Published in final edited form as:

Exp Brain Res. 2008 June ; 188(1): 159–164. doi:10.1007/s00221-008-1432-7.

Common synaptic input across motor nuclei supplying intrinsic muscles involved in the precision grip

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Abstract

To gain insight into the mechanism by which the nervous system orchestrates the activities of multiple muscles during voluntary motor behaviors, we measured the degree of synchrony in the discharge times across pairs of motor units recorded from two intrinsic hand muscles, the adductor pollicis (AdP) and first dorsal interosseous (FDI), in human subjects performing a precision grip. The magnitude of synchrony measured across muscles is thought to reflect the extent of divergent synaptic input delivered in common to the motor nuclei supplying the two muscles. Unlike the pronounced motor-unit synchrony observed across comparable extrinsic hand muscles during the precision grip, little synchrony was detected across these two intrinsic muscles. These results suggest that extrinsic and intrinsic muscles of the hand are controlled by descending pathways with distinctly different patterns of spinal connectivity—more widespread terminations across motor nuclei supplying extrinsic muscles whereas more focal input to individual motor nuclei innervating intrinsic muscles.

Keywords

Motor unit; Synchrony; Hand; Motor control; Precision grip; Finger

Introduction

The precision grasp of an object between the thumb and index-finger is executed using multiple muscles in the forearm and hand (Maier and Hepp-Reymond 1995a; Schieber 1995). While the mechanisms by which the central nervous system coordinates the activities of multiple muscles in the elaboration of a motor behavior such as the precision grip are not fully understood, recent findings have shed some light on this process. For example, two of the extrinsic muscles involved in the precision grip, one inserting on the distal segment of the thumb and the other on the distal segment of the index finger, appear to have their activities tightly coupled together by descending pathways that diverge to provide extensive common synaptic input across their respective motor nuclei (Winges and Santello 2004; Hockensmith et al. 2005).

There are also a host of intrinsic muscles that act on the thumb and index-finger and which also appear to play a significant role in generating finely graded forces associated with the precision grip (Maier and Hepp-Reymond 1995a, b). Indeed, the two muscles whose activities are most strongly correlated with precision-grip force are two intrinsic muscles, the adductor pollicis (AdP), a thumb adductor, and first dorsal interosseous (FDI), a muscle that flexes and abducts the index finger (Maier and Hepp-Reymond 1995a). Therefore, the purpose of this investigation was to determine whether the activities of these two intrinsic muscles that operate on the thumb and index-finger, like their extrinsic counterparts, are conjoined by divergent common synaptic input across their motor nuclei during the precision grip. The extent of common synaptic input across the motor nuclei supplying AdP and FDI was estimated by measuring the degree of short-term synchrony in the firing times of motor-unit pairs recorded from the two muscles (Sears and Stagg 1976; Kirkwood and Sears 1978) during a precision grip task. These data were compared to those obtained previously using similar procedures involving motor-unit pairs recorded from two extrinsic hand muscles (Hockensmith et al. 2005).

Materials and methods

Subjects

Fifteen experiments were performed on the dominant right hands of ten healthy human volunteers (6 females and 4 males) aged between 23 and 57 years. The procedures were approved by the Institutional Human Investigation Committee at the University of Arizona, and all subjects gave informed consent as required by the Helsinki Declaration.

Experimental setup

Subjects were seated in a dental chair with the right forearm supported on foam padding on a horizontal platform. The hand rested in a neutral supinated/pronated orientation (i.e., radial side up) with the wrist extended slightly. Single-unit electromyographic (EMG) activity was recorded using sterilized, lacquer-coated tungsten microelectrodes inserted percutaneously into the AdP and FDI muscles (Frederick-Haer & Co., Bowdoinham, Maine). Surface electrodes (4 mm diameter Ag-AgCl) attached to the skin overlying the radial styloid served as reference electrodes for each intramuscular electrode. Weak electrical stimulation was used initially and between each trial to verify microelectrode placement in AdP and FDI (0.5–5 mA, 1 ms duration, 1 Hz; S88 Stimulator, Grass-Telefactor, West Warwick, RI). Intramuscular EMG signals were amplified ($\times 2,000$) and band-pass filtered (0.1–3 kHz), and displayed on oscilloscopes. In a subset of six experiments, thumb and index-finger normal forces were monitored using thin, conformable force transducers (ConTacts C500, Pressure Profile Systems, Inc., Los Angeles, CA) placed over the pads of each digit and held in place by latex finger cots.

