2016; Ward et al., 2014).

One countermeasure for declines in sensorimotor function is to supplement the activation of muscle with electrical stimulation. In a double-blind, randomized trial, for example, Mani, Almuklass, Amiridis, et al. (2018), examined the impact of a 6-week intervention with neuromuscular electrical nerve stimulation (NMES) on the performance of older adults on clinical tests of motor function. In 18 treatment sessions, NMES was applied to the plantar flexor muscles of each leg at the maximal tolerable intensity while participants performed strong voluntary contractions. After the intervention, time to complete the test of walking endurance decreased and maximal walking speed increased after 9 treatment sessions (3x/week), but there were no further improvements after another 3 weeks of NMES. In contrast, tests of dynamic balance (chair-rise test and rapid stepping) increased progressively across the 6-week intervention.

To distinguish between the effects of electrical stimulation on the activation of motor and sensory nerve fibers, the stimulation can be applied at an intensity that targets sensory fibers. This can be accomplished by applying transcutaneous electrical nerve stimulation (TENS) at an intensity slightly above motor threshold, which elicits action potentials in several different types of sensory nerve fibers (Bergquist et al., 2011; Hardy et al., 2002; Moran et al., 2011; Radhakrishnan & Sluka, 2005; Walker et al., 2014). With this approach, we have shown that the supplementary sensory stimulation provided by TENS improves walking performance (maximal speed and walking endurance), dynamic balance, and manual dexterity in individuals with multiple sclerosis (MS) and walking endurance in healthy middle-aged adults (Almuklass et al., 2020; Carzoli et al., 2022; Cooper et al., 2011). Critically, the influence of TENS on the distance walked during the 6-min test by the healthy middle-aged adults differed when the stimulation was applied continuously compared with a bursting pattern. Although both TENS modes were able to increase the distance walked by middle-aged adults during the 6-min test compared with baseline values, the improvement was greater for the Burst mode than the Continuous mode.

The purpose of our study was to compare the influence of Continuous and Burst TENS on the performance of older adults on the 6-min test of walking endurance and on the ability to maintain balance during upright standing. Based on the findings of Carzoli et al. (2022), we hypothesized that the distance walked during the 6-min test would increase during the concurrent application of Continuous and Burst TENS and that the gains achieved with Burst TENS would be superior to those elicited by Continuous TENS. As potential explanatory variables for the expected changes in 6-min walk distance, we also hypothesized that the variability in key kinematic variables related to stride length and frequency would decline during the 6-min test and that postural sway during upright standing would decrease when TENS was applied concurrently to leg muscles.

METHODS

Participants

The study enrolled 26 healthy older adults (72 ± 5.4 yrs, range: 65–83 yrs; 4 men). Participants were recruited from the local community, and they completed a screening questionnaire to determine their eligibility for the study. Inclusion criteria were age range between 65 and 85 yrs and the ability to walk unaided for 6 min. Exclusion criteria were abnormal sensations in the lower limbs, diagnosis of diabetes mellitus, and history of stroke or seizure disorders. Eligible volunteers provided their consent before commencing the study, which was approved by the institutional review board at the University of Colorado Boulder (IRB #22–0072) and performed in accordance with the Declaration of Helsinki.

Experimental design

The participants visited the campus on two occasions to perform experiments that were separated by five to seven days. Both visits occurred at approximately the same time of day to minimize the influence of circadian rhythm on performance. The tasks that the subjects performed were the same for both visits and began with a 6-min walk test and, after 10 min of rest, was followed by the upright-standing balance tests. All the tasks were performed in the Recreation Center at the University of Colorado Boulder.

In each visit, there were two conditions that involved the same tasks but differed in that the TENS device was either not turned on (Baseline) or it was turned on while performing the tasks. The two conditions (Baseline + TENS) in each visit were separated by approximately 20 to 30 min of rest. Prior to beginning the 6-min walk tests, six tri-axial Opal^{TM} wireless inertial measurement units (IMUs), were attached to the wrists, feet (on top of shoes), chest, and lower back with Velcro straps or buckles (Version 2.0, APDM Inc., Portland, OR, USA). Each sensor contained 3-dimensional gyroscopes, accelerometers, and magnetometers and the detected signals were transmitted to a data-acquisition system, sampled at 128 Hz, and analyzed with gait-analysis software. Data from IMUs provided multiple kinematic measures during the 6-min walk.

TENS preparation

TENS was provided by two FDA-approved portable TENS units (LG TECELITE Therapy System) that delivered currents through pairs of conductive fabric electrode pads (Axelgaard Manufacturing, Lystrup, Denmark) attached to the skin over selected muscles. Four TENS electrodes were placed on each leg: two over the rectus femoris muscle (2 × 3.5 in and 2 × 5 in), and two over the tibialis anterior muscle (2 × 3.5 in). The two TENS devices were attached to the participants' waist band during each task. Monophasic rectangular pulses (0.2 ms) were delivered in a continuous mode at a frequency of 50 Hz in one visit and in burst mode (5 bursts/s) in the other visit. Each burst comprised seven pulses (0.2 ms each) at a rate of 100 Hz, thus a burst duration of 70 ms. The order for these two TENS modes was counterbalanced across participants.

The intensity of the TENS current was determined individually for each muscle during the first visit. While participants were relaxed and seated in a chair, the TENS intensity increased gradually until it was sufficient to elicit a muscle twitch. The current was kept at the same intensity for the second visit.

Six-Minute walk test

Participants were instructed to walk briskly around an oval track (~160 m) for 6 min. Each subject walked in the same direction (either clockwise or counterclockwise) for both visits. The distance walked in each minute was recorded using a meter wheel. In addition, one investigator walked with the participant as a precaution to minimize the risk of falling.

Balance testing

Participants were asked to stand barefoot on a balance plate (BTrackS; Balance Tracking Systems, Inc, San Diego, CA) with their feet together and their arms crossed over their chest. There were four balance conditions that were performed in the following order: rigid surface with open eyes (RO), rigid surface with closed eyes (RC), foam surface (Balance pad Airex [50 × 41 × 6 cm], Sins, Switzerland) with open eyes (FO), and foam surface with closed eyes (FC). Two 30-s trials were performed for each condition. Participants were asked to fixate on a marker placed at eye level approximately 1 m in front of them for the duration of each trial.

The balance plate has one force transducer at each corner and its signal was transmitted (sampling frequency of 25 Hz) to the data-acquisition system on a laptop (BTrackS; Balance Tracking Systems, Inc, San Diego, CA). The software detected the coordinates for the center-of-pressure location as a function of time and these data were used to calculate the sway-area rate (Davis, Allen, et al., 2020; Hufschmidt et al., 1980; Prieto et al., 1996) using a custom MATLAB code (MathWorks Inc, Natick, MA). Sway-area rate (mm^2/s) was calculated by summing the instantaneous x-y displacements for successive time points relative to the mean center of pressure location and dividing this value by trial duration (30 s). We have previously found that sway-area rate is significantly correlated with force control of the hip abductors and dorsiflexors during submaximal isometric contractions in young and older adults (Davis, Allen, et al., 2020).

Statistical analysis

The influence of TENS on the distance walked during the 6-min test was evaluated by comparing the two conditions (Baseline and TENS) between two experimental visits. To minimize the influence of day-to-day variations in walking performance, we used a linear mixed model that compared the baseline performance on the two sessions. In this model, the baseline conditions and time (distance walked each minute) were set as fixed effects and variability among participants was considered a random effect. We used another linear mixed model to compare the three conditions: baseline, continuous TENS, and burst TENS.

Assumptions of linearity, homoscedasticity, and normality of residuals were assessed with residual plots, histograms, and Q-Q plots. Different models were compared with Akaike information criterion (AIC), Bayesian information criterion (BIC), and log-likelihood. The final model's fixed effects were all three conditions, time (distance walked each minute), and its random effects were the individuals. P values were derived using the Satterthwaite approximations for which type 1 error rates are reduced (Luke, 2017) and Bonferroni corrected post-hoc tests were performed to determine differences between groups within conditions and minutes.

