Heteronymous reflex connections in human upper limb muscles in response to stretch of forearm muscles

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Manning CD, Bawa P. Heteronymous reflex connections in human upper limb muscles in response to stretch of forearm muscles. J Neurophysiol 106: 1489–1499, 2011. First published June 29, 2011; doi:10.1152/jn.00084.2011.—Torque motor produced stretch of upper limb muscles results in two distinct reflex peaks in the electromyographic activity. Whereas the short-latency reflex (SLR) response is mediated largely by the spinal monosynaptic reflex pathway, the longer-latency reflex (LLR) is suggested to involve a transcortical loop. For the SLRs, patterns of heteronymous monosynaptic Ia connections have been well-studied for a large number of muscles in the cat and in humans. For LLRs, information is available for perturbations to proximal joints, although the protocols for most of these studies did not focus on heteronymous connections. The main objective of the present study was to elicit both SLRs and LLRs in wrist flexors and extensors and to examine heteronymous connections from these muscles to elbow flexors (biceps brachii; BiBr) and extensors (triceps brachii; TriBr) and to selected distal muscles, including abductor pollicis longus (APL), first dorsal interosseous (FDI), abductor digiti minimi (ADM), and Thenars. The stretch of wrist flexors produced SLR and LLR peaks in APL, FDI, ADM, Thenars, and BiBr while simultaneously inducing inhibition of wrist extensors and TriBr. When wrist extensors were stretched, SLR and LLR peaks were observed in TriBr, whereas the primary wrist flexors, APL and BiBr, were inhibited; response patterns of FDI, ADM, and Thenars were less consistent. The main conclusions from the observed data are that: 1) as in the cat, afferents from wrist flexors and extensors make heteronymous connections with proximal and distal upper limb muscles; and 2) the strength of heteronymous connections is greater for LLRs than SLRs in the distal muscles, whereas the opposite is true for the proximal muscles. In the majority of observations, SLR and LLR excitatory peaks were observed together. However, on occasion, LLRs were observed without the SLR response in hand muscles when wrist extensors were stretched.

stretch reflex; spinal reflex; transcortical reflex; antagonist

TENDON TAPS OR ELECTRICAL stimulation of Ia afferents in the human arm muscles results primarily in the short-latency spinal reflex (SLR), although the existence of a longer-latency reflex (LLR) has also been reported (Baudry et al. 2009; Bawa et al. 1983; Deuschl et al. 1985; Lourenço et al. 2006; Tarkka 1986). With slightly slower stretch of the upper arm, forearm, and hand muscles, well-defined SLR (or M1) and LLR (or M2) responses are observed (Gienel et al. 1988; Hammond 1956; Kosland et al. 1991; Kurtzer et al. 2008, 2010; Lacquaniti and Soechting 1986a,b; Latash 2000; Lee and Tatton 1978; Marsden et al. 1976, 1981; Perreault et al. 2008; Smeets and Erkelens 1991), although SLR is not clearly present in a few of these studies (Kosland et al. 1991; Latash 2000). The SLR component of the stretch reflex is mediated primarily by the spinal monosynaptic reflex arc, whereas the longer-latency response likely arises via a transcortical loop (Cheney and Fetz 1984; Deuschl et al. 1985; Matthews et al. 1990; Matthews 1991; Palmer and Ashby 1992). The gain of the SLR depends on the afferent volley and the excitability of the spinal cord, including the excitability of the motoneurons and presynaptic terminals of Ia afferents. In addition to these factors, the gain of the LLR is suggested to depend on how the subject prepares to react to the imposed stretch (central set; Calancie and Bawa 1985; Colebatch et al. 1979; Evarits 1975; Hammond 1956; Lee and Tatton 1978; MacKinnon et al. 2000). Once the LLR volley arrives at the motoneuron pool, its effect will be determined by the refractoriness/inhibition left in the wake of the SLR. Furthermore, as the density of corticomotoneuronal synapses increases from the proximal to the distal muscles (Porter and Lemon 1993), the relative size of the LLR increases. Thus, in general, elbow flexors have dominant spinal reflexes, and the hand muscles exhibit prominent LLRs (Marsden et al. 1976; Matthews 1991; Smeets and Erkelens 1991). LLRs have also been reported in human lower limb (Schieppati et al. 1995; Zuur et al. 2009); this paper will focus exclusively on studies carried out on human upper limb muscles.

During any movement, the action is rarely produced by the contraction of a single muscle; synergistic action of many muscles is required to produce a movement (D’Avella et al. 2006; Fetz and Cheney 1980). The same is true of contractions resulting from stretch reflexes. For the spinal reflex (SLR), the homonymous and heteronymous connections of Ia afferents arising from muscles of both the hindlimb and of the forelimb in the cat and in humans have been examined quite extensively. Furthermore, the heteronymous connections do not confine themselves to the muscles of the same joint but extend to the muscles of the neighboring joints (cat: Eccles et al. 1957; Fritz et al. 1989; Willis et al. 1966; human: Alexander and Harrison 2003; Cavallari and Katz 1989; Cavallari et al. 1992; Créange et al. 1992; Marchand-Pauvert et al. 2000; McClelland et al. 2001). In general, the strength of the heteronymous connections for the monosynaptic reflex is much weaker than that to the homonymous muscle (Chalmers and Bawa 1997; Fritz et al. 1989; Pirrot-Deseilligny and Burke 2005). In the cat, heteronymous connections to muscles of the neighboring joints are found in both the proximal and the distal upper limb musculature (Fritz et al. 1989). In humans, clear distal-to-proximal connections have been demonstrated (Alexander and Harrison 2003; Cavallari et al. 1992; Créange et al. 1992; Lewis and McNair 2010; Marchand-Pauvert et al. 2000), but it has been suggested that proximal-to-distal connections do not exist in the human upper limb (Cavallari et al. 1992; Pierrot-

