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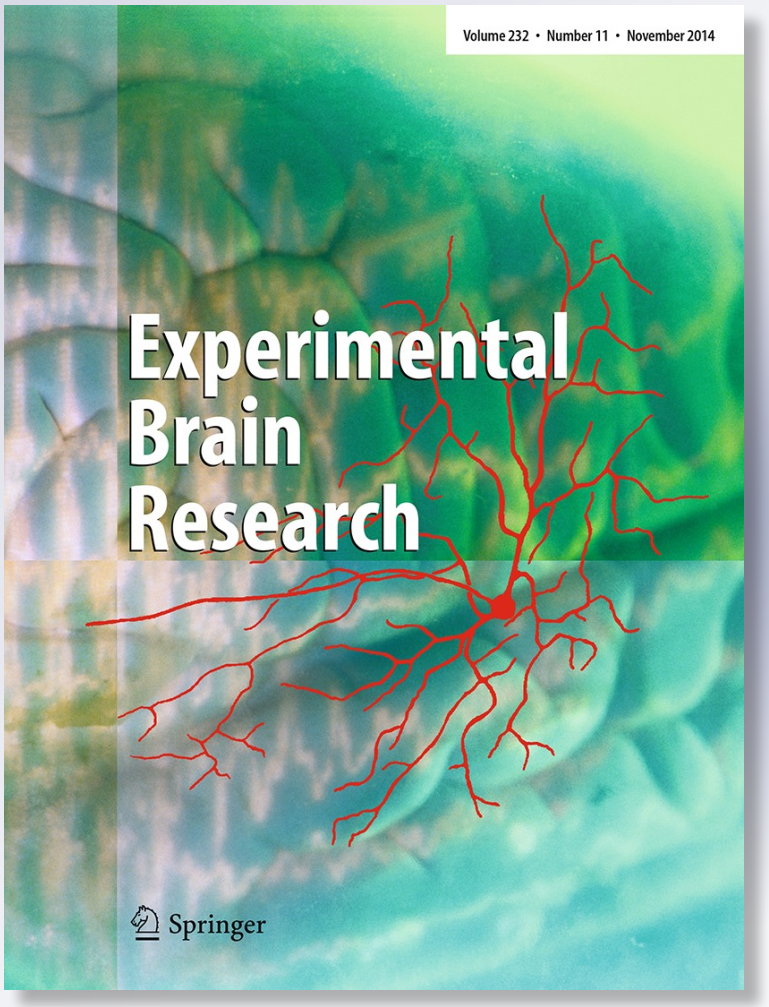

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RESEARCH ARTICLE

Stroke-induced synergistic phase shifting and its possible implications for recovery mechanisms

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Abstract Among other diminished motor capabilities, survivors of a stroke often exhibit pathological joint synergies. With respect to the upper limbs, these deficits diminish coordination in reaching, pointing, and daily task performance. Past research on pathological synergies suggests that the synergistic relationship between joints is different for flexion than in extension. One explanation for different flexion and extension synergies is that there exists a time difference between the joint being volitionally moved and the joint that moves in synergy. The goal of this research was to measure these synergistic time differences. The experiment included 11 hemiparetic subjects who performed rhythmic elbow motions at five different frequencies. A motion capture system was used to record the resulting shoulder synergies. Synergistic shoulder rotations were found to exhibit frequency-dependent phase lags (delays) and leads (advances) in the paretic arm. Furthermore, the synergistic leads and lags varied with frequency and were subject specific. We found that timing differences between joints in pathological movements are comparable to differences that were observed by other researchers for normal, able-bodied movement synergies. Moreover, the fact that pathological synergies were evident in rhythmic motion suggests that they are spinal in origin. A significant amount research exists relating to able-bodied spinal synergies. Thus, the supposition that pathological synergies are an expression of normal synergies would tie disabled movement into a larger body of work related to able-bodied synergies. The rehabilitation implications of this possible connection are discussed.

Keywords Stroke · Phase · Central pattern generator · Motor learning · Synergy · Rhythmic

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Introduction

Stroke is the leading cause of disability and the third leading cause of death in the USA (Rossini et al. 2003). Of the many undesirable affects resulting from a cerebral vascular accident (CVA) is the emergence of pathological muscle synergies (Dipietro et al. 2007). Pathological synergies are characterized by the involuntary recruitment of muscles around joints other than the joint being intentionally moved. These synergies are stereotypically described as flexor and extensor synergies. To take the arm as an example, when the elbow is voluntarily flexed, flexor synergy causes the fingers and wrist to flex, the shoulder humerus to externally rotate and abduct, and the scapula to retract. Often, both the upper and lower limbs, as well as the trunk, participate in synergistic patterns.

Many investigators have studied the role of cortical plasticity during neurorehabilitation from a CVA. However, few, if any, studies have specifically targeted the role of spinal plasticity. In related work to this paper, it was shown that pathological synergies are evident for discrete as well as rhythmic motion (Simkins et al. 2013a). Based on the idea that rhythmic motion is accomplished through spinal

mechanisms, it was proposed that pathological synergies observed in stroke survivors during rhythmic motion are spinal in origin.

Central pattern generators (CPGs) are believed to generate rhythmic motion (Grillner 1981). Though higher-level cortical processing is undoubtedly involved for rhythmic movements, evidence shows that CPGs are distributed along the spine (Scivoletto et al. 2007). Additionally, CPGs have the ability to generate complicated, multi-joint movement. Colloquially, the existences of spinal CPGs are evidenced by the proverbial (and factual) observation that a slaughtered chicken sometimes runs after its neck is severed. More formally, the existence of CPGs was demonstrated by the classic example of fictive walking in mesencephalic cats (Grillner 1981). Upper limbs CPGs have also been described in humans using FMRI (Schaal et al. 2004).

