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Amplitude- and Velocity-Dependency of Rigidity Measured at the Wrist in Parkinson's Disease

Douglas Powell¹, A. Joseph Threlkeld¹, Xiang Fang², Anburaj Muthumani¹, and Rui-Ping Xia¹

¹Rehabilitation Science Research Laboratory, Department of Physical Therapy, Creighton University, Omaha, NE 68178, USA

²Division of Biostatistics, Office of Research and Compliance, Creighton University, Omaha, NE 68178, USA

Abstract

Objective—Quantify the effects of increased amplitude and rate of muscle stretch on parkinsonian rigidity.

Methods—Eighteen subjects with Parkinson's disease participated in this study. Subjects' tested hand was passively displaced through 60° and 90° ranges of wrist flexion and extension at velocities of 50°/s and 280°/s in both treated and untreated conditions. Joint angular position, resistance torque, and surface electromyography (EMG) of the wrist flexors and extensors were recorded. Rigidity was quantified by normalized work scores and normalized angular impulses for flexion and extension, separately. Reflex responses of stretched and shortened muscles were quantified by mean EMG and EMG ratio. A series of ANOVAs was performed to determine the effect of amplitude, velocity and medication on selected variables.

Results—Both work scores and angular impulses revealed that the larger displacement amplitude and the higher velocity were associated with significantly greater rigidity, increased EMG ratio and mean EMG of stretched muscles. Dopaminergic medication was not associated with a reduction in rigidity.

Conclusions—Parkinsonian rigidity is modulated by the amplitude and rate of muscle stretch.

Significance—These findings shed light on the biomechanical underpinnings and physiological characteristics of rigidity and may inform clinical rigidity assessment in Parkinson's disease.

Keywords

Parkinson's disease; Rigidity; Dopaminergic medication; EMG; Kinetics

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Corresponding Author: Douglas Powell, Ph.D., Rehabilitation Science Research Laboratory, Dept. of Physical Therapy, Creighton University, 2500 California Plaza, Omaha, NE 68178, USA, Phone: 1-(402) 280-5679, Fax: 1-(402) 280-5692, dwp0817@gmail.com, douglaspowell@creighton.edu.

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1. Introduction

Parkinson's disease (PD) is a chronic, progressive neurodegenerative movement disorder characterized by bradykinesia, muscle rigidity, resting tremor and postural instability (Lang and Lozano, 1998; Fahn and Sulzer, 2004). As a cardinal symptom of PD, rigidity forms an integral part of clinical diagnosis. Rigidity is also used to evaluate the effectiveness of treatment, due to its positive response to dopaminergic medication and surgical intervention (Temperli *et al.*, 2003; Schapira *et al.*, 2009). Parkinsonian rigidity is defined as an increased resistance to passive movement of a limb and is felt as a constant and uniform resistance persisting throughout the entire range of motion (Fung and Thompson, 2002). A clinical rigidity score utilizing the Unified Parkinson's Disease Rating Scale (UPDRS) is based on the examiner's perception of resistance to examiner-imposed movements of the subject's wrist, elbow, neck and ankle joints (Fahn and Elton, 1987; Goetz *et al.*, 2008). The nature of this assessment is qualitative and highly subjective, since it is largely dependent on examiners' individual interpretations and experience (Prochazka *et al.*, 1997).

Numerous studies have been conducted to explore the underlying physiological mechanisms of rigidity. Electromyographic (EMG) studies show that the short-latency stretch reflex was normal in PD (Rothwell *et al.*, 1983; Delwaide *et al.*, 1986; Bergui *et al.*, 1992; Meara and Cody, 1993). However, the long-latency stretch reflex was reported to be exaggerated in individuals with PD, as compared to healthy controls (Rothwell *et al.*, 1983; Tatton *et al.*, 1984; Cody *et al.*, 1986).

Besides abnormal muscle responses to passive stretch, a shortening reaction (i.e. an anomalous muscle activation in response to passive shortening) has also been described in PD (Westphal, 1880). While the shortening reaction exists in healthy individuals, it was demonstrated to be accentuated in parkinsonian rigidity (Andrews *et al.*, 1972; Berardelli and Hallett, 1984) and was suggested to be responsible for the pathophysiology of rigidity (Rondot and Metral, 1973; Angel, 1983).

During the past several decades, considerable efforts have been made to quantify rigidity utilizing biomechanical measures. A variety of quantitative methods were developed to assess the dynamics of joint stiffness associated with rigidity (Teravainen *et al.*, 1989; Prochazka *et al.*, 1997; Lee *et al.*, 2002). The underlying approaches measure the resistance to externally generated passive movement about the examined joint. Traditionally, parkinsonian rigidity is considered to be independent of velocity in contrast to spasticity which is velocity-dependent (Lance, 1980). The notion of the velocity-independence of rigidity might be anecdotal. A limited number of studies have provided evidence which raised questions about the accuracy of this view. Lee *et al.* (2002) studied velocity related properties of hypertonia at the elbow joint in subjects with PD and in participants with hemiparesis. The investigators concluded that both rigidity and spasticity have approximately equal velocity-dependent properties. Quantitative measures of trunk rigidity in subjects with PD also revealed a velocity-dependency feature (Mak *et al.*, 2007).

