Resistance training reduces force tremor and improves manual dexterity in older individuals with Essential Tremor

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ABSTRACT

Background. Although symptoms of Essential Tremor (ET) are typically controlled with medication, it is of interest to explore additional therapies to assist with functionality. The purpose of this study was to determine if a generalized upper-limb resistance training (RT) program improves manual dexterity and reduces force tremor in older individuals with ET.

Methods. Ten Essential Tremor and 9 controls were recruited into a dual group, pretest-posttest intervention study. Participants performed 6-weeks of upper-limb RT, and battery of manual dexterity and isometric force tremor assessments were performed before and after the RT to determine the benefits of the program.

Results. The 6-week, high load, RT program produced strength increases in each limb for the ET and healthy older group. These changes in strength aligned with improvements in manual dexterity and tremor- most notably for the ET group. The least affected limb and the most affected limb exhibited similar improvements in functional assessments of manual dexterity, whereas reductions in force tremor amplitude following the RT program were restricted to the most affected limb of the ET group.

Conclusions. These findings suggest that generalized upper limb RT program has the potential to improve aspects of manual dexterity and reduce force tremor in older ET patients.

Key words: Force tremor; upper limb; isometric contraction.

INTRODUCTION

Essential Tremor is the most common progressive neurological disorders in older adults, affecting approximately 4% of people age 40 years and over, and up to 14% of people over 65 years (Louis et al., 1996; Dogu et al., 2003). ET is commonly characterized by increased kinetic, intention, and sometimes postural tremor compared to age-matched peers which often result in serious functional limitations and decreased quality of life (Louis, 2005; Benito-Leon & Louis, 2006). While symptoms may be partially controlled with medication, positive effects may only be seen in ~50% of patients, with this number declining over time as patients become desensitised to the medication (Lyons et al., 2003; Louis, 2005).

Although the pathophysiology of ET is not well understood, ageing is consistently associated with increased prevalence and incidence rates (Benito-Leon & Louis, 2006). As such, interventions that reduce tremor and improve upper limb function in healthy older populations may also be beneficial to individuals with ET. In healthy older adults, resistance training (RT) can significantly reduce postural tremor amplitude (Keogh, Morrison & Barrett, 2010) and reduce digit force variability (Keen, Yue & Enoka, 1994; Laidlaw et al., 1999; Keogh, Morrison & Barrett, 2007). Given that RT-related improvements in minimizing force variability is potentially scaled, where the greatest amount of improvement in older individuals occurs for those with the largest amount of variability (Tracy & Enoka, 2006), RT may provide considerable benefit to older individuals with ET who typically have one limb which is more affected with tremor than the other.

Surprisingly, only two studies have examined the effect of RT on older individuals with ET. The first study by Bilodeau and colleagues (Bilodeau et al., 2000) revealed that a 4-week high-load (and not low-load) training program of isometric index finger abduction exercises was able to improve the ability to maintain steady abduction forces of that same index finger.

These findings were, in part, due to the resultant increase in strength, whereby the ET patients improved their ability to maintain steady state abductions at the same absolute intensity pre- to post-training (i.e. lower relative load post training). Interestingly, while training the small hand muscle improved finger abduction force steadiness in ET subjects, there were no improvements in postural tremor amplitude, activities of daily living, or functional tasks such as controlled water pouring and drawing Archimedes spirals. These results reflect task-specificity associated with training a single muscle, and it may be possible that more widespread changes in upper limb function would have occurred with a more generalized RT program.

A second study by Sequeira and colleagues (Sequeira, Keogh & Kavanagh, 2012) employed a 6-week high-load RT program that separately exercised muscles of each forearm and upper arm, with the goal of increasing overall upper-limb strength in a group of individuals with ET. Manual dexterity was assessed with the Purdue Pegboard Test (PPT) and significant improvements were identified following RT when ET subjects used individual limbs to perform the test. Of particular interest was that the greatest improvements in manual dexterity occurred for the most affected limb, whereby ET patients had a 15% improvement in PPT scores compared to 10% improvement for the least affected limb. Given that ET is an asymmetric disorder, and this study identified improvements by exercising each limb individually, there may be benefits in targeting each limb so that the greatest outcome may be derived for the most affected limb. Collectively, the works of Bilodeau (Bilodeau, Keen et al., 2000) and Sequeira (Sequeira, Keogh et al., 2012) illustrate that RT has the potential to reduce tremor and improve hand function in individuals with ET. However it is currently not clear if 1) RT simply reduces age-related tremor instead of targeting symptoms of ET, or if 2) RT causes improvements across a spectrum of functional tasks that individuals are exposed to on a daily basis.

