

NEURAL MECHANISMS UNDERLYING MUSCLE SYNERGIES INVOLVED IN  
THE CONTROL OF THE HUMAN HAND

by

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## ABSTRACT

The dexterity of the human hand depends largely on the ability to move the fingers independently, the execution of which requires the coordination of multiple muscles. How these muscle ensembles are recruited by the central nervous system is not clear. Therefore, the objective of this dissertation was to identify some of the neural mechanisms whereby certain hand muscles are recruited into functional groups, or muscle synergies, needed for the generation of specific hand and finger movements.

We characterized the organization of synaptic inputs onto the motor neurons supplying different compartments of a multi-tendoned finger flexor, the flexor digitorum superficialis (FDS). We found that the motor neurons controlling different finger compartments of the FDS do not receive entirely segregated inputs, and that the motor neurons supplying adjacent compartments receive substantially more common synaptic input than motor neurons supplying compartments further apart. The FDS and another multi-tendoned finger flexor, the flexor digitorum profundus (FDP), both insert onto each finger and function together to flex the fingers. Surprisingly, we found that the motor neurons controlling the compartments of FDS and FDP to the same finger receive completely independent inputs, despite similar mechanical functions of the two muscles. Thus, there is more neural coupling between motor neurons supplying compartments of the same muscle that move different fingers than there is between motor neurons supplying the compartments of two different muscles that move the same finger.

Although the motor neurons supplying the flexors of the tips of the thumb [flexor pollicis longus (FPL)] and index finger [index compartment of the flexor digitorum

profundus (FDP2)] receive substantial shared synaptic input during a precision grip task, the removal of the normal tactile feedback from the digit pads did not change the amount of common input to the two motor neuron pools, indicating these last-order divergent neurons do not require tactile afferent inputs for activation. Finally, in contrast to the substantial shared input to motor neurons supplying these two *extrinsic* muscles (FPL and FDP2), the motor neurons supplying two *intrinsic* muscles of the thumb [adductor pollicis (AdP)] and index finger [first dorsal interosseous (FDI)] were shown to receive few shared inputs during precision grip.

**CHAPTER 1: INTRODUCTION**

Humans, like some other primates, have the capacity to move the fingers fairly independently enabling precise manipulation of objects and the generation of numerous gestures. Typing and playing the piano, for example, are complex behaviors in which control over individual finger movement is crucial. Yet movements of individual fingers require the activation of multiple muscles (Schieber 1995). For instance, during a simple behavior such as touching the tip of the index finger to the thumb, or during selective flexion of only one joint within a single finger, several muscles show significant activity on electromyographic (EMG) recordings (Close and Kidd 1969; Darling and Cole 1990; Schieber 1990). How the central nervous system (CNS) coordinates the activities of multiple muscles to produce even simple finger movements is not yet well understood. The goal of this dissertation, therefore, was to identify some of the neural mechanisms whereby selected hand muscles are recruited into functional ensembles needed to generate specific voluntary motor behaviors of the hand and fingers.

Motor neurons supplying hand muscles in higher order primates are specialized in that they receive a large proportion of their synaptic input directly from the motor cortex (Lawrence and Kuypers 1968a; Heffner and Masterton 1983; Palmer and Ashby 1992; Porter and Lemon 1993). Because finger movements, even those involving a single digit, require the participation of multiple muscles, two hypothetical schemes can be considered as to how such corticospinal inputs might be organized to recruit the various muscles needed to perform a particular task (Schieber 1990; Stephens et al. 1999). In one scheme, each muscle is controlled by a distinct set of corticospinal axons that selectively impinge upon individual spinal motor nuclei, which, in turn, project to specific muscles. In this

‘labeled-line’ like scheme, muscle selection would depend largely upon which cortical regions were activated. In a second scheme, individual corticospinal axons ramify to supply multiple motor nuclei; activity in such corticospinal neurons would then tend to enlist multiple muscles simultaneously. Therefore, selection of the set of muscles needed to perform a particular motor task would largely depend upon the pattern of divergence of the activated corticospinal axons across multiple motor nuclei.

At present, there exists virtually no anatomical information on the spatial pattern of terminal projections of corticospinal axons within the primate spinal cord needed to distinguish between the two organizational schemes. It is possible, however, to assess indirectly the pattern of divergence of synaptic inputs across motor nuclei in the human spinal cord based on the relative timing of discharges of motor units located in different muscles. In concept, the presence of presynaptic fibers that diverge to provide common excitatory input to two motor neurons should elicit concurrent excitatory postsynaptic potentials in the two neurons and thus slightly increase the probability that the two neurons will be brought to firing threshold simultaneously (Kirkwood and Sears 1978). Neurons receiving such common excitatory input, therefore, should discharge synchronously slightly more often than would be expected due to chance. Such synchrony is manifest as a narrow peak around time zero in the cross-correlation histogram constructed from the relative firing times of two concurrently active motor units. The magnitude of the synchrony peak is thought to represent the proportion of common to non-common synaptic inputs impinging upon the two neurons (Kirkwood and Sears 1978). For this dissertation, therefore, the extent of synchrony among motor units

was used to evaluate the degree to which coordinated activity across hand muscles could be attributed to divergence of descending pathways providing common synaptic inputs across sets of motor nuclei.

One prominent feature of the muscular organization of the hand is that the primary finger flexors and extensors are located in the forearm (extrinsic hand muscles) and each gives rise to four parallel tendons that cross multiple joints and insert onto the four fingers (Wood Jones 1941). Each of these muscles appears to be comprised of four compartments, one for each tendon. A question arises as to how the synaptic inputs to the motor neurons supplying different compartments of these multi-tendoned muscles are organized. Namely, does the subset of motor neurons innervating a particular muscular compartment receive a distinct set of synaptic inputs, or are synaptic inputs distributed across motor neurons that supply multiple compartments? To address this question, therefore, in the first study of this dissertation we characterized the organization of synaptic inputs to motor neurons supplying one of these multi-tendoned muscles, the flexor digitorum superficialis (FDS). Results from this study indicated that motor neurons controlling different finger compartments of FDS do not receive entirely segregated inputs. Furthermore, motor neurons supplying adjacent compartments received substantially more common synaptic input than motor neurons supplying compartments further apart, indicating there is more neural coupling between adjacent fingers. Such coupling may partially explain the tendency for neighboring fingers to move less independently than non-adjacent fingers.

Another intriguing aspect of the neuromuscular organization of the hand is that multiple muscles insert onto the same digit. For instance, the FDS and another multi-tendoned extrinsic muscle, the flexor digitorum profundus (FDP), both insert onto each finger and together function to flex the fingers. It is reasonable to anticipate that the activities of these two muscles must be tightly coordinated in order to enable coordinated digit flexion. Therefore, in the second set of experiments of this dissertation, the possibility that divergent last-order inputs serve to link the activities of these two muscles together was investigated. Surprisingly, results from this study indicate that motor neurons controlling the compartments of FDS and FDP to the same finger receive entirely independent inputs, despite the similar mechanical functions of these two muscles. Thus, the origin of the tightly coordinated activity of these two muscles does not appear to be at the level of last-order spinal inputs.

One example of the dexterous behavior of the human hand is the fine manipulation of objects between the index finger and thumb tips during precision grip. The extrinsic hand muscles are considered to provide the primary grip force while the muscles located within the hand (intrinsic muscles) primarily act to position and stabilize the digits and only secondarily contribute to the grip force (Long et al. 1970; Chao et al. 1989). The precise matching of thumb and index finger contact forces that is required for a stable precision grip (Westling and Johansson 1984) might be mediated through pathways that diverge extensively to engage the motor nuclei supplying the thumb and index finger muscles as a functional unit (Hockensmith et al. 2005). Indeed, Hockensmith et al. (2005) recently demonstrated a high degree of common synaptic input

across the motor nuclei supplying the muscles that flex the tips of the thumb [flexor pollicis longus (FPL)] and the index finger [index compartment of the FDP (FDP2)] during a precision-like grip. While the origin of this divergent input is likely to be cortical, is it possible that tactile afferents arising from the distal pads of the index finger and thumb could also provide potent divergent excitatory input across the motor nuclei involved in this task. This possibility was investigated in the third study of this dissertation by comparing the extent of common synaptic input to the motor neurons supplying the FPL and FDP2 muscles during a precision grip task in the presence and absence of normal tactile feedback from the digit pads of the index finger and thumb. A similar strong degree of common synaptic input across the two motor nuclei was present in the precision grip task with and without normal tactile input. This suggests that tactile afferents do not have a significant influence on the extent of common synaptic input across motor pools supplying the FPL and FDP2.

Finally, little is known about the coordination of the intrinsic muscles of the hand. For instance, is the neural coupling across motor nuclei supplying different intrinsic muscles similar to that found across extrinsic muscles during a task such as the precision grip? We addressed this question in the fourth set of experiments of this dissertation. Results from this study indicate that intrinsic muscles controlling the thumb and index finger are weakly coupled together during the precision grip, implying that their respective motor nuclei receive relatively independent synaptic inputs. These findings are in agreement with the concept that the extrinsic muscles have a primary role in developing the opposing, but matching, contact forces set up between the fingertips and

objects that must satisfy the requirements of static equilibrium and, therefore, might involve greater coupled control, while the intrinsic muscles function more for precise joint positioning needed to orient the digits appropriately for grasping objects possessing an infinite variety of physical dimensions and thus might require greater independent control.

In subsequent chapters, the literature related to the neuromuscular organization of the hand is first reviewed, then the results of each of the four studies are described, and finally some general implications of this work are presented.

**CHAPTER 2: BACKGROUND AND LITERATURE REVIEW**

This chapter begins with a review of behavioral observations related to grasping behavior and independence of finger movements. This is followed by brief comments on the anatomical and biomechanical features of the hand motor system. Subsequent sections of the chapter review the organization of inputs onto motor neurons supplying hand muscles, the concept of muscle synergies within the context of strategies to simplify motor control of the hand, and the concept of motor unit synchrony with implications to hand function. The final section of this chapter will briefly summarize the research aims of this dissertation.

### **Classification of grasp**

Napier (1956) classified prehensile movements of the human hand into general categories of the power grip and the precision grip, and stated that these patterns “either separately or in combination, provide the anatomical basis for all prehensile activities, whether skilled or unskilled”. Power grip is defined as the static posture, or the dynamic movement towards “a clamp formed by the partly flexed fingers and the palm” with the thumb lying generally in the plane of the palm (Napier 1956). The precision grip, also inclusive of static and dynamic function, is such that an object is “pinched between the flexor aspects of the fingers and the opposing thumb” (Napier 1956). Landsmeer (1962) coined the term “precision handling” in reference to holding or manipulating an object between the tips of the finger(s) and thumb, noting that the main purpose of the precision grip is to “operate the object with precision by means of the fingers”. Lister (1977) further delineated hand function into eight basic categories: precision pinch, pulp pinch, key pinch, chuck grip, hook grip, span grip, power grasp, and flat hand. The key pinch,

the tip pinch, and the pulp pinch are all considered precision grips according to the classification by Napier (1956). Lister (1977) uses the term “precision pinch” only in reference to the opposition of the thumb and index finger nail tips, as lifting a pin from a flat surface. Similarly, Chao et al. (1989) define three types of precision grip between the index finger and thumb: the key pinch as the side opposition of the index finger to thumb pad, the tip pinch as the juxtaposition of the tips of the index finger and thumb such that the distal joints are flexed, and the pulp pinch as the juxtaposition of the pads of the index finger and thumb such that the distal joints are extended.

Heffner and Masterton (1975, 1983) developed an “index of dexterity” for 69 different mammals with which to correlate features of their corticospinal tracts. The index ranges from 1 for mammals with fused or restrained digits that appear specialized for locomotion, to 7 for mammals with opposable thumbs capable of precision grip in opposition to each finger and that appear specialized for manipulation. They found a positive correlation between the index of dexterity and the presence and density of the corticospinal tract projections into portions of the spinal cord innervating muscles of the forelimb. Details and implications of these findings will be discussed in a later section of this chapter.

### *Precision grip*

Because the precision grip is a motor behavior of particular focus in this dissertation, a detailed description of this type of grip is provided here. The precision grip requires complex stabilization of three joints each in the thumb and index finger and in the joints of the wrist as well. It also requires the maintenance of compression forces

and the arch-like position between the index finger and thumb (Chao et al. 1989). Furthermore, in order for the object to be securely held, the contact forces developed by the thumb on the object must precisely match and counterbalance those exerted by the index finger. Multiple muscles are recruited to accomplish this task (Smith and Bourbonnais 1981; Buys et al. 1986; Johansson and Westling 1988; Maier and Hepp-Reymond 1995a), but according to biomechanical constraints (Chao et al. 1976) and kinetic analyses (Forrest and Basmajian 1965; Close and Kidd 1969; Long et al. 1970), the extrinsic muscles seem best suited for providing continuous and stable contact forces, whereas the intrinsic muscles appear to be better situated to adjust and stabilize the position of the joints (Hepp-Reymond et al. 1996).

The contact forces and the manner by which the hand and digits are stabilized varies with the type and conformation of the precision grip (Chao et al. 1989). For example, the magnitude of contact forces are similar for the tip pinch and pulp pinch, but is nearly double for the key pinch (Chao et al. 1989), yet the relative amount of EMG activity of the intrinsic and extrinsic muscles varies across all three types of grip (Forrest and Basmajian 1965; Close and Kidd 1969; Chao et al. 1989; Valero-Cuevas et al. 2003). This leads to inconsistency in the relationships between contact forces and the intensity of individual muscle activity. Such complexity in the relationship between contact forces at the fingertip and muscle activity is particularly evident in the thumb and will be discussed later in this chapter.

### **Independence of finger movement**

Although the fingers are used together in many types of grasp, the fine dexterity of the hand is derived largely from the ability to move and control single digits relatively independently. Extension and flexion of the fingers is primarily accomplished through the activity of the multi-tendoned extrinsic muscles, each with distinct compartments that appear to operate on separate digits (Fleckenstein et al. 1992; Lieber et al. 1992; Segal et al. 2002; Keen and Fuglevand 2003; 2004b). However, the degree of individuation of finger movement is not complete, since movement of adjacent fingers occurs when attempting to move a single finger. For example, the activity of single motor-units within individual digit-compartments of FDP (Kilbreath and Gandevia 1994) and FDS (Butler et al. 2005) was recorded during voluntary isometric flexion of each of the remaining fingers. The results of these studies revealed that the recruitment thresholds of the motor units within the non-instructed digits occurred at ~2.5% (FDP) and 50% (FDS) of the maximal voluntary contraction (MVC) of the instructed digit. Similarly, from simultaneous intramuscular EMG recordings in more than one compartment of the FDP muscle during isometric flexion of individual digits, Reilly and Schieber (2003) found significant amounts of EMG activity during isolated flexion of the adjacent digit. And finally, flexion force occurred not only on the intended finger, but also on adjacent fingers in subjects instructed to flex the distal IP joint of only one finger (Reilly and Hammond 2000).

The mechanisms by which force is distributed across the multiple tendons of a muscle onto separate digits have recently been investigated and have highlighted three factors that may play a role in the incomplete individuation of finger movements (Keen

and Fuglevand 2003; Lang and Schieber 2004; 2004b; Schieber et al. 2005). First, intertendinous connections between the distal aspects of a multi-tendoned muscle may serve to transmit force across compartments, resulting in unintended movement of the adjacent finger. Secondly, muscle fibers of a single motor unit may not be confined to a single compartment, particularly if they reside near the border of the adjacent compartment, resulting in force being generated across compartments. Keen and Fuglevand (2003, 2004b), however, have shown that neither of these factors appear to play a major role in coupling finger movements together. Thirdly, the branching of descending inputs onto motor neurons supplying adjacent compartments could provide common input to motor units within both compartments resulting in motor unit activity across the compartments when intending to move only one finger. In order to better understand the mechanisms underlying grasping behavior and individuation of finger movement, it is essential to consider the anatomical, biomechanical, and neural factors influencing movement of the digits.

### **Anatomical Considerations**

There are 29 bones in the human forearm, wrist, and hand. The long bones of the forearm are the radius and ulna from which arises the origin of many of the muscles discussed below. The wrist consists of eight carpal bones arranged in two horizontal rows. The proximal row of carpals meets the distal end of the radius and ulna, and the distal row approximates the five metacarpal bones in creating the five carpometacarpal (CMC) joints. Within the hand itself the metacarpals extend distally to join the five phalanges, or digits, creating the five metacarpophalangeal (MCP) joints. Each digit

contains a proximal, middle, and distal phalanx, with the exception of the thumb, which has only a proximal and distal phalanx. Therefore, each finger has a proximal and a distal interphalangeal (IP) joint, whereas the thumb has only a single IP joint (Agur 1991; Brand and Hollister 1999).

The motors of the human hand consist of 15 extrinsic muscles residing outside the hand in the forearm with tendons inserting onto the bones of the wrist and hand. Three of these extrinsic muscles are multi-tendoned muscles that each produces four tendons, one to each of the four fingers; four are single-tendoned muscles that insert onto individual digits; and six insert onto bones of the wrist and hand that act to position the hand by altering the wrist posture. In addition to these are 19 intrinsic muscles that reside within the hand itself (Agur 1991; Platzer 1992). Together these muscles insert onto the bones of the wrist, hand, and forearm, creating a complex anatomical and biomechanical system. In this dissertation, the term *digit* refers to the thumb and fingers, with digit 1 (D1) indicating the thumb, then *fingers* only refer to the index (D2), middle (D3), ring (D4), and little (D5) digits.

### *Extrinsic muscles*

#### *Multi-tendoned extrinsic muscles to the finger*

The two extrinsic finger flexors, flexor digitorum profundus (FDP) and flexor digitorum superficialis (FDS), have an unusual tendinous arrangement with the four tendons of the FDS each inserting onto the palmar aspects of the middle phalanges of digits 2-5 with bifurcating tendons, creating tunnels through which each of the four FDP tendons travel distally to insert onto the palmar aspects of the distal phalanges of digits 2-

5 (Walbeehm and McGrouther 1995). Both extrinsic flexors originate from the anterior aspects of the radius and ulna in the forearm, thus pass across all the joints of the wrist and fingers between origin and insertion and exert at least some degree of influence at each joint. However, the primary action of the FDP is flexion of the distal interphalangeal (IP) joints and assisting the primary action of FDS in flexion at the proximal IP joints (Brand and Hollister 1999).

The FDS anatomy is unique when compared to the other multi-tendoned muscles of the hand, having a more complex arrangement of the muscular compartments and greater variation and anomalies across subjects (Wood Jones 1941; Ohtani 1979; Brand and Hollister 1999). For instance, the deep layer of the muscle consists of a humeroulnar head with a single proximal belly that gives rise to an intermediate tendon that then divides into two muscle bellies each giving rise to the tendons of the index and little fingers, respectively. The superficial layer has both a radial and humeroulnar head and is composed of two bellies that each gives rise to the tendons of the middle and ring fingers, respectively. Of all the muscle components, the middle finger component is the most discrete. Although the index and little finger components each have their own muscle bellies arising from the intermediate tendon, the common proximal belly connects this tendon to its origin. The ring finger component also has its own muscle belly, but often has accessory muscle slips from the proximal common muscle belly, from the intermediate tendon, or from the little finger component.

In addition to the complex arrangement of the muscular compartments of the FDS, there are a number of anomalies noted specifically of the FDS tendon to the little finger,

including absence of the tendon, doubling of the tendon, and attachments to other tendons of the FDS or FDP (Furnas 1965; Kaplan 1969; Gonzalez et al. 1997). An absent FDS tendon to the little finger would preclude the ability to volitionally flex the proximal IP joint in isolation, leaving flexion of this joint to occur only in conjunction with flexion of the distal IP joint by the action of the FDP.

The third multi-tendoned extrinsic muscle, the extensor digitorum (ED), is situated in the posterior compartment of the forearm and originates from the lateral aspect of the distal humerus and from the posterior surface of the proximal radius. Its distal tendons pass dorsal to the wrist and finger joints, thus acting as the primary extensor of the fingers and assisting in wrist extension. As with the other multi-tendoned muscles, ED has four tendons arising from the muscle, that each insert onto digits 2-5, but on the dorsal aspect of the phalanges.

#### *Single-tendoned muscles to the fingers*

The extensor indicis (EI) is situated in the posterior compartment of the forearm and arises from the distal third of the ulna. It inserts, together with one of the tendons of ED, onto the dorsal aspect of the index finger and acts to extend the index finger in isolation. The extensor digiti minimi (EDM), also located in the posterior compartment of the forearm, arises together with the ED, extensor carpi radialis brevis (ECRB), and extensor carpi ulnaris (ECU) from the common extensor tendon from the lateral epicondyle of the humerus. It inserts together with the ED onto the dorsal aspect of the little finger and acts in isolated extension of the little finger (Agur 1991; Platzer 1992).

