Effects of Aging on the Regularity of Physiological Tremor
*Molly M. Sturman¹, David E. Vaillancourt¹, Daniel M. Corcos ¹-⁴

¹Department of Movement Sciences, ²Department of Bioengineering, and
³Department of Physical Therapy
University of Illinois at Chicago
Chicago, IL 60612

⁴Department of Neurological Sciences
Rush Presbyterian-St. Luke’s Medical Center
Chicago, IL 60612

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Mailing Address:
Molly M. Sturman
Department of Movement Sciences (M/C 994)
University of Illinois at Chicago
808 South Wood, 690 CME
Chicago, Illinois 60612
Tel: (312) 355-2541
Fax: (312) 355-2305
msturm3@uic.edu
Abstract

The purpose of this investigation was to determine the effects of healthy aging on the regularity of physiological tremor under rest and postural conditions. Additionally, we examined the contribution of mechanical reflex factors to age related changes in postural physiological tremor. Tremor regularity, tremor-EMG coherence, tremor amplitude, and tremor modal frequency were calculated for four age groups (young: 20-30 y, young-old: 60-69 y, old: 70-79 y, and old-old: 80-94 y) under resting and loaded postural conditions. There were six important findings from this study. First, there were no differences between the young and elderly subjects for any of the dependent variables measured under the rest condition. Second, postural physiological tremor regularity was increased in the elderly. Third, postural physiological tremor-EMG coherence was also increased in the elderly, and there was a strong linear relation between peak tremor-EMG coherence in the 1-8 Hz frequency band and regularity of tremor. This relation was primarily driven by the increased magnitude of tremor-EMG coherence at 5.85 Hz and 6.83 Hz. Fourth, enhanced mechanical reflex properties were not responsible for the increased magnitude of tremor-EMG coherence in the elderly subjects. Fifth, tremor amplitude was not different between the four age groups, but there was a slight decline in tremor modal frequency in the oldest age group in the unloaded condition. Finally, despite the increases in postural physiological tremor regularity and the magnitude of low frequency tremor-EMG coherence with age, there was a clear demarcation between healthy aging and previously published findings related to tremor pathology.
Key Words: physiological tremor, aging, regularity, tremor-EMG coherence, mechanical reflex, amplitude, frequency
**Introduction**

In the most general sense, tremor is defined as any involuntary, approximately rhythmic, and roughly sinusoidal movement that can be detected in an oscillating limb (Elble and Koller, 1990). Tremor is present in all individuals, occurring at rest (resting tremor) (Brumlik, 1962; Marsden et al., 1969) and during postural maintenance of the limb (postural tremor) (Schafer, 1886; Halliday and Redfearn, 1956; Marshall and Walsh, 1956). Tremor is also a frequent symptom of movement disorders, such as essential tremor (ET) and Parkinson’s disease (PD) (Elble and Koller, 1990; Deuschl et al., 1998). These pathologies are more prevalent among elderly individuals (Kelly et al., 1995; Waite et al., 1996; Elble, 1998) with prevalence rates for ET reaching 4.8% in individuals over 65 years (Benito-Leon et al., 2003), and the incidence of PD increasing from 0.50/100,000 in individuals aged 30–39 years to 44/100,000 in individuals over 50 years (Van Den Eeden et al., 2003).

Physiological tremor in healthy individuals is classically characterized as a low amplitude postural tremor with a modal frequency of 8-12 Hz (Elble and Koller, 1990). Physiological tremor measured at rest is a normally occurring, low amplitude oscillation determined by mechanical limb properties and cardioballistics (Brumlik, 1962; Marsden et al., 1969; Elble and Koller, 1990). In addition to amplitude and frequency, both physiological and pathological tremors can be characterized by the degree of regularity (measured with Approximate Entropy (ApEn)) in the limb acceleration signal and the amount of coherence between limb acceleration and muscle output (tremor-EMG coherence). For healthy physiological tremor, regularity and tremor-EMG coherence below 10 Hz are low (Vaillancourt et al., 2003; Sturman et al., 2004). In contrast to
healthy physiological tremor, patients with ET have an abnormal postural tremor with increased amplitude, regularity, tremor-EMG coherence below 10 Hz, and a modal frequency between 4-12 Hz (Elble and Koller, 1990; Vaillancourt et al., 2003). Tremor in PD is classified as a resting and/or postural tremor, which also has increased amplitude, regularity, and tremor-EMG coherence below 10 Hz. The modal frequency of resting tremor in PD is between 3-5 Hz and postural tremor frequency ranges from 4-12 Hz (Findley et al., 1981; Elble and Koller, 1990; Deuschl et al., 1998).

Previous research on postural physiological tremor has argued that the amplitude and modal frequency of physiological tremor in the elderly could be a form of undiagnosed pathological tremor, such as essential tremor (Moretti et al., 1983; Elble, 1995; Elble, 1998; Louis et al., 2000). However, recent research has not found changes in the amplitude and modal frequency of tremor with age (Raethjen et al., 2000; Elble, 2003). Regularity and tremor-EMG coherence, both of which are markers for tremor pathology, have not been examined in physiological tremor as a function of healthy aging. However, changes in the regularity of physiological output from elderly individuals have been detected in the absence of changes in the mean and variance of the dependent variables used to describe physiological function (Pincus, 2001). Recent research has also shown increased motor unit to motor unit coherence below 10 Hz among elderly individuals (Semmler et al., 2003).

The first purpose of this study is to investigate the effects of healthy aging, on the regularity and tremor-EMG coherence of physiological tremor under resting and postural conditions. In addition, in order to replicate previous research, we will also investigate the effects of healthy aging on the amplitude and modal frequency of physiological
tremor. Due to the decrease in muscle activity in a resting limb state and previous research which did not find age related changes in physiological resting tremor (Kelly et al., 1995; Raethjen et al., 2000), it is hypothesized that age will not affect the neurophysiological characteristics of tremor measured at rest. However based upon previous research demonstrating the sensitivity of regularity in detecting age related changes in physiological function (Pincus, 2001) and the presence of increased motor unit to motor unit coherence among elderly individuals during an active limb state (Semmler et al., 2003), we predict that age will increase postural tremor regularity and the magnitude of tremor-EMG coherence below 10 Hz.