Protocol

Subjects were instructed to lightly grasp an unsupported wooden dowel (18 cm long $\times$ 1 cm in diameter, 9 gm) that was placed between the thumb and index-finger by the experimenter, and to hold the dowel in a vertical orientation while keeping the other digits from contacting the dowel or the grasping digits. The microelectrodes were gently manipulated during this

task until action potentials of motor units could be clearly identified on each electrode. Subjects were then instructed to sustain a light grasp of the dowel such that both motor units remained active. Intramuscular EMG signals were recorded for 5–10 min or until the action potentials could no longer be clearly discriminated. Subjects received visual and audio feedbacks of the motor unit discharges, and 1–2 min of rest between trials. After each trial at least one of the two microelectrodes was adjusted until a presumed different motor unit was identified. Occasionally this required removal and reinsertion of the microelectrode into a new site, after which placement verification with electrical stimulation was performed as described. For comparison purposes, in some trials both microelectrodes were inserted into the AdP in order to record pairs of AdP motor units during the grip task. Successive trials were performed for up to 2 h. Intramuscular EMG signals were digitally sampled at 12.5 kHz per channel using the Spike 2 data-acquisition and data-analysis system (Cambridge Electronics Design, Cambridge, UK).

Data analysis

Cross-correlation analysis of the discharge times of motor-unit pairs was carried out in the same way as we have described previously (Keen and Fuglevand 2004; Hockensmith et al. 2005; McIsaac and Fuglevand 2006, 2007). In brief, off-line discrimination of motor-unit action potentials from each intramuscular recording was performed using a template-matching algorithm (Spike 2, Cambridge Electronics Design; Cambridge, UK). Cross-correlation histograms (1 ms bins, ± 100 ms) were constructed from the discharge times of the discriminated motor units from separate electrodes. The central peak in the histogram was identified using the cumulative sum (cusum) procedure, which involves progressively summing the differences in the number of counts in each bin of the histogram from the mean bin count (Ellaway 1978). The baseline mean was calculated as the mean count in the first and last 60 ms of the histogram. A rise in the cusum near time zero was used to identify the central peak in the histogram. The boundaries of this peak were defined as the bins corresponding to 10 and 90% of the difference between the minimum and the maximum cusum values (Schmied et al. 1993). The magnitudes of the central peaks in the cross-correlograms were quantified using the common input strength (CIS) synchronization index. CIS was calculated by the number of counts within the peak above the baseline mean divided by the duration of sustained tonic firing in the two units (Nordstrom et al. 1992). CIS reflects the rate of extra synchronous spikes (extra synch. spikes/s) above that expected by chance.

When no clear peak was evident in the cross-correlogram, the above technique for identifying the region of the histogram for which to calculate the CIS was unreliable. Therefore, for cases of non-significant peaks in which the number of counts within the peak was less than three standard deviations above the mean (z score < 1.96) (Schmied et al. 1993), the CIS was automatically calculated for an 11 ms region of the cross-correlogram centered at time zero (Semmler and Nordstrom 1995). All CIS values, regardless of the method used for calculation were included in the analysis.

The CIS data collected here for intrinsic muscles were compared to that obtained for extrinsic muscles of the thumb (flexor pollicis longus, FPL) and index-finger (index finger

compartment of flexor digitorum profundus, FDP) under similar, but not identical, task conditions (Hockensmith et al. 2005). In that study, leather cuffs that encircled the volar surfaces of the distal segments of the thumb and index-finger were attached to separate isometric force transducers. Subjects were instructed to squeeze the thumb and index-finger gently against the cuffs to mimic grasping of an object, while motor-unit activity was recorded from the two muscles. The analysis methods were identical to that used in the present study. Like the present investigation, there were ten right-handed subjects tested with an age range of 22–43 years in the Hockensmith et al. (2005) study. One subject was common to both studies.

A one-way ANOVA was used to determine whether mean CIS values were significantly different among the combinations of paired motor-unit recordings during the precision grip: both units within AdP (AdP–AdP), one unit in AdP and the other in FDI (AdP–FDI), and one unit in FPL and one unit in FDP (FPL–FDP, Hockensmith et al. 2005). A number of investigations previously have examined the extent of synchrony within FDI (Datta and Stephens 1990; Nordstrom et al. 1992), and therefore, such experiments were not repeated here. Tukey's post hoc analysis was used to identify differences in CIS across motor unit combinations. Values are reported as means $\pm$ SD with a probability of 0.05 selected as the level of statistical significance.