#### *Single-tendoned extrinsic muscles of the thumb*

Of all the digits of the human hand, the thumb demonstrates the greatest independence of movement (Hager-Ross and Schieber 2000). The four extrinsic muscles of the thumb act to flex, extend, and abduct (move away from the plane of the hand) the thumb in addition to exerting secondary actions at the wrist. The flexor pollicis longus (FPL) originates from the anterior aspect of the radius. Distally the FPL inserts onto the distal phalanx of the thumb and thus acts to flex the distal joint of the thumb as well as the two most proximal joints of the thumb and the wrist. The other three extrinsic thumb muscles all originate on the dorsal aspect of the forearm. The abductor pollicis longus (APL) inserts onto the first metacarpal and one of the carpal bones of the wrist, acts to abduct and extend the thumb at its base, and generates some abduction and flexion at the wrist. The extensor pollicis brevis (EPB) has similar actions as the APL at the wrist and the base of the thumb, but inserts onto the proximal phalanx of the thumb, thus it acts as primary extensor of the MCP joint. The extensor pollicis longus (EPL) inserts onto the distal phalanx of the thumb and thus serves to extend the distal joint of the thumb as well as both proximal joints and extends and abducts the wrist (Agur 1991; Brand and Hollister 1999).

#### *Wrist muscles*

In addition to the torques produced at the wrist from the actions of extrinsic finger and thumb muscles, more isolated movements at the wrist are generated by wrist muscles (Agur 1991). These include the extensor carpi radialis longus and brevis (ECRL/B) and extensor carpi ulnaris (ECU) located on the dorsum of the forearm that both extend the wrist and, respectively, abduct (radially deviate) and adduct (ulnarly deviate) the wrist.

Located on the anterior aspect of the forearm is the flexor carpi radialis (FCR) that flexes and abducts the wrist, and flexor carpi ulnaris (FCU) that flexes and adducts the wrist. An additional anterior forearm wrist flexor is the palmaris longus (PL) inserting onto the palmar aponeurosis at the base of the hand. The primary wrist extensors and flexors originate from common tendons at the lateral and medial epicondyles of the humerus, respectively, thus generating torques about the elbow in addition to the torques acting on the wrist (Agur 1991; Platzer 1992). Not all the muscles residing in the forearm have been noted here, rather only the muscles that cross the wrist and thus act upon the hand have been reviewed.

#### *Intrinsic muscles*

Intrinsic muscles of the hand are generally divided into three categories by anatomical location; the interosseous and lumbrical muscles of the four fingers, the hypothenar muscles to the little finger, and the thenar musculature of the thumb.

#### *Intrinsic finger muscles*

The intrinsic muscles to the four fingers consist of seven interossei and four lumbrical muscles. The four lumbricals are unique in that, rather than originating from a bony surface, they each arise from the radial sides of the four FDP tendons within the palm of the hand and insert onto the dorsal aponeurosis of each finger (Brand and Hollister 1999; von Schroeder and Botte 2001). The action of the lumbricals cause flexion of the MCP joints and extension of the IP joints when the FDP tendons (the origin of the lumbricals) are taut.

The seven interosseous muscles originate between the metacarpal bones and insert onto the ulnar (medial) or radial (lateral) aspect of digits 2-5 such that the four dorsal interossei act to spread the fingers apart (abduct) and the three palmar interossei bring them together (adduct) in the plane of the palm (Agur 1991). The first dorsal interosseous (FDI) is of particular importance in the precision grip and is discussed in additional detail. Like other dorsal interossei, the FDI is bipennate with the superficial and larger head arising from the ulnar (medial) side of the first metacarpal of the thumb, and the deep, smaller head arising from the radial (lateral) and palmar sides of the second metacarpal of the index finger. The FDI inserts onto the lateral tubercle at the base of the proximal phalanx of the index finger (Masquelet et al. 1986; Chao et al. 1989). Therefore, activity of FDI not only elicits abduction of the index finger at the MCP joint, but also causes flexion of the MCP joint, particularly when the deep head of the FDI, which lies anterior to the axis of MCP joint, is active (Masquelet et al. 1986; Chao et al. 1989).

The three hypothenar muscles include the abductor digiti minimi, the flexor digiti minimi brevis, and the opponens digiti minimi, and when active they abduct, flex and bring the little finger into the posture of thumb-opposition, respectively. The latter two muscles also assist in cupping the palm, as they arise from the ulnar aspect of the thick, fibrous flexor retinaculum that spans the two rows of carpal bones on the palmar side of the wrist.

#### *Intrinsic thumb muscles*

The four thenar muscles are the flexor pollicis brevis (FPB), the opponens pollicis (OP), the abductor pollicis brevis (AbPB), and the adductor pollicis (AdP). All four

thenar muscles have fibers that arise from the radial aspect of the flexor retinaculum and the underlying lateral carpal bones. In addition, the AdP arises more distally from the second, third and fourth metacarpals (Platzer 1992; Witthaut and Leclercq 1998). The thenar muscles insert at different sites near the base of the thumb close to the MCP joint, or on the radial aspect of the first metacarpal (in the case of the OP). Collectively the thenar muscles generate movements of the thumb into adduction, flexion, and abduction, as occurs with different types of grasping against the palm or fingers.

However, each thenar muscle is involved in movement of the thumb in more than one cardinal anatomical plane. Furthermore, movement of the thumb along any direction is usually accomplished through simultaneous, yet differential, activity of multiple muscles (Kaufman et al. 1999; Pearlman et al. 2004). For example, adduction of the thumb towards the palm is elicited primarily by activity of the AdP and secondarily by actions of the FPB and OP. Abduction of the thumb is achieved by activity of the AbPB and partly by FPB. Opposition and flexion of the thumb towards the little finger is accomplished mainly by activity of the OP assisted by FPB and the AdP. And finally, extension of the thumb towards the back of the hand is accomplished mainly by activity of the extrinsic muscles reviewed earlier; the EPL/B, and the APL (Platzer 1992).

One reason underlying the complex, multi-directional movements of individual thenar muscles is the multiple orientations of fibers within a single muscle. For example, the transverse fibers of the AdP are fan-shaped in orientation, arising from the palmar aspect of the second and third metacarpals, whereas the oblique fibers arise from the base of the second, third, and fourth metacarpal bones and the deep palmar ligaments covering

the distal row of carpal bones of the wrist (Mardel and Underwood 1991; Platzer 1992; Witthaut and Leclercq 1998). The two heads converge to insert via the ulnar sesamoid bone of the MCP joint onto the base of the proximal phalanx of the thumb. Therefore, the line of force generated by the muscle can vary significantly depending upon which fibers are activated (Brand and Hollister 1999).

### **Biomechanical considerations**

#### *Multi-joint systems of the index finger and thumb*

From a biomechanical perspective, the human hand can be regarded as a complex linkage system of bony segments intercalated with intricately-articulated joints across which ligaments, tendons and muscles span (Chao et al. 1989; Giurintano et al. 1995). In general, the thumb and index finger can each be modeled as 4-segment and 3-joint linkage systems (Chao et al. 1989; Brand and Hollister 1999). The two most distal joints of each finger have essentially single axes of rotation (oblique-oriented flexion-extension axis), and the proximal joint (MCP) has two axes, none of which are perpendicular to the bones or to one another, which creates conjunct rotations and allows the two-axis joint to move in all three anatomic planes (Napier 1955; Chao et al. 1989; Giurintano et al. 1995; Brand and Hollister 1999). In the thumb, the distal joint has one flexion-extension axis, and the MCP and CMC joints each have flexion-extension and abduction-adduction axes that are offset from the cardinal anatomical planes. The fact that the three digital joints are arranged in series and that the action of a single muscle tendon that crosses a two-axis joint will have an effect on both axes, contributes to the complexity of digit and hand positioning (Chao et al. 1989; Giurintano et al. 1995; Brand and Hollister 1999).

### *The fingers*

The finger has been described as a polyarticular system composed of two biarticular systems spanned by the extensor tendon of the ED and the two flexor tendons of the FDP and FDS (Landsmeer, 1962, 1963). One biarticular system, in which the joints move in coordination, consists of the distal and proximal IP joints with the intercalated middle phalanx. The other biarticular system, in which the joints can be moved independently, consists of the proximal IP and MCP joints with the intercalated proximal phalanx. Prevention of the “zigzagging tendency” that is inherent in such a mechanical system acted upon only by two distally-attached muscles is achieved by the addition of muscles having attachments onto more proximal segments of the system (Landsmeer, 1962, 1963), for example, by FDS, the interossei, and the lumbricals. Within this two-biarticular system are tightly coupled relationships of joint positions as well as highly correlated muscle activity (Darling et al. 1994). For example, Darling et al. (1994) found that in isolated finger movements, the two IP joints were coordinated to act as a unit while the MCP joint could be controlled independently of the distal joints. The relationship for positions between the two IP joints were linear, as were the positions between the MCP and proximal IP joints, but the latter had more variability and greater proximal IP to MCP joint movement ratios. In addition, the activities of FDS and FDP were highly correlated during finger flexion involving both IP joints.

The relationships between the tendon tension of the extrinsic flexor muscles and the output force at the tip of the finger has been investigated during various finger positions in cadaveric studies (Valero-Cuevas et al. 2000), and during various static and

dynamic finger tasks in vivo (Schuind et al. 1992; Dennerlein 2005; Kursa et al. 2005). The contribution to tip force was found to be greater for FDP than for FDS, except when the wrist was held in a highly flexed posture (Kursa et al. 2005). For both muscles, the output force on the fingertip was linearly related to tendon tension (Valero-Cuevas et al. 2000; Dennerlein 2005).

### *The thumb*

Thumb motion can be thought of as occurring around the surface of an inverted cone, the base of which is delineated by the thumb tip and the apex of which is near the CMC joint at the base of the thumb. The thumb pad faces the axis of the cone as the thumb circumducts into positions of opposition to the fingers for grasping, accomplished through rotation (pronation), flexion and abduction-adduction of the CMC and MCP joints (Napier 1956; Chao et al. 1989; Kaufman et al. 1999).

Several biomechanical models of the thumb have been developed (Cooney and Chao 1977; An et al. 1979; Giurintano et al. 1995; Valero-Cuevas et al. 2003), but all are limited in their accuracy in predicting even a simple static force output at the thumb tip due to the complexity of thumb mechanics (Valero-Cuevas et al. 2003). For example, a recent study by Pearlman et al. (2004) explored the relationship of thumb-tip force vectors and the eight muscles (4 intrinsic, 4 extrinsic) of the thumb, and found that thumb-tip force did not scale linearly with tendon tension. They suggest that the carpal bone at the base of the thumb and part of the CMC joint, the trapezium, does not create a rigid base, rather it moves slightly in a load-dependent manner, thus affecting joint seating and causing the thumb to act as a “floating digit”. Indeed, Valero-Cuevas et al.

(2003) suggest that all currently available mechanical descriptions of the thumb are over-idealized and that more elaborate descriptions are required to capture the complexity of articulations.

In summary, the muscular and skeletal machinery of the hand can be characterized as a highly complex biomechanical system. The following section addresses some of what is known about how the nervous system controls this remarkable apparatus.

### **Inputs to motor neurons supplying the muscles of the hand**

Voluntary movement of the hand is mediated by descending commands that operate on complex spinal circuitry. The organization of the descending pathways and spinal neural circuitry has been investigated over the last 150 years resulting in some understanding of the basic elements and principles of their inter-connectivity within the spinal cord (Baldissera et al. 1981). Inputs onto spinal motor nuclei arise from a variety of sources, including supraspinal descending pathways, spinal interneurons, and peripheral afferents. The major descending inputs that have been shown to influence spinal interneurons and motor neurons evoking limb movement include the corticospinal, rubrospinal, reticulospinal, and vestibulospinal pathways (Baldissera et al. 1981; Kuypers 1981). Lawrence and Kuypers (1968a, b) divided these into two functional categories: a lateral descending system consisting of the cortico- and rubrospinal tracts that primarily influence motor neurons supplying distal muscles, and a medial descending system consisting of the reticulo- and vestibulospinal tracts that primarily influence motor neurons supplying the axial and proximal muscles. Therefore, the medial pathways are

not likely to be prominently involved in voluntary control of the hand (Nyberg-Hansen and Mascitti 1964; Nyberg-Hansen 1965; Peterson et al. 1979). Because the lateral descending pathways have been shown to connect to interneurons and motor neurons supplying distal musculature (Houk et al. 1988; Porter and Lemon 1993), they are briefly reviewed here.

### *Supraspinal inputs*

The control of skilled distal limb and hand movements is mediated primarily by the corticospinal and rubrospinal systems (Lawrence and Kuypers 1968a; Lawrence and Kuypers 1968b; Ghez 1975). Both systems in the primate terminate in similar patterns and onto similar areas, including directly onto motor neurons supplying distal muscles of the forelimb in the dorsolateral portion of the anterior horn in the gray matter of the cervical spinal cord of the monkey (Baldissera et al. 1981; Kuypers 1981). Therefore, a review of anatomical, lesion, and electrophysiological studies of the corticospinal and rubrospinal systems is presented.

Evolutionarily, the corticospinal tract has increased in relative size and changed location within the white matter of the spinal cord (Schoen 1964; Phillips and Porter 1977) such that in the human it consists of over one million fibers originating from multiple cortical sites (Nolte 1999). Most of the primate corticospinal fibers cross at the medulla and descend in the lateral funiculus, whereas roughly 15% of the descending fibers remain uncrossed and descend in the anteromedial funiculus of the spinal cord (Kandel et al. 2000; Altman and Bayer 2001). The rubrospinal tract also travels in the lateral funiculus along the entire length of the spinal cord in the goat, cat, and monkey (Kuypers

et al. 1962; Nyberg-Hansen and Brodal 1964; Schoen 1964). While the rubrospinal tract is well developed in ungulates and carnivores, it is poorly developed in humans and is thought to have been 'replaced' by the much larger corticospinal tract (Schoen 1964; Nathan and Smith 1982).

The terminal projections of the corticospinal tract have been extensively studied by Kuypers (1981) who categorized mammals into four groups based on the terminal distribution of corticospinal fibers, by the extent of penetration down the cord, and by depth of penetration within the laminae of the spinal gray matter. For instance, group one includes animals, such as the goat and rabbit, in which the cortical fibers reach only the cervical and thoracic cord, and terminate exclusively in the dorsal part of the dorsal and intermediate zones (lamina IV and medial parts of laminae V and VI) which mainly contain sensory neurons projecting to supraspinal levels and short propriospinal neurons. Group two consists of animals such as the rat, cat, and dog, in which cortical fibers reach the entire length of the cord and penetrate slightly more ventral to terminate onto laminae V, VI, and VII of the intermediate zone. Group three mammals, such as the raccoon and rhesus monkey, have dense corticospinal terminations throughout the intermediate zone, including lamina VIII in which lie the long propriospinal neurons and motor neurons of distal extremity muscles. Finally, group four mammals, such as the chimpanzee and human, have corticospinal terminations into the same areas, but in greater abundance. Thus, compared to other mammals, higher primates have a greater number of direct corticomotoneuronal connections, not only onto neurons supplying hand and finger muscles, but also to neurons supplying more proximal arm musculature. The term

“propriospinal neuron” refers to an intrinsic spinal cord neuron, the axon of which terminates in remote segments of the cord, whereas neurons intercalated in reflex pathways of limb segments are referred to as “interneurons” (Baldissera et al. 1981) and will be discussed in greater detail in a later section.

In the monkey, the distribution of rubrospinal fibers parallels that of the corticospinal tract in location and pattern, although quantitatively fewer in fiber number by at least 100 times (Larsen and Yumiya 1980; Kuypers 1981). Rubrospinal fibers descend the entire length of the spinal cord and project not only to the intermediate zone, but also to motor neurons (Holstege et al. 1988; Ralston et al. 1988). The densest distribution of rubrospinal fibers to motoneuronal cell groups is found among those innervating the musculature of the forelimb digits (Holstege et al. 1988).

Associated with the number of corticospinal fibers that directly contact motor neurons, is the variation in digital dexterity and performance of skilled movements (Heffner and Masterton 1975). For example, the cebus monkey, who is able to pick up small objects using a precision-type grip, has substantial corticomotoneuronal projections in the ventral horn of the spinal cord where motor nuclei to distal hand muscles reside (Bortoff and Strick 1993). By comparison, the squirrel monkey, who must pick up small objects using a swiping motion of all fingers together as in a power-type grip, has sparse corticomotoneuronal connections in the same spinal area. Although this evidence is merely correlative, it supports findings of electrophysiological and lesion studies suggesting that corticomotoneuronal connections are necessary for the performance of dexterous tasks.

The importance of direct descending connections, particularly the corticospinal connections, to motor neurons for the control of distal muscles has also been demonstrated in primates in early lesion studies by Lawrence and Kuypers (1968a; 1968b). Arm and hand movement impairment was most severe after a complete bilateral lesion of the pyramidal tract. However, several weeks postlesion, monkeys recovered to essentially normal movement with the exception of the inability to retrieve a small food pellet from the smallest well, seemingly as a result of the permanent inability to use their fingers independently. In contrast, monkeys in whom the rubrospinal tract was lesioned demonstrated weakness and slowed movement of the affected hand that completely resolved within a week. However, pyramidotomized monkeys in whom the rubrospinal tract was subsequently lesioned demonstrated lasting deficits in independent distal extremity and hand movements, as well as an inability to flex the extended arm. Yet the same limb was only minimally impaired in movements involving the trunk and limb together, such as climbing. With recovery, these animals regained the ability to close the hand only as a part of a total arm movement, never as an isolated movement. Lawrence and Kuypers (1968a,b) concluded that the rubrospinal pathway mediates independent distal limb movement, particularly the hand, and that the corticospinal pathway not only superimposes speed and agility of movement, but also confers the ability for the high degree of fractionation of movements, that is exemplified by independence of finger movement.

Evidence from electrophysiological studies also suggests there are direct connections onto motoneurons from the corticospinal (Preston and Whitlock 1961; Fetz

and Cheney 1980; Buys et al. 1986; Lemon et al. 1986; Porter and Lemon 1993) and rubrospinal tracts (Shapovalov et al. 1971; Mewes and Cheney 1991; Belhaj-Saif et al. 1998; Belhaj-Saif and Cheney 2000). Early studies investigating the corticospinal connections onto motor neurons in the spinal cord used intracellular recordings of post-synaptic potentials in spinal motor neurons in response to weak stimulation of the motor cortex (Baldissera et al. 1981; Kuypers 1981). Results from experiments in monkeys demonstrated there were excitatory post-synaptic potentials (EPSP's) with latencies consistent with monosynaptic corticomotoneuronal connections (Preston and Whitlock 1961). Inhibitory post-synaptic potentials (IPSP's), however, were shown to involve disynaptic pathways via inhibitory interneurons (Jankowska et al. 1975).

Another electrophysiological technique used to explore mono- and disynaptic spinal connections from the cortex is by spike-triggered averaging of EMG activity from distal limb muscles during specific tasks (Fetz and Cheney 1980; Kuypers 1981; Cheney and Fetz 1985; Kasser and Cheney 1985). Recordings of single cortical cell discharge spikes are used as a trigger from which to average short segments of recorded muscle EMG. The EPSP's produced in spinal motor neurons by the cortical neuron will increase the likelihood of the motoneurons firing and manifest as a rise in the averaged muscle EMG at an appropriate latency, referred to as post-spike facilitation. Conversely, post-spike suppression is seen as a dip in the averaged muscle EMG, indicating the suppressive effect on motor neurons by IPSP's from inhibitory interneurons activated by the descending cortical discharge. The brief latency of post-spike facilitation supports

the existence of direct corticomotoneuronal (Fetz and Cheney 1980; Lemon et al. 1986) and rubromotoneuronal (Cheney and Fetz 1980; Mewes and Cheney 1991) connections.

Furthermore, it has been demonstrated using spike-triggered averaging in monkeys that a single cortical neuron (Buys et al. 1986; Lemon et al. 1986), or a single rubral neuron (Cheney et al. 1988; Mewes and Cheney 1991) can facilitate more than one muscle controlling the hand and wrist. These findings suggest the divergence of descending axons onto motor neurons innervating synergistic muscles. Supporting the electrophysiological findings are two anatomical studies of Shinoda and colleagues. They demonstrated extensive terminal ramification of a single corticospinal axon (Shinoda et al. 1981), and to a lesser extent in a rubrospinal axon (Shinoda et al. 1977), both within and across different motor nuclei supplying muscles of the hand and fingers in the monkey.