Changes in sway-area rate during the balance tests and spatiotemporal data retrieved from the IMUs during the 6-min walk were also analyzed using similar linear mixed model and assumptions for each TENS condition and baseline. Again, conditions were set as fixed effects and participants as random effects. Data were analyzed utilizing Python (Ver. 3.11.5) with an α

value set to 0.05. The results in the text were expressed as means ± SD. Given the absence of a difference between the baseline values, the data were averaged for visualization.

RESULTS

All the participants (height = 1.70 ± 0.16 m, range: 1.50 - 2.28 m; body mass = 65 ± 11 kg, range: 52 - 91 kg) attended the two visits except for one person who was unable to attend the second visit, which was the Burst TENS condition. These missing values were replaced with the sample average for that condition. Also, one participant mistakenly received Continuous TENS during both visits and was excluded from the analysis. In total, we analyzed data on 26 trials.

The average TENS currents applied to the four muscle groups for the two TENS conditions were as follows: right anterior thigh = 21 ± 4.2 mA; left anterior thigh = 21.6 ± 4.2 mA; right tibialis anterior = 20.4 ± 3.2 mA; left tibialis anterior = 20 ± 3.6 mA.

There was no significant difference in the distance walked in each minute during the two Baseline conditions across sessions ($p < 0.57$; Table 1). The linear mixed model showed a significant effect of condition and minute separately ($p < 0.001$ for both), but no interaction between them ($p = 0.413$). To achieve the highest goodness of fit, the final model excluded the interaction effect. Post-hoc results indicated that participants walked significantly less distance during the 6-min test when TENS was applied compared with the No TENS condition at Baseline (Table 1). This main effect was significant for both TENS modes (Fig. 1; $p = 0.01$ for Continuous TENS and $p = 0.001$ for Burst TENS). Post-hoc results for the effect of time found a significant difference between the 1st and 3rd minutes ($p = 0.04$) and the 2nd and 3rd minutes ($p = 0.04$).

Table 1. The distance walked (m) during each minute of the test for the 6-min walk performed on four occasions.

Minute	**Baseline 1**	**Baseline 2**	**Continuous TENS**	**Burst TENS**
First	96.9 ± 8.7	97.1 ± 9.8	94.7 ± 9.7	94.2 ± 10.2
Second	94.5 ± 10.3	95.7 ± 10.5	94.6 ± 9.7	94.1 ± 10.4
Third	93.9 ± 10.6	95.1 ± 10.3	93.2 ± 10.1	93.3 ± 10.7
Fourth	93.8 ± 10.2	95.0 ± 10.4	93.6 ± 10.3	93.8 ± 11.2
Fifth	94.0 ± 10.6	94.6 ± 10.8	93.7 ± 10.8	93.8 ± 10.4
Sixth	94.6 ± 10.8	94.9 ± 10.8	93.3 ± 11.3	93.2 ± 10.6

Mean ± SD.

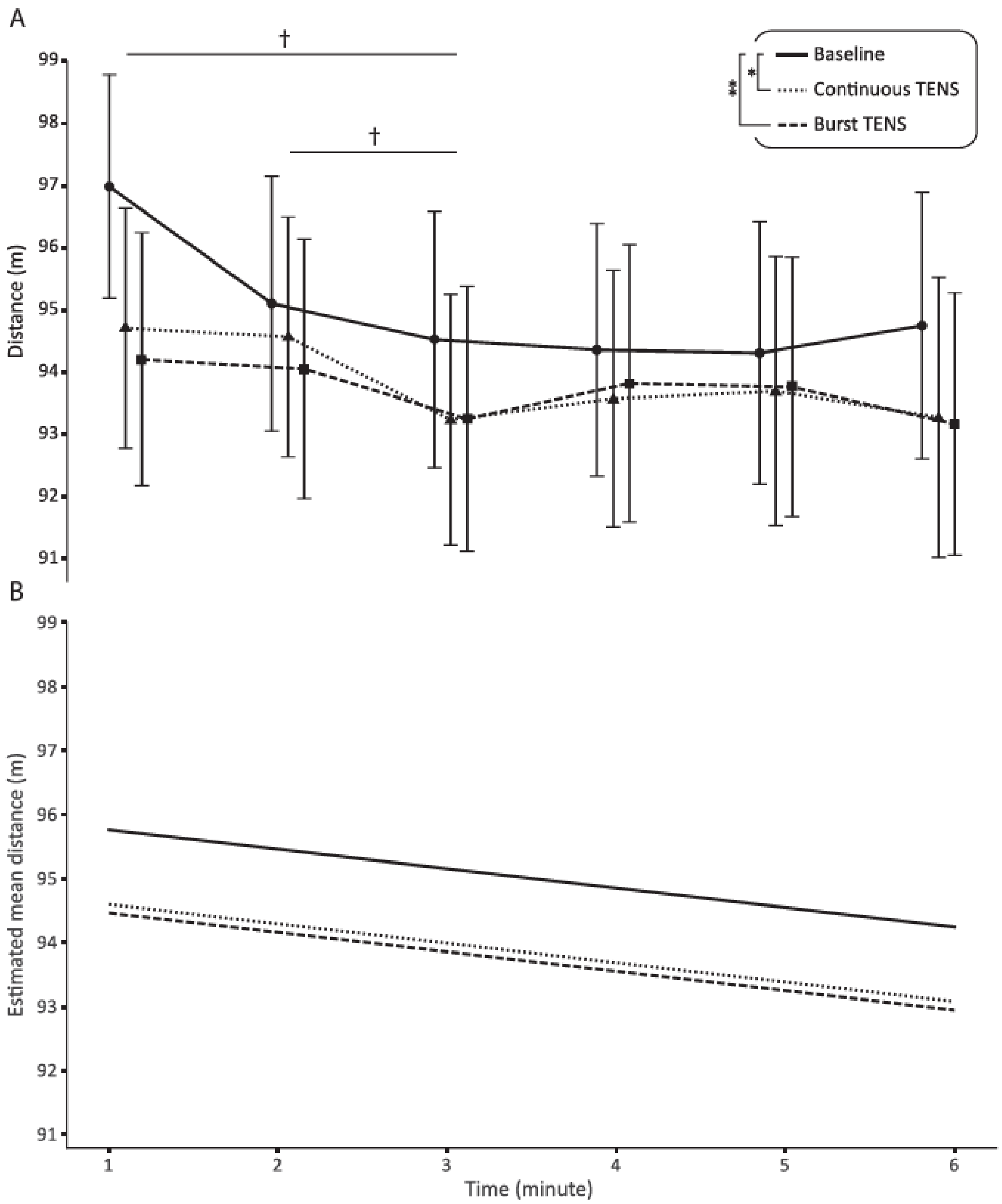

Figure 1. The 6-min walk test. (A) The absolute distance (m) walked in the 6-min test for the two Baseline and the two TENS modes. Lines connect data for the same participant. (B) The estimated mean values for the three conditions as derived from the model. * $p < 0.05$ relative to Baseline; ** $p < 0.005$ relative to Baseline; and † $p < 0.05$ between minutes.

The influence of TENS on the 6-min distance was not accompanied by significant changes in any of the kinematic measures averaged across the 6-min walk for either TENS mode. Despite the absence of significant differences for the average values, there were significant differences in the minute-by-minute values for stride length and stride frequency. These differences are summarized in Table 2, which lists the mean and coefficient of variation for stride frequency and stride length in Minutes 1 and 6 for each of the four conditions (Table 2). The mean and the coefficient of variation for stride frequency were significantly greater in Minute 1 compared with Minute 6 within each TENS mode. The changes observed for stride length comprised an increase in the coefficient of variation in Minute 1 relative to Minute 6 for both TENS modes, and a shorter mean stride length in Minute 1 during both TENS modes that was less than the Baseline value. The most consistent effect was a statistically significant reduction in the coefficient of variation for stride frequency and stride length, but this effect was observed for all three conditions (Baseline and the two TENS modes).

Table 2. Differences in stride frequency and length between Minutes 1 and 6 of the 6-min walk test and between TENS conditions relative to the preceding Baseline value. *P < 0.05 relative to Min 1. †P < 0.05 relative to Baseline.

