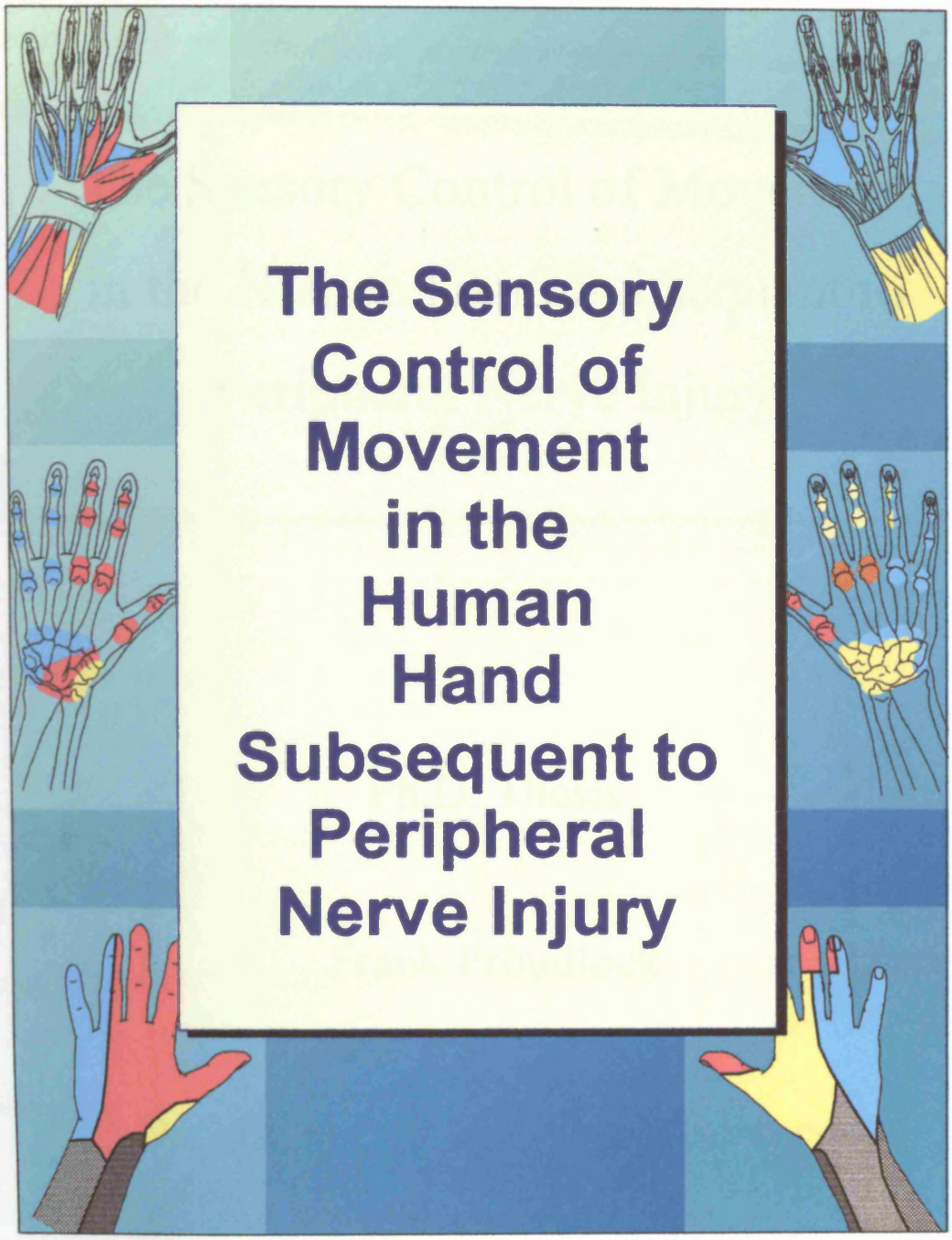
The Sensory
Control of
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in the
Human
Hand
Subsequent to
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The Sensory Control of Movement in the Human Hand Subsequent to Peripheral Nerve Injury

Ph.D. Thesis

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Contents

Abstract

This study presents the first comprehensive study into the recovery of kinaesthesia in man subsequent to peripheral nerve injury (PNI). An AC induction motor was used to apply movements to the models of the thumb carpometacarpal joint, little finger metacarpophalangeal joint and index finger metacarpophalangeal joint for investigating median, ulnar and mixed nerve (ulnar and median) innervation, respectively.

Thumb: High kinaesthetic acuity was present in the thumb following local anaesthesia of the median nerve. Median and radial nerve anaesthesia demonstrated that much of this remaining sensation was due to the contribution of the radial nerve. Kinaesthesia in median PNI subjects was characterised by high movement detection but inconsistent grading of movement.

Little Finger: Ulnar nerve anaesthesia resulted in profound kinaesthetic loss. Some subjects could detect at least some movements but could not grade amplitudes and velocities, sometimes sensing movements in the extension: flexion plane. Subsequent to ulnar PNI, kinaesthetic sensation varied from no sensation to kinaesthetic acuity approaching normal levels. Of the three models, the little finger provided the most complete model for assessing kinaesthetic recovery.

Index: Both ulnar and median nerve anaesthesia had a small but detrimental effect on the ability to sense movement in the index indicating that muscle and skin/joint proprioceptors both contribute to kinaesthesia. Median and ulnar nerve anaesthesia had opposite effects on the ability to grade movements, causing underestimation and overestimation of amplitudes, respectively. Median PNI resulted in variability in the ability to grade movement, whereas ulnar PNI resulted in consistent exaggeration of amplitude.

The three intrinsic muscles, abductor pollicis brevis, first dorsal interosseus and abductor digiti minimi all generated 8-10 Hz tremor, both in the normal hand, and subsequent to PNI and carpal tunnel syndrome (CTS). These findings provide further evidence for the central origin of 8-10 Hz pulsatile output.

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I would like to thank the staff of the Adrian building workshop for the care given to the construction of equipment and for the positive encouragement they have offered me in trying to explore novel ways of applying movements to human hands.

I am indebted to the many volunteers, members of staff and the general public, who have been willing to take part in the study. I would especially like to thank those volunteers who courageously offered themselves for application of local anaesthesia to the hand.

"In all thy ways acknowledge Him, and He shall direct Thy paths." Proverbs ch.3 v.6.

Commonly Used Abbreviations

Tests

Dn: Detection

VT: Visual Tracking

VR: Visual Repeat

IR: Ipsilateral Repeat

CR: Contralateral Repeat

MM: Movement Matching

0.5^{cutoff}: Percentage of moves responded to by the subject within a 0.5second time period

VRD: Visual Response Delay (time taken to respond to movement during VT test)

PRD: Proprioceptive Response Delay (time taken to respond during MM test)

Muscles

AbPB: Abductor Pollicis Brevis

AbDM: Abductor Digiti Minimi

1DI: First Dorsal Interosseus

AP: Adductor Pollicis

FPB: Flexor Pollicis Brevis

CHAPTER 1: INTRODUCTION

1.1. Overview

The human hand is a tool of unparalleled versatility. It is able to execute actions throughout the spectrum of human movement, coping with tasks as diverse as threading a needle to supporting one's own body weight. The unique capabilities of the hand are attributable to the fact that it acts as both a sensory and motor implement. When manipulating and palpating objects, the hand brings into contact a highly specialized receptor population giving it an essential role in sensory exploration. Yet, this sensory feedback also provides the basis for the extraordinary motor capabilities of the hand in the control of movement and force. Accordingly, the human hand represents an outstanding example of the integration of sensory and motor systems.

Proprioception is the sense of position, movement and force around the joints of the body. In hand function, proprioception permits the exploration of the physical qualities of objects, such as size, shape and mass. More importantly, proprioception has a crucial role in providing constant feedback of position, movement and force, for the fine control of movement. Proprioception, and in particular kinaesthesia (sense of movement), is dependent upon afferent input derived from mechanoreceptors present in muscles, joints and skin (Gandevia & Burke, 1992; Willis & Coggeshall, 1992).

Peripheral nerve injury (PNI) results in widespread sensory and motor loss due to axonal degeneration distal to the site of injury and consequent denervation of motor end plates and sensory receptors. The peripheral nervous system, however, has a potent regenerative capacity due to the ability of axons to sprout and regrow along remaining endoneurial tubes. Many studies have investigated reinnervation of proprioceptors in animal models, but no study has addressed the issue of how proprioception recovers at the level of human perception.

The human hand provides an excellent model for examining the recovery of proprioception following nerve injury, for a number of reasons:

- There is a wealth of experimental data concerning the relative contributions of proprioceptors found in skin, joint and muscle in the normal hand.
- The high frequency of occurrence of median and ulnar nerve injuries at wrist level permits ready investigation of the reinnervation of skin, joints and musculature of the hand.
- Because of the importance of proprioception for hand function, proprioceptive measures can be compared and correlated with clinical measures of hand function to give further insight into how the recovery of proprioception relates to hand function.

1.2. The Specialisations of the Human Hand

1.2.1. The Sensory Specialisations of the Human Hand

1.2.1.1. Sensory Receptors

The hand is the primary organ of touch, and the large surface area of the hand is densely innervated by highly sensitive and discriminative tactile mechanoreceptors (Johansson & Vallbo, 1980, 1983; Vallbo & Johansson, 1984). The median nerve for example, supplying a large proportion of palmar skin, innervates an estimated 17,000 tactile units (Johansson & Vallbo, 1979a). Moreover, these units have extremely low thresholds, and comparison of psychophysical touch thresholds with microneurographical recordings from cutaneous afferents indicate that the input from one afferent is sufficient to reach consciousness (Johansson & Vallbo, 1979b).

Intrinsic muscles of the hand also contain a disproportionately high concentration of receptors. Small distal muscles such as lumbricals or intrinsic thumb muscles, weighing only a few grammes, have as a similar number of muscle spindles and Golgi tendon organs as much larger forearm muscles (Scott & Panesar, unpublished observations)

1.2.1.2. Sensory Cortical Areas

Proprioceptive and tactile inputs project through the dorsal column-medial lemniscal pathway and terminate predominantly in the primary sensory cortex (S1), where the hand area has a particularly large representation (Pons *et al.,* 1987). Peripherally and centrally generated gating influences aid in discriminating between relevant and irrelevant information (Chapman, Tremblay & Ageranoiti-Bélanger, 1996). The hand representation of S1 has a distinctive hierarchical arrangement. Tactile and proprioceptive inputs are segregated in the rostral areas of the hand representation of S1 but are increasingly more integrated in caudal regions. Neurons of the caudal S1 have large, complex receptive fields, which respond to particular modes of action such as stretching, grasping and manipulation by the hand (Iwamaru *et al.*, 1993). The most caudal areas of S1 have a role in bilateral sensation in the hand (Iwamaru *et al.*, 1994, 1998).

Proprioceptive information is utilized by a number of cortical and subcortical structures. In the posterior parietal cortex, proprioceptive information is integrated with auditory and visual information for the recognition of objects (Stein, 1995, Andersen *et al.*, 1998). The cerebellum is thought to be involved in the predictive control of movement, integrating proprioceptive feedback with an efferent copy of outgoing commands to estimate the sensory outcome of the motor systems (Glickstein, 1998; Miall, 1998). The cerebellum may thus have a role in anticipatory control of grip force (Wing, 1996). The basal ganglia processes proprioceptive information to initiate and coordinate the control of movement (Mano, Hamada & DeLong, 1993). Both the cerebellum and basal ganglia receive proprioceptive inputs via the thalamus.

1.2.2. The Motor Specialisations of the Human Hand

1.2.2.1. Biomechanical Specialisations Of The Hand

A number of biomechanical specialisations are present in the hand, including:

- Its position at the most mobile extremity in the body (Kapandji, 1981).
- A large number of degrees of freedom provided by 19 bones and 17 articulations under the control of highly specialized intrinsic and extrinsic musculature.
- The highly mobile carpometacarpal joint of the thumb, which rotates the thumb throughout the range of circumduction, allowing opposition of the thumb with the other digits. (Brand & Hollister, 1993).
- The specialized gripping surface of the palmar hand which include papillary ridges to increase friction, cushion like palmar fat pads to provide resistance to pressure, and anchoring of the skin to the fascial plane (Thomine, 1981).

1.2.2.2. Cortical Control Of The Hand

The Corticomotoneuronal Projection

Although the hand possesses many anatomical specialisations, the versatility of the human hand is eminently determined by a powerful cortical control system exerting its influence through a direct pathway called the corticospinal (CS) tract. An all important component of the CS tract is the corticomotoneuronal (CM) projection which forms monosynaptic connections with the motoneurons of hand muscles (reviewed in Armand *et al.*, 1996; Lemon, 1993, 1997). The CM projection mediates independent control of the digits by the primary motor cortex. Four lines of evidence demonstrate that the CM projection is necessary for the performance of relatively independent finger movements (RIFM):

1. RESPONSE TO STIMULI: Activation of CM neurons by transcranial magnetic stimulation (TMS) elicits the largest responses in hand motoneurons (Rothwell *et al.*, 1991).
2. LESION STUDIES: Lesioning of the medullary pyramids in primates results in the loss of highly fractionated and skilled hand movements (Lawrence & Kuypers, 1968). Stroke induced lesions of M1 and its output pathways in humans, also cause preferential loss of function in the distal musculature of the upper limb (Turton *et al.*, 1996).
3. DEVELOPMENT: In the infants of monkey and man, CM connections appear in parallel with RIFM (Armand *et al.*, 1996).
4. COMPARATIVE ANATOMY: The extent of development of the CM system in primate species is correlated to manual dexterity (Armand *et al.*, 1996, Lemon, 1997).

Patterns of Synergy

Studies in the macaque have shown that neurons of the CS tract do not project to individual muscles, but rather to small groups of target muscles called muscle fields. This muscle 'synergy' has been demonstrated anatomically (Shinoda *et al.*, 1981) and physiologically, using spike triggered averaging techniques (Cheney & Fetz, 1985; Cheney, Fetz & Mewes, 1991). The muscle fields usually consist of anatomical or task related agonists.

The relationship between CM neurons and target motoneurons is surprisingly flexible. For example, in the primate, Lemon *et al.* (1986) have demonstrated that CM cells, which control hand muscles, fire during precision grip tasks but not during power grip tasks, although the amount of activity in the target muscle is usually higher. These task dependent, flexible synergies have also been demonstrated in the human, by correlating intramuscular EMG recordings from intrinsic muscles in both the amplitude and time domains (Hepp-Reymond, Huesler & Maier, 1996).

Multiple representations of muscles and movements within the motor cortex are thought to provide the basis for flexible synergies, so that CM connections converge onto hand motoneurons and affect the balance of a movement rather than have overall control (Lemon, 1993, Kleinschmidt, Nischke & Frahm, 1997). Bennett and Lemon (1996) have recently shown that certain CM projections appear to control temporal levels of activity in synergistic muscles and fire when the activity in two synergistic muscles is out of phase. It is suggested that the fast-conducting neurons of the CS tract may shape the pattern of muscle activity during RIFM, whereas slow-conducting neurons may provide background drive for the control of posture and grip force (Lemon, 1997).

The Consequences of Direct Cortical Control

The CM projection typically bypasses spinal mechanisms, to allow flexible cortical synergies to have their effect. This has a number of important consequences:

1. PROXIMAL AND DISTAL MUSCLES HAVE DIFFERENT SEGMENTAL CIRCUITRY

Illert, Kümmel & Scott (1996), list a number of anatomical differences between proximal and distal connections in the cat:

- ***Ia afferents*** from proximal muscles send divergent projections to motoneurons of synergistic muscles, which aid in eliciting responses such as the tonic stretch reflex (Davidoff, 1992). For more distal musculature, Ia afferent projections are more localized and only have a limited effect on motoneuron output.
- ***Recurrent Inhibitory Projections,*** mediated by Renshaw cells, are found in lower numbers on motoneurons of distal muscles. This has also been consolidated by physiological studies in the human (Davey *et al.*, 1993). Recurrent inhibition may have a role in the control of posture by increasing muscle stiffness to compensate for applied loads (Illert, Kümmel & Scott, 1996).
- ***Skeletofusimotor Innervation*** or β-innervation, the motor innervation from α-motoneuron collaterals to intrafusal muscle spindle fibres, is greater in distal cat muscles compared to more

proximal muscles (Scott, Kümmel & Illert, 1995; Illert, Kümmel & Scott, 1996). β-innervation causes the simultaneous contraction of extrafusal and intrafusal fibres enabling the muscle spindle to measure the error between the actual move and the intended output. Under isometric conditions, β-innervation can cause the spindle to act as a force encoder. Both mechanisms would be important for the fine manipulatory tasks performed by distal hand muscles.

2. AFFERENT INPUT HAS A DIRECT EFFECT ON CORTICOSPINAL TRACT OUTPUT

- ***Muscle Afferents*** directly influence corticospinal tract function. Macefield *et al.* (1993) have shown that anaesthesia of muscle afferents in the ulnar nerve causes a significant fall in α-motoneuron firing rates during maximal voluntary contraction. Similarly, when the hand is positioned to disengage the distal interphalangeal joint of the forth digit, there is a reduction in the common drive to motor units in the disengaged muscle (Garland and Miles, 1997).
- ***Cutaneous Afferents*** have a role in modifying the contribution of the CM system during a precision grip task. TMS has demonstrated that the CM system is particularly active during phases of precision grip tasks where sensory feedback is crucial, such as during onset of grip or during the unexpected application of a load (Johansson, Lemon & Westling, 1994; Lemon, Johansson & Westling, 1995). Using peripheral nerve microstimulation and averaged EMG recordings it has also recently been demonstrated that the input from one cutaneous afferent is sufficient to have short and long latency influences on the motor unit pool of intrinsic hand muscles (McNulty, Türkey & Macefield, 1999).
- ***Cortical Reflexes:*** Although spinal stretch and unloading reflexes exist in human distal hand muscles (Angel & Weinrich, 1986), their role appears to be subordinate to that of long loop cortical reflexes in distal hand muscles. By measuring the phase lag of EMG responses to sinusoidal stimuli applied to tendons of distal and proximal muscles, Matthews (1994) has clearly demonstrated that the latency of the distal muscle response is much greater than for the proximal muscle due to the involvement of long latency reflexes.

Other Cortical Areas Involve in Hand Control

In addition to M1, evidence from retrograde tracing studies (Dum & Strick, 1991; Roullier, 1996), cortical lesioning (Freund, 1987) and brain scanning techniques (Shibasaki *et al.*, 1993; Boeker *et al.*, 1994) have demonstrated that other cortical areas control hand movements. Two premotor areas are worthy of particular mention:

- SUPPLEMENTARY MOTOR AREA: Studies of cerebral blood flow and lesioning studies have demonstrated that the SMA is involved in programming complex sequences of movements, and in controlling bilateral hand movements (Roland *et al.*, 1980; Shibasaki *et al.*, 1993; Weisendanger, 1993). The SMA receives major inputs from the basal ganglia and has a

function in the initiation and timing of movements as generated from internal cues (Passingham, 1987; Tanji, 1994; Cunnington, Bradshaw & Iansek, 1996; Rizzolatti, 1996a).

- PREMOTOR CORTEX: In contrast to the SMA, the PM cortex receives inputs predominantly from the cerebellum and is involved in the selection and guidance of movements using visual information (Wise, 1985; Passingham, 1987; Rizolatti, 1996b). Two areas of the PM cortex can be distinguished. The dorsal PM is involved in the preparation of forth coming movements and contains neurons which code the position of an intended limb movement (Boussaoud, 1995). The ventral PM is concerned with the execution of visually guided movements and contain neurons which fire during particular manual tasks such as precision or power grip (Rizzolatti *et al.*, 1988; 1996b).

1.2.2.3. Pulsatile Output To The Hand

When measuring physiological tremor in the digits during position holding, a number of authors have emphasised the presence of a small but consistent 8-10 Hz peak in the periodogram of the acceleration record (Halliday & Redfearn, 1956; Stiles & Randall, 1967; Hagbarth & Young, 1979; Marsden, 1984). More recently, large and consistent 8-10Hz discontinuities have been described in velocity and acceleration records during slow extension: flexion movements in the long digits (Vallbo & Wessberg, 1993; Wessberg, 1995; McAuley *et al.*, 1999) and during a position holding task against an elastic load using the index finger (McAuley, Rothwell and Marsden, 1997). It has been suggested that this 8-10Hz oscillation may be a manifestation of central timing device to coordinate movements (for further discussion see Vallbo & Wessberg, 1993; Wessberg, 1995; McAuley, Rothwell and Marsden, 1997; Farmer, 1998). This pulsatile output is particularly evident in low inertia systems such as the eye or digits (McAuley *et al.*, 1999).

MECHANISMS GENERATING 8-10Hz TREMOR

A number of mechanisms have been implicated in the generation of 8-10 Hz tremor (Marsden, 1984):

- ***The natural resonance of the sytem:*** This is dependent upon elastic, viscous and inertial mechanical components in the system (Timeshenko, 1955). The resonating frequency is driven by muscle activity and cardioballistic effects (Stiles & Randall, 1967). The hand at the wrist joint has a resonating frequency of around 8-12 Hz (Lakie, Walsh & Wright, 1986; Reitsma, 1994)
- ***The combined effects of onset firing rates of recruited motor units and the low pass filtering properties of muscle:*** When motor units are recruited, they fire at around 8 Hz (Milner-Brown Stein & Yemm, 1973). However, as the firing rate increases the muscle acts as a low pass filter so that frequencies above 20 Hz are removed altogether (Mannard & Stein, 1973). For example, electrical stimulation of the ulnar nerve between 5 and 25 Hz results in a sharp decay in the

amplitude of movements in the digits between 10-16 Hz, so that amplitudes at 25 Hz are hardly visible (Allum, Dietz & Freund, 1978). These effects would highlight amplitudes within the range of 8-12 Hz.

- ***The stretch reflex:*** By driving the forearm through a range of sinusoidal frequencies, Joyce and coworkers, found that the passive limb assisted the oscillations between 6 and 13 Hz, and resisted oscillations above or below these frequencies (Joyce, Rack & Ross, 1974). However, no 8-10 Hz modulations are observed in muscle spindle microneurographical recordings during position holding (Hagbarth & Young, 1979). These findings suggest that the stretch reflex assists but does not generate 8-10 Hz tremor during position holding.
- ***A central oscillator:*** In contrast to postural tremor, 90% of Ia afferents and 50% of II afferents fire in phase with the 8-10Hz oscillations during slow movements, as revealed by spike triggered averaging techniques of microneurographical spindle recordings (Wessberg & Vallbo, 1995). This prompts the question whether the slow movement associated discontinuities are generated by the stretch reflex. Evidence confirming that they are not was provided by Wessberg & Vallbo (1996) who applied 3° perturbations during slow finger movements to generate stretch reflex responses. They found that these responses were too small and slow to be able to generate the 8-10Hz discontinuities. This implies that the origin of the movement tremor is through some oscillatory device in the CNS. Vallbo and Wessberg also showed that the individual discontinuities associated with slow movements are actually structured so that each discontinuity is typically characterised by an acceleration, a deceleration and a standstill phase (Vallbo & Wessberg, 1993). It was apparent from rectified EMG traces that these three phases are generated by an agonist driving phase, followed by an antagonist braking phase, followed by a pause period.

  Further evidence for the central origin of 8-10 Hz discontinuites was also recently provided by McAuley and coworkers (1999) who discovered that 10 Hz oscillations in finger movements are related to 10 Hz oscillations seen during smooth tracking movements in the eye. Coherence analysis demonstrated that the two oscillations were linked when simultaneously attempting to track sinusoidal moves with the digit and eye. The link was still present during periods when the feedback of either the digit position or the target were withheld from view. When the eyes or fingers performed similar but independent moves, no link between the oscillations was evident, indicating that the correlation is task specific. This implies that a common central oscillator has an influence over these two very distinct motor systems.

It has been suggested that the inferior olive may provide the source of the 8-10 Hz output since neurons in this region undergo synchronous depolarisation and hyperpolarisation at cycles of 10Hz and are associated with movement (Llinás, 1988, 1991; Welsh & Llinás, 1997). The output of the inferior olive through climbing fibre inputs onto Purkinje cells of the cerebellum could provide a mechanism for controlling coordinated motor activities (Llinás, 1991).

THE ROLE OF A CENTRAL OSCILLATOR

The advantage of a central timing device for the cordination of neuronal activities of various conduction delays was first suggested by Bernstein (1967). Llinás & Yarom (1986) also describe a pacemaker for sensorimotor integration in the cerebellum and brainstem.

A pulsatile modulation of *efferent* signals would reduce the computational complexity in controlling movements. For example, Vallbo & Wessberg, proposed a method in which the pulsatile output would provide simple mechanism for generating slow movements (Vallbo & Wessberg, 1993, 1996; Wessberg, 1995). An 8-10 Hz clock would drive a double pulse generator which produces an agonist burst followed by an antagonist burst. A pulse height controller would then provide a simple means of controlling the velocity of the move.

A pulsatile modulation of *afferent* signals would have the advantage of minimising the effects of noise and interference and aiding the integration of afferent information arriving at different times due to peripheral and central conduction delays. Suggestions that the pulsatile output may be a particularly important feature in relation to the interpretation of proprioceptive information and the control of internally generated movements, is highlighted by two findings. Firstly, spindle afferent feedback is highly correlated to the pulsatile output (Wessberg & Vallbo, 1995) and secondly, the coherence between the pulsatile output during two different task related activites is not dependent on visual feedback (McAuley *et al.*, 1999).

1.3. Proprioception

1.3.1. Definition and Importance

Proprioception can be accurately described as 'biomechanical sense'. The body can be modelled biomechanically as a series of levers, each with a defined position, velocity and acceleration and which are subject to torques applied either externally or internally through muscles (Kreighbaum & Barthels, 1996). Consequently, proprioception includes:

- **Sense of position, velocity and acceleration:** also termed *kinaesthesia*. Position sense is thought to be an independent from velocity and acceleration sense (Horch, Clark & Burgess, 1975; Clark *et al.*, 1979, 1985; Taylor and McCloskey 1990).
- **Sense of torque:** also called 'sense of effort'.

As biomechanical sense, proprioception represents the interface between sensory and motor systems, providing afferent feedback of the consequences of motor output.

As a sensory attribute, proprioception is important for acquiring information about the physical features of objects needed for recognition (Lederman & Klatzy, 1996) and for the education of the motor systems (Gordon et al, 1993; Johansson, 1996a). More importantly, proprioception provides the ongoing feedback of movement and force necessary for the fine control of movement. This is perhaps best illustrated in sufferers of large fibre sensory neuropathy which

results in loss of tactile and proprioceptive sensation (Rothwell *et al.*, 1982; Marsden, Rothwell & Day, 1984; Sanes *et al.*, 1985; Fleury *et al.*, 1995; Nougier *et al.*, 1996).

Rothwell *et al.* (1982) described a subject suffering from severe peripheral sensory neuropathy of the forearm and hands. He was able to perform a wide range of tasks including independent rapidly alternating flexion and extension movements of the fingers. He was able to move the thumb through to three different positions and could apply three different forces at the thumb digit tip, all in the absence of visual feedback. However, he was not able to estimate the weight of objects or maintain a fixed position of the thumb in the absence of visual feedback. His hands were useless for many tasks performed in daily life, such as fastening buttons and writing.

Fleury and coworkers also noted that deafferentation results in a loss of sense of force as measured by weight discrimination (Fleury *et al.*, 1995), and in the sense of a positional frame of reference, as seen by the accumulation of errors when attempting to perform constant alternating moves of a fixed amplitude (Nougier *et al.*, 1996).

1.3.2. The Neural Basis Of Proprioception

Overview

FEEDFORWARD: Corollary Discharge

Descending commands can be generated in the absence of afferent feedback and have been observed during anaesthesia of muscle afferents (Gandevia *et al.*, 1990; Macefield *et al.*, 1993) and subsequent to large fibre sensory neuropathy (Rothwell *et al.*, 1982; Sanes *et al.*, 1985). Subthreshold commands can also be elicited during which no movement occurs and consequently there is no feedback from receptors (Gandevia & Rothwell, 1987). Whether these commands can result in sensations of movement or force has been the subject of some debate (for reviews see McCloskey, 1981; Matthews, 1988).

The perception of outgoing motor commands or 'corollary discharge' has been described in other physiological systems. Corollary discharge provides accurate information about eye position after deafferentation of extraocular muscles in the primate (Guthrie, Porter & Sparks, 1983). Efference copy has also been described in the electric fish by Bell (1982), in which a outgoing command minimises the effects of electric organ induced activity. In the human, corollary discharge can be difficult to analyse since it takes place completely in the CNS. The majority of investigations have either looked at the sensations arising in the absence of afferent feedback, or at conditions which cause a discrepancy between the motor command and its usual effect. The weight of evidence suggests that corollary discharge does not elicit sensations of movement, but is important in the interpretation of kinaesthetic afferent information. Conversely, corollary discharge seems to have a fundamental role in the sense of effort (McCloskey, 1981; Matthews, 1988).

FEEDBACK: Sensory Receptors

Mechanoreceptors present in muscle, skin and joint have all been scrutinised under precisely and carefully controlled mechanical stimuli using animal models. The responses of proprioceptors during imposed and voluntary movements in humans, have also been investigated using the technique of microneurography (Hagbarth & Vallbo, 1969). Further insights concerning the relative contribution of these receptors to kinaesthesia and sense of force have come from psychophysical experiments involving the selective removal or stimulation of one or a number of contributing proprioceptors. The role of peripheral receptors in kinaesthesia is unequivocal (for reviews see Goodwin et al, 1972; McCloskey, 1978, Gandevia & Burke, 1992; Willis & Coggeshall, 1992, Jones, 1994, 1996). However, role of proprioceptors in sense of effort still remains uncertain (McCloskey, 1981).

1.3.3. Responses of Receptors to Mechanical Stimuli

1.3.3.1. Muscle Receptors

Two receptors, the muscle spindle and Golgi tendon organ, relate different information in accordance with their anatomical position in the muscle. The muscle spindle, whose intrafusal fibres lie in parallel with extrafusal muscle fibres, conveys information relating to muscle stretch. The Golgi tendon organ (GTO), arranged in series to muscle fibres, encodes the contractile tension generated within the muscle.

The Muscle Spindle

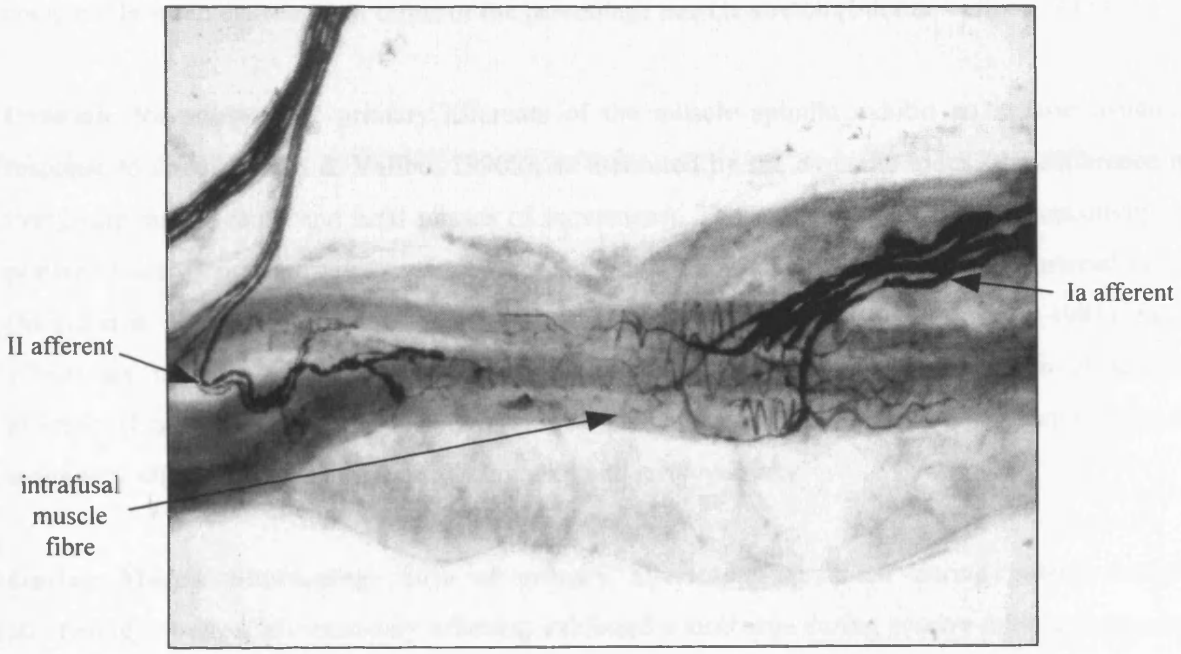
STRUCTURE

The intricate structure and function of the muscle spindle has been described by a number of authors (Matthews, 1972; Boyd, 1980; Hunt, 1990; Poppele, 1993; Gladden, 1995; Proske, 1997). Briefly, the muscle spindle capsule contains three main physiological components:

1. **Intrafusal Fibres:** Three types of intrafusal fibre; bag_1, bag_2 and chain fibres can be distinguished by their viscoelastic and contractile properties (Boyd, 1981). The viscous or thixotropic, polar regions of the bag fibres confer a dynamic sensitivity upon the sensory afferents which spiral around the central region (figure 1.1.).
2. **Sensory Innervation:** Large fibre myelinated primary Ia afferents form anulo-spiral endings around the central region of each intrafusal fibre. In the deefferented spindle, Ia afferents respond to passive ramp movements with a burst of activity during the acceleration phase, proportionally to the velocity of stretch and with small static component during the hold phase (Hunt, 1990, Poppele, 1993). Smaller myelinated II afferents innervate mainly bag_2 and chain fibres. These afferents signal muscle length.

3. **Motor Innervation:** *Fusimotor innervation,* originating from γ-motoneurons, accounts for as much as one half of the axons supplying a muscle (Boyd & Davey, 1968). γ_D efferents innervate solely bag_1 fibres and greatly enhance the dynamic response, whereas γ_S efferents, innervate bag_2 fibres or chain fibres and enhance the static response (Barker *et al.*,1973; Celichowski *et al.*,1994). γ_S efferents also have a role in maintaining responses during muscle shortening (Proske, 1995, 1997). The role of *skeletofusimotor innervation* or β-innervation is still an area of controversy (Grill & Rymer, 1987). Proximo-distal differences in the degree of β-innervation suggest that this hardwired system is well suited for fine manipulatory tasks carried out by distal muscles (Illert, Kümmel & Scott, 1996).

Figure 1.1: A teased silver preparation of a cat muscle spindle (courtesy of Dr J.J.A Scott)



RESPONSES OF HUMAN MUSCLE SPINDLES

The technique of microneurography introduced by Hagbarth and Vallbo (1969), has permitted recordings of single primary afferents to be made in awake human subjects using fine microelectrodes inserted percutaneously into nerves. Muscle spindle primary afferents, secondary afferents and Golgi tendon organs can be distinguished by features such as their static discharge, response to ramp and sine moves, response to twitch contractions and activity during isometric contractions (Vallbo *et al.*, 1979; Edin & Vallbo, 1990a).

Response In The Relaxed Muscle

The output of the human muscle spindle in passive movements appears to be unbiased by tonic fusimotor input, as suggested by low resting discharges and an absence of spontaneous alterations in activity (Vallbo, 1974a; Vallbo *et al.,* 1979). It is not possible to invoke a fusimotor response in relaxed muscle by either training or by engaging in mental or motor tasks (Vallbo *et al,*

1979, Burke, 1981; Gandevia & Burke, 1985). However, Gandevia *et al.* (1994) have recorded a small number of fusimotor responses following electrical stimulation of the hand dorsal skin. The absence of fusimotor influence greatly simplifies the output the spindle in relaxed muscle:

Static Response: Both primary and secondary afferents show a monotonic increase in firing rate with position (Vallbo, 1974a; Hulliger, Nordh & Vallbo, 1982; Edin & Vallbo, 1990b). The proportion of spindles firing also increases as a function of joint position, with primary afferents being recruited later than secondaries (Vallbo, 1974a). Less than 10% of spindle afferents exhibit a resting discharge at intermediate muscle lengths.

The static position sensitivity in humans appears to be as much as five times lower than that in the cat when expressed as a firing rate per millimetre of muscle. However, the sensitivity is comparable when expressed in terms of the percentage muscle stretch (Edin & Vallbo, 1990b).

Dynamic Response: The primary afferents of the muscle spindle exhibit an intense dynamic response to stretch (Edin & Vallbo, 1990b), as measured by the dynamic index (the difference in firing rate during ramp and hold phases of movement). The extraordinary dynamic sensitivity of primary endings means that they inappropriately fire because of artifacts such as arterial pulse (McKeon & Burke, 1981) and twitches in adjacent motor units (McKeon & Burke, 1983). Such effects are negligible compared to the ensemble input from the whole population of spindle afferents (Cordo 1996). Grill and Hallett (1995) have also demonstrated that the dynamic index in secondary afferents also significantly increases with ramp velocity.

During Muscle Shortening: 80% of primary afferents were silent during passive muscle shortening, whereas, all secondary afferents exhibited a discharge during passive muscle shortening (Edin & Vallbo, 1990b).

Response In The Active Muscle

During Isometric Conditions: Due to the influence of fusimotor drive, both primary and secondary afferent discharge increases with force of contraction under isometric conditions (Vallbo, 1974b). Like skeletomotor neurons, fusimotor neurons also have an order of recruitment (Burke, Hagbarth and Skuse, 1978).

During Isotonic Conditions: In contrast to relaxed muscle, spindle discharge during muscle contraction is poorly correlated to joint position (Vallbo, Hulliger & Nordh, 1981; Hulliger, Nordh & Vallbo, 1982) although information about the occurrence and direction of a movement can be ascertained from the spindle output during movements (Hulliger, Nordh & Vallbo, 1985). These directional responses become much greater during faster movements, but as the load increases,

directional responses diminish and the spindle begins to behave much more like a tension transducer (Burke, Hagbarth & Löfstedt, 1978).

During Natural Voluntary Movements: During *fast* voluntary movements, there is a fusimotor induced response in the agonist muscle during the contraction and a stretch induced response in the relaxed antagonist (Hagbarth, Wallin & Löfstedt, 1975). During *slow* voluntary movements, spike triggered averaging techniques of microneurographical spindle recordings show that 90% of Ia afferents and 50% of II afferents fire in phase 8-10 Hz fluctuations evident in velocity and acceleration profiles (Vallbo & Wessberg, 1993,1996; Wessberg, 1995).

Complications

Interpretation of Spindle Output: Although spindle responses in the active muscle are less consistent than in a passive muscle, thresholds of movement detection are lower when the muscle is contracted (Paillard & Brouchon, 1968; Gandevia & McCloskey, 1976; Colebatch & McCloskey, 1987; Taylor & McCloskey, 1992). Further complications result from the after effects of muscle contraction which cause resting discharge to increase due to the thixotropic character of intrafusal fibres (Wilson, Gandevia & Burke, 1995; Hagbarth, 1996). The CNS appears to be able to accurately derive position and velocity information regardless of these complications. Doubtless, corollary discharge has a contribution to the derivation of this information (McCloskey, 1981; Matthews, 1988).

Fusimotor & Skeletofusimotor Systems: The marked differences between the response of muscle spindles during active and passive movements can only be accounted for by the action of fusimotor and skeletofusimotor systems (Vallbo 1974a, 1974b; Burke, Hagbarth and Skuse, 1978; Hulliger, Nordh & Vallbo 1982, 1985). However, fusimotor systems are activated simultaneously with skeletomotor systems (Vallbo *et al.* 1979). Although studies in the cat have demonstrated that the degree of fusimotor drive can be varied according to the kinaesthetic demands of the task (Prochazka, 1986; Prochazka *et al*, 1985; Hulliger *et al.*, 1989), in the human, spindle discharge and motor activity appear to be invariably linked for different tasks. Levels of spindle discharge do not differ significantly during the process of learning of a new motor task (Al-Falahe & Vallbo, 1988; Al-Falahe, Nagaoka & Vallbo, 1990) or during various conditions of standing (Aniss *et al.* 1990). Although different levels of spindle discharge can be produced when performing identical routine and precision finger movements (Kakuda, Vallbo & Wessberg, 1996), the increase in spindle discharge seen during precision movements is always associated with increased skeletomotor activity.

It is still not clear whether the link between spindle discharge and motor activity in the muscle is due to α-γ coactivation or β-innervation. Evidence in favour of α-γ coactivation is given by Burke, Hagbarth & Skuse (1979). Application of a partial pressure block, effective in abolishing

skeletomotor activity during an attempted maximal voluntary contraction, has little effect on the increased spindle discharge that usually accompanies a voluntary contraction. Partial anaesthesia with lidocaine, which selectively anaesthetises small γ-motoneuron efferents, does eliminate the contraction induced increase in spindle discharge. However, this effect was observed in proximal musculature which may be under a different balance of fusimotor/skeletofusimotor control compared with distal musculature (Scott, Kümmel & Illert, 1995; Illert, Kümmel & Scott, 1996).

The Golgi Tendon Organ

These encapsulated structures, found at the musculotendinous junction, have a less elaborate structure and function than the muscle spindle. The Ib afferent terminal interweaves amongst the network of collagenous tendon fibres within the capsule and depolarises when tension is developed during muscle contraction (Swett & Schoultz, 1975). Up to 20 motor units may insert into the GTO and each one modulates the GTO output (Jami, 1992).

ANIMAL STUDIES

During *isometric* tetanic contractions, the GTO generates a three phased response corresponding to the rise and plateau phase of the tension:

- As tension increases, an initial frequency peak is produced by the GTO with an amplitude proportional to the rate of rise in tension (Fukami & Wilkinson, 1977).
- An exponential fall in firing rate following the frequency peak is inversely related to the rate of rising tension (Davies, Petit & Scott, 1995).
- As the tension plateaus, the firing frequency remains constant, firing at a rate that is proportional to the tension (Petit, Davies & Scott, 1994).

Experiments carried out under *isotonic* conditions demonstrate that the GTO output is linearly related to the contractile force as generated by either individual motor units or groups of motor units (Petit, Scott & Reynolds, 1997). In summary, the GTO is a highly sensitive force transducer, which reflects the overall contractile tension developed within the motor units in series with the structure.

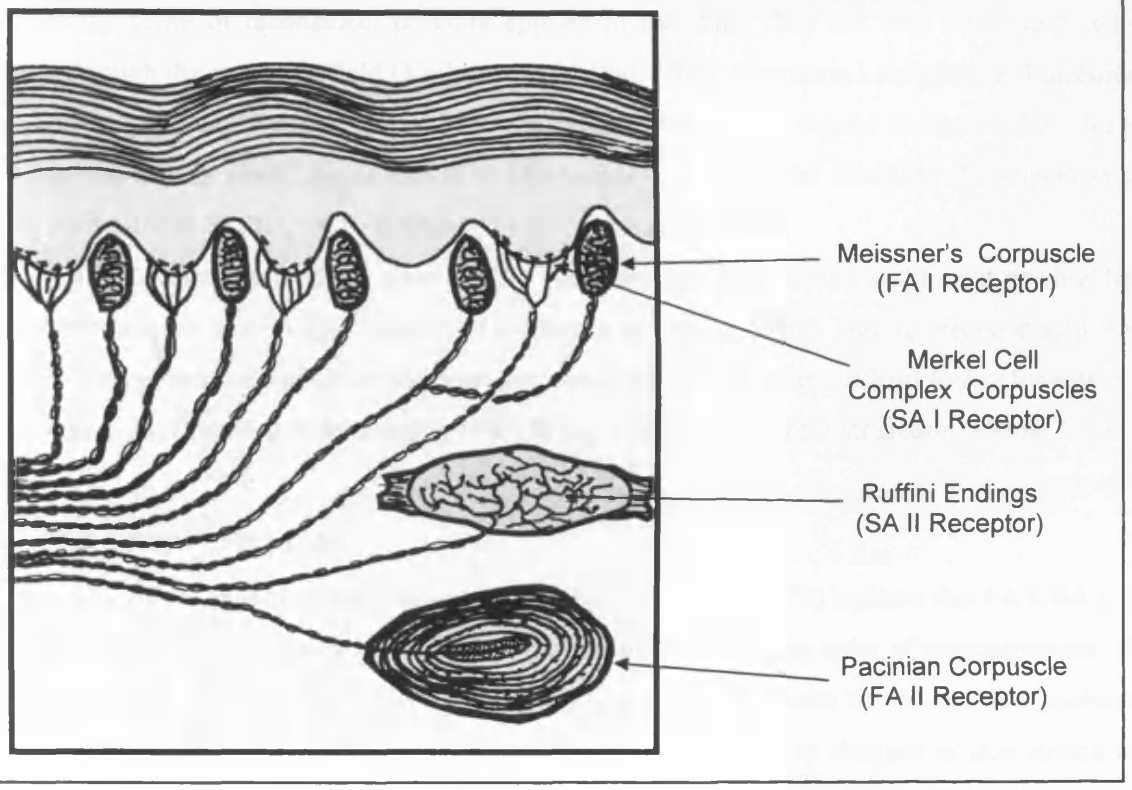
HUMAN STUDIES

Microneurographical studies of Golgi tendon organs are much less frequent than those of the muscles spindle. Available data indicates that responses of human GTOs are similar to those in animals (Vallbo, 1974a; Edin & Vallbo, 1990c). No resting discharge exists except at extreme joint angles. During movement, the tendon organ output is highly correlated to both the torque and EMG activity (Edin & Vallbo, 1990c). Each GTO reflects the overall torque produced in the motor units connected in series and shows step increases in firing rate as additional motor units are recruited (Vallbo, 1974a).

1.3.3.2. Cutaneous Receptors

Mechanoreceptors in the skin have primarily been studied with a view to understanding tactile rather than proprioceptive mechanisms, with the result that the emphasis has been placed on glabrous receptors of the hand (reviewed in Iggo, 1977; Johansson & Vallbo, 1983; Vallbo & Johansson, 1984; Willis & Coggeshall, 1992). Four types of glabrous receptors can be distinguished according to receptive field properties, response to stimuli and location in the skin (Knibestöl, 1973, 1975; Johansson & Vallbo 1979a, 1980; reviewed in Vallbo & Johansson, 1984). Two of these receptors are rapidly adapting (FA I and FA II receptors) and code for transient changes in indentation and flutter/vibration, and two receptors are slowly adapting (SA I and SA II receptors) and respond to static indentation and skin stretch, respectively. Of the 17,000 units in the median nerve, the proportions of FA I, FA II, SA I and SA II receptors are 43%, 13%, 25% and 19%, respectively (Johansson & Vallbo, 1979a).

Figure 1.2: The location of the four principal cutaneous mechanoreceptors



FA I and SA I receptors have small receptive fields with distinct borders and multiple low threshold zones and are found in high concentrations at the digit tips. FA II and SA II receptors have much larger receptive fields, no delimiting borders and single low threshold zones (Knibestöl, 1973, 1975; Johansson & Vallbo, 1979a, 1980, Vallbo & Johansson, 1984). FA I, FA II, SA I and SA II receptors are thought to correspond to Meissner's corpuscles, Pacinian corpuscles (or smaller Golgi Mazzoni complexes), Merkel cell complexes and Ruffini endings, respectively (figure 1.2).

Response To Mechanical Stimuli

Rapidly adapting receptors: Using microneurography, Johansson, Landström & Lundström (1982a) have shown that human FA I receptors respond to vibration in the range of 8-64Hz (sensed as flutter), and FA II receptors respond to frequencies between 128-400Hz (sensed as vibration). In addition, FA I receptors code the velocity of indentation and FA II receptors respond to acceleration or higher derivatives (Knibestöl, 1973, 1975). Rapidly adapting receptors have extremely low thresholds, and comparison of psychophysical touch thresholds indicate that the input from one afferent is sufficient to reach consciousness (Johansson *et al.*, 1979b; Vallbo & Johansson, 1984). The smaller receptive field size of FA I receptors is consistent with their role in two point discrimination (Johansson & Vallbo, 1979a). The ability to detect a moving raised dot also relies on FA I receptors which highlights their importance in spatiotemporal discrimination (LaMotte and Whitehouse, 1986).

Slowly adapting receptors SA I receptors exhibit static and dynamic responses to indentation and mediate the sense of mechanical pressure applied to the skin. They are very sensitive to edges cutting through the receptive field (Knibestöl & Vallbo, 1980; Johansson Landström & Lundström, 1982b; Phillips & Johnson, 1981a, 1981b). SA II receptors exhibit regular background discharges and respond during stretching of the skin, commonly in a particular direction (Chambers *et al.*, 1972; Knibestöl & Vallbo, 1970; Knibestöl, 1975; Johansson, 1978).

The small receptive field sizes of SA I receptors and high density at the digit tips highlight their importance in spatial discrimination (Johansson & Vallbo, 1980). During precision grip, SA I and SA II receptors are important for providing feedback of both grip and load force (Johansson & Westling, 1984; Westling & Johansson, 1987, Wing, 1996; reviewed by Johansson, 1996a, 1996b).

Role In Proprioception

Microneurographical recordings made by Hulliger *et al.* (1979) indicate that FA I, SA I, SA II and FA II glabrous receptors all fire during movement in increasing order of responsiveness. The deep location of the Pacinian corpuscles and Ruffini endings between the dermal and epidermal layers (Iggo, 1977) means that they are ideally located to respond to changes in skin stretch and compression during movements of the digits (see figure 1.2.). In particular, Ruffini endings (SA II receptors) consist of afferent nerve endings interwoven amongst fibrils connected to the collagenous structures in the dermis and are suitably positioned to measure the tension developed during skin stretch (Chambers *et al.*, 1972). Accordingly, FA II receptors are the most sensitive cutaneous receptors to finger movements with 100% firing during 0.1Hz ramp full range movements (Hulliger *et al.* 1979). 81% of SA II receptors also exhibit static responses coding for stretch resulting from changes in digit position.

The radial nerve which supplies the dorsal hairy skin of the hand may be an important source of cutaneous proprioceptive feedback since it is translated and stretched during digital movements. Microneurographical recordings of the radial nerve have demonstrated that 90% of the cutaneous afferents respond to digit movement (Edin and Abbs, 1991). By applying precise stretches to the dorsal skin, Edin (1992) has also shown that both SA I and SA II receptors have acute dynamic and static sensitivities to skin stretch.