The effect of movement amplitude is much less understood and has rarely been investigated in parkinsonian rigidity. We could locate only one study that assessed the effect of displacement amplitude on rigidity (Teravainen *et al.*, 1989). The movement amplitude examined in the above study was confined within $\pm 30^\circ$ of wrist motion; much smaller than the achievable range of motion in patients with PD having a clinical rigidity score under 4 on the UPDRS. The range of joint motion examined by clinicians often varies with some moving the segment back and forth rapidly in the mid-range, and others focusing on the extremes of range of motion or even the entire range of motion while utilizing slow stretches (Prochazka *et al.*, 1997). This clinical inconsistency increases the need to objectively

explore the influence of displacement amplitude on rigidity, including an expanded range of motion.

Although rigidity has been studied for decades, the majority of previous studies focused on measurement of one element, either examining muscle EMG responses without including joint torque resistance to imposed movement (Lee and Tatton, 1975; Cody *et al.*, 1986) or quantifying joint torque resistance alone (Teravainen *et al.*, 1989; Fung *et al.*, 2000). In addition, few studies have investigated the changes in physiological measures of rigidity resulting from the dopaminergic medication therapy despite the known responsiveness of rigidity to medication. No previous study has used quantitative measures of both EMG and joint kinetics to analyze the effects of multiple factors and their interactions on parkinsonian rigidity.

Therefore, the purpose of the current study was to investigate the effects of amplitude and velocity of passive movement and of dopaminergic medication on parkinsonian rigidity. It was hypothesized that (1) increased movement amplitude would be associated with greater levels of rigidity, (2) increased movement velocity would result in greater rigidity, and (3) dopaminergic medication would reduce rigidity across all conditions.

2. Methods

Participants

Eighteen subjects with idiopathic PD (7 men, 11 women) participated in this study. Subjects' ages ranged from 46 to 77 years, with an average of 64.1 ± 9.0 (SD). Each subject was assessed for inclusion using a verbal medical history and the Motor Section (Part III) of the UPDRS. Subjects were included if they (1) were between 40 and 80 years of age, (2) were treated using dopaminergic medication, (3) had the presence of clinical rigidity of 2 or 3 (mild to moderate or marked) in one or both arms when dopaminergic medication was temporarily withdrawn, and (4) had minimal tremor (≤ 1 , slightly and infrequently present) in the tested arm in the untreated condition. Subjects were excluded if cognitive impairments prevented them from giving informed consent, understanding instructions or providing adequate feedback. Subjects were also excluded if they had insufficient wrist range of motion (less than 50° in either flexion or extension) or a history of upper extremity impairment that would affect wrist motion. Table 1 presents all participants' clinical characteristics and medication information. The study was conducted in accordance with the Declaration of Helsinki. The experimental protocol was approved by the Institutional Review Board of Creighton University, Omaha, Nebraska, USA. All subjects provided written informed consent prior to participation in the study.

Experimental protocol

Each subject was initially evaluated using the Motor Section (Part III) of the UPDRS (Fahn and Elton, 1987); the subject was then seated in a height adjustable chair. The subject's hand exhibiting greater rigidity according to the UPDRS was placed in a manipulandum attached to the shaft of a servomotor. With the subject's shoulder and forearm in neutral position and the elbow in approximately 120° of flexion, the center of wrist joint rotation was aligned with the center of rotation of the servomotor. The forearm was stabilized with a vacuum bag splint, preventing forearm pronation and supination. The metacarpal restraints of the manipulandum restricted other motions of the wrist allowing only flexion and extension.

Subjects were instructed to remain relaxed to their best ability during the wrist flexion and extension movements generated by the servomotor. The movement applied was ramp-and-hold trajectory with one-second hold, including one flexion and one extension movement in each trial. The hand was displaced through central ranges of $60^\circ (\pm 30^\circ)$ and $90^\circ (\pm 45^\circ)$

motion at constant velocities of 50 °/s and 280 °/s. Four trials were collected for each of the four combinations of displacement amplitude with movement velocity. All combinations of range and velocity were randomly presented, and each trial was followed by a 30-second rest to minimize motor adaptation and fatigue.