	Baseline		**Continuous TENS**		**Baseline**		**Burst TENS**	
	Min 1	**Min 6**	**Min 1**	**Min 6**	**Min 1**	**Min 6**	**Min 1**	**Min 6**
Stride Frequency (steps/min)								
Mean	126 ± 10	123 ± 9 *	125 ± 10	122 ± 10 *	127 ± 11	124 ± 9 *	126 ± 12	124 ± 10
CoV	1.9 ± 1.1	1.39 ± 0.37 *	1.9 ± 0.7	1.5 ± 0.8 *	1.9 ± 1.3	1.54 ± 0.75 *	1.71 ± 0.72	1.42 + 0.56 *
Stride Length (m)								
Mean	1.41 ± 0.13	1.40 ± 0.13	1.37 ± 0.13 †	1.38 ± 0.14	1.40 ± 0.12	1.39 ± 0.14	1.36 ± 0.12 †	1.38 ± 0.13
CoV	2.5 ± 1.4	1.97 ± 0.56 *	2.5 ± 1.0	2.15 ± 0.78 *	2.18 ± 0.73	2.09 ± 0.94 *	2.32 ± 0.72	1.95 ± 0.57 *

Mean ± SD. CoV = Coefficient of variation. Min = minute. m = meter.

The average sway-area rate for each balance test at in the absence of TENS was the following: RO 29 ± 15 mm^2/s, RC 100 ± 55 mm^2/s, FO 75 ± 36 mm^2/s, FC 507 ± 235 mm^2/s. It is noteworthy that eight participants (6-min distance at baseline 547 ± 68 m) were not able to complete the balance condition in which they stood on a foam surface with eyes closed. There were no statistically significant changes in the sway-area rate values for any balance condition when TENS was applied concurrently to the anterior upper and lower leg muscles of both limbs.

DISCUSSION

Contrary to our hypothesis that supplementary TENS during walking would improve the walking endurance for adults aged 65 to 85 years, the main finding of our study was a significant decrease in the distance walked during the 6-min walk test during the concurrent application of TENS. Moreover, the decrease in the distance walked was similar for both TENS modes.

To obtain more information on the decrease in the distance walked during the 6-min test, we examined the distance walked in each minute of the test. There was no difference in the distance walked in each minute during the two Baseline tests, which underscores the reliability of test and suggests that the repeat performance did not elicit a significant practice effect. The distance walked in each minute decreased during the first part of the 6-min test, but similarly for all conditions; that is both Baseline tests and the two TENS modes. The decrease in distance walked was statistically significant at the third minute of the test. The decrease in the distance walked provides a measure of fatigability (Jones et al., 2020; Phan-Ba et al., 2012) that was not influenced by the application of TENS.

Supplementary sensory stimulation

As indicated in the introduction, our hypothesis was based on the findings of previous studies in which we demonstrated that the concurrent application of TENS elicited statistically significant increases in the distance walked during tests of walking endurance performed by middle-aged adults and by people with multiple sclerosis. First, Carzoli et al. (2022) found that the increase in the distance walked by the middle-aged adults during the 6-min test during application of TENS was statistically significant with large effect sizes. Moreover, the effect was greater during the application of Bursting TENS compared with Continuous TENS. Second, Almuklass et al. (2020) measured the distance walked by people with multiple sclerosis during the 6-min test with and without the concurrent application of Continuous TENS. The distance walked was significantly greater during the application of TENS with a large effect size. Third, Alenazy et al. (2021) examined the influence of nine treatment sessions with TENS (Continuous and Bursting) on the distance walked during a test of walking endurance by people with multiple sclerosis. TENS was applied to limb muscles while participants were seated in a relaxed position. The intervention elicited a statistically significant increase with a moderate effect size in the distance walked during the test of walking endurance.

There are several differences between the protocols used in these three previous studies and the one used in our current study. The key differences include stimulus intensity, stimulus mode, and the target muscles. When electrical stimulation is applied to peripheral nerves, an important feature is whether the intensity is below or above motor threshold (Enoka et al., 2020). At intensities below motor threshold, action potentials are elicited in sensory fibers and propagated into the CNS where they are distributed widely from the spinal cord up to the cerebral cortex. In addition to engaging sensory fibers that propagate signals centrally, stronger currents also evoke muscle contractions by eliciting action potentials in motor fibers. Our studies with TENS began with the premise that it could partially compensate for the decline in sensory function experienced by persons with multiple sclerosis (Hebert et al., 2011; Hilgers et al., 2013; Zackowski et al., 2009). Others have shown, for example, that intermittent electrical stimulation delivered through custom-made gloves with built-in electrodes contacting each fingertip improved four domains of sensorimotor function in patients with subacute stroke (Kattenstroth et al., 2018). This group also demonstrated that a single 45-min session of electrical stimulation improved two-point discrimination and increased the grey-matter volume of the associated somatosensory cortex (Schmidt-Wilcke et al., 2018).

Based on these findings, our approach in both healthy individuals and persons with multiple sclerosis has been to maximize the activation of sensory fibers without evoking meaningful muscle contractions. To achieve this goal, the applied TENS current has been set slightly above motor threshold to activate a spectrum of sensory fibers (Bergquist et al., 2011; Hardy et al., 2002; Moran et al., 2011; Radhakrishnan & Sluka, 2005; Walker et al., 2014). Participants typically perceive this stimulus as ≤ 5 on a 10-point discomfort scale. In our studies, motor threshold is defined as the minimal current needed to elicit observable twitches in the target muscles while a participant is seated. Subsequently, the TENS current is usually adjusted when the person stands to compensate for slight displacements of the nerve fibers relative to the stimulating electrode pads (Carzoli et al., 2022). In contrast to our previous studies, the TENS current was not adjusted in the current study when the participants went from sitting to standing, which meant that the effectiveness of the supplementary sensory feedback was likely less than that in our previous work and may explain some of the differences on the observed outcomes.

Another difference among our studies has been the influence of stimulus mode on the distance walked in the 6-min test. In our initial work, the applied TENS comprised continuous trains of monophasic pulses at a rate of 50 Hz (Almuklass et al., 2020). To minimize the depressive effects of changes in nerve excitability (Cuypers et al., 2010; John Luu et al., 2021; Tigerholm et al., 2020; Trevillion et al., 2010; Vance et al., 2014), we subsequently also examined the influence of TENS when it was applied as bursts of stimuli (Alenazy et al., 2021). In a comparison of stimulus modes, Carzoli et al. (2022) found that the distance middle-aged adults could walk during the 6-min test increased during the concurrent application of TENS and that the benefit was greater when the stimulation was applied in a Burst mode instead of the Continuous mode. In contrast, we found no statistically significant effect of stimulus mode on the 6-min walk distance of older adults in the current study. One important difference between these two studies was that the middle-aged adults performed the test by walking back-and-forth along a 60-m walkway (Carzoli et al., 2022), whereas the older adults in the current study walked around a 160-m track. The difference in venue was necessitated by our access to facilities during the Covid-19 pandemic.

Source of the impairment

Although differences in TENS intensity and mode of application may have contributed to the discrepancies in the distance walked in the 6-min test across studies, they likely do not explain the observation that the decrease in distance was uniform across the test. This finding suggests that the application of TENS reduced the ability of older adults to walk briskly. TENS can depress the responsiveness of sensory nerve fibers, as is evident by its clinical use in the management of pain. However, the hypoalgesia elicited by TEN is only present at strong intensities (Dailey et al., 2020; Vance et al., 2014). Alternatively, an over-abundance of sensory feedback, such as that elicited by the concurrent application of TENS to two sets of muscles (dorsiflexors and hip flexors) in both legs, may have compromised the ability of the older adults to incorporate critical sensory information into the control of the locomotor rhythm. For example, feedback provided by stretch receptors in the hip flexor muscles enables the switch from the stance to the swing phase during the gait cycle and feedback from load receptors in the foot modulate the amplitude of muscle activation during the stance phase (Frigon et al., 2021).

The TENS protocol used in the current study may have disrupted such signals and required the older adults to adjust their control strategy during the early part of the 6-min walk test.