An important feature of CPGs is that they actuate pools of muscles. Because rhythmic motion, such as locomotion, can involve a complicated interplay of many muscles, some have suggested that the CPG be divided into two parts (Rybak et al. 2006). In the first part, a "rhythm-generating network" is used to regulate the frequency, or speed of movement. A second CPG network handles the complicated sequence of muscle activations for each period of motion. The second mechanism is termed the "pattern formation" (PF) network. According to this view, the PF generates a volley of neurological activity directed at motor pools.

The foregoing description of the PF is analogous to what some have termed "synergy." The term "synergy" has been used in a variety of contexts throughout the literature. The therapeutic community often uses this term to describe undesirable movement patterns in hemiparetic individuals. However, term "synergy" is often used in different contexts to describe desirable aspects of movement (Tresch and Jarc 2009). Therefore, hemiparetic synergy is hereafter referred to as "pathological synergy." For lack of a better word, the synergies that relate to normal, coordinated movement in neurologically intact individuals are simply referred to as "normal synergies." Normal synergies have been investigated by a number of researchers for animal movement (Cheung et al. 2005), normal human movement (Kargo and Giszter 2008), and hemiparetic movement (Cheung et al. 2009; Clark et al. 2010; Gizzi et al. 2011). In the context of this work, normal synergies are assumed to relate to the activation of motor pools to accomplish a task, or possibly, to achieve submovements of a task (Novak et al. 2002; d'Avella et al. 2003; Kargo and Giszter 2008). Importantly, this definition of normal synergy does not distinguish between motor pools being activated for rhythmic tasks or discrete tasks. For example, the pool of muscle activations needed to kick a ball and the pool of muscles needed to move the leg through one period of walking are both referred to here as instances of normal synergy.

One rational for subcortical motor control is that it is needed to overcome latencies associated with afferent feedback. Because of the time delays associated with sending information from the periphery to and from the brain, normal synergies associated with rhythmic movement are modulated directly by the spinal cord (Grillner 1981). In this way, the CNS can coordinate and adjust muscle contractions for the execution of tasks that require rapid responses to disturbances. Such a disturbance requiring correction might include stepping on an uneven surface while running. Accordingly, it is believed that afferent feedback channels route directly to the spine and that CPGs are capable of adjusting normal synergies directly based on afferent feedback. This aspect of synergy was also demonstrated for discrete movements in frogs. It was shown that the spine modulates wiping synergies in frog legs through direct afferent feedback (Cheung et al. 2005; Kargo and Giszter 2000).

In this work, we consider the possibility that pathological synergies are an altered expression of normal synergies. As a means of comparison, we measured relative timing differences between joints and evaluate them against timing differences of able-bodied, multi-joint movement (Archambault et al. 1999; Ivanenko et al. 2006; Kelso 1984; Wadman et al. 1980). Timing differences for pathological synergy were measured using rhythmic motion.

Methods

Apparatus

A Vicon motion capture system (Vicon Motion Systems, Oxford, UK) was used to gather all data. Ten ceiling mounted cameras were aimed at the subject's paretic arm. Fourteen motion capture markers were attached to the paretic hand, forearm, upper-arm, and thorax, see Fig. 1. The motion capture system had a temporal resolution of 10 ms (a 100 Hz sampling rate) and submillimeter spatial resolution for marker position. The extraction of joint angles from marker position data is described in the "Data analysis" section.

Subjects

Eleven hemiplegic subjects participated in this research. All subjects provided written consent, and this research was approved by the University of California, Santa Cruz, Internal Review Board. A modified Fugl-Meyer (Duncan et al. 1983; De Weerdt and Harrison 1985) (mFM) assessment was performed on all subjects. The Fugl-Meyer was "modified" in that the hand was not assessed. One goal of this study was to consider as wide a range of impairments as

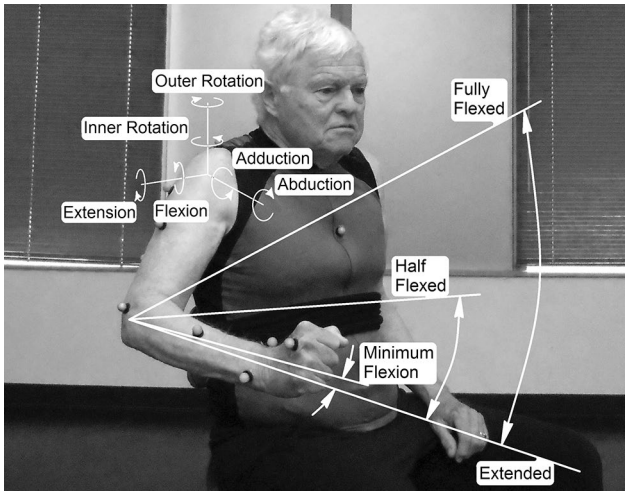

Fig. 1 Depicted is a hemiparetic subject in the extended position. The directions of rotation for shoulder are defined for flexion, extension, inner, and outer rotation. The different ranges of motion for the elbow are also depicted

possible. Notwithstanding, the mFM scores ranged from 1 (high impairment) to 14 (low impairment). Subjects ranged in age from 54 to 82 years old. Six of the 11 subjects were female. All subjects were in their chronic phase post-stroke, greater than 6 months since their most recent CVA. Even though one subject scored 14 on the mFM, all subjects exhibit some level of disability in their most affected side. A control group of 11 neurologically intact subjects also participated in this research. However, the controls exhibited very small amounts of movement other than the joint being intentionally moved. Therefore, phase calculations were indeterminate, and no phase results are reported for controls.