The purpose of this study was to determine if a 6-week upper-limb RT program improves manual dexterity and reduces force tremor in older individuals with ET. This is the first study to combine a battery of clinical assessments that are representative of real-world tasks, and laboratory-based assessments of force tremor, to determine if a generalized RT program has a positive effect on movement in individuals with ET. It was hypothesised that following the RT program both the ET and healthy older group would exhibit improved manual dexterity and reduced force tremor. It was also hypothesised that changes in manual dexterity and force tremor would be greater in the ET group compared to the control group, indicating that RT alleviates symptoms of ET rather than just declines in motor control due to the ageing process.

METHODS

Subjects

Ten ET and 9 controls were recruited to participate in the study (Table 1). ET participants had to be 60 years or over with a diagnosis for at least one year that was confirmed by a Neurologist. ET participants were excluded if they had osteoarthritis, a recent history (< 3 years) of upper limb musculoskeletal injury, or any history of upper limb surgery.

Participants remained on any prescribed medications throughout the study, and no changes in dosage occurred throughout the training period. The revised Washington Heights-Inwood Genetic Study of Essential Tremor (WHIGET) tremor rating scale was used to determine tremor severity during screening (scale of 0-4). No participant had a formal history of RT, and all participants abstained from alcohol and caffeine at least 4 hours prior to any testing. All procedures were approved by the Institutional Human Research Ethic Committee and written informed consent was obtained from all subjects prior to participation.

< insert Table 1 about here >

Experiment design

The current study was a dual group, pretest-posttest intervention design. ET and control participants performed 6-weeks of RT, and assessments of manual dexterity and force tremor were performed immediately before and after the 6-week exercise intervention.

Resistance training protocol

Three exercises formed the basis of the protocol: bicep curl, wrist flexion and wrist extension. All exercises in this study were performed using dumbbells, and each exercise was performed separately for each limb (Keogh, Morrison et al., 2007). Every training session was supervised by an Accredited Exercise Physiologist and exercise sessions were performed twice a week with a minimum of 48 hours between sessions.

Prior to commencing the training study, a determination of 5 repetition maximum (5RM) was performed as a measure of maximum strength for each exercise. Before the 5RM assessments, all participants performed a 5 min warm up consisting of static stretches and unloaded dynamic movements of the wrist, elbow and shoulders. Stretches and dynamic movements were performed through the joint's full range of movement, and care was taken to avoid harm or excessive discomfort. The same warm up was used prior to each training session throughout the 6-week period.

The first set for each exercise performed in the training sessions used a load corresponding to 40-50% of the participant's 5RM. The final three sets, separated by rest periods of 2-3 min, used loads that could only be lifted for 8-10 repetitions (Keogh, Morrison et al., 2010). The number of sets and repetitions, as well as the length of the rest periods between sets, was consistent with recent position statements by the American College of Sports Medicine on the optimal exercise prescription for improving functional performance in older adults (ACSM. et al., 2009). Once the subject could perform 10 repetitions in each set of a particular exercise, the load for that exercise was increased by ~1 kg for the next session (Keogh, Morrison et al., 2010). Training sessions were typically 45-55 min in duration.

Functional assessment

Four clinical tests of upper limb function and manual dexterity were employed in the current study (for a review of tests see: (Yancosek & Howell, 2009)). The Purdue Pegboard Test (PPT) assessed fine manual dexterity by placing a maximum number of small pins (diameter 2.5 mm) in a vertical column on a board within a 30 s period. The Nine-hole Peg test (9HPT) is a timed measure of manual dexterity where nine larger wooden pegs (diameter 10 mm) were inserted into a board and then removed as fast as possible. Ten objects were used in a timed Modified-Moberg pick up test (MMT) which was performed with eyes open, eyes closed, and eyes closed while naming each object being manipulated. An additional MMT test was performed where tweezers were used to pick up 5 objects, thus requiring a greater level of fine motor control compared to using the fingers alone. Two subtests of the Modified-Jebsen Hand Function test (MJHFT) were used to assess activities common to everyday life. Page turning was simulated by flipping over 5 playing cards that were spaced 25 mm apart on a table, and eating activities were simulated by picking up 5 kidney beans spaced 25 mm

apart with a spoon, and placing each bean in a cup held with the opposite hand. Prior to all functional tests participants were given ~ 3 min of familiarization, and no participant indicated that they needed additional time to familiarize themselves.

Force tremor assessment

Force tremor was quantified as variability in index finger abduction force during two submaximal, isometric contractions (10% and 60% MVC). The palmar surface of the hand was placed flat on a custom-designed device that measured index finger abduction force (Kenway, Bisset & Kavanagh, 2014). Abduction force was measured at the proximal interphalangeal joint of the index fingers with a Ultra Precision Mini Load Cell (Transducer Techniques, MDB-5). Force data was collected at 1000 Hz using Spike2 software (Cambridge Electronic Design), where three 15 s trials were collected for the most affected limb and the least affected limb for the 10% MVC and 60% MVC isometric contractions. Prior to experimental testing, maximum voluntary contraction (MVC) was determined using the same apparatus, but with Applied Measurements Xtran load cells with a range of 250 N to accommodate for the larger forces associated with maximal contractions (Kenway, Bisset et al., 2014; Kenway, Bisset & Kavanagh, 2015).