Difference in the properties of corticomotoneuronal and rubromotoneuronal cells emphasizes functional specialization. For instance, the facilitatory effect on motor neurons by rubromotoneuronal cells is much weaker in magnitude than that produced by corticomotoneuronal cells. Furthermore, rubromotoneuronal cells have stronger preference for facilitation of extensor than flexor muscles of the over the entire upper limb than do corticomotoneuronal cells, and more rubromotoneuronal cells demonstrate cofacilitation of agonist-antagonist muscles at the wrist and elbow than corticomotoneuronal cells (Mewes and Cheney 1991; Belhaj-Saif et al. 1998). Therefore, corticomotoneuronal pathways appear to be critical in mediating control of the hand and fingers for independent and highly fractionated finger movements, whereas the

rubromotorneuronal pathways might be more important for coordination of the fingers, hand, and arm as a whole during reach-and-grasp tasks.

### *Interneuronal inputs*

In general, of the thousands of inputs onto a typical motor neuron, only a fraction is from direct descending connections. However, large differences across motor neurons supplying different muscles might occur. For example, the majority of inputs to hand motor neurons might be from descending pathways (Porter and Lemon 1993).

Nevertheless, the majority of the inputs onto most spinal motor neurons arise from interneurons within the cord (Jankowska and Lundberg 1981). Interneurons are not merely relay stations of information, but perform important integrative functions (Jankowska and Lundberg 1981). Such premotoneuronal networks can function to selectively integrate information from numerous sources that may be important to achieve precise timing and balance of activity within and across motor neuron pools. This information comes, not only from descending pathways, but also ascending and descending propriospinal pathways, local segmental interneurons, and sensory afferents from the periphery. Some of the proposed benefits from this type of organization include the flexibility of control and the possibility of rapidly updating central descending commands for movement by unexpected changes in peripheral input (Baldissera et al. 1981; Jankowska 2001).

### *Segmental interneurons*

Among the interneurons providing synaptic input onto motor neurons supplying the forelimb are segmental interneurons mediating reflex pathways. Although early

electrophysiological experiments demonstrated that most spinal reflex actions are mediated by local interneurons (Brooks and Eccles 1947b). These same interneurons, receive extensive convergence from several descending pathways and other primary afferents (Baldissera et al. 1981; Jankowska and Lundberg 1981). Consequently, these pre-motoneuronal interneurons function to integrate information from multiple sources and are not exclusively involved in simple reflex behaviors.

#### *Propriospinal interneurons*

Another interneuronal system supplying inputs onto forelimb motor neurons is a system of propriospinal neurons located in the cervical spinal segments of C3-C4, the existence and role of which in humans has been the subject of vigorous debate (Burke 2001; Pierrot-Deseilligny 2002; Lemon and Griffiths 2005). The structure and function of the C3-C4 propriospinal system of the cat, in which there are no monosynaptic corticomotoneuronal projections (Illert et al. 1976), has been extensively investigated through behavioral experiments of target reaching and food retrieval, and described by Lundberg and his group (Baldissera et al. 1981; Alstermark and Lundberg 1992; Lundberg 1999). Findings from experiments in which the rubro- and corticospinal tracts, or the propriospinal system, or both were lesioned, demonstrate that the C3-C4 propriospinal system appears to mediate the multi-jointed forelimb movements in target-reaching, while control of the distal paw musculature involved in food-taking is mediated through cortico- and rubrospinal pathways projections to segmental interneurons (Sasaki et al. 1996; Lundberg 1999).

In the human and the macaque monkey, however, the evidence of a functional propriospinal system is scant, yet strongly debated (Pierrot-Deseilligny 2002; Lemon and Griffiths 2005). Findings from experiments in the cat, and in squirrel and macaque monkeys indicate that the propriospinal system becomes progressively weaker and the corticospinal connection increases in strength from lower to higher mammals (Alstermark and Lundberg 1992; Maier et al. 1998; Nakajima et al. 2000). These structural differences across species coincide with the variations in dexterity described earlier.

One conclusion that can be drawn from these studies is that the C3-C4 propriospinal system is unlikely to be responsible for significant transmission of cortical commands to upper limb motor neurons in humans and primates with dexterous hand function and strong corticomotoneuronal connections (Lemon and Griffiths 2005). An alternative conclusion is that the C3-C4 propriospinal system with its feedforward and feedback inhibitory mechanisms in humans functions to more accurately focus the descending commands for highly dexterous movements, as compared to the cat (Pierrot-Deseilligny 2002).

#### *Peripheral inputs*

While descending and interneuronal pathways influence the motor neurons supplying muscles of the hand, afferent information from muscle and cutaneous receptors also exerts influence on hand motor neurons.

#### *Muscle afferents*

Muscle spindle primary Ia afferents, relaying information about muscle length and rate of length change, contact virtually all motor neurons in the homonymous motor

nucleus and many motor neurons of synergistic muscles (Clough et al. 1968; Henneman and Mendell 1981).

### *Tactile afferents*

Tactile feedback is particularly crucial in the prehensile functions of the hand, as anesthesia of the thumb and finger tips causes marked impairment in manipulation tasks (Johansson et al. 1992; Monzee et al. 2003). Tactile information is mediated by four types of encapsulated mechanoreceptors in the skin, each giving rise to afferent fibers that, like the muscle afferents, ascend to the somatosensory cortex via the dorsal column-medial lemniscal pathway (Kandel et al. 2000). Two of the four afferents are slowly adapting, the slowly adapting type 1 (SA I) and slowly adapting type 2 (SA II), and each produce a sustained discharge in response to sustained skin deformation. The other two, the rapidly adapting type 1 (RA I) and Pacinian/rapidly adapting type 2 (RA II), respond only during the dynamic phase of skin deformation (Johnson et al. 2000; Kandel et al. 2000). Each receptor type transmits different aspects of tactile perception, such that the SA I fibers are activated by pressure and transmit information regarding the form and texture of the object touched, the SA II fibers are activated by skin stretch and mediate information used in the formation of hand postures and forces acting upon the hand, the RA I fibers are activated by stroking the skin and carries information of skin motion and is important in grip control to prevent the object from slipping, and the RA II fibers mediate vibration information (Chapman et al. 1996; Johnson et al. 2000; Kandel et al. 2000). Although principle central branches of the tactile afferent axons ascend the spinal cord in the ipsilateral dorsal column, secondary branches terminate in the dorsal horn of

the spinal segment in which it enters, affecting motor neurons via interneurons (Macefield et al. 1990; McNulty et al. 1999). For example, electrical stimulation of the digital nerves that possess only cutaneous afferents, elicits a cutaneomuscular reflex, recorded as a triphasic modulation of ongoing muscular activity during a steady voluntary contraction of the muscle (Caccia et al. 1973; Datta and Stephens 1981; Jenner and Stephens 1982; Evans et al. 1989). Brief latencies of the first excitatory and inhibitory components indicates that they are spinally mediated, whereas the longer latency component implies a transcortical or supraspinal loop (Rosen and Asanuma 1972; Datta and Stephens 1981). Furthermore, studies in a patient with damage to the motor cortex demonstrated an exaggerated initial excitatory component and loss of the long-latency components (Jenner and Stephens 1982). Tactile information, therefore, influences the activity of motor neurons supplying hand and finger muscles from both spinal and supraspinal levels.

The significant role of tactile input in motor control has been shown, not only in cutaneomuscular reflexes of the upper limbs, but also in the modulation of evoked grip responses (Johansson et al. 1992). Johansson et al. (1992) found that digital anesthesia during control of precision grip to unpredictable load changes led to significant impairment of normal grip force modulation during the initial aspect of the loading phase of precision grip. Likewise, in experiments in which the digits were cooled to produce anesthesia of the fingers that gripped an object while subjects repetitively moved the same arm and hand, Nowak and Hermsdorfer (2003) found digit cooling caused impairment in the scaling of the grip to load force ratio. Together these findings suggest

tactile afferent information might play a significant role in modulation of spinal motor output and the organization of common synaptic input to motor neuron pools.

Furthermore, tactile information projecting via supraspinal pathways could be influenced by other sensorimotor information generated or integrated through supraspinal, including cortical, mechanisms.

There is strong anatomical and physiological evidence in the non-human primate that there is direct tactile afferent information (via the thalamus) to primary motor cortex organized in “input-output columns”, whereby an area of motor cortex responds to an afferent receptive field that overlies its efferent zone, or “muscle field” (Rosen and Asanuma 1972; Asanuma et al. 1974; Murphy et al. 1978; Wong et al. 1978; Asanuma et al. 1980). Furthermore, ablation of the sensory cortex did not significantly alter the activity of receptive field neurons in the motor cortex. It is clear ascending tactile information is available to motor cortex neurons which presumably might be used in generating motor commands through direct corticospinal projections onto motor nuclei of the underlying muscles. Indeed, Shinoda et al. (1981), Cheney and Fetz (1980), and Lemon et al. (1986) demonstrated that corticospinal axons in non-human primates not only project monosynaptically onto the motor nucleus of a given muscle, but also diverge to supply more than one motor nucleus.

### **Muscle synergies**

Inputs to motor neurons supplying the arm and hand from cortical and other supraspinal areas, from within the spinal cord, and from the periphery all influence the activity of muscles controlling hand dexterity. The interactions of these influences and

the mechanisms involved in the coordinated control of muscles used for skilled hand and finger movements, however, are still largely unknown. One mechanism might be to control groups of muscles together that are used in a particular task. In considering such a control strategy, the question arises as to whether the central nervous system is organized for the control of individual muscles, or for the control of groups of muscles that are used together in performing a task. The control of individual muscles would allow flexibility in muscle selection depending on the task and the environment, but would require the management of multiple parameters by the central nervous system (Macpherson 1991; Hepp-Reymond et al. 1996). Conversely, the control of sets of muscles whose activity is obligatorily linked together, while less flexible, would reduce the number of parameters needed to be managed by the nervous system (Macpherson 1991; Hepp-Reymond et al. 1996).

The term “muscle synergy”, as used in this dissertation, refers to muscles acting together in the production of a motor task, without the presumption of the source of their coupled activity. One possible source of this coordinated muscle activity could arise from divergent descending pathways that simultaneously serve to engage different motor nuclei innervating synergistic muscles. The extent of such divergence across motor nuclei can be estimated by measuring the degree of synchrony in the discharge of motor units located in different muscles (Bremner et al. 1991b; Maier and Hepp-Reymond 1995b; Winges and Santello 2004; Hockensmith et al. 2005), as described briefly in the next section.

### **Motor unit synchrony**

Direct assessment of the distribution of synaptic input to motor neurons is not possible in humans, but can be estimated using cross-correlation analysis of the discharge times between pairs of motor units (Kirkwood and Sears 1978). The concept underlying cross-correlation analysis is that if presynaptic fibers diverge to provide common excitatory input to two neurons, then this should elicit near simultaneous excitatory postsynaptic potentials in the two neurons and thus slightly increase the probability that the two neurons will be brought to firing threshold simultaneously (Perkel et al. 1967; Kirkwood and Sears 1978). Neurons receiving common excitatory input, therefore, should discharge near-simultaneously slightly more often than would be expected due to chance. Such a statistical coincidence in their discharge can be seen as a peak around time zero in the cross-correlation histogram (cross-correlogram), and is referred to as short-term synchrony. The magnitude of this peak represents the proportion of common to non-common synaptic inputs impinging upon the two neurons (Kirkwood and Sears 1978).

The implication of significant motor unit synchrony across muscles, or across different compartments of a multi-tendoned muscle, is that the motor neuron pools supplying the muscles/compartments receive substantial common synaptic input to facilitate cooperative or synergistic muscle/compartment activity (Santello and Fuglevand 2004). The divergent synaptic input, therefore, might be one source for coordinating muscles used synergistically for voluntary tasks of the hand and fingers.

### **Summary**

Control of the muscles of the human hand and fingers involves the integration of information from supraspinal, intraspinal, and peripheral afferent pathways, in order to manage the anatomical and biomechanical complexity of the hand. One strategy the nervous system might employ to accomplish this complex control is by the grouping of muscles through descending divergent inputs across the associated motor nuclei, an estimate of which can be made using measures of motor unit synchrony.

### **Specific research aims**

The main goal of this work is to identify some of the neural mechanisms whereby hand muscles are recruited into functional groups needed for the generation of hand and finger movements. Since nearly all natural movements involve more than one muscle, the specific aims are designed to identify control strategies and how various muscles and muscle compartments are functionally grouped during simple isometric tasks involving the fingers and thumb.

As mentioned previously, the FDS is one of two primary finger-flexor muscles with four tendons to the four fingers. There are currently no published studies on the organization of the synaptic inputs to motor neurons innervating compartments of the FDS muscle. Therefore, the first aim of this dissertation was designed to fill this gap.

Flexion of an individual finger is accomplished by the action of both primary finger flexors, the FDS and FDP. The tight coordination of these two muscles might involve substantial common synaptic input across their motor nuclei to facilitate effective finger flexion. Thus, the second aim of this study was to determine whether the activities

of FDS and FDP are coupled together during finger flexion by divergent synaptic input to their respective motor nuclei.

The contact forces exerted by the thumb and index finger must be exactly matched during precision gripping. This matching appears to be enabled by the presence of divergent inputs across the motor nuclei involved in this task (Hockensmith et al. 2005). Therefore, the third specific aim was to determine whether such divergent input depends upon activity arising from tactile afferents originating from the pads of the index finger and thumb.

And finally, the control of precision grip forces not only involves extrinsic muscles, but also requires the control of intrinsic muscles. The neural coupling of intrinsic muscles during a precision grip is unknown. The fourth specific aim of this dissertation, therefore, was to determine if the organization of synaptic inputs to intrinsic muscles of the index finger and thumb were similar to that found for the extrinsic muscles during the precision grip.

**CHAPTER 3: GENERAL METHODS**

The following materials and methods apply to all experiments of this dissertation, unless otherwise noted in chapters 4-7.

#### *Subjects and experimental setup*

All experiments were carried out on healthy, adult human volunteers. All 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. Subjects were seated comfortably in a dental chair with their forearm resting supported on an adjustable platform.

#### *Force and electromyographic recordings*

Flexion force of the digits was measured by four force transducers (Grass Instruments, Warwick, Rhode Island, model FT-10, range 0-5 N, sensitivity 780 mN/mV) mounted in a custom-built manipulandum. The force signals were amplified (x1000, World Precision Instruments, Sarasota, Florida) and displayed on an oscilloscope.

Single-unit EMG activity was recorded with sterilized, lacquer-coated tungsten microelectrodes inserted percutaneously into the target muscles (Frederick-Haer & Co., Bowdoinham, Maine, 1- to 5- $\mu$ m tip diameter, 5- to 10-  $\mu$ m uninsulated length, 250- $\mu$ m shaft diameter,  $\sim$  200 k $\Omega$  impedance at 1000 Hz after insertion). Surface electrodes (4 mm diameter Ag-AgCl) attached to the skin overlying the radial styloid served as reference electrodes for each microelectrode. A moistened, silver-impregnated Velcro strap placed around the upper arm served as the ground electrode. Weak electrical stimulation (0.1 - 5 mA, 0.2-1 ms pulses, 1 Hz; S88 Stimulator, Grass Instruments) was used initially to verify electrode placement in the target muscles based on observation of

the evoked motor responses. Two microelectrodes were inserted in two different locations to record the activity of different motor units on each electrode. Each microelectrode was adjusted in depth and angle until the isolated movement of the target digit was elicited upon stimulation.

For experiments in chapters 4, 5, and 7, in an attempt to minimize inadvertent re-analysis of the same motor-unit pairs recorded on separate trials, pairs of surface electrodes were applied to the skin overlying each muscle compartment within which the microelectrodes were placed. The EMG signals detected with these surface electrodes were subsequently spike-triggered averaged in off-line analysis (see below) to extract the surface EMG signature associated with discharge of recorded motor units (Lemon et al. 1990).

The intramuscular and surface EMG signals were amplified (x 2000) and band-pass filtered (100 – 3000 Hz, and 10 – 1000 Hz, respectively; Grass Instruments), and displayed on oscilloscopes. Intramuscular EMG signals were also routed to a two-channel audio amplifier.

#### *General protocol*

Subjects performed low intensity isometric contractions of the target muscles. The microelectrodes were gently manipulated during the contraction until action potentials of individual motor units could clearly be identified on each electrode. Subjects then sustained weak contractions of the muscles such that both units remained active. Subjects were not given specific instructions on the force of the contraction; rather they were instructed to maintain the discharge of the motor units at low rates (~8-

12 Hz) for the duration of the 3-5 minute trial. Pilot studies indicated the 3-5 minute trials provided sufficient discharges (~3000/unit) needed to be able to clearly discern peaks in the cross-correlation histograms. Subjects received visual and auditory feedback of the motor unit discharges and 1-2 minutes of rest between trials to prevent fatigue. After each recording, at least one of the two microelectrodes was adjusted until a presumed different motor unit was identified. Occasionally this involved the removal and reinsertion of an electrode to a new site, after which placement verification with electrical stimulation was performed as described. Successive trials were performed for up to two hours. Flexion force, surface EMG, and intramuscular EMG signals were digitally sampled at ~ 2.0, 2.5, and 12.5 kHz, respectively, using the Spike 2 data-acquisition and data-analysis system (Cambridge Electronics Design, Cambridge, UK).

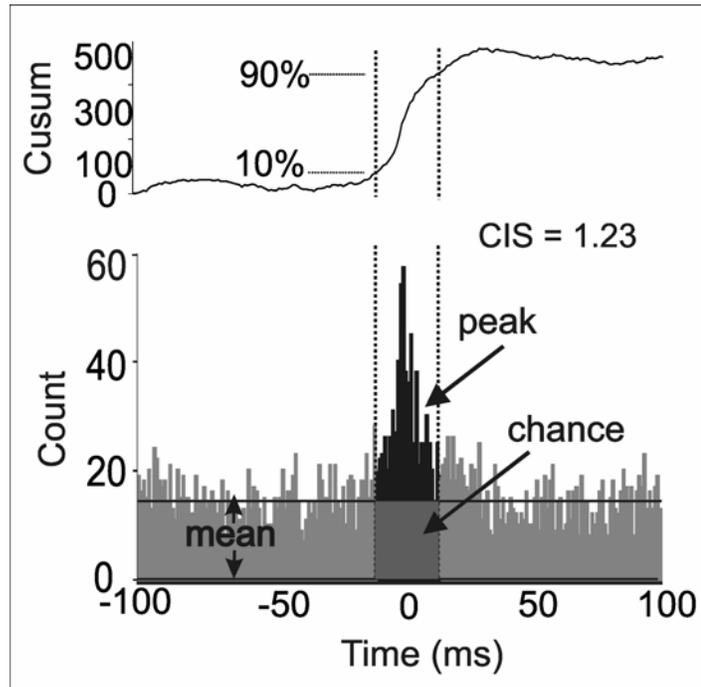
#### *Data analysis*

In off-line analysis, motor unit action potentials were discriminated from intramuscular recordings using a template-matching algorithm (Spike 2, Cambridge Electronics Design). Cross-correlation histograms (1 ms bins,  $\pm 100$  ms) were constructed from the discharge times of the discriminated motor units recorded from separate electrodes (Fig. 3.1). 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 delineate the central peak in the histogram. The boundaries of this peak were defined as the bins

corresponding to 10% and 90% of the maximum cusum values (Schmied et al. 1993).

The magnitudes of the central peaks in the cross-correlation histograms were quantified using a synchronization index, referred to as common input strength (CIS). The CIS was calculated by the number of counts within the peak above the baseline mean divided by the duration of the recording, which represents the rate of extra synchronous impulses (extra synch. imp./s) above that expected by chance (Nordstrom et al. 1992). In addition, we calculated the index  $k'$ , which is the ratio of the mean bin count contributing to the cross-correlogram peak to the number expected by chance (Ellaway and Murthy 1985) in order to make direct comparisons between our study and those that have used  $k'$  as their synchrony index in studies of other multi-tendoned extrinsic finger muscles.

When no clear peak was evident in the cross-correlation histogram, the technique described above for identifying the region of the histogram for which to calculate CIS or  $k'$  was unreliable. Therefore, for cases of non-significant peaks in the histograms, CIS and  $k'$  were calculated for an 11 ms region of the histogram centered at time zero (Semmler and Nordstrom 1995). In order for the histogram peak to be considered significant, the average count within the peak needed to be greater than 3 standard deviations above the baseline mean ( $z$  score  $\geq 1.96$ ) (Schmied et al. 1993). All CIS and  $k'$  values, regardless of the method used for calculation, were included in the analysis.



**Figure 3.1.** Example cross-correlogram depicting the timing of discharges of one motor unit relative to the timing of discharges of the other unit. The central peak of the histogram is defined as the area bounded by the 10<sup>th</sup> and 90<sup>th</sup> percentiles of the cusum. The magnitude of the central peak is quantified by the common input strength (CIS), representing the rate of extra synchronous impulses (extra imp./s) above that expected by chance.

For experiments in chapters 4, 5, and 7, spike-triggered averaging of the surface EMG based on the discharge times of the discriminated motor units was performed after each experimental session to verify that each motor unit pair recorded was not duplicated in subsequent trials of the same experiment. The identity of motor units was based on visual inspection of amplitude and shape of the spike-triggered average potentials. Duplicated motor-unit pairs were then dropped from further analysis.