Consistent with this interpretation, we found some statistically significant minute-by-minute differences in the kinematic variables. Average stride length was shorter during Minute 1 for the two TENS modes compared with the Baseline values, but there were no statistically significant differences in stride frequency for either condition or time (Table 2). In contrast, the coefficient of variation for stride length was greater during Minute 1 than Minute 6 within each TENS mode, and mean stride frequency was slower but more variable (coefficient of variation) during Minute 1 than Minute 6 within each TENS condition. These findings indicate that the older adults made some statistically significant adjustments in stride frequency and stride length when TENS was applied to their leg muscles during the 6-min walk.

One way to examine this association more closely would be to reduce the ambiguity of the sensory feedback by triggering the application of TENS with the occurrence of specific kinematic events during the gait cycle, such as foot-strike and toe-off. It has been shown, for example, that the recovery of locomotor abilities in rodents exposed to a spinal cord injury is most effective when electrical stimulation of the sensory nerves is applied during the stance phase and not during the entire gait cycle (Wenger et al., 2016). Moreover, the translation of this therapeutic approach to humans has demonstrated that the timing of the electrical stimulation during the gait cycle needs to be optimized for everyone (Rowald et al., 2022). In addition, the muscles that were targeted in our current study (dorsiflexors and hip flexors) were those that constrain walking performance in people with multiple sclerosis (Almuklass, Davis, Hamilton, Hebert, et al., 2018), whereas the performance capabilities of the calf muscles appear to be more important for older adults (Clark et al., 2013). However, one of the predictor variables that could explain mobility loss in older women over a 9-year period was the strength of the dorsiflexor muscles (Stenholm et al., 2015).

Standing balance

The decline in walking endurance during the application of TENS was not accompanied by changes in any performance metric derived from the tests of upright standing balance. This result indicates that the disturbances in sensory feedback (proprioceptive, visual, and vestibular) imposed by the balance conditions were not further compromised by the concurrent application of TENS. Although they used a slightly different balance protocol, Sadeghi-Demneh et al. (2013) also found that sub-motor threshold TENS did not influence balance when older adults stood on a firm surface with feet apart and the eyes either open or eyes closed. Similarly, Rugelj et al. (2020) found that the concurrent application of TENS to the plantar surfaces and lower posterior shanks of both legs at an intensity above sensory threshold did not influence center-of-pressure kinematics when older adults stood on a rigid surface with eyes open or closed. The absence of an effect of TENS during the eyes-closed condition in these studies is consistent with the conclusion that older adults reduce their reliance of proprioceptive feedback to control standing balance due to declines in receptor sensitivity and the integration of proprioceptive signals within the CNS (Baudry & Duchateau, 2020; Henry & Baudry, 2019; Mildren et al., 2020; Papavasileiou et al., 2022).

In support of this interpretation, the values for our measure of postural sway (sway-area rate) were greater when standing on a rigid surface with eyes closed (100 ± 55 mm2/s) compared with when standing on the foam surface with eyes open (75 ± 36 mm2/s). Davis, Allen, et al. (2020) found a similar difference (221 ± 65 mm/s2 vs. 154 ± 57 mm/s2) in a group of older adults who had large values for sway area rate. In contrast, Davis, Allen, et al. (2020) found that individuals with low values for sway area rate was similar for the two conditions (54 ± 24 mm/s2 vs. 59 ± 19 mm/s2). These data suggest that the ability of older adults to maintain balance while standing upright depends more on visual feedback than proprioceptive feedback.

Nonetheless, in a companion paper we report that logistic regression models based on force-plate and kinematic data obtained during the standing balance tasks (RO, RC, FO, and FC) were able to discriminate between older adults who were categorized and slow and fast walkers (M. S. Alenazy, Al-Jaafari, Folkesson-Dey, et al., 2023). The supplementary stimulation provided by TENS did not alter the power of the models to explain the variance in 6-min distance, which was walked at a brisk pace, but it did reduce the explanatory power for a 2-min test walked at a preferred pace. In three of the four models derived from the balance conditions (RO, RC, and FO) during which TENS was delivered concurrently, sway-area rate was the strongest discriminatory variable to the two walking-speed groups. Despite not influencing the amount of postural sway during the balance tests, the derived metrics were able to distinguish between the older adults who were classified as either slow or fast walkers.

LIMITATIONS

As mentioned in the preceding discussion, one potential limitation in our current study was the failure to adjust the intensity of the TENS stimulation when participants went from sitting to sitting, as we have done previously (Carzoli et al., 2022). However, the approach used in the current study was adequate to elicit meaningful gains in walking endurance of people with multiple sclerosis after a 3-week intervention of TENS. A more significant concern was the choice of test muscles. Although stimulation of the dorsiflexors and hip flexors has proven effective for people with multiple sclerosis, the plantar flexors may be a more effective target than the dorsiflexors for older adults (Clark et al., 2013). Moreover, studies on locomotor recovery in individuals with a spinal cord injury suggest that more attention should be paid to the timing of the TENS stimulation during the types of protocols used in our study (Gill et al., 2018; Wenger et al., 2016).

Although it is possible that the fixed order of the experimental conditions in each session with the Baseline condition being performed before the TENS modes may have confounded the results, any potential influence seems to have been minimal. The reason for this conclusion was the similarity of the distance walked in each minute of the test for the two Baseline tests and the two TENS modes. These results are s consistent with the absence of an order effect on the walking endurance of middle-aged adults when two burst modes were administered in a counterbalanced order within a single session (Carzoli et al., 2022).

Conclusions

In contrast to expectations, we found that the concurrent application of TENS to two sets of muscles in each leg reduced the distance walked by healthy older adults during the first part of the 6-min test of walking endurance. Moreover, the initial depressive influence of TENS was evident for both stimulus modes (Continuous and Burst stimulation). However, the participants were able to make adjustments that accommodated the supplementary sensory stimulation and to walk at the same average speed for much of the test. Consistent with the findings of other investigators, the concurrent application of TENS did not influence the ability of older adults to maintain standing balance during conditions that compromised the relative contributions of proprioceptive, visual, and vestibular sensory systems.

Chapter V

Temporal Variability in Stride Kinematics During the Application of TENS: A Machine Learning Analysis

Medicine and Science in Sports and Exercise 56: in press, 2024

ABSTRACT

Introduction: The purpose of our report was to use a Random Forest classification approach to predict the association between transcutaneous electrical nerve stimulation (TENS) and walking kinematics at the stride level when middle-aged and older adults performed the 6-min test of walking endurance. ***Methods***: Data from 41 participants (aged 64.6 ± 9.7 years) acquired in two previously published studies were analyzed with a Random Forest algorithm that focused on upper and lower limb, lumbar, and trunk kinematics. The four most predictive kinematic features were identified and utilized in separate models to distinguish between three walking conditions: burst TENS, continuous TENS, and control. SHAP analysis and linear mixed models were used to characterize the differences among these conditions. ***Results***: Modulation of four key kinematic features – toe-out angle, toe-off angle, and lumbar range of motion (ROM) in coronal and sagittal planes – accurately predicted walking conditions for the burst (82% accuracy) and continuous (77% accuracy) TENS conditions compared with control. Linear mixed models detected a significant difference in lumbar sagittal ROM between the TENS conditions. SHAP analysis revealed that burst TENS was positively associated with greater lumbar coronal ROM, smaller toe-off angle, and less lumbar sagittal ROM. Conversely, continuous TENS was associated with less lumbar coronal ROM and greater lumbar sagittal ROM. ***Conclusion***: Our approach identified four kinematic features at the stride level that could distinguish between the three walking conditions. These distinctions were not evident in average values across strides.

INTRODUCTION

Mobility is essential for older adults to maintain an independent lifestyle (Groessl et al., 2007; Metz, 2000; Yeom et al., 2008). It is often characterized by measures of habitual and maximal walking speed (Middleton et al., 2016; Suetta et al., 2019b). Moreover, previous findings indicate that long-distance walking tests, such as two or six-minute tests, can predict several health-related outcomes in older adults, including the risk of disability, cardiovascular disease, and mortality rate (Casanova et al., 2011; Newman et al., 2006; Vestergaard, Patel, et al., 2009). Among the physiological and psychological adaptations that decrease mobility in older adults (Beauchamp et al., 2014; Callisaya et al., 2009; Clark et al., 2013; Slobodová et al., 2022; Tiedemann et al., 2005; T. Wu & Zhao, 2021), declines in sensorimotor function seem to be critical (Lange-Maia et al., 2016; Ward et al., 2014).