Visual feedback was kept consistent between-subjects and from pre-training to post-training for all force tremor assessments. The target force was provided as a black horizontal line, and the abduction force exerted by the subject was displayed as a progressing green line. For all trials the target line was projected in the centre of a $4\text{ cm}\cdot\text{s}^{-1}$ scrolling plot on a 50 x 28 cm PC monitor. The scaling of the y-axis was adjusted for each subject and condition so that the same relative information was displayed pre- to post-training. A short familiarization period

of ~ 5 min occurred prior to force tremor assessment so that subjects were familiar with performing 10% MVC and 60% MVC isometric contractions.

Finger abduction force was low-pass filtered with a 4th order Butterworth filter set with a cut-off frequency of 40 Hz. Absolute tremor amplitude was quantified using the standard deviation (SD) of force. As tremor amplitude is influenced by the magnitude of force being generated, the coefficient of variation (CV) of force was calculated to provide a normalized measure of force tremor. Force data were examined in the frequency domain using Welch's averaged periodogram method (frequency resolution: 0.130 Hz). The peak power, normalized peak power (the proportion that peak power comprises of the total signal power), and the frequency of peak power were extracted from the power spectra between 0-4 Hz and 4-12 Hz. The lower frequency bandwidth was chosen as activity in this band reflects isometric force control in response to visual feedback. Alternatively, the higher frequency bandwidth is able to capture the power and frequency content commonly associated with tremor in ET and healthy individuals. All data analysis was performing using custom designed Matlab software (R2011b, Mathworks).

Statistical analysis

As the control group was free from pathological tremor, we matched limbs by exploiting the fact that even in a healthy older group there will be one limb with greater tremor amplitude. From the time-domain force tremor analysis of the healthy older group, the limb with the greater amplitude was identified and matched to the most affected limb in the ET group.

Given that ET tremor-related dependent variables are typically skewed (Elble et al., 2006; Heroux, Pari & Norman, 2009; Budini et al., 2014), and there may be responders and non-responders to stimuli in short-term RT intervention studies (Sequeira, Keogh et al., 2012), improvements (or declines) due to the 6-week RT program were determined with Wilcoxon sign-ranked tests. These tests examined the change in pre- and post-RT data, and determined if 5RM, functional assessments, and force tremor assessments, significantly improved due to RT. A two-way repeated measures ANOVA was then used to examine main and interaction effects of group (ET, healthy older) and limb (most affected, least affected) for changes in 5RM and functional assessment tasks. In the event of identifying an interaction effect, Tukey's HSD multiple comparison tests were used to determine if the intervention preferentially affected either group or limb. A three-way ANOVA was used to examine main and interaction effects of group, limb, and contraction intensity (10% and 60% MVC) for force tremor measurements. Once again, this analysis was performed on pre- to post-RT changescores and Tukey's HSD multiple comparison tests were used in the event of a significant interaction. Statistical analyses were performed using SAS 9.3 (SAS Institute Inc.) and the level of significance was set at 0.05.

RESULTS

Strength

5RM prior to resistance training

A main effect of group ($F(1, 109) = 17.04, p < 0.001$) was identified for 5RM values prior to undertaking the RT protocol, where the ET group had a greater overall 5RM (4.4 ± 1.6 kg) compared to the healthy older group (3.6 ± 1.2 kg). A group by muscle by limb interaction

was identified for pre-RT measures ($F(11, 102) = 3.62, p < 0.001$), where 5RM bicep curl for the ET group was greater than the healthy older group for the most affected ($F(1, 102) = 3.96, p = 0.049$) and least affected limbs ($F(1, 102) = 3.99, p = 0.048$, Figure 1a). Furthermore, 5RM bicep curl was significantly greater than 5RM wrist extension for the ET group's most affected ($F(1, 102) = 3.95, p = 0.049$) and least affected limbs ($F(1, 102) = 5.30, p = 0.023$).

< insert Figure 1 about here >

Change in 5RM due to resistance training

Wilcoxon sign-ranked tests revealed the 6-week RT program caused significant improvements in bicep curl, wrist extension and wrist flexion 5RM for each limb of each group (all p 's < 0.02 , figure 1b). A main effect of group was identified ($F(1, 109) = 9.27, p = 0.002$) where the overall change in 5RM for the ET group ($67 \pm 39\%$) was greater than the improvement in 5RM for the healthy older group ($42 \pm 32\%$). No group by muscle by limb interaction was identified for changes in 5RM due to RT.