1.3.3.3. Joint Receptors

Animal Studies

HISTORY OF JOINT RECEPTORS

The role of articular receptors in proprioception still remains controversial (see the review by Proske, 1988). Original work by Boyd & Roberts (1953) and Skoglund (1956) seemed to indicate that afferents in the cat posterior articular nerve (PAN) supplying the knee, adequately coded for joint position. Consequently, joint afferents were originally considered to be the principal mediators of kinaesthesia. Over a decade later, stimulation of muscle spindles by succinyl choline application and fusimotor stimulation demonstrated that the PAN was actually contaminated by afferents from the popliteus muscle. A large proportion of the receptors responding during mid range movements were, in fact, muscle afferents rather than joint afferents (Burgess and Clark, 1969; Clark & Burgess, 1975; McIntyre, Proske & Tracey, 1978).

Using single unit recordings, most authors record low mid-range firing in joint afferents, with significant levels of firing only occurring towards the extremes of the joint range of motion (Burgess & Clark, 1969, Clark & Burgess, 1975; Millar, 1973; Grigg and Greenspan, 1977; Tracey, 1979; Heppelmann, Heuss & Schmidt 1988). This implies that joint receptors only have a limited role in kinaesthesia, or more specifically, position sense, and instead signalled end points of the range of motion. In contrast, Ferrell and co-workers have maintained that there is a significant amount of joint afferent activity within the mid ranges for joint receptors to code for position sense. After removal of the popliteus muscle, Ferrell (1980) recorded that 17.8% of receptors in the PAN still fire during mid range positions. Using multiunit recordings of cat elbow joint afferents, Baxendale and Ferrell (1983) always found some receptors discharging at intermediate angles.

JOINT PROPRIOCEPTORS

Controlled stretch and compression forces applied to isolated sections of joint capsule have uncovered the properties of two types of mechanoreceptor which are likely to have a specific role in proprioception (reviewed in Grigg, 1994):

1. Ruffini Endings

Joint Ruffini endings (type I receptors) consist of a collagenous network continuous with the structures of the joint capsule (Zimny, 1988) and are found in high concentrations in the

'flexion' aspect of the joint which is stretched during extension movements (Grigg & Hoffman, 1982). By applying 2-dimensional in-plane stretching to isolated sections of the cat knee, Grigg and coworkers found that Ruffini endings:

- Encode capsule stress (i.e. applied load) rather than capsule strain (i.e. change in length) (Grigg & Hoffman, 1982; Fuller, Grigg & Hoffman, 1991).
- Respond to uniaxial stress not to compressive stress (Grigg & Hoffman, 1996).
- Fire specifically with regard to direction (Grigg & Hoffman, 1982; Khalsa, Hoffman & Grigg, 1996).
- Fire specifically to local stresses as indicated from applying 2-dimensional stress gradients (Khalsa, Hoffman & Grigg, 1996).

Although joint Ruffini endings have the potential to provide accurate and meaningful position feedback, during passive movements joint capsules remain unstressed for most anatomical positions, except towards limits of movement (Hoffmann & Grigg, 1989). Grigg & Greenspan (1977), however, have demonstrated that contraction of muscles can activate joint afferents even during intermediate angles. Thus, joint afferents may provide an important source of proprioceptive feedback during active movements (Ferrell, 1985; Millar, 1973).

2. Paciform Capsules And Golgi-Mazzoni Endings

Type II joint receptors, equivalent to Paciform capsules and Golgi-Mazzoni endings, are widely distributed around the inner surface of the joint capsule and have been traditionally classified as rapidly adapting receptors, since they exhibit transient responses to tensile loading (Zimny, 1988). However, almost all type II endings show slowly adapting responses to local compression (Grigg, Hoffman & Fogarty, 1982). These responses are specific to compression of the inner surface of the capsule since compression of the outer surface does not activate type II afferents. Pacinian capsules are the predominant mechanoreceptors found in primate MCP joints where it is suggested they have a role in sensing movements (Sathian & Devanandan, 1983).

OTHER ARTICULAR RECEPTORS

Large, Golgi tendon organ like corpuscles (type III receptors) located in joint ligaments, and free nerve endings (type IV receptors) found throughout joint capsules, respond to 'noxious' rotations of the joint (Schiable & Schmidt, 1983a, 1983b; Fuller, Grigg & Hoffman, 1991). A number of proprioceptors also exist in periarticular tissue such as menisci (see Zimny, 1988).

ROLE OF JOINT RECEPTORS IN LIMIT DETECTION

Several studies have highlighted the role of joint receptors in providing protection against joint instability. Sectioning of the anterior cruciate ligament in dogs results in severe osteoarthritis if accompanied by sectioning of the nerves to the knee joint (O'Connor *et al.*, 1992). Ferrell also suggests that disturbances in joint proprioceptive feedback, resulting from conditions such as

rheumatoid arthritis, could contribute to joint deformity by reflexly altering muscle tone around a joint (Ferrell, 1995).

Microneurography

Only a small number of studies have investigated responses in human joint receptors (Burke, Gandevia & Macefield, 1988; Macefield, Gandevia & Burke, 1990; Edin, 1990; reviewed by Macefield, 1995).

Recordings taken from nerves supplying palmar and dorsal aspects of the hand have indicated that there are anatomical variations in the responses of joint receptors to movement. Burke, Gandevia & Macefield, recording from median and ulnar nerve fascicles, found that the majority of afferents had high thresholds, no background discharge at rest, and fire only towards the range limit of movement (Burke, Gandevia & Macefield, 1988; Macefield, Gandevia & Burke, 1990). The majority of afferents responded to biaxial or multiaxial movements.

In contrast, Edin (1990) recording joint afferents from the radial nerve supplying the dorsum of the hand, found all responses were unidirectional, increasing discharge in flexion, and manifested a background discharge at rest. This implies that, unlike joint receptors located in the palmar hand, dorsally located receptors can adequately code for position and movement.

1.3.4. Proprioceptive Sources And Perception

From the large body of data amassed from the mechanical responses of animal and human proprioceptors, it is clear that slowly and rapidly adapting responses relating to position, movement and force derive from all three sources of muscle, joint and skin. However, whether these responses can affect conscious perception is a different issue. On entering the CNS, processes such as, integration, filtering and contrast enhancement can result in a large modification of the signal reaching the cortex (Chapman, Tremblay & Ageranoiti-Bélanger, 1996). Incoming signals may also be interpreted in the light of outgoing corollary discharge signals (McCloskey, 1981, Matthews, 1988). A number of methods have been used to investigate the sensations arising from different afferents sources, including selective stimulation of receptors and afferents and selective removal of specific proprioceptive sources.

1.3.4.1. Kinaesthesia

Corollary Discharge

Evidence suggests that corollary discharge does not evoke sensations of movement. Kinaesthetic sensations do not result from attempting to move when under conditions of anaesthesia, ischaemia or neuromuscular block (Goodwin, McCloskey & Matthews, 1972; Gandevia *et al.*, 1990; McCloskey & Torda, 1975). Conversely, stimulation of muscle or cutaneous

afferents by passive movement or other means does evoke sensations of movement, even though no corollary discharge is generated (see section 'Selective Stimulation Of Receptors'). Although phantom limb sensations of position occur in approximately 90% of amputees, sensations of movement below the level of amputation are usually accompanied by contractions of muscles in the stump (reviewed in McCloskey, 1981). In all, there is no hard evidence in favour of corollary discharge influencing the conscious perception of kinaesthesia.

It is, however, likely that corollary discharge does contributes to the accurate derivation of kinaesthetic information by taking account of previous and current descending commands. Movement detection thresholds are lower in the contracted muscle than in the relaxed muscle (Paillard & Brouchon, 1968; Gandevia & McCloskey, 1976; Colebatch & McCloskey, 1987; Taylor & McCloskey, 1992). Nevertheless, the behaviour of muscle spindles in the active muscle is more complex than in the relaxed muscle (Vallbo, 1974a; 1974b). Corollary discharge is also likely to play an important role in timing rapid movements where sensory feedback mechanisms are too slow to be of any use (McCloskey *et al.*, 1983b; Taylor & McCloskey, 1990b).

Selective Stimulation Of Receptors

MUSCLE RECEPTORS

Tendon Vibration: Compelling evidence favouring the importance of muscle afferents in proprioception, was first provided by the classic experiments of Goodwin, McCloskey and Matthews, (1972) in which tendon vibration was used to induce proprioceptive illusions of movement. Goodwin *et al.* found that vibration of human biceps and triceps tendons was able to induce illusions of both position and movement in the direction of muscle stretch even when the elbow and overlying skin were anaesthetised. Evidence confirming that the illusions were mediated by muscle spindles was later provided by microneurography in which tendon vibration was found to cause phase locking of both primary and secondary afferents (Burke *et al.*, 1976).

Tendon vibration has been shown to induce errors of both position and velocity. Position error dramatically increases between 25 and 50Hz whereas velocity error increases slowly up to 75Hz and decreases at higher frequencies (Roll and Vedel, 1982; Sittig, Denier and Gielen, 1987). Sittig *et al.* (1987) also demonstrated that disturbance of slow movements by vibration matches that of position error, whilst the disturbance of fast moves matches velocity error. Under loaded conditions, tendon vibration can only induce positional errors when applied to the lengthening antagonist (Inglis, Frank & Inglis, 1991). This emphasises the importance of the lengthening muscle in kinaesthesia.

Pulling Exposed Tendons: Circumstances arising during surgery have been exploited to observe the sensations resulting from pulling exposed tendons in man (Gelfan & Carter, 1967; Moberg, 1972; Matthews & Simmonds, 1974). Some authors observed sensation of movement (Matthews

and Simmonds, 1974) whereas others did not (Gelfan & Carter, 1967; Moberg, 1972). However, the conditions accompanying surgery are not ideal for conducting psychophysical tests. In a more carefully controlled environment, D. McCloskey became the willingly volunteer for a study in which he allowed his extensor hallucis longus tendon to be surgically exposed, cut and the proximal end attached to a vibrator/ramp generator (McCloskey *et al.*, 1983a). Ramp stretches of 0.75mm applied at 2.5mm/s, (equivalent to 7.5° and $25°s^{-1}$), were successfully detected using a margin of 70% correct detection.

CUTANEOUS RECEPTORS

Skin Stretching: Edin and Johansson (1995) have used digital nerve anaesthetic blocks of the index finger to remove sensation distal to the middle of the proximal phalanx permitting the experimenters to manipulate and stretch skin over the MCP joint without the knowledge of the subject. Applying skin stretch over the dorsal MCP joint and pushing skin proximally towards the palmar MCP joint induced illusions of PIP joint flexion in all subjects. Conversely, during a PIP joint flexion movement, the subject could be 'tricked' into thinking the digit was still extended by resisting the normal pattern of skin stretch. Illusions of joint movements produced by skin stretching have also been demonstrated by Collins and Prochazka (1996), although not so conclusively. Stretching of the skin over the dorsum of the hand using adhesive tape was able to induced illusions in 58% of subjects.

Electrical Stimulation: Using a number of electrode configurations on the dorsum of the hand, Collins and Prochazka (1996) found that electrical stimulation could induce movement illusions in 35% of subjects. Gandevia (1985) also found that digital nerve stimulation could also induce a sense of movement in 58% of subjects. Many subjects sensed a rapid oscillating movement, presumably because of the stimulation of rapidly adapting receptors.

Selective Stimulation Of Afferent Fibres

Microstimulation of individual afferents is possible through the application of trains of voltage pulses through microelectrodes previously used to identify the afferents by microneurographical techniques (Torebjörk, Vallbo & Ochoa, 1987).

Muscle Afferents: No perceptual sensation results from the stimulation of single muscle afferents (Vallbo *et al.*, 1984; Macefield, Gandevia & Burke, 1990), which implies that summation of responses from muscle afferents is required for muscle afferent input to reach consciousness. Electrical stimulation of the ulnar nerve at the wrist is able to induce illusory sensations of movement in the digits, presumably through this mechanism (Gandevia, 1985).

Cutaneous Afferents: In contrast to muscle afferents, perceptual sensations resulting from the microstimulation of tactile cutaneous afferents indicate that the responses of single FA I, FA II and SA I units are sufficient to reach consciousness (Vallbo *et al.*, 1984). Continuous stimulation of all

FA II units and many FA I receptors invokes a sense of flutter-vibration and occasionally non-cyclical stimuli (Vallbo *et al.*, 1984; Schady, Torebjörk & Ochoa, 1983; Macefield, Gandevia & Burke, 1990). SA I unit microstimulation produces a frequency dependent sense of indentation (Ochoa & Torebjörk, 1983; Vallbo *et al.*, 1984). No sensations are evoked by stimulation of SA II units (Ochoa & Torebjörk, 1983; Vallbo *et al.*, 1984). An isolated incident was recorded by Macefield *et al.* (1990), in which stimulation of two SA II afferents located near nail beds evoked sensations of passive movement of distal joints.

Joint Afferents: Joint afferent microstimulation is able to elicit perceptual sensation in the majority of subjects (Macefield, Gandevia & Burke, 1990). Half of these subjects felt a deep sensation, whereas the other half felt sensations of joint displacement. This also indicates that the input from one joint afferent fibre is sufficient to reach perceptual levels.

Selective Removal Of Other Proprioceptive Sources

A number of methods have been used to exclude the contribution of specific proprioceptive sources including anaesthesia, anatomical disengagement of muscle and joint replacement:

MUSCLE DISENGAGEMENT OF THE DISTAL INTERPHALANGEAL JOINT

Contribution of Muscle Afferents OR Skin & Joint afferents: When all the long digits are held extended and the middle digit flexed maximally at the proximal interphalangeal (PIP) joint, it becomes impossible to flex or extend the distal interphalangeal (DIP) joint because the long digit flexors and extensors are held at inappropriate lengths. Gandevia & McCloskey (1976) first recognised the value of this model in providing effective disengagement of the muscle. By applying extension and flexion ramp moves to the DIP joint, they found that muscle disengaged caused a deterioration in the ability to detect moves at all velocities ($1.5°s^{-1}$ to $10°s^{-1}$). However, the deterioration was much worse at lower velocities, so that at $1.5°s^{-1}$, detection scores were 7 or 8 times less than when the muscle was engaged.

Using digital anaesthetic blocks, Gandevia & McCloskey (1976) also looked at the effect of removing cutaneous and joint innervation. The results were perplexing, with some subjects sensing very few movements, and others having normal thresholds of detection. Additional tests showed that tensing the muscle had a significant effect in improving detection. A further paradigm was later introduced by Gandevia *et al.* (1983), in which all the long digits were flexed at the PIP joint, engaging only the flexor muscles. Superior detection was evident during the engagement of both muscles, which stresses the importance of both agonist and antagonist muscles in their contribution to kinaesthesia.

In all, the findings of Gandevia & McCloskey (1976) indicates that both muscle receptors and cutaneous / joint receptors provide sources for kinaesthesia, but that the sensitivity is greatest with all proprioceptive machinery intact. Impairments recorded during anaesthesia of the fingers

adjacent to the middle digit led the authors to suggest that cutaneous receptors had a role in offering a non-specific facilitatory input to kinaesthesia.

Contribution of Joint Receptors: Intra-articular anaesthesia applied to the DIP joint by Ferrell, Gandevia and McCloskey (1987) during muscle disengagement was used to investigate the contribution of joint receptors to movement detection. DIP joint anaesthesia impaired correct detection scores across a range of velocities, whereas, intra-articular injection of dextran, a high molecular weight molecule which expands the joint capsule, enhanced detection of movement. Ferrell et al, concluded that joint afferent input can also contribute to kinaesthetic performance. In a similar study carried out by Clark, Grigg and Chapin (1989), intra-articular anaesthesia of the joint caused only a 'modest but significant' reduction in the detection of 10° movements. Their conclusion was that joint receptors contribute only a little to normal proprioception in the relaxed hand.

ANAESTHESIA OF PROXIMAL INTERPHALANGEAL JOINT

Digital nerve anaesthesia eliminates the contribution of local joint and cutaneous afferents to kinaesthesia in the proximal interphalangeal (PIP) joint. Early studies undertaken by Provins (1958) examined the effect of a digital nerve block on the ability to sense a slow velocity movement ($37.8°min^{-1}$). Digital anaesthesia increased mean thresholds from 6.1° to 15.6° in the passive finger. Provins recorded no change in threshold when the muscle was contracted.

The PIP joint model was also later used by Ferrell and coworkers (Ferrell & Smith, 1987, 1988, 1989; Ferrell & Milne, 1989) in which the index finger PIP joint was randomly moved to one of four different positions (100°, 125°, 150° & 175°) and the subject then asked to matched the position with the contralateral hand. Application of digital nerve blocks caused a significant increase in error of the matched move (Ferrell & Smith, 1988). Yet a different pattern of position matching emerged depending on which finger was anaesthetised (Ferrell & Milne, 1989). If the anaesthetised finger was used to match the movement, then the subject exaggerated the position of the finger, i.e. range expansion. If the move was applied to the anaesthetised finger, then the subject underestimated the position, i.e. range compression. In other words, anaesthesia of the skin and joint resulted in an underestimation of the applied displacement. When the anaesthetised matching digit was subsequently loaded, then subjects tended to estimate postion with considerable flexion errors (Ferrell & Smith, 1989). This indicates that cutaneous/joint sensation may be important during conditions where spindle feedback is more ambiguous, i.e. in loaded conditions when fusimotor drive is high.

JOINT REPLACEMENT

Following metacarpophalangeal and metatarsophalangeal joint replacements, subjects could sense crudely applied moves of about 10° amplitude and $2\text{-}3°s^{-1}$ velocity or faster (Cross and McCloskey, 1973). Using more discriminative measures, Barrack *et al.* (1983) found that total knee

replacement resulted in impaired detection and matching of slow velocity movements. However, similar thresholds were also measured in the unoperated knee, indicating that a marked loss in proprioception was caused by the degenerative disease.

Position Sense

By applying very slow velocities, which fall below thresholds of movement detection, it has been shown by Clark and coworkers that position sense exists independently of velocity sense (Horch, Clark & Burgess, 1975; Clark *et al.,* 1979, 1985, 1986). This was first demonstrated in the knee (Horch, Clark & Burgess, 1975; Clark *et al.,* 1979), and later, in both the ankle joint and metacarpophalangeal joint of the hand (Clark *et al.,* 1985). Some disagreement exists concerning static position sense in the proximal interphalangeal joints of the hand. Clark *et al.* (1986) recorded that amplitudes as high as 35° were not sensed in the PIP joint when applied at very slow velocities. Taylor and McCloskey (1990a), however, did not observe any significant differences between position sense thresholds in the MCP, PIP and DIP joints of the digits.

By anaesthetising the ulnar nerve, which paralyses the abduction: adduction musculature of the MCP joint, Clark *et al.* (1985) found that static position sense of ±2.5° displacements dramatically fell when muscle afferent input was missing. Injection of local anaesthetic into the MCP joint space, however, had no significant effect on the position sense. Clark *et al.* concluded that muscle receptors are the prime proprioceptive source for static position sense. In contrast, Taylor and McCloskey (1990a) used the DIP joint model to show that there was no significant difference in position sense during muscle disengagement.

1.3.4.2. Sense of Effort

Corollary Discharge

In contrast to kinaesthesia, corollary discharge appears to have a fundamental role in sense of effort (reviewed in McCloskey, 1981; Gandevia, 1987). Evidence comes from the fact that perceived heaviness is always greater in conditions of muscle weakness such as fatigue (McCloskey, Ebeling & Goodwing, 1974), partial neuromuscular paralysis (Gandevia & McCloskey, 1977) and motor stroke (Brodal, 1973). There is also a strong correlation between the descending command and sense of effort evident from the strong link between α-motoneuron excitability and perceived heaviness (Aniss, 1988).

Role Of Proprioceptors

The role of peripheral receptors with respect to sense of effort still remains controversial:
FACILITATION: Modification of afferent input can cause excitation or inhibition of descending commands (Gandevia et al, 1990) and subsequently influences perception of heaviness. For

example, tendon vibration of loaded muscles causes an increase in perceived heaviness, whereas tendon vibration of antagonistic muscles results in loads feeling lighter (McCloskey, Ebeling & Goodwing, 1974). Likewise, cutaneous anaesthesia can make loads feel heavier, whereas, electrical stimulation of the skin causes them to feel lighter (Gandevia & McCloskey, 1977; Gandevia, McCloskey & Potter, 1980; Kilbreath *et al.*, 1995).

CALIBRATION: Afferent input may have a more specific role in sense of effort in permitting calibration of the consequences of motor output (Gandevia & McCloskey, 1978). A number of examples illustrate this:

- the deafferented subject is only able to estimate weight when the consequences of his lifting actions are visible to him (Fleury, 1995).
- When matching tension during tendon vibration of the agonist muscle, the subject is aware of a discrepency between the force sensation and the actual force, and adjusts the tension until it is correctly matched (McCloskey, Ebeling & Goodwin, 1974).
- Roland and Ladegaard-Pedersen (1977) notes that subjects can still effectively match forces produced by compression springs following partial neuromuscular block with gallamine.

EVOKING SENSATIONS OF FORCE: There are suggestions that peripheral receptors may have a more direct role in sense of effort:

- Under isotonic conditions, output from the Golgi tendon organ efficiently codes contractile tension (Petit, Scott & Reynolds, 1997).
- Sophisticated mechanisms controlling load and grip forces when lifting objects between the finger tips are mediated by sensory feedback provided by cutaneous receptors at the digit tips. (Johansson & Westling, 1984; Westling & Johansson, 1987; Kinoshita *et al.*, 1997; reviewed in Johansson, 1996a, 1996b; Wing, 1996).
- Henningsen, Knecht and Henningsen (1997) have shown that control of fine forces in the absence of visual feedback is better when either muscle /and or cutaneous afferent feedback is provided.

Anatomical specialisations In Sense Of Effort

The technique of weight matching with the ipsilateral and contralateral hands has been used to compare the discriminative abilities of various human hand muscles (reviewed in Gandevia & Kilbreath, 1995). Kilbreath & Gandevia found that the flexor pollicis longus muscle of the thumb was particularly well specialized in comparison to first dorsal interosseus, flexor digitorum profundus and adductor pollicis muscles of the hand (Kilbreath & Gandevia, 1992; 1995). The differences, however, were not due to cutaneous sensitivity but rather neural control mechanisms, since local anaesthesia did not improve accuracy. Gandevia and Kilbreath (1995) have also

demonstrated that proximal upper limb musculature was significantly better than distal musculature at weight matching relative to the maximal contraction of the muscle.

Fatigue

The phenomenon of fatigue is closely related to sense of effort. Changes in CNS drive, failure of neuromuscular transmission and contractile failure have all been implicated as possible mechanisms in fatigue (reviewed in Bigland-Ritchie & Woods, 1984). Further consideration of the diverse processes involved in fatigue is beyond the scope of this thesis.

1.3.5. Summary

Animal models have demonstrated that proprioceptors from all three sources of muscle, joint and skin provide information which can be used to derive joint position, movement and torque (Gandevia & Burke, 1992). Human psychophysical tests also indicate that that sensory receptors in muscle, joint and skin can all evoke kinaesthetic sensations. In the hand, the sense of movement is optimal when all the proprioceptive machinery is intact (Gandevia & McCloskey, 1976). There are suggestions that some receptors may have a more specific role. Joint receptors may be particularly important in sensing movements towards the end range of motion (Clark & Burgess, 1975). Muscle receptors may mediate position sense (Clark *et al.*, 1985). Cutaneous receptors may have a potential role in providing unbiased kinaesthetic feedback during conditions of loading when fusimotor drive is high (Ferrell & Smith, 1989).

The role of sensory receptors in the sense of force is more ambiguous (McCloskey, 1981). At the least they appear to have a role in the facilitation (Gandevia et al, 1990) and calibration (Gandevia & McCloskey, 1978) of movements. It is possible that they may have a more direct role in evoking sensations of force (Johansson & Westling, 1987; Petit, Scott & Reynolds, 1997).

The importance of sensory receptors to kinaesthesia and sense of force is fundamental in understanding the consequences of peripheral nerve injury upon proprioception. A nerve transection will result in a loss of sensory innervation in the muscle, skin and joint depending on innervation patterns of the nerve. Functional recovery of proprioception is, therefore, dependent upon the degree and specificity of reinnervation of these sensory receptors and in the reestablishment of appropriate mechoreceptive responses. Processes of peripheral and central plasticity may also play a role in accommodating for changes in connectivity occurring during reinnervation.

1.4. Peripheral Nerve Injury In The Hand

There are three issues pertaining to recovery of proprioception in the hand following peripheral nerve trauma:

1. ***Innervation Patterns Of The Hand:*** A single nerve transection will result in a loss of specific sensory sources depending on the muscle, skin and joint innervated by that particular nerve. Since all three sources appear to have some role in proprioception, an appreciation of the innervation patterns of each of the nerves supplying the hand is the first stage in understanding the effect of PNI on proprioception. However, such considerations are only theoretical and need to be corroborated by quantitative and functional assessments of the proprioceptive consequences of removing the sensory contribution of each nerve innervating the hand.

2. ***Factors Influencing The Successful Reestablishment Of Connections:*** Motor and sensory structures may degenerate as a result of prolonged denervation (Zelená, 1994). The type and degree of injury, the mixed content of the nerve and the subsequent surgical resuturing of the nerve will all influence the number of axons entering the distal segment and the specificity of the reinnervation of end organs (Dellon, 1981; Banks & Barker, 1989, 1991; Zelená, 1994; Scott, 1996). Mechanisms of neurotropism and neurotrophism act to assist the degree and specificity of recovery (Griffin & Hoffman, 1993). Specificity of reinnervation influences the recovery of appropriate mechanoreceptive responses in proprioceptors (Lewin & McMahon, 1991a & 1991b). Practically, the degree of reinnervation of proprioceptors and the capacity to derive meaningful sensory information from reinnervated proprioceptors can be assessed by measuring the ability of PNI subjects to detect and grade movements.

3. ***Mechanism Of Plasticity:*** Inappropriate reinnervation will result in abnormal proprioceptive sensations. Mechanisms of peripheral and central plasticity act to adapt for changes in connectivity and receptor firing patterns. The efficacy of these mechanisms in realistic terms will be evident from the recovery of proprioception during the rehabilitation of long-term PNI subjects (Kaas, 1991; Florence *et al.*, 1994).

1.4.1. Innervation of the Hand

The typical patterns of innervation of the three nerves supplying the hand are described in most standard anatomical texts (eg. Gray's Anatomy, 1995, Palastanga, Field & Soames, 1994). Figures 1.3. - 1.6. illustrate the routes taken by the nerves supplying the hand, along with typical innervation patterns of muscle, skin and joint by each nerve.

Figure 1.3.

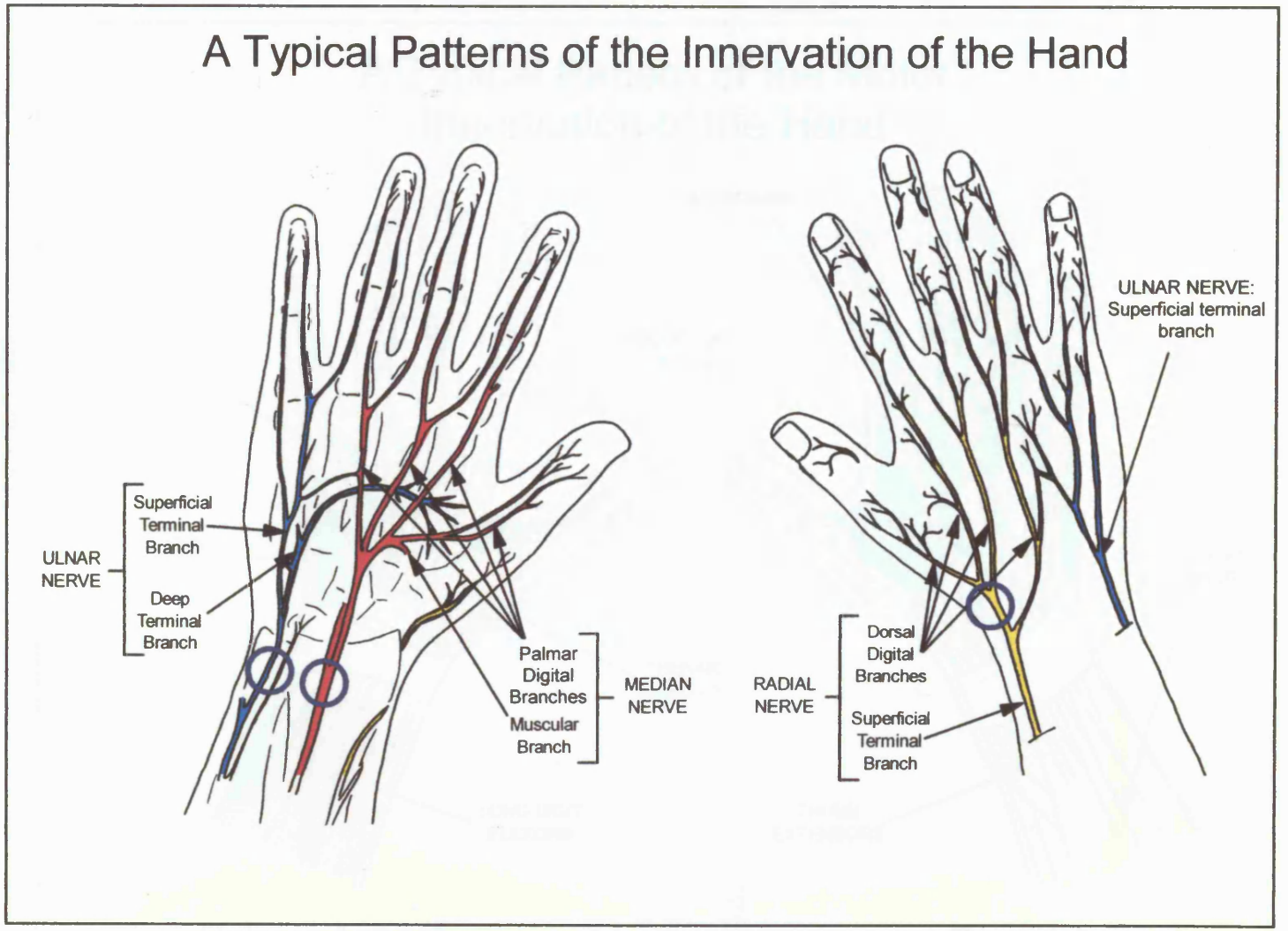

A Typical Patterns of the Innervation of the Hand
ULNAR N.
MEDIAN N.
RADIAL N.
Site of application of local anaesthetic
ULNAR NERVE
Superficial Terminal Branch
Deep Terminal Branch
Palmar Digital Branches
Muscular Branch
MEDIAN NERVE
ULNAR NERVE: Superficial terminal branch
RADIAL NERVE
Dorsal Digital Branches
Superficial Terminal Branch

Figure 1.4.

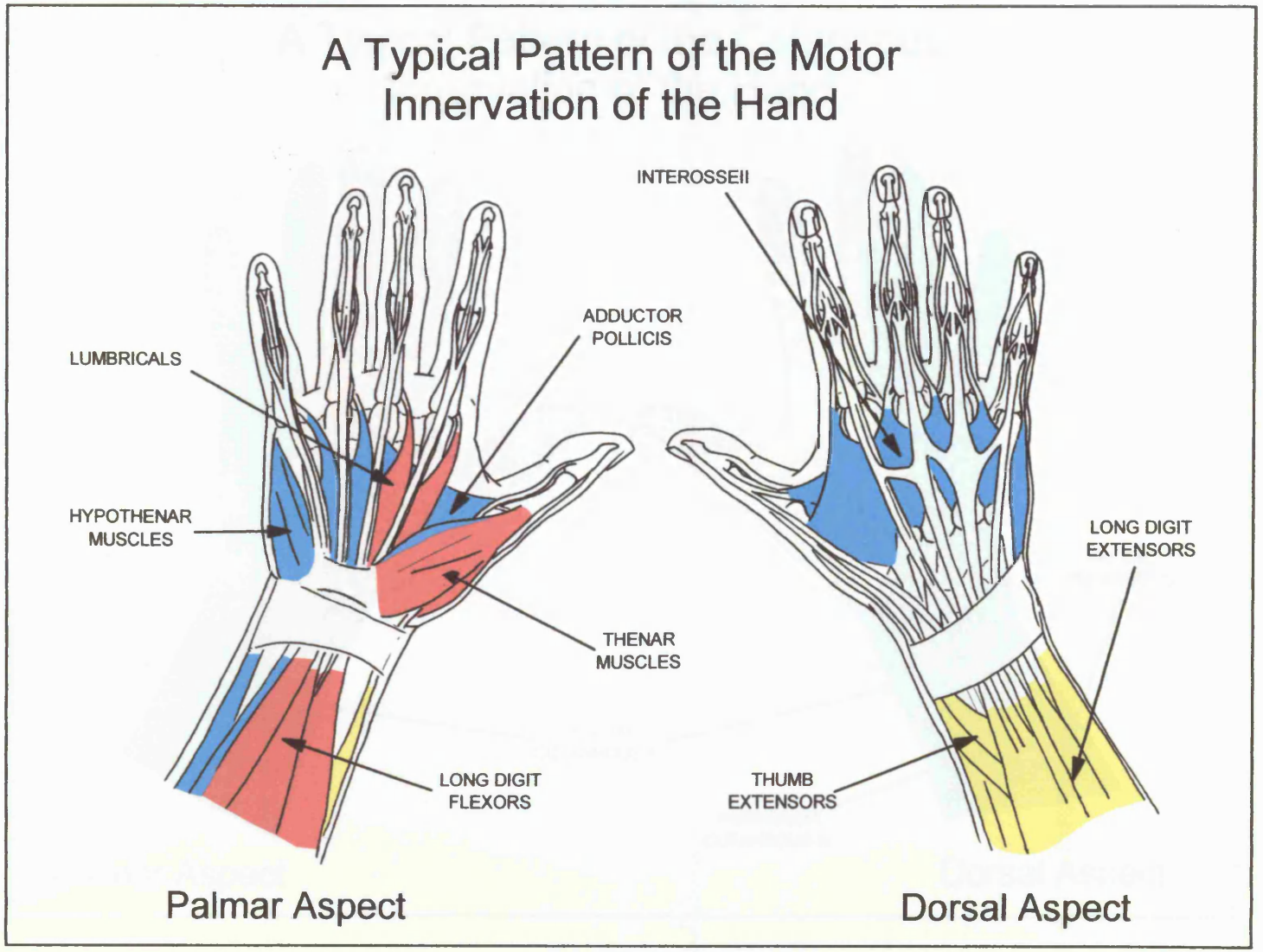

A Typical Pattern of the Motor Innervation of the Hand
ULNAR N.
MEDIAN N.
RADIAL N.
LUMBRICALS
ADDUCTOR POLLICIS
HYPOTHENAR MUSCLES
THENAR MUSCLES
LONG DIGIT FLEXORS
INTEROSSEII
LONG DIGIT EXTENSORS
THUMB EXTENSORS
Palmar Aspect
Dorsal Aspect

Figure 1.5.

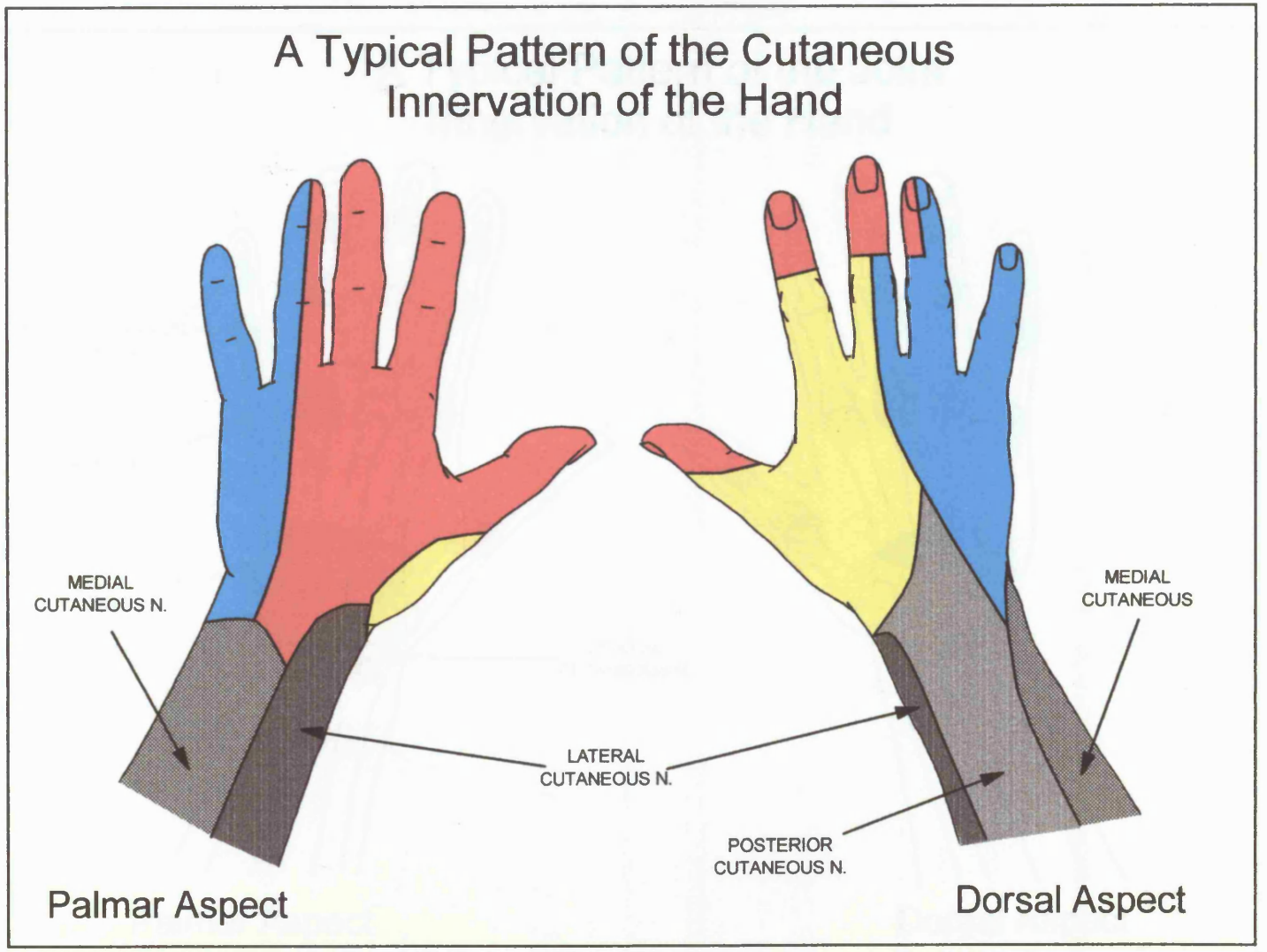
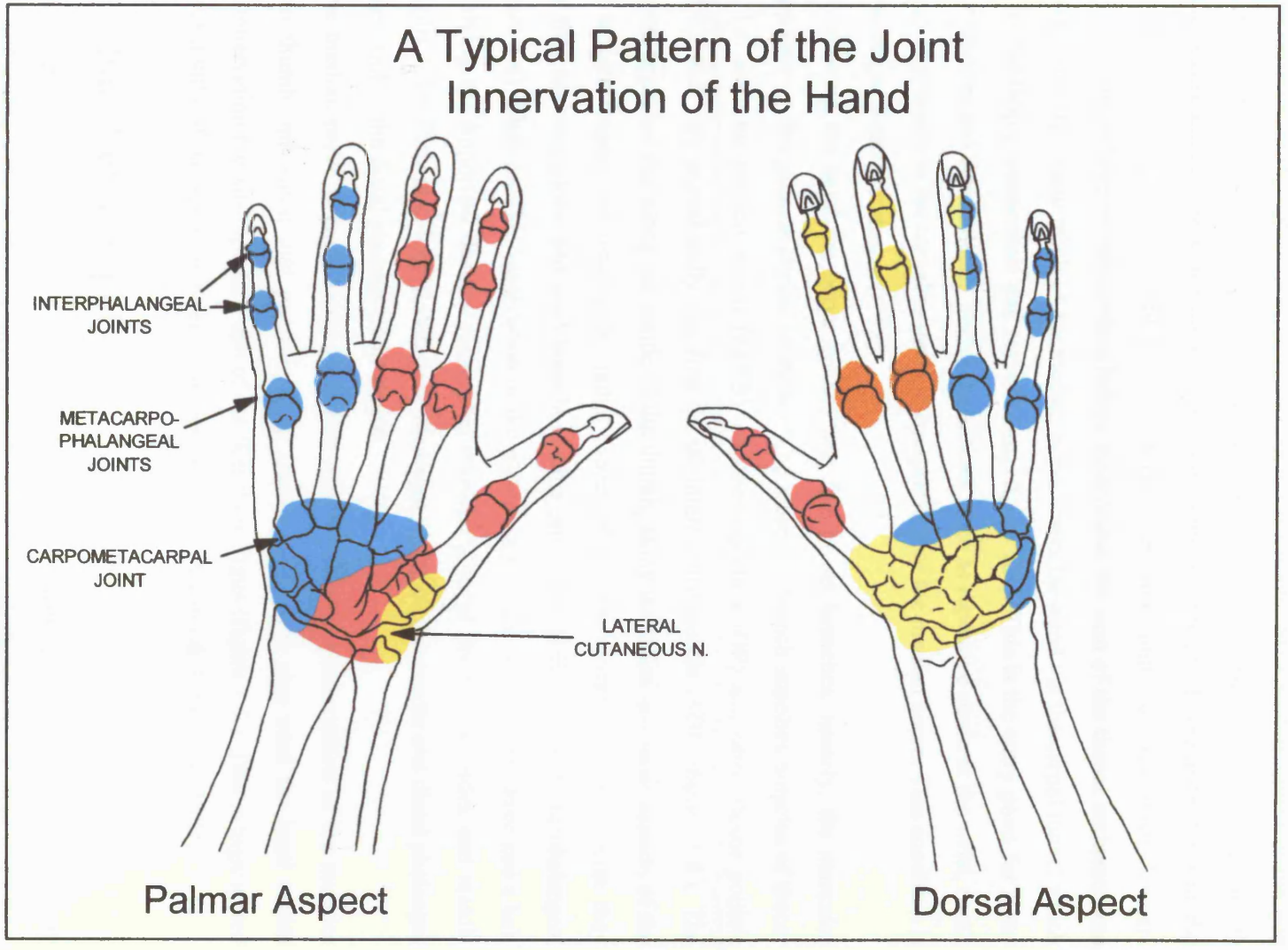

A Typical Pattern of the Cutaneous Innervation of the Hand
ULNAR N.
MEDIAN N.
RADIAL N.
MEDIAL CUTANEOUS N.
LATERAL CUTANEOUS N.
POSTERIOR CUTANEOUS N.
MEDIAL CUTANEOUS
Palmar Aspect
Dorsal Aspect

Figure 1.6.


A Typical Pattern of the Joint Innervation of the Hand
ULNAR N.
MEDIAN N.
RADIAL N.
INTERPHALANGEAL JOINTS
METACARPO-PHALANGEAL JOINTS
CARPOMETACARPAL JOINT
LATERAL CUTANEOUS N.
Palmar Aspect
Dorsal Aspect

1.4.1.1. Median Nerve Supply

The median nerve originates from spinal roots C6-C8 and takes a deep course in the arm close to the brachial artery. In the proximal forearm the *anterior interosseus nerve* branches to supply digit flexors and also provides some innervation to the wrist joints. In the distal forearm, the median nerve lies more superficially and divides to form the *palmar cutaneous branch* which enters into the deep fascia and flexor retinaculum before innervating the skin of the thenar eminence and of the central palm. The main trunk of the median nerve enters the hand via the carpal tunnel which is formed by the flexor retinaculum and carpal bones (figure 1.3.). This is the entry point for many digit flexor tendons and consequently certain conditions, such as repetitive strain at the wrist, result in a build up of pressure in the carpal tunnel and compression of the median nerve. This condition is described as carpal tunnel syndrome (CTS).

On entering the hand the nerve divides into five or six branches, namely, the *muscular branch*, and four or five *palmar digital branches*. The muscular branch supplies muscles of thenar eminence, i.e. abductor pollicis brevis (AbPB), opponens pollicis (OP) and often flexor pollicis brevis (FPB), and very occasionally the first dorsal interosseus muscle (1DI) (figure 1.4.). The palmar digital branches run along the inside of the thumb, along the radial and ulnar aspects of the index and middle fingers and usually the radial aspect of the ring finger. On their course they supply the first two lumbricals and send branches to the metacarpophalangeal and interphalangeal joints (figure 1.6). They provide innervation of the palmar skin of the most lateral three and a half digits supplying the important densely innervated terminal pads of the thumb, index and middle fingers (figure 1.5.). They also supply skin over the dorsal aspect of the middle and distal phalanges of the fingers and of the distal phalanx of the thumb.

The median nerve is particularly important with regard to the innervation of the muscles involved in thumb opposition and precision grip (figure 1.4.). It is also vital for hand tactile sensation, innervating the all-important tips of the first three digits (figure 1.5.). This is highlighted by the fact that 90% of the nerve supplies cutaneous receptors (Vallbo & Johannson, 1984).

1.4.1.2. Ulnar Nerve Supply

The origin of the ulnar nerve is typically C8 and T1 with a communication frequently originating in C7. The nerve follows a more medial course through the upper arm than that of the median nerve. *Muscular branches* in the proximal forearm supply long digit flexors, whereas a more distal *palmar cutaneous branch* supplies the skin of the ulnar aspect of the palm. Proximal to the wrist the ulnar nerve also divides to give the *dorsal branch* which courses dorsally, supplying flexor carpi ulnaris, and further divides into two or three branches of the dorsal digital nerves. These supply both skin and joints of the little and ulnar aspect of the ring finger. The possibility of a third digital nerve originating from the ulnar nerve means that adjacent sides of the proximal two thirds of the ring and middle fingers may be innervated by the ulnar nerve or, alternatively by the

radial nerve. The *superficial terminal branch* divides into two *palmar digital nerves,* one of which supplies the medial side of the little finger, and the other joins the median nerve to supply facing sides of the ring and little finger (figure 4.3.).

The *deep terminal branch* of the ulnar nerve passes through the muscles of the hypothenar eminence, crossing the hand before it terminates (figure 1.3.). It is a very important branch with regard to intrinsic musculature. It supplies branches to the muscles of the hypothenar eminence, i.e. abductor digiti minimi (AbDM), flexor digiti minimi (FDM) and opponens digiti minimi (ODM). It also supplies all the palmar interossei (1 to 4PI), dorsal interossei (1 to 4DI) and the third and fourth lumbricals (LUM3 & LUM4) (figure 1.4.). It then terminates on the adductor pollicis (AP) and sometimes innervates the FPB. These two muscles are important in providing power during grip. Although precise patterns are not altogether certain, the deep terminal branch also provides branches to intercarpal, carpometacarpal and intermetacarpal joints (Fukumoto *et al.*, 1993).

Compared to the median nerve, the ulnar nerve is much less significant as a cutaneous nerve (figure 1.5.), but it is vital for its contribution to intrinsic hand musculature (figure 1.4.). It is essential for the control of finger movements in the coronal plane. The ulnar nerve is responsible for innervating all the skin, joint and intrinsic musculature along the medial aspect of the hand (see figures 1.4 to 1.6.).

1.4.1.3. Radial Nerve Supply

In relation to nerve injury in the distal forearm, the radial nerve is considered to be the least significant of all the three nerves supplying the hand. This is because no intrinsic hand musculature are supplied by the radial nerve. In the upper arm and forearm a large number of muscles are innervated by branches arising from the radial nerve, including most of the long digit flexors and a number of muscles moving the thumb, i.e. extensor pollicis longus (EPL), abductor pollicis longus (APL) and extensor pollicis brevis (EPB).

Only cutaneous and articular branches, arising from the *superficial terminal branch,* enter the hand (figure 1.3.). This branch divides to form four or five *dorsal digital nerves* supplying the dorsal aspects of the hand and digits. The first two branches supply the radial and medial sides of the thumb up to the nail bed. The third branch supplies the lateral aspect of the index finger up to the centre of the middle phalanx. The fourth and fifth branches supply adjacent sides of the index and middle and the middle and ring fingers, respectively. The middle and ring fingers are innervated by the radial nerve up to proximal interphalangeal joints (figure 1.5.). The digital nerves supply branches also to the metacarpophalangeal and proximal interphalangeal joints (figure 1.6.). The deep terminal branch of the radial nerve provides articular innervation of the intercarpal and intermetacarpal joints and also, notably, the radial aspect of the carpometacarpophalangeal joint of the thumb (Fukumoto *et al.*, 1993).

The radial nerve has been implicated as an important proprioceptive source of joint and skin afferents for sensing movements in the digits (Edin, 1990; Edin and Johansson, 1995).

1.4.1.4. Anomalous Nerve Supplies

Nerve anomalies occur because of unusually high origins of the nerve or communicating branches between nerves causing nerve fibres to run in a different nerve, either temporarily or permanently (Meals & Calkins, 1991). The nerve supply to the muscles of the thenar eminence, especially the FPB muscle, can be highly variable due to communicating branches such as the Martin-Gruber communication. Other less frequent anomalies include an ulnar innervated AbPB and OP muscles, and a median innervated 1DI muscle. Cutaneous innervation patterns can also differ, particularly around areas of overlap between two nerves (Jolley *et al.*, 1997).

1.4.1.5. Contribution of Each Nerve to Proprioception

Although anatomical innervation patterns of the nerves supplying the hand can be described in some detail, the functional importance of each nerve to proprioception in the digits is still only a matter of conjecture. To provide a more quantitative measure of the contribution of each nerve to proprioception, local anaesthetic blocks were applied to median, ulnar and radial nerves using short lasting lignocaine and longer lasting marcaine. Accordingly, the loss in the ability to sense and grade movements and forces in the digits following single or combined peripheral nerve anaesthesia gives a clear indication of the functional contribution of each nerve to proprioception. The anaesthetic models also allow the establishment endpoints of the range of proprioceptive recovery. At one end of the spectrum is normal proprioceptive hand function. At the opposite end of the spectrum is the proprioceptive acuity evident when a nerve offers no afferent or efferent contribution at all.