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Deseilligny and Burke 2005). The existence of bidirectional SLR connections has been reported for both elbow and shoulder muscles (McClelland et al. 2001). Heteronymous connections for LLRs have been studied for muscles of the proximal joints including the shoulder and the elbow (Gielen et al. 1988; Koshland et al. 1991; Kurtzer et al. 2008, 2010; Lacquaniti and Soechting 1986a,b; Latash 2000; Perreault et al. 2008; Soechting and Lacquaniti 1988). The majority of these studies perturbed two joints simultaneously, which makes extracting information on the heteronymous connections difficult. The protocols were not designed to study heteronymous connections for LLRs as had been done by the studies for SLRs (Gielen et al. 1988).

To summarize, there have been two sets of studies: in the first set of studies, the experimental protocols were designed primarily to examine heteronymous connections of SLRs; they used tendon taps or electrical stimulation of spindle Ia afferents to elicit monosynaptic reflexes. The second set of studies, which have dealt with the distribution of LLRs, generally perturbed more than one joint (Kurtzer et al. 2008, 2010; Lacquaniti and Soechting 1986a,b; Latash 2000; Perreault et al. 2008; Soechting and Lacquaniti 1988). Their main aim was to examine whether the distribution of LLRs in a group of synergists was the same as for the upcoming voluntary activity in those muscles. For such complex perturbations, it would be difficult to study patterns of heteronymous activity. A muscle shortened by the perturbation at one joint may receive excitatory heteronymous activity from another stretched muscle(s). In short, there is a lack of data available for the heteronymous connections for LLRs without any interference from voluntary activity. Therefore, the purpose of our study was to generate both SLRs and LLRs in wrist flexors and extensors and search for heteronymous distribution of SLRs and LLRs in selected proximal and distal muscles using a simple single-joint perturbation protocol. In addition to recording electromyographic (EMG) activity from the stretched wrist flexors and extensors, EMG was recorded proximally from elbow flexor biceps brachii (BiBr) and elbow extensor triceps brachii (TriBr). For distal muscles, we chose an assortment of four muscles innervated by the ulnar nerve [first dorsal interosseous (FDI) and abductor digiti minimi (ADM)], the median nerve (most muscles of the thenar eminence, collectively termed Thenars), and the radial nerve [abductor pollicis longus (APL)]. Whereas FDI, ADM, and Thenars are located in the hand, APL is located on the dorsal side of the forearm. Since SLRs are weak distally and become larger proximally, we hypothesized that heteronymous connections for SLRs would be weak distally and stronger proximally. Conversely, for LLRs, we hypothesized that distal projections would be weaker, whereas proximal projections would be weak. Since some of the previous studies on the elbow/shoulder muscles (Gielen et al. 1988; Kurtzer et al. 2008) have shown differential occurrence of SLRs and LLRs, our next question was to examine whether, and under what conditions, SLRs and LLRs occur differentially. This question was addressed while perturbing only one joint segment and without any voluntary reaction to ensure the results are indicative of reflex activity alone.

**METHODS**

Intramuscular EMG data were collected during 19 experiments conducted on 6 right-handed male subjects ranging in age from 21 to 25 yr. Individuals who had clearly defined musculature in their forearms were recruited as subjects to ensure correct intramuscular electrode placement. Surface EMG data were collected during 10 additional experiments on 10 subjects (age range 19–28 yr, 3 female); 2 of these subjects were from the previous group, including 1 of the authors. The number of muscles recorded during each session ranged from 3 to 7. Experimental procedures were approved by the Ethics Review Board of Simon Fraser University. All subjects gave signed consent before undertaking the experimental procedures.

**Experimental Setup**

The subject was seated comfortably in a chair with his/her right forearm resting in a semiprone position on a padded horizontal platform (i.e., palm perpendicular to the horizontal platform). The elbow was flexed at 100°, and the wrist joint was fixed directly over the axis of rotation of the torque motor shaft. A vertical handle, parallel to the shaft of the torque motor and connected to the shaft by a horizontal bar (10-cm distance from center of the shaft to center of the vertical handle), was placed against the palm of the hand close to the metacarpophalangeal joint. A rotation of the shaft of the torque motor rotated the vertical handle; rotation of the handle rotated the wrist, which produced a stretch of either the wrist flexors or wrist extensors as required by the experimenters. Lateral movement of the wrist was prevented with two padded stops placed against the distal end of the wrist. The setup produced rotation only of the wrist and no movement at any of the other joints. Square pulses from Grass S88 Stimulator (150–200 ms in duration) triggered the power amplifier at a rate of 0.2 pulses/s (range 0.1–0.3 pulses/s), and the power amplifier generated rotation of the shaft of the brushless direct current (DC) torque motor (Aeroflex TQ 82W-1C; manufactured for 0 vibration). This motor is free of any vibration. See Calancie and Bawa (1985) for more details of the equipment.