The second purpose of this study is to determine if mechanical reflex oscillations affect physiological tremor in older individuals more so than in young individuals. Both mechanics and reflexes play a role in the peripheral component of physiological tremor, which is described by the mechanical reflex oscillator hypothesis (Stiles and Pozos, 1976). According to this hypothesis, the nervous system contributes to physiological tremor by setting the muscle stiffness and driving asynchronous contractions of motor units, with the inertia and stiffness of the limb determining the resonant frequency of tremor. If enhancement of the mechanical reflex component of tremor is contributing to the increased low frequency tremor-EMG coherence with age, we expect to find an age by load interaction, whereby load is preferentially affecting the magnitude of tremor-EMG coherence below 10 Hz in the elderly subjects. Alternatively, if there is no interaction between age and load, then enhanced mechanical reflex oscillations do not play a role in the increased magnitude of tremor-EMG coherence among elderly subjects.
The third purpose of the study is to examine physiological tremor measured under resting and postural conditions using a load manipulation with the same neurophysiological tools that have previously been employed for pathological tremors (Vaillancourt et al., 2003; Sturman et al., 2004). This will establish normative data for the regularity of physiological tremor as a function of healthy aging.

**Methods**

**Subjects**

A total of forty healthy subjects were enrolled in the study. These individuals were assigned to four different age groups with 5 females and 5 males in each group: young group (n=10; range 20-30 years; mean + standard deviation 24.4(SD=3.2)), young-old group (n=10; range 60-69 years; mean 65.8(SD=3.6)), old group (n=10; range 70-79 years; mean 73.5(SD=3.0)), and old-old group (n=10; range 80-94 years; mean 82.8 (SD= 4.4)). The data from ten patients with PD and six patients with ET are also presented. The data from the ET patients has been published elsewhere (Vaillancourt et al., 2003) as has the data from the PD subjects (Sturman et al., 2004). Informed consent was obtained from all subjects prior to the inception of the study, and all study procedures were approved by the local Institutional Review Board (University of Illinois at Chicago, Chicago, Illinois).

Subject height and weight information for the young and elderly subjects was collected, and a height to weight ratio was calculated (cm/kg) for each subject. The Yale Physical Activity Survey for Older Adults (Dipietro et al., 1993) and the Folstein’s Mini-Mental Status Examination (Folstein et al., 1975) were administered to all subjects before
data collection began. Exclusion criteria were determined a priori and included elite physical condition or extremely frail physical condition, cognitive impairments (scores below 29/30 on the Mini-Mental Status Examination), diabetes, uncontrolled hypertension or angina, alcoholism, or bed rest. Subjects were also excluded from the experiment if they were known to have any neurological pathologies, an apparent resting or postural tremor detectable with clinical tremor rating scales, or a family history of PD or ET. The purpose of the exclusion criteria was to exclude elderly subjects that were tremulous or that had health problems. We excluded one individual from the old group and one individual from the old-old group. The individual considered for the old group had an action tremor that received a 1 on the Tremor Rating Scale (Fahn et al., 1993), and the physical condition of the individual considered for the old-old group was extremely frail due to severe osteoarthritis.

Tremor data is presented in Tables 1 and 2 (mean + standard deviation) from six individuals with ET and ten individuals with PD. The data from the patients was collected while they were off treatment. All data analysis procedures and dependent variable calculations were performed in exactly the same way for both the patients and the young and elderly subjects. These procedures are described in detail in the following paragraphs. It is important to note that both patient groups were moderately to severely impaired. The data from both groups of patients are presented in order to provide a direct comparison between physiological tremor in the elderly and tremor in two different pathologies.
**Apparatus**

Subjects were positioned in a 42 cm high straight back chair. If necessary, foot support was provided to ensure that the knee and hip angles were both 90°. The arm of the chair served as the supportive surface for the subject’s forearm. The supportive surface measured 43 cm in length and was 58 cm from the ground. The subject’s dominant forearm was positioned on the supportive surface so that the ulnar styloid process was aligned with the end of the surface. In this position the elbow joint was flexed to approximately 90°, the shoulder joint was slightly abducted, and the forearm was pronated. A small table was positioned approximately 30 cm in front of the subject. The height of the table was adjusted to be level with the subject’s hand when the wrist and fingers were in a neutral position (0° of flexion and extension) as shown in Figure 1. The table served as the visual target to enable the subject to maintain the wrist in a neutral position. The width of the table edge was 1.3 cm.

Insert Figure 1 about here

A calibrated Coulbourn type V 94-41 miniature solid-state piezoresistive accelerometer was taped 2 cm proximal to the middle of the second metacarpophalangeal (MCP) joint (Figure 1). A Coulbourn Lab Linc V System V72-25A resistive bridge strain gage transducer with an excitation voltage of ± 5V amplified the changes in electrical resistance of the acceleration signals. The accelerometer’s resolution was 0.01 m/s², and a 12 bit A/D converter sampled the acceleration signal at 1000 Hz.

Surface electromyography was used to measure the neuromuscular activity in the extensor digitorum (Figure 1). Electrode placement was determined by muscle palpation during active wrist and finger extension, and EMG output was inspected by viewing a
digital oscilloscope. The EMG signal was amplified (gain 1000) and bandpass filtered by the Bagnoli system with a low cutoff of 20 Hz and a high cutoff of 450 Hz (Delsys Inc., Boston, MA). Data from each trial was saved to the hard disk of the data collection computer and analysis and processing was performed offline.