Experimental methods that were specific to each set of experiments are outlined within the appropriate chapters under the MATERIALS AND METHODS sections.

**CHAPTER 4: MOTOR UNIT SYNCHRONY WITHIN AND ACROSS  
COMPARTMENTS OF THE HUMAN FLEXOR DIGITORUM SUPERFICIALIS**

## **ABSTRACT**

A peculiar feature of the muscular organization of the human hand is that the main flexors and extensors of the fingers are compartmentalized and give rise to multiple parallel tendons that insert onto all the fingers. Previous studies of motor unit synchrony in extensor digitorum (Keen and Fuglevand 2004) and flexor digitorum profundus (Reilly et al. 2004; Wings and Santello 2004) have indicated that synaptic input to motor neurons supplying these multi-tendoned muscles is not uniformly distributed across the entire pool of motor neurons but instead appears to be partially segregated to supply subsets of motor neurons that innervate different muscular compartments. Little is known, however, about the organization of the synaptic inputs to the motor neurons supplying another multi-tendoned finger muscle, the flexor digitorum superficialis (FDS). Therefore, in this study, we estimated the extent of divergence of last-order inputs to FDS motor neurons by measuring the degree of short-term synchrony among motor units within and across compartments of FDS. The degree of synchrony for motor unit pairs within the same digit compartment was nearly double that of pairs of motor units in adjacent compartments and more than four times that of pairs in nonadjacent compartments. Therefore, like other multi-tendoned muscles of the hand, last-order synaptic inputs to motor neurons supplying the FDS appear to supply predominately subsets of motor neurons innervating specific finger compartments. Such an organization presumably enables differential activation of separate compartments to facilitate independent movements of the fingers.

## **INTRODUCTION**

Motor neurons supplying the hand muscles of humans and other primates are thought to receive substantial synaptic input directly from the motor cortex (Lawrence and Kuypers 1968a; Heffner and Masterton 1983; Palmer and Ashby 1992; Porter and Lemon 1993; Bennett and Lemon 1996). This privileged monosynaptic input is thought to underlie the unique dexterity associated with voluntary movements of the hand (Lemon et al. 2004). In general, these inputs appear to diverge extensively to contact many neurons within a motor nucleus (Lawrence et al. 1985; Mantel and Lemon 1987) and also ramify to contact multiple motor nuclei (Asanuma et al. 1979; Fetz and Cheney 1980; Shinoda et al. 1981; Buys et al. 1986). However, the precise organization of these descending inputs to motor neurons supplying specified hand muscles, and in particular, the multi-tendon muscles that serve as the main flexor and extensors of the fingers, is not fully understood.

In humans, there are three multi-tendon extrinsic finger muscles, two flexors (flexor digitorum superficialis, FDS; flexor digitorum profundus, FDP) and one extensor (extensor digitorum, ED), that are located in the forearm and that give rise to four parallel tendons that cross multiple joints and insert onto the four fingers. Recent studies of ED (Keen and Fuglevand 2004a) and FDP (Reilly et al. 2004; Winges and Santello 2004) indicate that synaptic inputs to motor neurons supplying these multi-tendoned muscles do not appear to be uniformly distributed across the entire motor nucleus but instead appear to be partially segregated to preferentially supply subsets of motor neurons that innervate separate muscular compartments that insert on different digits. Little is known, however, about the organization of the synaptic inputs to the motor neurons supplying the FDS.

Therefore, in this study, we used an approach similar to that used previously (Reilly et al. 2004; Wings and Santello 2004; Keen and Fuglevand 2004a) to estimate the extent of divergence of last-order synaptic inputs to FDS motor neurons by measuring the degree of short-term synchrony among motor units within and across compartments of FDS.

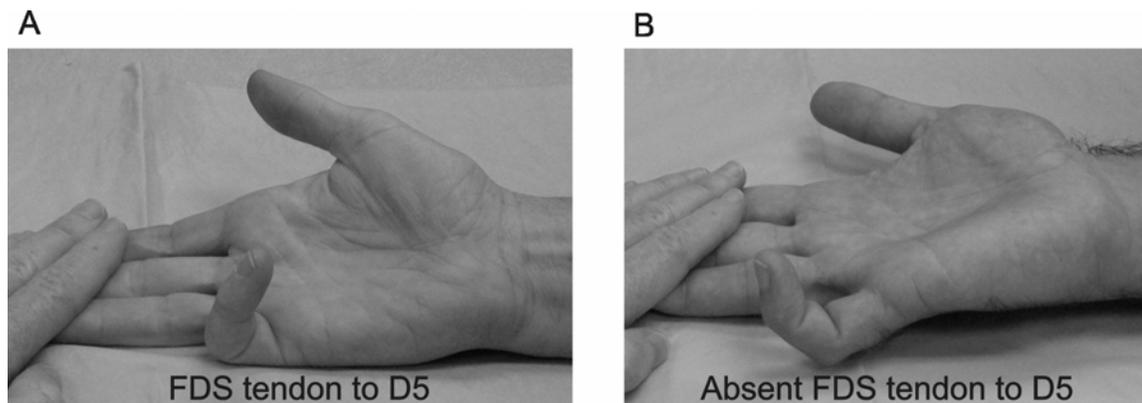
## **MATERIALS AND METHODS**

### *Subjects and test muscle*

Forty-one experiments were performed on the right FDS muscle in 28 healthy human volunteers (20 women, 8 men, ages 19-54 years). Procedures were approved and informed consent was given by all subjects as described in General Methods, Chapter 3.

The FDS originates from the humerus and proximal ulna and typically gives rise to four tendons that insert on the middle phalanges of digits 2 – 5. One of the main functions of FDS, therefore, is to flex the proximal IP joint without concurrent flexion of the distal IP joint, which is controlled by FDP. There are a number of anomalies noted specifically of the FDS tendon to the little finger, including absence of the tendon (Furnas 1965; Kaplan 1969; Gonzalez et al. 1997). An absent FDS tendon to the little finger would preclude the ability to isolate volitional flexion to the proximal IP joint, leaving flexion to occur through the action of the FDP to the distal segment (Fig. 4.1B).

Therefore, prior to each experiment we screened for the presence of an FDS tendon to the little finger by having each subject attempt to flex selectively the proximal IP joint of the little finger (Stein et al. 1990) (Fig. 4.1A, B). We subsequently attempted to record from the little finger compartment of the FDS only in those subjects who successfully performed this maneuver.



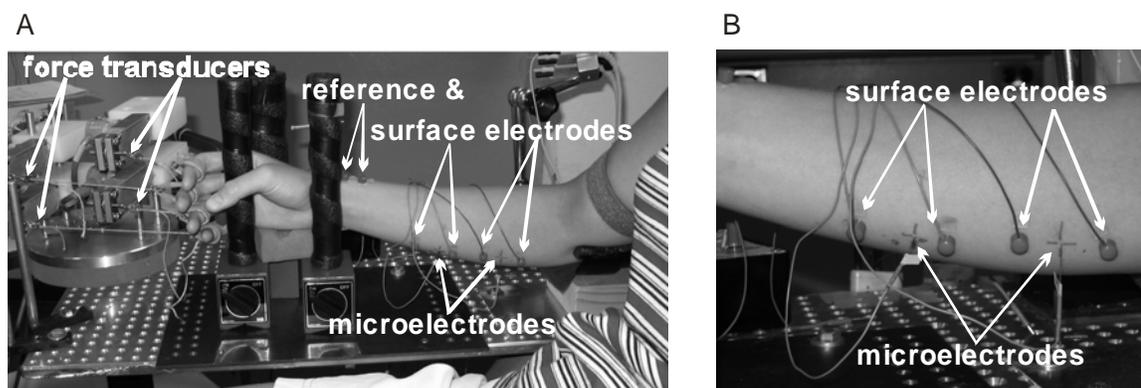
**Figure 4.1.** Flexor digitorum superficialis (FDS) to the little finger (D5) has been shown to have variable anatomy. Clinical examination revealed many subjects with absent or non-independent D5 tendons (Stein et al. 1990). A) Subject with independent FDS function in D5. B) Subject with incomplete FDS function in D5.

#### *Experimental setup*

Subjects were comfortably seated in a dental chair with the right arm supported on a horizontal platform and the proximal forearm and elbow stabilized in a padded trough. The forearm and hand were maintained in a mid-supinated (neutral) orientation by padded vertical posts placed in contact with the dorsal and palmar aspects of the hand. An additional narrow vertical post was placed just distal to the MCP joints to contact the volar surface of the proximal phalanges of digits 2 – 5 and served to hold the MCP joints in a neutral orientation. The proximal IP joints of each finger were maintained in a slightly flexed configuration ( $\sim 30^\circ$  flexed from full extension) by narrow leather bands around the middle phalanges of each digit that were attached to separate force transducers (Fig. 4.1A).

#### *Force and EMG recording*

Flexion force of the digits was measured by four force transducers (see General Methods, Chapter 3). Each transducer was aligned with the direction of pull orthogonal to the long axis of the middle phalanx of each digit. Force signals were amplified and displayed on an oscilloscope (see General Methods, Chapter 3) (Fig. 4.2A).



**Figure 4.2.** Hand and forearm (A) and close-up (B) views of experimental setup. Arm was supported on platform with the wrist and hand stabilized by padded bars on magnetic stands. **A**, Four force transducers were attached to the middle phalanges of each finger to measure the flexion force at all proximal IP joints. A surface electrode over the radius served as reference for each microelectrode. **B**, Microelectrodes were inserted into FDS compartments. Surface electrodes placed over FDS compartments recorded global EMG activity.

Single-unit EMG activity was recorded with microelectrodes inserted into the FDS muscle (see General Methods, Chapter 3) (Fig, 4.2A, B). Two microelectrodes were inserted into FDS at different locations to record the activity of separate motor units on each electrode. In some trials, the two electrodes were placed into the same compartment, and in other trials the electrodes were placed in separate compartments. Weak electrical stimulation was used initially and between each trial to identify the compartment location of each electrode and to verify microelectrode placement in FDS (see General Methods, Chapter 3). Each microelectrode was adjusted in depth and angle until an individuated

movement of the proximal IP joint of the target digit was elicited upon stimulation. After electrical stimulation, additional pairs of surface electrodes were applied to the skin overlying each muscle compartment within which the microelectrodes were placed, in order to record surface EMG signals. Surface and intramuscular EMG signals were recorded and subsequently analyzed as described in General Methods, Chapter 3.

#### *Protocol*

Subjects were instructed to perform low-force isometric flexion of all 4 digits primarily at the proximal IP joint to activate the FDS muscle. The remainder of the protocol is as described in General Methods, Chapter 3.

Previous studies have indicated that motor unit synchrony can be modulated based on the type of task performed (Bremner et al. 1991). Therefore, in a subset of experiments, we evaluated the degree of motor-unit synchrony in FDS associated with flexing a single digit compared to that associated with flexing with all four fingers together. All of these experiments involved trials in which both microelectrodes were inserted into the same compartment.

#### *Data analysis*

Off-line analysis was performed as described in detail in General Methods, Chapter 3. Briefly, cross-correlation histograms were constructed from the relative timing of discharges of two motor units recorded from separate electrodes. A central synchronous peak in each histogram was identified using the cusum procedure (see General Methods, Chapter 3). The magnitude of the central peak of the cross-correlogram was quantified by calculating the number of counts within the peak above

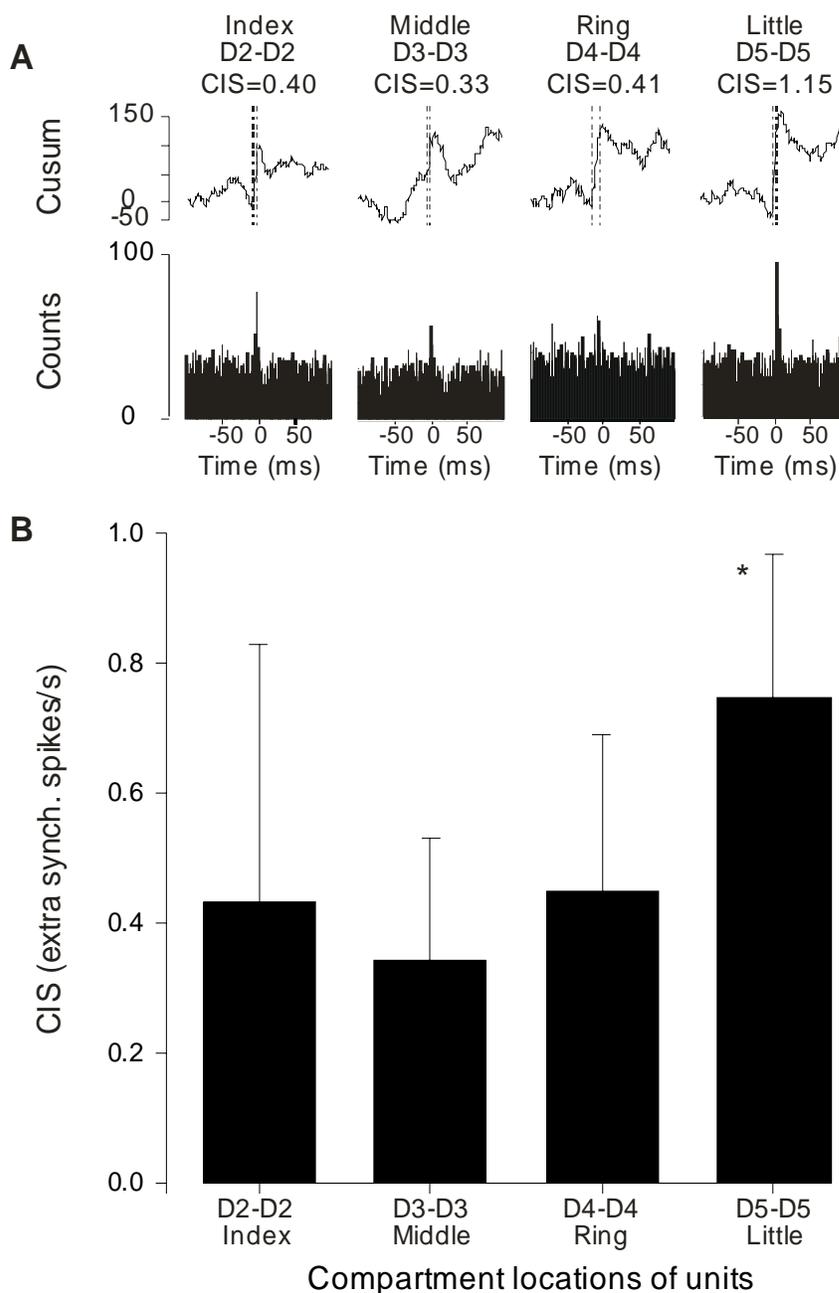
the baseline mean divided by the duration of the recording, referred to as the common input strength (CIS) index of synchrony. In the absence of a clear peak in the cross-correlogram, the above method for identifying the region of the histogram for calculation of CIS is unreliable. For such cases of nonsignificant peaks in the cross-correlograms, therefore, CIS was automatically calculated for an 11ms region of the histogram centered at time 0 (Semmler and Nordstrom 1995). The significance criterion for the peak in the cross-correlogram was if the average number of counts in the peak region was  $> 3$  SD's above the mean count ( $z$  score  $\geq 1.96$ ) (Schmied et al. 1993).

Statistical analyses were based on CIS values only ( $k'$  values were calculated to enable comparison with other studies). Trials in which both microelectrodes were situated within the same compartment of FDS are referred to as intra-compartmental whereas trials in which the microelectrodes were located in different compartments are referred to as extra-compartmental. A one-way ANOVA was used to determine whether intra-compartmental CIS values varied across the four muscle compartments. In addition, a one-way ANOVA was used to determine whether CIS values differed depending on the extent of compartmental separation between the recorded motor unit pairs (i.e. same compartment, adjacent compartments, two compartments apart, three compartments apart). Values are reported as means  $\pm$  SD with a probability of 0.05 selected as the level of statistical significance.

## **RESULTS**

A total of 393 FDS motor units were recorded during 163 trials and were used to generate 234 cross-correlation histograms. In 58 trials, more than one motor unit was

discriminated on an electrode, yielding multiple correlations. Based on our functional test, FDS tendons to digit 5 were found in only 12 of 28 (43%) subjects tested (see Fig. 4.1). Therefore, the total number of trials involving recordings from the D5 compartment was less than that for the other compartments of FDS (see below). The mean firing rate for all recorded motor units was  $10.2 \pm 1.6$  Hz and the mean number of events used to generate the cross-correlograms was  $2,270 \pm 737$ . Of the 234 cross-correlograms generated, 115 had significant synchrony peaks using the criteria described in METHODS. The average peak duration assessed from the cusum of these cross-correlograms with significant peaks was  $8.9 \pm 3.0$  ms. The average CIS for all pairs of FDS motor units, including those with non-significant peaks, was  $0.32 \pm 0.26$ .



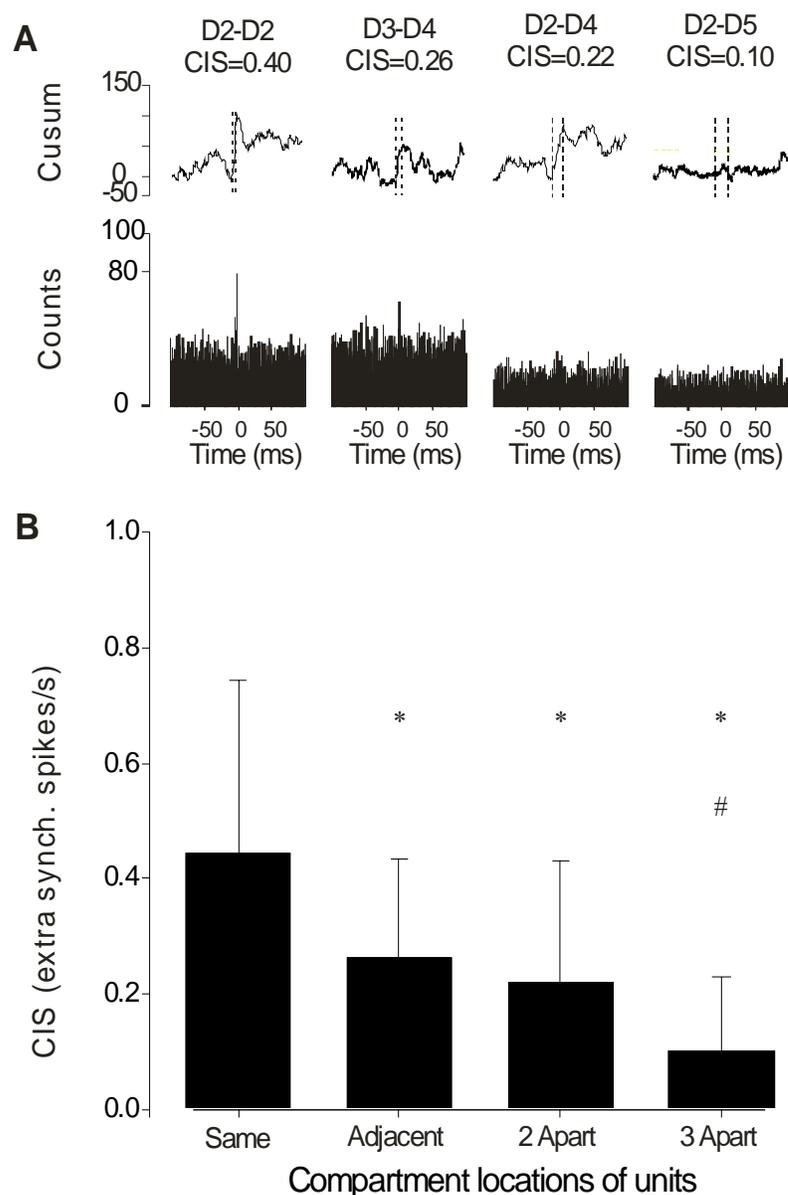
**Figure 4.3.** CIS values for intra-compartmental pairs of motor units in FDS. **A**, Example cross-correlograms for motor unit pairs residing in the Index (D2-D2), Middle (D3-D3), Ring (D4-D4), and Little (D5-D5) finger compartments of FDS. Trace above each correlogram is the cusum used to delineate the correlogram peak (dotted lines). **B**, Mean  $\pm$  SD CIS values for all intra-compartmental unit pairs as in **A**. \* Significantly different ( $P < 0.05$ ) from all other intra-compartmental pairs. synchron., Synchronous.