Surface EMG signals were recorded from the wrist and finger flexor muscles: flexor carpi radialis (FCR), flexor carpi ulnaris (FCU), and flexor digitorum superficialis (FDS), and extensor muscles: extensor carpi radialis (ECR), extensor carpi ulnaris (ECU), and extensor digitorum communis (EDC) using a multi-channel surface EMG system (Delsys, Inc., MA, USA). Electrode placements followed previously published recommendations (Perotto, 1994) and were confirmed by manual muscle testing. EMG signals were amplified ($\times 10$ k) and band-pass filtered (20–450 Hz) before being sampled at 1000 Hz for each EMG channel. Torque resistance at the wrist was measured using a strain gauge torque transducer (TRT-200, Pacific Scientific, CA, USA), while angular position of the wrist joint was measured using an emulated encoder output from the servomotor controller (SC904 series, Pacific Scientific, CA, USA). Torque and position signals were recorded at 1000 Hz and 100 Hz, respectively. Data capture was controlled by computer code written in LabVIEW 2009 (National Instruments, Texas, USA).

Subjects with PD were initially tested after an overnight withdrawal from dopaminergic medication (OFF-MED) for at least 12 hours (Jahanshahi *et al.*, 2010) when the majority of the beneficial effects of dopaminergic therapy was eliminated (Defer *et al.*, 1999). After the OFF-MED tests were completed, the subject's regular dose was self-administered in the laboratory, followed by a 30- to 60-minute period of rest. The effect of medication was validated verbally by the subject. After the efficacy of medication was established, the testing protocol was repeated in the on-medication state (ON-MED).

Data analyses

Customized code written in MATLAB 2010 (MathWorks, MA, USA) was applied to analyze torque and EMG data and to quantify rigidity of the wrist in subjects with PD. Rigidity was assessed by calculating the integral of torque with respect to joint angle (Nm-deg) for the movement being investigated, referred to as rigidity work score (Fung *et al.*, 2000; Xia *et al.*, 2006). The rigidity work score was normalized to range of motion to validate comparisons between conditions with different displacement amplitudes. The angular impulse was calculated as the torque value integrated with respect to time (Nm-sec) and was normalized to the duration of time required to complete a given range of motion for the movement being examined. The slope of the torque-angle plot was obtained using linear regression analyses for the flexion and extension movements, separately (Xia and Rymer, 2004; Xia *et al.*, 2006). Inertial components of the imposed torque, just after movement onset, were excluded from the analyses (Figure 1). This component covered about a 5° range for the 50 °/s velocity and nearly 15° for the 280 °/s velocity.

EMG signals were full-wave rectified and low-pass filtered with a cutoff frequency of 20 Hz. EMG activity for each muscle was averaged within the movement duration for flexion and extension, respectively, and then normalized to the background EMG activity by dividing by the mean EMG amplitude during the 100 ms prior to the onset of movement as previously suggested (Rothwell *et al.*, 1983). Normalized mean EMG values were grouped by function (flexors or extensors) and represented by the sum of the EMG (i.e. Flexors = FCR + FCU + FDS; Extensors = ECR + ECU + EDC). For example, the mean EMG of stretched muscles was calculated as an average of normalized mean EMG of the extensors during the flexion motion and the average of normalized mean EMG of the flexors during the extension motion (Xia *et al.*, 2009; Powell *et al.*, 2011). The mean EMG of shortened muscles was calculated as the average of normalized mean EMG signals of the flexors

during flexion and the average of normalized mean EMG signals of the extensors during extension.

In addition to stretched and shortened muscle responses, EMG ratios were also calculated. The normalized EMG activity of stretched muscles was divided by the normalized EMG activity of shortened muscles during each movement. Specifically, during the imposed flexion movement, the extensor muscles were stretched while the flexor muscles were shortened. Thus the normalized mean EMG in the stretched extensor muscles was divided by the normalized mean EMG in the shortened flexor muscles obtaining an EMG ratio for the flexion movement. EMG ratio has previously been used to represent the interaction of the stretch reflex and shortening reaction and shown to be a robust index for characterizing parkinsonian rigidity (Meara and Cody, 1992; Xia *et al.*, 2009).

Statistical analyses

A three-way (amplitude $\times$ velocity $\times$ medication; $2 \times 2 \times 2$) analysis of variance (ANOVA) was performed to determine the main effects and interaction effects of movement amplitude, movement velocity and medication on dependent variables associated with the flexion and extension phases of the movement as well as the entire cycle of flexion and extension (total movement). In the presence of a statistically significant interaction effect, post hoc analyses were performed, including tests of simple effects which determined the effect of one factor at each level of the other factor using Student's *t*-tests. Dependent variables were rigidity work score, angular impulse, torque-angle slope, EMG of stretched muscles, EMG of shortened muscles and the EMG ratio of stretched-shortened muscles. For all statistical tests, differences were considered significant when there was less than a 5% chance of making a type I error ($p < 0.05$). The statistical analyses were performed using SAS 9.2 (SAS Institute Inc., Cary, NC, USA).