One strategy that can be used to attenuate the impact of declines in sensorimotor function on mobility is to provide supplementary sensory stimulation, such as applying transcutaneous electrical nerve stimulation (TENS) during the performance of prescribed activities (Enoka et al., 2020). TENS devices pass a current between electrodes placed on the skin overlying target muscles and thereby elicit action potentials in a wide range of sensory fibers (Bergquist et al., 2011; Moran et al., 2011; Radhakrishnan & Sluka, 2005). However, there have been mixed findings on the influence of TENS on the distance walked during a six-minute test of walking endurance. In a study on middle-aged adults, Carzoli et al. (2022) found that one type of TENS (burst stimulation) increased the distance walked by an average of 16 m and another type of TENS (continuous stimulation) increased it by an average of 6 m. In contrast, two other studies (Alenazy, Al-Jaafari, Daneshgar, et al., 2023; Alenazy, Al-Jaafari, Folkesson-Dey, et al., 2023) found that the distance walked in 6 min by older adults was less during the application of TENS (both burst and continuous stimulation).

Based on average kinematic values derived from inertial measurement unit (IMU) recordings, neither study was able to identify the adjustments elicited by TENS that could explain the change in the distance walked in the six-minute test (Alenazy, Al-Jaafari, Daneshgar, et al., 2023; Carzoli et al., 2022). One explanation for these contrasting results could be the use of averaged or cumulative kinematic data, such as stride length or frequency, instead of comparing kinematic values for each stride. An alternative approach is to perform a non-linear analysis to evaluate the temporal variability across conditions (Harbourne & Stergiou, 2009; Ting et al., 2009). This can be accomplished with machine learning algorithms (Harris et al., 2021; Khera & Kumar, 2020; Kim et al., 2022; Liuzzi et al., 2023). For instance, a Random Forest algorithm can identify key predictor variables and assess their impact on the observed predictions via ensemble learning. Due to robustness against imbalanced datasets, outliers, and overfitting, this approach has been used to characterize gait conditions (Luo et al., 2020; Muñoz-Ospina et al., 2022).

The purpose of our report was to use a Random Forest classification approach to evaluate the association between TENS and walking kinematics at the stride level. The analysis was performed on kinematic data acquired during the 6-min test of walking endurance that we have published previously (Alenazy, Al-Jaafari, Daneshgar, et al., 2023; Carzoli et al., 2022). We formulated three hypotheses: 1) Both TENS conditions would be associated with common key kinematic features during six-minute walking tasks in the two cohorts (healthy middle-aged and older adults); 2) The kinematic features would be able to distinguish between the TENS and control conditions; and 3) The impact of burst TENS on walking kinematics is more distinguishable in healthy adults than that of continuous TENS.

METHODS

Participants

This report is based on previously published data (Alenazy, Al-Jaafari, Daneshgar, et al., 2023; Carzoli et al., 2022) involving 56 healthy middle-aged and older adults who performed six-minute tests of walking endurance. Because IMU data were not recorded for some participants and others experienced technical issues, the analysis was performed on data from 41 of these participants (64.6 ± 9.7 yrs; range: 43-83 yrs; 10 men). Participants were free of any self-reported neurological and walking impairments, diabetes mellitus, and abnormal sensations in the lower limbs. All participants provided informed written consent and the experimental protocols were approved by the University of Colorado Boulder (IRB #22-0072 and #19-0835) and performed in accordance with the Declaration of Helsinki.

Experimental protocol and devices

The experimental protocols were similar, but not identical, in the two studies. In one study (Alenazy, Al-Jaafari, Daneshgar, et al., 2023), participants performed the six-minute test of walking endurance while performing the control condition (electrodes attached but no current applied) or receiving either burst TENS, or continuous TENS. Two of the tests (control and either burst or continuous TENS) were performed on one day, and two on a second day (control and the other TENS condition). The order of the burst and continuous TENS conditions was counterbalanced across the days. In the other study (Carzoli et al., 2022), participants performed the walking test with the control condition and continuous TENS on one day, and then two burst TENS conditions (slow and fast) on the other day. The order of burst TENS conditions was counterbalanced across participants. The protocol for each day included a rest period of at least

30 minutes between conditions. The current report focuses on the common conditions across these protocols, extracting data from the control condition, continuous TENS, and fast burst TENS of Carzoli et al. (2022) and the first control condition, continuous TENS, and burst TENS from Alenazy, Al-Jaafari, Daneshgar, et al. (2023).

In these studies, participants wore six tri-axial Opal™ IMUs (Version 2.0, APDM Inc, Portland, OR, USA; sampling frequency 128 Hz) that were positioned over the sternum, L2/L3 region of the lower back, wrists, and feet (Figure 1A). Along with these IMUs, TENS electrodes were placed over tibialis anterior and rectus femoris muscles (Almuklass et al., 2020). The TENS devices (LG-TEC Elite, LG Med Supply, Cherry Hill, NJ, USA) were attached to the participants and connected to the electrodes (5 × 13 cm and 5 × 9 cm; Axelgaard Manufacturing, Lystrup, Denmark). The continuous TENS condition comprised monophasic rectangular pulses (200 μs) at 50 Hz, whereas the burst condition involved 5 bursts of 7 monophasic rectangular pulses (150/200 μs) each second. The TENS devices were turned off during the control condition. The TENS current was set at an intensity that was sufficient to elicit a muscle twitch, but not a functionally meaningful muscle contraction. The instruction for each six-minute test was to walk at a brisk pace either back-and-forth along a 60-m walkway (Carzoli et al., 2022) or around an oval track (Alenazy, Al-Jaafari, Daneshgar, et al., 2023).

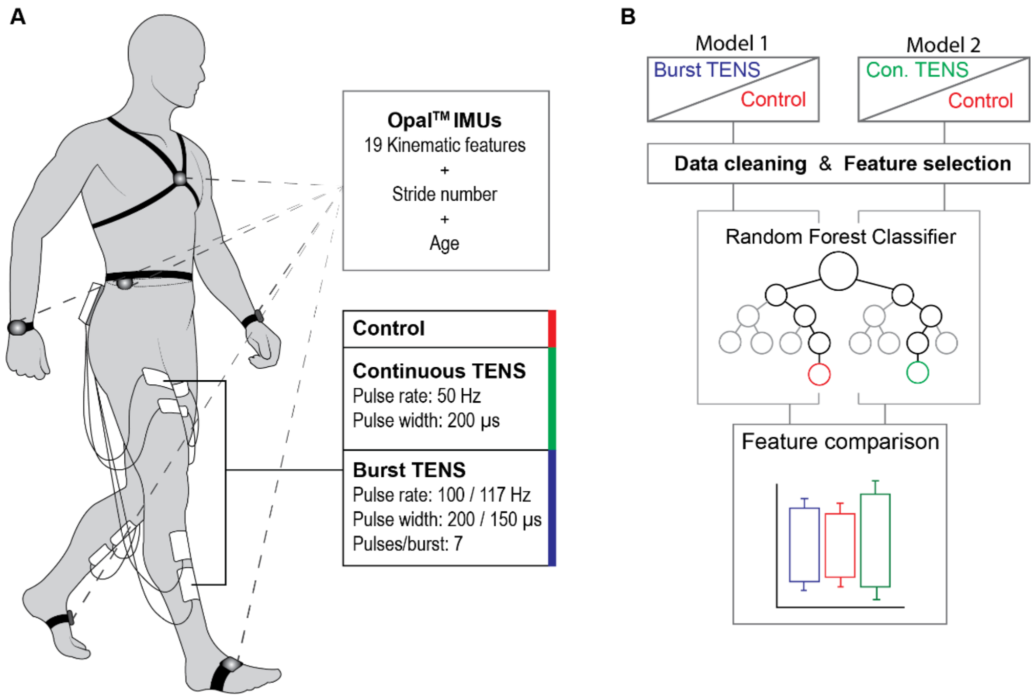

Figure 1. Setup and analysis modeling. (A) Schematic placement of the six inertial measurement units (IMUs) on feet, wrists, lower lumbar area, and chest for recording kinematic variables during each 6-min walk. The TENS devices were attached to a waistband and connected to electrodes that were placed on the anterior thigh and over tibialis anterior of both legs. The three TENS conditions are indicated in the boxes: control condition (red), continuous TENS (green), and burst TENS (blue). (B) Diagram of the schematic model. Each TENS condition (continuous or burst) was paired separately with a control condition. After data editing and feature selection for each model, two random-forest classifier algorithms were applied, and the features were compared with statistical analysis and Shapley Additive Explanations (SHAP).