Protocol

All subjects were seated in a metal chair. A strap was used to fixate subject's thorax to the backrest of the chair. All subjects were asked to rhythmically cycle their elbow from a common orientation. Many subjects had difficulty moving their elbow to a fully extended position. Therefore, for the extended position, the elbow was bent at 90° as if the forearm were resting on a chair armrest, see Fig. 1. The 90° extended positions were selected because many hemiparetic subjects were unable to fully extend their elbow to 180°. From the extended position, subjects were instructed to rhythmically flex and extend only their elbow in a smooth, sinusoidal motion. During this motion, they were told to avoid movement in any other joints, to the best of their ability. Only the synergistic responses in the shoulder are considered. This interaction was selected because the shoulder is known to exhibit a strong pathological synergy with the elbow (Trumbower et al. 2010; Sangani et al. 2007).

Table 1 Oscillatory elbow flexion–extension

Frequency	Description of one cycle
$f_1 = 0.33$ Hz	From extended position to fully flexed, and then back
$f_2 = 0.83$ Hz	From extended position to fully flexed, and then back
$f_3 = \max$	From extended position to fully flexed, and then back
$f_4 = \max$	From extended position to half of the fully flexed position and then back to the extended position
$f_5 = \max$	From extended position through a minimum amount of flexion and then back to the extended position

Subjects were asked to cycle their paretic elbows in their sagittal plane at 5 different frequencies, as given in Table 1 (Kautz and Brown 1998). For each frequency, three repeats were collected. Notice in Table 1 that the frequencies for f_1 and f_2 are given as exact values. The first two frequencies were set to the beat of a metronome (Thaut et al. 2002). The frequencies for f_3, f_4, and f_5 are listed as "max" (maximum). The maximum frequencies reflect that subjects were instructed to move their arms as rapidly as possible through the specified amplitude. Table 1 also provides a description of amplitudes. For an oscillation requiring half amplitude at f_4, subjects were asked to flex their elbow from the extended position through an angle that was approximately half as far as what was achieved for full flexion. Because the amplitude was reduced to half, subjects achieved higher frequencies for half amplitude oscillations than for full amplitude oscillations. Finally, for f_5, subjects were asked to oscillate their elbow from the extended position through the smallest possible flexion angle, at their fastest possible speed. Such a motion more or less resembled an elbow tremor in that the elbow oscillated rapidly through an angle of 2°–4°. Given that f_5 was executed through the smallest possible angle at the subject's maximum speed, f_5 frequencies were the highest.

Data analysis

Discrete Fourier transforms (DFT) were performed using the fast Fourier transform function in Matlab to determine frequencies of all waveforms. In this context, a waveform is described by the angular position of a joint versus time. The outputs of DFT are arrays of complex conjugates. In principle, taking the arctangent of the real and imaginary parts of the complex conjugates yields the phase at a given frequency. However, an accurate measure of phase using DFT requires that the dataset being evaluated for *each* frequency precisely start and end on some integer number of periods. This was impractical for the dataset at hand. Though DFT was not a capable measure of phase, it did reliably identify

dominant frequency modes. Thus, all frequencies were calculated using DFT.

A modified version of cross correlation was used to determine phase. The idea behind cross correlation is to successively shift one function relative to another function and to take the products of the overlapping areas. When the functions have maximum overlap, the product of their areas is maximized. The amount of shift required to maximize the product of the areas thus measures a time difference, or for the purposes of this research, the phase difference between the elbow being voluntarily moved and the joint moving in synergy. Because the experimental protocol required only a minimum of five cycles, edge effects tended to dominate phase calculations using ordinary cross correlation. Convolution intervals are closely related to cross correlation. One means for eliminating the edge effects associated with short, periodic signals is to use a method called circular convolutions. For this analysis, circular convolutions were adapted to cross correlation. This was accomplished using the circshift() function in Matlab to circularly shift the array of response angles by n increments. The circular shifting function is defined here as $h(n)[m]$ where m is a dummy variable. Since a circular shift is used, dummy variable m need only sum data across one period. Therefore, summation need only span the interval from 0 to the number of samples over one period, N, and the following expression is obtained,

$$(f \circ h)[n] = \sum_{m=0}^{N} f[m] \cdot h(n)[m] \tag{1}$$

where h is the synergistic shoulder response that is shifted by n increments. The discrete function f represents the array of elbow angles. The expression (1) is therefore best described as a discrete, circular, cross correlation function. As was described previously, the amount of phase between h and f is determined by finding the number of increments, $n_{\max}$, that maximizes (1). Expressing phase in terms of $n_{\max}$ is an indirect way to describe phase. However, the angular phase difference between f and g is easily expressed in degrees by multiplying $n_{\max}$ by $360/N$. Finally, calculating a phase difference between the elbow and the shoulder, $\Delta\Phi$, according to (1) results in a phase difference that spans the interval (0, 360). However, this interval would suggest that the shoulder always leads the elbow, thus precluding the possibility of a lag. Therefore, it is assumed that $|\Delta\Phi| < 180°$.

Phase was estimated by successively indexing n in (1) by the sampling period, $T_s = 0.01$ s. No interpolation was done between sampling epochs. Because the sampling time remained constant for the various frequencies, the granularity of successive phase shifts was also varied. Therefore, the magnitude of successive phase shifts scaled with the elbow frequency, f_e. The incremental phase shifts, $\Delta\Phi_{\text{Incremental}}$, were therefore

$$\Delta\Phi_{\text{Incremental}} = 360 \times T_s \times f_e \tag{2}$$

where $\Delta\Phi_{\text{Incremental}}$ is the incremental phase shift in degrees, T_s is the sampling time in seconds (as required by the camera sampling rate), and f_e is the elbow frequency in Hz. At $f_e = 0.33$ Hz for f_1, the incremental phase shifts according to (2) are only in 1.2° increments for n. Thus, f_1 phase estimates had relatively good resolution (within a degree). The highest achievable frequency for most subjects was around 3 Hz for f_5. According to (2), the successive phase shifts for 3 Hz are $\Delta\Phi_{\text{Incremental}} = 10.8°$. Therefore, the phase resolution was finer for lower frequencies and somewhat coarse for highest frequencies.