1.4.2. Classification of Peripheral Nerve Injury

The first classification of nerve injuries was given by Seddon (1943):

1. ***Neuropraxia*** is the name given to a localised conduction block with no mechanical disruption of the axon. A neuropraxic conduction block can result from an acute compression injury (Rudge, 1974). Removal of the compression will cause a return to normal conduction although the time taken to recover may vary from a few minutes to a number of weeks.

2. ***Axonotmesis*** is disruption of the axon causing interruption of the axonal transport systems. Distal to the lesion, the axon degenerates and the proximal segment undergoes chromalytic changes in preparation for regrowth. Since the endoneurial tubes remain intact, axons regenerate with end organ specificity yielding excellent recovery. Chronic compression injuries often result in axonotmesis. Entrapments result in weakness, clumsiness, paraesthesia, numbness, pain and localised demyelination along internode sections at the compression site (Eversmann, 1993). Compression of the median nerve in the carpal tunnel (carpal tunnel syndrome or CTS) is the most frequent type of nerve entrapment in the upper limb (Kuntzer, 1994).

3. ***Neurotmesis*** or transection of the nerve has a profound effect on both peripheral and central structures of the nervous system. The most significant difference between axonotmesis and neurotmesis is that axons may be directed along alternative routes, including different nerve fascicles, non-neural tissue and often may not even cross the scar tissue barrier. This results in unsuccessful or inappropriate reinnervation of end structures. Central mechanisms of plasticity may play a role in accommodating for the differences in connectivity.

Following nerve trauma epineural repair of the nerve must be performed if there is to be any chance of functional reinnervation of target structures. Commonly, perineural repair of the transected nerve is also performed by the surgeon in an attempt to improve the degree and specificity of recovery (Scott, 1986; Shaw, Wilgis & Brushart, 1993)

1.4.3. Degeneration of the Nervous System

1.4.3.1. Changes in the Distal and Proximal Segment

The pivotal event in axonal degeneration is axotomy, which causes disruption of cytoskeletal microtubules and neurofilaments involved in axonal transport (reviewed in Bowe *et al.*, 1989; Griffin & Hoffman, 1993; Ide, 1996). Following disruption of the axolemma membrane, an influx of Ca^{2+} causes activation of proteases, which begin to convert the elaborate cytoskeleton into granular debris (Zimmerman & Schleapfer, 1982). Loss of synaptic transmission results after a number of days depending on the length of the distal stump which continues to transport materials. Eventually, myelin forms ovoid structures containing disorganised whorls of myelin, which are degraded by both macrophages and Schwann cells (Stoll *et al.*, 1989). Macrophages, the majority of which are recruited from the circulation, remove cytoskeletal debris and myelin (Schiedt & Friede, 1987).

Following axotomy, the cell body and axon of the proximal stump undergo profound alterations in preparation for regeneration of the severed axon. Chromalytic changes include somatic enlargement, displacement of the nucleus to the periphery, rough endoplasmic reticulum break up and dispersal, an increase in the number of free ribosomes, and an increase in the mRNA content coding for the cytoskeletal proteins and growth associated proteins such as GAP-43 (Griffin & Hoffman, 1993; Skene, 1989; Ide 1996). Dendritic trees are retracted, somatic excitablility increases and excitability of the initial segment decreases (de la Cruz, Pastor & Delgado-Garcia, 1996).

1.4.3.2. Changes in Target Structures

Muscle undergoes rapid and profound atrophy following denervation, as quantified by measuring weight, cross-sectional area or protein content (Davis & Keirnan, 1981). These changes are mediated by the expression of myogenic regulatory factors (Adams *et al.*, 1995).

Muscle Receptors: Mature *muscle spindles* do not degenerate but may undergo some atrophy following denervation (Poppele, 1993). Motor denervation causes the polar regions to atrophy, whereas sensory denervation causes the equatorial regions to shrink. *Golgi tendon organs* do not appear to undergo any atrophy subsequent to denervation (Zelená, 1994).

Cutaneous Receptors: *Meissner corpuscles* atrophy significantly, for example, in the rhesus monkey they are reduced to half their normal size after 4 months of denervation (Ide, 1982). *Pacinian Corpuscles* are much more resistant to atrophy. In the cat, only atrophy of the inner core is evident after 6 months (Zelená, 1994). In rat hairy skin, two populations of *Merkel cell receptors* exist. Approximately 60% of Merkel cells do not survive denervation whereas the remnant undergoes atrophy slowly (Nurse, Macintyre & Diamond, 1984, Mills, Nurse & Diamond, 1989, Dubový & Aldskogius, 1996). However, no equivalent study has been carried out in glabrous skin. *Ruffini endings* have only been studied in joint receptors where they are little affected by denervation (Sasamura, 1986).

1.4.4. Regeneration of the Nervous System

1.4.4.1. Growth Cone Elongation and Guidance

In regeneration of the PNS, axonal extension is concentrated to a defined region called the growth cone comprised of filopodia and lamellapodia extending on a fine meshwork of actin filaments (Bixby & Harris, 1991; Griffin & Hoffman, 1993; Ide, 1996). Fast and slow axonal transport systems are critical for growth cone function. The additional plasma membrane needed for axonal extension is supplied by the fusion of vesicles, carried by fast anterograde transport. Slow anterograde transport carries actin and tubulin filaments needed for the assembly of the cytoskeletal structure of the axon at the growth cone (Reviewed in Ide, 1996). The rate of this slow transport system is the limiting factor of the rate of axonal extension and is equivalent to 2-4mm/day (Wujek & Lasek, 1983, Watson *et al.*, 1989). Since the velocity of slow retrograde transport decreases with age, so also, does the rate of axon regeneration (Watson *et al.*, 1989).

Unlike the CNS, axons in the PNS possess a powerful potential for regrowth because of the favourable conditions that exist in the distal segment of peripheral nerve. Both positive and negative influences upon the growth cone elongation act specifically to direct axons towards targets (Griffin & Hoffman, 1993; Gomez, Snow & Letourneau, 1995):

1) The Basal Lamina Layer: The Schwann cell basal lamina layer provides a surface on which regenerating axons vigourously grow (Ide, Osawa & Tohyama, 1990). Adhesion molecules, the most notable being laminin, provide a surface on which cytosketal components can be built up during axonal extension (Letourneau, Condic & Snow, 1994; Ide, 1996).

2) Expression of Adhesion molecules by Schwann Cells: Schwann cells of the PNS provide a supportive role in the regrowth of axons by expressing immunoglobulins and cadherins both of

which promote neurite outgrowth (reviewed in Bixby and Harris, 1991; Ide, 1996). In contrast, oligodendrocytes of the CNS express proteins which inhibit the outgrowth of neurites (Caroni, Savio & Schwabb, 1988).

3) Production of Neurotrophins: Nerve growth factor (NGF) and brain derived growth factor (BDNF) are both expressed by Schwann cells and target structures following axotomy (Heumann *et al.*, 1987, Meyer *et al.*, 1992). Neurotrophin-3 (NT-3) also appears to mediate trophic interactions in proprioceptive and tactile fibres (Snider & Wright, 1996; Airaksinen & Meyer, 1996).

4) Neurite Outgrowth Inhibition: Some substances such as certain membrane glycoproteins can inhibit neurite outgrowth by causing growth cone collapse (Patterson, 1988; Walter, Allsop & Bonhoeffer, 1990). .

5) Collateral Pruning: Following reverse grafting experiments, similar numbers of axons initially reinnervate correct and incorrect nerve branches. Over a number of weeks, inappropriate collateral branches are eliminated or 'pruned', even in the absence of target structures (Brushart, 1993).

1.4.4.2. Reinnervation Of Motor Targets

The time period of denervation is a critical factor in the recovery of muscle. Denervation periods of more than one month in the rat result in profound loss of muscle mass and force production (Kobayashi *et al.*, 1997). Prolonged denervation rather than prolonged axotomy results in reduced reinnervation implying that the deterioration of the muscle is the underlying mechanism behind poor reinnervation (Fu and Gordon, 1995a, 1995b).

The homogeneous organisation of motor units is maintained after reinnervation, not only following crush injury, but also subsequent to nerve transection and repair. Cross reinnervation experiments with fast and slow muscle nerves have demonstrated that the motor nerve can induce the transformation of the constituent muscle fibres of motor units from one type to another (Buller, Eccles & Eccles, 1960; Close, 1965; Bagust, Lewis & Westerman, 1981; Chan *et al.*, 1982; Lewis, Rowlerson & Webb, 1982). It is thought that the firing rate of the regenerating axon induces this transformation (Salmons & Sreter, 1976). Consequently, in a muscle of mixed motor units, the proportions of motor unit types is maintained after reinnervation (Foehring, Sypert & Munson, 1986a & 1986b; Gordon & Stein, 1982), as well as the recruitment order of the motor units (Cope & Clark, 1993).

An important difference between normal and reinnervated motor units is that, following transection, reinnervated muscle fibres of the motor unit are clumped together instead of being dispersed throughout the muscle (Dubowitz, 1967; Karpati & Engel, 1968). Many authors also record the presence of enlarged motor units (Chan *et al.*, 1982; Dum *et al.*, 1986; Gordon & Stein, 1982, Fu & Gordon, 1995a & 1995b). EMG recordings from mouse hindlimb muscles also show that transection and reinnervation interferes with agonist and antagonist coordination due to inappropriate innervation by efferents from other motor neuron pool (Wasserchaff, 1990).

In all, peripheral nerve trauma has a profound effect on the organisation of peripheral circuitry and, in particular, the size and distribution of motor units (Fu & Gordon, 1995a & 1995b). Since a number of authors have emphasised the central origin of 8-10 Hz pulsatile output (Wessberg, 1995; Wessberg & Vallbo, 1996; McAuley *et al.*, 1999) it would of interest to investigate how such dramatic peripheral disturbances affect the nature of 8-10 Hz pulsatile output. The majority of studies have measured oscillations in the digits when performing extension: flexion moves predominantly under the control of extrinsic forearm muscles (Vallbo & Wessberg, 1993; Wessberg, 1995; McAuley *et al.*, 1999). The present study contains an analysis of the 8-10 Hz tremor associated with slow movements and position holding in intrinsic hand musculature. The frequency of occurrence and amplitude of 8-10 Hz tremor in normal intrinsic musculature was compared to that generated by reinnervated musculature following median and/or ulnar nerve injury and repair.

1.4.4.3. Reinnervation Of Sensory Targets

Subsequent to nerve trauma there are four alternatives for regenerating axons:

- Axons may not reach target structures either because they do not cross the scar tissue barrier at the site of the trauma or alternatively because they enter nerve connective tissue or foreign tissue resulting in fronds of regenerating fibre or neuroma formation.
- An axon may enter its original endoneurial tube and reinnervate correct target structures. This commonly follows nerve crush.
- The axon may enter a different endoneurial tube and be directed towards a target structure of a similar modality.
- The axon may enter a different endoneurial tube but be directed towards a target structure of a different modality.

In the case of misdirected axons, mechanisms of peripheral and central plasticity have a role in reinterpretting the new patterns of sensory and motor connectivity.

1. Unsuccessful Reinnervation

FACTORS INFLUENCING SUCCESS

A number of factors influence the amount of axons successfully reinnervating target structures:

- Inappropriate and unsuccessful reinnervation is dramatically improved by epineural and perineural primary repair of the transected nerve (Sunderland, 1978; Scott, 1986; Shaw, Wilgis & Brushart, 1993). Alternatively, when the injury site is not cleanly sectioned or when surrounding tissue is damaged, the nerve is resectioned and a secondary repair performed. The loss of length is made up by mobilisation of the nerve or using nerve grafting techniques. Delayed repair of 6 weeks results in no significant additional loss in sensory innervation (Barker, Berry & Scott, 1990).

- The mixed content of a nerve also influences the degree of successful reinnervation since it influences the proportion of available targets. For example, Banks and Barker (1989, 1991) compared the reinnervation of spindles in the tenuissimus muscle, which contains Ia and II afferents but no Ib or cutaneous afferents, to reinnervation in the common peroneal nerve, which is a mixed nerve of multiple fascicles of cutaneous and muscle afferents. Loss of spindle afferents was 52% of Ia and 49% of II fibres in the tenuissimus compared to a 79% of Ia and 86% of II afferents in the peroneus brevis muscle. Conversely, Horch and Linsey (1981) found that in the cat cutaneous nerves, 75% of fibres crossed the transection site, reestablishing functional connections.
- It is suggested that the more distant location of Golgi tendon organs from the nerve entry point compared to the spindle may account for the poorer innervation of tendon organs following transection (Collins, Mendell & Munsen, 1986).

PROPERTIES OF UNSUCCESSFUL AFFERENTS

Two collaborating groups have investigated the mechanical sensitivities of afferents fibres which have not reached target structures by artificially inducing neuroma formation (Johnson & Munson, 1991; Proske, Iggo & Luff, 1995). They found that although both cutaneous and muscle afferents responded to mechanical vibration, most muscle afferents had a static discharge whereas cutaneous afferents did not. Three types of muscle afferent discharge were evident:

- Ia afferents had an intermittent or bursting resting discharge at rest
- II afferents had a steady resting discharge and low thresholds to stretches applied to the cuff
- Ib afferents had no resting discharge but had high stretch thresholds

Administration of colchicine demonstrated that the mechanosensitivity was caused by disruption of retrograde transport systems (Proske, Iggo & Luff, 1995). It is likely that the mechanosensitivity of muscle afferents mediates both Tinel's sign and neuroma sensitivity.

EXPANSIVE REGENERATIVE REINNERVATION

When structures are left denervated due to unsuccessful reinnervation, expansive regenerative reinnervation (ERR) may come into force in which newly reinnervating axons expand their connections to cover the denervated areas (Wiesenfeld-Hallin, Kinnman & Aldskogius, 1989; Dubový & Aldskogius, 1996). In the skin, collateral sprouting from already established connections only takes place in C-fibre axons but is not known to occur in mechanoceptor axons (Devor *et al.*, 1979), However, ERR of mechanoreceptive axons into foreign skin following nerve crush is known to take place in the rat hindpaw although there appears to be no functional recovery of foreign glabrous skin in the rat (Diamond, Holmes & Coughlin, 1992b Diamond *et al.*, 1992; Weisenfeld-Hallin, Kinnman & Aldskogius, 1989). ERR also occurs in the motor system resulting in expanded motor units in comparison to their original size (Chan *et al.*, 1982; Dum *et al.*, 1986; Gordon & Stein, 1982, Fu & Gordon, 1995).

2. Reinnervation Of Correct Structure: Effects Of Nerve Crush

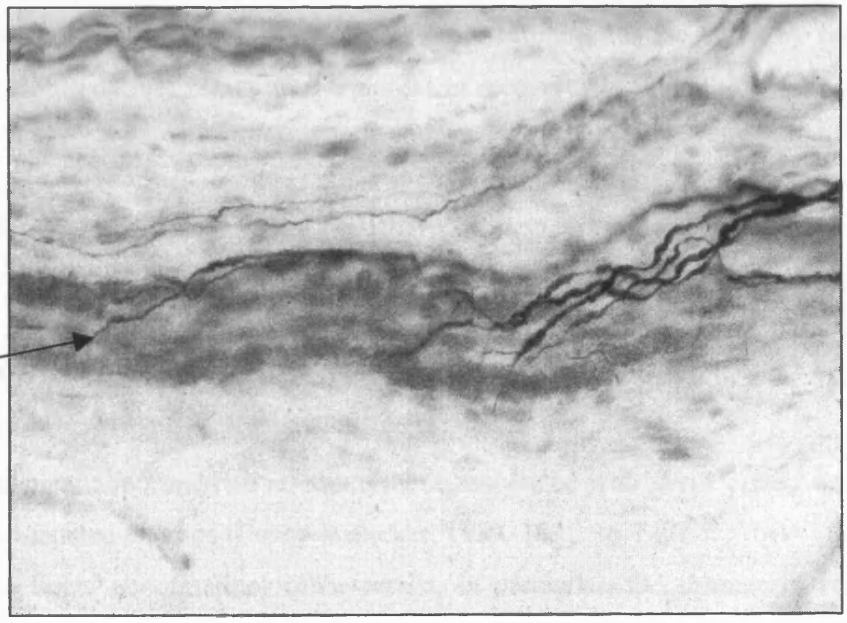
Due to redirection of axons to original targets, functional recovery subsequent to nerve crush is highly successful.

MUSCLE RECEPTORS

Muscle Spindles: Anatomically, regenerated endings are often abnormal. Primary endings are usually reduced in size, with a smaller number of annulospirals, than in the normal spindle (Barker, Scott & Stacey, 1985; 1986; 1988; Scott, 1996). Following prolonged denervation, a diffuse network of tapering axons often form instead of annulospiral endings (see figure 1.7.). For example, following cat common peroneal nerve crush, the average number of regenerated terminal bands falls from 29 in the normal spindle, to 10 bands after 50 days denervation and 0.6 bands after 134 days denervation (Barker, Scott & Stacey, 1985). Sometimes hyperinnervation of spindles by primary afferents occurs. Secondary endings will sometimes grow through the equatorial region and innervate both poles.

Even though spindles may possess anatomical abnormalities, the functional recovery of spindles following nerve crush is excellent (Hyde & Scott, 1983; Barker, Scott & Stacey, 1986; 1988). Phasic, tonic and background discharges of reinnervated spindles, all recover at different rates. The phasic response recovers very rapidly, within a number of weeks in the cat. The static response slowly reappears over one or two months. Finally, the resting discharge is restored so that after 4 months, 90% of muscles spindles show background firing (Hyde & Scott, 1983). Recovery of fusimotor and skeletofusimotor innervation subsequent to nerve freezing and nerve crush, respectively, have also been shown to recover to normal levels of innervation (Scott, 1985; 1987).

Figure 1.7. A teased silver preparation of a reinnervated cat muscle spindle following prolonged crush of 134 days (courtesy of Dr J.J.A. Scott).



Golgi Tendon Organs: In early stages, reinnervated tendon organs manifest phasic responses, however 6 weeks after common peroneal nerve crush in the cat, over 80% of afferents fire tonically during a steady contraction, (Scott, Davies & Petit 1995; Scott, Petit & Davies, 1996). Overall, firing rates following reinnervation are less, but the reduced force generation and increased fatiguability of recovering skeletal muscle also contribute.

CUTANEOUS RECEPTORS

Meissner Corpuscle (FA I Receptors): These are the first cutaneous receptors to recover after nerve crush (Sanders & Zimmerman, 1986). Within one or two months the diminished size of corpuscle returns to normal in the rat (Ide, 1982). Although the rapidly adapting character of receptors is present from the earliest stages, thresholds remain high for a number of months after nerve crush. They return to normal values by 8 weeks in the rat (Sanders & Zimmerman, 1986) and 3-5 months in the baboon (Terzis & Dykes, 1980).

Pacinian Corpuscle (FA II Receptors): Patterns of Pacinian corpuscle reinnervation following crush injury are complicated by interspecies variation. In the rat, the FA II receptor recovers later than FA I and SA I receptors (Sanders & Zimmerman, 1986). They are characterised by initial hyperinnervation with 74% of corpuscles having more than one terminal, 3 to 18 months after nerve crush (Zelená, 1984). Cat crural Pacinian corpuscles, however, do not exhibit the same degree of hyperinnervation and new inner cores form around any additional terminals (Zelená, 1994). With respect to receptor physiology, tuning curve thresholds fall over the course of six months, although the slope of the tuning curve does not change over this time period (Sanders & Zimmerman, 1986).

Merkel Cells (SA I Receptors): Just as denervation causes the degeneration of a large proportion of Merkel cells, so reinnervation induces neoformation of SA I receptors (Burgess *et al.*, 1974). Thus, in the rat, normal numbers of Merkel cells are restored by 6-10 weeks after nerve crush (Nurse, Macintyre & Diamond, 1984). Elevated dynamic sensitivities return to normal after two months in the rat (Sanders & Zimmermann, 1986). The static response, as measured by rate of adaption, however, approaches normal values after 6 months of recovery.

JOINT RECEPTORS

Only reinnervated Ruffini endings in the joint have been studied where the receptors are reinnervated by 30 days after nerve crush in the rat (Sasamura, 1986).

3. Reinnervation Of Incorrect Structure Of A Similar Modality

MUSCLE RECEPTORS

Muscle Spindles: Anatomical abnormalities resemble those associated with nerve crush, such as reduced annulospiral and tapered endings (Banks & Barker, 1989, 1991; Ip, Luff & Proske, 1988). Unlike nerve crush, functional abnormalities often persist, in particular, the absence of resting discharge and a failure to fire in the plateau phase of a ramp hold and stretch (Gregory, Luff &

Proske, 1982; Banks, Barker & Brown, 1985; Banks & Barker, 1989, 1991). Some muscle afferents remain unclassifiable, responding briefly only during maximal contraction or during electrical stimulation (Gregory, Luff & Proske, 1982).

All three types of muscle afferents, Ia, II and Ib afferents appear to be able to establish functional connections with all three sites (Collins, Mendell & Munson, 1986; Banks & Barker, 1989). In addition, reinnervation does not seem to be greatly affected by the fact that motor units may be of a different type (Gregory, Luff & Proske, 1982; Ip, Luff & Proske, 1988).

Evidence suggests that both γ and β efferents reestablish connections following nerve section (Brown & Butler, 1976; Gregory, Luff & Proske, 1982; Scott, 1987). However, Gregory, Luff & Proske (1982) found that fusimotor innervation consisted of only γ_s efferents and that skeletofusimotor innervation consisted of predominantly β_s efferents following reinnervation. Scott (1987) also found that the ratio of static to dynamic β efferent connections was much higher following transection and reinnervation.

Golgi Tendon Organs: Reinnervated GTOs frequently showed abnormal responses, most commonly an absence of maintained discharge during steady contraction (Gregory, Luff & Proske, 1982; Scott, Davies & Petit, 1995; Scott, Petit & Davies, 1996). On-off responses to the onset and termination of contraction are also encountered. Abnormalities in tendon organ reinnervation may result from a loss of both the afferent supply as well as from the rearrangement of motor unit structure following recovery. Scott *et al.* (1995, 1996) found that, although half of recorded GTO's had an abnomal response to contraction of the whole muscle, all GTO's responded normally to at least one motor unit. This implies that the reorganisation of motor units following reinnervation plays a crucial role in producing abnormalities.

RECOVERY OF CUTANEOUS RECEPTORS

Meissner Corpuscle (FA I Receptors): In reinnervating glabrous primate skin, tuning curves of FAI receptors are of a similar shape to normal curves. However, thresholds are as much as twenty times greater after 2 months, returning to near normal values after 10 months (Terzis & Dykes, 1980). Perception of flutter and moving touch as mediated by Meissner corpuscles, is the first tactile sense to return after median nerve repair in the human (Dellon, 1981). Dellon suggests that the relative ease with which Meissner corpuscles recover could be due to the high axon/corpuscle innervation ratio increasing the probability that a regenerating axon may reach a Meissner corpuscle. FA I receptors are also important for touch thresholds which return to normal levels one year after nerve injury (Mackel *et al.*, 1983). Skin grafting in primates has demonstrated that no new Meissner corpuscles can form after development (Dellon, 1981). This is crucial for the selection of suitable areas of skin for grafting onto the finger pads.

Pacinian Corpuscle (FA II Receptors): Studies of the functional recovery of FA II receptors following nerve transection is lacking. Terzis and Dykes (1980) in their experiments on

reinnervated glabrous baboon skin only recorded the responses from three possible FA II afferents out of the 79 afferents all of which had abnormal tuning curve sensitivities.

In the human, anatomical studies of reinnervated skin after nerve injury show no innervation of the Pacinian corpuscles of volar skin (Carlstedt, Lugnegard & Andersson, 1986) but multiple reinnervation of corpuscles in digital skin (Ide, Nitatori & Munger, 1987). As in the cat, additional terminals were accompanied by extra inner cores. The slow recovery of FA II receptors can be mapped by the sensitivity to 256 Hz vibration which appears 6 to 9 months after median nerve microsurgical repair (Dellon, 1981). The difficulty by which Pacinian corpuscles are reinnervated may be a consequence of the mechanical hindrances that exist as regenerating fibres growing into deeper tissues.

Merkel Cells (SA I Receptors): Merkel cells recover successfully following transection with 70-80% of receptors becoming innervated and functional after six months in rat touch domes (Nurse, Macintyre & Diamond, 1984). The rate of adaption in monkey glabrous skin only returned to normal values after 10 months (Terzis & Dykes, 1980).

The sensation of constant touch or pressure, mediated by Merkel cells, is easily measured in humans used Weinstein's filaments for threshold, and two point discrimination for receptive field size. Both may return to normal values after several years following nerve repair (Mackel *et al.*, 1983; Dellon, 1981). SA I receptive fields are usually smaller than their normal counterparts (Mackel *et al.*, 1983). They are also distributed at higher concentrations in proximal parts of the hand, such as the palm, than in the normal situation.

4. Reinnervation Of Incorrect Structure Of A Different Modality

A comparison of receptive field properties and cord dorsum potentials shows that muscle afferents preferentially reinnervate muscle receptors and likewise cutaneous afferents prefer to reinnervate cutaneous receptors (Koeber, Mirnics & Mendell, 1995). However, functional connections can be established across modalities.

Cross reinnervation experiments of muscle and cutaneous nerves in the rat demonstrate that functional connections retain some of the properties of the original afferent. 79% of muscle afferents form low threshold connections when innervating skin, however, a much higher percentage of these responses are slowly adapting compared to the normal situation (Lewin & McMahon, 1991b). In addition, many receptors undergo habituation, i.e. a slowly adapting response turns into rapidly adapting response with successive stimulation. Receptive fields of skin reinnervated by muscle neurons are in a similar location to the normal situation, indicating that at least some features are determined by the target structure.

When cutaneous neurons reinnervate muscle the number of stretch sensitive units falls to 41%, compared to 88% in the normal muscle and 67% in muscle reinnervated by muscle afferents

(Lewin & McMahon, 1991a). Of this 41% of stretch sensitive units, nearly all are rapidly adapting responses. The other 59% forms stretch insensitive connections which respond to muscle probing.

1.4.4.4. Mechanisms of Plasticity Following Reinnervation

Axonal regeneration is severely restricted in the CNS, however, other mechanisms of plasticity exist such as collateral sprouting (Woolf *et al.*, 1995), short and long term changes in synaptic efficiency as mediated by excitatory amino acids, peptides and neurotrophins (King & Thompson, 1995). The mechanisms fall into two categories in relation to peripheral nerve injury. There are plastic changes to counteract the effect of denervation and there are also reorganisational changes following the consequences of inappropriate reinnervation. These changes take place at all levels of the sensory and motor pathways.

Plastic Changes In The Spinal Cord

The arrangement of primary afferent terminal fields in the normal spinal cord is highly structured both in the rostrocaudal and dorsolateral planes and lends itself to study following axotomy (reviewed in Willis & Coggeshall, 1991).

Following Denervation: Following partial axotomy, collateral sprouting of spared primary afferent terminals into denervated areas is evident from the expansion of terminal arborisations in the spinal cord (Molander, Kinnman & Aldskogius, 1988; Woolf, Shortland & Coggeshall, 1992; LaMotte & Kapadia, 1993). In addition, axotomy induces short and long term changes in excitability which have the potential to render silent connections in the denervated area effective to other remaining inputs (Wall, 1983; King & Thompson, 1995).

Following Reinnervation: Expanded rostrocaudal arborisation patterns are evident subsequent to reinnervation following nerve crush or nerve transection (Florence *et al.*, 1993, 1994). Collateral sprouting also occurs in the dorsolateral plane of the spinal cord subsequent to axotomy and reinnervation. Expansion of A-fibre terminals into lamina II of the dorsal horn follows both nerve crush and nerve transection and may be a possible mechanism for allodynia and hyperalgesia (Koerber *et al.*, 1994; Woolf *et al.*, 1995). Inappropriate reinnervation is known to increase the excitablity of dorsal horn cells (Lewin & McMahon, 1991; Koerber *et al.*, 1994).

Plastic Changes In The Cortex

Following Denervation: Models of denervation in the primate include single digit and double digit amputations (Merzenich *et al.*, 1984), median and ulnar nerve transection and ligation (Merzenich *et al.*, 1984; Garraghty & Kaas, 1991; reviewed in Kaas, 1991) and whole dorsal root rhizotomy (Pons at al., 1991). Although there is some disagreement as to the degree of recovery, deprived cortical areas generally become responsive to adjacent cutaneous areas often with a surprisingly structured topographic arrangement. For example, following median and ulnar nerve injury, the

adult monkey cortical areas 3b and 1, regain a map of the volar surface of the hand in a matter of months (Garraghty & Kaas, 1991). Similarly, transcranial magnetic stimulation has also been used to demonstrate that there is a reorganisation of the corticospinal tracts following spinal cord injury in man (Topka *et al.*, 1991). A reduction in the expression of the inhibitory neurotransmitter γ-aminobutyric acid (GABA) has been suggested as one possible mechanism for the reemergence of new connections in the deprived cortex (Garraghty, Florence & Kaas, 1990).

Following Reinnervation: Reinnervation of the primate hand following nerve transection and repair results in highly abnormal patterns of the cortical representation of the hand (Paul *et al.*, 1972; Wall *et al.*, 1986; Florence *et al.*, 1994). Receptive fields are larger and often multiply represented. The somatotopic arrangement is also disordered and fractured. Often, the abnormalities of cortical representation are a reflection of inappropriate peripheral innervation (Florence *et al.*, 1994). For example, when the terminal arborisation of axotomised primary afferents are wide spread, this also results in an expansion of the cortical representation. The results seem to indicate that, unlike the widespread changes accompanying complete sensory deprivation (Garraghty & Kaas, 1991), there is a limit to cortical plasticity following peripheral nerve injury and recovery.

Recovery of Proprioception in Man Subsequent to PNI

Although a wealth of information has accumulated relating to the recovery of proprioception in animal models, clinical knowledge of functional proprioceptive recovery subsequent to nerve trauma in the human hand is still at a basic level. No objective or functional tests of proprioception are in current clinical practice and measures of proprioception are restricted to the sense of very crude manually applied movements of digits and limbs. There is almost a silence in the hand surgery literature relating to recovery of proprioception following reinnervation. Only one clinical study to date has incidently related proprioceptive loss to nerve injury in the human hand (Moberg, 1983). However, here the emphasis was placed upon the effects of cutaneous denervation at the time of a peripheral lesion.

Animal models have shown that peripheral nerve trauma and subsequent reinnervation affects the *number* of sensory receptors able to influence conscious perception, in accordance with the proportion of reinnervated proprioceptors (Banks and Barker, 1989, 1991). It also effects the normality of responses derived from proprioceptors, since reinnervated receptors often exhibit increased thresholds and alterations in rapidly adapting or slowly adapting characteristics (Terzis & Dykes, 1980; Banks and Barker, 1989; Lewin & McMahon, 1991a & 1991b). Accordingly, reinnervation following PNI is not only likely to affect the ability to *detect* movements in relation to the proportion of proprioceptors successfully reinnervated, but is likely to influence the ability to *grade* the amplitude and velocity of movements, in connection with the normality of proprioceptor responses. These factors must be taken into consideration when devising tests to assess the recovery of proprioception in the hand.

1.5. Clinical Studies on Motor and Sensory Recovery

A number of measures are in current clinical use to give an indication of other sensory, motor and autonomic functions (Dellon, 1981; Tubiana, Thomine & Mackin, 1996). These have been extensively used to chart the recovery of the hand following nerve injury:

1.5.1. Charting Recovery

1.5.1.1. Measures of Sensory Recovery

MEASURES OF SLOWLY ADAPTING CUTANEOUS AFFERENTS

- ***Two-Point Discrimination*** measures the recovery of the receptive field size of the Merkel cell complexes (Johansson & Vallbo, 1980). Typical values in the normal hand show a high intersubject variability, but range from 1 - 6 mm for the terminal pad of the digits and 4 - 12 mm for other parts of the hand, eg. dorsum, thenar and hypothenar eminence (Dellon, 1981; Dellon, MacKinnon & Crosby, 1987). 2-PD has the potential to recover to normal values, following nerve injury, but typically does not (Dellon, 1981; Mackel, 1983).
- ***Semmes-Weinstein Monofilaments:*** Criticism has been levelled at the test because of the change in the elastic modulus of the filaments with temperature and humidity, as well as variation in filament tip size and shape (Levin, Pearsall & Ruderman, 1978). However, Weinstein's filaments are one of the few tests which provide a quantitative measure of cutaneous detection threshold sensitivity. They predominantly measure sensitivity of SA I receptors which code for indentation of the skin (Knibestöl & Vallbo, 1980).

MEASURES OF RAPIDLY ADAPTING CUTANEOUS AFFERENTS

- ***Moving Two-Point Discrimination:*** The moving two point discrimination test was devised as a measure of the innervation density of the rapidly adapting system which has a particular importance in sensory exploration (Dellon, 1978, 1981; Dellon, MacKinnon & Crosby, 1987). Dellon found that the moving 2-PD is higher than classical 2-PD and that recovery of moving 2-PD is earlier and superior following peripheral nerve repair (Dellon, 1978). Moving 2-PD has the potential to recover to normal values but usually does not (Dellon, 1981; Mackel, 1983).
- ***Vibration Sense:*** Two tuning forks, with resonant frequencies of 30 Hz and 256 Hz can be used to distinguish recovery of Meissner corpuscles (FA I receptors) and Pacinian corpuscles (FA II receptors), respectively (Dellon, 1980). The sense of 30 Hz vibration is the first tactile sense to reappear during reinnervation after PNI.

OTHER MEASURES OF TACTILE SENSE

Several tests have used object recognition as a means of testing sensory function. The most commonly used test is Moberg's picking-up test (Moberg, 1958; Brink & Mackel, 1987) in which a blind-folded subject picks up and identifies a series of small objects (eg. nut, screw, key, safety pin,

penny), after prior manipulation under full vision. The time taken for each object to be recognised is also recorded. The test measures both precision grip and tactile gnosis. Median nerve injury results in significant delays in the time taken to recognise objects and patients will use fourth and fifth digits and sometimes the dorsum of the hand for sensory exploration.

1.5.1.2. Order of Sensory Recovery

Subsequent to nerve repair, submodalities recover at different rates (Dellon, 1981). The recovery of the signs, in order of appearance, are:

1. Pain and temperature - C-fibre reinnervation
2. Sense to 30 Hz vibration - FA I receptor reinnervation (all or none)
3. Moving 2-PD - FA I receptive field reinnervation (graded)
4. Constant touch -Semmes-Weinstein - SA I receptor reinnervation (graded)
5. Classical 2-PD - SA I receptive field reinnervation (graded)
6. Sense to 256 Hz vibration - FA II receptor reinnervation (all or none)

Mechanisms for the early recovery of pain and temperature may be due to collateral sprouting (Devor *et al.*, 1979) or the smaller diameter of afferent fibres which can regenerate more rapidly (Dellon, 1981). The differential rates of recovery of low frequency vibration, moving touch, constant touch and high frequency vibration can be explained by the ease with which Meissner corpuscles, Merkel cell complexes and Pacinian corpuscles can be innervated. Dellon (1981) recomends charting the emergence of each submodality in digits 1, 2 and 5. Once recovered, Moberg's picking-up test can be used to chart further recovery.

1.5.1.3. Measures of Motor Recovery

The most widely used tests of motor recovery are the British Medical Research Council Motor Functional Assessment (MRC grading) (Reviewed in Wade, 1994; Tubiana, Thomine & Mackin, 1996). The gradings are:

0: No contraction
1: Palpable contraction but no visible movement
2: Movement with gravity eliminated
3: Movement against gravity
4: Movement against resistant but subnormal
5: Normal power

The Jamar grip strength test can also used as a general measure of motor recovery.

1.5.1.4. Correlation of Clinical Measures to Proprioception

In the current study, assessments of kinaesthetic sensation in the digits were compared to clinical measures of sensorimotor function. Particular emphasis was laid upon Weinstein's test due to its advantage as a quantitative measure of cutaneous sensitivity. In addition to recording filament sensitivities at the digit tips, cutaneous thresholds were also recorded in areas of skin stretched during applied movements (see methods section).

1.5.2. Improving Recovery: Sensory Re-education

Some of the first sensory re-education programs were devised by Parry (1976), in which patients tried to identify various household objects whilst blindfolded. Dellon later introduced a two phase sensory education program appropriate to the sequence of recovery (Dellon, 1981, 1987). The early phase involves the subject trying to distinguish between constant touch and movement until vibration sense of 256 Hz returns to the finger tips. This is taken as an indication that all the modalities of tactile fibres have returned. When the subject can distinguish between constant touch and movement at the finger tip the later stage of manipulation and identification of household objects can commence. The test can be made more difficult by using smaller objects and also by placing them in media such as coffee beans or rice. Both classic and moving 2-PD, object recognition and paraesthesias improve as a result of sensory re-educated (Parry, 1976; Dellon, 1981; Imai, Tajima & Natsumi, 1991).

Due to lengthy times needed to follow longitudinal studies, the re-education programs were not employed as part of the current study.

1.6. Aims Of The Study

The primary objective behind the present investigation is to provide the first comprehensive study of the recovery of kinaesthesia in man subsequent to peripheral nerve injury. In addition, the current study contains an investigation into the nature of this pulsatile output in normal intrinsic hand musculature and its character subsequent to both peripheral nerve injury and carpal tunnel syndrome. In summary, the aims of the study are:

- To design, construct and test equipment for measuring kinaesthesia and tremor in the hand.
- To develop models and tests using the equipment, suitable for the investigation of median, ulnar and radial nerve contributions to kinaesthesia and tremor.
- To investigate kinaesthesia in the normal, anaesthetised and peripheral nerve injured hand.
- To investigate the nature of 8-10 Hz pulsatile output in normal intrinsic hand musculature, subsequent to peripheral nerve injury and carpal tunnel syndrome.
- To write software programs for analysing data.

- To correlate data with clinical measures of recovery of muscle, skin and joint

The discussion section also contains a pilot study into the investigation of the recovery of sense of force subsequent to PNI.

1.6.1. Equipment

A number of methods have previously been used to apply movements for investigating proprioception, including electromagnetic servo devices (Cody *et al.*, 1987; Matthews, 1994, 1997; Petit, Scott & Reynolds, 1997), stepper motors (Gagne, 1987; Pap, Machner & Awiszus, 1997; Sharma *et al.*, 1997), DC motors under positional or velocity servo control (Clark and Burgess, 1987) and DC brushless torque motors (Hulliger, Nordh & Vallbo, 1982; Vallbo & Wessberg, 1993). The design, construction and evaluation of a novel system, which uses slip control of an AC induction motor has been included in the design section of the present study. It is also found in summary form in the recent publication "Use of an AC induction motor system for producing finger movements in human subjects" (Proudlock & Scott, 1998).

The use of lasers to record hand tremor has been recently introduced (Beuter, Geoffroy & Cordo, 1994) as an alternative to accelerometry. A high resolution optical displacement laser transducer (resolution = 3μm, Micro-epsilon® Messtechnik, LD 1605-20) was used to record tremor in the present study.

1.6.2. Models Used

In the current investigation, three models were used to assess kinaesthesia, sense of force and pulsatile output subsequent to median, ulnar and mixed nerve injury (Figures 1.8.-1.10.):

1.6.2.1. Model 1: Median Nerve Innervation

The median nerve may arguably be the most important nerve for proprioception in the hand since it innervates vital sensory structures such as the glabrous skin, intrinsic musculature of the thumb and the first two lumbrical muscles (Peck, Buxton & Nitz, 1984). Finding suitable models for investigating reinnervation by the median nerve is hindered by the fact that there is no single plane of movement in any digit in the hand where the muscle, skin and joints are all innervated by the median nerve. The movement described provides the most complete single joint model available for investigating median nerve injury.

Movement: *Abduction-adduction of the thumb carpometacarpal joint*

Using the definition of thumb abduction: adduction as movement occurring in the sagittal plane and thumb extension: flexion as movement occurring in the frontal plane (see Tubiana, 1981 for the various systems used to describe thumb movement), the model chosen to study median nerve

innervation was abduction with 30° flexion and adduction with 30° extension of the carpometacarpal joint of the thumb (simplified to thumb abduction: adduction). It is equivalent to the action performed when bringing the thumb from the relaxed position to a position at right angles to the plane of the palm (see figure 1.8.). This action, vital for thumb opposition, is absent following median nerve paralysis because of the loss of the action of muscles in the thenar eminence.

Innervation

Musculature: The median nerve innervates intrinsic thenar eminence muscles including AbPB, OP and often FPB. Unfortunately, ulnar nerve innervated intrinsic muscles and extrinsic thumb musculature may provide an additional source of sensation.

Skin: The median nerve innervates all the palmar skin as well as the dorsal skin up to the interphalangeal joint. The skin covering the dorsal aspect of the thumb MCP and CMC joint is innervated by the superficial branch of the radial nerve (see figure 1.5.).

Joint: The innervation of the thumb is uncertain. Possible contributions may derive from the anterior interosseus nerve, the posterior interosseus nerve, the superficial branch of the radial nerve, and the palmar aspect from the lateral (antebrachial) cutaneous nerve (Fukumoto *et al.*, 1993). The innervation of the thumb CMC joint is not significantly affected by median and ulnar nerve injury at wrist level.

Surface EMG Recording: *Abductor Pollicis Brevis*

1.6.2.2. Model 2: Ulnar Nerve Innervation

The medial third of the hand is completely innervated by the ulnar nerve and provides a good model for investigating nerve regeneration. It is limited, however, in that the fourth and fifth digits have poor motor control.

Movement: *Abduction-adduction of the little finger metacarpophalangeal joint*

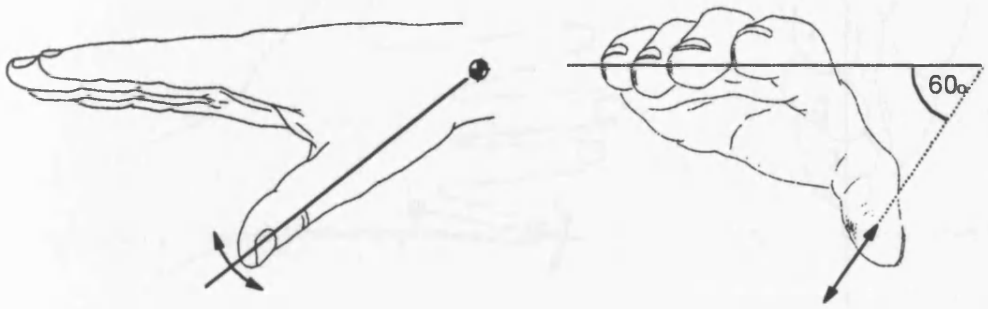
This action spreads the little finger for grasping large objects. It is the only plane of movement in any digit where muscle, skin and joint are innervated by a single nerve (figures 1.3.-1.6.).

Innervation: All the intrinsic musculature of the hypothenar eminence is innervated by the ulnar nerve, including the AbDM and 4PI muscles which abduct and adduct the little finger, respectively. Only the extrinsic muscles, extending the little finger (EDM and EDC), and flexing the finger (FDS and FDP) remain following ulnar nerve transection at wrist level. All skin around the MCP joint and the capsule itself, is innervated by the ulnar nerve.

Surface EMG Recording: *Abductor digit minimi.*

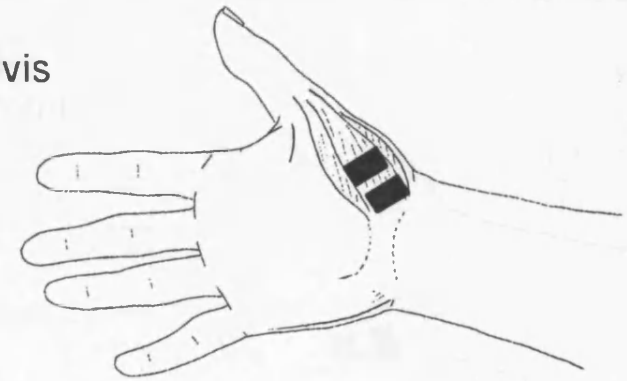
FIGURE 1.8. MODEL 1: MEDIAN NERVE INNERVATION

MOVEMENT: Flexion: Abduction / Extension:
Adduction of the CMC Joint of the Thumb



EMG RECORDING:
Abductor Pollicis Brevis

Movement:
Abduction-Flexion

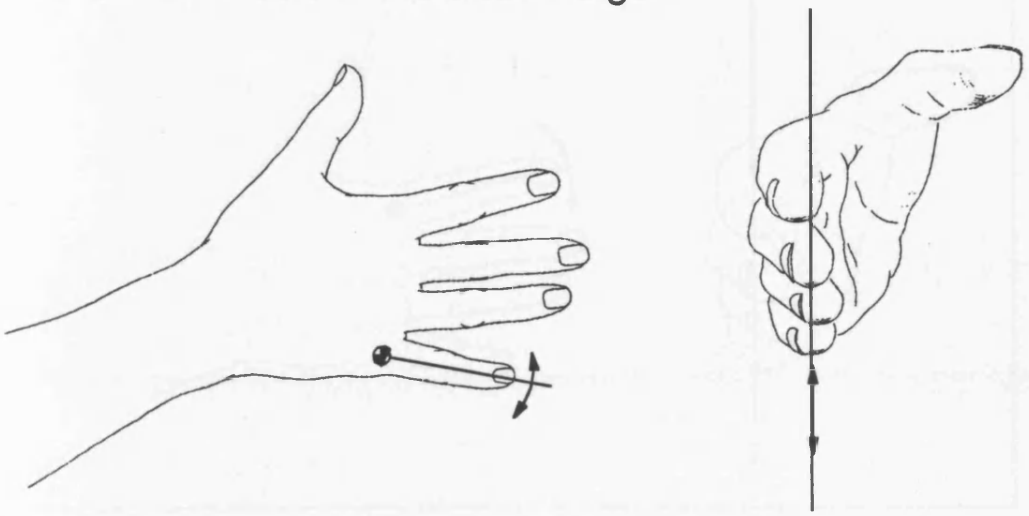


Electrode Positions

MOTOR INNERVATION	*Mostly Median N. with contribution from extrinsics and Ulnar innervated intrinsics*
CUTANEOUS INNERVATION	*Predominantly Median N. with some Radial N. on the hand dorsum*
JOINT INNERVATION	*Anterior and Posterior Interosseus N. and possibly the Superficial Radial N. and Lat. Cutaneous N.*

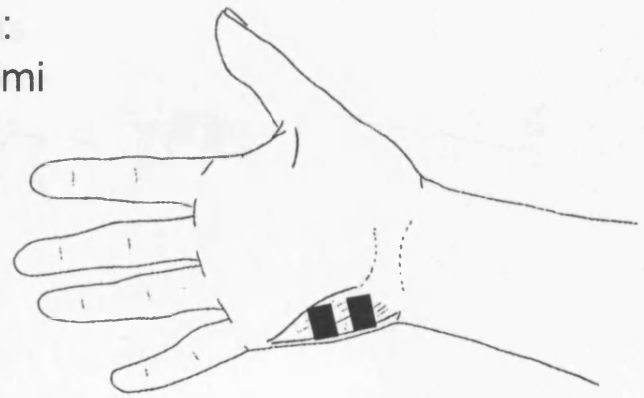
FIGURE 1.9. MODEL 2: ULNAR NERVE INNERVATION

MOVEMENT: Abduction: Adduction
of the MCP Joint of the Little Finger



EMG RECORDING:
Abductor Digiti Minimi

Movement:
Abduction

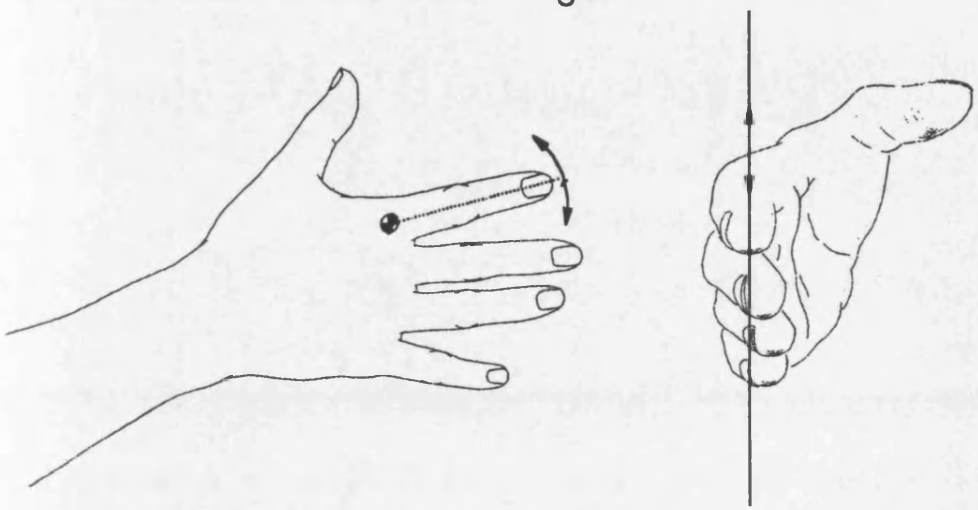


■ Electrode Positions

MOTOR INNERVATION	*Ulnar N.*
CUTANEOUS INNERVATION	*Ulnar N.*
JOINT INNERVATION	*Ulnar N.*

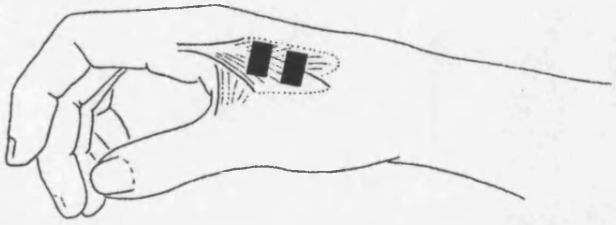
FIGURE 1.10. MODEL 3: MIXED NERVE INNERVATION

MOVEMENT: Abduction: Adduction
of the MCP Joint of the Index Finger



EMG RECORDING:
First Dorsal Interosseus

Movement:
Abduction



▮ Electrode Positions

MOTOR INNERVATION	*Mostly Ulnar N.*
CUTANEOUS INNERVATION	*Predominantly Median N. with some Radial N. on the Dorsum*
JOINT INNERVATION	*Predominantly Median N. with the possibility of Radial N.*

1.6.2.3. Model 3: Mixed Nerve Innervation

The index finger provides an appropriate model for distinguishing between joint/skin sensation and muscle sensation because of innervation by different nerves. It has been previously used to investigate the receptors mediating position sense (Clark *et al.*, 1985).