For intramuscular EMG recordings, hook electrodes (221-285S-730; Chalgren Enterprises) were used to record activity simultaneously from up to 7 arm and hand muscles, including flexor carpi radialis (FCR), flexor carpi ulnaris (FCU), extensor carpi radialis (ECR), extensor carpi ulnaris (ECU), extensor digitorum communis (EDC), APL, and FDI. Since there was less chance of cross talk, most of the data from BiBr and TriBr were collected with surface EMG electrodes (GS27). For the additional 10 experiments, bipolar surface EMG data were collected from wrist flexors and extensors, BiBr, TriBr, FDI, ADM, and Thenars. In each experiment, a ground electrode was placed either around the wrist or on the upper arm. Grass preamplifiers amplified and band-pass filtered (30 Hz to 3 kHz) all EMG signals. Once all the electrodes were positioned correctly, the subject’s hand was secured in the manipulandum; flexor loads stretched wrist flexors by extending the wrist joint, and extensor loads stretched wrist extensors by flexing the wrist joint. The subject was instructed not to grasp the vertical handle with his or her fingers and that, on perceiving the stretch, he/she was to let the wrist be rotated and then bring the handle back to the starting position at a comfortable speed using only the wrist muscles. The subject received visual feedback of wrist position on a computer monitor (using Spike2 software; Cambridge Electronics Division, Cambridge, United Kingdom) to return their wrist to the starting position and wait for the onset of the subsequent stretch. Generally, the muscles to be stretched were preloaded by 0.125 Nm to provide background activity in the muscles; the background activity ranged from 5 to 15% of maximal voluntary contraction (MVC). To examine reflex activity in BiBr and TriBr, the subject was asked to flex isometrically or extend his/her elbow to produce background activity in these muscles. Wrist abduction (radial deviation) produced background activity in APL. For FDI, ADM, and
Thenars, subjects were asked to voluntarily activate these muscles by ~10% MVC. Visual and auditory feedback was provided to the subject so that he/she could maintain a constant level of muscle activity during these different patterns of background muscle contractions. Under each condition of examining a particular group of muscles, ~25 flexor loads and 25 extensor loads were applied; each load pulse was 0.875 Nm in amplitude irrespective of the size of the subject. This load pulse (150–200 ms in duration) resulted in different angular velocities of rotation in different subjects and within the same subject, depending on the loading conditions.

Analysis

Data were collected on 2 personal computers, 1 using Signal and the other using Spike2 software via 2 separate 1401plus interfaces (Cambridge Electronics Division). All signals were sampled online at a rate of 5 kHz. During the experiment, Signal provided feedback to the experimenter about the response to each perturbation, whereas Spike2 was used to give continuous visual feedback to the subject (wrist position and EMG of selected muscles) and for offline analysis. Offline data analysis using Signal software involved frame-by-frame inspection for obvious artifacts and erroneous frames. Before averaging the responses for each condition, DC offset was removed from each of the EMG channels, and the signal was rectified. Averages were generated for all frames relevant to each of the conditions studied (20–25 responses per average). Averages obtained with Signal software provided a visual representation of the excitatory peaks and inhibitory responses across all recorded muscles simultaneously.

The excitatory reflex peaks were observed between approximately 30 and 100 ms in primary wrist flexors and extensors of most of the subjects; SLR peak between 30 and 60 ms, LLR peak between 60 and 100 ms. The onset and duration of each peak varied between subjects and conditions. Vertical cursors were placed around 30, 60, and 100 ms before the stimulus onset. To assess the presence of significant excitatory or inhibitory responses across all recorded muscles simultaneously.

Statistics

There is a large inter- and intrasubject variability in the onset and offset of SLR and LLR peaks, and the intrasubject variability arises from loading conditions. Furthermore, the responses could be excitatory or inhibitory for the same stretch. Thus population mean ± SD values of reflex peak profiles as a function of poststimulus time were not meaningful. Instead, Table 2 provides the frequency with which the two excitatory peaks and inhibitory responses were observed in various muscles during the stretch of wrist flexors and extensors.

RESULTS

The purpose of this study was to examine reflex responses of some synergistic muscles in the upper limbs of human subjects and of muscles antagonist to those that were stretched. A limitation of this protocol was that, on stretch perturbation, it was not possible to differentiate between homonymous and heteronymous responses in the stretched group as each muscle of the group was stretched simultaneously. Consequently, results are presented considering FCR and FCU as a unit of the primary wrist flexors when flexors were stretched and ECR, ECU, and EDC as a unit of primary wrist extensors when extensors were stretched. Although EDC is primarily a finger extensor, a stretch of this muscle could not be prevented with our experimental setup when ECR and ECU were stretched. Since the magnitude of the load used for stretching the wrist was the same for flexors and extensors, as well as for every subject, it produced a range of rates at which the wrist was rotated. In the first 60 ms after the onset of the load pulse, the wrist rotation ranged from 9 to 24° (i.e., angular velocity of 150–400°/s).