Inverse kinematics was calculated from motion capture marker trajectory data using Vicon Bodybuilder™ scripts. Phase and DFT were performed using custom Matlab scripts. Statistical calculations were performed using Minitab Statistical Software (Minitab Inc., State College, PA, USA).

Results

Phase estimation

Most hemiparetic subjects were unable to cycle their elbow much beyond 3 Hz (Swinnen et al. 2002). The achievable frequencies for f_1 and f_2 were synced to a metronome, but the speed for higher frequencies was self-selected. The mean achievable frequencies in Hz for f_3, f_4, and f_5 were 1.76 ± 1.87 (SD), 1.63 ± 0.70, and 3.04 ± 1.53, respectively. These speeds are slow enough that arm dynamics are believed to play an insignificant role (Bennett et al. 1992).

Depicted in Fig. 2 are two subjects. One subject exhibited little amounts of "drift" while the other exhibited large amounts of "drift." In this context, "drift" refers to the gradual shifting of the joints as they oscillate in synergy. The affects of drift were particularly evident at higher frequencies, f_4 and f_5, because the amplitudes were reduced. For the lower frequencies, such as Fig. 2a, the elbow input and the synergistic response of the shoulder are roughly sinusoidal and the drift is proportionally small compared to the synergistic oscillations. However, for the highest frequency depicted in Fig. 2b, the drift was proportionately large relative to the amplitude. As is evident from Fig. 2b, drift diminishes the periodicity of the input (elbow) and output (shoulder). Accordingly, the phase for high drift subjects is less certain, and the confidence intervals were typically larger, or could not be determined.

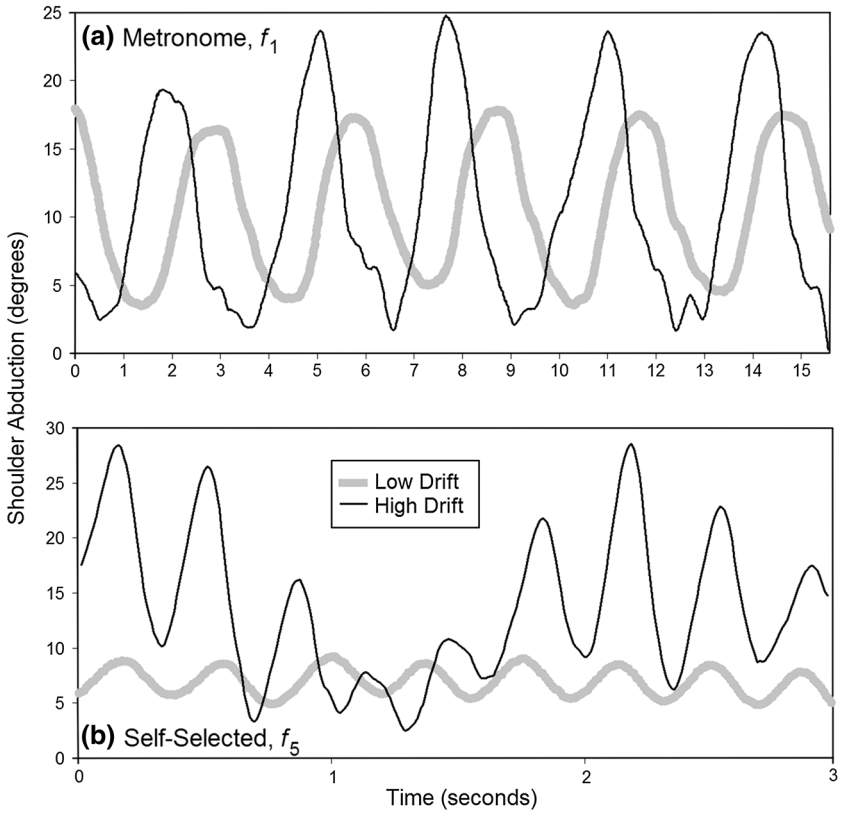

Fig. 2 Shown is the synergistic movement of the shoulder in abduction. Data were plotted from Subject 1 (*bold gray*) who exhibited small amounts of drift and Subject 11 (*black*) who exhibited large amounts of drift. Subject 11 data were shifted slightly upward on the vertical axes for purposes of comparison. At lower frequencies in (**a**), the drift is proportionately smaller and both subjects exhibit mostly sinusoidal movement. At higher frequencies in (**b**), the *bold gray line* remains sinusoidal; however, *black line* exhibits large drift

Phase differences

There were significant differences in phase between subjects for most frequencies. In an effort to evaluate how consistent phase leads and lags were between subjects, one-way ANOVAs were performed. Because it was possible that the phases might differ between the different axes of the shoulder, a separate ANOVA was performed for each of the three shoulder axes. Additionally, it is possible that the phase could change from one frequency to the next. Therefore, ANOVAs were performed for each shoulder axes as well as for each frequency. The ANOVA p values are given in Table 2. Assuming an alpha level of 0.05, then $p < 0.05$ indicates a significant difference. Thus, subjects exhibited significant differences for 9 out of 15 of the frequencies–axes combinations.