Movement: *Abduction-adduction of the index finger metacarpophalangeal joint*
This action is accompanied by a small degree of rotation. Index finger abduction-adduction has an important role in fine manipulatory tasks involving the index finger and thumb.

Innervation: The 1DI and 2PI muscles, controlling abduction and adduction, are both innervated by the ulnar nerve. Palmar skin and joint are innervated by the median nerve, whereas dorsal skin and joint are innervated by the superficial radial nerve. A number of extrinsic muscles control index finger extension and flexion and may act as additional proprioceptive sources.

Surface EMG Recording: *First dorsal interosseus*

1.6.3. Methods Used

1.6.3.1. Kinaesthesia

MOVEMENT REPRODUCTION TESTS

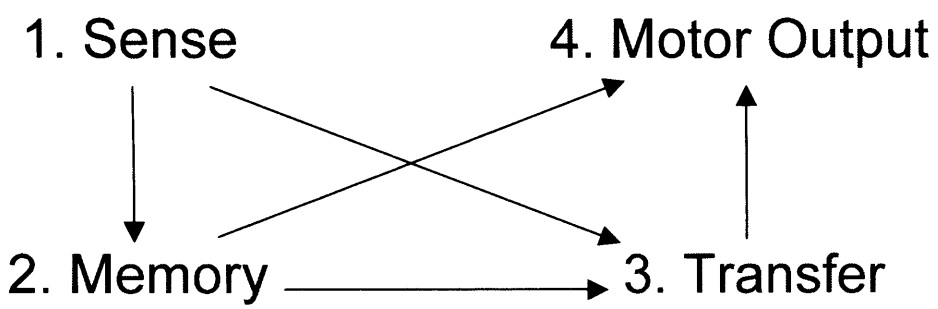
The two most frequently used methods for measuring kinaesthesia have been the percentage of correct responses in sensing the direction of an applied move (eg. Gandevia & McCloskey, 1976; Gandevia *et al.*, 1983; Hall & McCloskey, 1983; McCloskey *et al.*, 1983a; Ferrell, Gandevia & McCloskey, 1987; Clark, Grigg & Chapin, 1989; Refshauge *et al.*, 1995) or the threshold amplitude of detection of an applied slow velocity move (eg. Barrack *et al.*, 1983; Taylor & McCloskey, 1992; Hall *et al.*, 1994). Very slow subthreshold velocities have also been used to look at position sense (Horch, Clark & Burgess, 1975; Clark *et al.*, 1985, 1986, 1989; Taylor & McCloskey, 1990a). These methods test the ability to sense movements but give little indication as to whether the movement amplitude and velocity are graded correctly.

Following transection and reinnervation, mechanoreceptive responses may show abnormal tonic and phasic afferent firing patterns in response to movement (Terzis & Dykes, 1980; Sanders & Zimmerman, 1986; Banks & Barker, 1989; Lewin & McMahon , 1991a & 1991b; Scott, Petit & Davies, 1996; Scott, 1996). For example, cross reinnervation experiments of muscle and cutaneous nerves in the rat demonstrate that many muscle afferents form low threshold connections but a high percentage of these connections are slowly adapting (Lewin & McMahon, 1991b). Conversely, when skin reinnervates muscle, the number of stretch sensitive units falls to half of the proportion of units in the normal muscle (Lewin & McMahon, 1991a). Nearly all of the responses are rapidly

adapting. The ability to grade movements relies on appropriate slowly and rapidly adapting responses in response to movement. It is important therefore, that current methods for measuring kinaesthesia include a measure of the ability to grade movements.

Of the known methods used for investigating kinaesthesia, the movement reproduction tests used by Ferrell and coworkers, in which subjects repeat movements applied to the digits with the contralateral hand, presents the most appropriate measure of the ability to grade movement (Ferrell & Smith, 1987, 1988, 1989; Ferrell & Milne, 1989; Ferrell & Craske, 1992). However, the physiological processes involved in performing a contralateral repeat task are complex (figure 1.11.). The movement is first sensed (1), a process involving peripheral and central sensory pathways and the primary sensory cortex. The movement is retained in the memory (2) and the information is transferred from the ipsilateral to the contralateral cortex (3). Repetition of the movement (4) is also a complex sequence involving movement planning, initiation and execution using motor cortical and subcortical structures. It is possible that errors could result at any stage in the sequence.

Figure 1.11. Processes Involved In The Contralateral Repeat Test



In the current study, movement reproduction with the contralateral hand was also used as the basis for assessing position and velocity sense. However, a number of other tests were also peformed to examine the loss of information at each stage of the repeat process. The numbers in brackets refer to figure 1.11.:

1. ***Detection (Dn):*** The subject verbally reports the direction of the moves. This is purely a sensory test (1).
2. ***Visual Tracking (VT):*** The subject tracks a visual target the movement using the visual feedback signal of the digit position. This gives an indication of the motor control of the subject (4). The tests can be performed on ipsilateral and contralateral sides.
3. ***Visual Repeat (VR):*** The subject repeats the movement carried out during the VT in the absence of visual feedback. This gives an indication as to how well the memory preserves a copy of the movement (2).

4. ***Ipsilateral Repeat (IR):*** After the application of a movement, the actuator switches to a free movement mode and the subject repeats the move with the same hand. This involves the processes of sense (1), memory (2) and motor output (4).
5. ***Contralateral Repeat (CR):*** After applying a movement to the ipsilateral hand, the subject then repeats the movement with the contralateral hand. This involves the processes of sense (1), memory (2), transfer (3) and motor output (4). A comparison of IR and CR test results give an indication of the information loss during the transfer process.
6. ***Movement Match (MM):*** The subject simultaneously matches ipsilateral hand movements with the contralateral hand. It involves sense (1), transfer (3) motor control (4) but not memory (2). Results from this test can also be used to look at time dependent parameters such as velocity reproduction and the delay in response to the start of movement.

MOVEMENTS APPLIED

The ipsilateral repeat test is particularly important as a control test in PNI subjects since the normal hand can be used both to sense and repeat movements. Since the unpowered AC induction motor has no detent torque, the resulting free movement permits movements to be repeated ipsilaterally with relative ease. The disadvantage of the IR test is that the actuator must always end the movement at the resting position of the digit, so that no movement occurs when the motor switches off. This means that each movement must be in two phases, i.e. movement away from and movement towards the resting position. A further complication is added by the fact the resting positions of the index and little fingers are in close proximity to the other digits. To simplify the repeating process all moves perfomed consisted of a symmetrical abduction and adduction movement seperated by a 0.5 second hold period.

A pseudorandom sequence of ramp abduction and adduction moves were used in all tests to assess kinaesthesia in the three models mentioned. After consideration of the threshold plots given by Gandevia *et al.* (1983) for the DIP joint, 9 moves with amplitudes of 3°, 6° and 12° and velocities of $1.5°s^{-1}$, $3°s^{-1}$ and $6°s^{-1}$ were initially used to test kinaesthesia. It soon became apparent that the majority of these movements were sensed by both normal and PNI subjects, and consequently, 1.5° amplitude moves were also added to the movement sequence.

CONTRIBUTIONS OF EACH NERVE TO KINAESTHESIA

Although the innervation patterns of the three nerves supplying the hand are well documented, the contribution of each nerve as a proprioceptive source has never been assessed from a functional standpoint. In an attempt address this issue, median, ulnar and radial nerves were anaesthetised locally using lignocaine and marcaine. Shortened protocols were used when applying lignocaine blocks because of the restriction in time over which the block lasts. The results of the tests also demonstrated how complete each model was for providing a measure of innervation of a particular nerve.

RECOVERY OF KINAESTHESIA SUBSEQUENT TO PNI

When possible full kinaesthetic tests were performed on PNI subjects. In addition, ipsilateral tests, i.e. visual tracking, visual repeat and ipsilateral repeat tests were performed as controls for the injured hand.

1.6.3.2. Sense of Force

Considerable difficulties were associated with investigating the sense of force in nerve injured subjects primarily because of the dramatic loss in strength following reinnervation. These issues are developed further in the discussion section.

1.6.3.3. Pulsatile Output

In assessing the recovery of the pulsatile output following reinnervation, the presence of 8-10Hz tremor in intrinsic hand musculature first had to be established. Most studies have described kinetic tremor during slow extension-flexion movements of the long digits, which are predominantly controlled by extrinsic musculature (Vallbo & Wessberg, 1993, 1996; Wessberg, 1995; Wessberg & Vallbo, 1995, 1996, McAuley, Rothwell and Marsden, 1998). In the current investigation, 8-10Hz tremor was examined during abduction: adduction movements of the thumb, index and little fingers, primarily under the control of intrinsic musculature. The 8-10Hz pulsatile output was then measured in the same models subsequent to peripheral nerve injury during slow movements and during position holding. In addition, pulsatile output was also investigated in a group of subjects suffering from carpal tunnel syndrome (i.e. chronic median nerve compression at wrist level) using the model of thumb abduction: adduction movements. This allowed comparison of nerve trauma to nerve compression.

Repeat experiments of those performed by McAuley, Rothwell and Marsden (1998) were also carried out to investigate the nature of higher frequencies of oscillation apparent under elastic load conditions. Two springs of different spring constants were used to observe the effect of varying mechanical conditions upon frequencies of oscillation.

CHAPTER 2: DESIGN

2.1. Overview

A number of pieces of equipment were necessary for investigating motor control, kinaesthesia and tremor in the hand:

1. UPPER LIMB STABILISATION: Apparatus was constructed which permitted comfortable stabilisation of the hand and arm for a number of hours.

2. MOTOR CONTROL ASSESSMENT:

- ***Control of Movement:*** A visual display providing a moving target and feedback of the digit position was used to assess motor control in the digits.
- ***Force Output:*** Strain gauge equipment was used to measure the maximal voluntary contraction force of intrinsic hand musculature.

3. MEASURING KINAESTHESIA: An actuator capable of applying movements and forces to the digits was designed and constructed. Three modes of control were required from the actuator:

- **Movement Application:** The actuator must be able to perform a range of linear and sinusoidal moves for testing kinaesthesia, including very slow moves (down to $0.02°s^{-1}$) for investigating absolute position sense.
- **Repetition of Movement:** The actuator must be able to rapidly switch from movement application to free movement (or zero torque), so that moves can be repeated by the subject.
- **Load Conditions:** To assess the ability of subjects to compensate for applied loads, it was desirable that the actuator was capable of generating a number of different load conditions. These included a fixed load, an elastic load (proportional to position), a viscous load (proportional to velocity) and an inertial load (proportional to acceleration).

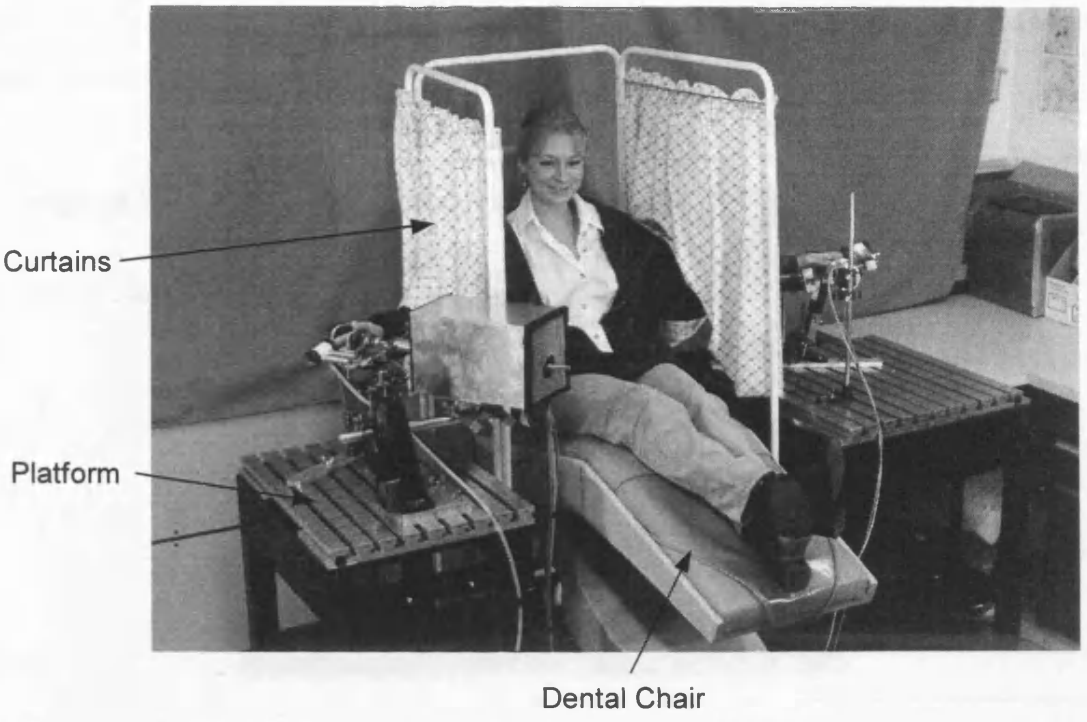
2.2. Upper Limb Stabilisation

Apparatus was constructed to stabilise the hand and the arm in a comfortable position for a number of hours. The equipment was designed to keep extraneous vibration to a minimum and allowed for subject variation with respect to height, arm length and hand size.

Seating: A dental chair was acquired (fig. 2.1.) permitting the shoulders to be placed at any level with respect to the rest of the apparatus.

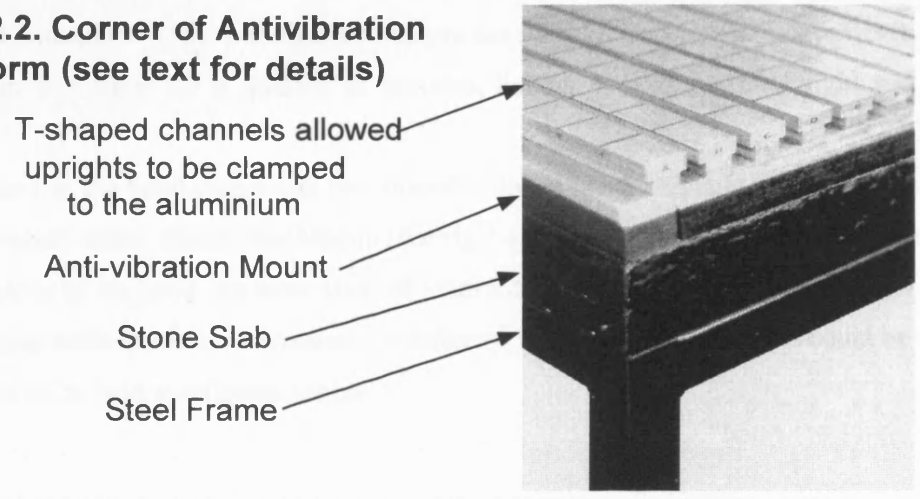
Curtains: Two curtains were hung from a frame placed around the dental chair depriving vision of the hands to the subject.

Figure 2.1. Seating Arrangement and Upper Limb Stabilisation (see text for details)



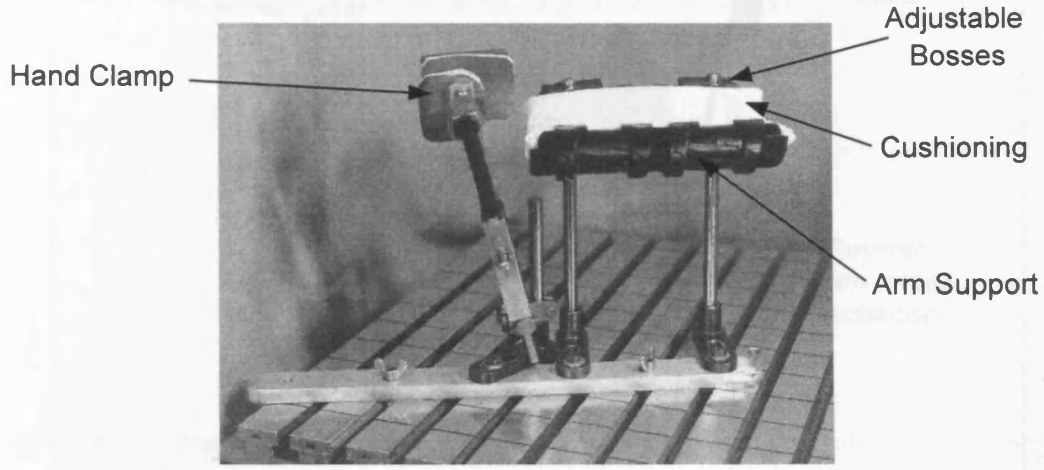
Platforms: Two platforms were constructed and situated either side of the dental chair (see fig. 2.1.). A solid aluminium base forming the top of the platform was arranged as a series of T-shaped channels and served as a base to which uprights and other apparatus could be clamped. Grids marked out on the top of each platform allowed the identical positioning of equipment on both sides. One platform was particularly suited for tremor recording. It consisted of a heavy steel construction. A large stone slab and anti-vibration mount were used to minimise extraneous vibration (see fig. 2.2.).

Figure 2.2. Corner of Antivibration Platform (see text for details)



Arm Supports: PVC guttering, velcro® and cushioning were used to construct arm supports. They were attached to uprights using adjustable bosses and could be fixed at a range of heights and angles (see fig. 2.3.). An upper arm support was used to strap the arm for further stabilisation during tremor recording.

Figure 2.3. Arm Stabilisation (see text for details)

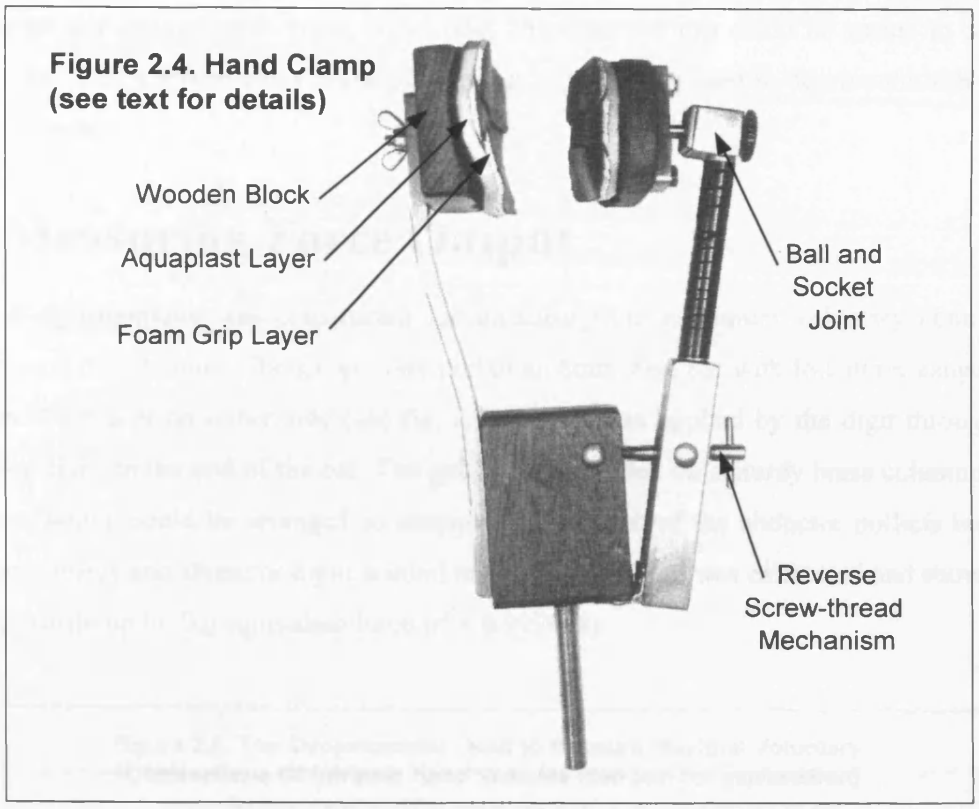


Hand Clamps and Supports: Hand stabilisation was critical for measuring tremor in the digits. A hand clamp was specifically constructed to provide:

- comfort during clamping over prolonged periods of time.
- minimal slip and rotation of the hand
- free movements of the thumb and fingers
- access for laser and EMG recording leads

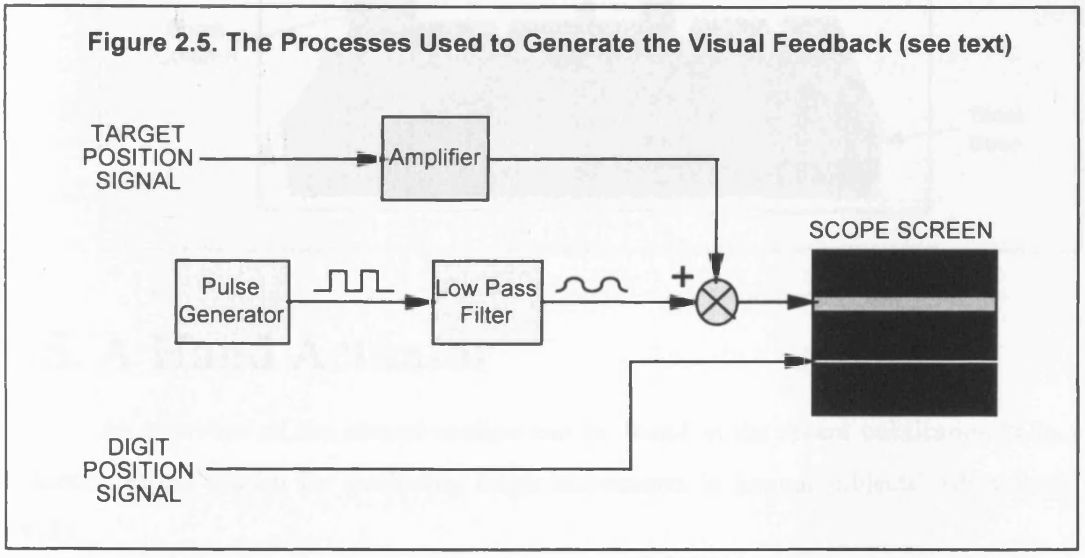
A number of materials were tested for their suitability for forming hand moulds, including latex, dental moulding compounds and potting compouds. A solution was met using an orthopaedic material called Aquaplast® (Smith & Nephew Rolyan Inc., USA). This polymer becomes malleable after placing in hot water for a number of minutes, but on cooling becomes rigid and weight bearing.

The basis of the hand clamp was two shaped wooden blocks brought together using a split, normal and reversed screw thread, mechanism (see fig 2.4.). The Aquaplast® layer inside the blocks provided a contour of the hand. An inner layer of foam rubber 'squash grip' provided a high friction surface and compressibility to accommodate for different hand shapes. The blocks could be tilted to allow the clamp to be held at different angles.



2.3. Visual Feedback

A digital oscilloscope sweeping at 100Hz was used to provide visual feedback of the digit and a target position for the subject to follow (see fig. 2.5.).



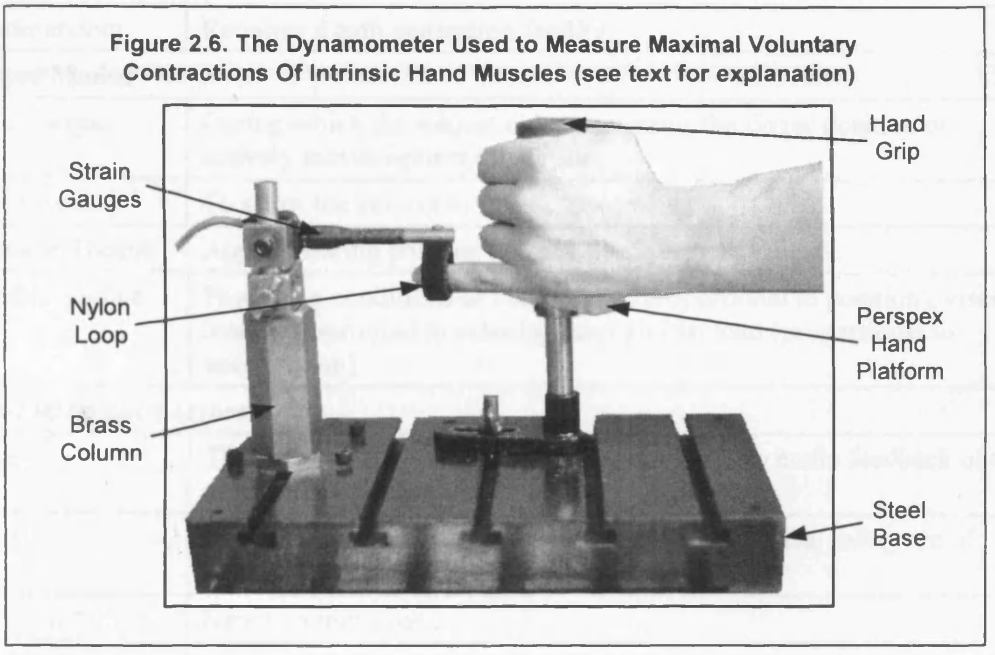
A target voltage signal was generated using a sequencer program created in Spike2 for Windows® (Cambridge Electronic Design). The gain or amplitude of the target movement could be controlled using an amplifier. To distinguish the target signal from the digit position feedback, a quasi-sinusoidal signal, generated using a pulse generator and a variable low pass filter, was added

to the target cue converting it into a broad line. The filter settings could be varied to control the width of the line. A screen cover made of blackout material was used to deprive the subject of the visual feedback.

2.4. Measuring Force Output

A dynamometer was constructed for measuring the maximum voluntary contraction of intrinsic hand musculature. The gauge consisted of an 8mm steel bar with foil strain gauges bonded to flattened surfaces on either side (see fig. 2.6.). Force was applied by the digit through a thick nylon loop fixed to the end of the bar. The gauge was mounted on a sturdy brass column fixed to a steel base, which could be arranged to measure the strength of the abductor pollicis brevis, first dorsal interosseus and abductor digiti minimi muscles. The gauge was calibrated and showed a near perfect linearity up to 7kg equivalent force ($r^2 = 0.999958$).

Figure 2.6. The Dynamometer Used to Measure Maximal Voluntary Contractions Of Intrinsic Hand Muscles (see text for explanation)



2.5. A Hand Actuator

An overview of the current section can be found in the recent publication "Use of an AC induction motor system for producing finger movements in human subjects" (Proudlock & Scott, 1998).

2.5.1. Original Specifications

Table 2.1. Original Specifications For A Hand Actuator	
Limits	
Angle Range	±30° maximum
Resolution	0.02° or less
Velocity Range	0.02-200° s^{-1} with smooth operation down to minimum velocities.
Torque Range	5 x 10^{-3} to 4 Nm^{-1}
Feedback	
Position	Position feedback from right and left hands
Velocity	Velocity feedback from right and left hands
Torque	Torque feedback from right and left hands
Movements	
Triangle / Ramp	With variable amplitude and velocity
Sinusoidal	With variable amplitude and frequency
Pseudorandom	Requires a path generation facility
Torque Modes	
Fixed Torque	During which the subject either maintains the finger position or actively moves against the torque
Zero Torque	To allow the subject to repeat movements.
Transient Torque	Applied during position holding or movement repeats.
Variable Torque	Producing conditions of elastic load (proportional to position), viscous load (proportional to velocity), and inertial load (proportional to acceleration).
Other Relevant Factors	
Noise	The actuator must run very quietly providing no audio feedback of the movement to the subject
Safety	Restrictions on the range of movement and electrical safety are of critical importance
Vibration	Kept to a minimum
Ease of Use	A user friendly system reduces the need for outside assistance

2.5.2. Alternatives

Electromagnetic vibrators with length and force feedback have been used extensively to apply movements and forces in a number of physiological applications (eg. Gandevia and McCloskey, 1976; Gandevia *et al.* 1983, Matthews, 1994, 1997; Petit, Scott & Reynolds, 1997). In the present context, electromagnetic vibrators were inpractical due to their limited range of motion. Four other alternatives were considered and actively explored to assess their viability:

A) A Pneumatic System

Pneumatic systems can be used to produce movements with very smooth velocity profiles. Using electromagnetic regulators to control pressure on either side of an actuator and an optical encoder to provide feedback of position, the pneumatic system can be configured as a servo loop system. Both rotary and linear pneumatic actuators are commercially available.

Advantages

- Because the force is generated externally, high torques can be applied using a small, light actuator which assists the manoeuvrability of the setup.
- It is able to apply smooth, vibration free movements.
- Provided compressors are located at a distance from the experimental setup, the pneumatic system is a very quiet system.
- Electrical noise is minimal.
- Actuators are relatively cheap. A range of actuators could be purchased to allow high versatility.
- The system can be made very safe. Cylinders have a restricted travel, and rotary actuators can be fitted with angle limiting devices. The system offers no electrical hazard.

Disadvantages

- A serious disadvantage of the pneumatic system is that resident static friction ('stiction'), existing at the interface between the barrel and the rubber seal, causes a problem when trying to generate movements with a smooth start up, such as sine waves.
- Compressors are noisy and need to be located at a distance from the actuator.
- An electromagnetic clutch must be added in series to permit free movement.
- Position and force loop feedback systems are not commercially available which means a custom built system must be constructed requiring outside technical expertise.

The pneumatic system control option was explored at some length. Low friction actuators (SMC®) and fittings were purchased and tested. However, unsatisfactory progress was made.

B) A Stepper Motor System

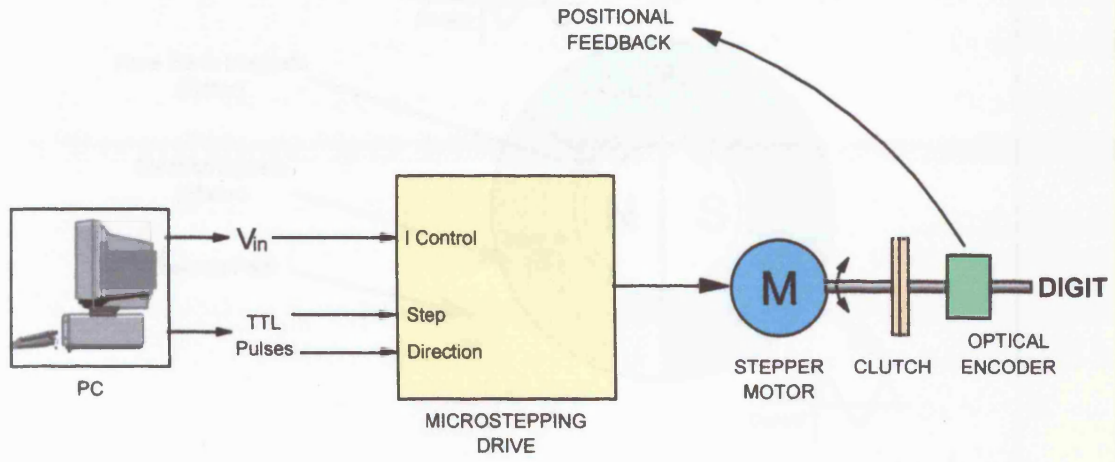
Stepper motors are a simple, low cost and effective means of applying movements for physiological applications (Gagne, 1987; Pap, Machner & Awiszus., 1997; Sharma *et al.*, 1997). The resolution of stepper motors can be greatly enhanced using microstepping, whereby the current to the motor windings is proportioned to further divide each step. Because they work on a 'feedforward' mechanism, a PC can be easily configured to control a microstepping system (Fig. 2.7.). The torque is controlled using a voltage input signal (torque is proportional to current), and

the step and direction using simple TTL pulses. An uncoupling device such as an electromagnetic clutch must be added in series to allow free movement of the digit. An optical encoder would provide position feedback.

Advantages

- Stepper motors and their control systems are cheap, rugged and reliable.
- Since control is open loop, it is easy for a novice to set up a system using a PC, an input/output card and high level language commands from a PC.
- Microstepping offers resolution in excess of 100 000 steps per turn.

Figure 2.7. A Simple Microstepping Control System (see text for explanation)



Disadvantages

- Because no feedback loops exist, an extraneous force can easily produce a position error. If the phase between steps is lost then it is only recovered in the next step of the stepper motor, resulting in large errors.
- It is difficult to configure stepper motors for torque control. High detent torque severely restricts minimum torque. Torque ripple also occurs between steps requiring complex algorithms to electrically dampen oscillations (Gagné, 1986).
- Stepper motors have a high current consumption and run hot.
- Stepper motor systems are noisy and produce a pitch which is proportional to velocity. Audio feedback can be eliminated using ear defenders, but this would severely restrict the normal interaction between the subject and the researcher.

Because of the related disadvantages, a stepper system was rejected as a viable option.

C) A DC Brushless Motor System

In the DC brushless motor, currents to the electromagnetic coils of the stator field are sinusoidally modulated so that the rotor field is maintained at 90° to the stator field. Thus, typically, the three R, S and T phases are controlled with sinusoidally modulated currents, 120° out of phase with respect to each other (see figure 2.8.). Because electromagnets supply the outer stator field, this creates a shorter thermal path to the motor exterior allowing greater power and, hence, larger torques can be generated. The rotor however, requires expensive 'rare earth magnets' which do not demagnitize over time.

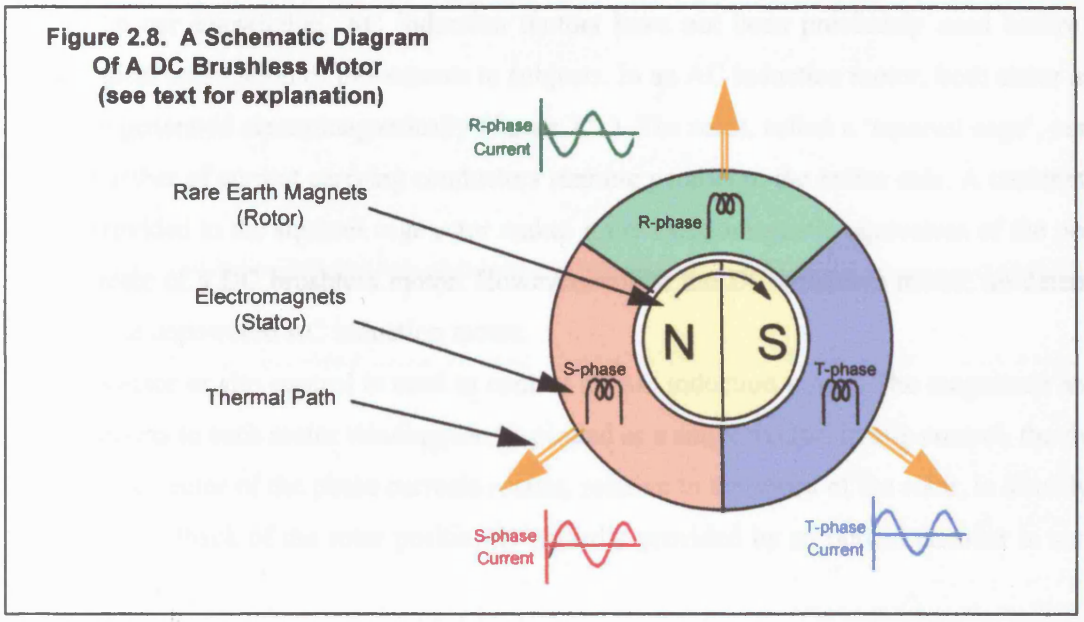


Figure 2.8. A Schematic Diagram Of A DC Brushless Motor (see text for explanation)

DC brushless motors have successfully been used to apply movements and impose various load conditions to human finger joints (eg. Al-Falahe & Vallbo, 1988, Vallbo & Wessberg, 1993). Previous system have been custom built by control systems specialists, but more recently, 'off the shelf' control modules have become commercially available, which allow the layman to set up and control DC brushless systems. The advantages and disadvantages of a DC brushless system are:

Advantages

- For a fixed position, there is a near perfect linear relationship between current and torque.
- The low inertia of the rotor means that high dynamic capabilities are possible.
- High torque is generated from a relatively small motor size.
- 'Off the shelf' control modules running from Windows® compatible software are commercially available meaning that technical expertise is not required.

Disdvantages

- A detent torque resulting from the permanent magnets means that an electromagnetic clutch is needed to achieve zero torque.
- Because DC brushless motors contain rare earth magnets, they are relatively expensive.

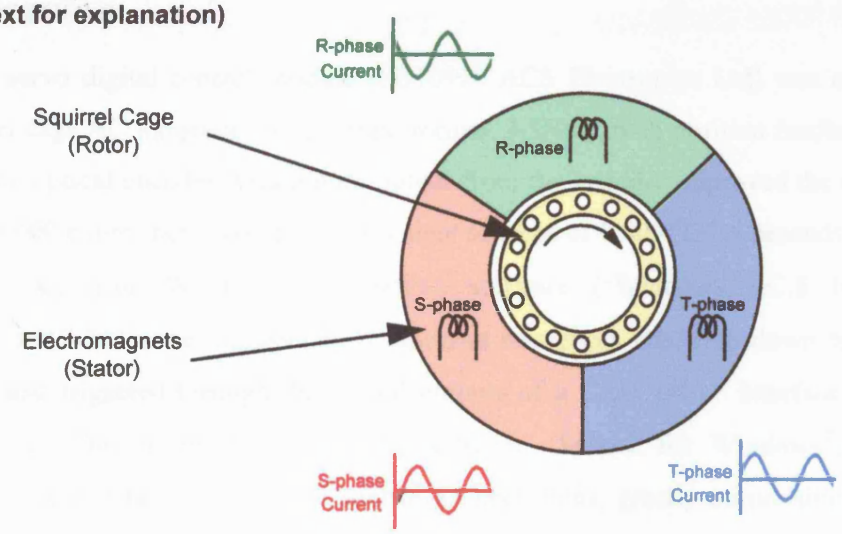
A DC brushless motor was tested using a control module but this option offered less advantages than an equivalent AC induction motor system which did not have the problems associated with detent torque.

D) An AC Induction Motor System

To our knowledge, AC induction motors have not been previously used before for the physiological application of movements to subjects. In an AC induction motor, both stator and rotor fields are generated electromagnetically (figure 2.9.). The rotor, called a 'squirrel cage', consists of a large number of current carrying conductors running parallel to the motor axis. A constant current supply provided to the squirrel cage rotor makes it the electromagnetic equivalent of the permanent magnet rotor of a DC brushless motor. However, unlike the DC brushless motor, no detent torque exists in the unpowered AC induction motor.

Vector or slip control is used to control an AC induction motor. The magnitude and phase of the currents to each motor winding can be plotted as a single vector. In slip control, the frequency at which the vector of the phase currents rotates, relative to the speed of the rotor, is directly related to torque. Feedback of the rotor position is typically provided by an optical encoder in series with the motor shaft.

Figure 2.9. A Schematic Diagram Of An AC Induction Motor (see text for explanation)



The advantages and disadvantages of the AC induction system are listed:

Advantages

- AC induction motors are very reliable and cheap, costing less than a quarter of the price of a comparable DC brushless motor.
- The larger inertia of the squirrel cage rotor means that the velocity profiles of movements are very smooth.
- AC induction motors run quietly.
- In the unpowered motor, free movement is possible.
- 'Off the shelf' control modules running from Windows® compatible software have recently become commercially available meaning that technical expertise is not required.

Disadvantages

- Because of the squirrel cage, AC induction motors are large and heavy.
- The linearity in the relationship of torque to current is not as good in AC induction motors as in DC brushless machines.

Compared to the other three options, the AC induction motor system offered the greatest benefits with the minimum complexities. A cheap system could be readily set up to offer accurate control with a high degree of versatility. The system also represented a novel approach to tackling the problem of applying smooth slow physiological movements to human subjects. An outline of the mechanical and electrical setup of an AC induction motor system follows.

2.5.2. Actuator Setup

2.5.2.1. Overview

An AC servo digital control module (SB1091® ACS Electronics Ltd) was configured to control a squirrel cage AC induction motor (max. torque: 3.5Nm), with position feedback provided by an 10 000 line optical encoder. Quadrature output from the encoder improved the resolution of the system to 40 000 counts per revolution, equivalent to steps of 0.009° (32.4 seconds of arc). The control module ran from Windows® compatible software ('Windows®A.C.S Interface' or WACSI®), via an RS-232 serial connection. Command sequences could be down loaded to the control module and triggered through the digital outputs of a CED 1401+ interface (Cambridge Electronic Design). This meant that recording software (Spike2 for Windows®, Cambridge Electronic Design) could be configured to control all operations, greatly minimising the running complexities of experiments.

2.5.2.2. Mechanical Arrangement

Support: A 'Brown-Schuster' myograph stand was modified to support the 7kg weight of the housed motor (see figures 2.10. and 2.11.). The stand was mounted on an aluminium plate (25mm thick) fixed with locking nuts to the base platform. The motor ran along two parallel square section cross rails (20mm thick) supported by the stand. The motor could also be rotated on its base, aided by a PTFE layer to reduce friction.

Housing: The motor was housed in an aluminium casing (165mm x 175mm x 285mm) which was electrically isolated from both the motor and the base. The housing was used to shield the effects of the high frequency current pulses delivered to the motor phases.

Attachment of the Encoder: An optical encoder fixed to the rear of the motor was connected to the motor shaft using a nickel bellows coupling which minimised shaft misalignment errors (see figure 2.11.).

Attachment of the Digit: Ranges of pneumatic splints, of various diameters, were constructed to account for different digit diameters. The splints were attached directly to the motor shaft via a steel cross piece and were inflated to a pressure of 20 mmHg using a sphygmo-manometer (see figures 2.10., 2.11. and 2.12.). The splints reduced the effects any resident system vibration. Inertial masses were added to counterbalanced the weight of the splint.

Figure 2.10. The Hand Actuator And Support: A modified Brown-Schuster myograph stand was used to support the actuator. The stand permitted three degrees of planar movement and one degree of rotational movement (indicated by the arrows). Rail clamps fixed the actuator to the bottom rail. Angle restricting mechanisms are elaborated further in figure 2.14.

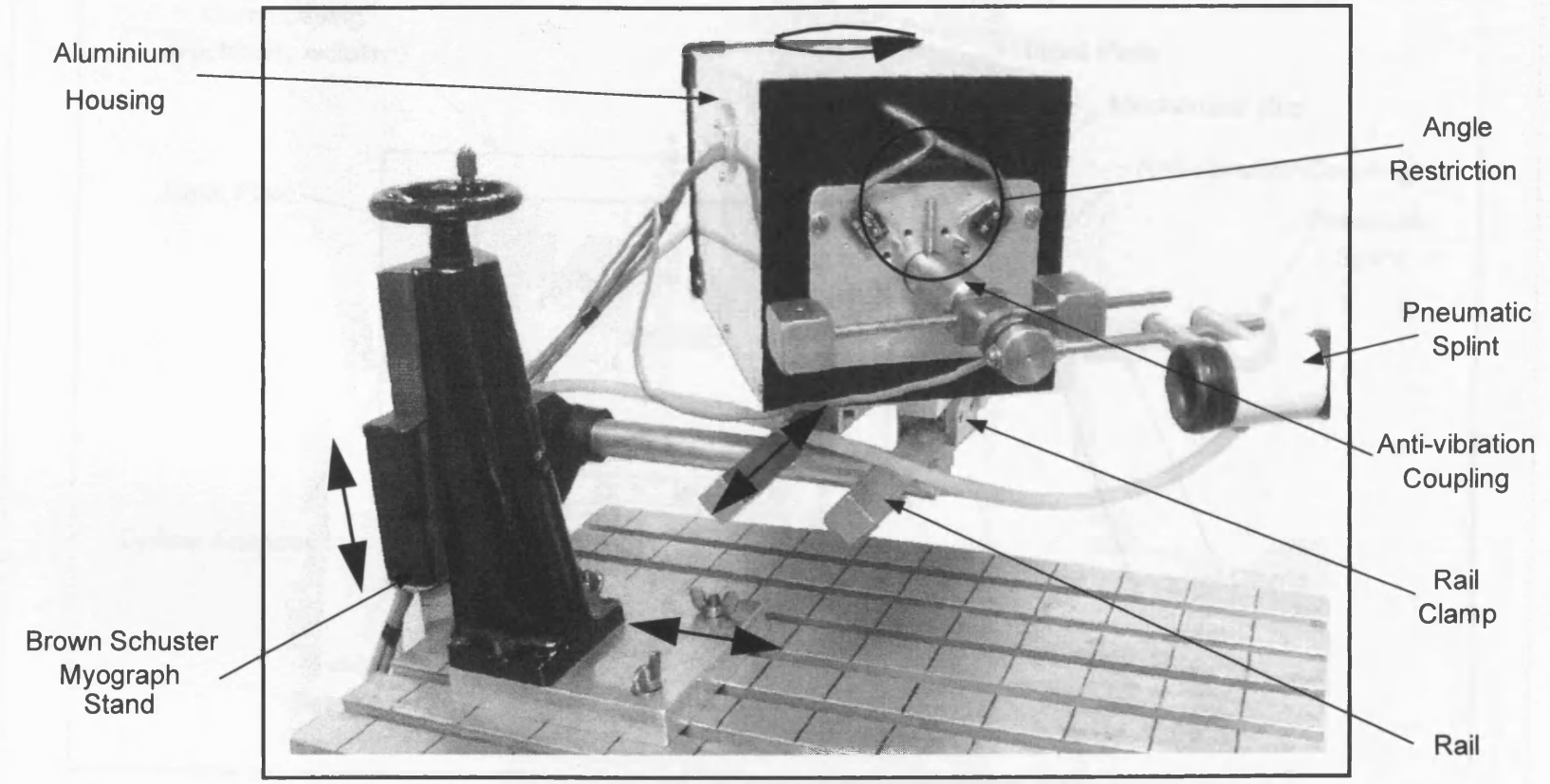


Figure 2.11. A Schematic Diagram Of The Actuator: An optical encoder is fixed to the rear plate of the motor and connected to the motor shaft with a nickel bellows coupling. At the front of the actuator, mechanical stops restrict the range of motion. The pneumatic splint is connected to the motor shaft via an antivibration coupling with inertial masses to dampen vibration. The foot of the motor can rotate aided by a low friction PTFE layer. Rail clamps hold the actuator on the bottom rails.

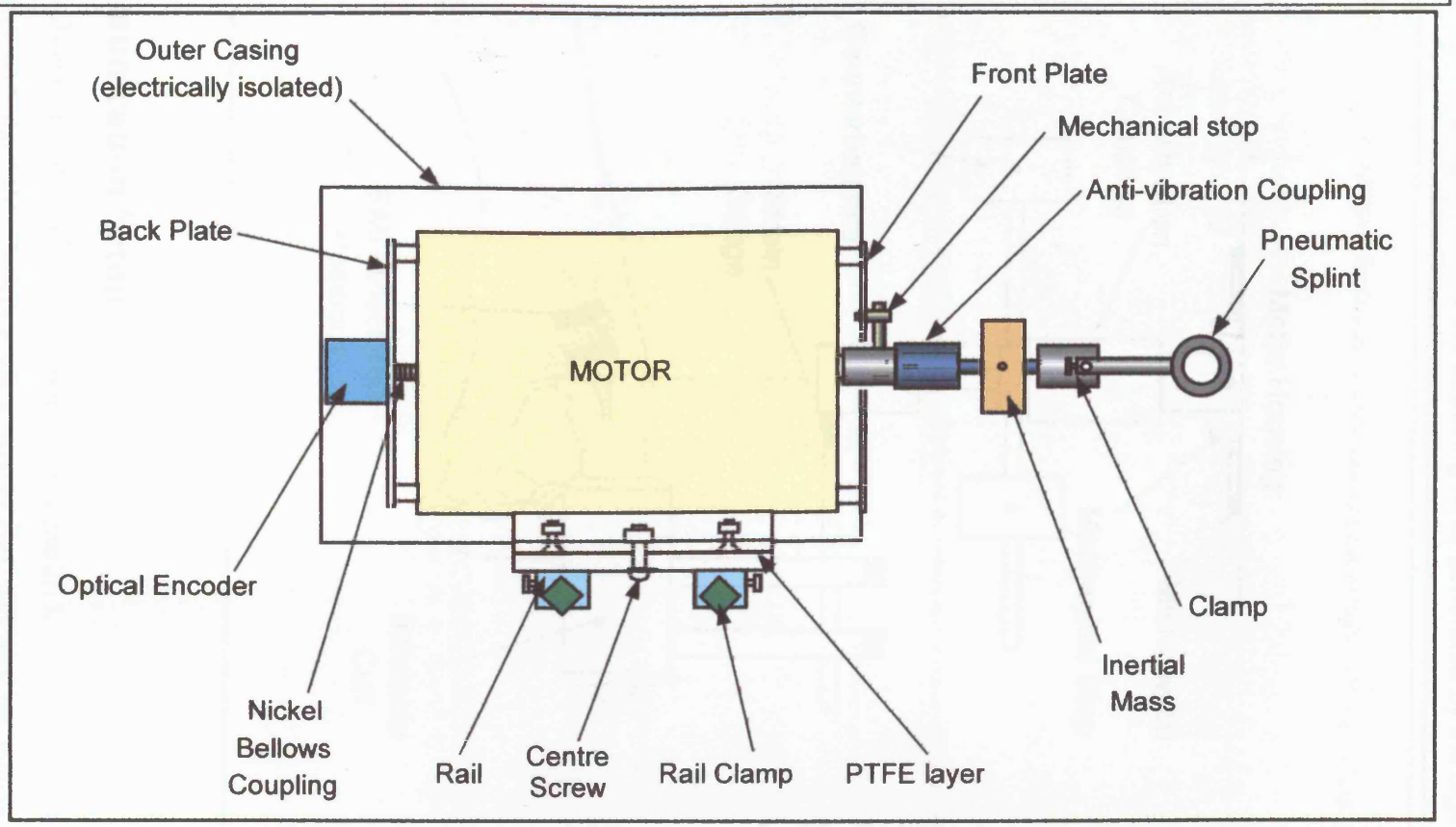
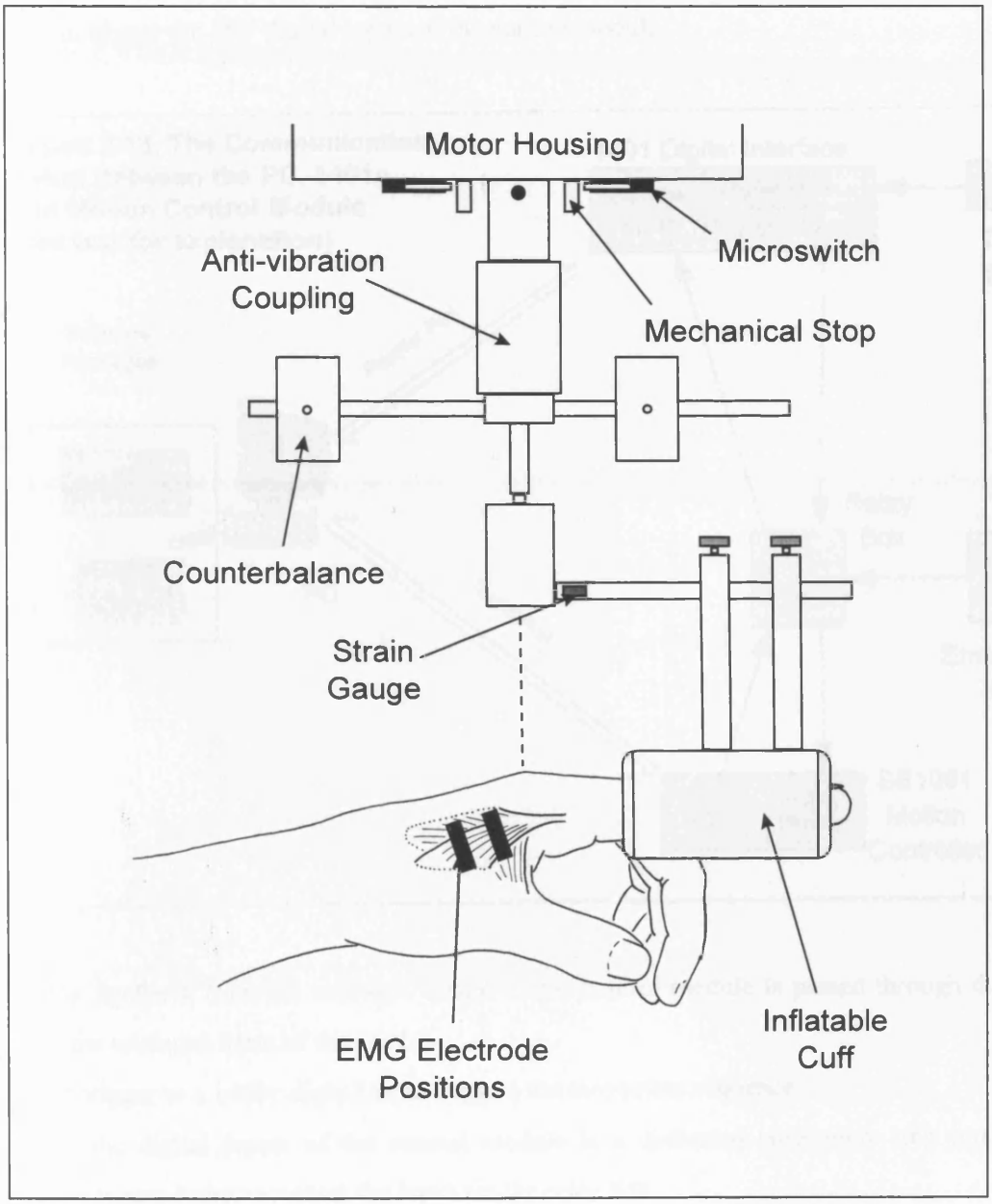


Figure 2.12. An outline diagram of the digit attachment to the motor shaft. The range of motion is restricted using electrical (microswitch) and mechanical stops. An antivibration coupling reduces unwanted vibration. Counterbalances act to balance the weight of the pneumatic splint into which the digit fits. Strain gauges records the opposing force generated by the digit.