Figure 4.3A shows four examples of intra-compartmental cross-correlograms for each compartment of FDS and their respective CIS values. The labels at the top indicate the compartment within which both of the microelectrodes were located. The mean (SD) intra-compartmental CIS values for each compartment are shown in Fig. 4.3B. Ninety-four motor-unit pairs in total were recorded from within the same compartment. These had substantial mean CIS values of  $0.43 \pm 0.40$  ( $n = 28$ ),  $0.34 \pm 0.19$  ( $n = 28$ ),  $0.45 \pm 0.24$  ( $n = 28$ ), and  $0.75 \pm 0.23$  ( $n = 10$ ) for D2 through D5 compartments, respectively. A one-way ANOVA revealed a significant difference ( $p = 0.002$ ) between compartments in CIS values for intra-compartmental pairs. Post hoc analysis using the Newman-Keuls method identified this difference to include only comparisons involving the D5 compartment (i.e., D2-D5, D3-D5 and D4-D5). No other intra-compartmental comparisons were significantly different from one another.

One hundred forty extra-compartmental motor-unit pairs were recorded from FDS. These were categorized according to the respective locations of each recorded motor unit in the pair and the degree of separation between compartments. The adjacent group consisted of motor-unit pairs from D2-D3 (CIS =  $0.26 \pm 0.81$ ,  $n = 35$ ), D3-D4 (CIS =  $0.27 \pm 0.17$ ,  $n = 39$ ), and D4-D5 (CIS =  $0.26 \pm 0.18$ ,  $n = 10$ ). The two-apart group included motor-unit pairs from D2-D4 (CIS =  $0.16 \pm 0.15$ ,  $n = 31$ ) and D3-D5 (CIS =  $0.36 \pm 0.28$ ,  $n = 13$ ). The three-apart group included the motor-unit pairs of D2-D5 (CIS =  $0.10 \pm 0.13$ ,  $n = 12$ ). Figure 4.4A shows four examples of cross-correlograms, one for an intra-compartmental pair of motor units and three for each of the groups of extra-compartmental pairs, with their respective CIS values. Figure 4.4B shows the mean (SD)

CIS values for all pairs recorded within the same compartment ( $0.45 \pm 0.30$ ,  $n = 94$ ), for pairs in adjacent compartments ( $0.26 \pm 0.17$ ,  $n = 84$ ), for pairs two-compartments apart ( $0.22 \pm 0.21$ ,  $n = 44$ ), and for pairs three compartments apart ( $0.10 \pm 0.13$ ,  $n = 12$ ). A one-way ANOVA revealed a significant effect of compartment separation on CIS ( $p < 0.001$ ). Post hoc analysis with Dunn's method indicated all extra-compartmental pair groups had significantly smaller CIS values than the intra-compartment pairs ( $p < 0.05$ ). Furthermore, a Newman-Keuls post hoc test showed that the CIS values for pairs of units located three compartments apart were significantly smaller than for pairs from all other extra-compartment groups ( $p < 0.05$ ). There was no significant difference in CIS values for pairs of units in adjacent compartments compared to pairs two-compartments apart.

In an additional set of trials, intra-compartmental pairs of motor units were recorded while subjects were instructed to flex only the digit associated with the compartment within which the microelectrodes were situated. The mean CIS value recorded during this single digit task ( $0.5 \pm 0.25$ ,  $n = 28$ ) was not significantly different ( $p = 0.17$ , Mann-Whitney test) from that for intra-compartmental pairs recorded during the task involving flexion of all four fingers ( $0.45 \pm 0.3$ ,  $n = 94$ ).



**Figure 4.4.** CIS values for all intra-compartmental and extra-compartmental unit pairs of different degrees of separation in FDS. **A**, Example cross-correlograms for motor unit pairs residing in the same compartment (D2-D2), adjacent compartments (D3-D4), two compartments apart (D2-D4), and three compartments apart (D2-D5). **B**, Mean  $\pm$  SD CIS values for combinations of unit pairs as in **A**. \* Significantly different ( $p < 0.05$ ) from same-compartment pairs. # Significantly different ( $p < 0.05$ ) from all other compartment pairs. synchron., Synchronous.

## **DISCUSSION**

The present study demonstrates that the degree of synchrony for motor units in the FDS follows a general pattern with the greatest synchrony for pairs of units within compartments and progressively less synchrony for pairs of units in compartments separated by increasingly lateral distances. Therefore, like other multi-tendoned muscles of the hand, last-order projections to FDS motor neurons do not appear to be uniformly distributed across the entire FDS motor nucleus, but instead tend to be segregated to supply subsets of motor neurons innervating different compartments. Consequently, differential activation of motor neurons supplying specific compartments of FDS may facilitate movements of individual fingers. Nevertheless, extra-compartmental synchrony is indicative of some across-compartment divergence of synaptic input that may contribute to the inadvertent movement of adjacent fingers during intended movement of only one finger (Kilbreath and Gandevia 1994; Hager-Ross and Schieber 2000; Zatsiorsky et al. 2000; Butler et al. 2005).

### **Anatomical complexity of the FDS muscle**

The FDS anatomy is unique when compared to the other multi-tendoned muscles of the hand, having a more complex arrangement of the digital compartments and greater variation and anomalies across subjects (Wood Jones 1941; Ohtani 1979; Brand and Hollister 1999). For instance, the deep layer of the muscle typically consists of a single proximal belly that gives rise distally to an intermediate tendon from which two muscle bellies emerge each giving rise to the tendons of the index and little fingers, respectively. In the present experiments, we sampled from the distal, single-digit compartments.

Future work is needed to evaluate the motor unit organization of the intriguing proximal belly and how its activity is coordinated with that of its two daughter bellies.

In addition to the complex arrangement of the muscle-belly components, there exist surprisingly high proportions of anomalies associated with the FDS tendon to the little finger. Indeed, only 43% of our sample population had a functional FDS tendon to the little finger of the right hand. This is in agreement with the percentage (42%) reported by Stein and colleagues (1990) using more extensive clinical tests of FDS. It remains for future investigations to determine whether absence of an FDS tendon to the little finger leads to detectable functional impairment in certain types of manipulative tasks.

### **Synchrony and inferences about common synaptic input**

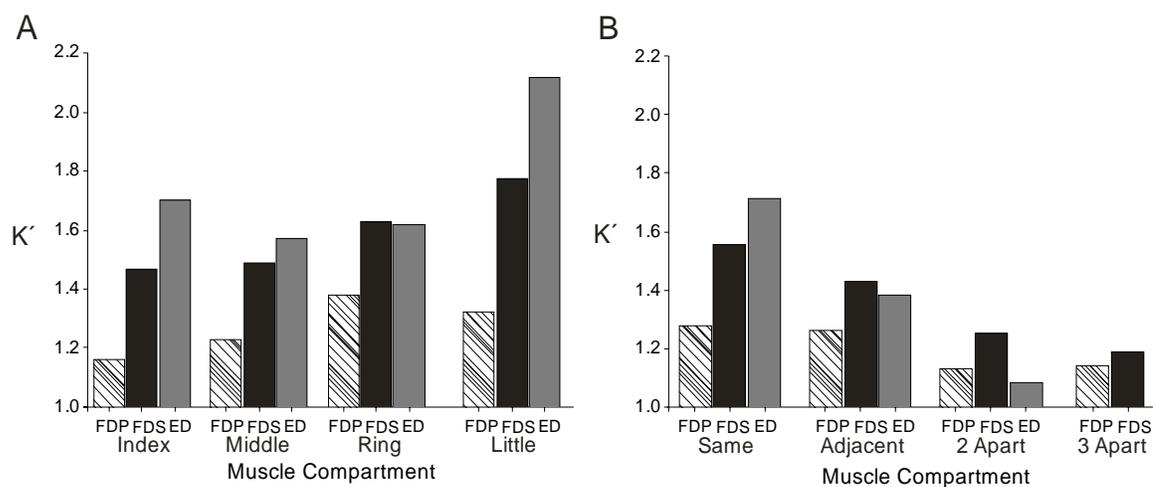
Investigations into the organization of the distribution of synaptic input within and across motor nuclei in the spinal cord of cats and monkeys using anatomical, histological, and electrophysiological methods support the idea that spinal inputs, including those arising in the cerebral cortex, may diverge to influence several motor nuclei simultaneously (Mendell and Henneman 1971; Shinoda et al. 1981; Fetz and Cheney 1980; Buys et al. 1986). Direct assessment of the distribution of synaptic input to motor neurons is impractical in humans, but can be estimated using cross-correlation analysis of the discharge times between pairs of motor units (Kirkwood and Sears 1978). As described in Chapter 2 of this dissertation, the concept underlying cross-correlation analysis is that if presynaptic fibers diverge to provide common excitatory input to two neurons, then this should elicit near simultaneous excitatory postsynaptic potentials in the

two neurons and thus slightly increase the probability that the two neurons will be brought to firing threshold simultaneously (Perkel et al. 1967; Kirkwood and Sears 1978). Neurons receiving common excitatory input, therefore, should discharge near-simultaneously slightly more often than would be expected due to chance. Such a statistical coincidence in their discharge can be seen as a peak around time zero in the cross-correlogram. Central peaks in the cross-correlograms can also occur due to some degree of synchronized firing of presynaptic neurons, but these generally are of broader duration (>10ms) than the peaks due to branched last-order inputs (Kirkwood et al. 1982). Although the average peak duration for motor-unit pairs tested in the present study was < 10ms, the possibility cannot be discounted of the contribution of synchronized presynaptic input. Regardless, the magnitude of this peak represents the proportion of common to non-common synaptic inputs to the two neurons (Kirkwood and Sears 1978). Short-term synchrony is thought to be of central rather than peripheral origin, since it is not abolished by lesions of the dorsal roots (Kirkwood et al. 1982), yet is significantly reduced after lesions to descending pathways (Kirkwood et al. 1982; Datta et al. 1991).

### **Synchrony in multi-tendoned finger muscles**

Substantial synchrony has previously been shown to exist for motor-units pairs within intrinsic hand muscles (Datta and Stephens 1990; Bremner et al. 1991a; Bremner et al. 1991b; Bremner et al. 1991c; Nordstrom et al. 1992). From the limited data available, significant motor unit synchrony has also been shown to exist across different hand muscles, but to a lesser extent by about half than for within-muscle pairs (Bremner et al. 1991b; Maier and Hepp-Reymond 1995b; Huesler et al. 2000). Our findings (see

also Keen and Fuglevand, 2004a) of nearly double the amount of synchrony for motor-unit pairs within a compartment (CIS = 0.45) versus across adjacent compartments (CIS = 0.26) and compartments two apart (CIS = 0.22) is similar to previous results of synchrony across hand muscles. This suggests that the extent of divergent last-order inputs onto motor neurons supplying different compartments of multi-tendoned hand muscles is generally similar to the shared input across motor neurons supplying neighboring hand muscles.



**Figure 4.5.** Comparison of synchrony index values of the three multi-tendoned extrinsic finger muscles in humans. **A**, Mean  $K'$  values for *intra-compartmental unit pairs* located within the Index, Middle, Ring, and Little finger compartments of FDP (hatched bars) FDS (black bars) and ED (gray bars). **B**, Mean  $K'$  values for *intra- versus extra-compartmental unit pairs* located within the *Same* compartment, *Adjacent* compartments, compartments that were *2 Apart*, and compartments that were *3 Apart* for FDP, FDS, and ED, as in panel A. Note that no data were available for ED compartments that were *3 Apart*. Mean FDP data adapted from (Reilly et al. 2004). *synch.*, Synchronous.

Figure 4.5 illustrates the average levels of synchrony for each of the three multi-tendoned extrinsic finger muscles, as reported here for FDS and previously reported for ED (Keen and Fuglevand 2004a) and FDP (Reilly et al. 2004). For comparison purposes, the present data and that of Keen and Fuglevand (2004a) were re-analyzed using the  $k'$  synchrony index (see METHODS). Figure 4.5A shows the intra-compartmental  $k'$  values for each finger compartment of the three muscles while Figure 4.5B shows  $k'$  values for different degrees of compartment separation between motor unit pairs. Interestingly, both intra- (Fig. 4.5A) and extra-compartmental (Fig 4.5B) motor-unit synchrony is generally greatest for ED, intermediate for FDS, and least for FDP. Because synchrony can be considered to reflect the extent of neural coupling across motor units, these findings are consistent with the idea that the digital compartments of the flexor muscles possess greater independence and control than that of the extensor muscles of the fingers (Bremner et al. 1991b; Porter and Lemon 1993). Likewise, the lower levels of synchrony for FDP compared to FDS implies that the inputs to the subsets of motor neurons supplying separate finger compartments are more segregated for FDP than for FDS which might enable a greater degree of independence for movements involving the distal segments of the digits.

The pattern of synchrony we found for FDS in which the magnitude decreases with increasing separation between pairs of units is also consistent with previous observations in the ED and FDP during isometric force production (Bremner et al. 1991b; Reilly et al. 2004; Keen and Fuglevand 2004a) (Fig. 4.5B). Interestingly, Butler et al. (2005) demonstrated a similar pattern in the degree of coactivation across compartments

of FDS during attempts to isolate voluntary flexion of a single finger, but to a lesser extent than the degree of coactivation across compartments of FDP found by Kilbreath and Gandevia (1994). Likewise, comparing the present findings of synchrony patterns in FDS to the synchrony patterns in FDP reported by Reilly et al. (2004), it is clear the strength of synchrony declines with increased separation of units (Fig. 4.5B). Taken together these results suggest less independent corticospinal control of adjacent fingers than of fingers further apart. Motor unit pairs with greater synchrony are thought to receive a larger proportion of common inputs, suggesting less independence of finger movement with high extra-compartmental synchrony (Datta and Stephens 1990; Bremner et al. 1991a; Bremner et al. 1991b; Nordstrom et al. 1992)

### **Effect of task on motor unit synchrony**

Modulation of motor unit synchrony as a function of the task performed was shown by Bremner et al. (1991c). Therefore, we designed the present study to include a subset of experiments in which motor unit synchrony was assessed during flexion of an individual finger and flexion of all four fingers together. There was no significant difference in the degree of synchrony within digital compartments of the FDS between the tasks. Interestingly, two groups using different tasks have reported similar CIS values for pairs of motor units located in the two muscles that flex the distal segments of the thumb [flexor pollicis longus (FPL)] and index finger (FDP) (Winges and Santello 2004; Hockensmith et al. 2005). Wings and Santello recorded single motor unit activity during a five-digit grasp, while Hockensmith et al. (2005) recorded during a precision-

like grip with the thumb and index finger, yet the strength of motor unit synchrony across FPL and FDP to the index finger was remarkably similar.

### **Conclusion**

The degree of synchrony for pairs of motor units within a compartment of the FDS was greater than for pairs of motor units in adjacent and non-adjacent compartments, indicating that synaptic inputs to the population of FDS motor neurons are not uniformly distributed, but instead are roughly segregated to supply four separate sub-pools of motor neurons. Additionally, the pattern of decreasing synchrony strength with increasing separation of motor units in the FDS, as with the other multi-tendoned extrinsic hand muscles, suggests this distributed input may result in the unintended flexion of adjacent fingers when attempting to flex only one finger. Less motor unit synchrony within finger flexor muscles implies the CNS has greater independent control over motor neurons of the flexor muscles than the extensor muscles of the fingers. Greater control of finger flexion may reflect the need for finely graded flexion forces during highly dexterous tasks and manipulation of small objects.

**CHAPTER 5: COORDINATION OF TWO FINGER FLEXORS: MOTOR UNIT  
SYNCHRONY ACROSS THE HUMAN FLEXOR DIGITORUM PROFUNDUS  
AND THE FLEXOR DIGITORUM SUPERFICIALIS**

## **ABSTRACT**

Short-term synchrony was measured for pairs of motor units located in compartments of two multi-tendoned extrinsic flexor muscles that insert onto the same digit during an isometric finger flexion task. Surprisingly, synchrony for pairs of motor units residing in these neighboring muscles that both act to flex the same finger was negligible. Furthermore, the degree of synchrony across these muscles (FDS and FDP) that insert on a single finger was significantly less than the synchrony across compartments of one muscle (FDS) that inserts onto different fingers. These results suggest that the coordinated activity of the two long finger flexors are controlled by mechanisms other than divergent descending pathways providing common synaptic input to the motor nuclei innervating these muscles.

## **INTRODUCTION**

The coordinated action of multiple muscles underlies nearly all movements. For instance, several muscles are simultaneously active in the forearm and hand in humans and nonhuman primates during movements of individual fingers (Darling and Cole 1990; Darling et al. 1994; Schieber 1995; Valero-Cuevas et al. 1998). There is general consensus that the ability to coordinate muscles during precise movements of the fingers is related to direct connections from the motor cortex to the motor neurons supplying hand muscles (Heffner and Masterton 1975; Bortoff and Strick 1993; Porter and Lemon 1993; Sasaki et al. 2004). Such pathways may selectively target the individual motor nuclei innervating the specific muscles that participate in a finger movement, or they may diverge to supply multiple motor nuclei with excitation and thereby compel several

muscles to operate in unison during the elaboration of finger movements (Fetz and Cheney 1980; Shinoda et al. 1981; Buys et al. 1986; Schieber 1990; Hepp-Reymond et al. 1996). The second scenario, while affording less flexibility than the first, might provide a mechanism of reliable activation of a set of muscles into synergistic groups as needed to perform a particular motor task.

Coordinated movement of the multi-jointed human finger represents a fundamental motor behavior involved in manual dexterity. Finger flexion, for example, involves tightly coupled joint motions at the proximal and distal interphalangeal (IP) joints (Darling et al. 1994). The muscles responsible for flexion of the IP joints are the flexor digitorum profundus (FDP), the sole flexor of the distal IP joint, and the flexor digitorum superficialis (FDS) that flexes the proximal IP joint together with the FDP. A descending pathway that diverges to supply the motor nuclei innervating the FDP and FDS with common synaptic input might provide the neural substrate to couple together the movements of the distal and proximal IP joints during flexion.

In order to gain insight into mechanisms by which the CNS enlists muscles to perform a manual task, we estimated the extent of common, last-order synaptic input from the discharge times of motor unit pairs recorded from compartments of FDP and FDS that insert on the same finger during voluntary isometric finger flexion (Sears and Stagg 1976; Kirkwood and Sears 1978).

## **MATERIALS AND METHODS**

### *Subjects and test muscles*

Ten experiments were performed on 10 right-handed, healthy human volunteers (5 females) between the ages of 21 and 54 years. The Institutional Human Investigation Committee approved the procedures, and all subjects gave informed consent. Motor unit recordings were made from FDP and FDS, finger flexor muscles residing in the ventral forearm that each typically gives rise distally to four tendons that insert onto the anterior surfaces of digits 2-5 (index – little fingers). Both muscles can cause flexion at any of the joints over which they pass (wrist, MCP, and IP joints), but the FDS inserts onto the middle phalanx, while the FDP continues distally to insert onto the distal phalanx of each finger. Thus, the FDP is the only muscle to flex the distal IP joints and assists the FDS as the primary flexor of the proximal IP joints. We sampled motor unit activity from the divisions of the FDS and FDP that both insert onto the index (D2) or onto the middle (D3) finger.

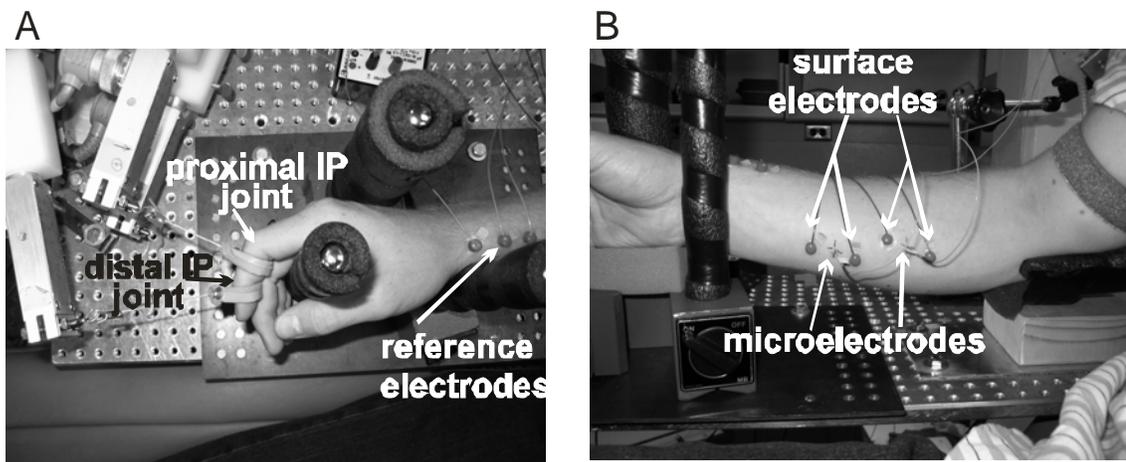
#### *Experimental setup*

The setup for the experiments in this chapter is identical to that for the experiments in the previous chapter (see General Methods, Chapter 3; and Materials and Methods, Chapter 4), with the exceptions noted below.

Subjects were seated with the forearm supported on a platform as previously described with the proximal IP joint resting in  $\sim 40^\circ$  of flexion and the distal IP joint resting in  $\sim 20^\circ$  of flexion. Leather cuffs were placed around the middle and distal phalanges of either the index or middle finger and were attached by lightweight cables to two force transducers (Fig. 5.1).