Responses of Primary Wrist Flexors and Extensors

With intramuscular electrodes in FCR, FCU, ECR, ECU, and EDC, reflex responses were tested when the primary
muscles were slightly preloaded and then stretched. Clear SLR and LLR peaks were observed in all the stretched muscles. Figure 1 shows the time course of reflex responses in flexors (FCR) at the top and the extensors (ECR) at the bottom. The SLR and LLR peaks were generally well-defined for flexors but rarely for extensors.

The onset of SLR could be measured only when there was background activity in a muscle, and the onset of LLR was not always clear in every subject and every muscle. The shortest values were measured for each muscle in each subject, and means ± SD (in milliseconds) of these values for the population of subjects are shown in Table 1. In every subject, FCR values were always the shortest and most clearly defined.

Since the antagonists had little or no background activity when the stretched muscles were preloaded, inhibition could not be observed. To observe inhibition, the antagonists were preloaded by 0.25–0.375 Nm. Reflex peaks were clearly observed in the stretched muscles with concomitant inhibition of the antagonist muscles. As has previously been shown (Calancie and Bawa 1985), the amplitude of SLR was dependent on the antagonist muscles. As has previously been shown (Calancie and Bawa 1985), the amplitude of SLR was dependent on the antagonist muscles.

Table 1. Onset latencies of SLRs and LLRs

<table>
<thead>
<tr>
<th>Muscle</th>
<th>SLR Onset, ms</th>
<th>LLR Onset, ms</th>
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<tbody>
<tr>
<td>FCR</td>
<td>29.6 ± 2.1</td>
<td>56.8 ± 4.4</td>
</tr>
<tr>
<td>FCU</td>
<td>33.8 ± 2.6</td>
<td>58.9 ± 2.6</td>
</tr>
<tr>
<td>ECR</td>
<td>33.5 ± 3.4</td>
<td>57.5 ± 2.2</td>
</tr>
<tr>
<td>EDC</td>
<td>34.2 ± 1.7</td>
<td>58.6 ± 3.9</td>
</tr>
<tr>
<td>ECU</td>
<td>34.2 ± 3.1</td>
<td>57.8 ± 3.4</td>
</tr>
<tr>
<td>APL</td>
<td>37.2 ± 4.7</td>
<td>59.6 ± 2.9</td>
</tr>
<tr>
<td>FDI</td>
<td>37.8 ± 8.7</td>
<td>63.2 ± 4.4</td>
</tr>
<tr>
<td>ADM</td>
<td>34.0 ± 5.2</td>
<td>62.4 ± 4.6</td>
</tr>
<tr>
<td>Thenars</td>
<td>35.9 ± 8.8</td>
<td>63.2 ± 5.5</td>
</tr>
<tr>
<td>BiBr</td>
<td>29.1 ± 2.1</td>
<td>57.2 ± 4.0</td>
</tr>
<tr>
<td>TriBr</td>
<td>30.3 ± 3.6</td>
<td>56.8 ± 3.6</td>
</tr>
</tbody>
</table>

Values are means ± SD. Onset latencies of short- (SLRs) and longer-latency reflexes (LLRs) are provided for all muscles tested. The shortest values obtained for each subject are included in this table. FCR, flexor carpi radialis; FCU, flexor carpi ulnaris; ECR, extensor carpi radialis; ECU, extensor carpi ulnaris; APL, abductor pollicis longus; FDI, first dorsal interosseous; ADM, abductor digiti minimi; BiBr, biceps brachii; TriBr, triceps brachii.

30 and 100 ms in both FCR and FCU with simultaneous inhibition of ECR, ECU, and EDC. When the flexors were preloaded and extensors stretched, excitatory reflex activity is seen in ECR, ECU, and EDC, whereas FCR and FCU are inhibited during this period. SLR activity between 30 and 60 ms is almost nonexistent in extensors when flexors were preloaded. On the other hand, when the antagonists were preloaded, the gain of the LLR loop was still high in the stretched muscles. Inhibition of the antagonists started at 30 ms; it generally lasted from approximately 40 to 90 ms and was clearly stronger during the LLR period.

Heteronymous Connections

Table 2 summarizes the nature of responses in various heteronymous muscles both distal and proximal to the stretched forearm muscles. N is the number of averaged observations available for that muscle, and each was inspected for reflex excitation or inhibition. The numbers in the columns below “Inh,” “No,” and “Exct” indicate the number of times the averaged response of the muscle was inhibited, had no significant reflex response, or showed an excitatory peak, respectively. “Reb” indicates excitatory activity either following inhibition (rebound; Kranz et al. 1973) or an excitatory peak starting after 75 ms with no activity between 30 and 75 ms. The stretch of wrist flexors consistently excited APL, FDI, ADM, Thenars, and BiBr. The stretch of extensors excited TriBr and inhibited APL and BiBr; responses of other muscles were not clear or consistent, as described in more detail below for individual muscles.