3. Results

Quantification of parkinsonian rigidity assessed by torque measure

Figure 2 depicts torque-angle plots associated with two displacement amplitudes and two movement velocities obtained from a representative subject in the OFF-MED state. The illustrations display the effects of both amplitude and velocity on rigidity as reflected by normalized work score, i.e., the area within the torque-angle loop. The effect of movement amplitude is evident when comparing the 60° range of motion (upper panels) with the 90° range (lower panels). In the SLOW condition, the distance between the torque-angle traces remained relatively small and consistent throughout the entire range of movement (Figure 2A), whereas the 90° range of motion was associated with a progressively increasing distance between the two torque-angle traces until the movement approaches the end of the wrist flexion where there was a dramatic increase in the distance (Figure 2C). This increase is attributable to the steeper torque-angle plot near the end-range of the 90° range of flexion movement. A similar effect of movement amplitude was also observed in the FAST condition with greater distances between the flexion and extension portions of the torque-angle traces when the wrist was displaced through 90° of excursion (Figure 2D) in comparison to the 60° range of motion (Figure 2B).

Figures 3 and 4 show summary results of rigidity work score and angular impulse averaged in all participants. The greater amplitude of movement caused significant increases in work score ($p < 0.001$; Figure 3) and angular impulse ($p = 0.003$; Figure 4). Both the work score and angular impulse were consistently higher with the greater movement amplitude for all velocity conditions and medication states (Figure 3A cf. 3B; Figure 4A cf. 4B). The changes in the total work score and angular impulse were dominated by increases related to the

flexion movement (work score: $p < 0.001$; angular impulse: $p < 0.001$), but there was no significant change in rigidity scores for the extension movement (work score: $p = 0.161$; angular impulse: $p = 0.466$).

There was a presence of velocity effect on work score and angular impulse. Specifically, the FAST condition was associated with greater work scores: Total ($p < 0.001$), Flexion ($p < 0.001$) and Extension ($p < 0.001$). In comparison to the SLOW condition, the FAST condition increased angular impulse: Total ($p < 0.001$), Flexion ($p < 0.001$) and Extension ($p < 0.001$). Dopaminergic medication had no significant effect on work scores (Total: $p = 0.314$; Flexion: $p = 0.272$; Extension: $p = 0.772$) or angular impulses (Total: $p = 0.333$; Flexion: $p = 0.287$; Extension: $p = 0.637$). There were no significant interactions among movement amplitude, velocity and medication. However, the amplitude $\times$ velocity interaction did approach significance for work score ($p = 0.070$) and angular impulse ($p = 0.059$) associated with the extension component of rigidity.

The torque-angle slope characterizes and quantifies the uniform nature of parkinsonian rigidity. Figure 2 portrays the uniform pattern of rigidity under two displacement amplitudes and two movement velocities. In the SLOW conditions (left panels), the torque-angle curves were steeper for both flexion and extension in the 90° range of motion (Fig. 2C) compared to the 60° range of motion (Fig. 2A). The resistance to movement (quantified by torque) progressively increased through most of the flexion phase until the movement approached terminal flexion (+45°) where the steeper increase in torque occurred. A similar trend was observed in the torque-angle plot during the FAST conditions (Figures 2B and 2D); however, the increase in slope appeared to have a later onset in the movement, passing approximately 30° of wrist flexion. In addition, the mean slopes of the torque-angle plots were consistently flatter for the extension movement (the upper traces) than the flexion movement (the lower traces) across all four panels.

Table 2 lists summarized results of the torque-angle slopes from all the subjects. There were no significant differences between the 60° and 90° ranges of motion ($F = 3.47$, $p = 0.082$). The FAST condition was associated with significantly greater torque-angle slopes ($F = 22.64$, $p < 0.001$). The extension component of the torque-angle slope was significantly flatter than the flexion component ($F = 14.53$, $p = 0.002$). There was no significant effect of medication on the slope of the torque-angle plot ($F = 1.80$, $p = 0.196$). However, the slope became steeper as a result of medication therapy regardless of the amplitude and velocity condition.

Electromyographic (EMG) activation of forearm muscles in parkinsonian rigidity

Joint position and EMG activities of the flexors and extensors across the wrist during the imposed extension movement are shown in Figure 5. A stretch reflex and shortening reaction are visualized when a representative subject was tested in the OFF-MED (A) and ON-MED (B) conditions. In this example, the stretch reflex was observed in the wrist flexors and the shortening reaction was exhibited in the wrist extensors. Both phenomena were evident in the OFF-MED condition, whereas the magnitude was substantially reduced for both stretch reflex and shortening reaction in the ON-MED condition.