#### *Force and EMG recording*

Flexion force of the proximal and distal IP joints was measured by two force transducers mounted in a custom-built manipulandum (Fig. 5.1A). One force transducer was aligned with the direction of pull orthogonal to the long axis of the middle phalanx for measuring proximal IP joint flexion force and the second transducer was aligned with the direction of pull orthogonal to the long axis of the distal phalanx to measure distal IP joint flexion force of the tested digit.



**Figure 5.1.** Top of hand (A) and inside of forearm (B) views of experimental setup. Arm was supported on platform with the wrist and hand stabilized by padded bars on magnetic stands. **A**, Two force transducers were attached to the middle and distal phalanges of a finger to measure the flexion force at the proximal and distal IP joints, respectively. A surface electrode over the radius served as reference for each microelectrode **B**, Two microelectrodes were inserted, one each into the FDS and FDP compartments of the same finger. Surface electrodes placed over FDS and FDP recorded global EMG activity.

Initial placement of the microelectrodes was determined by use of anatomical maps generated from previous intramuscular EMG recordings of the forearm muscles, then followed by palpation of the muscle during isolated flexion of the proximal IP joint for the FDS and of the distal IP joint for the FDP of the digit associated with the target muscle compartment (Fig. 5.1B). Weak electrical stimulation was used initially and

between each trial to verify microelectrode placement in target ED compartments of FDS and FDP as described in the General Methods section of Chapter 3. Each microelectrode was adjusted in depth and/or angle while weak current pulses were delivered until an individuated movement of either the proximal IP joint for the FDS or the distal IP joint for the FDP of the target digit was evoked. After electrical stimulation, additional pairs of surface electrodes were applied to the skin overlying each muscle compartment within which the microelectrodes were placed, in order to record surface EMG signals (see General Methods, Chapter 3) (Fig. 5.1B).

#### *Protocol*

Subjects were instructed to perform low-force isometric flexion of a single finger at the proximal and distal IP joints simultaneously. The identification and recording of motor unit action potentials were performed as described in the General Methods section of Chapter 3.

#### *Data analysis*

Off-line analysis of motor unit action potentials was performed using a template-matching algorithm, as described in the General Methods section of Chapter 3. Briefly, cross-correlation histograms were constructed from the relative timing of discharges of two motor units recorded from separate electrodes. A central synchronous peak in each histogram was identified using the cusum procedure (see General Methods, Chapter 3). The magnitude of the central peak of the cross-correlogram was quantified by calculating the number of counts within the peak above the baseline mean divided by the duration of the recording, referred to as the common input strength (CIS) index of synchrony. In the

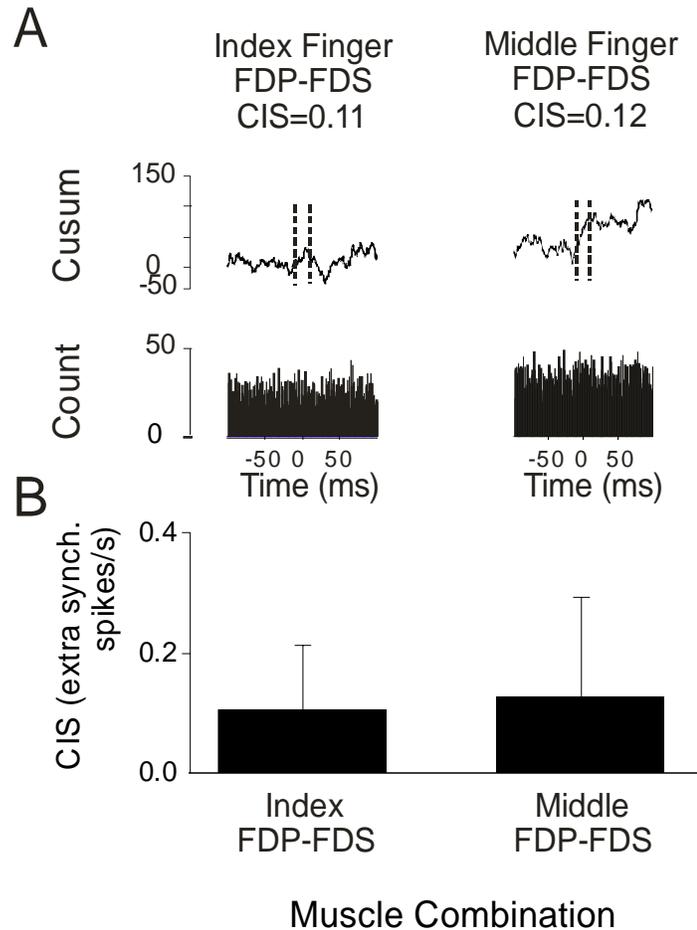
absence of a clear peak in the cross-correlogram, the above method for identifying the region of the histogram for calculation of CIS is unreliable. For such cases of nonsignificant peaks in the cross-correlograms, therefore, CIS was automatically calculated for an 11ms region of the histogram centered at time 0 (Semmler and Nordstrom 1995). The significance criterion for the peak in the cross-correlogram was if the average number of counts in the peak region was  $> 3$  SD's above the mean count ( $z$  score  $\geq 1.96$ ) (Schmied et al. 1993).

A two-tailed Student's  $t$ -test was used to compare the differences in the degree of synchrony for pairs of motor units recorded from FDS and FDP within compartments to the same finger. Differences between FDS-FDP motor-unit pairs to the index and to the middle fingers were also assessed using the Student's  $t$ -test. Values are reported as means  $\pm$  SD with a probability of 0.05 selected as the level of statistical significance.

## **RESULTS**

A total of 196 motor units were recorded, 97 in the FDP (39 in D2 and 58 in D3 compartments) and 99 in the FDS (39 in D2 and 60 in D3 compartments) during weak voluntary flexion of the two distal segments the index finger or the middle finger. Since the motor unit activity was recorded only during low force contractions, the sampled units were restricted to low-threshold types only. The mean firing rate for all recorded motor units was  $9.9 \pm 1.4$  Hz and the mean number of spikes per units used in the analysis was  $3,868 \pm 1,427$ . The discharge times of units recorded on different electrodes were used to generate 85 cross-correlation histograms. In 17 trials, more than one unit was discriminated on an electrode, providing more than one cross-correlation per trial.

Figure 5.2A shows example cross-correlograms for motor units pairs recorded in FDS - FDP muscle compartments to the index and middle fingers. Of the 85 correlograms, 10 (4 from Index, 6 from Middle finger pairs) had significant peaks (mean peak duration of  $7.7 \pm 2.7$  ms) and 75 had non-significant peaks (88%). Overall, synchrony for FDS and FDP pairs of motor units residing in either the index finger (CIS =  $0.11 \pm 0.11$ ) or middle finger (CIS =  $0.12 \pm 0.16$ ) compartments was very weak (Fig. 5.2B), particularly when compared to previous findings of synchrony for pairs of units within and across compartments of ED (Keen and Fuglevand 2004a), FDP (Reilly et al. 2004), and FDS (McIsaac and Fuglevand 2005). There was no significant difference in CIS between Index FDS-FDP and Middle FDS-FDP motor unit pairs ( $p = 0.598$ ).



**Figure 5.2.** CIS for pairs of motor units located in the compartments of the FDP and FDS muscles to a single finger. **A**, Example cross-correlograms for pairs of motor units residing within the index compartments of the FDP and FDS muscles (Index FDP-FDS), and unit pairs residing in the middle finger compartments of the FDP and FDS muscles (Middle FDP-FDS). The traces above each correlogram are the cusum used to identify the peak (dashed lines) in the correlogram. **B**, Mean  $\pm$  SD CIS values for the Index and Middle finger motor-unit pairs as in **B**. synch., Synchronous.

## DISCUSSION

We used cross-correlation analysis of the discharge times of motor units located in the same digit compartment of the two multi-tendoned extrinsic finger flexors, FDS and FDP, to estimate the degree to which their coordinated activity in flexing the IP joints of a single digit might be related to divergent synaptic input across motor nuclei activated

during finger flexion. Unexpectedly, we found little synchrony between motor unit pairs located in FDS and FDP compartments acting on the same digit, despite being neighboring muscles that perform similar actions. These results imply that the tightly coupled movements of the proximal and distal IP joints do not arise as a consequence of divergent synaptic input to the pools of motor neurons supplying the FDP and FDS muscles.

### **Limitations**

The task used in the present experiments involved isometric contractions of the proximal and distal IP joints against tethers fixed to the middle and distal phalanges, rather than the grasp of an object. This enabled measurement of flexion force for individual phalangeal segments of the finger during the contraction. Although there may be changes in motor unit synchrony that are task-dependent (Bremner et al. 1991c), previous findings of synchrony across tasks in FDS were not different (McIsaac and Fuglevand 2005) and synchrony in FDP and flexor pollicis longus were similar during a multi-digit grasp (Winges and Santello 2004) and a simulated precision grip (Hockensmith et al. 2005). Therefore, we believe the task itself used in the present experiments did not markedly affect our results of synchrony measures, but this remains to be evaluated.

### **Comparisons of within- and across-muscle synchrony**

The few studies that have investigated motor unit synchrony across muscles indicate that neighboring muscles, or muscles with similar actions, often exhibit significant synchrony (Bremner et al. 1991a; Bremner et al. 1991b; Gibbs et al. 1995;

Maier and Hepp-Reymond 1995a). The implication of high motor unit synchrony across muscles is that the motor neuron pools supplying the muscles receive substantial common synaptic input to facilitate cooperative or synergistic muscle activity. Therefore, we reasoned that motor unit synchrony across the two extrinsic finger flexors; FDP and FDS, to a single finger would be high during flexion of that finger.

Recent evidence suggests there is a degree of functional compartmentalization of multi-tendoned extrinsic finger muscles, with regions of the muscle selectively active during movement of only one finger (Reilly et al. 2004; Keen and Fuglevand 2004a; McIsaac and Fuglevand 2005) and the generation of motor unit force primarily on one finger as assessed with intraneural microstimulation of single motor axons (Keen and Fuglevand 2004b). Studies that have measured motor unit synchrony have found the greatest degree of synchrony for pairs of motor units located within a compartment, more moderate synchrony for pairs located in adjacent compartments, and less for pairs located in non-adjacent compartments (Reilly et al. 2004; Keen and Fuglevand 2004a; McIsaac and Fuglevand 2005). The degree of synchrony across motor unit pairs in different compartments of a multi-tendoned muscle is thought to correspond to the extent of coupling in the movements of the associated digits.

For example, we previously found adjacent-compartment synchrony for FDS and ED to have average CIS values of 0.26 (McIsaac and Fuglevand 2005) and 0.42 (Keen and Fuglevand 2004a), respectively. This represents about twice and four times the amount of synchrony among motor units acting on neighboring digits than that found in the present study for FDS-FDP motor-unit pairs acting upon the same digit. These results

suggest that the descending pathways that operate on the motor nuclei supplying the FDP and FDS muscles are highly independent, despite the high correlation of activities between these muscles found during simple finger flexion tasks (Darling et al. 1994).

Overall, these findings suggest that a high degree of synchrony across FDS and FDP motor units acting on the same finger is not required for coordinated finger flexion. In fact, a high level of synchrony might limit the flexibility of muscle synergies needed for effective grasp and manipulation of a wide array of objects in various hand and wrist postures. Perhaps the greater levels of synchrony found across digit compartments within muscles than was found across different muscles to the same finger reflects a strategy by the CNS to assure multi-digit control in grasp and manipulation while allowing the flexibility of individual finger orientation and positioning.

**CHAPTER 6: THE INFLUENCE OF TACTILE INPUTS ON THE  
COORDINATION OF MOTOR NEURONS SUPPLYING EXTRINSIC MUSCLES  
SUBSERVING PRECISION GRIP IN THE HUMAN HAND**

## **ABSTRACT**

The mechanisms by which the nervous system coordinates multiple muscles for the control of finger movements are not well understood. One possibility is that groups of muscles may be selected into synergies by last-order inputs that project across multiple motor nuclei. In this study we investigated the role that tactile input might play in coupling together the activities of motor units in two muscles involved in generating the precision grip. Cross-correlation analysis was used to assess the degree of synchrony in the discharge times of pairs of motor units recorded from index-finger and thumb flexor muscles while human subjects performed an isometric grip task. The magnitude of synchrony is thought to reflect the extent to which divergent last-order inputs provide common synaptic input across motor neurons. Synchrony was evaluated under two conditions: gripping with normal tactile input and gripping when tactile input from the digit pads was eliminated. Synchrony between motor units of index finger flexor and thumb flexor muscles, while substantial, was not significantly different across the two tactile-input conditions. These findings suggest that tactile input is not required to activate the divergent last-order inputs that couple together the activities of the index-finger and thumb flexor muscles during the precision grip.

## **INTRODUCTION**

The fine control of forces associated with the precision grip involves synergistic coordination among multiple muscles (Maier and Hepp-Reymond 1995a; Maier and Hepp-Reymond 1995b). Tactile feedback appears to be crucial for this fine control as digit cooling or local anesthesia of the thumb and index-finger tips in humans causes

significant deficits in force control during precision grip tasks (Rothwell et al. 1982; Johansson and Westling 1984; Sanes et al. 1985; Johansson et al. 1992; Teasdale et al. 1993; Fleury et al. 1995; Nowak and Hermsdörfer 2003). The specific mechanisms by which tactile information from the digits helps to orchestrate the activities of multiple muscles during a task such as the precision grip, however, remains unclear.

One possibility is that activity in tactile afferents arising from the distal pads of the index finger and thumb (Westling and Johansson, 1987; Johansson and Westling, 1987; Macefield et al. 1996) could engage both spinal and supraspinal pathways (Rosén and Asanuma, 1972; Lemon, 1981; Jenner and Stephens, 1982; Darton et al. 1985; Evans et al. 1989; Johansson et al. 1994; Deuschl et al. 1995; Macefield et al. 1996; Collins et al. 1999; McNulty et al. 1999) that provide divergent excitatory inputs across the motor nuclei involved in the precision grip. In this way, afferent activity initially triggered upon contact with an object could facilitate selection of the appropriate set of muscles needed to generate the precision grip (Collins et al. 1999).

One indirect means to characterize the organization of synaptic inputs to motor neurons involves cross-correlation analysis of the discharge times of pairs of concurrently active motor units (Sears and Stagg 1976; Kirkwood 1979; Farmer et al. 1997). The magnitude of short-term synchrony revealed by cross-correlation analysis is thought to represent the extent of last-order inputs that diverge to supply two motor neurons with common synaptic input. This approach has been used to show that coordination of activity in separate muscles that flex the distal segments of the thumb (FPL) and index finger (FDP2) during gripping tasks is related to the presence of potent divergent last-

order inputs across the associated motor nuclei (Winges and Santello 2004; Hockensmith et al. 2005). Consequently, the two muscles are compelled to operate in unison which facilitates the precise matching of normal forces exerted by the distal segments of the thumb and index finger during the precision grip (Forssberg et al. 1991; Hockensmith et al.).

We were interested, therefore, to determine whether the divergent input that appears to couple together the activities of FPL and FDP2 during the precision grip is dependent upon activity arising from tactile afferents. We addressed this issue by comparing the extent of synchronous discharge between motor units in FPL and FDP2 during a task that mimicked precision grip in the presence and absence of normal tactile feedback from the digit pads of the index finger and thumb.

## **MATERIALS AND METHODS**

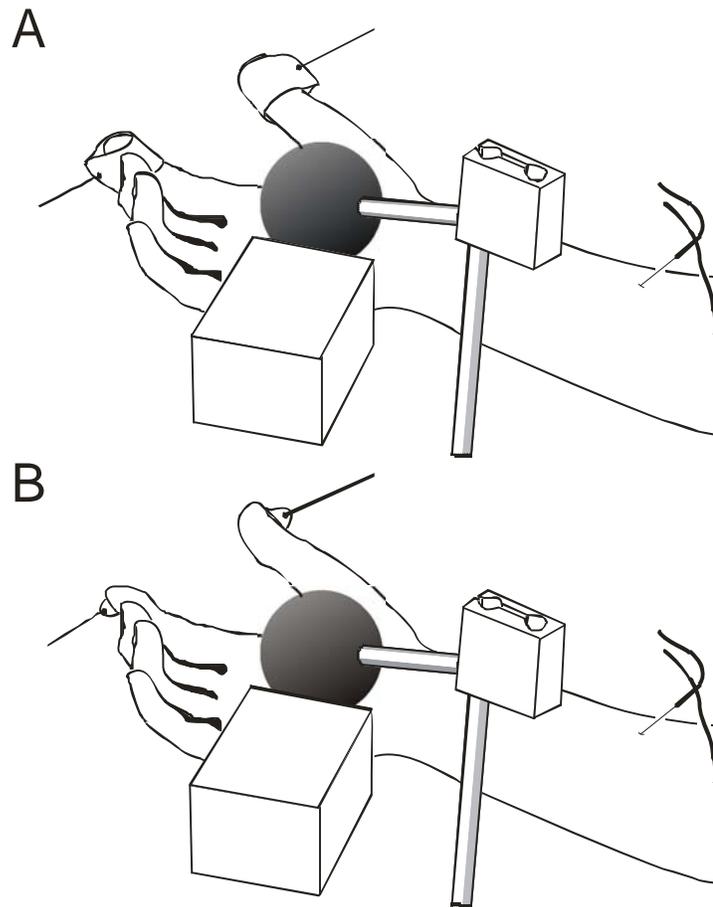
### *Subjects*

Ten experiments were performed on ten healthy human volunteers (six female and four male, ages 21-50 years). 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 and behavioral tasks*

Subjects were comfortably seated in a dental chair with the forearm and wrist supported on an adjustable platform and stabilized in a vacuum pillow and foam padding. Restraints were used to secure the wrist and hand in a position of  $\sim 70^\circ$  of forearm supination. Subjects performed a task to mimic precision grip by pinching the thumb and

index finger of the right hand towards each other against the resistance of two separate isometric force transducers attached to the two digits. This was done under two conditions. For one condition, the thumb and index digit pads exerted force against leather cuffs that encircled the volar surfaces of the distal phalanges and were attached to force transducers via nylon string. We refer to this as the Pad Contact condition (Fig. 6.1A). The second condition was one in which small plastic fittings were glued to the fingernails and were attached to the force transducers to eliminate input from the digit pads during the grip task. We refer to this situation as the No Pad Contact condition (Fig. 6.1B). For both conditions, the task involved a weak “grip” sustained for three to four minutes. Because the joint orientations and magnitudes of exerted forces were similar across conditions, the activities in muscle and joint receptors were comparable for the two conditions. The No Pad Contact condition, therefore, differed from the Pad Contact condition primarily by the absence of activity in finger pad tactile afferents and by the presence of activity in nail-bed afferents associated with the novel circumstance of tensile forces set up between the finger nail and the nail bed. Because the forces exerted were weak (see below), subjects did not report discomfort associated with the No Pad Contact condition. The advantage of this mechanical approach over an anesthetic one was that we could readily switch between tactile feedback conditions. This enabled, in many cases, the testing of the same pair of motor units under both conditions.



**Figure 6.1.** Experimental set up for recording motor-unit activity simultaneously from a thumb flexor (FPL) and index-finger flexor (FDP2) during a simulated pinching task. A rubber ball mounted on a frame and pressed into the palm helped secure the hand in a semi-supinated position. For one condition (**A**), the volar surfaces of the index finger and thumb exerted force against thin leather cuffs that were attached by string (arrows) to two force transducers. For the second condition (**B**), fittings glued to the fingernails were attached by string to the force transducers. In this latter condition, tactile afferents from the pad of the digits were not activated during the pinching task.

#### *Force and EMG recording*

Flexion forces of the digits were measured as described in the General Methods section of Chapter 3. Each transducer was aligned with the distal phalanx of the

associated digit along the direction of pull generated during the precision grip task (Fig 6.1).

Single-unit EMG activity was recorded with microelectrodes inserted into the FPL and FDP2 muscles of the thumb and index finger, respectively (Fig. 6.1), (see General Methods, Chapter 3). Microelectrode placement and verification was performed as described in the General Methods section of Chapter 3.

### *Protocol*

Subjects initially performed weak isometric flexion of the thumb and index finger in a simulated precision grip, to activate the FPL and FDP2 while the microelectrodes were manipulated until the potentials of at least one motor unit could be identified in each muscle. Subjects then sustained the grip (generally  $< 1$  N exerted by each digit) for three to four minutes. Subjects received audio and visual feedback of the discharging motor units and were instructed to keep the units firing at steady rates during the trial. Between trials, the connections between the force transducers and either the finger cuffs or the nail fittings were switched, alternating between conditions with pad contact and no pad contact of the digit pads. In an attempt to record from the same pair of units across conditions, care was taken between trials to maintain the same digit positions to minimize disruption of electrode placement. This was not always successful as one or both units tracked under one condition were sometimes lost during the subsequent trial to test the other condition. The order of tactile conditions alternated trial-by-trial between Pad Contact and No Pad Contact conditions. After each pair of conditions, the microelectrodes were repositioned until the action potentials of presumed new motor

units were identified, occasionally necessitating removal and reinsertion of the microelectrode at a new site. Each experiment lasted for up to two hours during which multiple trials were recorded.