Data processing

The spatiotemporal variables recorded by the IMUs during the six-minute walking tests were transmitted to a laptop and analyzed automatically by APDM's Mobility Lab (Version 2, APDM Inc, Portland, OR, USA). This system enabled the identification and analysis of successful strides. The automated processing of these kinematic measures, including their validation, was conducted using the Mobility Lab software as per the methodologies described by Morris et al. (Morris et al., 2019). In the study of Carzoli et al. (Carzoli et al., 2022), strides that included turning at the end of the 60-m walkway were identified and removed from the analysis. The average number of strides in each walking test was 350 ± 34 (average ± standard deviation) and we extracted 19 kinematic features from each stride along with stride number and age (Table 1). Because the asymmetrical measures between the left and right sides were among the least significant features, these values were averaged.

Table 1. Gait variables definition (Adapted from APDM, 2023).

Lower limb variables *	
Cadence (steps/min)	Number of steps per minute, with a step defined as the period from initial contact of one foot to the next initial contact of the other foot.
Double support (% stride time)	Percentage of stride time in which both feet are on the ground at the same time.
Stride duration (s)	Time from the initial contact of the left foot to the next contact of the left foot.
Walking speed (m/s)	Forward speed of the participant calculated from the forward distance traveled during a stride divided by stride duration.
Stance (% stride time)	Percentage of the stride in which the foot is on the ground.
Swing (% stride time)	Percentage of the stride in which the foot is not on the ground.
Circumduction (cm)	The distance that the foot travels perpendicular to the direction of forward displacement when swinging the leg forward.
Toe-off angle (degrees)	Angle of the foot at push-off. The pitch of the foot is zero when it is flat.
Toe-out angle (degrees)	Outward rotation of the foot relative to forward displacement during the stance phase.
Stride length (m)	Forward distance travelled by a foot during a stride.
Step duration (s)	Time from initial ground contact with one foot to ground contact with the other foot.
Upper limb variables *	
Swing velocity (degrees/s)	Maximal angular velocity during arm swing
Swing range of motion (degrees)	Angular displacement of arm swing
Trunk variables	
Coronal ROM (degrees)	Angular displacement of the thoracic spine in the coronal plane (roll)
Sagittal ROM (degrees)	Angular displacement of the thoracic spine in the sagittal plane (pitch)
Transverse ROM (degrees)	Angular displacement of the thoracic spine in the transverse plane (yaw)
Lumbar variables	
Coronal ROM (degrees)	Angular displacement of the lumbar spine in the coronal plane (roll)
Sagittal ROM (degrees)	Angular displacement of the lumbar spine in the sagittal plane (pitch)
Transverse ROM (degrees)	Angular displacement of the lumbar spine in the transverse plane (yaw)

* Lower and upper limb variables are calculated by averaging the left and right sides. ROM= range of motion

Data analysis

The resulting dataset comprised 40,246 strides. The primary objective of the Random Forest model was to classify the condition (Continuous TENS, burst TENS, and control) for each six-minute walking test. The dataset was organized into two subsets: one containing the control and Burst TENS conditions, and the other containing the control and Continuous TENS conditions. A Random Forest feature selection algorithm was applied to each subset separately (Figure 1B). To ensure robustness and generalizability of the feature selection procedure, the datasets were shuffled and subjected to a 10-fold cross-validation method with 70% training and 30% testing sets for each fold. The random forest feature selection algorithm was applied to the training sets for each fold separately, and the importance values of each feature were averaged across all 10 folds. The collinearity among the top-selected features was examined using Variance Inflation Factor (VIF).

The Random Forest models were optimized using GridSearchCV to find the best hyperparameters, ensuring an effective balance between model complexity and generalization ability. The hyperparameters tuned included: 1000 trees (n_estimators) to ensure comprehensive learning, Gini impurity criterion for optimal node splitting, a maximal depth (max_depth) of 10 to prevent overfitting, and the maximal number of features in each tree (max_features) set to the square root of 21, the total number of features. The datasets were grouped at the level of participant, ensuring that data from the same participant were not distributed across both the training and testing sets. The feature selection process applied within this framework identified the first four important features that were common across both datasets (Figure 2).

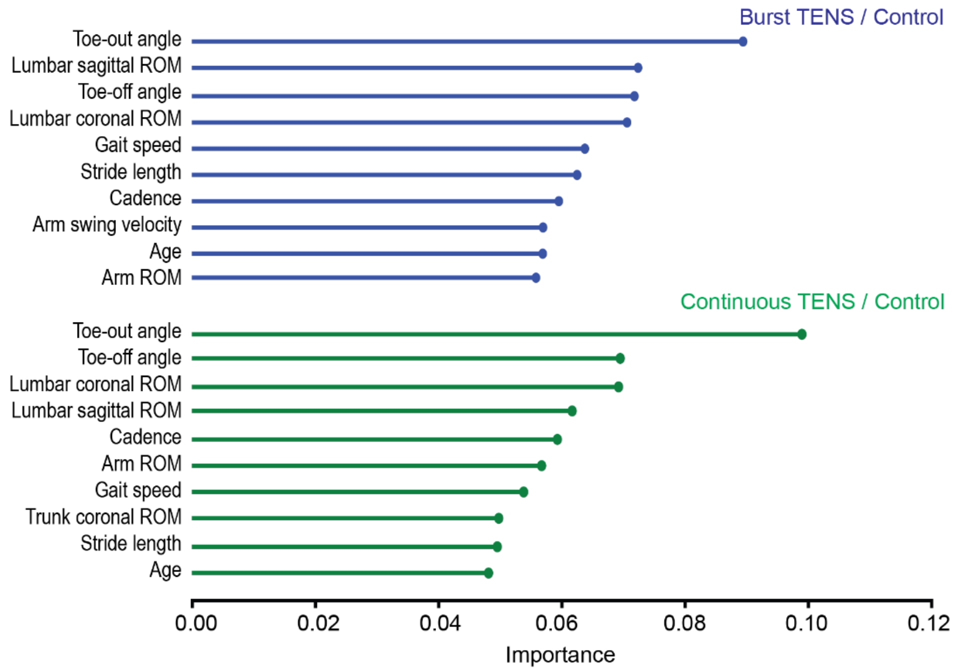

Figure 2. The most important selected features for each dataset as determined by Random Forest algorithms. The algorithm was applied separately to the burst TENS – control (blue) and continuous TENS – control (green) datasets. Data visualization was limited to the first 10 out of 21 features. The first four features were selected for each model. ROM = range of motion.

Subsequently, the models were retrained with the selected common features using the Random Forest Classifier with the same hyperparameters. Validation of both models was performed using a 10-fold cross-validation procedure. The overall performance of each model was determined by averaging the results of the ten tests. Along with performance accuracy, F1 score, and area under the curve (AUC), we report Cohen's Kappa (k) score to provide measures of agreement between the predicted and actual classifications. Interpretation of Cohen's Kappa (k) score was based on the ratings suggested by Landis and Koch (Landis & Koch, 1977): poor (0-0.2), fair (0.4-0.6), moderate (0.4-0.6), substantial (0.6-0.8), and almost perfect (0.8-10) agreement. Additionally, the sensitivity and specificity of each model were calculated using the confusion matrix generated from the performance of the test set.

To understand the individual contribution of each feature to the prediction of the model, SHAP (Shapley Additive exPlanation) analysis was conducted for each model. The SHAP framework uses game theory to assign each feature an importance value for a given prediction and provides insight into the direction and magnitude of its impact on the model output (Lundberg et al., 2020). The computed SHAP values for each model were visualized as density plots to observe the distribution and trend of its impact on the prediction of the three conditions (burst TENS, continuous TENS, and control conditions).