**Protocol**

The study examined two types of tremor. In the resting tremor condition, subjects were instructed to relax their forearm and hand muscles, and allow the wrist to dangle unsupported over the edge of the supportive surface for 30 seconds (Figure 1A) (Marsden et al., 1969; Burne et al., 1984; Raethjen et al., 2000; Duval et al., 2001). In the postural tremor condition, subjects were asked to maintain their wrist and hand in a neutral, extended position while keeping it level with the target for 30 seconds (Figure 1B-C) (Elble and Randall, 1976; Homberg et al., 1987; Raethjen et al., 2000). Loads of 1000, 500, 250, 100, and 0 grams were suspended from the subjects’ hand. A velcro strap, placed 1 cm proximal to the middle of metacarpophalangeal joints 2-5, secured the weights in their suspended position (Figure 1C). Subjects performed three trials in each condition and at least three minutes of rest was provided between trials. To ensure that fatigue was not present during the recording session, we analyzed the effect of trial in our data. This analysis showed no effect of trial; therefore, fatigue was not a factor. The resting tremor condition was always performed first followed by the postural tremor experiments. The order of the loaded conditions was randomized. Verbal and visual feedback was provided to the subjects regarding the maintenance of the target hand position. Additionally, hand and wrist initial position was checked by the experimenter prior to each trial.
Data Analysis

In order to quantify the differences in physiological tremor between young and elderly adults, data analysis examined the same four dependent measures for resting tremor and for postural tremor with different loads. The independent variables were age and load, and the dependent variables were regularity (measured with approximate entropy (ApEn)), magnitude of tremor-EMG coherence, amplitude, and modal frequency. Prior to data analyses, the acceleration and EMG signals were processed with the following techniques. The EMG signals were digitally rectified, and both the EMG and acceleration data were downsampled by a factor of 5 to 200 Hz (Vaillancourt and Newell, 2000). We analyzed the full wave rectified EMG signal in order to maximize the information about the temporal pattern of grouped motor unit firing potentials (Mima et al., 2001; Myers et al., 2003). This procedure has been used by many different groups when examining physiological and pathological tremor (Elble and Randall, 1976; McAuley et al., 1997; Halliday et al., 1999; Vaillancourt and Newell, 2000). The acceleration signal was digitally filtered using a 4th order Butterworth filter with a lowpass cutoff frequency of 30 Hz. For the calculation of tremor-EMG coherence in the 35-50 Hz bin, the acceleration signal was filtered at 50 Hz instead of 30 Hz. In addition to the 20-450 Hz analog bandpass filter (see p. 10) and after rectification, the EMG signal was digitally filtered using a 4th order Butterworth filter with a lowpass cutoff frequency of 60 Hz (Vaillancourt et al., 2003; Sturman et al., 2004). Data processing and time and frequency analyses were performed using software written in Matlab (The Mathworks Inc., Natick, MA).
Regularity (Approximate Entropy)

The regularity of tremor was quantified using approximate entropy (ApEn). This algorithm assesses the time-dependent structure of the acceleration signal and returns a value between 0 and approximately 2 which represents the predictability of future values in the time series based on previous values. An ApEn value of zero would correspond to a sine wave signal which has a high degree of short and long term predictability. On the other hand if a highly unpredictable signal such as white Gaussian noise is added to a sine wave, the ApEn value will increase. If a completely random signal such as pure white Gaussian noise is assessed with ApEn the value returned will be close to 2. This is because in a completely random signal future values in the time series are independent and unpredictable based upon previous values. The calculation of ApEn requires two input parameters: “m” is the window length, and “r” is a filter (Pincus, 1991). In this manuscript ApEn parameter settings of m = 2, r = 0.2 * standard deviation of the signal were used to be consistent with previous work from our laboratory (Vaillancourt and Newell, 2000; Vaillancourt et al., 2001; Vaillancourt et al., 2003; Sturman et al., 2004) and other laboratories (Pincus and Goldberger, 1994).

Tremor-EMG Coherence

Cross-spectral analysis was used to analyze the relation between the EMG and acceleration signals (tremor-EMG coherence). The cross-spectrum was calculated using Welch’s averaged periodogram method with no overlap between successive segments in the spectral calculation. Coherence between each respective signal was calculated and a 95% confidence interval was determined (Rosenberg et al., 1989; Farmer et al., 1993), which yielded a broadband of coherence that was significantly different from 0. The
magnitude of the peak coherence value in the coherence spectrum in the 1-8 Hz, 9-15 Hz, 15-30 Hz, and the 35-50 Hz bins was determined. To ensure that the binning method was discriminative enough, we also calculated peak tremor-EMG coherence in 3 Hz bins from 1-50 Hz (acceleration signal filtered at 50 Hz). The results were consistent with those in the 1-8 Hz, 9-15 Hz, 15-30 Hz, and 35-50 Hz bins and are not presented. The 1-8 Hz bin was further divided into 0.976 Hz bins, and the magnitude of tremor-EMG coherence was determined within the smaller bins. Only peak coherence values from the 1-8 Hz bin (Table 1, Table 2, Figure 4, and Figure 6A) are reported, since age did not affect the magnitude of peak tremor-EMG coherence in the higher frequency bins.

Amplitude

Autospectral analysis was used to quantify the amplitude of the acceleration signal (Jenkins and Watts, 1968; Elble and Koller, 1990; McAuley et al., 1997). This method for determining amplitude calculates the root-mean-square (rms) displacement of the acceleration signal from the modal frequency of tremor (Stiles, 1976). The unit of measurement for acceleration prior to autospectral analysis is m/s². In order to calculate the rms displacement of the acceleration signal, it is assumed that the tremor spectrum resulted from a periodic oscillation, which is a reasonable assumption for hand tremor. In this case, spectral analysis produces a narrow band of power. The sum of the three highest spectral values represents the majority of the variance of the tremor oscillations at the modal frequency (f), and the square root of this sum represents the rms acceleration at this frequency (f). Three spectral values are required to capture the overall variance of the acceleration signal. At this point the unit of measurement for the power spectral density of the acceleration data is m/s² divided by Hz (1/s), which gives m/s. By dividing
the rms acceleration by the square of $\omega (\omega = 2\pi f)$ the units are converted to displacement (cm). In this study, units of displacement (cm) are used to quantify tremor amplitude in the elderly in order to directly compare physiological tremor amplitude to pathological tremor amplitude which is measured clinically in centimeters (Fahn et al., 1993).

Modal Frequency – Acceleration Signal

The modal frequency of the acceleration signal was determined using auto-spectral analysis of the signal. The spectral resolution was 0.781 Hz. The peak of the tremor acceleration spectrum was designated as the modal frequency $f$ of tremor.