#### *Data analysis*

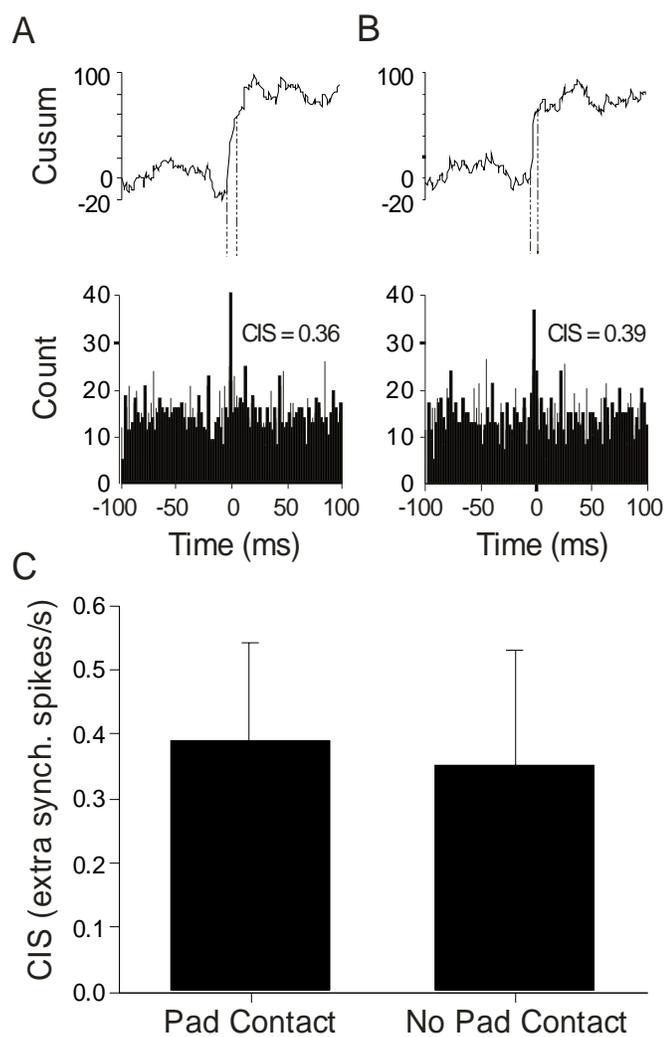
The discharges of individual motor units were identified, cross-correlograms were generated, and calculations of the central correlogram peak magnitudes were performed as described in the General Methods section of Chapter 3.

A Student's *t*-test was used to compare the CIS values for all recordings during digit pad contact to recordings with no digit pad contact. Values are reported as means  $\pm$  standard deviation with a probability of 0.05 as the level of statistical significance.

## **RESULTS**

A total of two hundred single motor units were recorded (98 from FPL and 102 from FDP2) during 78 trials, yielding 100 cross correlation histograms. In 22 trials, more than one motor unit was discriminated on an electrode, leading to multiple correlations. The mean firing rate for all recorded units was  $10.4 \pm 1.6$  Hz and the mean coefficient of variation in interspike intervals was  $0.17 \pm 0.04$ .

Figure 6.2 shows example cross-correlation histograms generated from FPL - FDP2 motor unit pairs, during Pad Contact (Fig. 6.2A) and No Pad Contact (Fig. 6.2B) conditions. The magnitude of motor unit synchronization was similar across the tactile conditions for these two trials (Pad Contact CIS = 0.36, and No Pad Contact CIS = 0.39).



**Figure 6.2.** Example cross-correlograms and associated CUSUMs for FPL-FPD2 motor unit pairs during pinching task in the Pad Contact (**A**) and No Pad Contact conditions (**B**). (**C**) The mean (SD) CIS values for all pairs of motor units recorded during Pad Contact and No Pad Contact Conditions.

Of the 100 FPL-FDP2 cross-correlation histograms constructed, 48 were from motor unit pairs recorded during the Pad Contact condition and 52 from the No Pad Contact condition. A *t*-test revealed no significant difference in the mean CIS across the tactile conditions ( $0.39 \pm 0.15$  for Pad Contact and  $0.35 \pm 0.18$  for No Pad Contact). A subset of 20 pairs of motor units were recorded during both tactile conditions. A *t*-test

also revealed no significant difference in the mean CIS values for this subgroup of motor units across conditions ( $0.43 \pm 0.11$  for Pad Contact and  $0.41 \pm 0.14$  for No Pad Contact).

## **DISCUSSION**

The main finding of the present study was that synchrony of motor unit pairs residing in thumb and index finger flexor muscles, FPL and FDP2 respectively, was not significantly different during gripping with digit pad contact compared to gripping with tactile input from the digit pads eliminated. Although a substantial degree of synchrony was found in both conditions, the elimination of tactile input did not significantly modulate the motor unit synchrony measured. Therefore, engagement of divergent synaptic inputs that appear to couple together the activities of the thumb and index finger muscles during gripping tasks (Winges and Santello 2004; Hockensmith et al. 2005) does not appear to depend directly upon feedback from tactile receptors.

Narrow synchronous peaks revealed in cross-correlation analysis of the discharge times of motor-unit pairs reflect primarily the extent of *last-order* inputs concurrently received by the associated motor neurons (Kirkwood et al. 1982). In concept, then, last-order inputs that ramify to supply both the FPL and FDP motor nuclei and which likely underlie the synchrony observed in the present study could originate from the cerebral cortex (Fetz and Cheney 1980), from propriospinal neurons (Sasaki et al. 2004), from segmental spinal interneurons (Jankowska 1992), or from peripheral sensory afferents (Mendell and Henneman 1971). Furthermore, because the relationship between the arrival of a common synaptic potential and the induction of synchronous discharge between two motor neurons is probabilistic and relatively weak (Kirkwood 1979), it

would seem necessary that the sources of common input be persistently active throughout the gripping task. Such a requirement would likely exclude a primary role of rapidly adapting tactile afferents in mediating the synchrony observed in the present study because such afferents are relatively silent during sustained periods of unperturbed gripping tasks (Westling and Johansson 1987; Macefield et al. 1996a). Slowly adapting tactile afferents, on the other hand, and in particular those characterized as having large receptive fields (i.e. SAII type), are tonically active during static gripping (Westling and Johansson 1987; Macefield et al. 1996a) and also appear to elicit short latency excitatory responses in motor neurons supplying muscles involved in gripping tasks (McNulty et al. 1999). Consequently, SAII tactile afferents would seem to be suitable candidates to provide divergent and sustained excitatory input to motor neurons supplying thumb and index finger muscles. While it is unlikely that such tactile afferents would provide direct synaptic input onto motor neurons, they might engage specific spinal interneurons whose axons ramify to supply FPL and FDP2 motor nuclei with common synaptic input.

The removal of normal tactile activity arising from the pads of the index finger and thumb in the present experiments, however, did not disrupt synchronous activity between FPL and FDP2 motor units. Consequently, we can conclude that the last order spinal or cortical neurons that provide divergent excitation across the FPL-FDP2 motor nuclei during sustained gripping tasks do not require input from tactile afferents in order to be activated. This is not to suggest that tactile input has an ancillary function in the control of the precision grip. Rather, feedback from tactile receptors appears to play a crucial role in facilitating the subtle moment-to-moment adjustments in grip forces

associated with dynamic manipulative tasks (Johansson and Westling 1984; Westling and Johansson 1984; Johansson and Westling 1987; Westling and Johansson 1987).

**CHAPTER 7: MOTOR UNIT SYNCHRONY ACROSS THE INTRINSIC  
MUSCLES, ADDUCTOR POLLICIS AND FIRST DORSAL INTEROSSEOUS,  
DURING PRECISION GRIP IN HUMANS**

## **ABSTRACT**

Short-term synchrony was measured for pairs of motor units located within and across intrinsic hand muscles activated during a precision grip task of the thumb and index finger. Surprisingly, little synchrony was found for pairs of units residing in the adductor pollicis muscle of the thumb and the first dorsal interosseous muscle of the index finger during the precision grip task. These results imply that the motor nuclei supplying the intrinsic muscles used in the precision grip receive relatively segregated synaptic inputs. The potential role of the intrinsic muscles in relation to the extrinsic muscles active in precision grip is discussed.

## **INTRODUCTION**

Exquisite volitional control of individual finger movements is a unique characteristic of hand dexterity in humans and some non-human primates. The precision grasp of an object between the thumb and index finger is executed using multiple muscles in the forearm and hand (Schieber 1995; Maier and Hepp-Reymond 1995a). The mechanism by which the CNS coordinates the activity of these muscles during grasping or other motor behaviors is not fully understood. However, as discussed in Chapter 2, a generally accepted idea is that the ability to differentially control digits and even segments of a single digit, relies in part upon monosynaptic and disynaptic connections between the motor cortex and the motor neurons innervating muscles of the hand (Heffner and Masterton 1983; Bortoff and Strick 1993; Porter and Lemon 1993; Sasaki et al. 2004). Thus, two schemes of CNS organization might encompass a range of mechanistic possibilities in the selection of specific muscle combinations needed to

perform particular tasks (Schieber 1990; Hepp-Reymond et al. 1996). In one scheme, the selection occurs through activation of separate corticospinal pathways that each recruit a specific muscle needed to perform the task. In the other scheme, muscle selection occurs through the divergent pattern of descending pathways across multiple motor nuclei (Fetz and Cheney 1980; Shinoda et al. 1981; Buys et al. 1986). Such a scheme might lead to reliable, yet less flexible, activation of sets of muscles needed to perform a task.

Fundamental to stable and accurate precision grip is the development of normal forces on the index finger and thumb (Forsberg et al. 1991). During precision grip of moderate or high force, extrinsic hand muscles that reside in the forearm yet act to flex the digits are considered to provide the primary grip force, while intrinsic muscles that reside within the hand primarily act to position and stabilize the digits (Long et al. 1970; Chao et al. 1989). However, during a low-force precision grip task, intrinsic muscles acting on the thumb and index finger appear to play a significant role in generating small and finely graded grip forces (Maier and Hepp-Reymond 1995a; Maier and Hepp-Reymond 1995b). Therefore, the tight coordination of the thumb and index finger forces required for precision grip might be accomplished through activation of a descending pathway that diverges to supply common input to the spinal motor nuclei innervating the intrinsic muscles like that known to supply motor nuclei acting on extrinsic muscles to the thumb and index finger (Hockensmith et al. 2005).

Therefore, in order to gain insight into the mechanism by which the CNS activates groups of muscles during a stereotyped manual task, we evaluated the extent of common input to motor pools supplying the intrinsic index finger flexor and abductor, first dorsal

interosseous, (FDI) and the intrinsic thumb adductor, adductor pollicis longus (AdP) during precision grip. The degree of common, last-order synaptic input was estimated from the magnitude of short-term synchrony of the firing times of motor-unit pairs recorded from the two muscles (Sears and Stagg 1976; Kirkwood and Sears 1978). For comparison, synchrony was also measured during a non-grip task that mimicked the positions of the digits during the grip task.

## **MATERIALS AND METHODS**

### *Subjects*

Sixteen experiments were performed on the dominant right hands of 10 healthy human volunteers (6 females, 4 males) between the ages of 23 and 57 years. 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 arm supported on foam padding on a horizontal platform and comfortably positioned with the shoulder slightly flexed and abducted, the elbow flexed to 120° in reference to the humerus, the forearm in neutral pronation/supination and wrist in the resting position of slight extension (~10°).

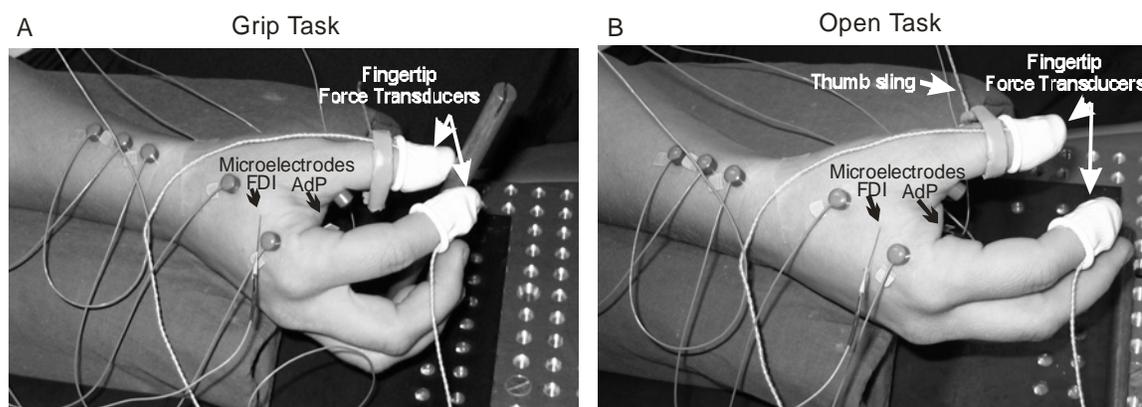
### *Force and EMG recording*

Single-unit EMG activity was recorded percutaneously from the AdP and FDI muscles. Microelectrode placement and verification was performed as described in the General Methods section of Chapter 3 (Fig. 7.1A, B). Each microelectrode was adjusted in depth and/or angle of position until an individuated thumb adduction (for AdP) or

index finger abduction (for FDI) was observed in response to stimulation. In a subset of experiments thumb and index finger tip forces were measured during the *Grip* task using thin, conformable force transducers (ConTacts C500, 0.8 mm thick, 0-40 N; Pressure Profile Systems, Inc., Los Angeles, CA) placed over the pads of each digit and held in place by latex finger cots (Fig. 7.1A, B).

### *Protocol*

Subjects were instructed to lightly grasp a wooden dowel (1.0 cm in diameter) between the thumb and index finger, keeping the remaining three fingers from contacting either the dowel or the grasping digits, constituting the *Grip* task (Fig. 7.1A). For the *Open* task, subjects were instructed to approximate the position when grasping the dowel, but to do so without allowing contact of the thumb and index pads, necessitating isometric co-contraction of muscles stabilizing the thumb and index finger (Fig. 7.1B). Occasionally, subjects had difficulty maintaining firing of the AdP in the *Open* task. In these cases, subjects were allowed to adduct the thumb against a thumb-sling anchored to a post fixed on the platform. The microelectrodes were gently manipulated during the contraction 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 or maintain a weak contraction that mimicked grasp such that motor units detected on both electrodes remained active. Intramuscular EMG signal recording, processing, and other aspects of the experimental protocol are as described in the General Methods section of Chapter 3.



**Figure 7.1.** Experimental arrangement and recording sites for two different tasks of the thumb and index finger. **A**, *Grip* task in which the subject grasps a dowel between the thumb and index finger. Note the force transducers attached to the tips of each digit. **B**, *Open* task in which the subject contracts the same muscles used when grasping the dowel, but to do so without allowing contact of the thumb and index pads, necessitating isometric co-contraction of muscles stabilizing the thumb and index finger. Note use of the thumb sling to assist isometric contraction of the thumb adductor for the duration of the recording (5 min).

#### *Data analysis*

The discharges of individual motor units were identified, cross-correlograms were generated, and calculations of the central correlogram peak magnitudes were performed as described in the General Methods section of Chapter 3. Briefly, cross-correlograms were generated from the relative discharge times of motor units recorded on separate electrodes, the central synchrony peaks of the histograms were identified using the cusum procedure (Ellaway 1978), and the magnitude of each peak was quantified using the common input strength (CIS) index of synchrony (Nordstrom et al. 1992). In the cases of nonsignificant peaks in the histogram, CIS was calculated for an 11 ms region of the histogram centered at time zero (Semmler and Nordstrom 1995). Synchrony peaks were

determined to be significant if the average number of counts in the peak region was  $> 3$  SD's above the mean count ( $z$  score  $\geq 1.96$ ) (Schmied et al. 1993).

Spike-triggered averaging of the surface EMG to single motor unit spikes was performed after each experimental session to verify that each motor unit pair recorded was not duplicated in subsequent trials of the same experiment. Duplicated motor-unit pairs were then dropped from further analysis.

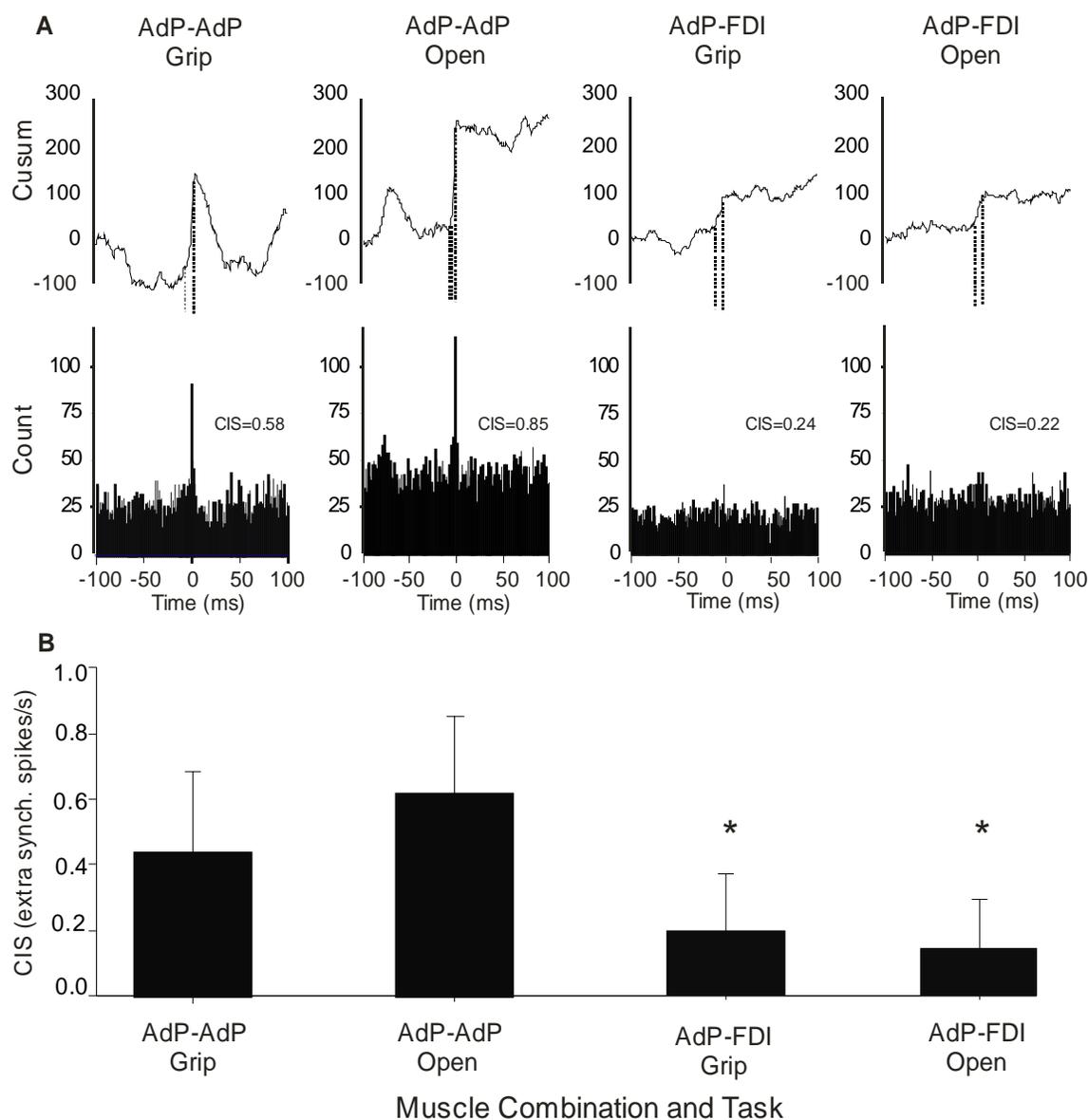
A one-way ANOVA was used to determine whether mean CIS values were significantly different among the combinations of paired motor unit recordings during the different tasks: both units within AdP during the *Grip* (AdP-AdP Dowel) and *Open* (AdP-AdP Open) tasks, and one unit each in AdP and FDI during the *Grip* (AdP-FDI Dowel) and *Open* (AdP-FDI Open) tasks. Tukey's *post hoc* analysis was used to identify differences in CIS across motor-unit combinations and tasks. Comparisons of the cross-correlogram peak durations for all combinations of unit pairs were made using a one-way ANOVA and Dunn's *post hoc* analysis. Values are reported as means  $\pm$  SD with a probability of 0.05 selected as the level of statistical significance.