Heteronymous responses of APL. APL is located on the dorsal side of the forearm and abducts the thumb, although its excitatory and inhibitory responses were consistently similar to those of FCR. Notably, however, its SLR peak was relatively small compared with LLR. APL responses are compared with those of FCR and ECR in Fig. 3. When wrist flexors were stretched (Fig. 3, left), LLRs were present in both FCR and APL, whereas ECR was inhibited. Conversely, when the extensors were stretched (Fig. 3, right), an LLR peak was seen in ECR with inhibition of APL and FCR. Table 2 shows that with flexor loads, APL always showed excitatory peaks. With extensor loads, APL was generally inhibited but showed occa-

Fig. 1. Typical intramuscular electromyographic (EMG) responses in wrist flexors and extensors to torque motor imposed stretch of the corresponding muscles. Flexor load extends the wrist (position trace upward in all figures), whereas the extensor load flexes the wrist (position trace downward in all figures). Short-latency reflex (SLR) and long-latency reflex (LLR) peaks were generally well-defined in the flexors but rarely in the extensors. Vertical cursors are located at 30, 60, and 100 ms to clarify the onset of SLR, LLR, and voluntary activities. With the stretch of flexors, reflex excitation is located between
sional excitation, which was confined to later parts of LLR period (the rebound period).

**Heteronymous responses of FDI, ADM, and Thenars.** Figure 4 illustrates responses of ADM, Thenars, and FDI when stretch was applied to wrist flexors (A, D, and G) and to extensors (B, C, E, F, H, and I). Because of consistency in responses with stretch of wrist flexors, only one example is provided for each muscle. Two examples are shown to reflect the variability of responses in these hand muscles when wrist extensors were stretched. Specifically, ADM (recorded with surface EMG electrodes) was always excited with flexor loads, although the SLR was not always significant (Fig. 4A). With extensor loads, results were not consistent; either inhibition (Fig. 4B) or excitatory peaks could be observed (Fig. 4C). Similarly, Thenars (surface recordings) were consistently excited by flexor loads (Fig. 4D), although SLR peaks were observed only in 4/11 averages. With the stretch of wrist extensors, no significant effect (Fig. 4E), inhibition (Fig. 4F), or late excitation could be observed. FDI was always excited with flexor loads (Table 2), however, the peak was not always significant at the SLR time. Figure 4G shows two clear peaks with flexor loads. Results with extensor loads were not consistent; clear excitatory peaks or inhibition was not seen as a general pattern. With extensor stretch, Table 2 shows that in 5/12 cases, clear excitatory peaks were observed starting at 60 ms with no excitation during SLR (Fig. 4H). In Fig. 4I, there is no clear excitation or inhibition in FDI. In conclusion, in the three hand muscles, stretch of wrist flexors led to consistent excitatory responses in all of these muscles. With the stretch of wrist extensors, these muscles could be inhibited, show no significant response, or show only LLR with an onset of ~60 ms.

**Heteronymous connections with proximal muscles, BiBr and TriBr.** With little or no background activity in BiBr and TriBr, no significant reflex responses were observed when wrist extensors or flexors were stretched. When background activity was present, clear excitatory and inhibitory responses were observed. With the stretch of wrist flexors, SLR and LLR were observed in BiBr. With the same stretch but background activity in TriBr, inhibition was seen in TriBr. This inhibition was followed, sometimes with a clear rebound peak (Fig. 5, left), or inhibition extended up to 100 ms. Conversely, with the stretch of the wrist extensors, reflex excitation was observed in TriBr, with inhibition of BiBr. As indicated in Table 2, late peak in BiBr (or TriBr) is interpreted as rebound activity rather than an LLR.

Table 2. Frequency of SLR and LLR responses observed with stretch of wrist flexors and extensors

<table>
<thead>
<tr>
<th>Stretch Flexors</th>
<th>N</th>
<th>SLR</th>
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<td></td>
<td></td>
<td>Inh</td>
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</table>

The frequency with which SLR and LLR responses were recorded in each muscle when wrist flexors were stretched (left) and when wrist extensors were stretched (right). N is the total number of observations for that muscle (each observation is an average of ~25 individual responses). Inh, inhibition; No, no significant effect; Exct, excitatory peak; Reb, excitatory burst with onset times between 75 and 90 ms. Excitatory activity with onset times >90 ms was considered voluntary.
The strength of a response of a tonically firing neuron is determined by computing the increase in its firing rate compared with the background rate (Cheney and Fetz 1984). Similarly, for surface EMG, mean percent increase in activity was computed during SLR and LLR periods for all six heteronymous muscles (see METHODS). Mean percent increase in activity of the heteronymous muscle was compared with concomitantly recorded activity of the homonymous muscle, namely, APL, FDI, ADM, Thenars, and BiBr were compared with FCR and TriBr with ECR. Results are shown in Table 3: columns 2 and 3 compare mean ± SE percent increase in activity during SLR and LLR periods for the six heteronymous-homonymous pairs. The mean for each pair is calculated over M observations (column 1), and selection of each pair required clear background EMG activity in both muscles. For the hand muscles, the strength of connections was stronger for LLR compared with SLR. The opposite was true for the proximal muscles; the mean SLR activity was higher compared with the mean LLR activity.