Statistical Analysis

Data were averaged across the three trials for each dependent variable. A one way ANOVA with a between subject factor of age (4) was used to determine significant differences in the resting tremor condition. A separate two way Age (4) x Load (5) ANOVA was used to evaluate the significance of the dependent variables for the postural tremor condition. A three way Age (4) x Load (5) x Bin (9) ANOVA was used to determine which frequency bins within the 1-8 Hz band had increased magnitude of tremor-EMG coherence. Tukey’s Honestly Significant Difference (HSD) post hoc analysis was used to evaluate which groups were significantly different if a main effect was obtained. Statistical analyses were deemed significant when alpha was less than 0.05. All statistical analyses were conducted using Statistica statistical software package (StatSoft Inc., OK).
3. Results

Resting Tremor

There were no significant differences between the four age groups in the regularity, magnitude of peak tremor-EMG coherence in any frequency bin, amplitude, or modal frequency for the resting tremor condition. Table 1 provides group means + standard deviation of each of the dependent variables for resting tremor.

Postural Tremor

Regularity and Tremor-EMG Coherence

Figure 2 quantifies the regularity of postural hand tremor in the four age groups calculated with ApEn. There was a main effect of age on ApEn ($F_{(3,36)}=2.99$, $p<0.05$). The age by load interaction ($p=0.59$) was not supported nor was the main effect of load ($p=0.60$). As illustrated by Figure 2, the ApEn values for the young group were higher than the values for the three elderly groups, and ApEn decreased as a function of age. Post hoc analysis using Tukey’s HSD revealed that only the ApEn values of the old-old group were significantly different from the young group ($p<0.05$).

Figure 3 is single subject data from a young (25 years) and old-old subject (81 years). This figure depicts the effects of mechanical load on the tremor autospectrum, EMG autospectrum, and the cross spectrum between the two signals. In Figure 3A and 3B, the addition of mechanical load shifts the accelerometric peak to a lower frequency for both the young and old-old subject. This suggests that mechanical resonance factors are influencing the modal frequency of physiological postural tremor. In contrast the
frequency of the peaks in both the EMG spectrum (Figure 3C and 3D) and the tremor-EMG coherence spectrum (Figure 3E and 3F) are not influenced by mechanical load in the young and elderly subject. This suggests a central modulation of tremor-EMG coherence. Additionally, a difference exists in the magnitude of peak tremor-EMG coherence between the young and elderly individuals which is most pronounced at or below ~10 Hz (Figure 3E and 3F). Although significant peak coherence occurred at 40 Hz in this trial for the old-old subject (3F), this was not a consistent finding.

Insert Figure 3 about here

The postural tremor condition yielded significant differences in the magnitude of peak tremor-EMG coherence in the 1-8 Hz frequency bin between the four age groups. This is depicted in Figure 4. Figure 4 depicts the across subject mean peak tremor-EMG coherence in the 1-8 Hz frequency band + standard deviation. There was a main effect of age for the magnitude of peak tremor-EMG coherence in the 1-8 Hz frequency band (F(3,36)=2.94, p<0.05). Post hoc tests confirmed that the main effect of age was due to the old-old subjects exhibiting a significantly greater magnitude of peak tremor-EMG coherence in the 1-8 Hz frequency band compared to the young subjects (p<0.05).

Tremor-EMG coherence analysis was also performed on the 9-15 Hz, 15-30 Hz, and 35-50 Hz frequency bins. There were no differences between the age groups in the magnitude of peak tremor-EMG coherence in the higher frequency bins (p’s>0.23).

Insert Figure 4 about here

In order to determine the specific frequencies within the 1-8 Hz bin that demonstrated an increased magnitude of tremor-EMG coherence among the elderly, we performed a more detailed analysis of tremor-EMG coherence across load in the 1-8 Hz
bin, which is depicted in Figure 5. Results from the three way (age x bin x load) ANOVA revealed a significant age by bin interaction ($F_{(24,288)}=2.77$, $p<0.01$) and a significant load by bin interaction ($F_{(32,1152)}=6.60$, $p<0.01$). The age x load x bin and age x load interactions were not significant. In order to interpret the significant age by bin interaction, we performed separate one way, between group ANOVAs that confirmed a main effect for age at 5.85 Hz ($F_{(3,36)}=5.26$, $p<0.01$) and 6.83 Hz ($F_{(3,36)}=4.03$, $p<0.01$). Tukey’s Post Hoc analysis revealed that a significant difference in the magnitude of tremor-EMG coherence existed between the young and old-old groups from 5.85 Hz – 6.83 Hz ($p<0.01$ for each bin). The old-old subjects also had greater tremor-EMG coherence compared to the young subjects at 7.81 Hz and 8.78 Hz, and this difference was close to reaching statistical significance ($p's=0.07$). To interpret the significant load by bin interaction, we performed separate one way, within subject ANOVAs that showed a main effect of load from 4.88 Hz – 8.78 Hz ($p's<0.01$), such that the magnitude of tremor-EMG coherence increased with load.

Figure 6 is a summary figure that depicts the relation between the magnitude of tremor-EMG coherence in the 1-8 Hz frequency band and ApEn, and illustrates how these two variables change with increasing age. In Figure 6A the relation between the magnitude of peak 1-8 Hz tremor-EMG coherence and ApEn is best described by a linear function with a y intercept of 0.78, a slope of –0.43, and a $R^2$ value of 0.70. For Figure 6B and Figure 6C the magnitude of tremor-EMG coherence at 5.85 Hz and 6.83 Hz is plotted versus ApEn. These two frequency bins were chosen because a significant difference in the magnitude of tremor-EMG coherence exists between the young and old-
old subjects at 5.85 Hz and 6.83 Hz. As expected the relation between the magnitude of tremor-EMG coherence and ApEn at 5.85 Hz and 6.83 Hz is linear with $R^2$ values of 0.59 and 0.57 respectively. These figures suggest that as the amount of squared correlation between the tremor and the muscle output increases, the regularity of tremor also increases as a function of age.