Functional assessments

Nine-hole Peg test and Purdue Pegboard Test

Wilcoxon sign-ranked tests revealed that significant improvements occurred in the 9HPT for the most affected limb ($W = 22.5, p = 0.019$) and the least affected limb ($W = 24.5, p = 0.009$) for the ET group (table 2). The PPT used smaller pegs and yielded similar results for the ET group, where the number of pegs completed in 30 s improved for the most affected limb ($W =$

14, $p = 0.012$), the least affected limb ($W = 22.5$, $p = 0.004$), and also when using both limbs to perform the test ($W = 21.5$, $p = 0.008$). The healthy older group only exhibited significant improvements for the PPT, where a greater number of pegs could be completed in 30 s for their equivalent most affected limb ($W = 18$, $p = 0.008$) and least affected limb ($W = 16$, $p = 0.031$), as well as when both limbs were used ($W = 10.5$, $p = 0.039$). Despite a range of improvements being detected for each group in the 9HPT and PPT following the 6-week RT program, no main or interaction effects were identified between groups or limbs.

< insert Table 2 about here >

Modified-Moberg Test

Similar to the pegboard-based functional assessments, RT had a positive impact on the manual dexterity tasks in the MMT- most notably for the ET group. Improvements occurred in the ET group for the most affected limb ($W = 17.5$, $p = 0.039$) and the least affected limb ($W = 21.5$, $p = 0.008$) when performing tasks with the eyes closed. Similar improvements were also observed when the eyes were closed and naming objects when manipulating objects with the most affected limb ($W = 21.5$, $p = 0.008$) and least affected limb ($W = 19.5$, $p = 0.019$). When manipulating objects with tweezers, the ET group had significant improvements for the most affected limb ($W = 16.5$, $p = 0.049$) and the least affected limb ($W = 19.5$, $p = 0.019$). For the MMT, the healthy older group improved following the RT program for the most affected ($W = 17$, $p = 0.025$) and least affected limb ($W = 17.5$, $p = 0.015$) when performing tasks with eyes opened. Once again, no main or interaction effects were identified between groups or limbs for the MMT.

Modified-Jebsen Hand Function test

Changes in manual dexterity emerged in the spoon control task component of the MJHFT, where improvements occurred for the most affected limb for the ET group ($W = 22.5, p = 0.031$) and the healthy older group ($W = 15, p = 0.039$) following RT. Only the ET group exhibited improvements for the least affected limb when demonstrating spoon control ($W = 21.5, p = 0.007$). This task also produced a significant interaction effect ($F(3, 34) = 2.58, p = 0.048$), where improvement in the time-to-complete the task was greater for the ET group's least affected limb compared to the corresponding limb in the older group following RT ($F(1, 34) = 7.37, p = 0.011$).

Tremor amplitude assessment

SD of force

Representative tremor data for an ET participant performing the 10% MVC and 60% MVC task is presented in Figure 2. Wilcoxon sign-ranked testing revealed that the ET group exhibited improvements in SD of force during the 60% MVC contraction for the most affected ($W = 27.5, p = 0.002$) and least affected limbs ($W = 19, p = 0.046$, Figure 3a).

< insert Figures 2 and 3 about here >

A main effect of group was detected ($F(1, 72) = 5.65, p = 0.021$) where SD of force reduced to a greater extent for the ET group (0.09 ± 0.11 N) compared to the healthy older group (0.01 ± 0.12 N). A main effect of intensity ($F(1, 72) = 7.21, p = 0.009$) indicated that the

reduced SD of force was greater for the 60% MVC condition (0.091 ± 0.201 N) compared to the 10% MVC condition (0.004 ± 0.051 N) for the ET group (Figure 3a).

A group by limb by intensity interaction was identified ($F(7, 68) = 3.01, p = 0.008$), and planned contrasts revealed that the ET group had greater improvements in SD of force than the healthy older group for the most affected limb when contracting at 60% MVC ($F(1,68) = 7.76, p = 0.007$, Figure 3a). Furthermore, improvements in SD were significantly greater for the most affected limb at 60% MVC compared to the most affected limb at 10% MVC for the ET group ($F(1,68) = 10.62, p = 0.002$).

CV of force

When SD of force was normalized to the amplitude of contraction, the ET group exhibited significant improvements following the RT program for the most affected limb at the 10% MVC intensity ($W = 23.5, p = 0.013$, Figure 3b). The ET group also had significant improvements at 60% MVC for both the most affected ($W = 25.5, p = 0.005$) and least affected ($W = 25.5, p = 0.005$) limbs.

A main effect of group was identified ($F(1, 72) = 8.28, p = 0.006$), where CV of force reduced to a greater extent for the ET group (2.6 ± 4.8) compared to the healthy older group (0.25 ± 1.1).

A group by limb by intensity interaction was identified ($F(7, 68) = 2.22, p = 0.043$), where planned contrasts revealed greater improvements in CV of force for the ET group than the healthy older group for the most affected limb when contracting at 10% MVC ($F(1, 68) = 7.81, p = 0.007$, Figure 3b). Furthermore, improvements in CV were significantly greater for the most affected limb at 10% MVC compared to the most affected limb at 60% MVC for the ET group ($F(1,68) = 4.64, p = 0.035$).