To evaluate the performance of hypothesis testing, four linear mixed models were applied to the identified features for each dataset. The model utilized a dataset where the features were averaged across strides during each walking test to reduce the inner variability within participants. To ensure the robustness of our models, the assumption of normality was checked by visually inspecting Q-Q plots and using the Shapiro-Wilk test on the population of each condition and the assumption of homoscedasticity was assessed by visually inspecting plots of residual vs actual values. In each of the mixed models, walking condition was included as a fixed effect, participants were set as the nested random effect within the fixed effect of condition, and intercept was set as random. When significant main effects were detected, we applied Bonferroni corrections to adjust for multiple comparisons.

All statistical tests were conducted using Python (Version 3.11), and the Random Forest algorithm and SHAP analysis were implemented using the Scikit-learn and SHAP libraries, respectively. The alpha value for all statistical tests was set at 0.05.

RESULTS

Our analysis included 26,135 strides for the burst TENS – control model and 27,684 strides for the continuous TENS – control model. The Random Forest feature-selection algorithm ranked all 21 features (19 kinematic variables, age, and stride number) in each model based on their importance for predicting the walking condition, as shown in Figure 2. The algorithm for burst TENS and control dataset showed 95% cross-validation accuracy using all 21 features. This accuracy was 92% for the continuous TENS and control dataset. In both algorithms, the features of toe-out angle, lumbar sagittal range of motion (ROM), toe-off angle, and lumbar coronal ROM were selected as the most important features. The VIF scores for the top four features (toe-out angle, toe-off angle, lumbar coronal ROM, and lumbar sagittal ROM) in the burst TENS and control model were 1.012, 1.018, 1.015, and 1.001, respectively. In the continuous TENS and control model, the VIF scores for these features were 1.009, 1.003, 1.015, and 1.02. These low VIF scores indicate minimal multicollinearity among the selected features in both models.

These four features were re-selected for the prediction models. The final Random Forest models demonstrated high prediction accuracy and substantial agreement between the predicted and actual classifications, particularly for the burst TENS – control model, which achieved an average cross-validation accuracy of 0.82 and a substantial Cohen's kappa score of 0.64. In comparison, the continuous TENS – control model showed a cross-validation accuracy of 0.77 and a moderate kappa score of 0.52. Detailed performance metrics of these two models are presented in Table 2.

Table 2. Performance and accuracy results from Random-Forest algorithms for the burst TENS – control and continuous TENS – control models. Both models comprised the first four kinematic features shown in Figure 2.

	Burst TENS – control	Continuous TENS – control
Cross-validation accuracy	0.82	0.77
Cohen's Kappa score	0.64	0.52
F1 score	0.82	0.77
Sensitivity	0.80	0.77
Specificity	0.83	0.75
Area under curve (AUC)	0.90	0.85

Linear mixed models

Linear mixed models were performed on the average data for each walking test to reduce the variability within each condition. Assumptions of normality and homoscedasticity were all visually inspected and met the criteria using Q-Q plot and residual-predicted values plots. None of the p-values for the Shapiro-Wilk test were significant. None of the main effects for condition were significant for three of the key features: lumbar coronal ROM (p-value = 0.88), toe-off angle (p-value = 0.07), and toe-out angle (p-value = 0.82). The only key feature with a significant main effect was lumbar sagittal ROM (p-value = 0.048). Bonferroni post-hoc analysis for this feature indicated a significant difference between continuous TENS and burst TENS (p-value = 0.049). Details of the values for each condition are shown in Table 3.

Table 3. Descriptive comparison of the four selected kinematic features (degrees) for the three conditions. Conditions were compared using linear mixed models. * $p < 0.05$ relative to the burst TENS condition.

Feature (degrees)	Control	Burst TENS	Continuous TENS
Lumbar coronal ROM	8.2 ± 2.3	8.3 ± 2.4	8.16 ± 2.3
Lumbar sagittal ROM	6.5 ± 1.6	6.2 ± 1.5	**6.9 ± 1.4***
Toe-off angle	40.3 ± 2.9	39.9 ± 3.0	40.0 ± 2.9
Toe-out angle	7.2 ± 4.8	6.9 ± 4.9	7.3 ± 4.7

Mean ± standard deviation. ROM = range of motion

SHAP analysis

Once the Random Forest classification models had been developed for the two datasets (burst TENS – control and continuous TENS – control), the influence of the four common kinematic features on the prediction of each model was assessed with a SHAP analysis (Figure 3). In this analysis, each data point corresponds to one stride, with the color intensity representing the magnitude of the angle, measured in degrees (°). Darker colors indicate angles with greater positive values, whereas lighter colors denote angles with lower values that may include negative angles. A positive SHAP value for a data point (stride) indicates a positive influence on predicting the presence of either TENS condition (either burst or continuous). Conversely, a negative SHAP value denotes prediction of the control condition and negative impact on prediction of the TENS condition.

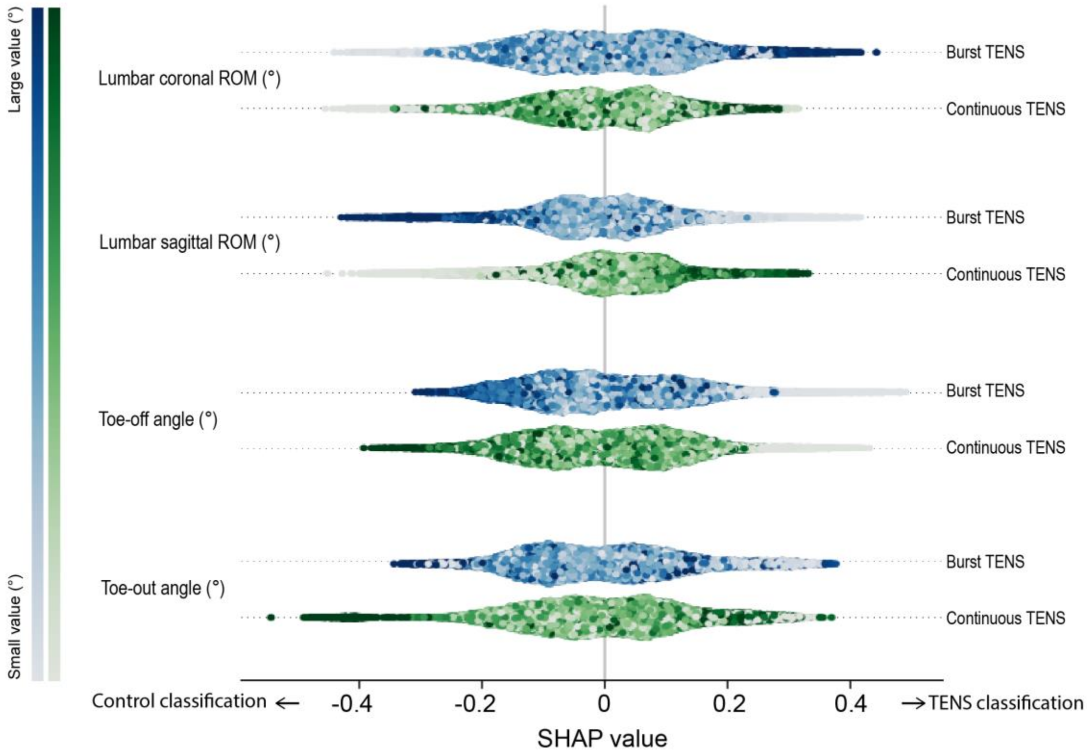

Figure 3. Density plots for SHAP values for the burst TENS (blue dots) and continuous TENS (green dots) models for the four kinematic variables. Each data point indicates a kinematic measure in one stride with 26,135 strides for the burst TENS – control condition and 27,684 strides for the continuous TENS – control condition (green color spectrum). The darkness of the color assigned to each data point qualifies the angle (º) of the selected kinematic variable in the stride. The distributions of SHAP values indicate that the influence of the feature on model prediction tends to be centered around the average SHAP value. Positive SHAP values denote a positive influence of the feature on the prediction of the TENS condition, whereas negative SHAP values represent a positive influence of the feature on the prediction of the control condition.