Insert Figure 6 about here

Amplitude and Modal Frequency

The effect of age on the amplitude of tremor did not reach the 0.05 significance level ($F_{(3,36)}=2.57$, $p=0.07$). Inspection of the data revealed that the old-old subjects had slightly greater tremor amplitudes compared to the young subjects (Table 2). Clinical rating scales for pathological tremor, classify tremor amplitude as moderate if it is greater than “slight, but perceivable” and less than 2 cm (Fahn et al., 1993). Therefore, even though tremor amplitude for the old-old subjects was higher, it did not reach pathological ranges. This is also illustrated in Table 2 where RMS values for PD (Table 2) and ET (Table 2) subjects are reported. As expected there was a main effect of load on the amplitude of tremor ($F_{(4,144)}=6.21$, $p<0.01$), such that tremor amplitude increased with load. However, an age by load interaction was not supported ($p=0.71$).

Insert Table 2 about here

In line with the increase in amplitude with added load, the modal frequency of tremor decreased with load ($F_{(4,144)}=86.25$, $p<0.01$) (Table 2). There was a significant age by load interaction ($F_{(12,144)}=3.37$, $p<0.01$). Due to the interaction, separate one way, between group ANOVAs were conducted at each load. There was a main effect of age at the 0 gram load ($F_{(3,36)}=2.83$, $p<0.05$). However, when loads from 100 grams to 1000
grams were added to the limb, the tremor frequency was similar in all four age groups (p’s >0.17). Independent sample t-tests confirmed a height to weight ratio difference between the young and old subjects (t_{18}=2.69, p<0.01) and the young and old-old subjects (t_{18}=2.29, p<0.05). Since the frequency of mechanical oscillations is inversely proportional to the square root of the combined inertia of the oscillating limb, increased limb inertia can reduce the modal frequency of oscillation (Stiles and Randall, 1967). Therefore, the elderly subjects were heavier than the young subjects, which may account for their lower hand acceleration frequencies at 0 grams.

**Discussion**

The purpose of this study was to investigate the effects of healthy aging on the regularity and tremor-EMG coherence of physiological tremor under resting and postural conditions using a load manipulation. Additionally, we determined the effects of aging on the amplitude and modal frequency of resting and postural physiological tremor. There were six important findings from this study. First, there were no differences between the young and elderly subjects for tremor regularity and the magnitude of tremor-EMG coherence measured under the rest condition. Second, postural physiological tremor regularity was increased in the oldest group of elderly subjects. Third, the magnitude of peak postural physiological tremor-EMG coherence in the 1-8 Hz frequency band was also increased in the oldest group of elderly subjects. There was a strong linear relation between the magnitude of tremor-EMG coherence at 5.85 Hz and 6.83 Hz and tremor regularity. Fourth, enhanced mechanical reflex properties were not responsible for the increased magnitude of tremor-EMG coherence in the 1-8 Hz
frequency band in the oldest age group. Fifth, tremor amplitude was not different between the four age groups, but there was a slight decline in tremor modal frequency in the oldest age group in the unloaded condition. Finally, despite the increases in postural physiological tremor regularity and the magnitude of tremor-EMG coherence in the 1-8 Hz frequency band with age, there was a clear demarcation between healthy aging and tremor pathology. These findings have important implications for the mechanisms of tremor in the elderly and provide normative aging data that we compare with previous work on ET and PD (Vaillancourt et al., 2003; Sturman et al., 2004).

**Resting Tremor**

The finding that age did not affect the amplitude and frequency of resting physiological tremor is consistent with previous research (Kelly et al., 1995; Raethjen et al., 2000). The novel results from the present study are that resting physiological tremor regularity and the magnitude of peak tremor-EMG coherence were not different between young and elderly subjects. Resting tremor is one of the cardinal signs of PD (Hughes et al., 1992b; Hughes et al., 1992a; Deuschl et al., 1998), and the presence of an obvious resting tremor is associated with pathology. Approximately 20%-30% of patients diagnosed with PD do not have a clinically detectable resting or postural tremor (Lance et al., 1963; Elble and Koller, 1990; Marsden, 1990). However, Vaillancourt and colleagues (2000) demonstrated that the ApEn measure was sensitive enough to detect a difference in tremor regularity between mild PD patients who did not have clinically detectable tremor and control subjects. Therefore, if an individual has increased tremor regularity and/or an increased magnitude of tremor-EMG coherence in the 1-8 Hz frequency band at rest (Table 1), it suggests some form of tremor pathology.
Postural Tremor

Relation between Tremor-EMG Coherence and Regularity

The regularity of postural tremor was greater among the elderly subjects compared with the young group. The ApEn measure has been used to assess the effects of aging on other physiological systems (Kaplan et al., 1991; Pincus et al., 1996) and to characterize pathological tremors (Vaillancourt and Newell, 2000; Vaillancourt et al., 2003; Sturman et al., 2004). ApEn has also been used to identify an age related increase in the regularity of force output during a constant, visuomotor, force production task (Vaillancourt and Newell, 2003). In the current study the magnitude of peak tremor-EMG coherence in the 1-8 Hz frequency band was increased among the oldest subjects, and there was a linear relation between the magnitude of low frequency tremor-EMG coherence and tremor regularity. The strong linear relation between low frequency peak tremor-EMG coherence and tremor regularity suggests similar mechanisms behind the age related changes in these two variables. Tremor-EMG coherence provides a predictive measure of motor unit synchronization (Halliday et al., 1999). Therefore, our data suggest that the aging process enhanced motor unit synchronization which increased the regularity of tremor measured behaviorally.

Potential Mechanisms for Increased Regularity and 1-8 Hz Tremor-EMG Coherence

During maintained voluntary muscle contraction, pairs of concurrently active motor units exhibit correlated discharge which is postulated to result from common presynaptic input to the motor neuron pool (Dietz et al., 1976; Datta and Stephens, 1990; De Luca and Erim, 1994; Farmer et al., 1997), and this common drive is thought to have central origins (De Luca and Erim, 2002). Both time and frequency domain analysis can
be used to quantify the correlated discharge of action potentials from motor units (motor unit synchronization) (Farmer et al., 1993; Halliday et al., 1999). It is known that the common descending input to motor neurons is responsible for motor unit synchronization in the 1-12 Hz and 16-30 Hz frequency bands (Farmer et al., 1993; Conway et al., 1995). Due to the established relation between motor unit synchronization, motor unit to motor unit coherence, and tremor-EMG coherence (Halliday et al., 1999), our finding of an increased magnitude of low frequency tremor-EMG coherence in the elderly subjects was most likely due to increased motor unit synchronization. Two potential mechanisms for this age related change could be increased gain in the mechanical reflex pathway or alterations in the common descending input to the motor neuron pool.