Results

A total of 129 motor units were recorded from ten subjects during precision grip of the thumb and index-finger. Only low-threshold motor units were sampled in this study due to the low-force nature of the grasping task (contact forces <1.5 N). The mean discharge rate for all motor units was 10.5 ± 1.9 Hz, and the average number of spikes/unit used in the analysis was $4,457 \pm 2,047$. The discharge times of units detected on separate electrodes were used to generate 72 cross-correlograms. In 11 trials more than one unit was detected on an electrode, providing for more than one cross-correlation per trial. Thirty-six of the correlograms were for AdP–FDI motor-unit pairs and 36 were derived from trials in which both of the units were within AdP. The total number of cross-correlograms contributed per subject ranged from 2 to 16 with a median of seven correlograms/subject. In the Hockensmith et al. (2005) study, correlograms were constructed from the firing times of 25 low-threshold pairs of motor units recorded from the extrinsic muscle pair, FPL–FDP. The overall average discharge rate for motor units recorded in that study was 9.8 ± 1.3 Hz.

Figure 1 shows three example cross-correlation histograms obtained for each combination of motor-unit pairs. These examples are all from the same subject; the one subject that participated in both the present investigation and in the Hockensmith et al. (2005) study. Figure 1a shows a cross-correlogram obtained during the precision grip for a pair of motor unit both residing within the AdP muscle. The prominent central peak indicates a high degree of synchrony (CIS = 1.20) for this pair of motor units. Similarly, Fig. 1b shows an example cross-correlogram for a pair of motor units, but in this case, one unit was from AdP and the other was from FDI (AdP–FDI). For this across-muscle combination of units associated with intrinsic muscles, virtually no central peak was discernable (CIS = 0.08). And finally, Fig. 1c shows an example cross-correlogram for an FPL–FDP pair of units

recorded in this same subject as part of the Hockensmith et al. (2005) study. In this case, there was a substantial degree of synchrony ($CIS = 0.74$) for this across-muscle combination of units from extrinsic muscles.

Overall, a large proportion (32/36 or 89%) of the cross-correlograms for AdP–AdP motor-unit pairs exhibited a significant peak (see “Methods”) whereas relatively few (6/36 or 17%) AdP–FDI cross-correlograms had a significant peak. The durations of these significant peaks were brief for both combinations of motor unit pairs recorded in the present investigation (7.9 ± 2.0 ms for AdP–AdP pairs, 9.2 ± 2.2 ms for AdP–FDI pairs). The peak durations for cross-correlograms obtained for FPL–FDP pairs (Hockensmith et al. 2005) were also relatively brief (9.4 ± 2.2 ms).

Figure 2 shows the mean (SD) CIS values for all within-muscle pairs (AdP–AdP) and for all across-muscle pairs (AdP–FDI) of motor units recorded from these intrinsic muscles during the precision grip. For comparison, also shown in Fig. 2 is the mean (SD) CIS value for 25 across-muscle pairs of motor units recorded from two extrinsic muscles (FPL and FDP) (Hockensmith et al. 2005). ANOVA revealed a significant effect of muscle combination on mean CIS value ($p < 0.001$). Post-hoc analysis indicated that the mean CIS values for AdP–AdP motor-unit pairs (0.55 ± 0.25) and FPL–FDP pairs (0.45 ± 0.27 , Hockensmith et al. 2005) were both significantly greater ($p < 0.0001$) than that recorded in AdP–FDI pairs (0.14 ± 0.15).

Discussion

We used cross-correlation analysis of the discharge times of motor units located in intrinsic hand muscles acting on the thumb (AdP) and index-finger (FDI) to estimate the degree to which their coordinated activity in generating grip force might be related to divergent synaptic input across motor nuclei activated during a precision grip task. In contrast to the high degree of synchrony exhibited between motor units residing in separate extrinsic muscles acting on the thumb and index-finger (Winges and Santello 2004; Hockensmith et al. 2005), here we found little synchrony for AdP–FDI motor-unit pairs, despite these being neighboring muscles and the primary intrinsic muscles used in a tip precision grip (Long et al. 1970; Maier and Hepp-Reymond 1995a; Brand and Hollister 1999). These findings suggest that the descending pathways that control the activities of intrinsic muscles provide more concentrated input to individual motor nuclei than those pathways destined for motor nuclei innervating extrinsic hand muscles. The functional significance of such differences in corticospinal organization is considered below.

Within- and across-muscle synchrony

Experimental and modeling studies have shown that the magnitude of the synchronous peak in cross-correlation histograms, constructed from the relative firing times of two concurrently active neurons, provides a noisy representation of the degree of common synaptic input to the two neurons (Perkel et al. 1967; Sears and Stagg 1976; Kirkwood and Sears 1978; Kirkwood 1979). Substantial synchrony has been shown previously to exist for most pairs of motor units within intrinsic hand muscles, including FDI (Datta and Stephens 1990; Bremner et al. 1991a; Nordstrom et al. 1992; Semmler and Nordstrom 1995; Huesler

et al. 2000) and within extrinsic hand muscles (Bremner et al. 1991b; Schmied et al. 1993; Keen and Fuglevand 2004). Likewise, we have shown here considerable synchrony among motor units within ADP, also an intrinsic hand muscle. Overall, such observations support the idea that descending fibers branch extensively to provide broadly distributed and potent input across motor neurons comprising a single motor nucleus (Lawrence et al. 1985; Mantel and Lemon 1987).