Oscillatory content of force tremor

RT did not significantly affect the power spectral content for the control group or the frequency of oscillations in the ET group. The primary frequency component in the 0-4 Hz bandwidth for the ET group was 0.55 ± 0.20 Hz for the most affected limb and 0.60 ± 0.21 Hz for the least affected limb. The main frequency component between 4-12 Hz for the ET group was 5.45 ± 0.97 Hz for the most affected limb and 5.65 ± 0.77 Hz for the least affected limb.

0-4 Hz and 4-12 Hz absolute peak power

The ET group's most affected limb exhibited reductions in the 0-4 Hz peak amplitude ($W = 19, p = 0.040$) and 4-12 Hz peak amplitude ($W = 19, p = 0.046$) during the 60% MVC contraction.

< insert Figure 4 about here >

A main effect of intensity ($F(1, 72) = 7.10, p = 0.010$) indicated that the change in absolute peak power was greater for the 60% MVC condition ($0.039 \pm 0.059 \text{ N}^2$) compared to the 10% MVC condition for the 0-4 Hz bandwidth ($0.006 \pm 0.009 \text{ N}^2$).

A group by limb by intensity interaction was identified for the change in absolute peak power in the 0-4 Hz ($F(7, 68) = 3.67, p = 0.009$) and 4-12 Hz bandwidths ($F(7, 68) = 5.22, p = 0.001$). Planned contrasts revealed that the ET group had greater improvements for absolute

peak power than the healthy older group for the most affected limb when contracting at 60% MVC in both the 0-4 Hz ($F(1,68) = 6.35, p = 0.011$) and 4-12 Hz bandwidths ($F(1,68) = 10.86, p < 0.001$, Figures 4a and b). Furthermore, improvements in absolute peak power were significantly greater for the most affected limb at 60% MVC compared to the most affected limb at 10% MVC in the ET group's 0-4 Hz ($F(1,68) = 8.67, p < 0.001$) and 4-12 Hz bandwidths ($F(1,68) = 7.99, p = 0.006$).

0-4 Hz and 4-12 Hz normalized peak power

When peak power in each bandwidth was normalized to the total signal power, the ET group exhibited significant improvements following the RT program for the most affected limb at the 10% MVC intensity ($W = 23, p = 0.009$).

A group by limb by intensity interaction was identified ($(F(7, 68) = 5.02, p = 0.001)$), where planned contrasts revealed a greater change in normalized peak power for the ET group than the healthy older group for the most affected limb when contracting at 10% MVC ($F(1,68) = 6.14, p = 0.012$, Figure 4d). Furthermore, changes in normalized peak power were significantly greater for the most affected limb at 10% MVC compared to the most affected limb at 60% MVC for the ET group ($F(1,68) = 6.09, p = 0.009$).

DISCUSSION

The results of this study suggest that undertaking a generalized upper limb RT program can improve aspects of manual dexterity and reduce force tremor in older ET patients. The least affected limb and the most affected limb for the ET group exhibited similar improvements in functional assessments of manual dexterity following the RT program. The RT intervention

also had a positive effect on function in the healthy older group, albeit to a slightly lesser extent. When force tremor was examined under controlled conditions, reductions in tremor amplitude occurred following the RT program. These improvements were restricted to the most affected limb of the ET group and were, in part, mediated by a reduction in the ~5.5 Hz frequency component of ET force tremor.

Improvements in manual dexterity

The 6-week RT program caused widespread improvements in clinical tests that assess manual dexterity and upper limb function. Even though there were some improvements in function for the healthy older group, the ET group improved performance in one or more sub-tests within the 9HPT, PPT, MMT, and MJHFT. The ET group displayed improvements in 7 out of 10 sub-tests, whereas the healthy older group displayed improvements in 4 out of 10 sub-tests (Table 2). It should also be noted that functional deficits for both the most affected and least affected limbs were improved with RT, which suggests that overall function can be improved even in the presence of a problematic limb (Sequeira, Keogh et al., 2012). The aforementioned findings, combined with the fact that that only three group-related differences were identified in the manual dexterity tests, suggests that RT may not entirely target the movement dysfunction associated with ET. Instead, it is likely that RT may also account for declines in function due to the normal ageing process.