Qualitatively, subject-to-subject differences were particularly evident for shoulder outer rotation. For example, shoulder outer rotation for Subject 8 lagged the elbow by a large margin while Subject 3 had a small lead. For perspective, this discrepancy is depicted graphically in Fig. 3 for one repetition for Subjects 3 and 8.

The phase difference for all subjects, all joints, and all speeds is depicted in Fig. 4. Notice that Fig. 4i–k showed a large lag around ±180° for rhythmic shoulder outer rotation. The other eight subjects had little to no phase difference of shoulder outer rotation with respect to the elbow.

Table 2 Significant differences between subjects

Frequency	Flexion (p)	Outer rotation (p)	Abduction (p)
f_1	0.59	0.06	**0.02**
f_2	**<0.01**	**<0.01**	**0.03**
f_3	**<0.01**	**<0.01**	**<0.01**
f_4	0.06	0.14	**0.04**
f_5	**<0.01**	0.09	0.09

Confidence intervals that do not cross the 0° phase line indicate that there was a significant phase difference between the elbow and the shoulder with 95 % confidence. These intervals are distinguished with emboldened CI whiskers. One unique feature about the confidence intervals in Fig. 4 is that they wrap from top to bottom. In other words, intervals that extend past the top of Fig. 4 reemerge at the bottom. Intervals that wraps from top to bottom assumed phase differences <±180°. The directions of rotation depicted in Fig. 2 are for the three axes of the shoulder: flexion, outer rotation, and abduction, see Fig. 1. These directions are consistent with the stereotypical axes of rotation (flexor synergy) for elbow flexion. As such, intervals below the 0° line suggest that the shoulder lags the elbow. Intervals above the 0° line suggest a lead.

In previous work using isolated joint rotations, shoulder *flexion* was associated elbow flexion (Simkins et al.

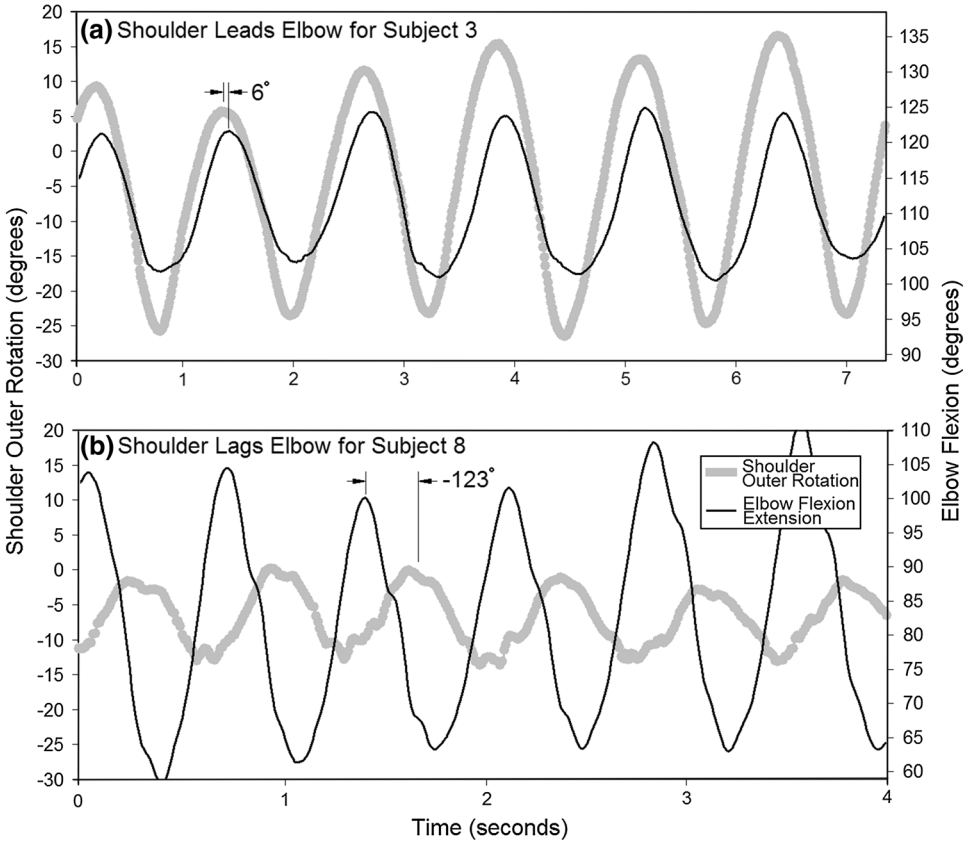

Fig. 3 Depicted are two subjects who exhibited very different synergistic shoulder rotation responses in terms of phase. The phase difference between the elbow and shoulder is at the f_3 speed for one repetition

2013b). However, the classic description of flexor synergy (Brunnstrom 1970) includes elbow flexion and shoulder *extension*. Therefore, to avoid confusion, the phase differences given in Fig. 4 assume that elbow flexion is synergistically coupled with shoulder flexion.

Phase calculations were not included in Fig. 4 for some data. For example, in Fig. 4h, Subject 8 exhibited highly erratic (quasi-periodic) shoulder rotation for almost all three repetitions at most frequencies, and it was unclear whether the phase estimate given by (1) were meaningful. Therefore, such phase estimates were excluded. In other cases, only one or two points are plotted. In cases that only two points were included, the confidence intervals were especially wide due to data scarcity. In cases where only one data point was available, the mean is plotted directly on the singular value and the confidence interval is undefined. For confidence intervals that span more than 360°, such as in Fig. 4d, the interval is depicted as a single line that extends from top to bottom.