2.5.2.3. Communication Setup

The electrical communication arrangement is given in figure 2.13.

- The PC interfaces with the 1401+ interface via a parallel port, and with the motion control module through a RS-232 serial connection.
- Input and output of data through the parallel port is controlled using 'Spike2 for Windows®' (Cambridge Electronic Design).

- Input and output of data through the serial port is controlled using 'Windows®A.C.S Interface' software (ACS Electronics Ltd).
- Command sequences are download to the controller through the RS-232 serial connection and can be triggered via the digital inputs of the control module.
- A relay box was constructed containing six relay switches which permit the 5V outputs of the 1401+ to trigger the 15V digital inputs of the control module.

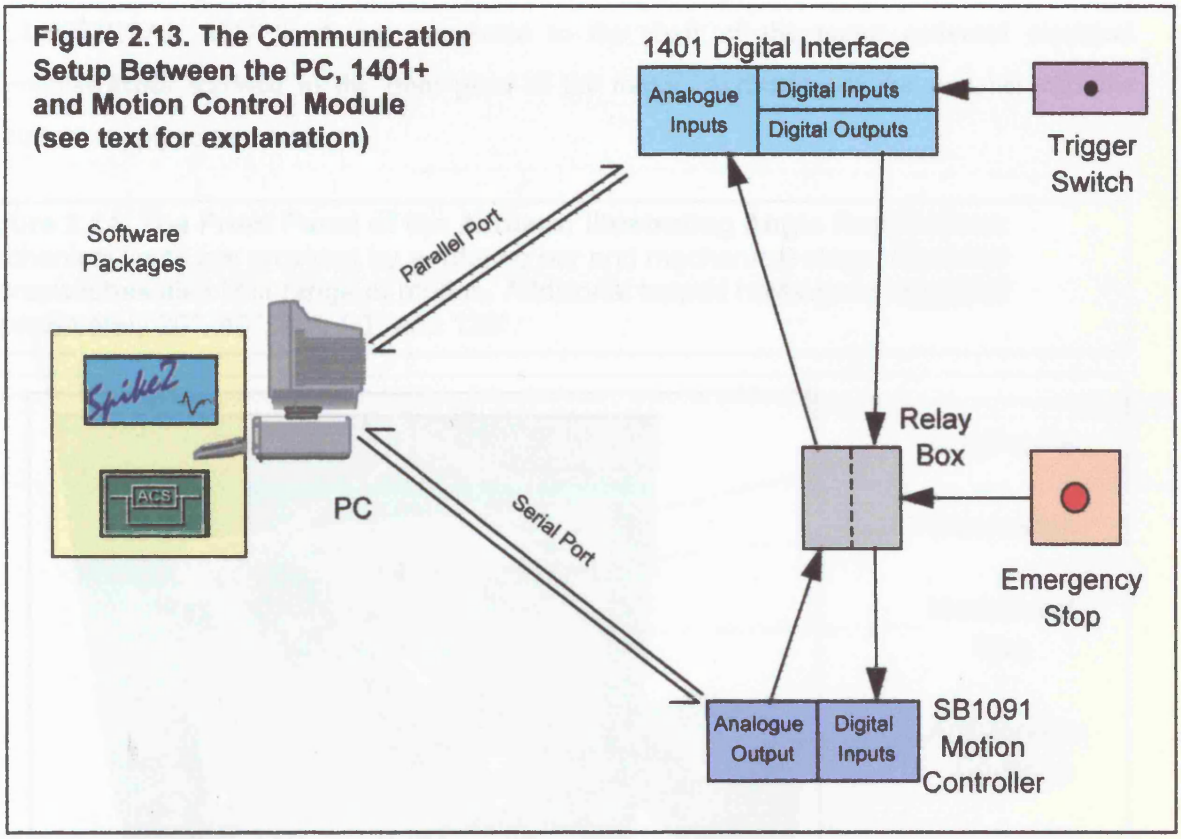


Figure 2.13. The Communication Setup Between the PC, 1401+ and Motion Control Module (see text for explanation)

- Position feedback from the analogue output of the control module is passed through the relay box to the analogue input of the 1401+.
- A hand trigger to a 1401+ digital input triggers the movement sequence.
- One of the digital inputs of the control module is a dedicated emergency stop input. The emergency stop button accesses the input via the relay box.

Earthing

The motor controller was placed in a shielded container which, along with the motor housing and base platforms, were earthed in a star configuration. Anti-surge filters were used in the power supplies to the motor controller, the PC and the 1401+ digital interface.

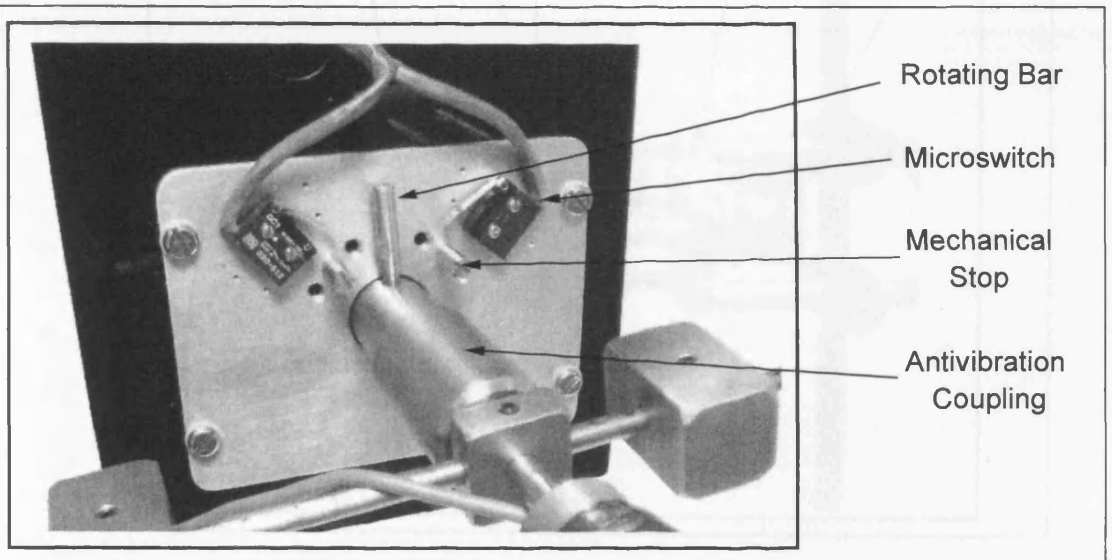
2.5.2.4. Safety

Mechanical Safety

Safety is of critical importance in experiments where movements and forces are applied to human hands, particularly injured hands. A series of safety stages were incorporated into the front plate of the actuator to restrict the range of motion of the motor (see figure 2.14.):

- SOFTWARE STOPS: Position limits were defined in the command language so that the motor would not move outside of set boundaries.
- ELECTRICAL STOPS: A bar connected to the shaft of the motor activated electrical microswitches screwed to the front plate of the motor. Activation of the switches cuts the current supply to the motor.

Figure 2.14. The Front Panel of the Actuator Illustrating Angle Restrictions: Mechanical limits are provided by a rotating bar and mechanical stops. Electrical microswitches also limit range of motion. Additional tapped holes gave ranges of approximately 20°, 40°, 60°, 90° and 120°.



- MECHANICAL STOPS: Steel bars screwed to the front plate of the motor in conjunction with a bar connected to the shaft of the motor served as physical limits of the range of motion. Since the motor draws more current when it hits the mechanical stop, a software current limit set in the program language provided further protection by deactivating the motor when this limit was transgressed.
- MANUAL EMERGENCY STOP: A push button switch activates a command which interrupts movement sequences and cuts the current supply to the motor.

A number of tapped holes in the front plate allow the electrical and mechanical stops to be positioned to give ranges of motion of 20°, 40°, 60° , 90° and 120°.

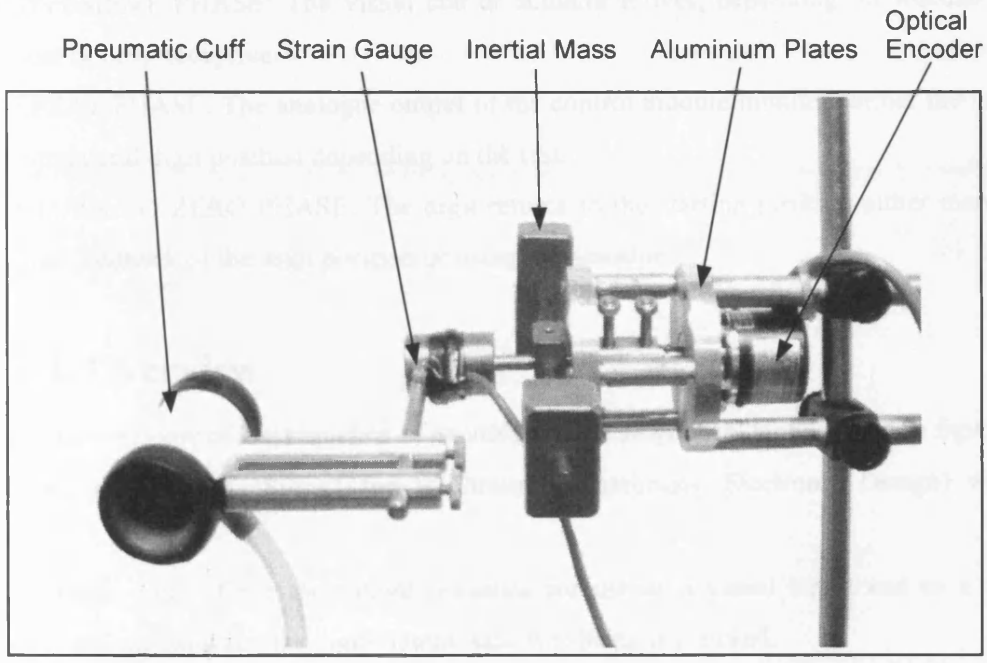
Electrical Safety

The SB1091 motion control module offered full protection against phase to phase shorting, phase to ground shorting and overheating. The subject was kept electrically isolated from all equipment.

2.5.2.5. A Second Position Encoder

A position encoder was constructed to monitor the position of the contralateral hand. A 2000 line optical encoder, with a quadrature output provided the position reading. This gave a resolution of 8000 counts per turn, equivalent to 0.045° steps.

Figure 2.15. A Second Position Encoder



Two parallel aluminium plates, separated by spacers, housed bearings through which the centre shaft passed (fig 2.15). The optical encoder was fixed to the rear of the plates and a pneumatic cuff to the front shaft. Inertial masses were also added to act as counterbalances and match the moments of inertia of the actuator. Strain gauges measured the torque. The control module was only able to display the output from one optical encoder at the same time. An exact copy of the movement carried out by the motor was also generated by the sequence programmer in Spike2 for Windows® to provide simultaneous displays of ipsilateral and contralateral movements, when monitoring from the second position encoder.

2.5.5. Command Sequences

2.5.5.1. Movements Required

For the current investigations two pseudorandom sequences of movements were generated:

- ***Ramp Moves:*** A sequence of 12 ramp abduction and adduction moves of amplitudes 1.5°, 3°, 6° and 12° and velocities 1.5°s^{-1}, 3°s^{-1} and 6°s^{-1}.
- ***Sine Moves:*** A sequence of 9 sinusoidal moves of frequencies 1Hz, 0.5Hz and 0.25Hz and amplitudes 3°, 6° and 12°. Four sinusoidal cycles were performed during each move. The sinusoidal test was implemented as a supplementary test for measuring kinaesthesia. It was not used in the current study.

There were three phases to each movement:

1. MOVEMENT PHASE: The visual cue or actuator moves, depending on whether the test is visual or proprioceptive.
2. REPEAT PHASE: The analogue output of the control module monitors either the ipsilateral or contralateral digit position depending on the test.
3. RETURN TO ZERO PHASE: The digit returns to the starting position either manually using visual feedback of the digit position or using the actuator.

2.5.5.2. Overview

An overview of the sequence of events during a single trial is illustrated in figure 2.16. The sequencer language of 'Spike2 for Windows®' (Cambridge Electronic Design) was used to generate:

- A voltage copy of the movement sequence for use as a visual target and as a copy of the ipsilateral signal when the contralateral side was being monitored.
- Commands to the 1401+ digital outputs to control the sequence and timing of movements.

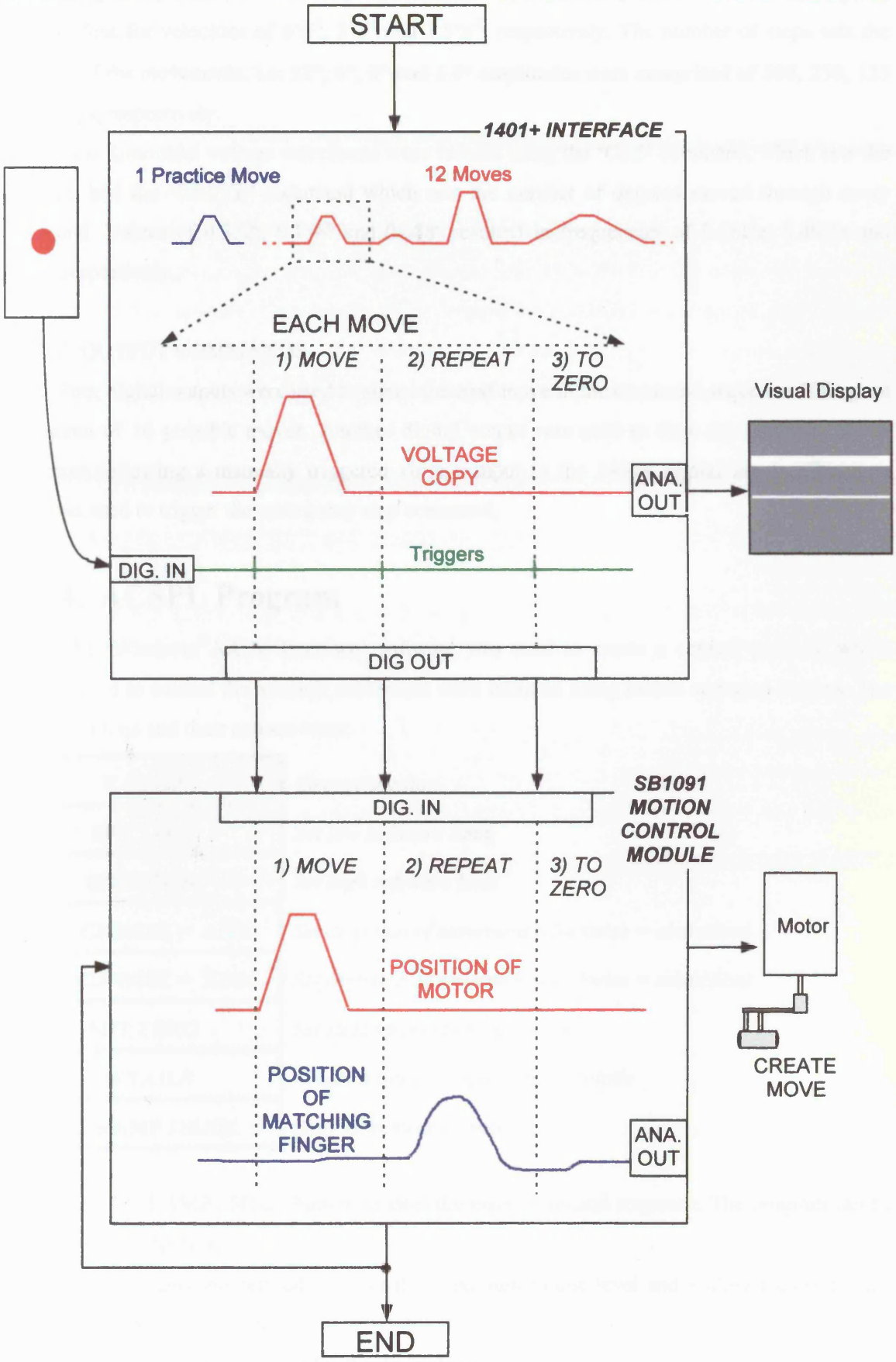
The ACS program language of the 'Windows®A.C.S. Interface' software (ACS Electronics Ltd, Israel) was used to:

- Generate movements in response to cues at the digital inputs.
- Switch the motor off in response to an emergency stop signal.
- Set software limits for the range of motion.

2.5.5.3. Spike 2® Sequencer Program

After creating an initial practice move, the program generates a pseudorandom sequence of movements using the 'branch' command which randomly moves to different parts of the movement sequence.

Figure 2.16. Overview of command sequences: The 1401+ interface generates a practice move followed by pseudorandom sequence of 12 moves. A voltge copy of the moves is generated at the analogue output. Triggers are also generated to control the timing and sequence of the moves. The SB1091 control module creates movements in the induction motor and reads the optical encoders to give a readout of the digit position at the analogue output (see text for a full description).



VOLTAGE COPY

Ramp Moves: The voltage copy of the ramp moves consisted of a rapid series of voltage steps created using a loop command. The loop time determined the 'velocity' of the movement, i.e. 4ms, 8ms and 16ms for velocities of $6°s^{-1}$, $3°s^{-1}$ and $1.5°s^{-1}$, respectively. The number of steps sets the amplitude of the movements, i.e. 12°, 6°, 3° and 1.5° amplitudes were comprised of 500, 250, 125 and 63 steps, respectively.

Sine Moves: Sinusoidal voltage waveforms were created using the 'CSZ' command, which sets the amplitude, and the 'CRATE' command which sets the number of degrees moved through every millisecond. Values of 0.352°, 0.176° and 0.088° resulted in frequencies of 0.98Hz, 0.49Hz and 0.24Hz, respectively.

DIGITAL OUTPUT COMMANDS

Four digital outputs were used to signal the next move in the command sequence. This gave a maximum of 16 possible moves. Another digital output was used to time the sequence of the movements following a manually triggered voltage input to the 1401+ digital inputs. The sixth output was used to trigger the emergency stop command.

2.5.5.4. ACSPL Program

The 'Windows®A.C.S. Interface' software was used to create a control panel in which programs used to control the actuator movement were initiated using mouse activated buttons. The specified buttons and their actions were:

E STOP	*Emergency stop*
SET LOW	*Set low software limit*
SET HIGH	*Set high software limit*
CLOCKWISE = ABD.	*Set direction of movement (clockwise = abduction)*
CLOCKWISE = ADD.	*Set direction of movement (clockwise = adduction)*
SET ZERO	*Set starting point of movement*
DETAILS	*Create a table to input subject details*
GO RAMP / SINE	*Start movement sequence.*

The 'GO RAMP / SINE' button initiates the main command sequence. The program can be broken down accordingly:

- Program constants are defined, such as the maximum torque level and scaling factors for the two optical position encoders.
- Then program prompts the user for the desired test.

- The direction of movement, current test and amplitude and velocity of each movement are returned to the user via the ACS terminal
- Following a timing cue, the desired movement is read from the digital inputs of the SB1091 control module.
- ***Ramp Movements:*** A linear point to point mode is used to create the ramp movements. Target position, linear velocity and linear acceleration are defined in encoder counts (eg. 3° is equivalent to 333 counts). Linear acceleration and deceleration were set at 1000 000 counts s^{-2}, equivalent to 9009°s^{-2}.
- ***Sine Movements:*** An arbitrary path generation mode was used to produce sinusoidal movements by following an array of points created from a sine table in the non-volatile memory of the control module. Four arrays were created to produce sinusoids of four different amplitudes (3°, 6°, 9° and 12°). The 'PathTime' command, defining the time in milliseconds between each point, was used to determine the frequency of the sinusoid.

2.5.6. Problems Encountered

NOISE: Reducing the current loop gain by a small amount reduced the noise to below levels of auditory threshold.

FRICTION: A small degree of static friction (stiction) was resident in both the AC induction motor and the optical encoder, which the subjects could perceive when trying to make active movements. Both the motor and encoder were disassembled and existing industrial lubricating grease was replaced with low viscosity clock oil. Also, radial springs added to stabilise motor bearings at high rotational speeds were removed to further reduce friction. The resultant radial stiction was below 2.5 X 10^{-3} Nm^{-1}. Friction levels below this could only be attained using active compensatory control mechanisms (Al-Falahe & Vallbo, 1988, Vallbo & Wessberg, 1993).

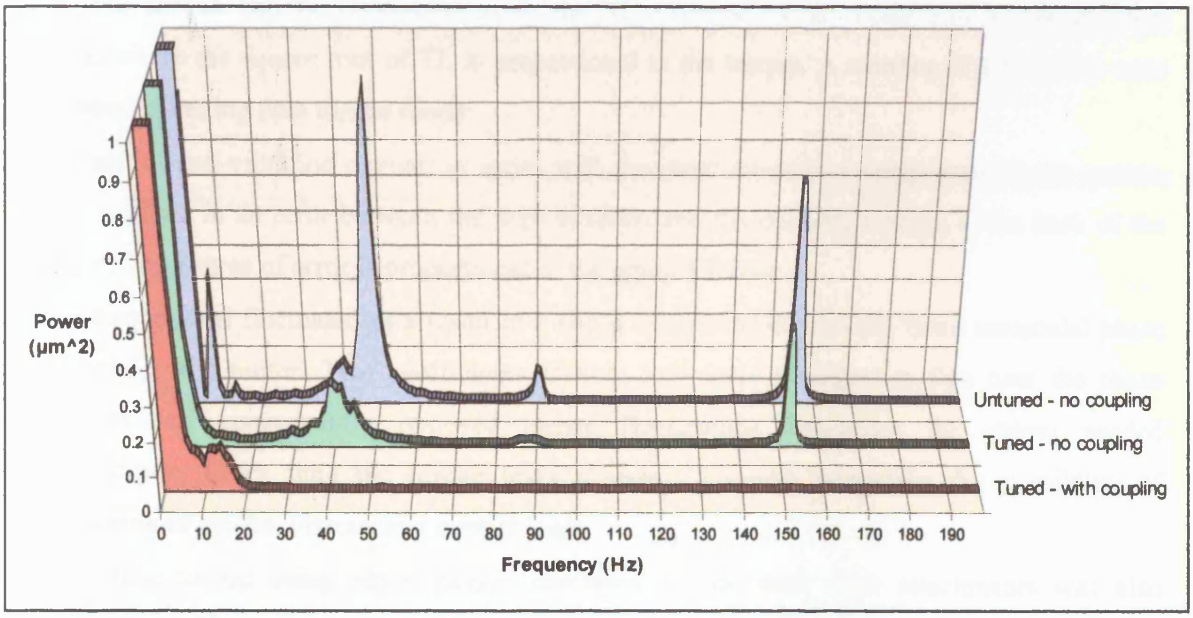
VIBRATION: Proprioceptive illusions can be induced by tendon vibration due to the stimulation of Ia muscle spindle afferents (Goodwin, McCloskey & Matthews, 1972). Sittig *et al* (1987), have demonstrated that perception of position and velocity, as well as performance of fast and slow non-visually guided movements in the forearm, are all influenced by tendon vibration in a frequency dependant manner. Although sensory illusions occur below 25Hz, the greatest errors in perception of both position and velocity occur between 50 to 100 Hz.

The SB1091 control system functions by hunting for a given encoder count and then seeking to maintain this position. A drift away from the target position is recognised when the control module registers an adjacent encoder count with the result that the motor tends to oscillate by ±1 encoder count. Steps were taken to reduce both the amplitude and the frequency of the

vibration and, in particularly, to ensure that frequencies above 25Hz were abolished. A number of different methods were used to reduce vibration:

- ***A New Optical Encoder:*** The 2000 line encoder supplied with the system was replaced with a higher resolution 10 000 line encoder, potentially reducing the amplitude of the vibration fivefold. The new encoder resulted in vibration of a smaller amplitude but also of a higher frequency.
- ***Tuning the System:*** Software was provided with the control module that permitted adjustment of the loop gains and filter characteristics (ACS adjuster, ACS Electronics Ltd, Israel). After some investigation it became apparent that the velocity loop controlled the vibration frequencies between 150 and 160 Hz whereas the position loop controlled frequency peaks around 40 or 60 Hz. Whilst keeping the system response fast and stiff, the velocity and position loop gains and bandwidths were reduced to minimise vibration. Figure 2.17. illustrates the effect of tuning in reducing the peaks between 40-60Hz, 80-90Hz and 150-160Hz. The power spectra presented in figure 2.17. were measured using an optical laser system (see tremor section) recording the displacement at 0.1m from the shaft axis.

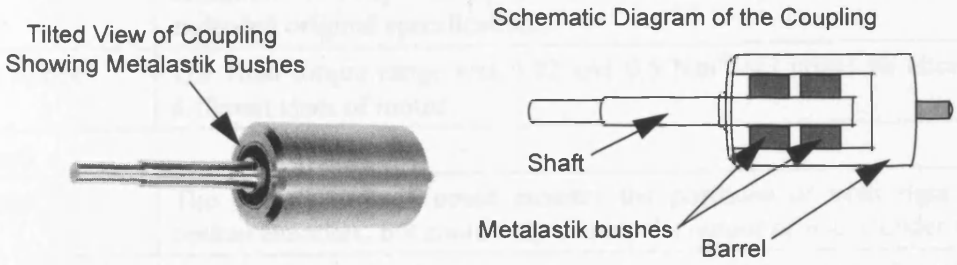
Figure 2.17. Reduction of system vibration using motor tuning and an antivibration coupling. Power spectra are calculated for recordings of displacement (using an optical laser), measured at 0.1m from the axis of rotation. The power spectra are of: the untuned system, ie. the motor as first connected to the controller; the tuned system, following optimisation of position and velocity loops; and the tuned system with the antivibration coupling in place (See text for full explanation).



- ***An Anti-Vibration Coupling:*** A wide range of compliant materials were tested for their dampening capacity by sandwiching them between two brass plates in series with the motor shaft. The materials included rubber, foam rubber and anti-vibration mount cut to different

dimensions. Two test couplings were subsequently constructed and tested. Although the couplings were effective at reducing high frequency vibrations they also resulted in shaft misalignment due to the load at the end of the shaft. A third coupling was constructed using two Metalastik® anti-vibration bushes surrounded by an outer barrel connected to the motor shaft (figure 2.18.). The digit attachments were then connected to the inner shaft of the coupling. The third coupling was effective at removing frequencies above 20Hz and minimised shaft misalignment (figure 2.17.).

Figure 2.18 Antivibration Coupling (see text for details)



- ***Inertial masses:*** These were located between the coupling and the digit (see figures 2.10. - 2.12.), and could be moved towards and away from the shaft to fine tune the dampening characteristics of antivibration coupling.
- ***Pneumatic cuffs:*** These acted to filter out any vibration not removed by other methods.

Control of Torque

The torque can be controlled using the TL (Torque Level) command in the program language, where the square root of TL is proportional to the torque. A number of difficulties were encountered in setting up a torque mode:

- The use of anti-vibration devices in series with the shaft introduces compliance to the system. This resulted in an error between the digit position and the encoder reading at the back of the motor. The degree of error is proportional to the applied torque
- The torque level fluctuated as a result of a slight mismatch between the three sinusoidal phase currents to the motor. Two coefficients (J16 & J17) were modified to fine tune the phase currents and consequently removed torque fluctuations. However, the values needed readjustment every time the torque level changed, severely restricting the possibility of simulating of elastic, viscous and inertial loads.
- Measuring torque using strain gauges cemented to the steel digit attachments was also problematic. Their close proximity to the motor meant that they were sensitive to the high frequency current pulses used to control the motor.

Using the actuator to investigate sense of force was rejected in favour of using a simple mass and pulley system (see the section on 'sense of force' in the discussion).

2.5.7. Final Specifications

The final design met most of the original specifications (see section 2.51.):

TABLE 2.2. FINAL SPECIFICATIONS FOR A HAND ACTUATOR	
Angle Range	Angle ranges of 20°, 40°, 60° , 90° and 120° were defined by software, electrical and mechanical stops.
Resolution	The system resolution was 40 000 counts per revolution, equivalent to 0.009° (or 32.4 seconds of arc). This was less than half the originally specified value.
Velocity Range	The minimum velocity was 1 count/sec equivalent to 0.009 $°s^{-1}$. The maximum velocity was up to 250 revolutions per second. Both values exceeded original specifications.
Torque Range	The final torque range was 0.02 and 0.5 Nm^{-1} but could be altered using different sizes of motor.
Feedback	
Position	The control module could monitor the positions of both right and left optical encoders, but could only display the output of one encoder at a time.
Velocity	Velocity was derived from the position signal off-line using digital filtering techniques.
Torque	Strain gauges were used to measure torque in the system.
Movements	
Triangle/Ramp	The 'linear point to point' mode was used to generate linear velocity movements.
Sinusoidal	The 'arbitrary path generation mode' was used to create sine waves by tracing a sine table stored in the control module.
Pseudorandom	A pseudorandom move could be created using a random array of points followed under 'arbitrary path generation' mode.
Torque Modes	
Fixed Torque	The level of torque was set using the TL command.
Zero Torque	No torque is present when the motor is not powered up.
Transient Torque	A time or position triggered change in torque can easily be created by modifying the TL value.
Variable Torque	It was not possible to simulate elastic, viscous and inertial loads due to torque fluctautions which vary with the degree of torque.
Other Relevant Factors	
Noise	Reducing the current loop gain could change the noise of the motor to below auditory threshold.
Safety	Software, electrical and mechanical stops were used to restrict range of motion. The system was electrically safe.
Vibration	Vibration was reduced by adding an antivibration coupling and pneumatic splints and tuning position and velocity loops. The compliance introduced into the system reduced the capabilities of the system for applying torque.
Ease of Use	Windows® compatible software made the system easy to use.

CHAPTER 3: METHODS

Informed consent was obtained from all subjects and the study was performed in accordance with local ethical approval under the Declaration of Helsinki. Transportation and attendance costs for PNI and CTS patients were covered.

3.1. Patient Recruitment

Normals: 41 subjects under the age of 45 were recruited for the purpose of investigating proprioception and tremor in the normal hand. In addition, 3 subjects over 45 were also recruited as controls for the PNI subjects. All normal subjects were free from any neurological disorders.

Anaesthetic Blocks: Local anaesthetic blocks were applied to peripheral nerves of 7 willing volunteers. The anaesthetic blocks included 7 median nerve blocks, 7 ulnar nerve blocks, 3 radial nerve blocks and 3 median & radial nerve blocks.

PNI subjects: In all, 48 PNI subjects were contacted drawing from a pool of subjects who had been admitted into Leicestershire hospitals between the years 1991-1996, and other subjects were contacted through local radio and newspaper advertising. Of 34 subjects who were willing to participate, 9 were unsuitable due to incomplete nerve trauma, neurological deficits or age, leaving 25 subjects who took part in some aspect of the study. Of the 25 subjects, 9 suffered from median nerve injury, 10 from ulnar nerve injury and 6 from median and ulnar injuries. None of the subjects suffered from any significant radial nerve damage at wrist level. The majority of nerve lesions were inflicted through glass injuries.

Normal hands of PNI subjects were also used as control data for injured hands using results from unilateral kinaesthetic trials (i.e. visual tracking, visual repeat and ipsilateral repeat tests) and tremor measurement.

CTS Subjects: 16 CTS subjects were recruited prior to carpal tunnel release. The subjects were selected on the basis of electrodiagnosis (slowing of motor and sensory conduction velocities). Tremor and weight matching ability (see discussion) was examined in these subjects.

3.2. Kinaesthesia

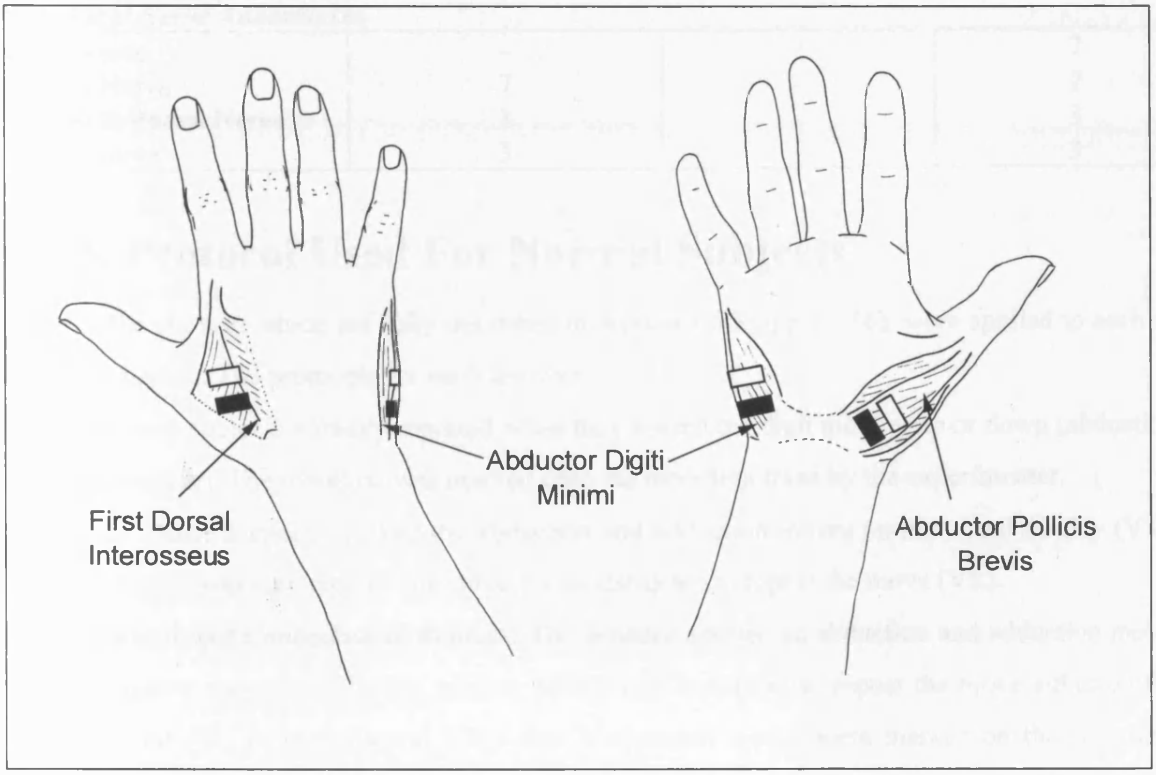
3.2.1. Models Used

The three models are described at length in section 1.6.2. (p49, p50 & p54) and illustrated in figures 1.8-1.10 (pp51-53). Because the axis of rotation of the motor is always vertical, the plane of hand was positioned vertically to perform abduction: adduction of the little and index fingers and 30° from vertical, to perform abduction: adduction of the thumb. A removable extension pin fitted into the end of the shaft aided the correct alignment of the joints.

3.2.2. EMG Recordings

Surface EMG recordings from AbPB, 1DI and AbDM muscles were recorded from the thumb, index and little finger models, respectively (figure 3.1.). Tab electrodes (Biotabs®, Medical & Surgical Bio-adhesives Ltd, UK) were cut down to 11 mm x 18 mm, and positioned away from the skin covering the joint of interest. Typically, the positive electrode was positioned over the belly of the muscle and the negative electrode towards the proximal tendon, approximating to a monopolar recording. The skin was abraded and sterilised before application of the electrodes. Resistances between electrodes were recorded before and after trials with the objective of values remaining below 20 kΩ over the course of recording.

Figure 3.1. Electrode positions used for recording EMG activity in relation to the anatomical positions of recorded muscles. The positive electrode is displayed in white and the negative electrode in black.



3.2.3. Movements Applied

A series of 13 abduction and adduction movements were applied during each trial, including a test move of 6° at $3°s^{-1}$ (not analysed) followed by a pseudorandom sequence of 12 moves of amplitudes, 1.5°, 3°, 6° and 12°, and velocities, $1.5°s^{-1}$, $3°s^{-1}$ and $6°s^{-1}$. The pseudorandom sequence was created by breaking into a loop sequence in one of four places (see section 2.5.5., p76). Each move consisted of an abduction move, a 0.5 second hold period and an identical adduction move. This was followed by a movement repeat phase and a phase where the matching digit was returned to zero. Each phase was initiated using a hand trigger input.

All subjects were instructed to remain relaxed throughout the course of the movements, although most subjects found this particularly difficult during movement repeat and matching tasks. Precedence was given to the subject concentrating on accurately reproducing the amplitude and velocity of the move, even at the expense of keeping the muscle relaxed.

3.2.4. Sample Sizes

The sample sizes for each model (including normal hands from PNI subjects) were:

Model	***1. Thumb*** *Median Innervation*	***2. Little Finger*** *Ulnar Innervation*	***3. Index Finger*** *Mixed Innervation*
Controls	55	30	47
Peripheral Nerve Injury			
Ulnar Nerve	-	9	10
Median Nerve	8	-	7
Median & Ulnar Nerve	6	6	6
Peripheral Nerve Anaesthesia			
Ulnar Nerve	-	7	7
Median Nerve	7	-	7
Median & Radial Nerve	3	-	3
Radial Nerve	3	-	3

3.2.5. Protocol Used For Normal Subjects

The six test, which are fully described in section 1.6.3. (pp 55-56), were applied to each of the three models. The protocols for each test was:

- ***Detection:*** subjects verbally reported when they sensed the digit moving up or down (abduction or adduction). The direction was marked onto the recording trace by the experimenter.
- ***Visual Tests:*** Subjects tracked the abduction and adduction moves on the visual display (VT). The display was covered and the subject was instructed to repeat the move (VR).
- ***Ipsilateral and Contralateral Repeats:*** The actuator applied an abduction and adduction move. If the move was sensed by the subject, he/she was instructed to repeat the move either on the ipsilateral (IR) or contralateral (CR) side. Undetected moves were marked on the recording trace. During CR tests, if there was a significant error between the position at the start and the end of the move, the visual display was shown to subject so that the digit could be returned to the zero position. During IR tests, the motor performed a move to return the digit to the zero position. To distinguish between the return to zero and movement phases, subjects were informed when the movement and the return to zero phases were occurring.
- ***Movement Matching:*** The actuator applied movements that were simultaneously matched with the contralateral hand. The experimenter varied the timing of each move and no cue was provided to the subject concerning the occurrence of the moves. The visual display was used to correct a significant deviation from the zero position during the test.

3.2.5. Protocol Used During Anaesthesia

Short lasting lignocaine and longer lasting marcaine were used to apply local anaesthetic blocks to median, ulnar and radial nerves. The site of application (figure 1.3., p28) was:

- *Median Nerve:* The insertion site was the ulnar side of the tendon of the palmaris longus, approximately 1-1.5 cm proximal to the base of the palm.
- *Ulnar Nerve:* The insertion was radial to flexor carpi ulnaris tendon, approximately 1-1.5 cm proximal to the base of the palm.
- *Radial Nerve:* The insertion site was the region of the anatomical snuffbox. A flap of skin was lifted to inject the anaesthetic.

Motor recovery from anaesthesia was charted using EMG readings of attempted maximal voluntary contractions and sensory recovery by applying a blunted point with pressure.

The short lasting lignocaine blocks were applied to 7 ulnar nerves, 3 radial nerves and 5 median nerves using 5mls max. of lignocaine (1%, plain). The onset of action of the block was 2-3 minutes and the duration was approximately 40 minutes. This called for a shortened protocol so that the order of events during lignocaine anaesthesia was:

- A full clinical assessment (section 3.5.).
- Sensory and motor tests relating to proprioception, i.e. the measurement of maximal voluntary contractions of AbPB, AbDM and 1DI muscles and of the sensitivities of the skin around the joint, in right and left hands.
- CR and MM tests using the models relevant to each anaesthetic block.
- If time allowed and wherever possible, Dn and IR tests were also performed.

Longer lasting marcaine blocks were applied to the median nerves of 4 subjects using 5 mls max. of marcaine (0.5% bupivacaine, plain). The time of onset was 5-7 minutes and the duration of the block approximately 3 hours. The extended anaesthesia allowed:

- An additional lignocaine radial block to be applied to look at the effects of combined median and radial anaesthesia (3 subjects).
- Full visual and proprioceptive tests to be performed (3 subjects).
- Sense of force tests in the index under median nerve anaesthesia (2 subjects, see discussion).

3.2.6. Protocol Used For PNI Subjects

When possible, full proprioceptive tests were performed on PNI subjects. However, in many cases, subjects could not perform VT, VR and IR tests well because of poor motor control. IR tests from normal hands were used as controls for CR tests of injured hands. Control subjects, needed for MM test data and when IR test data was not available, were matched with order of preference given to individuals, of similar age, sex, EMG activity (i.e. relaxed or contracted) and handedness.

3.2.7. Recording Configuration

Digit positions, surface EMG records and triggers were all recorded using a 1401+ digital interface, operating under Spike 2.21 for Windows® software (Cambridge Electronic Design). The sampling rates were:

1. Sequencer Output (used as a visual target or motor copy) 256 Hz
2. Digit Position (control module analogue output) 256 Hz
3. Left and Right EMG recordings 512 Hz

Data files were stored using 100MB zip disks® (Iomega Ltd, UK).

3.2.8. Other Considerations

Safety: Prior to each session, software stops were set and microswitches were tested to ensure restrictions on the range of motions were fully operational (see section 2.5.2.4., p74).

Temperature: Room temperature was monitored and maintained at approximately 20° C. Hand temperature was also recorded using DermaTherm perfusion monitors (Sharn$^{inc.}$, USA). If hand temperature was below 30°C, the hands were heated in warm water.

3.2.9. Analysis Programs

A program was written in the script language of Spike 2.21 for Windows® to analyse data from kinaesthetic tests. An outline of the script follows:

I. SETTING VARIABLES

Previous memory channels, cursors and toolbars were removed and global variables and arrays were defined and set. The subject inputs the test type that determines the selection of a predefined array that acts as a guide along a specific route through the script.

II. CREATING NEW CHANNELS

- **Smoothed Position Channel:** The motion control module analogue outputs a digital position signal with a 10bit resolution of 1024 steps (equal to 0.145°). The position signal was smoothed with a twenty five-point triangular window to improve locating maxima and minima.

- **Velocity Channels:** Two velocity channels were created using a 15-point linear window. The velocity trace of the visual cue was used to determine which move was under analysis. The velocity derived from the position feedback signal was used for setting cursor positions (eg. at the start of the movement) and for calculating the mean matched velocity.

- **EMG Channels:** To determine the mean level of muscle contraction, a rectified and integrated EMG trace was created using a 9-point triangular filter. An overestimate of the true contraction level results if there is either a DC shift or high electrical noise in the recording. To minimise these effects the DC level was first subtracted from the recording, and the signal filtered using a 125 point, 50 Hz notch filter.

III. CALCULATIONS

Amplitudes & Delays

The script works through each reproduced moves prompting the user to decide whether the whole move or only abduction or adduction phases have been sensed. A maximum of four cursors are automatically placed by the script for each move (figure 3.3):

Cursor 1 (ST): The start of the abduction movement. The cursor is placed at the first positive increment in velocity (i.e. when the velocity exceeds $1°s^{-1}$).

Cursor 2 (HI): The start of the adduction move. The cursor is placed at the first negative increment in velocity following the highest point (i.e. when the velocity falls below $-1°s^{-1}$).

Cursor 3 (LO): The end of the adduction movement. A cursor is placed at the lowest point following the adduction move

Cursor 4 (FIN): Positioned at the point when the digit comes to rest.

The user can adjust the cursors if they appear to be positioned inappropriately. After the user accepts the cursor positions the program proceeds to calculate the following amplitudes and delays:

Abduction Amplitude = Position at cursor 'HI' - Position at cursor 'ST'

Adduction Amplitude = Position at cursor 'LO' - Position at cursor 'HI'

Undershoot = Position at cursor 'LO' - Position at cursor 'FIN'

Error = Position at cursor 'FIN' - Position at cursor 'ST'

Abduction Delay = Time at cursor 'ST' - Time at abduction move trigger

Adduction Delay = Time at cursor 'HI'- Time at adduction move trigger

Sample calculations illustrated in figure 3.2. compare values produced by the script program to values calculated independently.

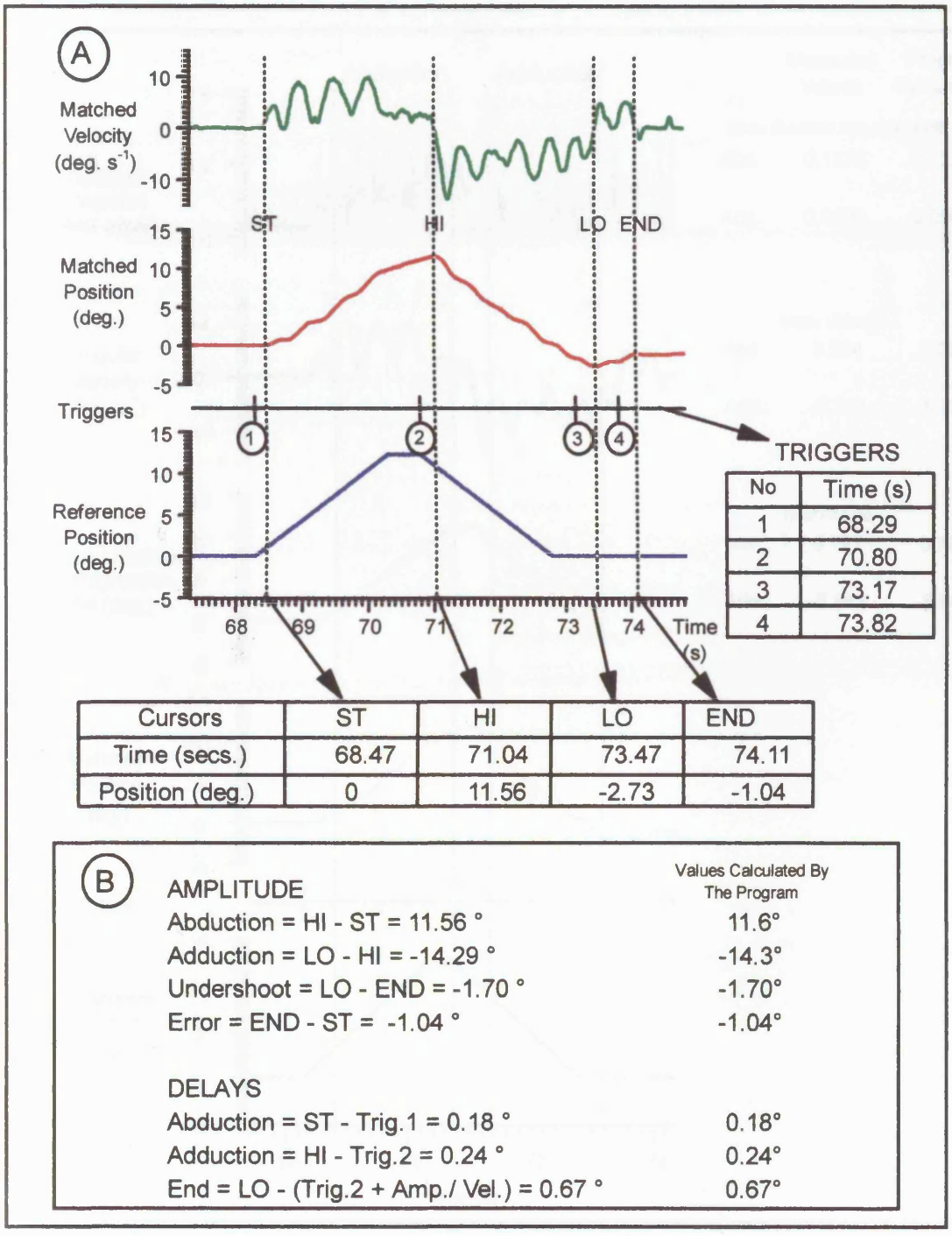
Velocities

Another four cursors are placed, ready to analyse the inner 75% of each of the ranges between cursors 'ST' and 'HI' and between cursors 'HI' and 'LO'. Again, the user can modify the cursor positions. The new cursor ranges are used to calculate (figure 3.3.):

Mean Velocity: The mean velocity trace over the specified range as measured from the velocity channel.