Surprisingly, one of the greatest improvements for the ET group coincided with one of the few between-group differences for the functional assessment: manipulating objects with the most affected limb and naming those objects when the eyes are closed. Since tactile discrimination and sensory perception play a dominant role in this test (Moberg, 1958; Moberg, 1960), it is possible that the benefits associated with RT may not be restricted to

motor function, but also aspects of sensory function. Other tasks that discriminated between the groups involved picking up objects with tweezers and a spoon, which emphasizes that the effects of RT on ET may not simply be a restricted to increasing strength. Prehensile control during object manipulation has a close association with cerebellar/purkinje cell activity (Smith & Buourbonnais, 1981; Goodkin & Thach, 2003), and although the effect of acute RT on cerebellar function has not been explored, these structures are implicated in ET movement dysfunction (Benito-Leon & Louis, 2006; Louis et al., 2014) and can be preserved in ageing with chronic exercise (Larsen, Skalicky & Viidik, 2000).

Based on the differences observed in the battery of functional tests that were employed in the current study, the overall increase in upper limb strength most likely improved elements of movement speed as well as accuracy of goal-directed movement (Yancosek & Howell, 2009). The results of the functional assessments provided a general indicator that RT was beneficial to the ET group, and to a lesser extent the healthy older group. However, a known feature of unrestrained multi-joint movement is that neuromuscular recruitment patterns can be altered to meet the requirements of the task (Wang, Zatsiorsky & Latash, 2006) and different coordination patterns can exist between individuals performing the same task (Chow et al., 2008). These features may mask some of the effects that RT has on the CNS with regard to movement, and may also explain why few group differences and no between-limb differences were identified for any functional assessment. The absence of between-limb differences transpired despite WHIGET, tremor assessments, and the ET subjects themselves indicating that one limb had greater movement dysfunction compared to the other. To resolve issues of multi-joint coordination, and to provide a more detailed assessment of tremor in ET patients, we examined fluctuations in finger abduction force.

Changes in force tremor dynamics

A useful method of determining how an intervention influences tremor characteristics is to examine the cumulative output of the motor system. This can be achieved by a variety of methods; however in the realm of force tremor a particularly useful model of examining tremor is to isolate movement a single joint which is driven by a single muscle. As such, several studies have examined small fluctuations in abduction force of the index finger, which is controlled by the first dorsal interosseous muscle (McAuley, Rothwell & Marsden, 1997; Vaillancourt, Larsson & Newell, 2003; Marmon, Gould & Enoka, 2011; Marmon et al., 2011; Kenway, Bisset et al., 2014). If the generalized RT program involving the biceps, wrist flexors, and wrist extensors causes adaptation at any level of the neuromuscular system, there will most likely be changes in motor output for this small hand muscle.

Arguably, the most important finding in this study was that RT had a significant impact on force tremor amplitude for the ET group- particularly for the most affected limb. The improvements following RT appear to have preferentially targeted the ET population, as the healthy older adults were not affected by the intervention, and group differences were identified between the ET and healthy older cohort. For the ET group, there was a reduction in the absolute force amplitude of tremor at the higher intensity contraction. This finding may have positive implications for individuals living with ET, as reducing the absolute amplitude of tremor may impact on how the ET patient perceives the severity of their condition and perform activities of daily living (Elble, Pullman et al., 2006; Chandran & Pal, 2013). In contrast, CV of force is independent of the overall amplitude of contraction, and provides greater insight to inherent changes tremor due to RT. Our results suggest that high-load RT assisted in reducing force tremor amplitude at high contraction intensities, but inherent changes in tremor dynamics also emerged when performing lower force-generating activities. These changes in tremor were most likely physiological and not simply due to increased strength following the RT program, as the targeting line was adjusted to account for changes

in strength throughout testing, and tremor-specific features of the ET participant's power spectrum was also altered pre- to post-RT.

Quantifying the frequency content of a tremor-related signal can be used to provide insight into the a variety of neurophysiological and mechanical processes, such as the contribution of central oscillators and peripheral reflexes to postural tremor, or the common oscillatory input to the pool of motoneurons innervating a muscle during isometric force tasks. The majority of power for an isometric contraction is located within the lower frequencies (< 4 Hz) (Kenway, Bisset et al., 2014) and variability of force corresponds to the spectral band representing neural drive to the muscle (Negro, Holobar & Farina, 2009; Dideriksen et al., 2012). As the low frequency 0-4 Hz absolute peak power in the ET group decreased with RT, it appears that the intervention assisted in being able to hold a 'steadier' contraction over the duration of the finger abduction task. While the lower frequency bandwidth is often attributed to visuomotor processing, the higher frequency reflects physiological tremor in healthy individuals and pathological tremor in special populations (McAuley & Marsden, 2000). As such, the reductions in the 4-12 Hz peak power for the ET most affected limb indicates that the RT program affected specific symptoms of ET rather than just age-related symptoms of tremor.