Mechanical resonance tremor of the hand is driven by random, unsynchronized firing of motor units in the forearm muscles, which causes an oscillation at the mechanical resonant frequency. This is the main mechanism for physiological postural tremor (Halliday and Redfearn, 1956; Stiles and Randall, 1967). However, the stretch reflex is a peripheral neural mechanism that can entrain motor units at the frequency of tremor if the period of tremor oscillation is twice the time delay of the reflex loop. This is a proposed mechanism for enhanced physiological tremor (Lippold, 1970; Hagbarth and Young, 1979). In enhanced physiological tremor, tremor amplitude, motor unit synchronization, and motor unit to motor unit coherence are increased (Logigian et al., 1988), while the modal frequency of tremor shifts with changes in the mechanical resonant frequency (Homberg et al., 1987). The oldest group of elderly subjects in this study had physiological tremor with an increased magnitude of tremor-EMG coherence in the 1-8 Hz frequency band and tremor modal frequencies that followed reductions in
the mechanical resonant frequency. If enhanced mechanical reflex oscillations were responsible for these changes, there should have been a significant interaction between age and load affecting the magnitude of tremor-EMG coherence in the 1-8 Hz frequency bin. In this study there was no evidence for an interaction between age and load on tremor-EMG coherence. Thus, increased gain in the mechanical reflex pathway is not a mechanism that explains the increased magnitude of tremor-EMG coherence in the 1-8 Hz frequency band in the oldest group of elderly subjects.

The absence of age related changes in the gain of the mechanical reflex pathway suggests that the mechanism for increased regularity and increased low frequency tremor-EMG coherence may be mediated via common descending input from the cortex to the motor neuron pool. Research examining the affect of aging on the common drive to the motor neuron pool did find differences between young and elderly subjects (Erim et al., 1999). However, other literature which examined the correlated discharge of action potentials from pairs of motor units in the time domain did not find an age related increase in motor unit synchronization (Kamen and Roy, 2000; Semmler et al., 2000). In contrast a separate study by Semmler and colleagues (2003) using the same sample of individuals where no differences in motor unit synchronization were found, did find a difference in the correlated discharge of action potentials from pairs of motor units between young and elderly subjects in the frequency domain (motor unit to motor unit coherence). The authors concluded that frequency rather than time domain analyses may be more sensitive to subtle, age related changes in the common descending input to the motor neuron pool (Semmler et al., 2003). Results from the current study support the
findings of Semmler and colleagues (2003) by demonstrating increased magnitude of tremor-EMG coherence at 5.85 Hz and 6.83 Hz in the elderly subjects (Figure 5).

The fact that the frequency of the peaks in the EMG spectrum and tremor-EMG coherence spectrum were unaffected by mechanical load (Figure 3) supports a centrally driven mechanism for tremor-EMG coherence in the young and elderly subjects in this study. Differences between young and elderly subjects in the ability to modulate the descending inputs to the motor neuron pool may explain the age related increases in regularity and the magnitude of low frequency tremor-EMG coherence. In young healthy subjects the actions of multiple neural oscillators interact in a coordinated fashion to produce motor output (Sosnoff et al., 2004), and the descending inputs to the motor neuron pool are more random, oscillating at a wide variety of frequencies (Semmler et al., 2003). With aging, the ability to modulate the input from multiple neural oscillators diminishes (Lipsitz, 2002; Vaillancourt and Newell, 2002), and the descending input to the motor neuron pool becomes more regular, oscillating at a specific frequency (Semmler et al., 2003). These age related changes may explain the presence of a well defined peak in the tremor-EMG coherence spectrum between 1-8 Hz which had a greater magnitude for the elderly subjects, and the more distributed pattern of tremor-EMG coherence across a wide range of frequencies with a smaller magnitude for the young subjects. Studies of coherence between motor cortical field potentials and EMG rarely demonstrate significant corticomuscular coherence at or around 10 Hz (Conway et al., 1995; Salenius et al., 1997; Kilner et al., 2000). One explanation for this finding is that a “desynchronizing central mechanism” prevents the motor neuron pool from synchronizing with low frequency cortical oscillations, thereby preventing excess
physiological tremor (Baker et al., 2003). Pathological conditions such as epilepsy have been shown to disrupt the “desynchronizing mechanism” producing strong low frequency corticomuscular coherence (Raethjen et al., 2002). With age the ability to desynchronize low frequency cortical inputs to the motor neuron pool could also diminish causing increased coherence at or below 10 Hz.

Effects of Aging on Amplitude and Frequency

The amplitude of physiological postural tremor was not statistically different between the four age groups. The fact that amplitude did not reach a statistical significance level of 0.05 is consistent with previous literature (Kelly et al., 1995; Raethjen et al., 2000; Elble, 2003). In this study tremor frequency was reduced by 1 Hz in the old-old group compared with the young group at the 0 gram load. However, when load was added to the limb, tremor modal frequency was the same between young and elderly subjects. This finding for load is congruent with current literature where no difference in modal acceleration frequency was found between young and elderly adults performing loaded abduction movements of the index finger (Burnett et al., 2000).

Previous research has demonstrated a decrease in tremor frequency with age (Marshall, 1961; Marsden and Watson, 1969; Wade et al., 1982; Birmingham et al., 1985; Kelly et al., 1995). In these studies the range of decline in frequency with age was approximately 1-4 Hz (Marshall, 1961; Marsden and Watson, 1969; Wade et al., 1982; Birmingham et al., 1985; Kelly et al., 1995). In contrast, more recent studies have not found any decline in tremor frequency with age in the presence and absence of mechanical load (Raethjen et al., 2000; Elble, 2003). Differences between the health and functional independence status of subjects in the above studies may explain the wide range (0-4 Hz) of age related
declines in tremor frequency reported in the literature. Subjects in the present study were excluded if they showed signs of neurological pathology, were deemed to be extremely frail, and/or resided in a skilled nursing facility.