In addition, several studies have examined the extent of synchrony between motor units residing in separate muscles or muscle compartments. In these studies, significant synchrony is often observed for neighboring muscles, or in muscles with similar actions, although the magnitude of such across-muscle synchrony is typically less than that found within muscles (Bremner et al. 1991b; Maier and Hepp-Reymond 1995a; Huesler et al. 2000; Keen and Fuglevand 2004; Wings and Santello 2004; Reilly et al. 2004; McIsaac and Fuglevand 2007). One notable exception, however, is for the extrinsic hand-muscle pair FPL and the index finger compartment of FDP (Wings and Santello 2004; Hockensmith et al. 2005). Synchrony recorded for pairs of motor units residing in these separate thumb and index-finger muscles during a precision grip was just as large as that for pairs of units both within the same muscle (Hockensmith et al. 2005). These results implied the existence of descending fibers that ramify extensively to operate on the two motor nuclei as a unit and thereby induce the two muscles to function together in the generation of the matched normal forces required during a precision grip (Hockensmith et al. 2005).

In the present experiment, we were interested to determine whether such divergence also serves to couple together the activities of two intrinsic muscles that are also critical participants in the precision grip (Maier and Hepp-Reymond 1995a). Little synchrony, however, was observed between AdP–FDI motor-unit pairs, suggesting that descending inputs more selectively target the motor nuclei supplying these two intrinsic hand muscles than their extrinsic counterparts. To a large extent, these observations parallel those based on more direct evaluation of cortical projections to spinal motor nuclei in the monkey. In those studies, individual pyramidal-tract neurons arising in primary motor cortex and targeting motor nuclei destined for forearm muscles often appeared to supply multiple motor nuclei (Fetz and Cheney 1980; Shinoda et al. 1981; Cheney and Fetz 1985) whereas cortical neurons innervating motor nuclei of intrinsic hand muscles tended to facilitate individual muscles (Buys et al. 1986).

Roles of intrinsic and extrinsic muscles in precision grip

The contrasting organizations of the descending pathways targeting extrinsic and intrinsic muscles seem in harmony with postulated differential functions of these two groups of muscles in the precision grip. Biomechanical (Chao et al. 1989) and EMG studies (Long et al. 1970) of the precision grip indicate that extrinsic muscles provide the primary gripping forces while intrinsic muscles largely act to orient the digits to interact with the object to be manipulated. Because gripping per se necessitates the production of precisely counterbalanced forces across two or more digits, it seems reasonable to speculate that the muscles primarily involved in the production of gripping forces have their activities securely linked together by divergent descending inputs across their respective motor nuclei. On the

other hand, because the fingers must interact with an extensive range of objects of varying shapes and sizes, it would seem fitting that intrinsic muscles be controlled by highly independent pathways that enable the fractionated actions needed to con-figure the digits to the unique dimensions of an object to be handled. The results of the present study provide some support for such differential control over the extrinsic and intrinsic muscles involved in the precision grip.

Acknowledgments

We are grateful to Amber Rice for technical assistance. This work was supported by a Douglas G. Stuart Pre-Doctoral Fellowship in Neuroscience (to TLM) and NIH Grant NS 39489 (to AJF).

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Fig. 1.

Example cross-correlograms obtained during precision grip from the same subject for (a) pair of motor units both recorded within AdP, and (b) a pair of motor units for which one unit was recorded from AdP and the other from FDI, and (c) a pair of motor units for which one unit was recorded in FPL and the other in FDP. In each case, discharge synchrony was quantified as the CIS (see “Methods”) based on the central peak in the correlogram (delineated using the cusum procedure, not shown) (*AdP* adductor pollicis, *FDI* first dorsal interosseous, *FPL* flexor pollicis longus, *FDP* flexor digitorum profundus, *CIS* common input strength)

Fig. 2.

Mean (SD) CIS for pairs of units both residing within the intrinsic muscle AdP (AdP–AdP within intrinsic), for pairs of units in which one unit was recorded from AdP and the other unit was recorded from FDI (AdP–FDI across intrinsic), and for pairs of units recorded across two extrinsic muscles (FPL–FDP across extrinsic, from Hockensmith et al. 2005). * significantly different ($p < 0.0001$) from AdP–FDI motor-unit pairs. (*CIS* common input strength, *AdP* adductor pollicis, *FDI* first dorsal interosseous, *FPL* flexor pollicis longus, *FDP* flexor digitorum profundus)