Velocity By Linear Regression: A regression line is fitted to the data in the position channel over the specified range, where the gradient of the line is the velocity estimate. The correlation coefficient is also calculated as an indication of the linearity of the movement.

Figure 3.2. A. Illustrates the positioning of cursors and subsequent calculation of AMPLITUDES AND DELAYS for a single move during a movement match test.
Four cursors are placed by the program at :
ST: The start of the movement, when the velocity rises above $1°s^{-1}$.
HI: The beginning of the adduction movement (i.e. maximum point).
LO: The end of the adduction movement (i.e. minimum point).
END: The point at which the movement comes to rest.
B. Gives the calculation of the parameters worked out by the script using the cursor positions in ***A.***
Values derived by the program script are given in the far right column.



TRIGGERS

No	Time (s)
1	68.29
2	70.80
3	73.17
4	73.82

Cursors	ST	HI	LO	END
Time (secs.)	68.47	71.04	73.47	74.11
Position (deg.)	0	11.56	-2.73	-1.04

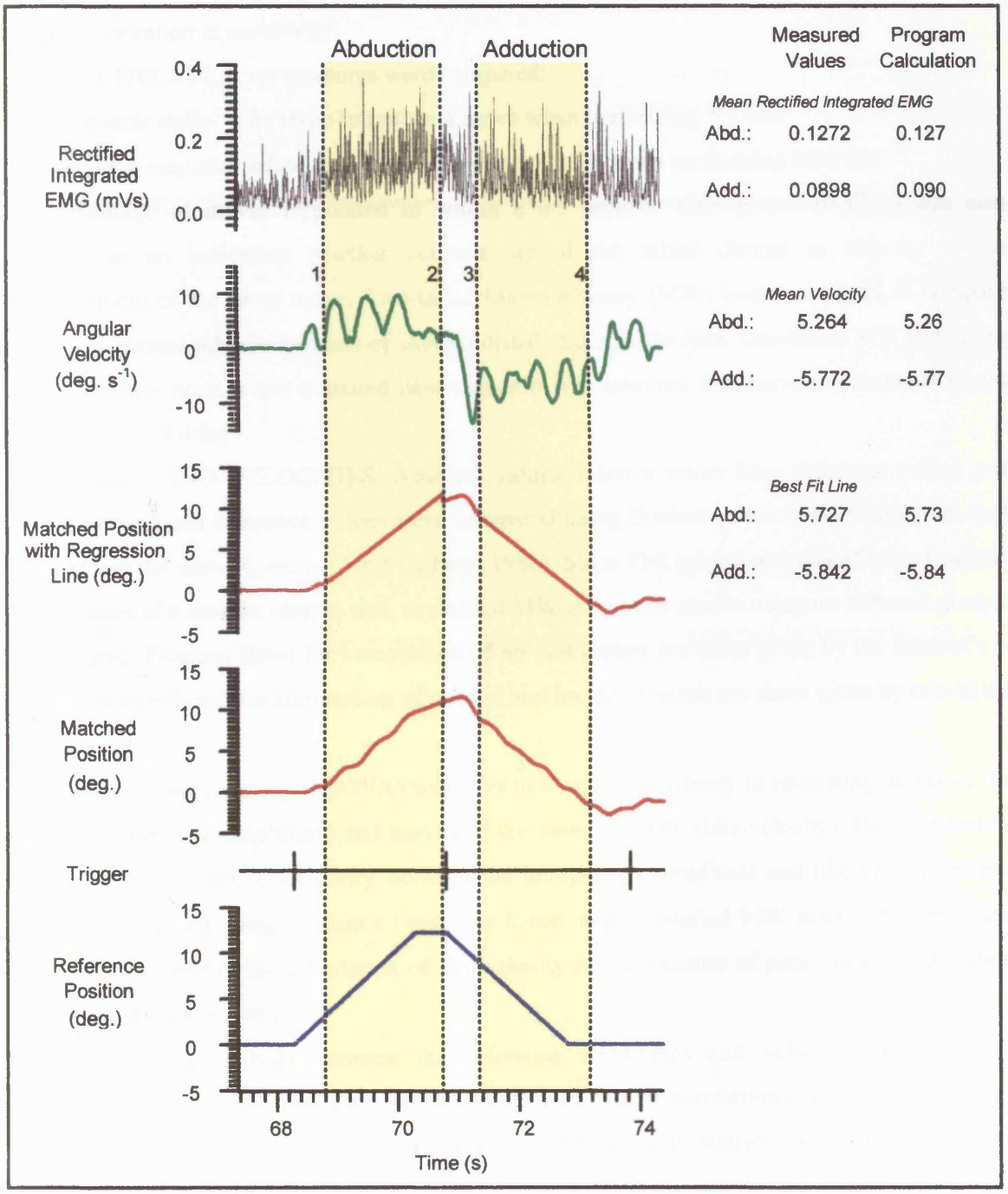
B

	Values Calculated By The Program
AMPLITUDE	
Abduction = HI - ST = 11.56 °	11.6°
Adduction = LO - HI = -14.29 °	-14.3°
Undershoot = LO - END = -1.70 °	-1.70°
Error = END - ST = -1.04 °	-1.04°
DELAYS	
Abduction = ST - Trig.1 = 0.18 °	0.18°
Adduction = HI - Trig.2 = 0.24 °	0.24°
End = LO - (Trig.2 + Amp./ Vel.) = 0.67 °	0.67°

EMG Levels

The mean of the rectified integrated EMG level recorded in the ipsilateral hand (the same side as the motor) during the period of the movement was used to give an indication of the level of contraction. The value was normalised using the background level of contraction measured during a period of muscle inactivity.

Figure 3.3. Illustrates the positioning of cursors and subsequent calculation of VELOCITIES AND MEAN RECTIFIED EMG LEVELS for a single move during a movement match test.
The cursors 1 to 4 define the analysis windows (shaded area).The program uses the regions to calculate the mean rectified integrated EMG, mean velocity, as well as the best fit line and correlation coefficient of the points over the range specified. The program draws in the regression line to give the user an idea as to whether a suitable range has been selected. The calculations derived by the program (in left hand column) were also checked using the 'cursor regions' option in Spike 2® for Windows (in right hand column).



IV. DISPLAY AND OUTPUT

After analysing all the movements, the data was copied as tab delimited text into a text file which could then be pasted and copied into a suitable spreadsheet.

3.2.10. Data Analysis

DETECTION TESTS: Tests of movement sense were all analysed separately since IR and CR tests measure sense of movement following an audible cue, whereas Dn and MM tests measure sense of movement in the absence of a cue. Two-tailed Mann-Whitney (MW) tests were used to compare data sets in normal subjects. One-tailed Mann-Whitney (MW) tests were used to compare normal and impaired hands (either PNI or anaesthesia), since it was assumed that nerve impairments would cause a deterioration in sensitivity.

RESPONSE DELAYS: Two measures were compared:

Visual response delay: time taken to initiate a move when performing VT test

Proprioceptive response delay: time taken to initiate a move when performing MM test

The percentage of moves responded to within a 0.5 seconds time period (0.5^{cutoff}) was also calculated as an indication whether subjects sensed the initial change in velocity at the commencement of the ramp move. Two-tailed Mann-Whitney (MW) tests were used to compare data sets in normal subjects because of skewed distributions in the data. One-tailed MW tests were used to compare normal and impaired hands since it was assumed that nerve impairments would result in extended delays.

AMPLITUDES AND VELOCITIES: Absolute values, relative errors from reference values and absolute errors from reference values were compared using Student's t-test (two-sample, unequal variance) and the more rigorous C-test (Scheer, 1986). Since PNI subject and anaesthetised subject data sets were of a smaller sample size, two-tailed MW tests were used to compare different groups. Unless stated, P-values listed for comparison of normal groups are those given by the Student's t-test and P-values listed for comparison of normal and impaired hands are those given by two-tailed MW tests.

Analysis of variance (ANOVA) was used to look at consistency in estimating moves of the same amplitude (like-amplitude) and moves of the same velocity (like-velocity). Because results indicated that there was consistency between the groups, like amplitude and like velocity *means* were also compared using Student's t-test, the C-test and two-tailed MW tests. 1.5° amplitude moves were omitted in the calculation of like-velocity means because of poor velocity estimation during these smaller moves.

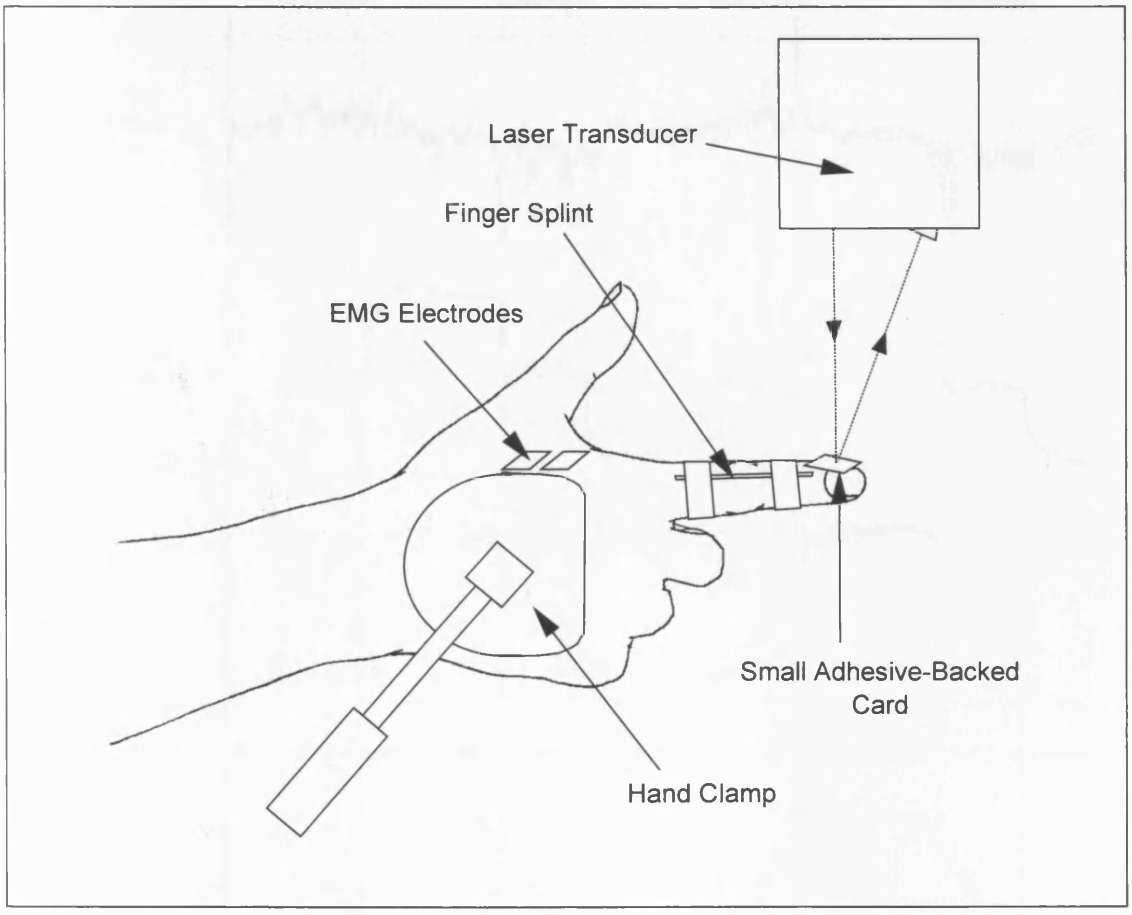
Regression analysis between the reference amplitudes and velocities and matched amplitudes and velocities from each subject was used to see if correlations between the two sets were significant. Gradients and intercepts of pooled data from all subjects were used to look for patterns in grading movements.

3.3. Tremor Recordings (Pulsatile Output)

3.3.1. Equipment

An optical displacement laser transducer with a range of 10mm and a resolution of 3μm (Micro-epsilon® Messtechnik, LD 1605-20) was used to record tremor in the thumb, index and little fingers (figure 3.4.). The laser was shone onto a small white adhesive backed card (15mm x 15mm) attached to the digit. The reading was taken at a distance of 57mm from the joint centre of rotation, at which position, displacement in millimetres approximates to the angle in degrees for small angles. Digits where splinted across interphalangeal joints. The hand and arm were firmly clamped using a hand clamp and upper limb stabilisation apparatus (section 2.2., pp 58-61). EMG recordings were identical to those used in section 3.2.2. (figure 3.1.).

Figure 3.4. **Set up for recording tremor using a laser transducer.** The digit is splinted using a light wooden splint. The laser beam is reflected off a card positioned so that displacement is recorded at 57mm from the joint centre. The hand is clamped for the duration of recording.



3.3.2. Protocols

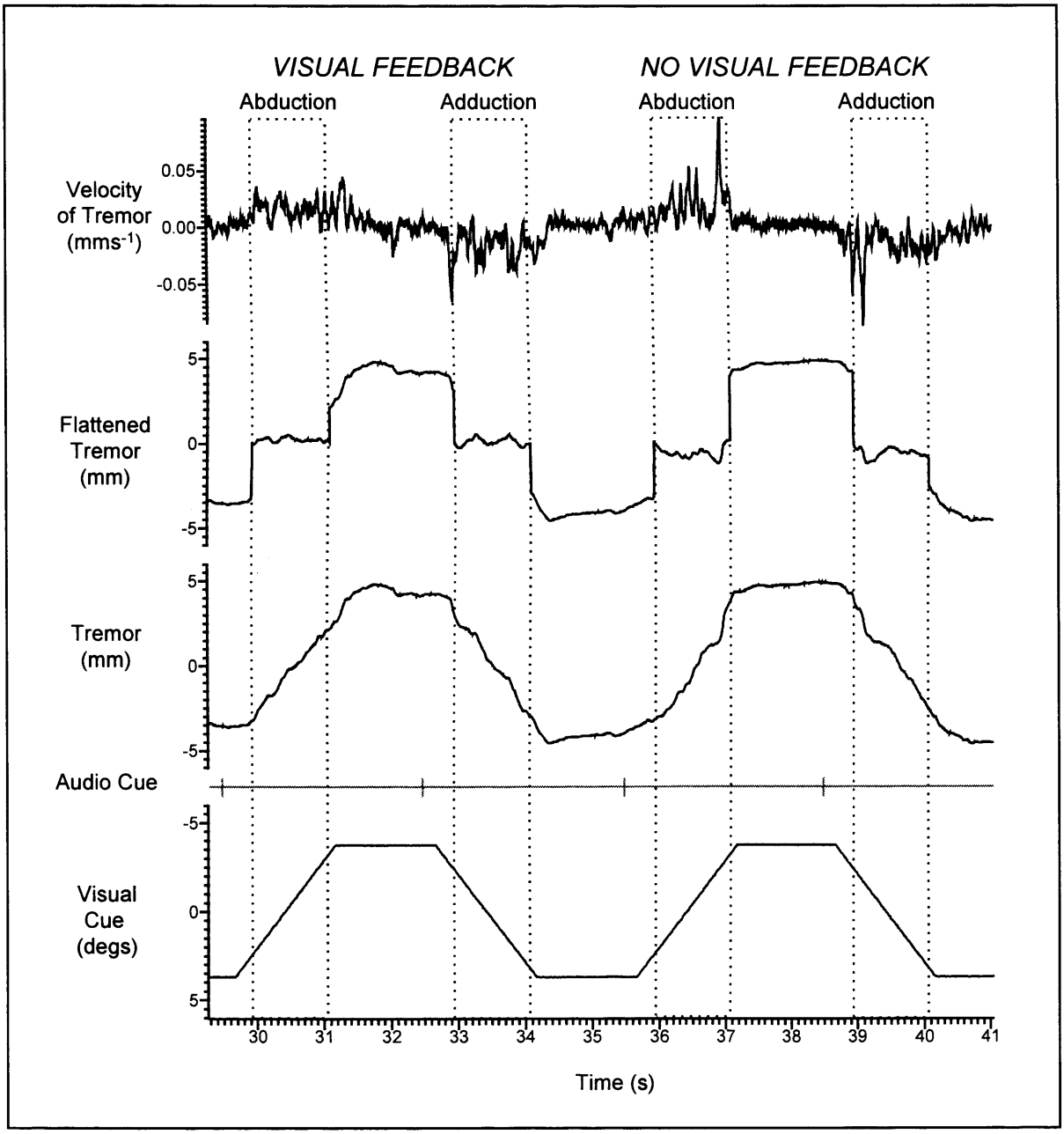
MEASURING PULSATILE OUTPUT EVIDENT DURING SLOW MOVEMENTS

When measuring the tremor associated with slow movements, or kinetic tremor, the same protocol was used for throughout. Feedback of the digit position was provided through the visual

display (see section 2.3., p61). The subject tracked a target created using the sequence language of Spike 2.21 for Windows® equivalent to alternate, 7.5° amplitude and $5°s^{-1}$ velocity, abduction and adduction moves, separated by a 1.5 second hold period (figure 3.5.).

The subjects had to perform an abduction move and adduction move when provided with visual feedback and then repeat the same sequence with the visual display covered. An audible cue was provided 300 milliseconds before each abduction and adduction move. A one second period was analysed from each move using spectral analysis. The subject repeated this process for a period of 3 minutes, resulting in 58 sweeps in all.

Figure 3.5. Sequence of events occurring when the recording of pulsatile output during movement. Abduction and adduction movements (here in the index finger) are performed with and without visual feedback The script flattens the finger position trace over the analysed region by subtracting the linear regression. An audio cue precedes each movement by 300ms.



A number of different trials were performed:-

1. Comparisons of Intrinsic Muscles: Kinetic tremor was recorded using the three previously mentioned models, i.e. abduction: adduction movements of the thumb, index and little fingers in 31, 35 and 10 normal subjects, respectively. All of the three models were predominantly controlled by intrinsic hand musculature. EMG recordings from AbPB, 1DI and AbDM, respectively were also recorded for each model.

2. Comparisons of Intrinsic and Extrinsic Musculature: Kinetic tremor was also measured during index finger flexion: extension moves in 10 subjects. Surface EMG recordings were taken from the EDC muscle. This allowed comparison of tremor generated predominantly through intrinsic musculature during index finger abduction-adduction movements with tremor generated primarily through extrinsic musculature during index finger flexion: extension movements.

3. Comparison to Tremor During Rest and Position Holding: Tremor was recorded with the digit at rest for one minute (60 sweeps). The tremor was also recorded during position holding in which the subject held the digit in an abducted position, 10° away from the resting position. Visual feedback, used to maintain the digit position was provided for 40 seconds and then removed for 40 seconds. This process was repeated resulting in 160 sweeps. The sample sizes for the thumb, index and little fingers were 28, 28 and 10 subjects, respectively, during position holding and 29, 35 and 10 subjects, respectively, during rest.

4. Tremor During Conditions Of An Elastic Load:

- *Extension: Flexion vs Abduction: Adduction:* Kinetic tremor was recorded during index abduction: adduction moves (n=10) and flexion: extension moves (n=7) under an elastic load of 2.5N applied using a spring with a constant of $25Nm^{-1}$. The spring applied forces against abduction and extension movement, respectively.
- *Varying the Spring Constant:* To investigate the oscillations evident during isometric contraction against an elastic load, a similar protocol was used to that of McAuley, Rothwell and Marsden (1997). Ten subjects had to perform ten isometric contractions for 6-second periods against an elastic load using the 1DI muscle action. 15-second rest gaps were allowed between each contraction to prevent fatigue. Each trial was performed at three different force levels (2.5N, 5N and 10N) and a strain gauge was used to set the applied load. Two different springs were used with spring constants of 25 Nm^{-1} and 45 Nm^{-1} instead of a single elastic band as used by McAuley, Rothwell and Marsden (1997). The longitudinal resonating frequencies of the springs were 23.5 Hz and 29.0 Hz, respectively.

  Using a spring of $25Nm^{-1}$ and a load of 2.5N, the same protocol was also used to compare tremor during an index finger extension task (n=7).

4. Tremor Subsequent to PNI: When possible, tremor during rest, position holding and slow movement was measured in 5 thumbs, following median nerve injury, and 12 index and 9 little fingers subsequent to ulnar nerve injury. Protocols were identical to those in 1. and 4.

5. Tremor Subsequent to CTS: Tremor during rest, position holding and movement was measured in 16 thumbs of CTS patients.

3.3.3. Recording Configuration

Data was recorded using a 1401+ digital interface operating under Spike2.21 for Windows® software (Cambridge Electronic Design). Sample rates used during tremor recording were:

1. Sequencer Output (visual display) 64 Hz
2. Tremor 512 Hz
3. EMG recordings 512 Hz

When measuring tremor under elastic load conditions, the sample rates for tremor and EMG channels were 2048 Hz. Data files were stored using 100MB zip disks® (Iomega Ltd, UK).

3.3.4. Tremor Analysis

A program was written in the script language of Spike 2.21 for Windows® to automate the calculation and analysis of power spectra of tremor and EMG data. An outline of the script follows:

I. TIDYING UP AND SETTING VARIABLES

Previous memory channels, cursors and toolbars were removed. Global variables and arrays were defined and set.

II. NEW CHANNELS

- ***Velocity:*** A velocity trace was derived from the smoothed position data using a simple 5 point linear filter. This trace was for display purposes only and not for deriving power spectra.
- ***Rectified EMG:*** A rectified EMG trace was created from the raw EMG data for treatment by spectral analysis. The DC level of the raw EMG data was first subtracted from the signal.

III. CALCULATION OF POWER SPECTRA

Tremor: Each ramp move was inspected before analysis. Cursors were set to ensure that the best part of the movement was analysed. The velocity trace was displayed to aid the process. The tremor trace within the accepted range was flattened by subtracting the regression line of the data from the trace (figure 3.5.). Each 1-second trace was analysed using a finite fast Fourier transformation of the block of 512 points, subsequent to the application of a raised cosine (Hanning) window. This

resulted in a frequency resolution of 1 Hz. Derivation of velocity and acceleration power spectra of tremor were performed in the frequency domain by multiplying the data by a weighting function (i.e. freq.^{2} in radians). This eliminates the attenuation of high or low frequencies when creating velocity and acceleration channels in the time domain by digital filtering techniques. The resulting spectra were then averaged together.

EMG: Raw and rectified EMG traces were also analysed using finite fast Fourier transformation of the block of 512 points following Hanning window application. Because of high electrical resistance of the glabrous skin of the hand, a 50Hz peak was often evident in the power spectra of the raw EMG. The peak was removed by setting the 3 bin values of 49, 50 and 51 Hz to the mean of the values of 48 and 52 Hz.

IV. STATISTICAL ANALYSIS

The script calculates a number of general statistical measures such as measures of area under the spectral curve, averages, measures of the spread of the data and significant peaks (for a review of statistical measures relating to the power spectrum, see Lindström and Petersén, 1983). Definitions and worked examples of these measures are given in appendix 3.1.

Measures of Area

Spectral moments of order are equal to the area under the spectral curve after the spectrum has been multiplied by the frequency raised to a specific power called the *order of moment.* The first and second moments of order are used to calculate further measures such as standard deviation. Higher spectral moments of order emphasise higher frequencies in the power spectrum. The root mean square of the power spectrum has been used extensively in EMG analysis as a measure of the contraction level of muscle.

1) Spectral moment of order zero (M_0) = Area under the spectral curve

2) First spectral moment of order (M_1) = Area under the spectral curve after multiplication by the frequency

3) Second spectral moment of order (M_2) = Area under the spectral curve after multiplication by the frequency^2

4) Root Mean Square (RMS) = $\sqrt{M_0}$

Averages

The mean, median and mode values are described as mean power frequency, median frequency and peak frequency, respectively:

5) Mean Power Frequency (MPF) = $\frac{M_1}{M_0}$

6) Median Frequency (MedF) = the frequency at which cumulative power $= \frac{\sum P}{2}$

7) Peak Frequency (PkF)

8) Power at Peak Frequency (P@PkF)

Measures of Spread

Standard deviation is a well-known measure of spread, but has the disadvantage of being very sensitive to high frequency noise since the second spectral moment of order is used in its derivation. An alternative measure is to use equivalent bandwidth, which only uses low moments of order in its calculation (Lindström and Petersén, 1983). The bandwidth of the maximum peak at half power is a more accurate estimate of peak frequency amplitude than maximum power (Timmer, Lauk & Deuschl, 1996). Linear interpolation was used to improve the accuracy of the calculation.

9) Standard Deviation (Stdev) = $\sqrt{\frac{M_2}{M_0} - \left(\frac{M_1^2}{M_0^2}\right)}$

10) *Equivalent Bandwidth (EquBW)* $= \frac{M_0^2}{\sum P^2(f)}$

11) *Minimum* $\frac{1}{2}$ *Power @ Peak Frequency (P1/2_lo)*

12) *Maximum* $\frac{1}{2}$ *Power @ Peak Frequency (P1/2_hi)*

13) *Power between P1/2_lo and P1/2_hi* (P@P1/2)

= Cumulative Power @ P1/2_hi - Cumulative Power @ P1/2_lo

Significant Peaks

The program also contained a procedure to find significant peaks in the power spectra. The following procedure is fully described by Timmer, Lauk & Deuschl (1996):

1) The Kolmogorov-Smirnov test (KS-test) was applied to test whether the power spectrum is significantly different from a white noise signal. The cumulative spectrum is normalised and drawn along with a white noise signal (a straight line). Confidence limits of P=0.05 are added. If the cumulative spectrum falls within the confidence limits then it does not significantly differ from a white noise signal and no further analysis can be carried out.
2) All positive peaks were located by calculating all negative points of inflection.
3) The confidence interval for the spectral curve is given by:-

$$\left(\frac{\nu S(f_k)}{\chi^2_{1-\alpha/2}(\nu)}, \frac{\nu S(f_k)}{\chi^2_{\alpha/2}(\nu)}\right)$$

where: $S(f_k)$ = spectral curve

α = confidence level = 0.025

$\chi^2 = \chi^2$ distribution

ν = degrees of freedom = 2 . no of averages used to calculate the spectrum

The equation is used to find the values of the upper confidence limit for the spectrum (figure 3.6.).

Figure 3.6. Power spectrum of an acceleration record with the upper confidence level shown. Significant peaks are given in table 3.3.

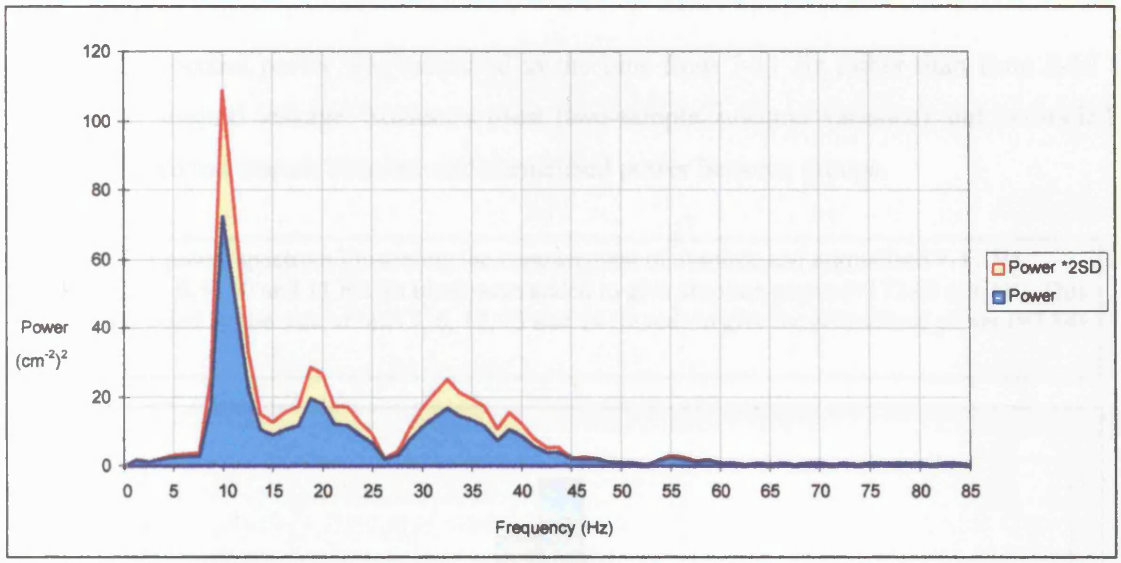


Table 3.3. The frequency and amplitude of the five largest significant peaks in the power spectrum shown in figure 3.6.

Peak	*Frequency*	*Power at Peak*	*Power* $(cm^{-2})^2$
P1	10 Hz	P@P1	72.31
P2	18 Hz	P@P2	19.27
P3	32 Hz	P@P3	16.87
P4	55 Hz	P@P4	2.33
P5	65 Hz	P@P5	0.85

4) A peak is deemed significant if the peak power is greater than the upper confidence level either side of the peak. The program, therefore examines the frequencies above and below each point of inflection to see if the upper confidence limit values fall below the peak amplitude. It then records the five largest significant peaks and their amplitudes. Figure 3.6. shows the power spectrum of an acceleration record with the upper confidence level. The five largest significant peaks for the graph are displayed in table 3.3 along with the amplitude of the peaks. Two different analysis ranges were examined, from 0-20Hz and from 0-70Hz.

V. DISPLAY AND OUTPUT

After all the spectra have been calculated and analysed, the script sets up a menu which copies frequency and power values of the spectra and results of the statistical analysis in to tab-delimited text files ready for copying into an appropriate spreadsheet.

3.3.5. Data Analysis

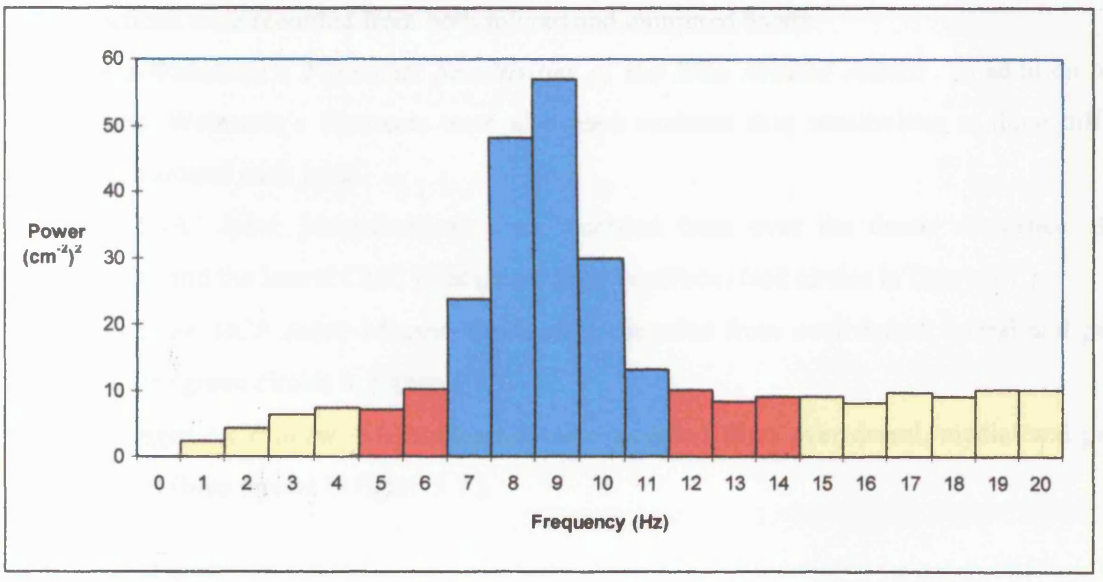
In addition to the analysis performed by the script, two indexes were generated to give an indication of the absolute and normalised power in the range of 7-11 Hz (figure 3.7.):

- **Absolute Power** = Total power in the bins of 7, 8, 9, 10 & 11 Hz

- **Normalised Power** $= \dfrac{\text{Total power in the bins of 7, 8, 9, 10 \& 11 Hz}}{\text{Total power in the bins of 5, 6, 12, 13 \&14 Hz}}$

The spectral power was measured in the bins from 7-11 Hz rather than from 8-10 Hz to account for spectral leakage. Student's t-test (two-sample, unequal variance) and two-tailed MW tests were used to compare absolute and normalised power between groups.

Figure 3.7. A power spectrum illustrating the measurement of absolute and normalised 7-11 Hz tremor. Bins 7, 8, 9, 10 and 11 Hz (in blue) were added to give absolute power (=172.03 $(cm^{-2})^2$). This value was divided by the sum of bins 5, 6, 12, 13 and 14 (in red) to give the normalised power (=3.84).



3.5. Clinical Assessment

Standard clinical tests were performed throughout by the same hand surgeon on PNI and CTS subjects. The tests were also performed on subjects prior to and immediately following local anaesthetic nerve block:

MOTOR TESTS

1) ***Manual MRC Testing:*** For the actions of the AbPB, AbDM and 1DI muscles.
2) ***Grip Strength:*** Recorded on left and right hands using a Jamar® hand dynamometer (Preston, USA) in positions II and III.

SENSORY TESTS

1) ***Semmes-Weinstein's Filaments Sensitivities at the Digit Tips:*** A series of 5 filaments applying forces of 0.7, 2, 20, 40 and 2000 mN (NeuroCommunication Research Laboratories, USA) were used to assess cutaneous sensitivities of the radial and ulnar aspects of the digit tips (yellow circles on figure 3.7).

Two Point Discrimination: Static 2-PD was also determined for the radial and ulnar aspects of each digit tip (Mackinnon-Dellon Disk-criminator®, USA).

ADDITIONAL SENSORIMOTOR TESTS

Two tests were performed to provide more relevant measures of skin and muscle innervation relating to proprioceptive reinnervation:

1) ***Maximal Voluntary Contraction:*** The best out of three maximal abduction contractions of thumb, index and little finger was used as a measure of the strength of AbPB, 1DI and AbDM muscles on normal and injured sides (see section 2.4., p62). The force was applied to the dynamometer just proximal to the nail bed. In the case of PNI subjects, maximal voluntary contractions were recorded from both injured and uninjured hands

2) ***Semmes-Weinstein's Filaments Sensitivities of the Skin Around Joints:*** In addition to the digit tips, Weinstein's filaments were also used evaluate skin sensitivities at three different positions around each joint:

- *Thumb CMC Joint:* Measurements were recorded from over the thenar eminence, dorsal webspace, and the lateral CMC joint (anatomical snuffbox) (red circles in figure 3.7.).
- *Index Finger MCP Joint:* Measurements were recorded from over dorsal, lateral and palmer MCP Joint (green circles in figure 3.7.).
- *Little Finger MCP Joint:* Measurements were recorded from over dorsal, medial and palmer MCP Joint (blue circles in figure 3.7.).

OTHER TESTS

Moberg's Pick-Up Test: A range of small objects of different size, shape and texture were placed in a tray, i.e. pencil, eraser, paper clip, elastic band, screw, rubber ball, plastic tweezers and pencil sharpener. After familiarising themselves with the feel of the objects, the subjects had to identify and pick up specified objects as rapidly as possible.

Skin Temperature: DermaTherm perfusion monitors (Sharn[inc.], USA) were used to measure the skin temperature along the lateral borders of the thumb, index finger and little finger, and over the thenar and hypothenar eminences.

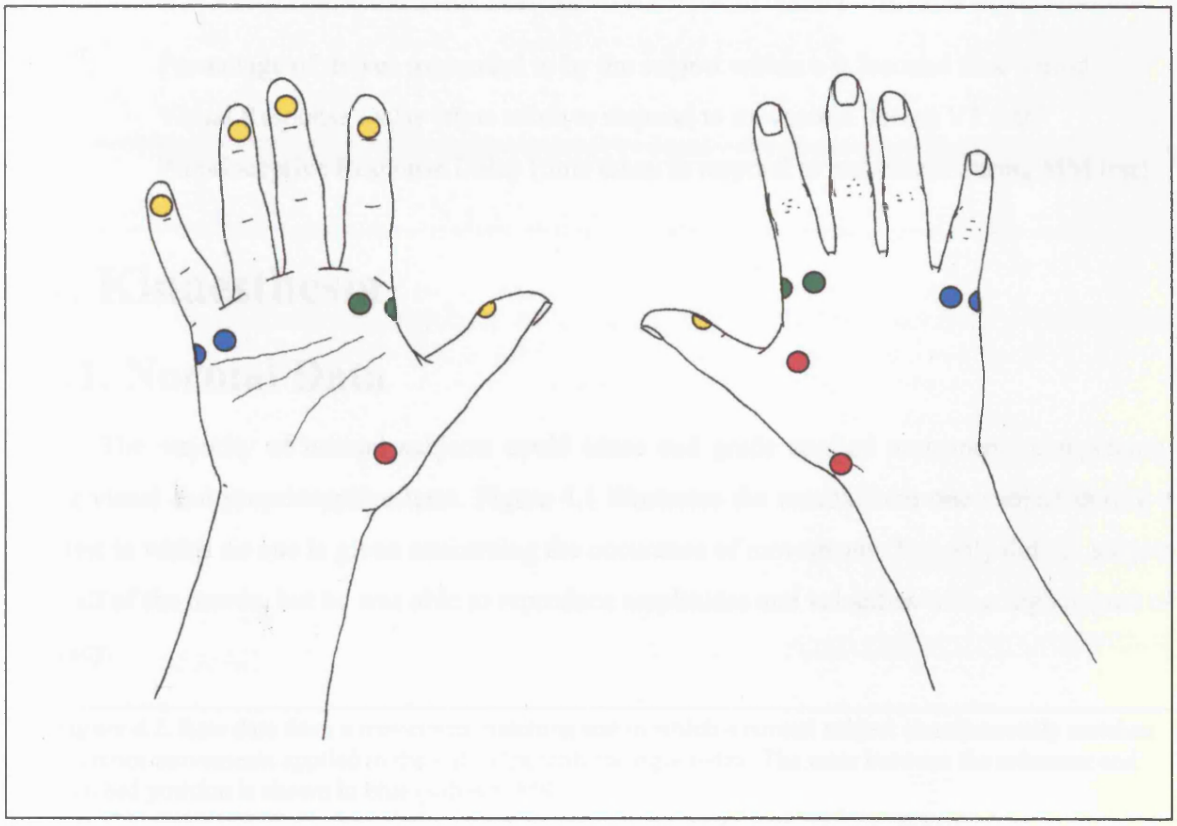
Injury Related: A number of different signs were examined in PNI and CTS subjects, including:

- **Tinel's Sign:** mechanosensitivity resulting from percussion of the nerve trunk distal to the site of the lesion.

- **Froment's sign:** a test for paralysis of the AP muscle. If positive, the subject will flex the terminal phalanx of the thumb on a unidigital pulp-to-pulp grip, for example when gripping and pulling a single sheet of paper.
- **Phalen's test:** shows compression of the median nerve at the carpal tunnel. On holding wrists in maximum flexion, subjects will begin to experience parasthesias.
- **Allen test:** used to decide whether the main arterial supply is from the radial or ulnar artery.

General symptoms: descriptions of the hand, i.e. site of injury, scarring and wasting. Also, documenting tingling, numbness, paraesthesias, pain, night waking, radiation, tenderness.

Figure 3.7. Points at which cutaneous sensitivities were evaluated using Weinstein's filament tests. Yellow markers, i.e. the digit tips are tested as a standard with an emphasis on tactile function. The other points are more representative of skin sensibility relating to kinaesthesia.
They are colour coded accordingly: model 1: thumb = red; model 2: little finger = blue; and model 3: index finger = green.



CHAPTER 4: RESULTS

To simplify the presentation of data, much of the results are summarised in tabular and graphical form displayed in the text. Full details of the results are given in a series of appendices presented in the form of Excel® spreadsheets (Microsoft Corporation, USA: see floppy disks).

ABREVIATIONS USED

VT: Visual Tracking

VR: Visual Repeat

IR: Ipsilateral Repeat

CR: Contralateral Repeat

MM: Movement Matching

0.5^{cutoff}: Percentage of moves responded to by the subject within a 0.5second time period

VRD: Visual Response Delay (time taken to respond to movement during VT test)

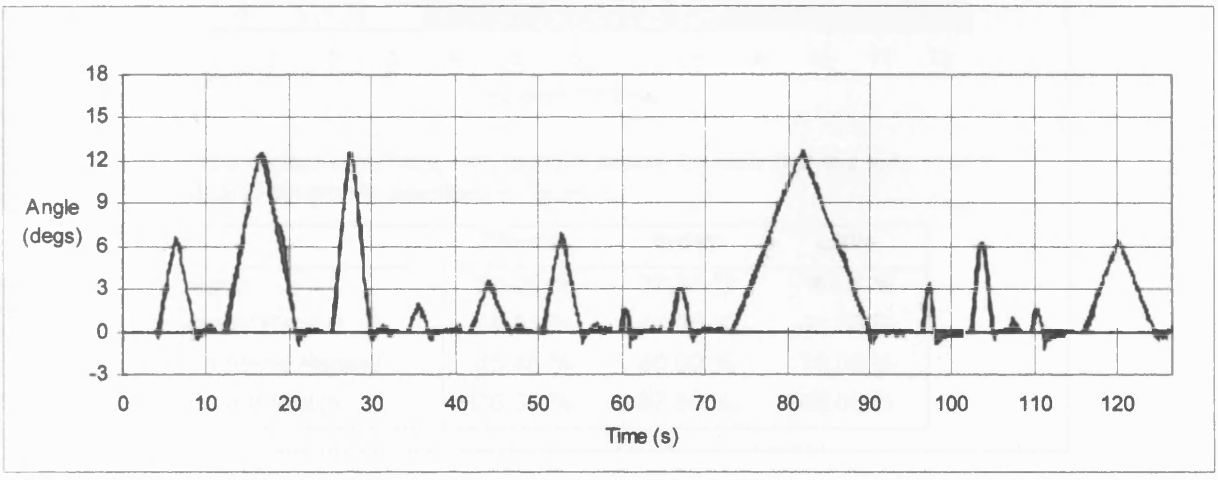
PRD: Proprioceptive Response Delay (time taken to respond to movement during MM test)

4.1. Kinaesthesia

4.1.1. Normal Data

The majority of normal subjects could sense and grade applied movements competently during visual and proprioceptive tests. Figure 4.1 illustrates the results from one subject during a MM test in which no cue is given concerning the occurence of movements. Not only did the subject sense all of the moves, but he was able to reproduce amplitudes and velocities with a high degree of accuracy.

Figure 4.1. Raw data from a movement matching test in which a normal subject simultaneously matches reference movements applied to the left index with the right index. The error between the reference and matched position is shown in blue (subject: MK).



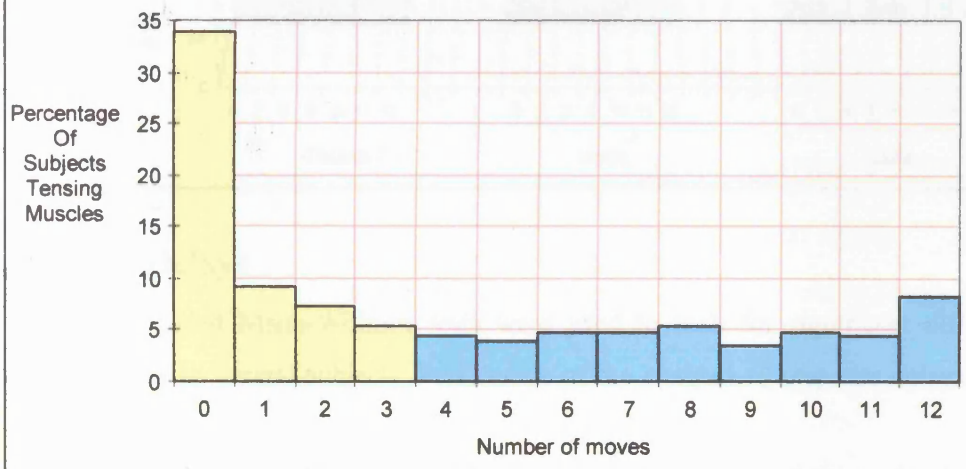
4.1.1.1. Levels Of Contraction

Although subjects were instructed to remain relaxed throughout the application of movements, varying degrees of EMG activity were encountered during each test and for each digit. To determine when muscles were tensed, mean rectified EMG patterns recorded from intrinsic muscles under anaesthesia were used to assess the degree of fluctuations in background noise resulting from movement artifact. Although the ratio of EMG during passive movement: EMG at the zero position fluctuated during the different amplitudes of movement, the value never exceeded 1.8. As a result, a ratio of 1.8 of mean rectified EMG activity: background EMG activity provided a safe cutoff point for distinguishing between tensed and relaxed muscles.

To simplify analysis, subjects were divided into two groups and were classified as 'relaxed' if three or less moves were above the threshold (yellow bins in figure 4.2.A.), and 'tensed' if more than three moves were above threshold (blue bins in figure 4.2.A.). Using such criteria indicated that there was wide variation in levels of contraction throughout all the tests. Figure 4.2.B. lists the percentage of subjects tensing muscles during the four proprioceptive tests in each of the three digits, according to the criteria. There was variation between both tests and digits, but subjects were generally most relaxed during detection tests.

Figure 4.2.

A. The number of moves during which subjects tensed muscles using data from all four proprioceptive tests (Dn, IR, CR & MM) and for all three digits. Criteria used to decide whether muscles were tensed or relaxed is given in the text. The even spread of data over the histogram indicates that the extent of muscle tensing is highly variable. The yellow bins represent subjects classified as 'relaxed' for further analysis, whereas the blue bins represent subjects with 'tensed' muscles.



B. The percentage of subjects with muscles tensed, for each digit and test, according to the criteria described in figure A..

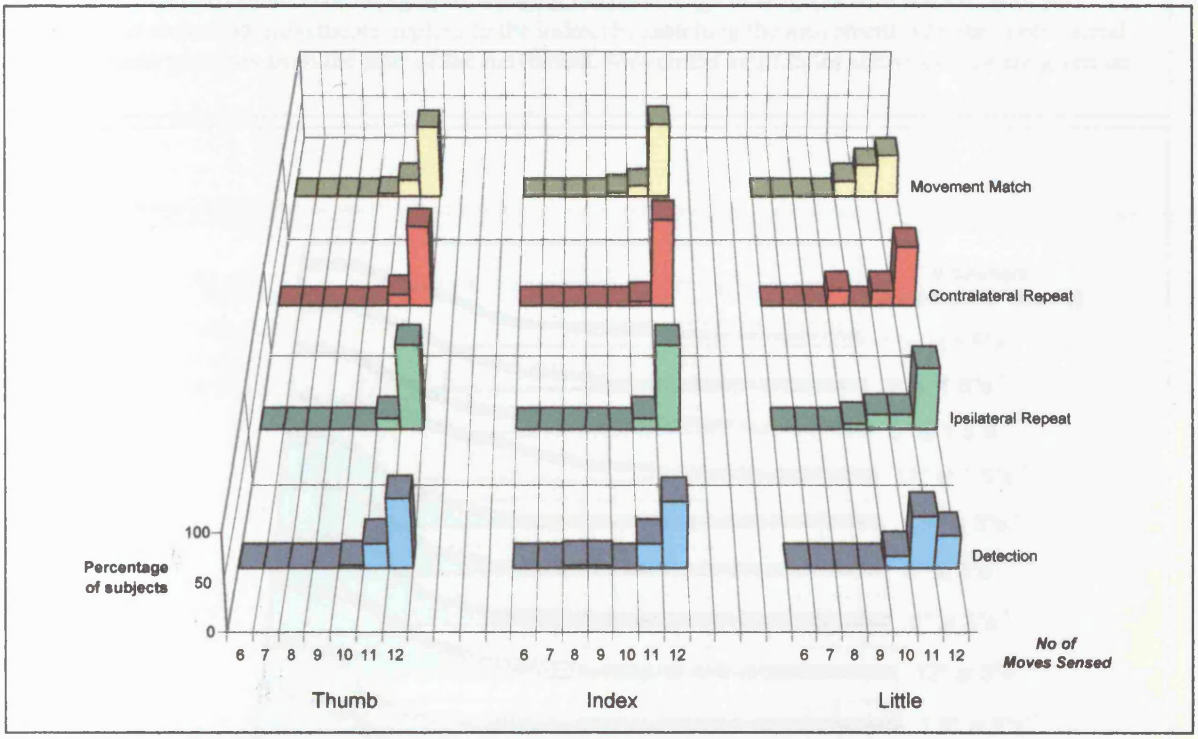
Test	Thumb	Index	Little
Detection	31.25 %	33.33 %	16.67 %
Ipsilateral Repeat	48.21 %	44.90 %	41.38 %
Contralateral Repeat	45.45 %	40.00 %	10.00 %
Movement Match	36.54 %	67.50 %	40.00 %

4.1.1.2. Sensing Movement

Detection Of Movement

Two tailed Mann-Whitney tests were used to look for significant differences between levels of detection in normal subjects. Over 75% of the moves were sensed regardless of the test or digit used (figure 4.3.). Both the thumb and index were significantly more sensitive in detecting movements than the little finger during Dn and MM tests ($\alpha<0.05$). There were no other significant differences between either tests, digits, dominant and non-dominant hands, abduction and adduction moves or tensed and relaxed digits (full details are given in appendix 4.1.).

Figure 4.3. The number of moves sensed by each digit during the four tests of kinaesthesia. Each bin represents the percentage of subjects sensing the particular number of moves specified along the x-axis.



Response Delays

Two tailed Mann-Whitney tests were used to look for significant differences between response delay in normal subjects. Full details of the analysis of response delays can be found in appendix 4.2.

Patterns: The proprioceptive delay and velocity of the movement were closely related (see the inverted cumulative 3-D graph in figure 4.4.) and consequently, *mean delays* of moves of the same velocity (or 'like-velocity' moves) were analysed in addition to individual moves. The percentage of moves responded to within a 0.5 second period (0.5^{cutoff}) was calculated as an estimate of how often subjects sensed the initial change in velocity.