Our results extend on Bilodeau and colleagues (Bilodeau, Keen et al., 2000), who revealed that a 4-week high load training program of isometric index finger abduction exercises improved the ability to maintain steady abduction forces in individuals with ET. The task-specificity identified in that study, along with the results of our generalized RT program, indicate that mechanisms of ET can be modified with high-load training. While selective benefits of RT on force tremor were identified, a surprising finding was that the RT intervention had little effect on force tremor in the healthy older group. The relationship between RT and fluctuations in isometric force is not always a clear one, particularly in older

populations. For example, studies examining force control in the knee extensors have found little, or no change, in the coefficient of variation of force during isometric contractions after RT (Tracy, Byrnes & Enoka, 2004; Manini et al., 2005). Others have identified that the greatest improvements due to RT are among older individuals who were least steady prior to undertaking the intervention (Tracy & Enoka, 2006). In regards to the FDI, two similar studies found that both a 4-week and 12-week high intensity RT program was able to reduce fluctuations in abduction force (Keen, Yue et al., 1994; Laidlaw, Kornatz et al., 1999), which was particularly notable at lower contraction intensities and during the initial 4 weeks of training (Keen, Yue et al., 1994; Laidlaw, Kornatz et al., 1999). The lack of results in our control group may reflect the health status of the group, whereby healthy individuals with minimal tremor may not be able further reduce their tremor with any form of intervention.

RT as a therapy for Essential tremor

The results of the baseline 5RM suggest that a compensation strategy may have existed for the ET group prior to RT. The 5RM bicep curl was greater than 5RM wrist extension for the ET group, which was not a feature of the control group, and largely contributed to the main effect of group for the assessment of strength. Given that one of the movement dysfunctions that manifest in ET is excessive tremor about the flexion-extension axis of the wrist (Louis, 2005; Heroux, Pari & Norman, 2011), there may be an overall reliance on using larger, more proximal muscles, when performing activities of daily living. Over a prolonged duration, this could lead to an increase in activity for the biceps relative to the wrist flexors or extensors. Nonetheless, it appears that RT for multiple muscle groups may offer a viable therapy for individuals with ET.

Although we have illustrated certain benefits of RT, we cannot rule out that some results may, in part, be attributed to a relative lack of physical activity in the ET group compared to the healthy group due to their disorder. If the ET group had lower physical activity in their daily routines, it would be expected that they would show the greatest improvements with exercise. Although we did not assess physical activity levels per se, the 5RM assessments did provide insight to physical capacity of the participants. Even though the ET group had a higher baseline 5RM, the capacity for improving strength was greater in the ET. That is, with the same training, over the same period of time, the ET group had significantly greater improvements in 5RM, which typically reflects a more sedentary population.

It should be noted that the ET participants in this study remained on their prescribed medication during training and testing. As their prescribed medications reduce tremor amplitude, future studies would benefit by assessing individuals in their “off” medication state. This design will determine whether RT lead to tremor reduction or whether the results seen are simply the result of the daily vagaries of medication efficacy. Although it was out of the scope of this study, future research should explore the interaction between ET medications and dose-response characteristics to exercise-related therapy, and determine what combinations of exercises (e.g. dexterity training (Budini, Lowery et al., 2014) and/or RT) provide the greatest benefits to individuals with ET.

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FIGURE CAPTIONS

Figure 1. 5RM at the commencement of the training study (baseline), and the change in 5RM due to 6 weeks of upper limb RT for the Essential Tremor and healthy older groups. Data is presented for bicep curl, wrist flexion, and wrist extension for the least affected and most affected limbs. Error bars represent one standard error of the mean. * difference between groups ($p < 0.05$), † difference between limbs ($p < 0.05$).

Figure 2. Representative data for an Essential Tremor patient performing the sustained 10% MVC (top row of panels) and 60% MVC tasks (bottom row of panels). Data is presented for the most affected limb pre- and post- the 6 week resistance training program. Note the overall increases in force output following RT. The shaded insets are tremor signals from 6 s to 14 s that have been scaled to the post-RT amplitude to illustrate that absolute measures of tremor (SD) should be combined amplitude normalized measures of tremor (CV) to reveal changes due to resistance training. Spectral peaks were identified in a 0-4 Hz bandwidth and a 4-12 Hz bandwidth.

Figure 3. Change in SD of force (a) and change in CV of force (b) for the Essential Tremor and healthy older groups. Data represents the change in dependent measures from pre- to post-RT for the most affected and least affected limbs. Positive values represent a reduction in SD or CV following the RT program. Error bars represent one standard error of the mean. * difference between groups ($p < 0.05$), † difference between limbs ($p < 0.05$).

Figure 4. Power spectral data for the most affected and least affected limbs of the Essential Tremor and control groups. Data in the top panels represent the pre- to post-RT change in amplitude of the dominant frequency component in the 0-4 Hz (a) and 4-12 Hz bandwidth (b). Data in the bottom panels represent the pre- to post-RT change in normalized amplitude of the dominant frequency in the 0-4 Hz (c) and 4-12 Hz bandwidth (d). Positive values represent a reduction in peak power amplitude following the RT program. Error bars represent one standard error of the mean. * difference between groups ($p < 0.05$), † difference between limbs ($p < 0.05$).