**Aging versus Disease**

Because of the increased prevalence of movement disorders among elderly individuals (Benito-Leon et al., 2003; Van Den Eeden et al., 2003; Strickland and Bertoni, 2004), it is important to distinguish healthy aging from neurological pathologies. Results from this study demonstrated a strong, linear relation between the magnitude of peak tremor-EMG coherence in the 1-8 Hz frequency band and ApEn (Figure 6A), and both of these variables were sensitive enough to detect age related changes in physiological tremor between the oldest and youngest groups of subjects. Examination of ApEn values in Tables 1 and 2 suggests that healthy physiological tremor in the oldest group of subjects is different from pathological tremor in PD or ET. For resting and postural physiological tremor plus or minus three standard deviations from the mean ApEn value for the old-old subjects yields ApEn scores that range from 0.84 to 0.54 and 0.77 to 0.59 respectively. Therefore, it requires an ApEn value which is at least three standard deviations below the mean of the oldest group of subjects to approach mean ApEn values of tremor in the PD and ET groups.

The 1-8 Hz tremor-EMG coherence data also suggest a demarcation between healthy aging and disease. For resting tremor, there is close to a four fold difference between the magnitude of tremor-EMG coherence in the 1-8 Hz frequency band for the old-old subjects and the PD subjects (Table 1). For the unloaded postural tremor condition, the magnitude of tremor-EMG coherence in the 1-8 Hz frequency band for the
PD patients was between 2 and 2.5 times greater than the magnitude of 1-8 Hz tremor-EMG coherence from the old-old subjects (Table 2). Similarly, the magnitude of the ET subjects’ unloaded, postural tremor-EMG coherence in the 1-8 Hz frequency band was approximately 1.5 times greater than that of the old-old subjects (Table 2). The relation between and sensitivity of ApEn and tremor-EMG coherence in the 1-8 Hz frequency band further support their usefulness as biomarkers of tremor for aging and disease.

**Summary**

The aging process does not affect the neurophysiological characteristics of physiological tremor measured at rest, and the most significant consequences of healthy aging on physiological tremor are found in postural tremor regularity and the magnitude of tremor-EMG coherence in the 1-8 Hz frequency band in the oldest group of elderly subjects. Results from the current study showed that enhanced mechanical reflex properties among elderly adults are not a mechanism that can explain the age related increases in regularity and tremor-EMG coherence in the 1-8 Hz frequency band. A potential mechanism that could explain the changes in these variables is the age related loss of the ability to modulate descending inputs from multiple neural oscillators (Erim et al., 1999; Sosnoff et al., 2004). This argument is strengthened by the fact that with age the descending inputs to the motor neuron pool become more regular, oscillating at specific frequencies (Semmler et al., 2003). Despite the significant increases in postural tremor regularity and the magnitude of tremor-EMG coherence in the 1-8 Hz frequency band with age, there was a clear demarcation between these healthy, elderly individuals and our previous investigations of tremor pathology.
Acknowledgements

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References


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Table Captions

**Table 1:** Resting tremor regularity (ApEn), maximal 1-8 Hz tremor-EMG coherence, amplitude (RMS), and frequency (Hz) values (mean ± standard deviation) for young (20-30 years), young-old (60-69 years), old (70-79 years), and old-old (80-94 years) subjects. For direct comparison between age and disease, values (mean ± standard deviation) for patients with Parkinson’s disease are also given.

**Table 2:** Postural tremor regularity (ApEn), maximal 1-8 Hz tremor-EMG coherence, amplitude (RMS), and frequency (Hz) values (mean ± standard deviation) values for young (20-30 years), young-old (60-69 years), old (70-79 years), and old-old (80-94 years) subjects. For direct comparison between age and disease, values (mean ± standard deviation) for patients with essential tremor and Parkinson’s disease are also given.
Figure Captions

Figure 1: Schematic of the experimental paradigm for (A) resting tremor, (B) postural tremor without a load, and (C) postural tremor with a load. An accelerometer was placed 2 cm proximal to the second MCP joint (A-C), surface EMG electrodes were placed over the extensor digitorum muscle (A-C), and a load was suspended from MCP joints 2-5 (C). The target is shown in Figures B-C for the postural tremor conditions.

Figure 2: Tremor regularity (measured with ApEn) for the young, young-old, old, and old-old subjects under the postural tremor condition. Each value represents the average across subjects in each age group at each inertial load (mean + standard deviation). N=10 for each age group.

Figure 3: (A) Autospectra of tremor for a young subject (25 years), (B) and an old-old subject (81 years). (C) Autospectra of the EMG signal for the same young subject, (D) and the same old-old subject. (E) Coherence between tremor and EMG for the same young subject, (F) and the same old-old subject. The solid line depicts postural tremor-EMG coherence under the 0 gram load, and the dash, dotted line represents postural tremor-EMG coherence under the 1000 gram load. The thick dotted horizontal line in (E) and (F) represents the 95% confidence interval for significant tremor-EMG coherence.

Figure 4: Maximal postural tremor-EMG coherence in the 1-8 Hz band collapsed across load from young, young-old, old, and old-old subjects (mean + standard deviation). N=10 for each age group.

Figure 5: Tremor-EMG coherence in the low frequency bins measured under the postural tremor condition from young, young-old, old, and old-old subjects. The
frequency bins were subdivided by 0.976 Hz into 9 bins. In each bin, mean tremor-EMG coherence is presented from each age group at each load from 0 grams (1), 100 grams (2), 250 grams (3), 500 grams (4), to 1000 grams (5).