Quantification of muscle activity, including the mean EMG values of the stretched and shortened muscles as well as the EMG ratios of stretched-shortened muscles from all participants, is presented for the imposed flexion and extension movements (Figures 6 and 7). During the flexion movement (Figure 6), the 90° range of motion was associated with significantly lower muscle activation levels in the stretched muscles ($F = 8.72$, $p = 0.005$) and significantly smaller EMG ratio ($F = 13.37$, $p = 0.001$) while the shortened muscles exhibited significant increases in muscle activity ($F = 6.58$, $p = 0.014$). Regarding the

velocity effect, the FAST condition resulted in significantly greater muscle activation in the stretched muscles ($F = 72.47$, $p < 0.001$) and EMG ratio ($F = 12.95$, $p = 0.001$), whereas no difference was found in the shortened muscles ($F = 0.30$, $p = 0.5864$). There was no significant effect of medication on EMG amplitude in the stretched muscles ($F = 3.42$, $p = 0.078$), shortened muscles ($F = 0.16$, $p = 0.693$) or EMG ratio ($F = 1.70$, $p = 0.201$) during the flexion phase of the movement, though overall EMG amplitudes were decreased with the administration of medication.

During the extension movement (Figure 7), a significant interaction effect between amplitude and velocity was identified for all three EMG variables: the stretched muscles ($F = 6.99$, $p = 0.001$), the shortened muscles ($F = 6.00$, $p = 0.016$), and the EMG ratio ($F = 17.85$, $p < 0.001$). In the stretched muscles, the 90° range of motion was associated with significantly increased mean EMG values compared to the 60° range of motion under the SLOW condition ($t = 2.02$, $p = 0.047$); however, no differences were detected between the two displacement amplitudes under the FAST condition ($t = -1.69$, $p = 0.094$). Further, the FAST condition was associated with significantly greater mean EMG values of the stretched muscles compared to the SLOW condition in both the 60° ($t = 7.45$, $p < 0.001$) and 90° ranges of motion ($t = 3.55$, $p < 0.001$). In the shortened muscles, the larger amplitude of motion did not cause significantly different mean EMG values in either the SLOW ($t = 1.58$, $p = 0.117$) or the FAST condition ($t = -1.57$, $p = 0.112$). In comparison of the FAST with the SLOW condition, there were not significant changes in mean EMG values of the shortened muscles in the 60° range of motion ($t = 1.56$, $p = 0.22$).

Conversely, in the 90° range of motion, the FAST condition was associated with greater mean EMG values of shortened muscles than the SLOW condition ($t = 4.88$, $p < 0.001$). The EMG ratio was significantly greater in the larger displacement amplitude under the SLOW condition ($t = 2.70$, $p = 0.008$). However, the 90° range of motion was associated with significantly smaller EMG ratios than the 60° range of motion in the FAST condition ($t = -3.23$, $p = 0.002$). The FAST condition was associated with significantly greater EMG ratios than the SLOW condition for the 60° range of motion ($t = 6.20$, $p < 0.001$); however, EMG ratios were not significantly different between the FAST and SLOW conditions, for the 90° range of motion ($t = 0.08$, $p = 0.933$). During the extension movement, there was no significant effect of medication on EMG amplitudes of stretched muscles ($F = 3.66$, $p = 0.069$), shortened muscles ($F = 0.42$, $p = 0.524$), or EMG ratios ($F = 1.75$, $p = 0.199$).

4. Discussion

Parkinsonian rigidity has been investigated across a number of upper and lower extremity joints with respect to the aberrant reflex responses in muscles acting on the given joint and the quantification of joint stiffness (Berardelli and Hallett, 1984; Gregoric *et al.*, 1988; Lee *et al.*, 2002; Mak *et al.*, 2007; Shapiro *et al.*, 2007; Xia *et al.*, 2009; Powell *et al.*, 2011), but the current study has investigated the amplitude-dependent nature of parkinsonian rigidity. This investigation is novel and directly relevant to the clinical examination of rigidity. In addition, the present study supports accumulating evidence that rigidity is modulated by movement velocity (Lee *et al.*, 2002; Mak *et al.*, 2007; Xia *et al.*, 2009).

Effect of amplitude on parkinsonian rigidity

The main finding of the current study was the modulation of parkinsonian rigidity by the amplitude of wrist motion. Comparing 60° to 90° of passive sagittal-plane movement, the greater displacement was associated with increased rigidity as quantified by work scores and angular impulses. This finding seems to contradict the clinical description of parkinsonian rigidity as increased and uniform resistance throughout the entire range of passive motion. While torque integral analyses applied in this study are time- and position-dependent, these

variables were then normalized to allow for making comparisons between different displacement amplitudes and between different time durations. The normalization procedure provides confidence that the observed increases in rigidity in response to the larger range of motion was not due to an artifact of the data processing methods.

There are a few possible explanations for the amplitude-dependency of parkinsonian rigidity. First, the stiffness due to shortening of the tendon, intramuscular connective tissues and other non-neural factors can dramatically increase the resistance to a passive motion with an increasing muscle stretch (Fung and Thompson, 2002). Muscle force generated by the passive motion is approximately proportionate to the muscle stretch, i.e. the well known length-tension relationship (Matthews, 1959). Evidence has indicated that the non-neural component also contributes to parkinsonian rigidity (Dietz *et al.*, 1981; Watts *et al.*, 1986; Dietz, 1987). The contribution of the non-neural component to joint stiffness was shown to be comparable to the neural contribution from increased reflex responses in parkinsonian rigidity (Xia *et al.*, 2010).