Differences between Digits: Proprioceptive reaction times were much slower in the little finger compared to the index finger and thumb. For example, all mean delays were significantly prolonged

in the little finger compared to either the thumb or index ($\alpha<0.05$) (table 4.1.). These differences were also evident when comparing 0.5^{cutoff} (table 4.2 and appendix 4.2, table 4.4., sheet 3).

Proprioceptive response delays were also significantly greater during slow adduction moves in the thumb compared to the index finger adduction moves. For example, average proprioceptive response delays (± standard error) for $1.5°s^{-1}$ adduction moves were 0.478s (± 0.061) in the index finger compared to 0.716s (± 0.089) in the thumb ($\alpha=0.037$) (table 4.1.).

There were also considerable differences in VRD between digits (table 4.1.), however, differences in VRD were much smaller in magnitude compared to differences in PRD indicating that motor control only has a minor contribution to the differences in PRD between the digits.

Figure 4.4. Inverted cumulative 3-D graphs showing the percentage of subjects who HAVE NOT yet responded to abduction movements applied to the index (by matching the movement with the contralateral finger) as time proceeds from the start of the movement. Movement amplitudes and velocities are given on the right.

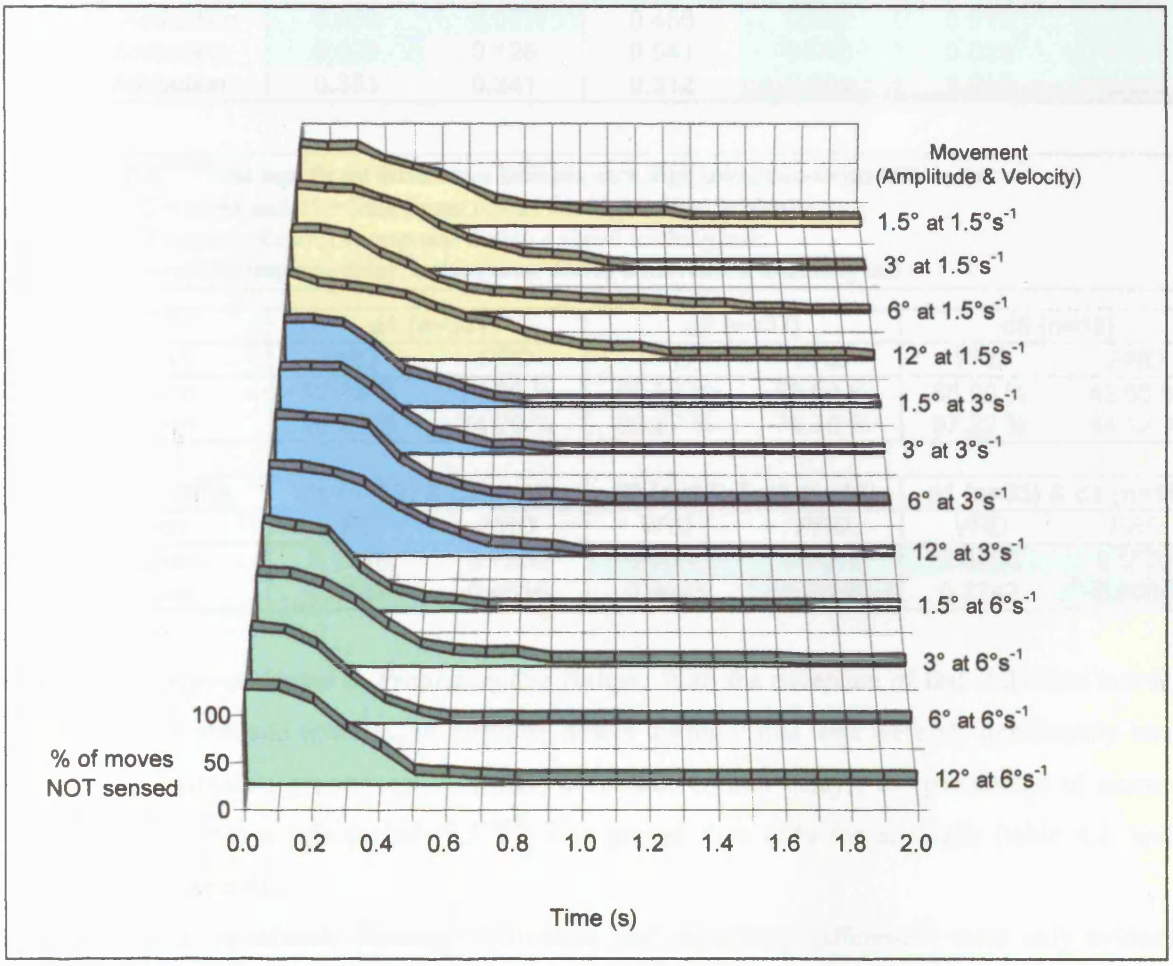


Table 4.1. **Mean response** delays for each velocity of movement and significant differences between each digit using two-tailed MW tests ($\alpha<0.05$ is highlighted in blue).
d1= thumb, d2 = index and d5 = little finger.
VRD = Visual response delay, i.e. response during a visual tracking task.
PRD = Proprioceptive response delay, i.e. response during a movement matching task.

Mean Delays	**d1 (n=33)**		**d2 (n=37)**		**d5 (n=15)**	
Velocity : Direction	*VRD (sec)*	*PRD (sec)*	*VRD (sec)*	*PRD (sec)*	*VRD (sec)*	*PRD (sec)*
1.5°/s : Abduction	0.298	0.738	0.299	0.612	0.396	1.003
3°/s : Abduction	0.267	0.399	0.298	0.432	0.349	0.603
6°/s : Abduction	0.279	0.310	0.247	0.331	0.334	0.458
1.5°/s : Adduction	0.132	0.716	0.050	0.478	0.145	1.168
3°/s : Adduction	0.078	0.393	0.036	0.283	0.101	0.641
6°/s : Adduction	0.064	0.264	0.034	0.230	0.097	0.412
Significant Diffs.	**d1 (n=33) & d2(n=37)**		**d2 (n=37) & d5 (n=15)**		**d1 (n=33) & d5 (n=15)**	
Velocity : Direction	*VRD (sec)*	*PRD (sec)*	*VRD (sec)*	*PRD (sec)*	*VRD (sec)*	*PRD (sec)*
1.5°/s : Abduction	0.484	0.512	0.025	0.001	0.081	0.000
3°/s : Abduction	0.397	0.181	0.019	0.000	0.074	0.001
6°/s : Abduction	0.545	0.352	0.009	0.006	0.004	0.015
1.5°/s : Adduction	0.038	0.037	0.456	0.002	0.013	0.000
3°/s : Adduction	0.026	0.126	0.541	0.000	0.009	0.000
6°/s : Adduction	0.381	0.341	0.312	0.001	0.049	0.000

Table 4.2. **0.5^{cutoff}** and significant differences between each digit using two-tailed MW tests.
d1= thumb, d2 = index and d5 = little finger ($\alpha<0.05$ is highlighted in blue).
VRD = Visual response delay, i.e. response during a visual tracking task.
PRD = Proprioceptive response delay, i.e. response during a movement matching task.

0.5^{cutoff}	**d1 (n=33)**		**d2 (n=37)**		**d5 (n=15)**	
Direction	*VRD*	*PRD*	*VRD*	*PRD*	*VRD*	*PRD*
Abduction	92.68 %	71.90 %	93.92 %	68.80 %	85.00 %	42.65 %
Adduction	96.21 %	74.29 %	98.87 %	79.70 %	97.22 %	44.12 %
Significant Diffs.	**d1 (n=33) & d2(n=37)**		**d2 (n=37) & d5 (n=15)**		**d1 (n=33) & d5 (n=15)**	
Direction	*VRD*	*PRD*	*VRD*	*PRD*	*VRD*	*PRD*
Abduction	0.9718	0.7209	0.0000	0.0000	0.0000	0.0000
Adduction	0.2167	0.4616	0.8938	0.0000	0.3742	0.0000

Differences between Visual & Proprioceptive Delays: With the exception of fast abduction moves ($6°s^{-1}$) in the thumb and little finger, response delays during visual tests were all significantly less than during equivalent proprioceptive tests. For visual reaction delays, the percentage of moves responded to within a 0.5s period (0.5^{cutoff}) was greater than 85% for all digits (table 4.2. and appendix 4.2., sheet 4).

Differences due to Muscle Tensing: Consistent and significant differences were only evident during adduction movements in the index finger, where longer delays were present in relaxed muscle. Mean delays and 0.5^{cutoff} for $1.5°s^{-1}$ and $3°s^{-1}$ moves were both significantly different ($\alpha<0.05$) (appendix 4.2., sheet 5).

Differences between Dominant and Non-Dominant hands: There were no significant differences between dominant and non-dominant hands (appendix 4.2, sheet 6).

Differences between Abduction and Adduction Moves: In the index finger, means of $1.5°s^{-1}$, $3°s^{-1}$ and $6°s^{-1}$ moves were all significantly less during adduction moves ($\alpha<0.05$) (appendix 4.2, sheet 7). In the thumb, only means of $3°s^{-1}$ adduction moves were significantly less ($\alpha<0.05$). However, visual and proprioceptive response delays for adduction moves demonstrated that many adduction moves were predicted. For example, for visual delays in the index, 42.3% of subjects began moves before time zero and 83.1% before 0.2s. For proprioceptive delays in the index, 11.4% began moves before time zero and 29.1% before 0.2s (appendix 4.2, sheet 8).

4.1.1.3. Grading Movement

Results are listed fully in appendices 4.3. and 4.4. (Excel® worksheets). Unless stated, significant differences listed are for the Student t-test (two-sample, unequal variance).

Matching Amplitudes

Overview: Amplitude matching was more accurate during visual tracking (VT) compared to repeat tests (VR, IR and CR). This was particularly true for smaller amplitudes that were consistently overestimated during repeat tests. Amplitude matching during MM was more accurate for small amplitudes compared to repeat tests but slightly worse for larger amplitudes. The thumb and index were both consistently better at matching amplitudes compared to the little finger.

VISUAL TRACKING

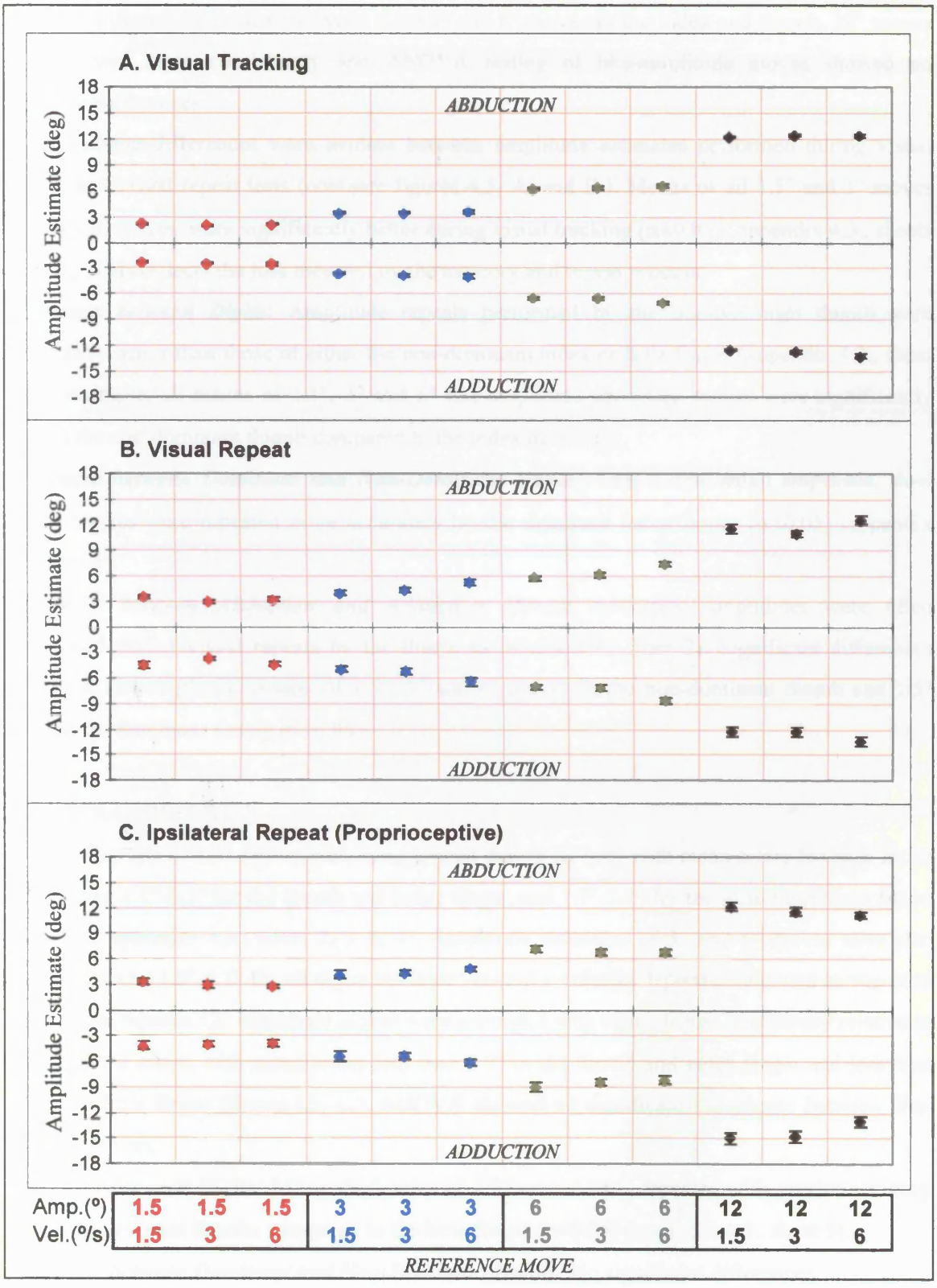
Patterns: Amplitude matching during visual tracking was highly accurate and consistent. For example, mean errors of like-amplitude abduction moves were less than 0.7° in the index and thumb and 1.1° in the little finger (figure 4.5.A.) (appendix 4.3., sheets 2, 3 & 4).

Differences between Digits: There were small but significant differences between the thumb and index finger when matching movements of 12° amplitude because of a propensity for the thumb to slightly overshoot movements. Amplitude matching in the little finger was consistently poorer than the thumb and index, particularly during smaller abduction moves (appendix 4.3., sheet 5).

Differences between Dominant and Non-Dominant Hands: There were infrequent differences present in all three digits, because of more accurate tracking by the dominant hand (appendix 4.3., sheet 2, 3 & 4).

Differences between Abduction and Adduction Moves: There was a consistent overshooting at the end of adduction moves, although the mean overshoots never exceeded more than 1° (appendix 4.3., sheet 2, 3 & 4).

Figure 4.5 Ability to reproduce amplitudes during ipsilateral tests in the non-dominant thumb. Mean estimates +/- standard errors of abduction moves are displayed above the axis, and of adduction moves below the axis. **A.** shows amplitude matching during visual tracking (VT), **B.** is during visual repeat (VR) and **C.** during a proprioceptive ipsilateral repeat test (IR).
The amplitude and velocity of each move for all three graphs are displayed along the bottom. Like-amplitude moves are colour coded (1.5° in red, 3° in blue, 6° in green and 12° in black).



VISUAL REPEAT

Patterns: During both abduction and adduction moves, in the thumb and index finger, a similar pattern emerged for repeating amplitudes (figure 4.5. B.). Moves of 1.5° amplitude were exaggerated by between 1.5-3.5° regardless of the applied velocity, but during 3° and 6° amplitude moves, there was a velocity dependent increase in error. ANOVA testing of like-amplitude moves showed significant differences between most 3° and 6° moves in the index and thumb. 12° moves were repeated more consistently and ANOVA testing of like-amplitude moves showed no significant differences.

Striking differences were evident between amplitude estimates performed during visual tracking and visual repeat tests (compare figures 4.5. A. and B.). Means of all 1.5° and 3° moves and many 6° moves, were significantly better during visual tracking ($\alpha<0.05$) (appendix 4.3., sheets 2, 3 & 4). This reflects the loss incurred by the memory and repeat process.

Differences between Digits: Amplitude repeats performed by the non-dominant thumb were significantly better than those of either the non-dominant index or little finger (appendix 4.3., sheet 5). For example, all means of 1.5°, 3° and 6° like-amplitude abduction moves were significantly better in the non-dominant thumb compared to the index ($\alpha<0.01$).

Differences between Dominant and Non-Dominant Hands: Only a few small amplitude, slow velocity moves were repeated more accurately by the dominant index finger ($\alpha<0.05$) (appendix 4.3., sheet 4).

Differences between Abduction and Adduction Moves: Adduction amplitudes were often exaggerated during visual repeats by the thumb (appendix 4.3., sheet 2). Significant differences existed for like-amplitude means of 1.5°, 3° and 6° moves in the non-dominant thumb and 1.5° moves in the dominant thumb ($\alpha<0.05$).

IPSILATERAL REPEAT

Patterns: Repeats of 1.5° moves were exaggerated during IR tests with mean errors for each move varying from 1.1°-3.5° for the thumb and index finger, and 1.7°-5.7° for the little finger (see figure 4.5. C. and appendix 4.3., sheet 2, 3 & 4). Amplitude estimates of 3° and 6° moves were also overestimated by 1.0°-4.1° for all digits but there was not a velocity dependent element as was seen during visual repeats. 12° amplitude moves were estimated with some degree of accuracy relative to the size of the move, with mean errors less than 2.7° in the thumb and index finger and less than 3.3° in the little finger (figure 4.5. C.). ANOVA showed no significant differences between like-amplitude moves.

Differences between Digits: Mean amplitudes of 1.5° moves were repeated with greater accuracy by the non-dominant thumbs compared to the little finger ($\alpha<0.05$) (appendix 4.3., sheet 5).

Differences between Dominant and Non-Dominant Hands: No significant differences.

Differences due to Contraction Level: No significant differences.

Differences between Abduction and Adduction Moves: Amplitude estimates were significantly larger during adduction movements in the thumb (see figure 4.5. C. and appendix 4.3., sheet 2). There were significant differences for all mean amplitudes in non-dominant thumbs ($\alpha<0.01$) and means of 3° and 12° moves in the dominant thumb ($\alpha< 0.05$) (appendix 4.3., sheet 3).

CONTRALATERAL REPEATS

Patterns: Estimates of amplitudes performed during ipsilateral and contralateral proprioceptive repeats were very similar (compare figures 4.5. C. and 4.6. A.) as indicated by the absence of significant differences between mean amplitudes for all digits (appendix 4.3., sheets 2, 3, & 4). The majority of like-amplitude moves performed during CR tests showed no significant differences when tested by ANOVA, although there were some exceptions (eg. during 3° abduction and adduction moves in the index finger).

Differences between Digits: Means of 1.5°, 3° and 6° like-amplitude abduction and adduction repeats were significantly larger in the little finger compared to the thumb and index (appendix 4.3., sheets 2, 3, & 4).

Differences due to Contraction Level: No significant differences.

Differences between Abduction and Adduction Moves: No significant differences.

MOVEMENT MATCH

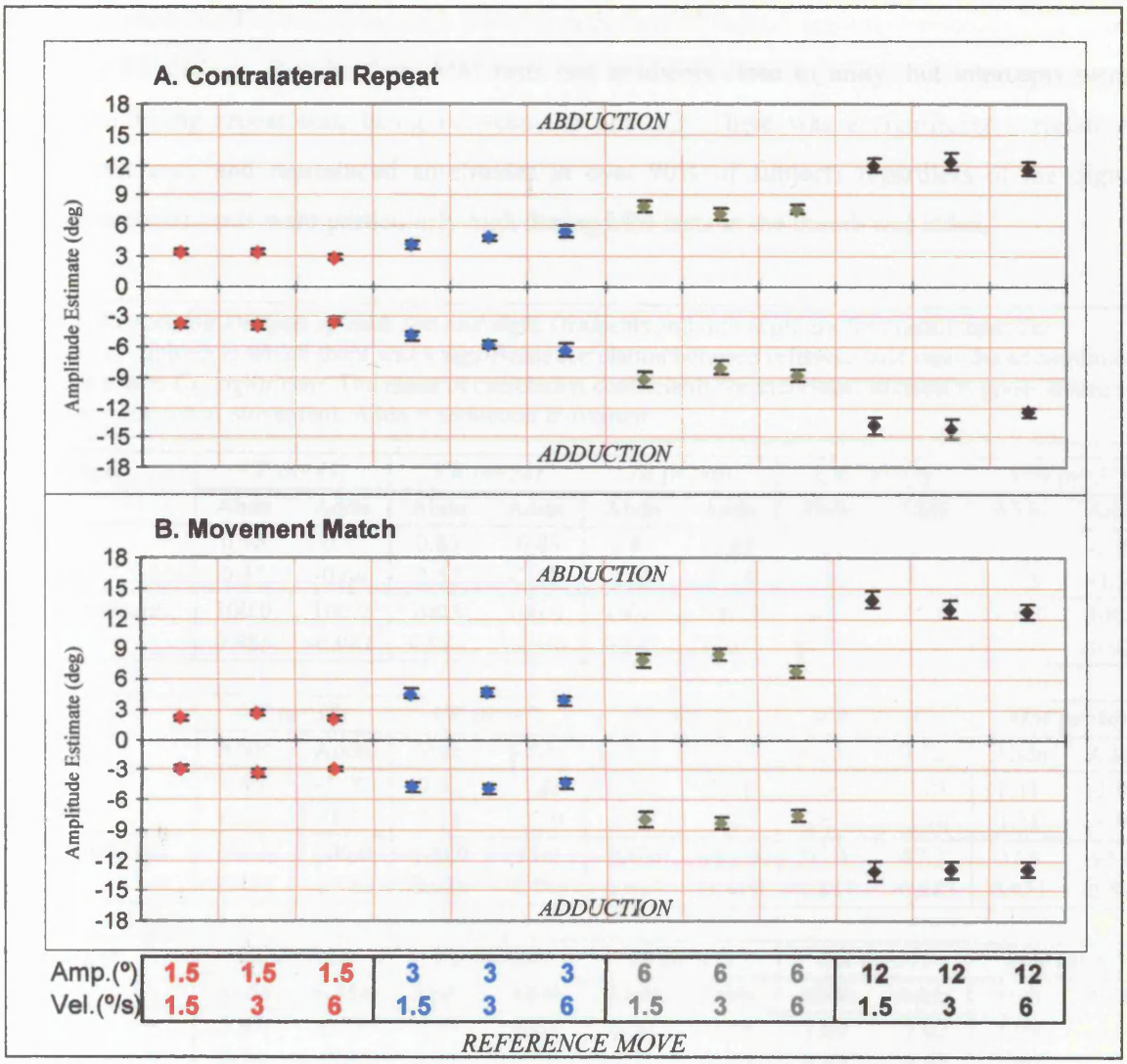
Patterns: Amplitudes were matched consistently during MM test for different velocities. ANOVA analysis yielded no significant differences between like-amplitude moves for any digit (figure 4.6. B. and appendix 4.3., sheets 2, 3, & 4). Mean errors, however, increased with amplitude. Small amplitudes were estimated with greater accuracy during the MM test compared to CR tests. This meant there was a significant difference between CR tests and MM tests, for many 1.5° and 3° abduction and adduction moves in all digits ($\alpha<0.05$).

Differences between Digits: No significant differences

Differences due to Contraction Level: No significant differences.

Differences between Abduction and Adduction Moves: $1.5°\&6°s^{-1}$ moves were significantly smaller when matched during thumb abduction moves of MM tests ($\alpha<0.05$).

Figure 4.6. Ability to reproduce amplitudes during proprioceptive tests in the thumb. Mean estimates +/- standard errors of abduction moves are displayed above the axis, and of adduction moves below the axis. **A.** shows amplitude matching during a contralateral repeat test (CR), and **B.** during movement matching (MM). The amplitude and velocity of each move for all three graphs are displayed along the bottom. Like-amplitude moves are colour coded (1.5° in red, 3° in blue, 6° in green and 12° in black).



REGRESSION ANALYSIS

Regression analysis of data from each individual subjects demonstrated that there was a high correlation between reference and reproduced amplitudes (Table 4.3.). Regardless of the test, the number of subjects in which there was a significant correlation between reference and reproduced amplitudes was over 94% for the thumb and index, and over 75% for the little finger.

Visual Tracking: Reference and reproduced amplitudes were significantly correlated in 100% of subjects regardless of the digit. Gradients were close to unity and intercepts close to zero in both abduction and adduction directions. Mean correlation coefficients were all over 0.97.

Repeats: During repeat tests in the thumb and index, gradients were between 0.8 and 1.0 and intercepts between 1.8° and 3.1° because of the overestimation of smaller moves. Intercepts were even higher during repeat tests by the little finger.

There was a significant correlation between reference and reproduced amplitudes in over 94% of subjects for the thumb and index, and over 75% of subjects for the little finger, however, mean correlation coefficients were much lower than during VT tests.

Movement Matching: Results from MM tests had gradients close to unity, but intercepts were lower than during repeat test, being between 0.8 and 2.3. There was a significant correlation between reference and reproduced amplitudes in over 90% of subjects regardless of the digit. Correlation coefficients were particularly high during MM tests in the thumb and index.

Table 4.3. Regression analysis of each test and digit. Gradients and intercepts are for pooled data. The proportion of subjects in which there was a significant correlation between reference and reproduced amplitudes is given in row *% CC significant.* The mean of correlation coefficients for individual subjects is given in *Mean CC.* Abdn = abduction movement, Addn = adduction movement.

Index Finger	***VT (n=42)***		***VR (n=38)***		***IR (n=46)***		***CR. (n=39)***		***MM (n=37)***	
	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn
Gradient	0.96	-0.97	0.83	-0.89	0.87	-0.88	0.86	-0.93	1.06	-0.97
Intercept	0.37	-0.64	2.52	-2.68	2.41	-3.08	2.91	-3.04	0.78	-1.37
% CC significant	100.0	100.0	100.0	100.0	100.0	100.0	100.0	97.5	100.0	100.0
Mean CC	0.986	-0.981	0.923	-0.910	0.893	-0.881	0.877	-0.876	0.941	-0.922

Thumb	***VT (n=39)***		***VR (n=37)***		***IR (n=41)***		***CR (n=36)***		***MM (n=36)***	
	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn
Gradient	0.99	-1.00	0.82	-0.82	0.82	-0.96	0.91	-1.01	1.11	-1.02
Intercept	0.40	-0.72	2.18	-2.79	1.89	-2.62	2.67	-3.10	1.21	-1.99
% CC significant	100.0	100.0	100.0	94.9	100.0	100.0	97.3	97.3	97.5	95.0
Mean CC	0.986	-0.983	0.935	-0.896	0.917	-0.910	0.887	-0.883	0.921	-0.898

Little Finger	***VT (n=18)***		***VR (n=20)***		***IR (n=21)***		***CR (n=17)***		***MM (n=17)***	
	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn
Gradient	0.97	-0.98	0.92	-0.88	0.96	-1.06	1.03	-1.02	1.09	-1.01
Intercept	0.78	-0.98	2.39	-3.06	3.47	-4.74	4.02	-4.97	1.60	-2.31
% CC significant	100.0	100.0	100.0	100.0	86.2	79.3	80.0	75.0	95.0	90.0
Mean CC	0.975	-0.970	0.925	-0.901	0.778	-0.801	0.778	-0.769	0.874	-0.843

Matching Velocities

Overview: Velocity matching was not as accurate or as consistent as amplitude matching. Velocities were accurately matched during VT tests, but there were consistent differences as the amplitude of the move varied. Velocities matched during proprioceptive tests were matched less accurately than during VT tests but amplitude had a minimal effect on matching. Slow movements and adduction movement velocity estimates were particularly large during repeat tests. Large amplitude moves were accurately matched during MM tests.

VISUAL TRACKING

Patterns: With the exception of some 1.5° amplitude moves, target velocities were matched with a high degree of accuracy (figure 4.7. A.). ANOVA testing yielded significant differences for $1.5°s^{-1}$ and $3°s^{-1}$ like-velocity moves ($\alpha<0.05$) although the majority of these differences were not significant if 1.5° amplitude moves were omitted from the analysis (appendix 4.4. sheets 2, 3 & 4).

Differences between Digits: The thumb and little finger tended to exaggerate velocities compared to the index finger particularly during adduction moves in the dominant hand. There were many significant differences between the index and the other two digits for all velocities of abduction and adduction moves ($\alpha<0.05$) (appendix 4.4. sheet 5).

Differences between Dominant and Non-Dominant Hands: There were significant differences between means of $3°s^{-1}$ and $6°s^{-1}$ like-velocity adduction moves in the thumb, $1.5°s^{-1}$ and $6°s^{-1}$ adduction moves in the index finger, and $6°s^{-1}$ abduction moves in the little finger (where $\alpha<0.05$). In all cases, estimates were larger in non-dominant hands (appendix 4.4. sheets 2, 3 & 4).

Differences between Abduction and Adduction Moves: There were occasional significant differences between abduction and adduction moves in the thumb and little finger, but frequently, adduction movements were significantly exaggerated in the index ($\alpha<0.05$) (appendix 4.4. sheets 2, 3 & 4).

VISUAL REPEATS

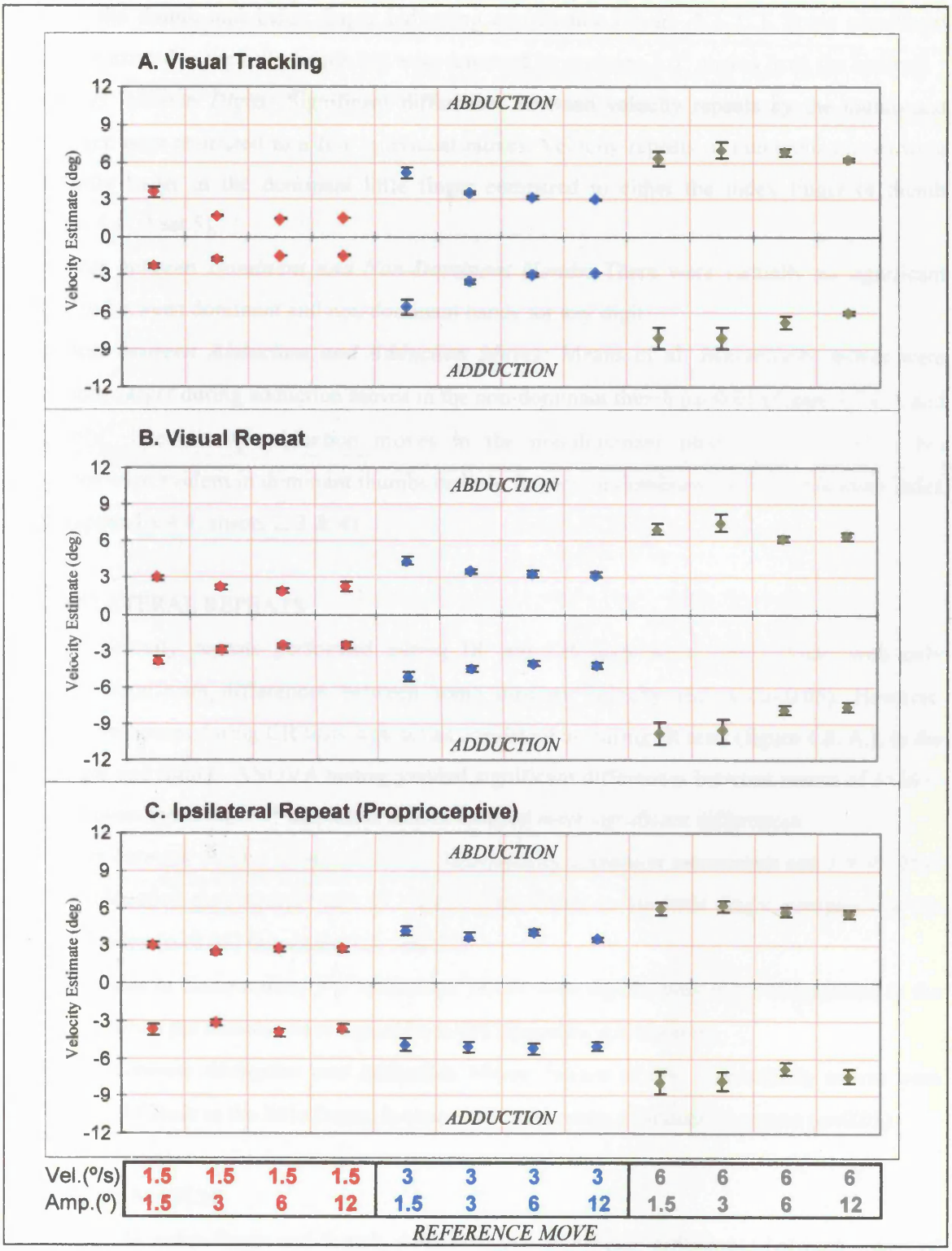
Patterns: Slow abduction moves and most adduction moves tended to be overestimated during VR tests, yielding significant differences between equivalent moves in VT and VR tests ($\alpha<0.05$) (figure 4.7. B.). As for VT tests, some 1.5° amplitude moves also tended to be overestimated during VR tests, as indicated by some significant differences between means of like-velocity moves. The siginificant differences were not present if 1.5° amplitude moves were omitted from the analysis (appendix 4.4. sheets 2, 3 & 4).

Differences between Digits: $1.5°s^{-1}$ and $3°s^{-1}$ abduction moves were significantly larger in the non-dominant thumb moves compared to the index finger. The little finger consistently overestimated velocities yielding many significant differences between like-velocity moves in the little finger and the thumb or index (appendix 4.4. sheet 5).

Differences between Dominant and Non-Dominant Hands: No significant differences.

Differences between Abduction and Adduction Moves: The thumb significantly overestimated adduction repeats as was evident from both the Student's t-test and the C-test ($\alpha<0.05$). Some adduction moves in the little finger were also overestimated during adduction ($\alpha<0.05$) (appendix 4.4. sheets 2, 3 & 4).

Figure 4.7. Ability to reproduce velocities during ipsilateral tests in the non-dominant thumb. Mean estimates +/- standard errors of abduction moves are displayed above the axis, and of adduction moves below the axis. **A.** shows velocity matching during visual tracking (VT), **B.** during visual repeat (VR) and **C.** during a proprioceptive ipsilateral repeat test (IR).
The amplitude and velocity of each move for all three graphs are displayed along the bottom. Like-velocity moves are colour coded (1.5° in red, 3° in blue and 6° in green).



IPSILATERAL REPEATS

Patterns: Slow moves were significantly exaggerated during IR tests, compared to VR tests (compare figure 4.7. B. and C.), whereas fast moves were estimated with greater accuracy (appendix 4.4. sheets 2, 3 & 4). ANOVA showed no differences between means of like-velocity moves in the thumb and index finger indicating consistency (figure 4.7. C.). Some significant differences existed in the little finger, but were removed by omitting 1.5° moves from the analysis.

Differences between Digits: Significant differences between velocity repeats by the thumb and index finger were restricted to a few individual moves. Velocity repeats of numerous moves were significantly larger in the dominant little finger compared to either the index finger or thumb (appendix 4.4. sheet 5).

Differences between Dominant and Non-Dominant Hands: There were virtually no significant differences between dominant and non-dominant hands for any digit.

Differences between Abduction and Adduction Moves: Means of all like-velocity moves were significantly larger during adduction moves in the non-dominant thumb ($\alpha<0.01$)(figure 4.7.C.), and during $6°s^{-1}$ like-velocity adduction moves in the non-dominant little finger ($\alpha<0.01$). No differences were evident in dominant thumbs or little fingers, or dominant and non-dominant index fingers (appendix 4.4. sheets 2, 3 & 4).

CONTRALATERAL REPEATS

Patterns: Velocity repeats performed during IR and CR tests were very similar, with only occasional significant differences between some medium velocity moves ($\alpha<0.05$). However, estimating velocities during CR tests was not as consistent as during IR tests (figure 4.8. A.). In the index finger and thumb, ANOVA testing yielded significant differences between means of 3° like-velocity moves. Omitting 1.5° amplitude moves reduced most significant differences.

Differences between Digits: Means of $1.5°s^{-1}$ like-velocity abduction movements and $1.5°s^{-1}$, $3°s^{-1}$ and $6°s^{-1}$ adduction movements were all significantly larger in the little finger compared to the thumb and index ($\alpha<0.05$) (appendix 4.4. sheet 5).

Differences due to Contraction: $3°s^{-1}$ abduction moves were significantly more exaggerated in the index finger when the muscles were tensed ($\alpha<0.05$) (appendix 4.4. sheet 6).

Differences between Abduction and Adduction Moves: Means of $6°s^{-1}$ like-velocity moves were significantly different in the little finger, because of exaggeration of adduction moves ($\alpha<0.05$).

MOVEMENT MATCH

Patterns: In the index finger and thumb, ANOVA gave significant differences between means of like-velocity moves for the majority of $1.5°s^{-1}$ and $3°s^{-1}$ moves during MM tests (figure 4.8. B.). Omitting 1.5° amplitude moves from the analysis reduced significant differences for the majority of moves. Generally, MM test results were more accurate than repeat tests, especially for slower

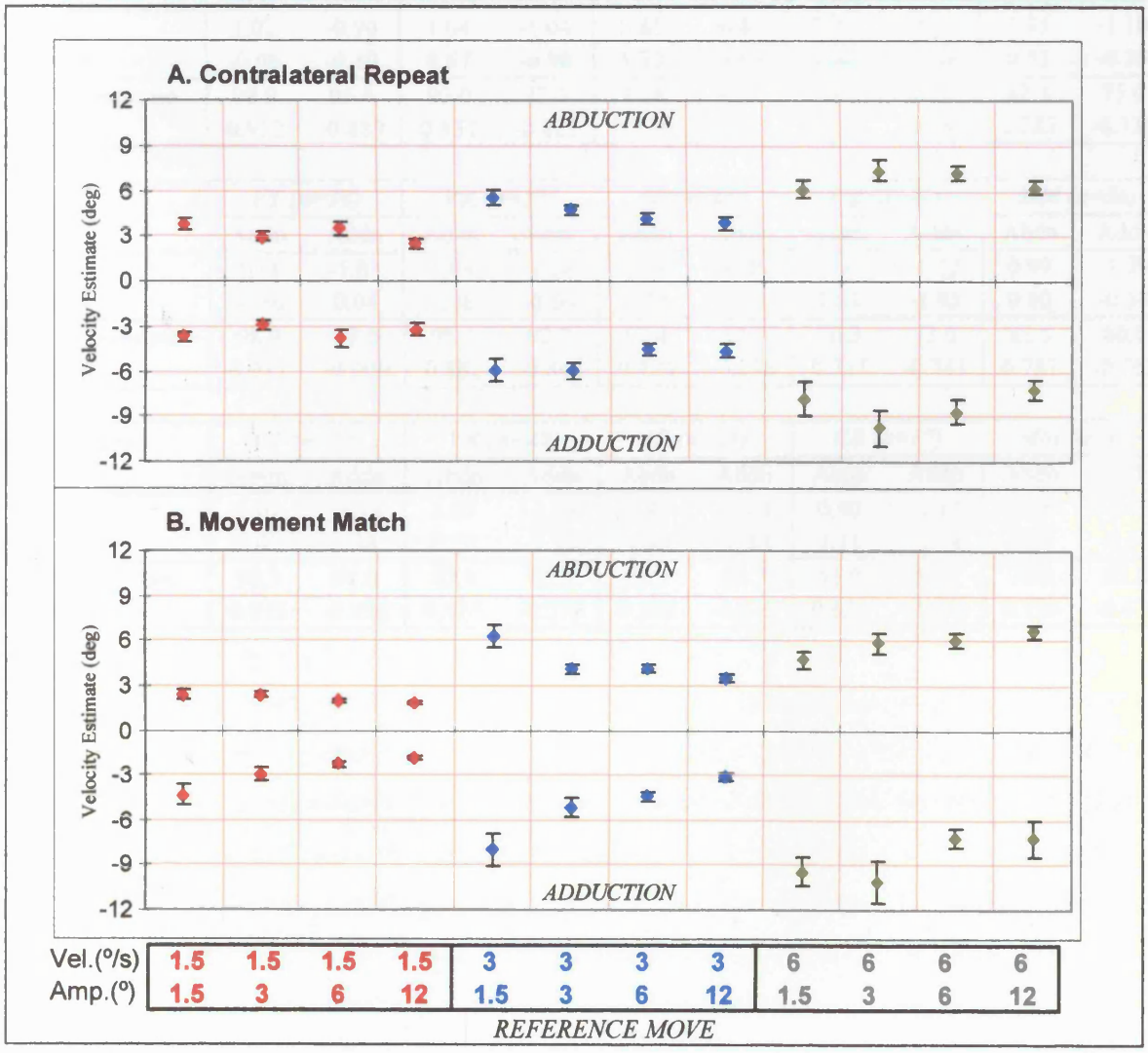
moves. This resulted in significant differences between CR and MM test estimates for the majority of $1.5°s^{-1}$ like-velocity means and some $3°s^{-1}$ like-velocity means (appendix 4.4. sheets 2, 3 & 4).

Differences between Digits: There were significant differences in $1.5°s^{-1}$ adduction estimates in the index finger and thumb due to overestimation by the thumb (α=0.05) (appendix 4.4. sheet 5).

Differences due to Contraction: There were significant differences between relaxed and tensed index fingers, for the majority of $1.5°s^{-1}$ and $3°s^{-1}$ adduction moves during MM (α<0.01), due to exaggerated velocity estimates when muscles were tensed. In the little finger, significant differences were restricted to two individual adduction moves ($3°\&6°s^{-1}$ and $6°\&6°s^{-1}$, where α<0.05) (appendix 4.4. sheet 6).

Differences between Abduction and Adduction Moves: Some fast and small move estimates were significantly exaggerated during adduction in the thumb and index.

Figure 4.8. Ability to reproduce velocities during proprioceptive tests in the thumb. Mean estimates +/- standard errors of abduction moves are displayed above the axis, and of adduction moves below the axis. **A.** shows velocity matching during a contralateral repeat test (CR), **B.** is during movement matching (MM). The amplitude and velocity of each move for all three graphs are displayed along the bottom. Like-velocity moves are colour coded (1.5° in red, 3° in blue and 6° in green).



REGRESSION ANALYSIS

The correlation between reference and reproduced velocities for individual subjects was not as significant as during amplitude matching, although the number of subjects in which there was a significant correlation was over 80% during visual tests, and over 50% during proprioceptive tests (table 4.4.). Results were improved by omitting 1.5° amplitude moves from the analysis.

Reference and reproduced velocities were most closely related during visual tests (VT and VR) and MM tests. Intercepts were much higher during proprioceptive repeat tests (IR and CR), especially during adduction moves. This was due to overestimation of slow velocities.

Table 4.4. Regression analysis of each test and digit. Gradients and intercepts are for pooled data. The proportion of subjects in which there was a significant correlation between reference and reproduced amplitudes is given in row *% CC significant.* The mean of correlation coefficients for individual subjects is given in *Mean CC.* Abdn = abduction movement, Addn = adduction movement.
1.5° moves were not included in the analysis.

Index Finger	***VT (n=42)***		***VR (n=38)***		***IR (n=46)***		***CR. (n=39)***		***MM (n=37)***	
	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn
Gradient	1.02	-0.90	1.04	-1.04	0.85	-0.81	0.95	-0.91	0.95	-1.10
Intercept	-0.06	-0.10	0.67	-0.98	1.73	-1.98	1.86	-2.05	0.73	-0.35
% CC significant	98.9	95.4	90.0	92.3	77.8	71.1	70.0	72.5	82.5	75.0
Mean CC	0.912	-0.889	0.831	-0.825	0.710	-0.645	0.738	-0.660	0.783	-0.738

Thumb	***VT (n=39)***		***VR (n=37)***		***IR (n=41)***		***CR (n=36)***		***MM (n=36)***	
	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn
Gradient	1.11	-1.03	1.09	-1.28	0.68	-0.86	1.00	-1.22	0.99	-1.29
Intercept	-0.16	0.04	0.36	-0.66	1.72	-2.41	1.83	-1.95	0.90	-0.54
% CC significant	98.9	97.6	96.3	92.7	67.4	52.2	70.3	73.0	82.5	80.0
Mean CC	0.917	-0.900	0.882	-0.846	0.725	-0.576	0.727	-0.741	0.787	-0.762

Little Finger	***VT (n=18)***		***VR (n=20)***		***IR (n=21)***		***CR (n=17)***		***MM (n=17)***	
	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn	Abdn	Addn
Gradient	1.02	-1.13	1.07	-1.31	0.96	-1.48	0.90	-1.42	1.25	-1.43
Intercept	0.05	0.18	0.88	-1.23	1.90	-2.38	3.11	-2.74	0.40	-0.62
% CC significant	98.3	91.0	82.9	85.5	51.7	51.7	55.0	50.0	70.0	65.0
Mean CC	0.855	-0.856	0.825	-0.774	0.585	-0.619	0.652	-0.633	0.728	-0.670

4.1.2. Nerve Anaesthesia And Nerve Injury Data

As with normal subjects, the degree of muscle contraction was highly variable during tests performed on PNI subjects. Control subjects were matched with order of preference given to individuals, of similar age, sex, EMG activity (i.e. relaxed or tensed) and handedness. When anaesthesia caused paralysis of muscles, a second set of controls was also compared in which subjects maintained relaxation of muscle throughout tests.

When available, data from ipsilateral tests performed with the normal hands of PNI subjects (i.e. VT, VR and IR tests) were used as control data for the contralateral side. Approximately two thirds of control data were in this form.

Unless stated, significant differences quoted in the text are those given by MW tests. One-tailed analysis was used for detection and response delays. Two-tailed analysis was used for comparison of amplitudes and velocities.

4.1.2.1. Motor Tests

Visual tracking tests were used to give an indication of motor recovery in PNI subjects who were able to perform the tests. There were no significant differences in delay or amplitude matching between thumbs of median or median & ulnar PNI subjects and controls (n=9) or between index fingers of ulnar or median & ulnar PNI subjects and controls (n=8). There were infrequent significant differences in velocity matching between index fingers of ulnar or median & ulnar PNI subjects and controls during some adduction moves (see appendices 4.8., 4.9. & 4.10.). These differences were also evident when comparing PNI injured hands and normal hands during VR tests.

4.1.2.2. Proprioceptive Tests

Model 1: The Median Nerve (The Thumb)

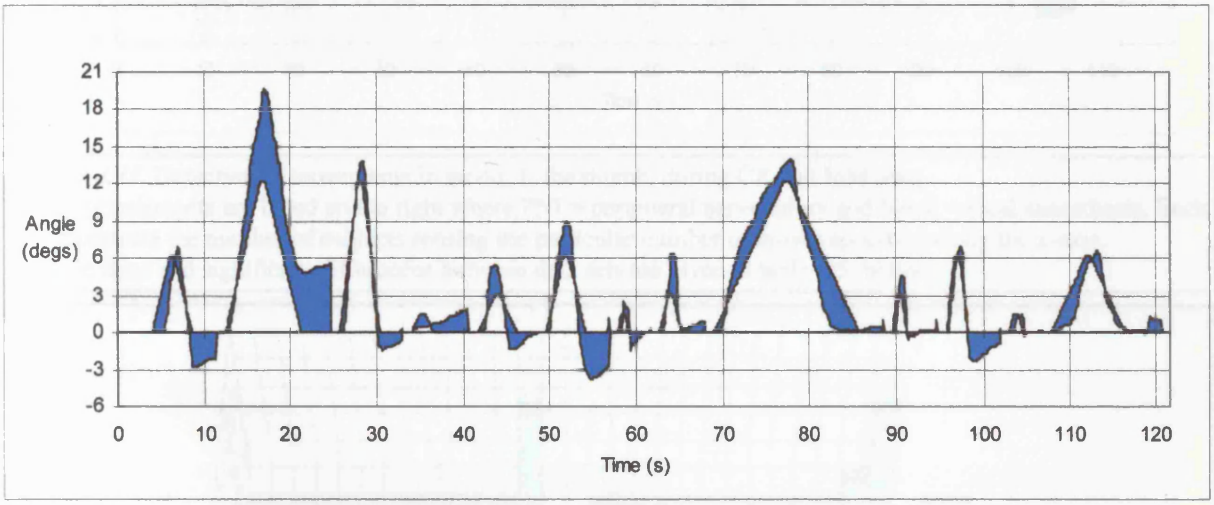
ANAESTHETIC MODELS

Median nerve anaesthesia

The seven volunteers could sense and grade movements with remarkable accuracy following median nerve anaesthesia, even though most subjects reported a feeling of 'deadness' in the digit (figure 4.9.). All anaesthetised subjects could sense over 75% of all movements, and there were no significant differences in detection of movements in comparison to controls ($\alpha<0.05$) (figure 4.11. and table 4.5.). Reference and matched amplitudes and velocities during anaesthesia were also highly correlated. For example, during MM test abduction moves the mean correlation coefficient was 0.936 for amplitude matching and 0.785 for velocity matching (table 4.7.A. and 4.7.B.). The size of the reproduced amplitudes and velocities were also similar to controls, as borne out by an absence of significant differences (appendices 4.6. and 4.7.) (figure 4.13.).

Median nerve anaesthesia did result in significantly longer delays, particularly for mid-range and faster velocity abduction movements (figure 4.12. and table 4.6.). For example, mean delays (±standard error) of $3°s^{-1}$ moves increased from 0.397s (±0.019) in control subjects to 0.648s (±0.144) during median nerve anaesthesia. These significant differences were still evident after replacing control data with that from subjects who maintained relaxation of muscles during the tests (appendix 4.5.).

Figure 4.9. Raw data from a movement matching test performed under **median nerve anaesthesia** in which a normal subject simultaneously matches reference movements applied to the left anaesthetised thumb with the right normal thumb. The error between the reference and matched position is shown in blue. (subject: JS)



Median and radial nerve anaesthesia

Although the sample size was only three subjects, median and radial nerve anaesthesia resulted in significant impairments during both CR and MM tests ($\alpha<0.05$) (figure 4.10. & table 4.5.). Detection was reduced to half of the moves in two of the three subjects (MM test) (figure 4.11.) and mean delays were increased by as much as 2-3 fold, during $3°s^{-1}$ and $6°s^{-1}$ velocity moves (figure 4.12.).