Notice that the phases in Fig. 4 sometimes appear to suddenly flip from lead to lag, and vice versa. For example, for f_2 in Fig. 4e, the mean shoulder phase has a large lag. However, for f_3, the shoulder has a large lead. This is a peculiarity of phase plots because Fig. 4 assumes that the phase is between $\pm 180°$. As a hypothetical example, consider a repetition whereby a joint has a calculated phase of 179° (lead) relative to the elbow. Assume that the next repetition has a calculated phase difference of 181° (still a lead). If both points were plotted on Fig. 4, the first repletion would appear as 179°. However, the second repetition would go off the top of the plot and reappear at the bottom at −179°. That might suggest that the second repetition is approximately 180° away from the first repetition, when in reality, both repetitions only differ by a couple of degrees. More to the point, there is some ambiguity as to whether or not our hypothetical repetitions were truly leads near 180°, or whether both were actually lags near −180°. In practice, this is an inescapable ambiguity in calculating phase from periodic data. Thus, when interpreting Fig. 4, it is helpful to look where the phase points fall as well as the trend of successive phase calculations versus frequencies.

Not including data with one individual value, or intervals that cross the 0° line, there were 33 leads and 16 lags. There were 96 intervals that crossed the 0°. Therefore, a phase difference was not resolvable with 95 % confidence for the majority of shoulder axes and frequencies. The number of leads, lags, and zero-crossings are given in Table 3.

For some subjects, the phase differences could change abruptly from one frequency to the next. Subjects who exhibited large phase swings are given in Fig. 4f–j, and

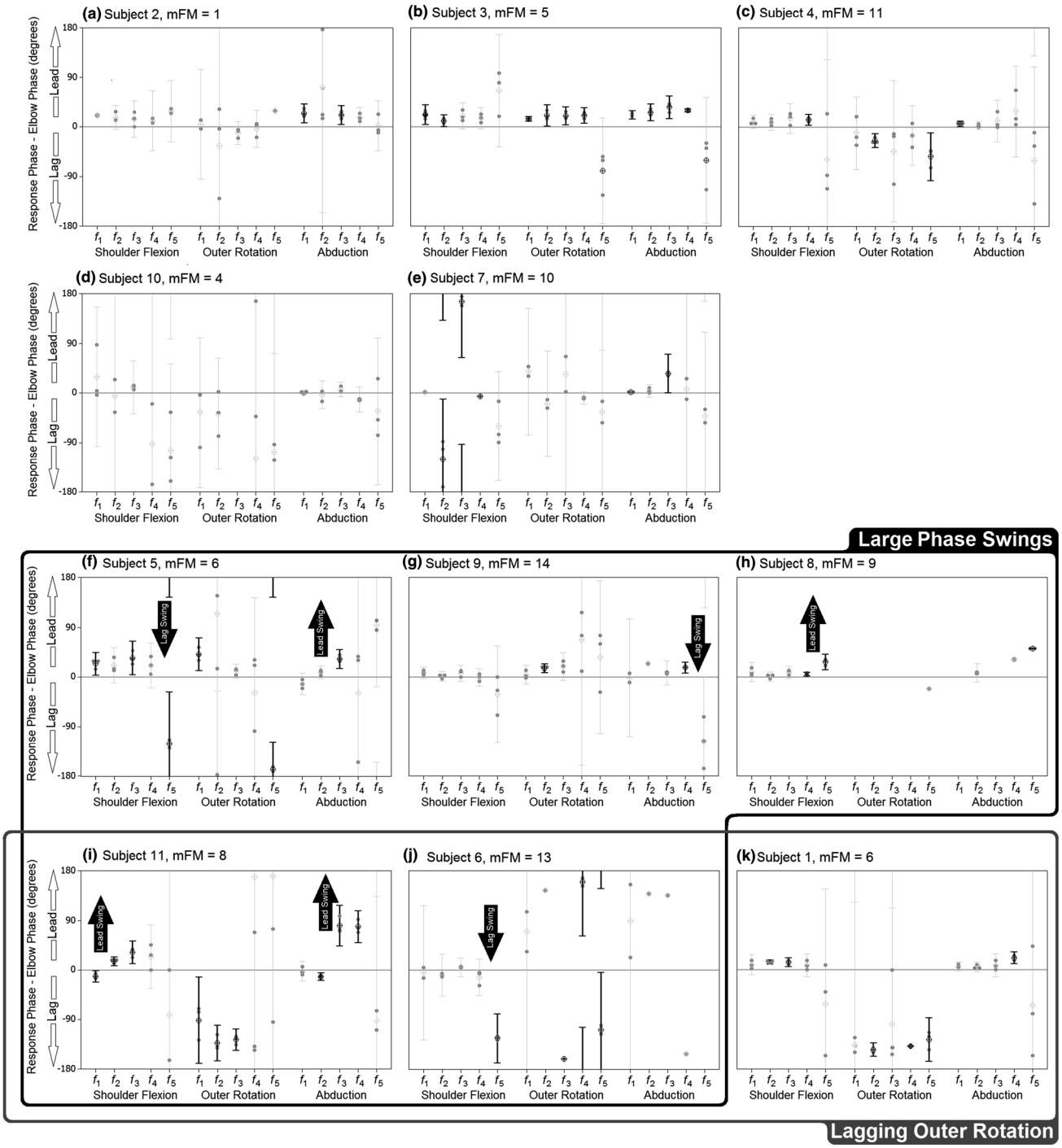

Fig. 4 Phase differences between rhythmic motion for the elbow (input) and the synergistic shoulder (output). The phase differences (output–input) are given as gray points for discrete values. The *whiskers* represent 95 % CIs. Mean values are given as *circles*. Phase plots are grouped for persistent 180° phase lags for a given joint axes (shoulder rotation). As frequency increases, *black arrows* point up for phase shifts to lead, or down for lag. Intervals that cross the 0° line is denoted by *thin gray lines*. *Bold black lines* denote intervals that do not cross the 0° line

arrows indicate the direction of the phase swing. A "large" swing is assumed to include cases in which the 95 % confidence interval (CI) for neighboring frequencies has no overlap. With four swings in the lead direction and three swings in the lag direction, it appears that swings in either direction are likely to occur. However, all three swings in the lag direction were for the highest frequency, f_4 to f_5. Referring to Table 3, pathological synergistic shoulder