Second, the neural reflex component may not maintain the uniformity of rigidity near the terminal portions of the larger range of motion (Figure 2). The findings of the current study suggest that with an increased joint excursion and greater muscle stretch, the stretch reflex dominates the shortening reaction, resulting in greater rigidity. Andrews *et al.* (1972) showed that the stretch reflex was facilitated by increasing muscle length and also suggested that the shortening reaction responded to changes in muscle length. In addition, Berardelli *et al.* (1983) demonstrated the enhanced long-latency stretch reflex and shortening reaction recorded from triceps surae and tibialis anterior in patients with PD, and suggested that the abnormal long-latency stretch reflex might be mediated by the group II afferents which are sensitive to changes in muscle length. Other than the spinal mechanism, supraspinal involvement has also been suggested (Andrews *et al.*, 1973; Angel, 1982; Diener *et al.*, 1987).

The shortening reaction is shown to play a mediating role in the uniform nature of parkinsonian rigidity within a moderate range of motion, i.e. 30° flexion/extension (Xia and Rymer, 2004), but little is known about the neurophysiology underlying the shortening reaction or its response to greater muscle stretch (45° flexion/extension). It has been recently demonstrated that parkinsonian rigidity has stronger correlations with the interaction of the stretch reflex and shortening reaction compared with the reflex responses in stretched muscles alone (Xia *et al.*, 2009). Finally, while the relatively normal short-latency stretch reflex is mediated by a spinal pathway, mediation of the long-latency stretch reflex may involve a trans-cortical pathway (Andrews *et al.*, 1972; Capaday *et al.*, 1991; Palmer and Ashby, 1992; Lewis *et al.*, 2004; Coxon *et al.*, 2005). In particular, it was revealed that increasing the amplitude of muscle stretch in the wrist flexors and extensors not only altered the short- and long-latency stretch reflexes, but also modulated corticomotor excitability (Coxon *et al.*, 2005). Using transcranial magnetic stimulation, Coxon *et al.* (2005) investigated changes in corticomotor excitability during passive wrist flexion and extension movements through ranges of motion similar to those used in the current study (60° and 90°). They reported that large-amplitude motions facilitated motor responses more than small-amplitude motions.

Furthermore, a recent imaging study has demonstrated that the primary motor cortex was hyperactive in people with PD and that changes in motor cortex activation following dopaminergic medication were highly correlated with parkinsonian rigidity (Yu *et al.*, 2007). It is possible that the interaction between the hyperactivity of motor cortex and increased corticomotor excitability associated with increased movement amplitude contribute to the observed increase in rigidity in the larger range of motion. In conjunction

with the segmental contributions to rigidity, supraspinal mechanisms (including the long-latency stretch reflex, changes in corticomotor excitability and hyperactive motor cortex) are likely to be responsible for the amplitude-dependent nature of rigidity in PD.

Effect of velocity on parkinsonian rigidity

In concert with previous research findings (Lee *et al.*, 2002; Mak *et al.*, 2007; Xia *et al.*, 2009), the current data lend further support to the velocity-dependent nature of parkinsonian rigidity. The muscle spindle responds to an increased rate of stretch by increasing the firing rate of the primary afferents, producing a greater reflex response as evidenced by the greater amplitudes of EMG activity (Figures 6 and 7). The long-latency stretch reflex may account for increased rigidity produced during the FAST wrist movement in the current study. The rate of muscle stretch needs to be sufficiently high in order to elicit the long-latency stretch reflex. The shortening reaction mediates the constant and uniform resistance of parkinsonian rigidity because its resultant muscle force counteracts the resistance to elongation produced by the stretched muscles (Xia and Rymer, 2004).

Joint torque resistance to passive movement is a broad reflection of the interaction between the stretch reflex in opposing muscle groups and the shortening reaction in assisting muscle groups (Xia *et al.*, 2009). Present EMG data support previous research findings by demonstrating that EMG ratios were consistently greater in the FAST than the SLOW condition for two ranges of motion, both medication states and for both flexion and extension movements. While the mean EMG amplitude of the stretched muscles increased with the increasing velocity, the mean EMG amplitude of the shortened muscles remained relatively unchanged during either the flexion or extension movements, except for one condition of 90° range of extension movement. This is in agreement with previous research that the shortening reaction is relatively independent of movement velocity (Rondot and Metral, 1973; Xia *et al.*, 2009). Therefore, the velocity-dependent changes in rigidity observed in the current study and in previous studies (Lee *et al.*, 2002; Mak *et al.*, 2007; Xia *et al.*, 2009) can be explained by the interaction of velocity-dependent increases in the antagonistic contribution of the stretch reflex and the unchanged contribution of the velocity-independent agonistic action of the shortening reaction.