**DISCUSSION**

The results of this study have shown that muscle afferents from wrist flexors and extensors form heteronymous connections with both the proximal and distal motoneuron pools tested in this study. With stretch of wrist flexors, excitation of APL, FDI, ADM, Thenars, and BiBr and inhibition of TriBr were observed accompanied by reciprocal inhibition of wrist extensors ECR, EDC, and ECU. Similarly, the stretch of wrist extensors excited TriBr while inhibiting BiBr, wrist flexors (FCR and FCU), and APL. The effect of extensor stretch on FDI, ADM, and Thenars was variable. Based on recordings from single motor units, the relative strength of heteronymous monosynaptic connections among the forearm muscles has previously been reported (Chalmers and Bawa 1997). On the extensor side, the values ranged from 0.4 (ECU-EDC) to 0.9.

**Fig. 3.** Abductor pollicis longus (APL) as heteronymous muscle of wrist flexors (intramuscular recordings). When stretch of wrist flexors produced SLR and LLR in FCR, SLR and LLR were also recorded from APL, whereas ECR was reciprocally inhibited. Stretch of extensors produced SLR and LLR in ECR with simultaneous inhibition of FCR and APL. These 2 responses of APL make it a heteronymous muscle for the wrist flexors and an antagonist of wrist extensors. The 3 vertical cursors are located at 30, 60, and 100 ms. POS, angular wrist position.

**Fig. 4.** Responses of abductor digiti minimi (ADM), Thenars, and first dorsal interosseous (FDI) during stretch of wrist flexors (A, D, G, and J) and wrist extensors (B, C, E, F, H, I, K, and L). During stretch of wrist flexors, ADM and FDI are excited during SLR and LLR periods and Thenars are excited only during LLR. When wrist extensors were stretched, one could observe inhibition (ADM (B) and Thenar (E)), excitation during LLR (ADM (C) and FDI (H)), or no clear effect (Thenar (E) and FDI (J)). Cursors are placed at 30, 60, and 100 ms; load pulse for stretch = 0.875 Nm.
(ECR-EDC), whereas for flexors, the values ranged from 0.5 to 0.6. In the present study, the values for heteronymous connections with muscles acting on the elbow and hand ranged from 0.11 to 0.29 for SLR and 0.07 to 0.52 for LLR. LLRs were stronger than SLRs distally, whereas the converse was true for the proximal muscles, thus the strength of the heteronymous connections is much higher for muscles acting at the same joint than for muscles acting on neighboring joints. Additionally, the patterns of heteronymous connections from wrist extensors to hand muscles were not consistent. These observations will be discussed in light of previous reports of heteronymous connections in the upper limb and the methodologies employed.

Different methods have been used to study reflex distributions, each with advantages and disadvantages. First, the use of tendon taps employed for selective stimulation of individual tendons excites Ia afferents only of the tapped muscle, allowing for clear differentiation of homonymous and heteronymous connections. The results are not complicated by activation of Ib afferents. The short time course of tap, however, results mostly in SLR with very little or no LLR. Second, weak electrical stimulation of a muscle or a mixed nerve excites Ia afferents of the short latency reflex, however, the stretch of a number of synergists is much higher for muscles acting at the same joint than for muscles acting on the elbow and hand. Despite these drawbacks, the use of a torque motor to stretch wrist flexors and extensors has provided information on heteronymous connections both for SLRs and LLRs. Furthermore, the stretch of a number of synergists together is more physiological and hence clinically more relevant. Importantly, the use of maximum allowable torque pulses produces strong homonymous reflexes, which, in turn, lead to stronger measurable heteronymous connections.

**Heteronymous Connections**

In this section, we will compare our results for heteronymous connections with those in the literature for monosynaptic reflexes without distinguishing between SLR and LLR (assuming SLR and LLR occur together). In the cat, Fritz et al. (1989) have shown heteronymous connections to be bidirectional in

<table>
<thead>
<tr>
<th>Muscle Pair</th>
<th>SLR (Mean ± SE)</th>
<th>LLR (Mean ± SE)</th>
<th>SLR Strength</th>
<th>LLR Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>APL-FCR (M = 30)</td>
<td>75 ± 9 (456 ± 63)</td>
<td>221 ± 23 (1,022 ± 124)</td>
<td>0.164</td>
<td>0.216</td>
</tr>
<tr>
<td>FDI-FCR (M = 28)</td>
<td>148 ± 56 (516 ± 88)</td>
<td>489 ± 118 (946 ± 141)</td>
<td>0.287</td>
<td>0.517</td>
</tr>
<tr>
<td>ADM-FCR (M = 22)</td>
<td>62 ± 20 (542 ± 100)</td>
<td>217 ± 28 (820 ± 121)</td>
<td>0.114</td>
<td>0.264</td>
</tr>
<tr>
<td>Thenar-FCR (M = 11)</td>
<td>43 ± 18 (397 ± 87)</td>
<td>228 ± 68 (653 ± 171)</td>
<td>0.11</td>
<td>0.349</td>
</tr>
<tr>
<td>BiBr-FCR (M = 28)</td>
<td>62 ± 6 (422 ± 48)</td>
<td>90 ± 14 (1,089 ± 124)</td>
<td>0.147</td>
<td>0.082</td>
</tr>
<tr>
<td>TriBr-ECR (M = 26)</td>
<td>39 ± 5 (201 ± 49)</td>
<td>84 ± 13 (1,262 ± 350)</td>
<td>0.199</td>
<td>0.066</td>
</tr>
</tbody>
</table>