**Figure 6:** The relation between regularity (ApEn) and tremor-EMG coherence in the 1-8 Hz frequency band measured under the postural tremor condition from young, young-old, old, and old-old subjects. Mean values for ApEn and 1-8 Hz tremor-EMG coherence are collapsed across subjects in each age group at each specific inertial load condition. (A) Tremor-EMG coherence in the 1-8 Hz frequency bin plotted versus ApEn, (B) Tremor-EMG coherence in the 5.85 Hz frequency bin plotted versus ApEn, (C) Tremor-EMG coherence in the 6.83 Hz frequency bin plotted versus ApEn. Standard deviations for ApEn and 1-8 Hz tremor-EMG coherence are presented in Table 2.
### Table 1: Resting Tremor

<table>
<thead>
<tr>
<th>Dependent Variables</th>
<th>Young (20-30 y)</th>
<th>Young-Old (60-69 y)</th>
<th>Old (70-79 y)</th>
<th>Old-Old (80-94 y)</th>
<th>Parkinson’s Disease</th>
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<tbody>
<tr>
<td>ApEn</td>
<td>0.70 ± 0.06</td>
<td>0.69 ± 0.04</td>
<td>0.71 ± 0.10</td>
<td>0.69 ± 0.05</td>
<td>0.53 ± 0.08</td>
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<tr>
<td>Coherence</td>
<td>0.16 ± 0.03</td>
<td>0.13 ± 0.03</td>
<td>0.14 ± 0.03</td>
<td>0.16 ± 0.03</td>
<td>0.62 ± 0.25</td>
</tr>
<tr>
<td>Amplitude (cm)</td>
<td>0.01 ± 0.01</td>
<td>0.01 ± 0.01</td>
<td>0.02 ± 0.02</td>
<td>0.02 ± 0.01</td>
<td>9.17 ± 8.2</td>
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<tr>
<td>Frequency (Hz)</td>
<td>8.09 ± 0.69</td>
<td>7.37 ± 0.77</td>
<td>7.29 ± 0.85</td>
<td>7.44 ± 0.86</td>
<td>6.07 ± 0.89</td>
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ApEn – approximate entropy
### Table 2: Postural Tremor

<table>
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<th>Dependent Variables</th>
<th>Load</th>
<th>Young (20-30 y)</th>
<th>Young-Old (60-69 y)</th>
<th>Old (70-79 y)</th>
<th>Old-Old (80-94 y)</th>
<th>Essential Tremor</th>
<th>Parkinson’s Disease</th>
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<td>ApEn</td>
<td>0 grams</td>
<td>0.72 ± 0.03</td>
<td>0.71 ± 0.04</td>
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<td>0.68 ± 0.03</td>
<td>0.57 ± 0.05</td>
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<td></td>
<td>100 grams</td>
<td>0.71 ± 0.04</td>
<td>0.70 ± 0.03</td>
<td>0.70 ± 0.06</td>
<td>0.69 ± 0.05</td>
<td>0.58 ± 0.04</td>
<td>0.59 ± 0.04</td>
</tr>
<tr>
<td></td>
<td>250 grams</td>
<td>0.72 ± 0.05</td>
<td>0.69 ± 0.02</td>
<td>0.69 ± 0.04</td>
<td>0.66 ± 0.05</td>
<td>0.57 ± 0.05</td>
<td>0.60 ± 0.05</td>
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<tr>
<td></td>
<td>500 grams</td>
<td>0.74 ± 0.06</td>
<td>0.70 ± 0.04</td>
<td>0.69 ± 0.07</td>
<td>0.67 ± 0.06</td>
<td>0.55 ± 0.04</td>
<td>0.57 ± 0.06</td>
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<td>1000 grams</td>
<td>0.74 ± 0.06</td>
<td>0.70 ± 0.07</td>
<td>0.68 ± 0.06</td>
<td>0.66 ± 0.03</td>
<td>0.53 ± 0.06</td>
<td>0.58 ± 0.04</td>
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<tr>
<td>Coherence</td>
<td>0 grams</td>
<td>0.16 ± 0.06</td>
<td>0.24 ± 0.10</td>
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<td>0.41 ± 0.16</td>
<td>0.61 ± 0.25</td>
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<td>100 grams</td>
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<td>0.24 ± 0.11</td>
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<td>0.27 ± 0.14</td>
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<td>0.57 ± 0.30</td>
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<td>0.21 ± 0.09</td>
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<td>0.41 ± 0.26</td>
<td>0.60 ± 0.27</td>
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<td>0.14 ± 0.04</td>
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<td>0.21 ± 0.11</td>
<td>0.24 ± 0.08</td>
<td>0.41 ± 0.24</td>
<td>0.58 ± 0.26</td>
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<tr>
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<td>1000 grams</td>
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<td>0.21 ± 0.11</td>
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<td>0.26 ± 0.11</td>
<td>0.44 ± 0.25</td>
<td>0.57 ± 0.26</td>
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<td>Amplitude (cm)</td>
<td>0 grams</td>
<td>0.04 ± 0.02</td>
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<td>0.06 ± 0.05</td>
<td>0.09 ± 0.08</td>
<td>4.67 ± 2.26</td>
<td>10.62 ± 8.97</td>
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<td>100 grams</td>
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<td>0.09 ± 0.07</td>
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<td>1.97 ± 1.82</td>
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<tr>
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<td>1000 grams</td>
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<td>0.07 ± 0.04</td>
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<td>1.84 ± 1.77</td>
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<td>500 grams</td>
<td>6.59 ± 0.75</td>
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<td>6.22 ± 0.29</td>
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ApEn – approximate entropy
A. Resting Condition  

B. Unloaded Postural Condition  

C. Loaded Postural Condition

Figure 1
Figure 2
Figure 3

(A) Young Subject

(B) Old-Old Subject

(C)

(D)

(E)

(F)
Figure 4

The graph illustrates the coherence (1-8 Hz) across different age groups: Young, Young-Old, Old, and Old-Old. The x-axis represents age (yrs.) with categories 20-30, 60-69, 70-79, and 80-94. The y-axis shows the coherence ranging from 0.0 to 0.4. The coherence values increase with age, with the oldest age group showing the highest coherence.

* denotes a significant difference.
Figure 5
Figure 6

Aging and Tremor Regularity

- Coherence (1-8 Hz)
- Coherence (5.85 Hz)
- Coherence (6.83 Hz)

Plot A:
- R² = 0.70
- Intercept = 0.78
- Slope = -0.43

Plot B:
- R² = 0.59
- Intercept = 0.73
- Slope = -0.30

Plot C:
- R² = 0.57
- Intercept = 0.73
- Slope = -0.24

Legend:
- Young
- Young-Old
- Old
- Old-Old