The angular impulses and work scores presented in this study are similar in magnitude to those previously reported and are derived from a larger sample size than the previous study (Xia *et al.*, 2006). Measures of rigidity were normalized to allow comparison between different movement velocities and amplitudes; however, the un-normalized work scores and angular impulses were within one standard deviation of previously reported data under similar movement conditions which was the 60° range of motion at 50 °/sec (Xia *et al.*, 2006). Furthermore, these data support previous research findings by demonstrating that rigidity is positively related to velocity (Lee *et al.*, 2002; Mak *et al.*, 2007; Xia *et al.*, 2009). While the correlation between rigidity and movement velocity was not examined in the current study, both measures of rigidity were significantly greater in the FAST condition compared to the SLOW condition.

Effect of medication on parkinsonian rigidity

Our results showed that dopaminergic medication did not significantly reduce rigidity as quantified by measures of EMG, torque scores, or torque-angle slope, irrespective of the displacement amplitude or movement velocity. A few explanations may underlie these findings. This may pertain to the uni-planar nature of the objective measurement of rigidity used in the current study. However, clinical assessment of rigidity incorporates three-dimensional movements. It may be possible that the improvements in clinically assessed rigidity resulting from medication therapy were not observed in the objective measures of

rigidity due to this limitation. On the other hand, the efficacy of medication in clinical examination was based on the global impression from multiple joints, including neck, upper extremity and lower extremity joints. Similarly, the lack of medication effect was found on quantitative measure of rigidity at the elbow joint in the uni-planar movement (Shapiro et al., 2007). Subjects were tested under four combinations of medication (Off vs. On) and deep brain stimulation (Off vs. On) status. Treatment by deep brain stimulation reduced rigidity as indicated by work score and by rigidity score on the UPDRS. The results suggested that the surgical treatment may be more effective in alleviating rigidity in the upper limb of parkinsonian patients than medications alone.

Another possibility lies in the background EMG activity level under the two medication conditions. It was previously suggested that the increased background EMG due to patients' inability to relax also contribute to parkinsonian rigidity. Analysis of the EMG data in the present study revealed an 11% decrease in background EMG amplitude when testing was repeated after the administration of dopaminergic medication. A small reduction in background muscle activity in the ON-MED state may well be a reason for the current results.

A possible reason for a lack of medication effect on measures of EMG amplitude pertains to the method used for EMG normalization. Previous research has suggested that rigidity is associated with the reflex activity, which is scaled to the pre-existing levels of background EMG because individuals with PD exhibit hypertonia and cannot fully relax their muscles (Rothwell *et al.*, 1983). In the present study, EMG amplitude was normalized to the mean background EMG prior to the onset of movement. However, dopaminergic medication is shown to reduce not only reflex magnitude but also the background muscle activation, although the change was relatively small. While no statistical tests were conducted, the effect of a reduced normalization value may be substantial. Therefore, the methodology used in this study may have contributed to the current observation, as medication therapy may have reduced both the background EMG and reflex magnitude, possibly masking the changes.

Conclusions

The present study is the first to directly investigate the effect of movement amplitude on parkinsonian rigidity, and one of few to have quantified the effect of movement velocity on rigidity. The findings of the current study indicate that both movement amplitude and movement velocity modulate parkinsonian rigidity, and suggest that these parameters should be considered when assessing rigidity using manually applied passive joint motions as in the UPDRS assessment. These data also provide a foundation from which the pathways mediating parkinsonian rigidity can be further explored.

HIGHLIGHTS

- Reflex responses of stretched muscles were augmented by increased movement amplitude and velocity of muscle stretch.
- Rigidity was enhanced by greater movement amplitude and velocity of the stretch
- Knowledge of the amplitude- and velocity-dependence of rigidity may aid in clinical examination of this symptom.

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Figure 1.

A representative sample of joint position (dotted) and joint torque (solid) signals recorded from one subject during the 60° range of imposed flexion and extension movements at 50°/s. Angular impulses and work scores were calculated for the periods of flexion and extension while the inertial components of torque, denoted by brackets, were omitted from the analysis.

Figure 2.

Comparison of torque-angle traces from a subject with PD in the OFF-MED state during passive movements in the 60° SLOW (A), 60° FAST (B), 90° SLOW (C) and 90° FAST (D) conditions. As indicated on the figure panel A, the lower portion of the torque-angle traces in each panel represents the flexion movement and the upper portion the extension movement.

Figure 3.

Mean normalized work scores for total, flexion and extension phases through 60° (A) and 90° (B) ranges of motion at 50°/s (SLOW) and 280°/s (FAST) obtained from all subjects in both medication states. The 90° range of motion was consistently associated with greater rigidity scores compared to the 60° range of motion. The same pattern held true for the faster velocity compared to the slow one. Error bars: standard deviation.