Table 1. Subject characteristics for the Essential Tremor and the control group.

		Essential tremor (n = 10)	Healthy older (n = 9)
Age (yr)		71 ± 5	69 ± 5
Height (cm)		174 ± 8	165 ± 8
Weight (kg)		84 ± 9	72 ± 16
BMI (kg/m ²)		30 ± 3	27 ± 5
WHIGET	Rating:		
	0.	n = 0	-
	1.	n = 4	-
	2.	n = 1	-
	3.	n = 4	-
	4.	n = 1	-

Table 2. Pre- and post-RT functional assessment outcomes for the Essential Tremor and healthy older group.

	Limb	Essential Tremor			Healthy older		
		Pre-RT	Post-RT	Improvement	Pre-RT	Post-RT	Improvement
9HPT (s)	Most affected	26.8 ± 4.8	25.0 ± 4.2	1.8 ± 1.7 [†]	21.8 ± 3.1	19.6 ± 2.5	2.8 ± 4.3
	Least affected	29.6 ± 6.7	25.6 ± 5.0	4.1 ± 3.5 [†]	22.3 ± 3.9	19.5 ± 4.0	2.1 ± 2.2
PPT- single hand (pegs/30 s)	Most affected	10 ± 4	12 ± 4	2 ± 1 [†]	13 ± 3	16 ± 3	2 ± 1 [†]
	Least affected	10 ± 2	13 ± 2	2 ± 1 [†]	14 ± 2	15 ± 2	2 ± 2 [†]
PPT- both hands (pegs/30 s)	-	15 ± 5	19 ± 6	4 ± 3 [†]	20 ± 5	22 ± 6	2 ± 2 [†]
PPT- assembly task (units/60 s)	-	21 ± 4	25 ± 7	4 ± 4	26 ± 6	28 ± 7	2 ± 2
MMT- eyes open (s)	Most affected	11.3 ± 3.6	10.0 ± 2.5	1.2 ± 2.7	8.7 ± 1.7	7.4 ± 1.1	1.3 ± 1.0 [†]
	Least affected	11.1 ± 1.9	10.4 ± 1.8	0.7 ± 1.1	8.7 ± 1.8	7.3 ± 1.1	1.3 ± 0.9 [†]
MMT- eyes closed (s)	Most affected	19.6 ± 5.8	17.8 ± 4.5	1.6 ± 1.9 [†]	14.2 ± 3.0	13.9 ± 2.9	0.3 ± 2.2
	Least affected	20.9 ± 5.1	19.0 ± 5.1	1.7 ± 1.3 [†]	14.6 ± 2.1	13.4 ± 3.4	1.2 ± 2.5
MMT- eyes closed naming (s)	Most affected	31.6 ± 8.4	24.1 ± 5.9	6.7 ± 4.8 [†]	21.6 ± 2.1	17.8 ± 2.7	3.7 ± 2.8 §
	Least affected	27.8 ± 5.1	24.4 ± 5.6	3.0 ± 3.1 [†]	19.3 ± 4.4	16.7 ± 3.8	2.5 ± 3.5
MMT - eyes open tweezers (s)	Most affected	12.9 ± 4.3	10.5 ± 2.5	2.2 ± 3.7 [†]	10.8 ± 3.2	8.9 ± 2.4	0.9 ± 2.7 §
	Least affected	15.4 ± 4.4	11.9 ± 2.3	3.2 ± 3.5 [†]	12.2 ± 4.7	8.8 ± 3.3	3.2 ± 3.7
MJHFT - spoon control (s)	Most affected	10.2 ± 2.6	8.8 ± 3.0	1.3 ± 0.9 [†]	8.2 ± 1.9	7.1 ± 1.3	1.1 ± 0.9 [†]
	Least affected	10.9 ± 4.0	8.6 ± 1.6	2.3 ± 2.8 [†]	8.0 ± 1.5	7.9 ± 2.0	0.1 ± 1.3 §
MJHFT - card turning (s)	Most affected	5.7 ± 1.4	5.2 ± 0.6	0.5 ± 1.0	5.2 ± 0.9	4.4 ± 0.6	0.7 ± 1.1
	Least affected	5.4 ± 0.6	4.7 ± 0.6	0.6 ± 0.7	5.0 ± 1.2	4.2 ± 0.6	0.7 ± 1.2

9HPT, Nine-hole Peg test; PPT, Purdue Pegboard test; MMT, Modified-Moberg Test; MJHFT, Modified-Jebsen Hand Function test.

§ significant difference detected from Wilcoxon Sign-Ranked test ($p < 0.05$).

† significant difference between ET and older group ($p < 0.05$).

**Most affected limb
pre-resistance training**

**Most affected limb
post-resistance training**

**Most affected limb power
spectra pre- to post-training**

0-4 Hz bandwidth

4-12 Hz bandwidth