Table 3 Summary of leads and lags

	f_1	f_2	f_3	f_4	f_5	Total
Shoulder flexion						
Leads	2	3	4	2	1	12
Zero	6	7	7	8	9	37
Lags	1	1	0	0	2	4
Shoulder rotation						
Leads	2	2	1	2	0	7
Zero	7	4	6	7	5	29
Lags	1	3	2	0	4	10
Shoulder abduction						
Leads	4	1	5	4	0	14
Zero	6	7	4	5	8	30
Lags	0	1	0	0	1	2

flexion leads outnumbered lags by 3 to 1. For shoulder abduction, leads outnumbered lags by 7 to 1.

In an effort to correlate phase relationships to subject attributes, various statistical tests were applied. Categories of investigation included age, impairment level, sex, and handedness. No statistically significant correlations were found between these categories and the phase relationships depicted in Fig. 4. Therefore, in terms of subject-to-subject differences with respect to phase, no specific correlations are reported.

Discussion

There are three principle takeaways from this work. First, the shoulder tends to lead the elbow. Second, large phase shifts were observed as oscillatory speeds increased. In the discussions that follow, we reference other research suggesting that these two aspects of movement are present in normal, multi-joint synergistic movement as well. Third, pathological, synergistic patterns persist for rhythmic movement. As was described in the "Introduction", and this is an important point, rhythmic motion is generated in the spine. The question naturally arises as to how these findings fit into what is known about synergies and hemiparesis. Our hypothesis is stated presently, and the claims are supported throughout the remainder of the "Discussion" section. Both pathological synergies and normal synergies are spinal, and both have similarities with respect to phase. Therefore, it is possible that pathological synergies are expressions of the same spinal mechanisms that regulate normal synergies associated with multi-joint movements such as running or swimming. It is also known that spinal synergies have motor learning mechanisms. This is almost obvious given that tasks, such as running or swimming, are learned and adjusted throughout life. Therefore, it is possible that the apparent reductions in pathological synergies that typically occur during the rehabilitation process are actually the results of spinal learning mechanisms, or subcortical plasticity.

An unusual feature of pathological synergies is that they are not exactly multi-joint movements, nor are they exactly isolated joint movements. In the case of this experiment, subjects intended to perform single joint movements, however, due to their pathological synergies, multi-joint movement resulted. The issue being considered presently is the possible relationship between normal synergies associated with multi-joint movement and pathological synergies. This hypothesis was proposed long ago just as synergies were first identified and documented. It was postulated that the brain might resort to movement vestigiality when the higher functioning motor system is damaged (Brunnstrom 1970). A relationship is being proposed here that includes more contemporary accounts of multi-joint movement. Accordingly, this discussion will first consider the possible similarities between pathological synergies and multi-joint movement of neurologically intact individuals, as reported in the literature.

Two aspects of pathological synergy stand out in this work. First, in most cases, the shoulder leads (i.e., moves before) the elbow. Another explanation for observed phase shifts is that they are caused by hysteresis in connective tissues. However, these effects are more prominent in load-bearing joints such as the ankle and not necessarily in the upper limbs (Given et al. 1995). For these reasons, synergistic muscle activation is assumed to be the predominant source of phase differences. Other research has shown that shoulder muscle activations often precede elbow muscle activations for able-bodied individuals. In a 2-joint reaching experiment using neurologically intact individuals, shoulder muscle EMG recordings preceded elbow EMG by 5–40 ms (Archambault et al. 1999). Likewise, for ballistic arm movements, the shoulder preceded the elbow by 15–25 ms (Wadman et al. 1980). Even though it was difficult to

directly correlate shoulder muscle activations to joint rotation (Archambault et al. 1999), such timing advances are comparable with most hemiparetic timing differences in the present study. The mean phase leads for f_2–f_5 with confidence intervals that did not cross the 0° line corresponded to time advances of between 9 and 55 ms for shoulder flexion, and 10–127 ms for shoulder abduction. Therefore, shoulder leads that resulted from hemiparetic elbow flexion appear to have comparable time advances to voluntary, multi-joint movements in neurologically intact individuals.

A second finding in this work was that the phase difference between the elbow and the shoulder might undergo phase swings across different frequencies. In studying muscle activation synergies for the lower limbs during human locomotion, it was found that there was "a consistent speed-dependent phase shift that corresponded to the shift in relative stance duration with walking speed" (Ivanenko et al. 2006). Large phase swings in locomotion are especially obvious for rhythmic speed increases associated with the transition from walking to jogging, or jogging to running. In quadrupeds, they would occur for transitions from trotting to galloping. For the rhythmic motion in the upper limbs, large swings in phase were also observed in bimanual circle drawing tasks (Kelso 1984). For bimanual circle drawing, the phase was found to shift abruptly for hand speeds of around 2.3 Hz. Perhaps coincidentally, the majority of phase swings for pathological synergies occurred somewhere between f_4 (1.6 Hz) and f_5 (3.0 Hz). Given these considerations, it is therefore *possible* that phase relations for hemiparetic movement are a reflection of normal synergies for multi-joint movement in that proximal joints tend to move before more distal ones and phase shifting occurs with changes in speed.