Visual inspection of the features and SHAP values indicates the relative influence of the stride-level variables on the model predictions (Figure 3). For example, in the burst TENS and control model (blue diagrams), a greater lumbar ROM in the coronal plane tends to predict the burst TENS condition, whereas a greater lumbar ROM in the sagittal plane and toe-off angle are more predictive of the control condition. Similarly, a larger lumbar ROM in the sagittal plane also predicts the continuous TENS condition and the larger the toe-off angles were associated with the control condition. The data for the toe-out angle was more mixed and did not show consistent predictions.

DISCUSSION

The main finding of our study was that the application of burst and continuous transcutaneous electrical nerve stimulation (TENS) to selected leg muscles of middle-aged and older adults during a test of walking endurance mainly influenced with four kinematic variables at the stride level. Differences in these variables were able to distinguish between the TENS and control conditions. Moreover, the association between burst TENS and the kinematic variables was stronger than that of continuous TENS.

Model performance and feature selection

Our analytical approach focused on walking kinematics at the level of individual strides. The kinematic data acquired during the burst TENS, continuous TENS, and control conditions were analyzed with a Random Forest algorithm to develop models that could predict the experimental condition. Each model was derived from one TENS condition (burst or continuous) and a control condition.

In both prediction models, four common kinematic variables were identified as the most important features: Two related to the foot (toe-off and toe-out angles) and two to the lower trunk (lumbar ROM in the coronal and sagittal planes). These features were consistent predictors across both age groups (middle-aged and older adults). Three of these variables (toe-off angles, toe-out angles, and lumbar ROM in the sagittal plane) were previously selected by Swanson and Fling as main determinants in discriminating fast walking patterns between middle-aged and older adults (Swanson & Fling, 2021). In contrast to our finding, the studies on middle-aged

(Carzoli et al., 2022) and older adults (Alenazy, Al-Jaafari, Daneshgar, et al., 2023) from which our data were derived, used walking distance as the primary outcome and reported opposing results for the two groups of participants. One of the limitations in these previous studies was the measurement of walking distance from cumulative and averaged stride lengths. Similar to our approach, the study on middle-aged adults found that toe-off angle was the only significant predictor of the increase in stride length and stride frequency when TENS increased average walking speed. In contrast, the most consistent adjustment associated with the decrease in 6-min distance experienced by older adults during the application of TENS was a reduction in the coefficient of variation in the minute-by-minute values for stride frequency and stride length. Our approach was to focus on this variability at a finer resolution: that is, a stride-level analysis.

The effectiveness of our model was particularly evident in the burst TENS condition, demonstrating higher sensitivity, specificity, AUC, cross-validation accuracy, F1 score, and substantial Cohen's Kappa score compared with the continuous TENS condition. This result is consistent with that for the study on middle-aged adults (Carzoli et al., 2022) but not older adults (Alenazy, Al-Jaafari, Daneshgar, et al., 2023). The superior benefit elicited by burst TENS, when it has been detected, is attributed to a reduction in the desensitization of the activated intramuscular axons to the applied electrical current (Almuklass et al., 2020).

Kinematic features and TENS

Our study examined four key kinematic features with a SHAP analysis and linear mixed models. SHAP analysis assigns a prediction score to each key feature within individual strides. Positive scores indicate a greater likelihood of the stride occurring within a TENS condition, whereas negative scores suggest an association with the control condition. Although the average score across all strides is a common measure in SHAP analysis, it was not reported in this study due to the uneven number of strides in each condition, which could skew the average value and bias the interpretation. However, most of our SHAP results revealed clear trends that identify those kinematic features most associated with the application of TENS.

In our study, linear mixed models were used to reduce variability within each task, focusing primarily on exploring linear associations. The nonsignificant findings from this type of analysis indicate its limitations in capturing only linear relations and the conventional approach of hypothesis testing. Moreover, linear mixed models were unable to compare conditions in the stride level due to the non-normal distribution and heteroscedasticity. In contrast, machine learning can identify relatively subtle but meaningful changes in variables regardless of their adjustments with linearity, normality, and homoscedasticity. For example, a SHAP analysis can provide a more complete evaluation of the adjustments in the kinematic variables during the application of TENS.

The Random Forest algorithm identified the toe-out angle as a significant kinematic predictor of walking conditions. Although the SHAP analysis did not show clear trends for this variable (Figure 3), data from Table 3 suggest that the continuous TENS condition was associated with a greater toe-out angle compared with the control condition. This trend was reversed during the burst TENS condition. These differential changes in toe-out angle were accompanied by adjustments in the lumbar ROM in both the coronal and sagittal planes. The burst TENS condition was characterized by smaller toe-out angles and greater lumbar ROM in the coronal plane. Conversely, the continuous TENS condition involved greater toe-out angles and lumbar ROM in the sagittal plane. The concurrent adjustments in lumbar ROM and toe-out angle indicate that the supplementary sensory feedback elicited by TENS altered the activation of the muscles that control these actions. Perhaps the adjustments in hip-muscle activity modulate toe-out angle, as has been demonstrated in studies on lateral balance stability (Afschrift et al., 2019; Rogers & Mille, 2003). Such changes could disturb walking stability, which might cause individuals to reduce walking speed to maintain balance (Alenazy, Al-Jaafari, Daneshgar, et al., 2023; Kongsuk et al., 2019; Menz et al., 2003). This change in balance during the walking task may explain the slower walking speeds observed in older adults due to their balance confidence (Alenazy, Al-Jaafari, Daneshgar, et al., 2023) than middle-aged adults (Carzoli et al., 2022).

The differential effects of the two TENS modes on lumbar ROM in the coronal and sagittal planes are difficult to explain. The greater benefits elicited by burst TENS are usually attributed to the reduction in responsiveness of intramuscular axons during prolonged high-frequency stimulation (Cuypers et al., 2013; Kiernan et al., 2004; Noto et al., 2011). The effect we observed cannot have been caused by differences in the applied current because the influence of TENS mode was evident in the data from two studies that used slightly different currents, but the applied current was similar for both modes. We are unable to explain why one of the variables that could distinguish between the continuous TENS and control conditions were lumbar ROM in the coronal plane, whereas the lumbar variable that distinguished the burst TENS from the control condition was ROM in the sagittal plane. This effect suggests that the adjustments elicited by the two TENS modes were more involved than simply modulating the responsiveness of intramuscular axons.

The model also highlighted the toe-off angle as an important kinematic predictor. Data from figure 3 and Table 3 reveal a larger toe-off angle in the control condition than TENS conditions. This aligns with previous studies in which the application of electrical stimulations at intensities close to motor threshold augments sensory feedback and motor performance in both healthy individuals (Almuklass et al., 2020; Carzoli et al., 2022) and those with neurological conditions

(Celnik et al., 2007; Rejc et al., 2017; Tyson et al., 2013). The application of TENS in stride kinematics can involve an increase in the hip flexion torque (Almuklass et al., 2020; Carzoli et al., 2022), which could decrease the propulsion force (Ohtsu et al., 2023), plantar flexion force (Neptune & Sasaki, 2005) during the stance-to-swing transition, and consequently reduce toe-off angle.

LIMITATIONS

Our dataset comprised a greater number of women than men, a factor we did not explore within our models. This sex difference may have influenced the results and limit the generalizability of our findings. Also, we did not investigate the potential kinematic consequences of differences in the location of TENS electrodes, which is an issue that should be addressed in a more systematic investigation. For example, the functional capabilities of the plantar flexor muscles are likely a greater limiting factor in constraining walking speed of older adults than are the dorsiflexor muscles (Clark et al., 2013). Moreover, the timing of the supplementary sensory feedback (TENS) was not gated by specific kinematic events, which can limit its effectiveness (Rowald et al., 2022).

CONCLUSION

The impact of burst and continuous TENS on walking kinematics during a six-minute test in healthy middle-aged and older adults was strongly correlated with four common kinematic variables. The significance of these variables was only evident with a machine-learning approach that examined the data with a stride-level analysis and not those that compared average values.

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