Figure 4.

Mean normalized angular impulse for total rigidity as well as rigidity for the flexion and extension phases of movement at 50°/s (SLOW) and 280°/s (FAST) with 60° (A) and 90° range of motion from all participants in the OFF-MED and ON-MED states. The faster velocity was associated with greater total rigidity as well as greater flexion components of rigidity. The 90° range of motion was associated with greater rigidity scores compared to the 60° range of motion. Error bars: standard deviation.

Figure 5.

Representative joint position and EMG tracings of the wrist flexors and extensors from a subject with PD during the wrist extension movement at 50°/s with 60° range of motion. In reflex was recorded in the wrist flexors. Dopaminergic medication greatly diminished the amplitude of these phenomena in the ON-MED condition (B). The onset of movement is indicated by the vertical line. Top panel: joint position (°); middle panel: average EMG of wrist flexor muscles; lower panel: averaged EMG of wrist extensor muscles.

Figure 6.

Mean EMG values of stretched and shortened muscles and EMG ratios during passive wrist flexion when the wrist was flexed through a range of motion equal to 60° (dark) and 90° (white) during the SLOW (A) and FAST conditions (B) in the OFF- and ON-MED states. Error bars: standard deviation.

Figure 7. Mean EMG values of stretched and shortened muscles and EMG ratios during passive wrist extension when the wrist was extended through a range of motion equal to 60° (dark) and 90° (white) during the SLOW (A) and FAST conditions (B) in the OFF- and ON-MED states. Error bars: standard deviation.

Table 1

Patients' clinical information

Patient	Age (yrs)	Disease Duration (yrs)	Gender	Arm tested	Rigidity (UPDRS) ^a		Medication Information ^b
					Off	On	
1	62	11	F	R	3	1	C/L 50/200 (×4); C/L/E 100 mg (×2); Pra 1.5 mg (×3)
2	67	13	F	L	3	2	C/L 25/100 (×3); R 1 mg (×3); S 5 mg (×2)
3	71	5	F	R	2	1	C/L 25/100 (×3)
4	69	3	F	R	2	2	Pra 1.5 mg (×3)
5	65	3	M	L	2	1	C/L 25/100 mg (×3)
6	59	8	M	R	2	1	C/L 25/100 (×3); R 1.0 mg (×3)
7	57	5	F	R	2	1	Az 1 mg (×1); C/L 25/100 (×3); R 3.0 mg (×3)
8	63	12	M	R	2	1	Am 100 mg (×1); C/L 25/100 (×2);
9	58	14	M	L	3	3	Am 100 mg (×2); C/L 25/100 (×3); Ct 200 mg (×3)
10	77	1	F	L	2	0	C/L 25/100 (×3)
11	67	10	M	R	2	1	Az 1.0 mg (×1); C/L 100 (×1); Ct 200 mg (×1)
12	63	7	F	R	2	1	Pra 1.5 mg (×3); S 1.0 mg (×1)
13	46	1	F	L	3	1	C/L 25/100 (×1); R 1.0 mg (×3)
14	73	2	M	L	3	2	C/L 25/100 (×3)
15	55	10	M	L	3	1	C/L 25/250 mg (×4); R 1 mg (×4)
16	72	4	F	L	2	1	C/L 25/100 (×1); R 3.0 mg (×4)
17	74	2	F	L	2	1	C/L 25/100 (×3)
18	48	2	F	L	2	1	C/L 25/100 (×3); Pra 1.5 mg (×1)

^aUPDRS (unified Parkinson's disease rating scale). Rigidity: 0 - absent; 1 - slight; 2 - mild to moderate; 3 - marked; 4 - severe.

^bAm - amantadine; Az - azilect; C/L - carbidopa/levodopa; ct - comtan; E - entacapone; Pra - pramipexole; R - ropinirole; S - selegiline.

Mean slopes of the Torque-angle plots during the imposed flexion and extension movements at the SLOW (50°/s) and FAST (280°/s) velocities under both medication conditions in all subjects with Parkinson's disease. Data shown in the table are presented as: mean (SD). Units are milli-Nm/deg.

Table 2

ROM	Medication	SLOW (50°/s)		FAST (280°/s)	
		Flexion	Extension	Flexion	Extension
60°	Off-Med	4.19 (2.43)	3.40 (1.62)	8.77 (5.26) ^a	7.16 (5.42) ^{a,b}
	On-Med	5.25 (3.60)	4.36 (2.86)	10.84 (8.97) ^a	7.53 (5.94) ^{a,b}
90°	Off-Med	5.31 (3.21)	3.72 (1.72)	7.52 (5.02) ^a	4.62 (3.19) ^{a,b}
	On-Med	6.26 (3.89)	4.30 (2.29)	8.08 (5.03) ^a	5.59 (4.05) ^{a,b}

Note:

^a significantly different than SLOW condition

^b significantly different than Flexion component