## **RESULTS**

A total of 198 motor units were recorded from ten subjects during 86 trials of grip and open tasks 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 tasks ( $< 1.5$  N). The discharge rate for all motor units was  $10.4 \pm 1.8$  Hz, and the average number of spikes used in the analysis was  $4073 \pm 1950$ . The discharge times of units detected on separate electrodes were used to generate 106 cross-correlograms. In 21 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 pairs of units both within AdP (12 during the *Grip* task and 24 during the *Open* task) and 70 correlograms were for AdP-FDI unit pairs (36 recorded during the *Grip* task, and 34 during the *Open* task). The mean CIS value for all within-muscle unit pairs (AdP-AdP) was  $0.55 \pm 0.24$  and for all across-muscle unit pairs (AdP-FDI) was  $0.17 \pm 0.17$ .

Figure 7.2A shows example cross-correlograms for the different combinations of motor unit pairs during two tasks of the thumb and index finger. A prominent central peak was seen in the cross-correlogram, indicating a high degree of synchrony for the pairs of motor units both residing within the same muscle (Fig. 7.2A, AdP-AdP Grip and AdP-AdP Open), as has been shown previously in the FDI (Datta and Stephens 1990; Nordstrom et al. 1992). The synchrony was considerably less, however, for unit-pairs across intrinsic muscles during both tasks (AdP-FDI Grip and AdP-FDI Open) (Fig. 7.2A). Figure 7.2B shows the mean  $\pm$  SD CIS values for pairs of motor units located within AdP and across AdP-FDI muscles during different tasks of the thumb and index finger. There was no significant difference ( $p = 0.121$ ) in CIS between unit pairs recorded from within the AdP during the task of grasping the dowel ( $0.44 \pm 0.24$ ) compared to the *Open* task ( $0.61 \pm 0.23$ ). Likewise, there was no significant difference ( $p = 0.250$ ) in CIS between AdP-FDI unit pairs recorded during the *Grip* ( $0.14 \pm 0.15$ ) versus the *Open* task ( $0.20 \pm 0.18$ ), although both were significantly less ( $p < 0.001$ ) than the AdP-AdP unit pairs during either task.



**Figure 7.2.** CIS for pairs of motor units located within AdP and across AdP-FDI muscles during different tasks of the thumb and index finger. **A**, Example cross-correlograms for pairs of motor units located both within AdP during the *Grip* task (AdP-AdP Dowel) and *Open* task (AdP-AdP Open), and with one unit each in AdP and FDI during the *Grip* task (AdP-FDI Dowel) and the *Open* task (AdP-FDI Open). The traces above each correlogram are the cusum used to delineate the central peak (dashed lines) of the correlogram. **B**, Mean  $\pm$  SD CIS values for the four combinations of motor unit pairs and task. synchron., Synchronous.

A large proportion of the cross-correlogram peaks were significant (see General Methods, Chapter 3) for the AdP-AdP motor unit pairs (89%), yet only 23% of the cross-correlogram peaks for the AdP-FDI unit pairs were significant. The durations of the correlogram peaks were relatively brief for all unit pair combinations ( $10.1 \pm 6.9$ ,  $8.4 \pm 2.2$ ,  $13.2 \pm 5.7$ , and  $12.4 \pm 6.7$  for AdP-AdP *Grip*, AdP-AdP *Open*, AdP-FDI *Grip*, and AdP-FDI *Open* combinations, respectively). The duration of the correlogram peak for the AdP-AdP unit pairs during the *Open* task was moderately, but significantly less ( $p < 0.05$ ) than for the AdP-FDI unit pairs during the *Grip* task. No other differences were significant.

## **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. Unexpectedly, we found a low level of synchrony between motor unit pairs across AdP and FDI, 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). Our results imply that the tightly coupled digit tip forces associated with a precision grip are not a consequence of common last-order synaptic input onto the motor pools supplying the AdP and FDI muscles.

### **Biomechanical and task considerations**

For the *Grip* task, subjects were asked to grasp the dowel between the tips of the thumb and forefinger with at least enough force to prevent slippage of the dowel and instructed to prevent collapse of the distal IP joints into full extension, which would change the task from a tip precision grip to a pulp precision grip (see the Classification of Grasp section of Chapter 2). No other instructions were given, or physical constraints used, which would preclude normal positioning of the multi-joint systems of the thumb and forefinger. Thus, although the tips of the thumb and index finger were in stable contact with the dowel and relatively stable with respect to one another, the more proximal segments of each digit were not constrained and slight positional adjustments in these segments were occasionally observed. For the *Open* task, subjects did not have an object (dowel) against which the index finger and thumb could develop matching contact forces, as was available in the *Grip* task. The gripping-type forces developed in the *Open* task, were matched instead, by the cocontraction of other muscles acting antagonistically to the AdP and FDI.

### **Implications of across-muscle synchrony**

Substantial synchrony has previously been shown to exist for motor-unit pairs within the FDI muscle (Datta and Stephens 1990; Bremner et al. 1991a; Nordstrom et al. 1992). The few studies that have investigated motor unit synchrony across muscles indicate that neighboring muscles, or muscles with similar actions, often exhibit significant synchrony that is generally half the level of synchrony found for unit pairs within a muscle (Bremner et al. 1991b; Maier and Hepp-Reymond 1995a; Huesler et al. 2000). The implication of significant motor unit synchrony across muscles is that the

separate motor neuron pools receive substantial common synaptic input to facilitate cooperative or synergistic muscle activity. Similar to previous studies, we found a high level of synchrony for unit pairs within AdP (CIS = 0.55), but only about a third the level of synchrony for pairs across AdP-FDI (CIS = 0.17) during a precision grip. Thus, our hypothesis of a substantial motor unit synchrony across the two intrinsic muscles with the highest correlation of EMG activity to precision grip force, AdP and FDI (Maier and Hepp-Reymond 1995a), was not supported by the present findings.

### **Task-dependence of synchrony**

A previous study by Bremner et al. (1991c) indicated that the degree of synchrony among motor units within an intrinsic hand muscle varied systematically depending on the type of task performed by the digits. The implication of that finding was that different tasks were associated with the activation of different descending pathways with different patterns and extents of divergence across spinal motor neurons. In the present study, we found no task-related difference in the magnitude of motor unit synchrony within the AdP or across AdP and FDI during precision grip of a dowel compared to the *Open*, non-grip task. It may be that our two tasks (*Grip* vs. *Open*) were not different enough to affect a change in the descending pathways activated. On the other hand, we and others have previously not been able to demonstrate a task-dependent effect on motor-unit synchrony under a variety of other task conditions (Winges and Santello 2004; McIsaac and Fuglevand 2006 accepted; McIsaac and Fuglevand 2005). Therefore, the generality of task-dependent switching in the descending pathways engaged (as reflected by changes in motor-unit synchrony) remains unresolved and warrants further exploration.

### **Roles of intrinsic and extrinsic muscles in precision grip**

Previous studies that have investigated the respective roles of intrinsic and extrinsic hand muscles activated during a precision grip have yielded mixed results. Conclusions drawn by Chao et al. (1989) from biomechanical studies of the index finger and thumb during precision grip, and by Long et al. (1970) from EMG studies of muscle activation during grip and manipulation tasks, agree that extrinsic muscles provide the primary grip force while the intrinsic muscles primarily act to position and stabilize the digits, and only secondarily contribute to grip force through thumb adduction (AdP) and index flexion at the MCP joint. However, Maier et al. (1995a) found that the AdP and FDI appeared to play significant roles in generating small and finely graded grip forces during a low force precision grip task ( $\leq 10\%$  maximum voluntary contraction). Moreover, Maier et al. (1995a) found that the highest correlations between EMG activity and grip force for AdP and FDI among the seven intrinsic and eight extrinsic muscles tested. Using cross-correlation analysis of multi-unit EMG signals, Maier et al. (1995b) reported synchrony between AdP and FDI in 83% of the experimental sessions, although how synchrony was quantified was not specified. In contrast, we found the magnitude of the motor unit synchrony across the intrinsic muscles AdP and FDI (mean CIS = 0.17) was less than half the magnitude of synchrony found across two extrinsic muscles that are also involved in generating a precision grip, FPL and FDP2 (mean CIS = 0.48, Winges and Santello 2004; mean CIS = 0.42, Hockensmith et al. 2005; mean CIS = 0.36, McIsaac and Fuglevand 2005). Taken together, these results support the idea that in the precision grip, divergent synaptic inputs serve to link together the activities of the

extrinsic muscles that generate grip forces in order to tightly coordinate the forces developed on each digit. On the other hand, intrinsic muscles appear to be much more independently controlled enabling the positioning of the digits in a wide array of configurations needed for gripping objects of various shapes and sizes.

### **Intrinsic thumb muscle behavior**

Although the grip force of the thumb acts at the tip-object interface, this output force is generated through a complex interaction of four intrinsic and four extrinsic thumb muscles, most of which span more than a single joint (Chao et al. 1989; Brand and Hollister 1999; Kaufman et al. 1999; Valero-Cuevas et al. 2003). As described in the Biomechanical Consideration section of Chapter 2, the complexity of the relationship between the activity of thumb muscles and the resultant output pinch force is highlighted by the results of Pearlman et al. (2004), in a study in which they found a non-linear relationship between intrinsic muscle tendon tension and thumb-tip output force. We, likewise, often noticed behavior of the AdP firing frequency relative to the force produced at the thumb-dowel interface that did not always appear to be a purely positive relationship. Several subjects reported occasionally having difficulty maintaining a steady firing of the AdP muscle, despite keeping a steady grip force. They described needing to “slightly reposition the thumb”, particularly with respect to CMC and MCP rotation, in order to reactivate the discharge of spikes that had ceased with no detectable change in the output force at the thumb tip. These observations support the idea that intrinsic muscles, particularly those of the thumb, are more involved in positioning of the digits than in contributing to steady contact forces between the digits and object.

## **Conclusion**

The degree of motor-unit synchrony across intrinsic muscles of the thumb (AdP) and index finger (FDI) that are active during precision grip was found to be low in the present study, implying that control of these muscles in grip force generation is not mediated by divergent descending inputs across their spinal motor pools. Extrinsic muscles, however, have previously been shown during precision grip to demonstrate significant across-muscle motor unit synchrony, implying a control strategy involving common last-order inputs across the FPL and FDP2 spinal motor pools. Therefore, it seems reasonable that the extrinsic thumb and index finger muscles are tightly coordinated by descending divergent input to couple and match the tip forces, whereas the intrinsic thumb and index finger muscles are more independently controlled to enable gripping of objects of different shapes. This independent control strategy may apply to a greater extent among the intrinsic thumb muscles, given the complexity of the musculoskeletal biomechanics of the thumb.

**CHAPTER 8: SUMMARY AND CONCLUSIONS**

The human hand, as the great physiologist and surgeon, Sir Charles Bell (1837), described, “is so beautifully formed,...its actions are so powerful, so free, and yet so delicate, as if it possessed a quality of instinct in itself, that there is no thought of its complexity as an instrument,...” (p. 16). As such, studies of the hand as a complex instrument have intrigued investigators for many years. The dexterous and highly coordinated movements of the hand provide humans with a wide repertoire of behaviors, such as communicating through sign language, manipulating coins while paying a bill, and tying shoelaces. In an effort to understand how the nervous system coordinates multiple muscles in the production of tasks such as these, the studies of this dissertation were designed to identify some of the neural mechanisms whereby hand muscles are recruited into functional groups, or muscle synergies, during voluntary motor behaviors of the hand and fingers.

The theoretical framework underpinning these studies related to two possible strategies by which the CNS might select muscles needed to perform a motor behavior. In one, the selection occurs supraspinally and depends on which corticospinal neurons are activated which in turn target specific motor nuclei to engage individual muscles in the task. In the other, selection occurs more at a spinal level by the pattern of divergence of the descending pathways across multiple motor nuclei to activate multiple muscles (Schieber 1990). The concept of motor unit synchrony was introduced as a method by which to estimate the degree of divergence of the last-order synaptic inputs onto motor neurons, and the technique of cross-correlation analysis was used to measure the strength of motor unit synchrony.

The first objective of this dissertation was to characterize the organization of inputs onto motor neurons supplying the multi-tendoned finger flexor muscle, the FDS. Similar to the two other multi-tendoned hand muscles (ED and FDP), the last-order projections to FDS motor neurons were found to be largely segregated to supply subsets of motor neurons innervating different compartments. The general pattern of synchrony was greatest for pairs of units within a digit-compartment and progressively less for pairs of units in compartments to fingers further apart, implying more independent control of fingers further apart. Comparison of synchrony patterns across the extensor, ED, and the two flexors, FDP and FDS, revealed the idea that there is less motor unit synchrony in the finger flexors compared to the extensors. In general, this finding implies there is greater independence and control of the digital compartments of the flexor muscles than the extensor muscles of the fingers (Bremner et al. 1991b; Porter and Lemon 1993).

These findings of synchrony patterns among the three multi-tendoned extrinsic hand muscles raised the question of synchrony across the two flexors, FDP and FDS. The level of synchrony of motor-unit pairs in different muscles, yet in compartments that each inserted onto the same finger, was very low. These results suggest that neural control of the FDP and FDS muscles to a single digit are relatively independent, despite the tight coupling of the proximal and distal IP joint movements and the high correlation of muscle activity found during finger flexion in previous studies (Darling et al. 1994). Thus, a high degree of motor-unit synchrony across FDS and FDP to the same finger is not required for coordinated finger flexion. Indeed, such coupling might limit the flexibility of muscle synergies needed for grasping under different conditions. Perhaps

the greater levels of synchrony found across digit-compartments within a muscle than was found across different muscles to the same finger reflects a strategy by which the CNS assures multi-digit control in grasp and manipulation while allowing flexibility of individual finger orientation and positioning.

The fine control of force-matching required during a precision grip between the index finger and thumb (Westling and Johansson 1984) might be mediated by divergent, descending pathways which engage the index-finger and thumb flexors as a muscle synergy (Hockensmith et al. 2005). While the origin of this divergent input is likely to be cortical, is it possible that tactile afferents in the distal pads of the index finger and thumb could provide a potent influence on motor neurons that are also associated with triggering and scaling grip force to prevent slip during a precision grip task (Johansson and Westling 1987; Macefield et al. 1996a). Upon investigation of this hypothesis, it was found that removal of the normal tactile activity from the digit pads did not disrupt the synchronous activity between motor unit pairs in the muscles flexing the tips of the thumb and index finger (FPL and FDP2). Consequently, we can conclude that the last order spinal or cortical neurons that provide divergent excitation across the FPL-FDP2 motor nuclei during sustained gripping tasks do not require input from tactile afferents in order to be activated. This is not to suggest that tactile input has an ancillary function in the control of the precision grip. Rather, feedback from tactile receptors appears to play a crucial role in facilitating the subtle moment-to-moment adjustments in grip forces associated with dynamic manipulative tasks (Westling and Johansson 1984; Johansson and Westling 1987 1987).

Although tactile afferent information did not mediate the degree of synchrony across the extrinsic muscles (FPL and FDP2) used in a precision grip task, the level of synchrony was substantial in both conditions. Little is known, however, about the control of the intrinsic muscles used in precision grip. Therefore, the final study of this dissertation examined the neural coupling of two intrinsic hand muscles that are active during a precision grip task (AdP and FDI) (Close and Kidd 1969; Long et al. 1970; Chao et al. 1989; Maier and Hepp-Reymond 1995a). The degree of motor unit synchrony across intrinsic muscles of the thumb (AdP) and index finger (FDI) was found to be low, in contrast to the high level of synchrony found across extrinsic muscles (FPL and FDP2). Therefore, extrinsic thumb and index finger muscles appear to be tightly coordinated by descending divergent inputs in order to precisely match the magnitudes of contact forces exerted by the thumb and index finger on the grasped object. The intrinsic thumb and index-finger muscles, however, are more independently controlled to provide positional adjustments of the joints in each digit and to more finely tune the tip forces of the precision grip.

## APPENDIX A: HUMAN SUBJECTS COMMITTEE APPROVAL

Human Subjects Committee

1622 E. Mabel St.  
P.O. Box 245137  
Tucson, Arizona 85724-5137  
(520) 626-6721

27 April 1999

Andrew Fuglevand, Ph.D.  
Department of Physiology  
Gittings Building, 117  
PO BOX 210093HSC #99-55 COORDINATION OF MUSCLE ACTIVITY DURING FINGER  
MOVEMENTS

Dear Dr. Fuglevand:

We received your 14 April 1999 letter and accompanying revised consent form for the above referenced project. All of the conditions as set out in our 23 March 1999 letter to you have been met. Therefore full Committee approval for this subjects-at-risk project is granted effective 27 April 1999 for a period of one year.

The Human Subjects Committee (Institutional Review Board) of the University of Arizona has a current assurance of compliance, number M-1233, which is on file with the Department of Health and Human Services and covers this activity.

Approval is granted with the understanding that no further changes or additions will be made either to the procedures followed or to the consent form(s) used (copies of which we have on file) without the knowledge and approval of the Human Subjects Committee and your College or Departmental Review Committee. Any research related physical or psychological harm to any subject must also be reported to each committee.

A university policy requires that all signed subject consent forms be kept in a permanent file in an area designated for that purpose by the Department Head or comparable authority. This will assure their accessibility in the event that university officials require the information and the principal investigator is unavailable for some reason.

Sincerely yours,

John D. Palmer, Ph.D., M.D.  
Chairman  
Human Subjects Committee

JDP:rs

Departmental/College Review Committee

DUE DATE:  
15 APRIL 2005

HUMAN SUBJECTS COMMITTEE  
PERIODIC REVIEW FORM

APPROVAL EXPIRES:  
4/27/2005

Andrew Fuglevand/#99-55/Physiol/Coordination of Muscle Activity During Voluntary Movements  
NAME OF INVESTIGATOR/PROJECT APPROVAL NUMBER/TITLE OF PROPOSAL

Human subjects approval for this activity expires on the date indicated above. Depending upon the activity status of the project, attachments may be required. Refer to IRB website ([www.irb.arizona.edu](http://www.irb.arizona.edu)) for detailed instructions. **Note:** If renewal is not granted before the expiration date, all study activities must stop at that time. If study procedures/treatment must be continued for subject safety, contact the IRB office immediately.

**Activity Status – check one box only**

Category A: attach items 1-13 listed on reverse

- Enrollment of new subjects in progress
- Enrollment not initiated, but still planned
- Enrollment closed to new subjects but current subjects are still undergoing study procedure or being entered into extensions and/or sub-studies

Category B: attach items 1-12 listed on reverse

- Enrollment closed, follow-up only (non-sensitive data collection via telephone contact, questionnaire and/or record review)
- Local data analysis only: no subject contact/no additional data collection (annual review required)

Category C: attach items 1-8 listed on reverse

- Concluded: enrollment and all participation/follow-up/local data analysis completed

Category D: no attachments required; complete and submit this form only

- Study not begun: permanent withdrawal of study

**Subject Numbers (local enrollment)**

If more than one study population is involved, report enrollment under number 2 of checklist (see reverse)

- a) Number of new subjects enrolled (consented) since last reporting period
- b) Total number of subjects enrolled (consented) since start of project
- c) Male/female ratio of total enrolled since start of project

84	
220	
126/94	

**Conflict of Interest Statement (COI):** see COI policies at [http://vpr2.admin.arizona.edu/rie/conflict\\_of\\_interest.htm](http://vpr2.admin.arizona.edu/rie/conflict_of_interest.htm)

- a) Do any of the investigators serve as a speaker or consultant to the sponsor, the manufacturer, or the owner of the test article?  Yes  No
  - b) Do any of the investigators (or their family members) derive a direct or indirect benefit equity and/or royalty relationship with the sponsor, manufacturer, or owner of the test article?  Yes  No
- If yes to either of the above, attach copy of U of A Conflict of Interest and Commitment Disclosure form.

*I certify that this research will be conducted in accordance with the currently approved protocol/amendments and that no changes to procedures or study documents will be made without the knowledge/approval of the IRB.*

Signature of Principal Investigator (required for all projects)	Date 4/5/05	Signature of Departmental Review Chair (not required for concluded or not begun studies)	Date 4-14-05
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<b>FOR COMMITTEE USE ONLY</b>	
<input checked="" type="checkbox"/> Approve <input type="checkbox"/> Disapprove Subject to the following conditions: N/A. Revised Consent Form (updating to current guidelines, including use of second person vs. first person), and personnel change (removing Soren Lowell) approved concurrently. Non-Competitive Renewal reviewed concurrently.	Period of Approval: <b>APR 27 2005</b> — <b>APR 27 2006</b>  Date Reviewed: <b>APR 26 2005</b>
David G. Johnson, M.D., Chair Biomedical/Continuing Review Committee	<input type="checkbox"/> Expedited Review <input checked="" type="checkbox"/> Full Committee Review

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