As was mentioned in the introduction, the PF network is thought to elicit rhythmic, multi-joint movement by enervating motor pools, i.e., normal synergies. Essentially, this process translates higher-level cortical commands into lower-level spaciotemporal patterns of muscle contractions. A hierarchy of control such as this has been advocated and substantiated through various experiments (Georgopoulos et al. 1986, 1991). In other words, motor commands are generated and encoded at higher levels, and decoded at a lower level into pooled muscle actuations that represent normal synergies. Such an arrangement is vaguely akin to multiplexing in electronics, whereby an encoded signal changes the state of many outputs.

The argument being put forth might suggest that normal synergies are generated exclusively in the spine. This is so because CPGs are thought to initiate and regulate rhythmic movement, and CPGs are known to exist in the spine. However, these statements do not preclude the possibility that supraspinal networks are at work. Specifically, some have suggested that the cerebellum retains and modulates internal models of movement as part of motor learning (Ramnani 2006). For these reasons, the adaptive properties being discussed in this work relate to the spine, but they also may include higher structures such as the brain stem and cerebellum. In any event, based on the idea that there is a hierarchy of descending commands, normal synergies and pathological synergies appear to be generated at the subcortical level.

It has been suggested that one of the effects of hemiparesis is the alteration of descending motor commands (Cheung et al. 2009). The hypothesis being proposed here is that alteration of descending commands causes the incorrect recruitment of normal synergies and that in turn manifests itself as pathological synergy. The relation of normal and pathological synergies might also help to explain drift. The spine has been shown to modulate muscle pools through afferent feedback (Kargo and Giszter 2000). Likewise, it was shown that CPGs might adjust normal synergies based on direct afferent feedback (Pearson 2000). It is also known that proprioception is often adversely affected following a CVA (Smith et al. 1983). Therefore, degraded proprioception could explain the observed drift in some subjects.

The foregoing hypothesis might explain aspects of the rehabilitation process. Motor recovery from a CVA is partially characterized by the emergence and ebb of pathological synergies. This process is sometimes divided into 6 stages. By stage 3, individuals begin to restore voluntary movement and the effects of pathological synergies are more severe. As recovery progresses to stage 4, the effects of pathological synergy begin to subside. Ideally, by stage 6, individuals regain normal movement (Brunnstrom 1970).

The reason that the relationship between pathological and normal synergy is potentially important in rehabilitation is because normal synergies are highly adaptable. In humans, only minorities of multi-joint (or multi-muscle) tasks are known a priori from birth. The majority of tasks, such as locomotion or throwing, are learned overtime. It therefore stands to reason that the normal muscle synergies that generate those movements are adaptable. A number of experiments have demonstrated leaning mechanisms, i.e., neuroplasticity, in the spine (Chen and Wolpaw 2002; Wolpaw and Chen 2006; Edgerton et al. 2005). Accordingly, altered reflexive activity in the less affected side of stroke survivors has been attributed spinal plasticity (Thilmann et al. 1990; Wolpaw 2007). These considerations would suggest the spinal plasticity is indeed at work post-stroke. Along those lines, spinal CPGs associated with locomotion exhibit surprising adaptability for asymmetric multi-joint movement in the case of both neurologically intact movement and hemiparetic movement (Reisman et al. 2007; Dietz et al. 1994).

Given that a CVA, by definition, is cortical and not spinal, the adaptive properties of the spine should remain intact. Therefore, it is possible that the restoration of movement, and subsequent reduction of pathological synergies, could be related to learning processes in the spine that are associated with normal synergy. In other words, it is possible that spinal adaptation to altered descending commands plays an important role in the restoration of motor function post-stroke. Following a CVA, the most dramatic improvements are typically obtained during the acute/sub-acute phase of recovery. The subacute phase typically spans between 1 and 3 months after the CVA. Thereafter, individuals enter a chronic phase, whereby further improvement is often slowed significantly. In light of theses observations, it is possible that subcortical adaptation is at work through the subacute phase. Given that stage 1 in the recovery process is characterized by flaccidity, virtually no effects of adaptation (subcortical plasticity) would be evident. By stage 2, individuals have minimal movement that is highly synergistic. By stage 3, early synergistic adaptations might manifest themselves as severe synergistic patterns. Later on, by stage 4 and 5, the synergistic patterns would subside. These reductions of synergy are analogous to the learned acquisition of any new task. Early in this learning process, some joints might move too much, others too little, but these errors are eventually reduced or removed and individuals become adept at the given task. Finally, the extent to which individuals attain stage 6, normal movement, could depend on the extent to which the CVA altered descending commands. If the alterations are severe enough, perhaps subcortical plasticity has done all it can and some pathological synergies would persist. Importantly, this model of recovery does not depend on the restoration of pre-CVA descending commands through cortical neuroplasticity.

Investigations of CVA rehabilitation often focus on neural plasticity in or around the cortical infarct (Johansson 2000). Likewise, spinal cord injury (SCI) research often focuses on neural plasticity in the spine. Such approaches are sensible because they focus on the site of the injury. However, an important characteristic of the CNS is that it makes use of compensation strategies when possible. For example, when some group of muscles is compromised by an injury, the CNS utilizes muscles outside effected group as a means of compensation to restore function. Such compensation strategies are well known for SCI (Behrman et al. 2006) and CVA (Krakauer 2006). Likewise, it is possible that lower-level spinal compensation is at work to compensate for higher-level cortical damage. Admittedly, these findings are far from conclusive evidence that spinal plasticity plays a central role in CVA recovery. The hypothesis is presented here, with some supporting evidence, as a consideration for future research.

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