APL, FDL, ADM, Thenar, and BiBr activity was compared with concomitantly recorded FCR activity. TriBr activity was compared with that of ECR. M is the total number of observations for each pair. Each selected observation required the presence of background activity in each simultaneously recorded heteronymous/homonymous pair.
the forelimb of the cat, yet a large number of studies in humans have suggested the projections to be only in the distal-to-proximal direction with no clear presence of proximal-to-distal connections (Cavallari and Katz 1989; Créange et al. 1992; Lourenço et al. 2006; Marchand-Pauvert et al. 2000; Pierron-Deseilligny and Burke 2005). However, using tendon taps, McClelland et al. (2001) have shown bidirectional heteronymous connections between the shoulder and elbow muscles for SLRs. For LLRs, proximal-to-distal heteronymous connections have been reported from elbow to wrist muscles (Koshland et al. 1991; Latash 2000). The difference in results for SLRs could largely be due to differences in methodology and the strength of the stimulus where a stronger homonymous response results in a stronger heteronymous response. The stimulus employed by Cavallari and Katz (1989), Créange et al. (1992), and Marchand-Pauvert et al. (2000) was weak, and Lourenço et al. (2006) acknowledged that the frequency of heteronymous connections in their previous paper (Marchand-Pauvert et al. 2000) was extremely low due to the weak stimulus. If, to start with, the underlying heteronymous connections to hand and elbow are weak, a weak stimulus will fail to excite the heteronymous pool and make the resultant response unobservable. Similarly, previous experiments testing only for SLR may have been influenced by the decrease in strength of SLR projections to the distal forelimb, rendering any connection unobservable (Marsden et al. 1976; Matthews 1991; Smeets and Erkелens 1991). The stimulus in our experiments was very strong, and afferent activity originated from multiple muscles of the forearm, making the input to the heteronymous pools additively stronger. As a result, we observed the heteronymous connections with greater frequency, particularly when wrist flexors were stretched.

With the stretch of the wrist extensors, reflex patterns were not as consistent: clear inhibition, appearance of LLR peak. In some subjects when the amplitude of the SLR peak was, when averaged over all subjects, larger than that working by cocontraction, FCR counteracts the undesired supinating force of APL. The finger muscle FDI was also consistently excited by the stretch of wrist flexors in our experiments. With stretch of wrist extensors, weak inhibition (at SLR latency) was sometimes observed. More consistent, however, was an excitatory peak starting at 60 ms and spanning the LLR period. FDI is an abductor and flexor (metacarpophalangeal joint) of the index finger. It also acts synergistically with EDC to extend the index finger by acting at the phalangeal joints. Thus it is not surprising that LLR was observed in FDI mirroring its shared action with EDC. The variable responses of ADM and Thenars with surface electrodes could be attributed to cross talk of activity from all other hypothenar and thanar muscles, respectively. Individual muscles of each of these groups are responsible for various functions, and hence each muscle could be excited by afferents of either wrist flexors or extensors, a distinction that our methodology will not allow. Cross talk, as inviting as it appears, may not be the real answer. The muscles of the hand allow for several degrees of freedom, and thus it would not be unexpected that they share connections with either wrist flexors, or extensors, as the task dictates (Lacquaniti and Soechting 1986b). The complexity of activation patterns of APL and other forearm/hand muscles are brought to our attention by studies from Van Oudenaarde and coworkers (1995, 1997). Voluntary activation of various combinations of muscles depends on the position of the hand and the forearm. The same argument may hold for all small muscles in the hand and around the wrist when considering the degrees of freedom around the wrist joint. With regard to ADM, it should be added that even though the manipulandum was designed to restrict the stretch to the forearm muscles, one cannot rule out the stretch of ADM when the hand was moved.

Heteronymous Connections to Elbow

Stretch of wrist flexors excited BiBr and inhibited TriBr, but the reverse was true with the stretch of wrist extensors. In the cat, IA afferents from FCR showed weak excitatory connections to BiBr motoneurons, whereas IA afferents from ECR, EDC, and ECU did not show any connections with motoneurons of BiBr or TriBr (Fritz et al. 1989). In humans, all studies have shown excitatory connections between FCR and BiBr (Cavallari and Katz 1989; Lewis and McNair 2010). Patterns reported by Cavallari and Katz (1989), however, showed excitatory heteronymous connections onto BiBr and inhibitory connections to TriBr, regardless of whether the group I afferent volley originated from electrical stimulation of the radial nerve or the median nerve at the elbow. Conversely, when working with shoulder and elbow muscles, Smeets and Erkелens (1991) observed a reciprocal relationship between BiBr and TriBr, when brachialis and BiBr were excited, TriBr was inhibited; when TriBr was excited, brachialis and BiBr were inhibited. A similar reciprocal relationship between BiBr and TriBr was reported by Lacquaniti and Soechting (1986a) and Perreault et al. (2008). Inconsistency in results could arise from differences in methods that excited different populations of muscle afferents at different anatomic positions and via different means of excitation. Another major difference we have with a few studies is the relative amplitudes of LLRs vs. SLRs in elbow extensors and flexors (Kurtzer et al. 2008). As mentioned in RESULTS, BiBr and TriBr heteronymous responses were small, and SLR was, when averaged over all subjects, larger than LLR. In some subjects when the amplitude of the SLR peak reached statistical significance, the amplitude of LLR peak did...
not always reach significance even though the peak was well-defined. From inspection of individual averages, it appears that in some subjects, SLR in the elbow flexors and extensors is followed by strong inhibition and that transcranial reflex activity arriving at the motoneurons during the LLR period is superimposed on this inhibition. This is akin to LLR following SLR with tendon taps, hence LLRs are reported very infrequently (Baudry et al. 2009). The inhibition in wake of SLR could arise from Renshaw cells (Pierrot-Desseiligny and Burke 2005), refractoriness of motoneurons, or some untested source of heteronymous inhibition.

In subjects where LLR was relatively larger and almost equal to SLR, it was still never dominant as it is in the hand and wrist muscles. Therefore, for studies that have reported very large LLRs compared with SLRs, it is suggested that the large amplitudes possibly result from changes in the central set of the subject and superposition of voluntary activity in the LLR period (see Fig. 1, Kurtzer et al. 2008).

Late Rebound Activity and Coupling of SLR and LLR

Most of the heteronymous connections in our study were strong and consistent, with both SLR and LLR occurring together. Weak or an absent SLR was correlated with the absence of background activity similar to what has been shown in detail by Smeets and Erkelens (1991). Two additional patterns of late excitatory activity were observed. One such pattern was the late activity in heteronymous muscles (post 75 ms) that could be explained as a postinhibition rebound peak following inhibition as it appears in Fig. 5 (Kranz et al. 1973). The second pattern was the appearance of a peak in hand muscles ~60 ms without any preceding excitation or inhibition during the SLR period. This was interpreted as a LLR, as it was temporally the same as LLR induced by stretch of the wrist flexors. This is an example where perturbations in opposite directions produce LLR in the same muscle. An analogous example for the distribution LLR was reported by Gielen et al. (1988) who reported reflex excitation of normal antagonists, BiBr and TriBr, when pronation torque was applied to the forearm (a perturbation that did not stretch TriBr). The authors proposed that even though the trigger for LLR is IA afferent, its distribution can be different from that of SLR. It must be pointed out that the above quoted study by Gielen and coworkers (1988) was done with single motor units, and appearance of both reflex peaks with the same motor unit is difficult (Calancie and Bawa 1985); for that reason, SLR might not always appear with LLR. A tonically firing motor unit will respond at the SLR time and could be totally refractory during LLR time. This was interpreted as a LLR, as it was surface or intramuscular EMG.

Conclusions

The main observations from the current study are that spindle afferents from wrist flexors and extensors make heteronymous connections with proximal and distal muscles. Quite frequently, the LLRs can appear in the same hand muscle with both flexor and extensor stretch, and the strength of heteronymous connections from the forearm to the elbow and hand muscles is weaker than the connections among the prime wrist flexors and extensors. The weak connections seem comparable with the less frequent and small amplitude connections in the cat (Fritz et al. 1989). Do these infrequent and weak responses (excitatory postsynaptic potentials or EMGs) have a functional meaning, or rather do they reflect biological noise? We suggest that although there may be some aberrant connections, the averaged responses, although small, do have functional significance. First, the variable frequency of appearance of LLRs with extensor stretch may depend on the postural set...
that can determine both the afferent activities and their network connections in the spinal cord. Depending on their motor training and postural set during the experiments, each subject will have different synergies, and we suggest that these synergies dictate the heteronymous reflex responses. The second role of weak connections relates to plasticity. In the past couple of decades, there has been ample proof of plasticity of the adult nervous system, and hence it is suggested that the weak connections, as such, do not contribute much to movement but provide a background substrate of connections on which coordinated movements can be built with practice. From a functional perspective, the pairing of the proximal muscles of the wrist with those acting at the hand is intuitive, as an unexpected perturbation to the wrist during a fall or loss of balance requires bracing of the distal limb and hand to regain postural stability. Wrist flexor stretch leads to consistent excitation of the hand muscles that function in both the finger abduction (spreading) and flexion (bracing) necessary to sustain the wrist with those acting at the hand is intuitive, as an unexpected perturbation to the wrist during a fall or loss of balance requires bracing of the distal limb and hand to regain postural stability. Wrist flexor stretch leads to consistent excitation of the hand muscles that function in both the finger abduction (spreading) and flexion (bracing) necessary to sustain the weight of the body. Thus it may be suggested that these heteronymous reflex connections have adapted into these synergistic patterns to allow for functionally relevant multijoint responses that far precede the onset of any voluntary response. Future investigations must consider simple SLR and LLR responses from single-joint perturbations to elucidate the heteronymous patterns associated with each joint and at both latencies. From this, more functionally relevant investigations involving multiple limb segments and voluntary reactions will have a physiological framework on which to move forward from.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

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