Although reproduced *abduction* amplitudes were highly correlated to reference amplitudes, there was a consistent underestimation of amplitudes matched particularly during CR tests but also during MM tests (figure 4.13.), as reflected in the regression equation of the data (table 4.7.A.). Underestimation was also evident during velocity matching in CR and MM tests, although not so to the same degree as during amplitude matching. Reproduced *adduction* amplitudes and velocities performed under anaesthesia, were poorly correlated to reference amplitudes and velocities for both CR and MM tests (table 4.7.A. & B.).

Figure 4.10. Raw data from a movement matching test performed under **median and radial nerve anaesthesia** in which a normal subject simultaneously matches reference movements applied to the left anaesthetised thumb with the right normal thumb. The error between the reference and matched position is shown in blue. (Subject: JS)

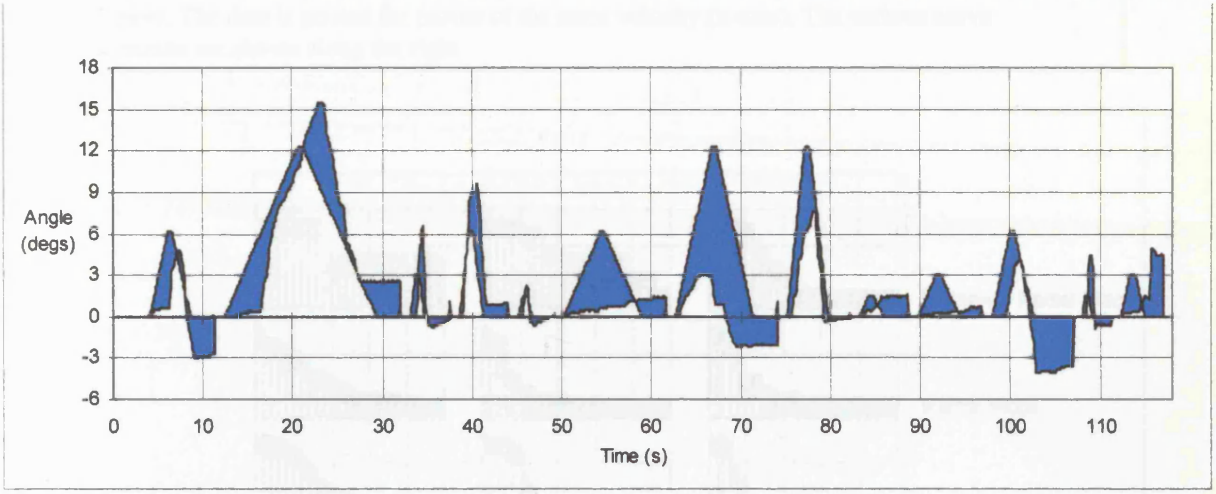


Figure 4.11. Detection of movements in model 1: the thumb, during CR and MM tests.
Nerve impairments are listed on the right where PNI = peripheral nerve injury and block = local anaesthesia. Each bin represents the number of subjects sensing the particular number of moves specified along the x-axis.
Sample sizes and significant differences between data sets are given in table 4.5. below.

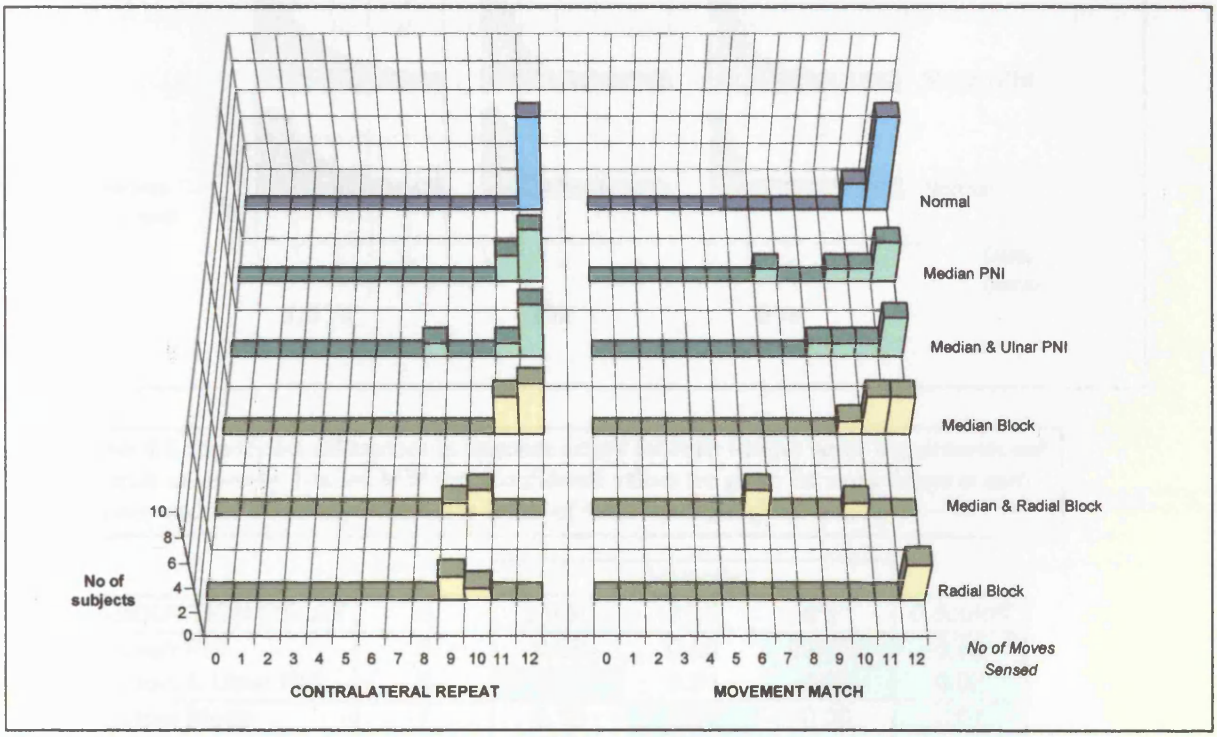


Table 4.5. Significant differences between various nerve impairments and control values in the ability to sense movements during CR and MM tests in the thumb. Confidence values given in the two right hand columns are results of 1-tailed MW tests. Confidence levels of < 0.05 are highlighted in blue.

Nerve	Impairment	*n*	*CR*	*MM*
Median	PNI	6	0.20	0.09
Median & Ulnar	PNI	6	0.33	0.14
Median	Anaesthesia	7	0.10	0.18
Median & Radial	Anaesthesia	3	0.05	0.05
Radial	Anaesthesia	3	0.05	0.55

Figure 4.12. Inverted cumulative 3-D graphs showing the percentage of subjects who HAVE NOT yet responded to abduction movements applied to the thumb as time proceeds from the start of the movement. The data is pooled for moves of the same velocity (x-axis). The various nerve impairments are shown along the right

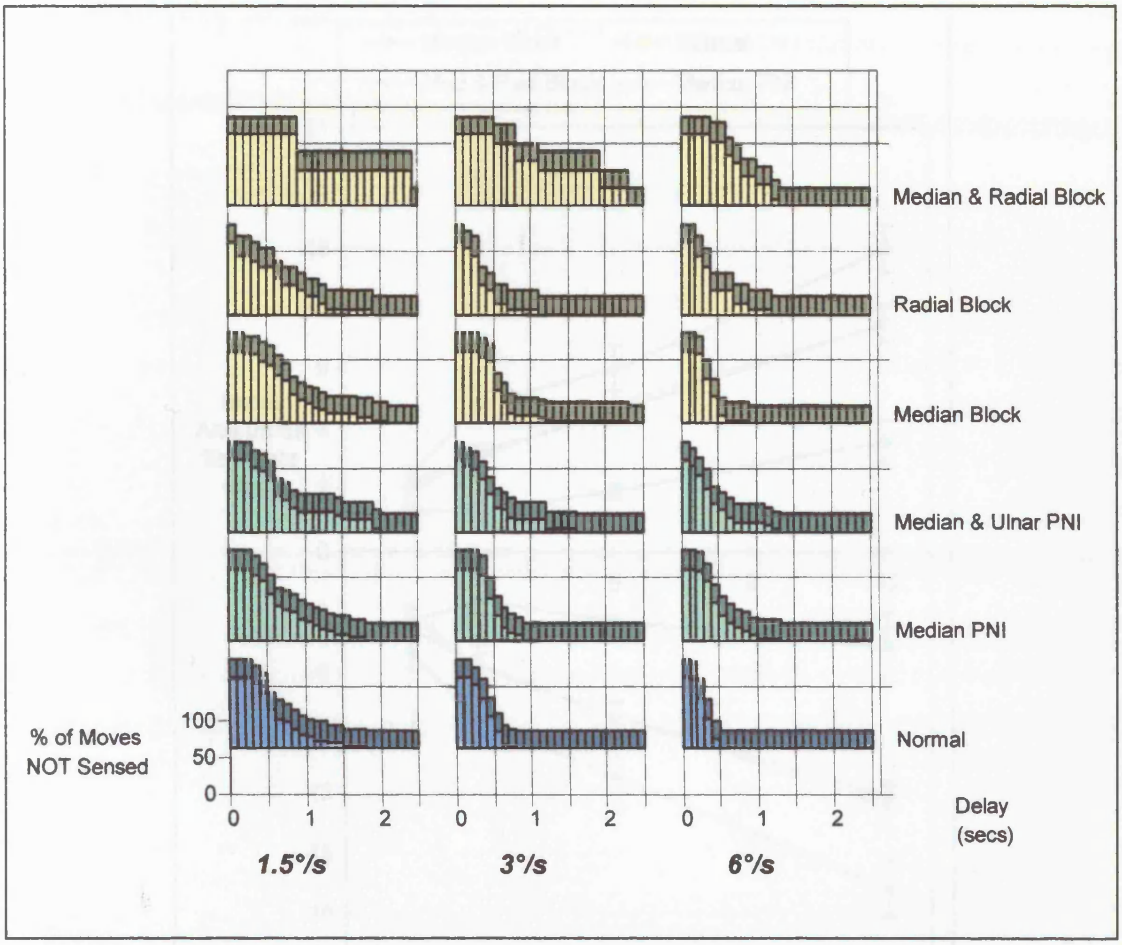


Table 4.6. Significant differences in response delays between various nerve impairments and controls as given by 1-tailed MW test. Confidence values are given for mean delays at each velocity and for 0.5cutoff. Confidence levels of <0.05 are highlighted in blue.

		Velocity			
ABDUCTION DELAY	*n*	*1.5°s^{-1}*	*3°s^{-1}*	*6°s^{-1}*	*0.5cutoff*
Median PNI	8	0.08	0.10	0.0001	0.03
Median & Ulnar PNI	6	0.01	0.34	0.05	0.02
Median Block	7	0.13	0.01	0.06	0.01
Median & Rad. Block	3	0.10	0.05	0.05	0.05
Radial Block	3	0.50	0.35	0.20	0.35

		Velocity			
ADDUCTION DELAY	*n*	*1.5°s^{-1}*	*3°s^{-1}*	*6°s^{-1}*	*0.5cutoff*
Median PNI	8	0.52	0.02	0.006	0.0002
Median & Ulnar PNI	6	0.47	0.09	0.02	0.09
Median Block	7	0.23	0.10	0.50	0.08
Median & Rad. Block	3	0.50	0.05	0.05	0.05
Radial Block	3	0.50	0.10	0.20	0.10

Figure 4.13. Mean estimates +/- standard errors of like-amplitude moves during CR tests in the thumb (model 1). Mean values of abduction moves are given above the x-axis and adduction values below. Values are given for normal hands, and various median (med.) and radial (rad.) nerve impairments caused by anaesthetic block or peripheral nerve injury (PNI).

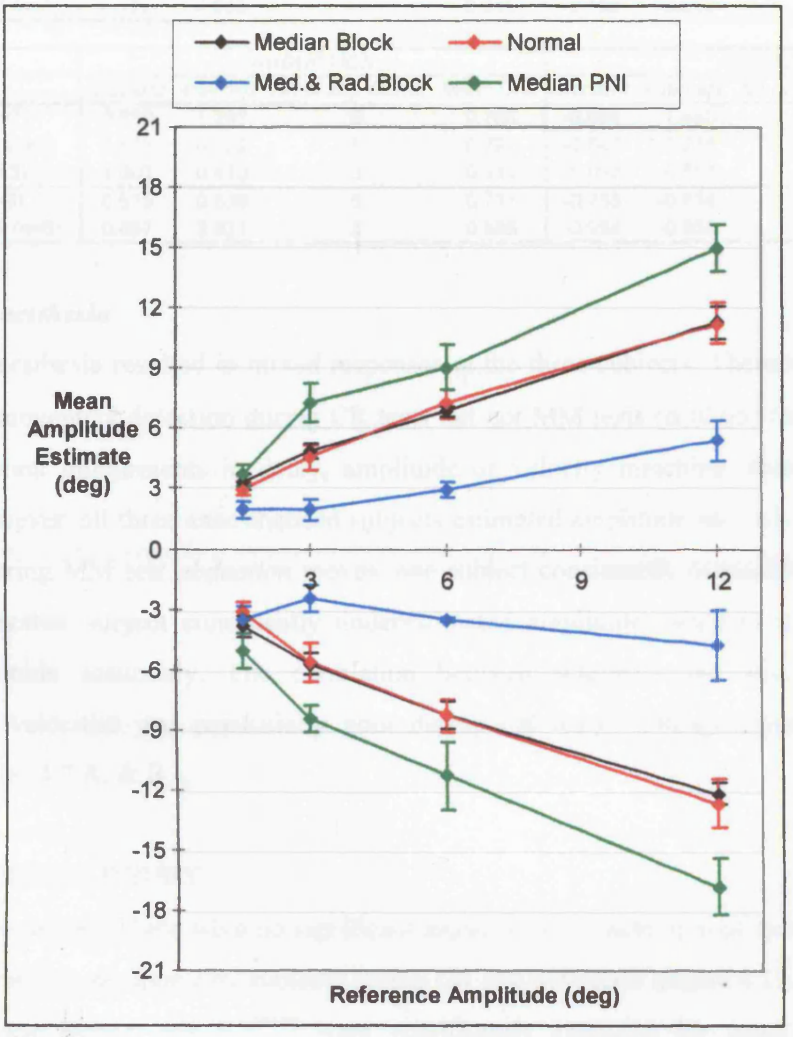


Table 4.7. Regression analysis of (A) amplitude and (B) velocity estimates in model 1: the thumb, under various nerve impairments. Gradients and intercepts are for pooled data. The proportion of subjects in which there was a significant correlation between reference and reproduced amplitudes and velocities is given in row *'No of Sig. Correl'*. Mean correlation coefficients are given in column *'Mean C.C'*. 1.5° moves were not included in the analysis of velocity estimates.

A. Regression analysis of amplitude estimates in model 1: the thumb, under various nerve impairments.

Contralateral Repeat	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Median Block (n=7)	0.744	2.410	7	0.892	-0.768	-3.181	7	-0.881
Med. & Rad. Block (n=3)	0.387	0.852	3	0.891	-0.238	-2.233	0	-0.434
Radial Block (n=3)	0.485	1.766	3	0.893	-0.523	-2.628	1	-0.625
Median PNI (n=8)	0.982	3.160	6	0.813	-1.029	-4.581	6	-0.773
Median & Ulnar PNI (n=6)	0.764	3.437	5	0.750	-0.797	-4.182	5	-0.730

Movement Match	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Median Block (n=7)	1.131	0.415	7	0.936	-0.983	-1.597	7	-0.932
Med. & Rad. Block (n=3)	0.370	2.327	3	0.905	-0.324	-2.754	1	-0.396
Radial Block (n=3)	0.823	1.480	3	0.907	-0.838	-1.971	3	-0.929
Median PNI (n=8)	0.781	0.488	7	0.880	-0.734	-1.453	6	-0.837
Median & Ulnar PNI (n=6)	0.729	1.743	5	0.832	-0.745	-2.322	5	-0.637

B. Regression analysis of velocity estimates in model 1: the thumb, under various nerve impairments.								
Contralateral Repeat	**ABDUCTION**				**ADDUCTION**			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Median Block (n=7)	0.888	1.341	5	0.785	-1.166	-1.268	5	-0.721
Med. & Rad. Block (n=3)	0.426	0.681	2	0.700	-0.197	-1.409	0	-0.412
Radial Block (n=3)	0.613	0.576	2	0.688	-0.685	-1.295	0	-0.565
Median PNI (n=8)	1.048	2.785	6	0.684	-1.616	-3.274	5	-0.756
Median & Ulnar PNI (n=6)	0.122	4.832	1	0.241	-0.196	-5.812	1	-0.432
Movement Match	**ABDUCTION**				**ADDUCTION**			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Median Block (n=7)	0.889	1.261	5	0.786	-0.956	-1.480	6	-0.766
Med. & Rad. Block (n=3)	0.538	0.632	1	0.791	-0.647	-1.238	1	-0.136
Radial Block (n=3)	1.003	0.470	3	0.846	-1.054	-0.563	1	-0.636
Median PNI (n=8)	0.615	0.639	5	0.711	-0.788	-0.834	5	-0.669
Median & Ulnar PNI (n=6)	0.697	2.021	3	0.595	-0.954	-0.938	4	-0.672

Radial nerve anaesthesia

Radial nerve anaesthesia resulted in mixed responses in the three subjects. There were significant impairments in movement detection during CR tests but not MM tests ($\alpha<0.05$) (table 4.5.) There were no significant impairments in delay, amplitude or velocity matching during radial nerve anaesthesia. However, all three anaesthetised subjects estimated amplitude and velocity differently. For example, during MM test *abduction* moves, one subject consistently overestimated amplitude and velocity, another subject consistently underestimated amplitude, whereas the third subject estimated amplitude accurately. The correlation between reference and matched *adduction* amplitudes and velocities was particularly poor during CR tests performed under radial nerve anaesthesia (tables 4.7.A. & B.).

PERIPHERAL NERVE INJURY

Detection of Movement: There were no significant impairments in detection of movement in either *median PNI* or *median & ulnar PNI* subjects during CR and MM tests (figure 4.11. and table 4.5.). However, response delays and 0.5^{cutoff} were significantly extended for many abduction and adduction moves, particularly faster moves (figure 4.12. and table 4.6.).

Grading Movement

Median PNI: Although there were significant correlations between reference and matched amplitudes in the majority of subjects during CR and MM tests, the pattern of amplitude estimation by median PNI subjects was variable (table 4.7.A.). In general, median PNI subjects tended to exaggerate amplitudes during CR tests (figure 4.13.) and underestimate amplitudes during MM tests. For example, mean amplitudes of 3° and 12° abduction and adduction moves were significantly larger in PNI subjects during CR tests and mean 12° abduction moves were significantly smaller during MM tests ($\alpha<0.05$) (appendix 4.6.). These patterns were also reflected in regression equations of the data (table 4.7.A.).

Significant correlations between reference and matched *velocities* were much lower compared to correlations in amplitude. Median PNI subjects also tended to overestimate velocity

during CR tests and underestimate velocity during MM tests (table 4.7.B.). For example, some abduction velocity repeats and the majority of adduction velocity repeats were significantly larger in PNI subjects during CR tests, and significantly smaller during MM tests compared to controls (appendix 4.10.).

Data from the six median & ulnar nerve injured subjects was also variable during both CR and MM tests due to overestimation of amplitude and velocity by some subjects and underestimation by others (appendix 4.9. and 4.10.). The correlation between reference and estimated velocities was particularly poor during CR tests (table 4.7.B.)

CORRELATION TO CLINICAL MEASURES

During median nerve anaesthesia, standard measures of sensory function indicated a profound impairment of sensation in the thumb. In the majority of cases, Weinstein's filament testing applied to the digit tip demonstrated that sensation was absent, although residual sensation was present but greatly diminished in two subjects (appendix 4.11.). Likewise motor function, measured using the thumb abduction action was typically reduced to MRC grade 0 or occasionally 1 and the mean force (± standard error) of the abduction action was reduced from 33.7 N (±2.7 N) in controls to 3.9 N (±1.5 N) during median nerve anaesthesia. Although the standard clinical measures suggest poor sensory and motor function, surprisingly high proprioceptive acuity was present in the digit subsequent to median nerve injury. Subjects were able to sense and grade amplitudes and velocities of movements with a similar degree of accuracy to the normal hand. Similar patterns were also evident during median or median and ulnar PNI.

A more accurate measure of sensory function reflecting proprioceptive acuity was that of cutaneous sensory thresholds at the three points around the CMC thumb joint (i.e. dorsal CMC joint, dorsal web space and thenar eminence, figure 3.7., p101). The mean sensation across the three points was still high during median nerve anaesthesia or subsequent to median PNI with the majority of subjects sensing the finest or second finest filament at each of the three locations. A dramatic loss in sensation at the three points occurred during combined median and radial nerve anaesthesia in which sensation was reduced to that of the coarsest Weinstein's filament (2 N) or no sensation at all. This was also accompanied by a deterioration in the ability to sense and grade movements in the thumb.

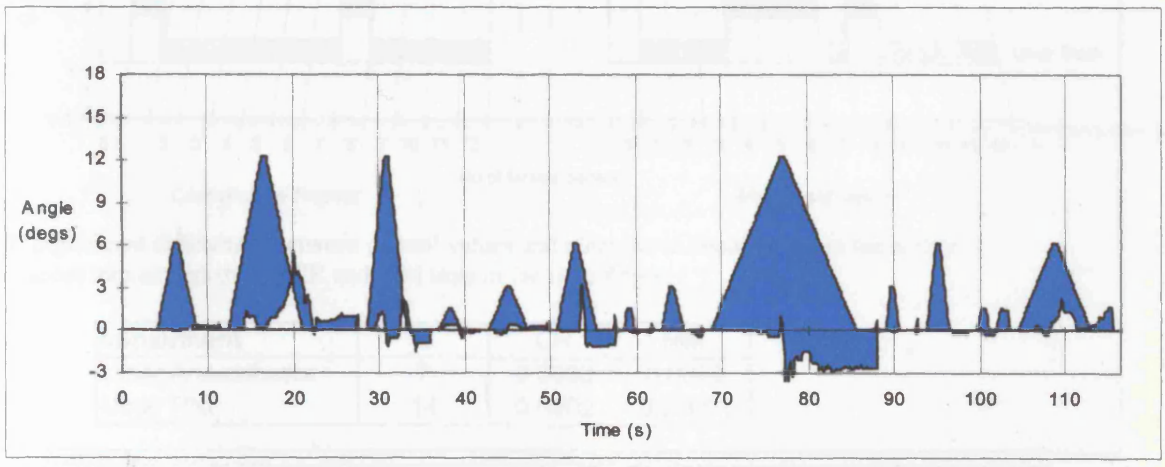
All subjects under median or median & radial nerve anaesthesia and many median PNI subjects used the ulnar innervated sensory areas of digits 4 and 5 to identify and pick up objects during Moberg's picking up test.

Model 2: The Ulnar Nerve (The Little Finger)

ANAESTHETIC MODELS

Detection of Movement: Although there was a dramatic loss in sensitivity to movement in the little finger during ulnar nerve anaesthesia, yielding obvious significant differences, the results were not absolute (figure 4.14. and 4.15.). Four out of the seven subjects could sense some movements in the little finger whilst anaesthetised. However, subjects described these movements as feeling indistinct or were not sure whether movements were being applied in the plane of extension: flexion rather than the plane of abduction: adduction. One subject reported that he distinctively felt abduction moves as extension moves and adduction moves as flexion moves (subject: JS).

Figure 4.14. Raw data from a MM test performed under **ulnar nerve anaesthesia** in which a normal subject simultaneously matches the reference movements applied to the left anaesthetised little finger with the right normal little finger. The error between the reference and matched position is shown in blue. (subject JP)

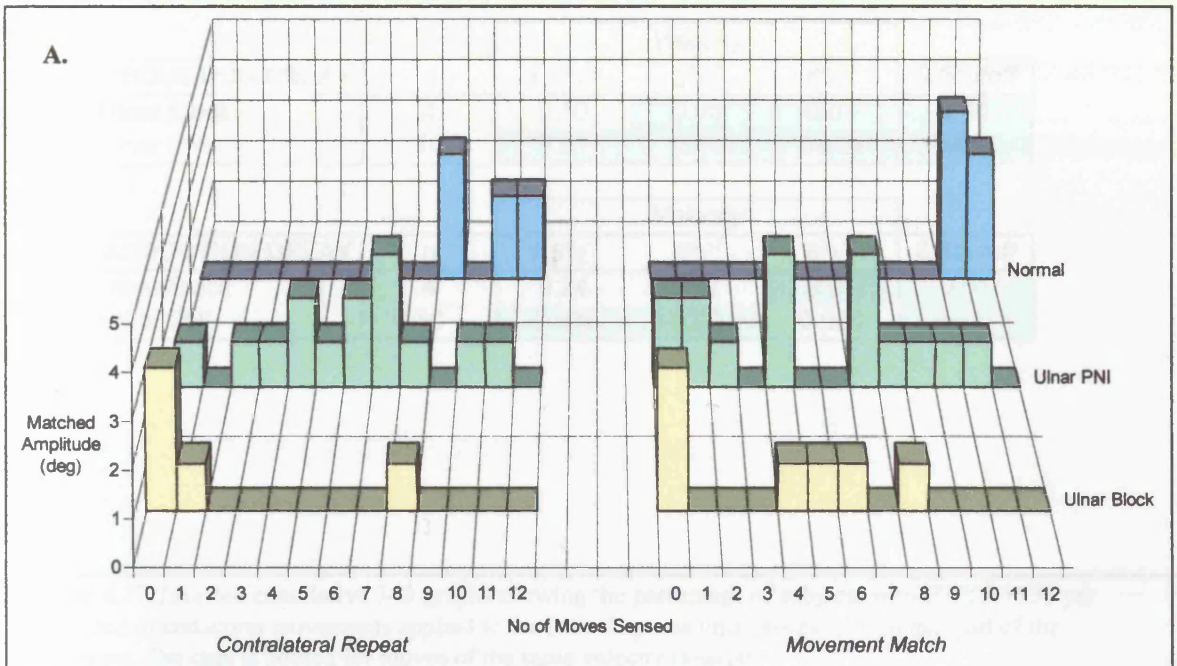


The little finger model also demonstrated that conditions of anaesthesia and PNI caused preferential loss in detection of smaller amplitude moves rather than slower velocity moves (figure 4.16.). This suggests that ability to sense movements appears to be dependant upon the amplitude of a move rather than its velocity.

***Response Delays*:** Response delays were significantly extended during anaesthesia, more obviously during faster moves (figure 4.17. and table 4.8.). For example, average delays for $6°s^{-1}$ abduction moves increased from 0.53s in normal subjects to 1.51s in anaesthetised subjects. Many slow velocity moves were not sensed, resulting in smaller sample sizes causing significant differences to be less apparent (appendix 4.8.).

Grading Movement: For the small number of moves which were sensed by ulnar blocked little fingers (22 moves by 4 subjects), there was no significant correlations between reference and matched amplitudes or velocities (tables 4.9.A. & B.). All the reference moves tended to be matched by moves of similar amplitude (4-7°) and of a low velocity (less than $4°s^{-1}$). The semblance of the matched moves to medium range amplitude moves meant that consistent differences between anaesthetised and normal hands were only evident for abduction and adduction moves of 12° ($\alpha<0.05$) (appendix 4.6.).

Figure 4.15.A. Detection of movements in model 2: the little finger, during CR and MM tests. Nerve impairments are listed on the right where PNI = peripheral nerve injury and block = local anaesthesia. Each bin represents the number of subjects sensing the particular number of moves specified along the x-axis. Sample sizes and significant differences between data sets are given in **B.** Confidence values given in the two right hand columns are results of 1-tailed MW tests.



B. Significant differences between control values and ulnar nerve impairments in the ability to sense movements during CR and MM tests in the little finger.

Impairment	n	CR	MM
Ulnar Anaesthesia	7	0.0003	0.0003
Ulnar PNI	14	0.0002	0.00001

Figure 4.16. The number of subjects sensing each move in the little finger subsequent to ulnar nerve anaesthesia, ulnar PNI and in the normal hand (MM test). Detection of movement appears to be dependant upon the amplitude of the move.

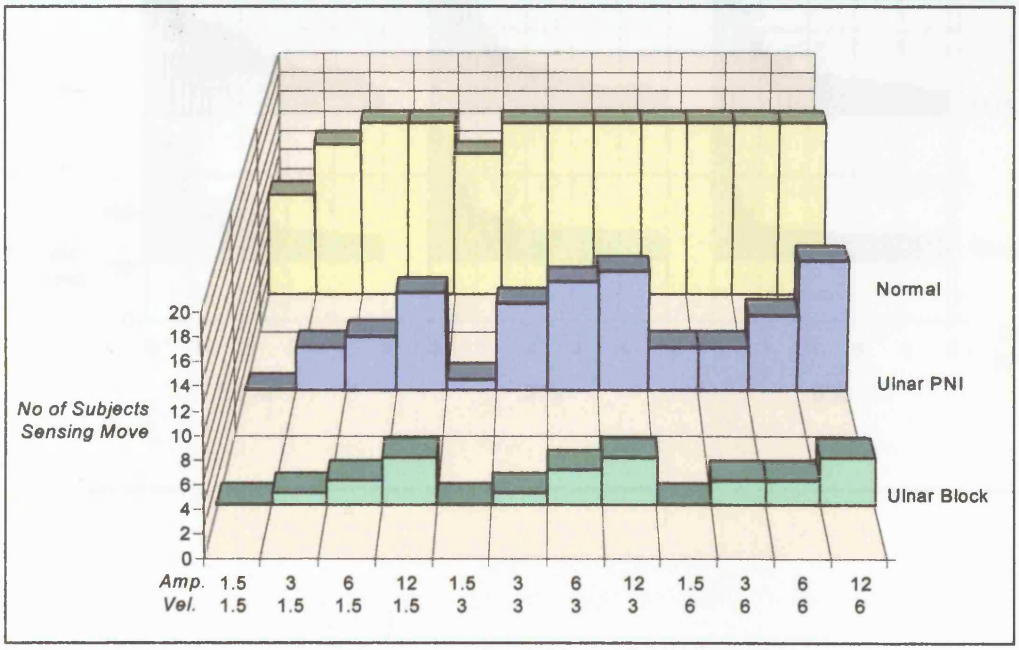


Table 4.8. Significant differences in response delays between ulnar nerve impairments and controls as given by 1-tailed MW test. Confidence values are given for mean delays at each velocity and for 0.5^{cutoff}. Confidence levels of <0.05 are highlighted in blue.

		Velocity			
ABDUCTION DELAY	*n*	*1.5°s^{-1}*	*3°s^{-1}*	*6°s^{-1}*	*0.5cutoff*
Ulnar Block	4	0.10	0.03	0.01	0.01
Ulnar PNI	10	0.01	0.01	0.004	0.001

		Velocity			
ADDUCTION DELAY	*n*	*1.5°s^{-1}*	*3°s^{-1}*	*6°s^{-1}*	*0.5cutoff*
Ulnar Block	4	0.24	0.17	0.01	0.01
Ulnar PNI	10	0.002	0.03	0.056	0.017

Figure 4.17. Inverted cumulative 3-D graphs showing the percentage of subjects who HAVE NOT yet responded to abduction movements applied to the little finger as time proceeds from the start of the movement. The data is pooled for moves of the same velocity (x-axis).
The various nerve impairments are shown along the right

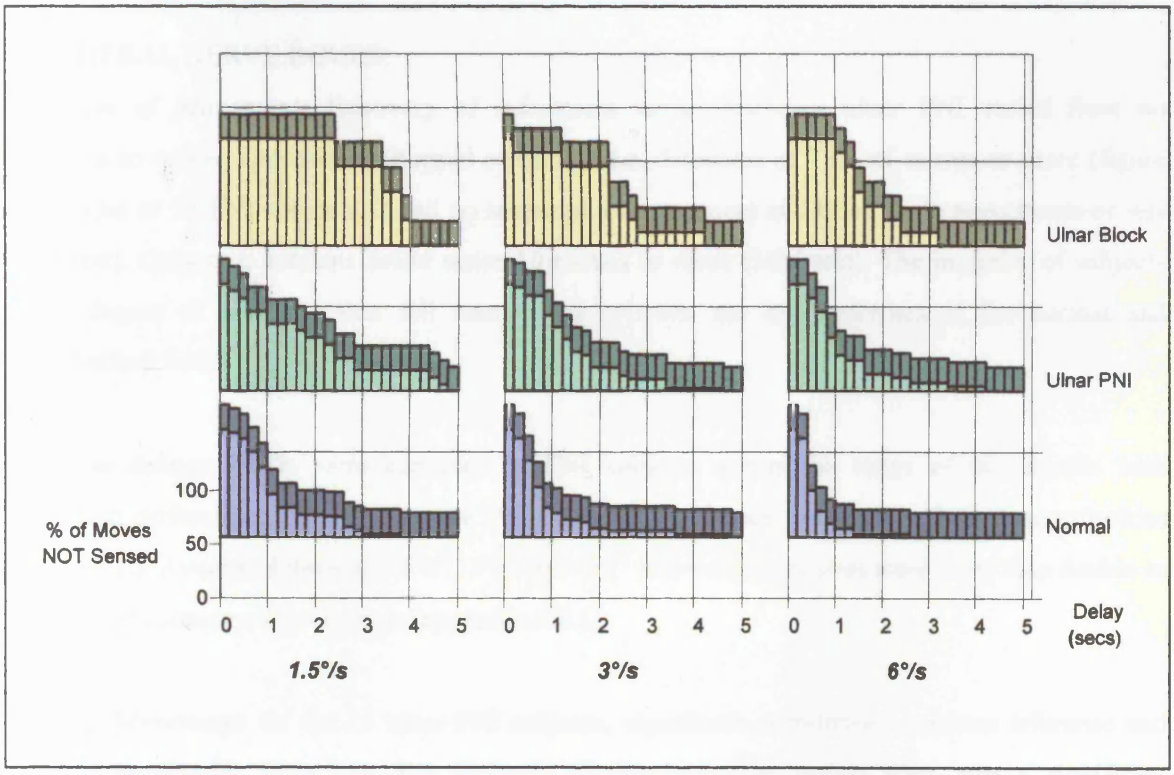


Table 4.9. Regression analysis of (A) amplitude and (B) velocity estimates in model 2: the little finger, under ulnar nerve impairments. Gradients and intercepts are for pooled data. The proportion of subjects in which there was a significant correlation between reference and reproduced amplitudes or velocities is given in row *'No of Sig. Correl'*. Mean correlation coefficients are given in column *'Mean C.C'*.
1.5° moves were not included in the analysis of velocity estimates.
Regression analysis was only performed on subjects who sensed 4 or more moves (which was only 1 subject during CR tests for ulnar anaesthetised subjects).

A. Regression analysis of amplitude estimates in model 3: the little finger, under ulnar nerve impairments.

Contralateral Repeat	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Ulnar PNI (n=11)	0.728	1.842	5	0.800	-0.766	-2.514	5	-0.760
Movement Match	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Ulnar Block (n=4)	-0.051	4.511	0	0.055	-0.017	-3.196	0	-0.109
Ulnar PNI (n=10)	0.655	2.048	6	0.593	-0.641	-3.546	6	-0.588

B. Regression analysis of velocity estimates in model 2: the little finger, under ulnar nerve impairments.

Contralateral Repeat	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Ulnar PNI (n=11)	0.284	2.751	1	0.404	-0.137	-5.966	0	-0.047
Movement Match	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Ulnar Block (n=4)	0.807	0.856	1	-0.055	-0.762	0.200	0	0.046
Ulnar PNI (n=10)	1.402	-0.532	5	0.455	-1.975	0.078	4	-0.532

PERIPHERAL NERVE INJURY

Detection of Movement: Recovery of movement sense following ulnar PNI varied from no sensation to values approaching normal sensation, i.e. detection of 75% of moves or more (figure 4.16.). Out of 15 PNI subjects, 2 had no sensation of movement and 6 felt three movements or less (MM test). Only two subjects could sense 10 moves or more (MM test). The majority of subjects had a degree of recovery that fell somewhere between the two extremes of the normal and anaesthetised hand.

Response delays: PRDs were extended in PNI subjects across the range of movements with significant differences existing between PNI and control subjects for means of all three velocities (table 4.11.). Average delays of $1.5°s^{-1}$, $3°s^{-1}$ and $6°s^{-1}$ like-velocity moves were more than double in PNI subjects compared to controls (appendix 4.8.).

Grading Movement: Of the 15 ulnar PNI subjects, significant correlations between reference and matched *amplitudes* were low. For example, during abduction moves there was a significant correlation between reference and reproduced amplitudes in 5 subjects during CR tests and 6 subjects during MM tests (table 4.9.A). There was large variation in the pattern of amplitude matching with some subjects overestimating and others underestimating. At least some subjects could reproduce amplitudes with the same degree of accuracy as control estimates. Because of large

standard errors in both control and PNI subject data, only 3° amplitude abduction moves were significantly different ($\alpha<0.05$) between groups for CR and MM tests. In both cases, this was because of exaggeration of moves by normal hands (appendix 4.9.).

A significant correlation between reference and matched *velocities* during *CR tests* was only evident in one subject for abduction moves and no subjects during abduction moves (figure 4.9. B.) (appendix 4.10). Mean estimates of faster moves, i.e. $3°s^{-1}$ and $6°s^{-1}$, were significantly slower than those of controls during CR tests ($\alpha<0.05$). Velocity estimation was better during *MM tests* and there was a significant correlation between reference and matched velocities for 5 subjects during abduction and 4 subjects during adduction. There was large variation in the pattern of velocity matching with some subjects overestimating and others underestimating and others reproducing velocities with the same degree of accuracy as control estimates.

CORRELATION TO CLINICAL MEASURES

Proprioceptive function correlated well with combined measures of sensory and motor function in the little finger. This included the sensory function measured either at the digit tip or around the MCP joint (appendix 4.11.). Motor function was equally represented by MRC grading or relative strength of the impaired digit compared to the normal digit. The wide variance of sensorimotor function in the subject groups of ulnar nerve anaesthesia, ulnar PNI and the normal digit allowed correlation between assessments of sensorimotor function and proprioceptive recovery. The correlation was optimal when measures of sensory and motor function were combined as a sum rather than as a product. For example, where:

Sensorimotor Index = MRC grade for little finger abduction +

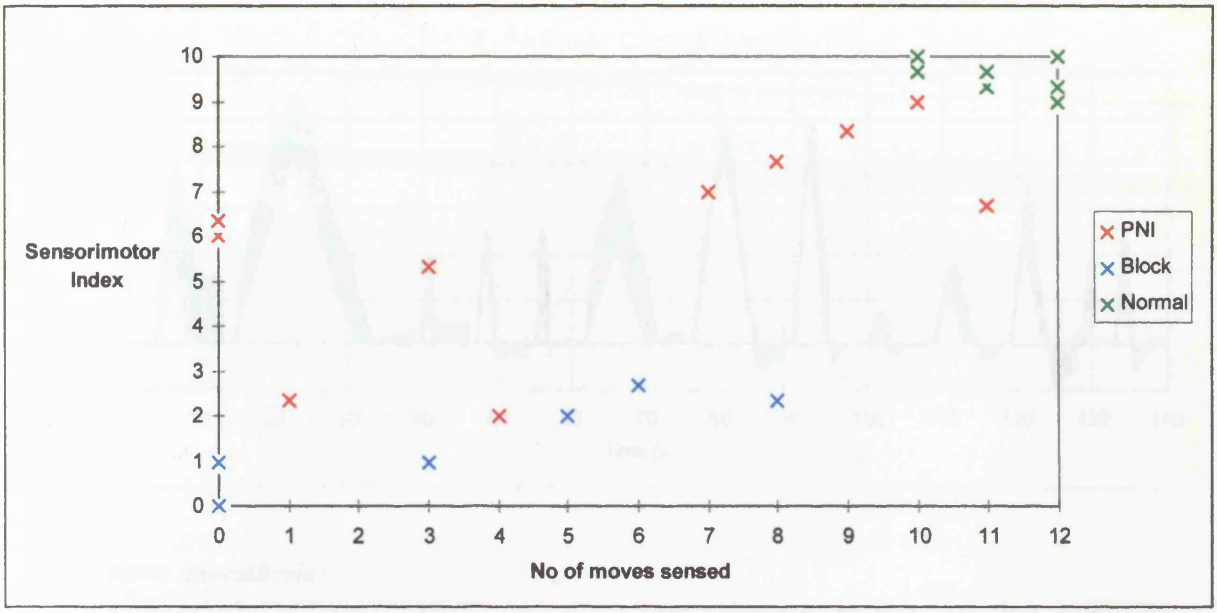
average Weinstein's filament sensitivity

(where 0= no sensitivity and 5=able to sense the finest Weinstein's filament)

The correlation coefficient between number of moves sensed and sensorimotor index, was 0.711 when average Weinstein's filament sensitivity was of radial and ulnar little finger pulp, and 0.723 when average Weinstein's filament sensitivity was of palmar, medial and dorsal skin around the little finger MCP joint (figure 4.18.).

Ulnar anaesthetised and PNI subjects used the median innervated area to explore and recognise objects during Moberg's pick-up test.

Figure 4.18. The correlation between number of moves sensed and sensorimotor index where: *Sensorimotor Index* = MRC grade for little finger abduction + average Weinstein's filament sensitivity of palmar, medial and dorsal skin around the little finger MCP joint. The correlation coefficient was 0.723.



Model 3: Mixed Innervation (The Index Finger)

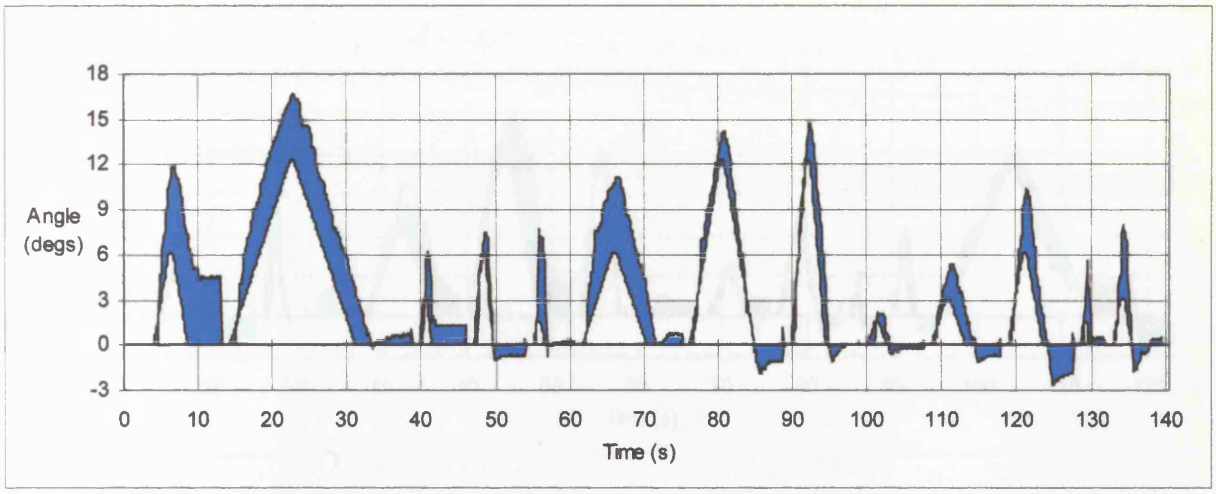
ANAESTHETIC MODELS

Ulnar nerve anaesthesia

There were significant deficits in both detection and delay following ulnar nerve anaesthesia (figure 4.19., figure 4.21. and figure 4.22.). The CR test was better than the MM test for discriminating between normal and impaired hands and yielded significant differences between the ulnar anaesthetised and normal hand ($\alpha<0.05$, 1 tailed) (table 4.10.). There were also significantly extended delays in response to $1.5°s^{-1}$ & $3°s^{-1}$ abduction moves and for 0.5^{cutoff} (abduction and adduction moves) subsequent to ulnar nerve anaesthesia ($\alpha<0.05$).

The correlation between reference and reproduced *amplitudes* for each subject was high, with average correlation coefficients all above 0.87 during CR and MM tests for both abduction and adduction moves. During CR tests, there were no significant differences in amplitude matching between control subjects and subjects under ulnar nerve anaesthesia, but during MM tests small abduction moves (1.5° & 3°) were significantly exaggerated during ulnar nerve anaesthesia ($\alpha<0.05$) (appendix 4.6.). Ulnar nerve anaesthesia also caused overestimation of *velocities* during both CR and MM tests, particularly during abduction moves and midrange moves. During both CR and MM tests, mean velocity estimates of $3°s^{-1}$ abduction moves were significantly larger in the anaesthetised hands (appendix 4.7.).

Figure 4.19. Raw data from a movement matching test performed under **ulnar nerve anaesthesia** in which a normal subject simultaneously matches reference movements applied to the left anaesthetised index with the right normal index. The error between the reference and matched position is shown in blue. (subject: YS)



Median nerve anaesthesia:

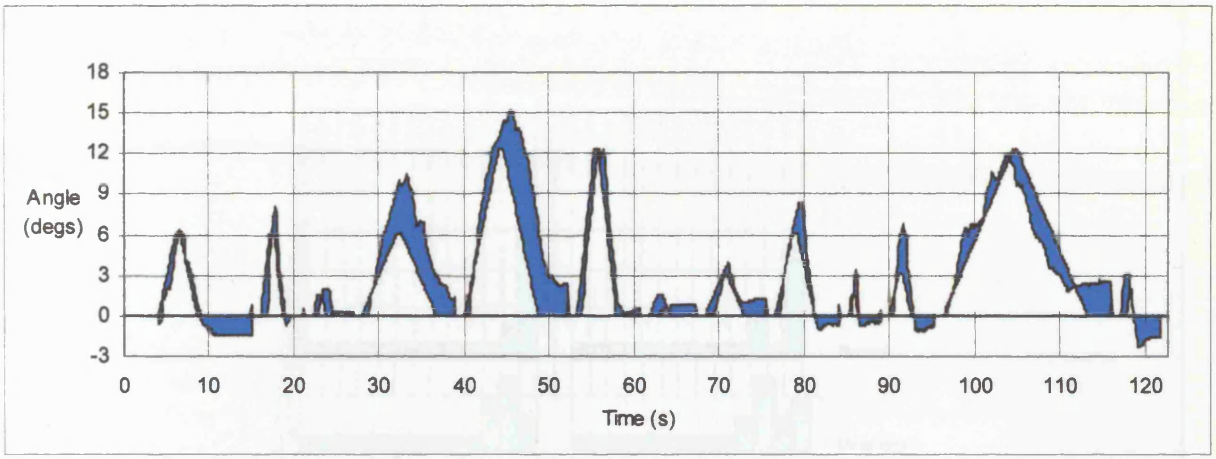
As for ulnar anaesthesia, there were also significant deficits in both detection and delay following median nerve anaesthesia (figure 4.20., figure 4.21. and figure 4.22.). There were significant impairments for the detection of movements during CR tests but not MM tests ($\alpha<0.05$, 1 tailed) (table 4.10.). Response delays were significantly extended during $1.5°s^{-1}$, $3°s^{-1}$ & $6°s^{-1}$ abduction moves and $3°s^{-1}$ & $6°s^{-1}$ adduction moves after median anaesthesia ($\alpha<0.05$).

There were no significant differences between controls and median nerve anaesthetised subjects for amplitude reproduction and only minor differences for velocity reproduction (appendices 4.6. and 4.7.).

Median & Radial nerve anaesthesia

Differences in detection of movement between median & radial blocked hands and controls were only significant for a confidence level of $\alpha=0.1$ (table 4.10.). There were also some significant differences in delay but only during $1.5°s^{-1}$ abduction moves ($\alpha<0.05$, 1-tailed MW test) (figure 2.22. and table 4.11.). Anaesthesia of median & radial nerves brought about underestimation of amplitudes of larger movements in comparison to controls. This resulted in significant differences between controls and anaesthetised hands in the ability to estimate amplitudes of large 12° abduction and adduction moves during CR tests (appendix 4.6.). Regression lines of CR test amplitude data from median & radial blocked subjects had gradients which were much smaller than control subjects (table 4.12.A. and figure 4.23.). These significant differences were not as apparent during MM tests.

Figure 4.20. Raw data from a movement matching test performed under **median nerve anaesthesia** in which a normal subject simultaneously matches reference movements applied to the left anaesthetised index with the right normal index. The error between the reference and matched position is shown in blue. (subject: YS)



Anaesthesia of median & radial nerves resulted in only minor differences in velocity matching during CR or MM tests compared to controls (appendix 4.7.). However, in only two out of the three subjects was there a significant correlation between reference and matched velocities (MM test) (table 4.12.B.).

Radial nerve anaesthesia

Differences in detection of movement and PRD between radial blocked hands and controls were only significant for a confidence level of α=0.1 (table 4.10. & 4.11.). As for anaesthesia of the median & radial nerves, radial nerve anaesthesia also caused subjects to significantly underestimate amplitudes of larger movements yielding significant differences between radially anaesthetised subjects and controls for means of 12° abduction and adduction moves during CR tests (appendix 4.6.). Consequently, regression lines of CR test data from radial blocked subjects had gradients which were much smaller than control subjects (table 4.12.A.). There were no significant differences between control and anaesthetised subjects during MM tests or for any velocity estimates (table 4.12.B.) (appendix 4.7.).

Table 4.10. Significant differences between various nerve impairments and control values in the ability to sense movements during CR and MM tests in the index. Confidence values given in the two right hand columns are results of 1-tailed MW tests. Confidence levels of < 0.05 are highlighted in blue.

Nerve	Impairment	*n*	*CR*	*MM*
Ulnar	PNI	9	0.05	0.03
Median	PNI	6	0.066	0.18
Median & Ulnar	PNI	6	0.013	0.02
Ulnar	Anaesthesia	7	0.01	0.10
Median	Anaesthesia	7	0.003	0.13
Median & Radial	Anaesthesia	3	0.07	0.20
Radial	Anaesthesia	3	0.07	0.50

Figure 4.21. Detection of movements in model 3: the index, during CR and MM tests.
Nerve impairments are listed on the right where PNI = peripheral nerve injury and block = local anaesthesia.
Each bin represents the number of subjects sensing the number of moves specified along the x-axis.
Sample sizes and significant differences between data sets are given in table 4.11. below.

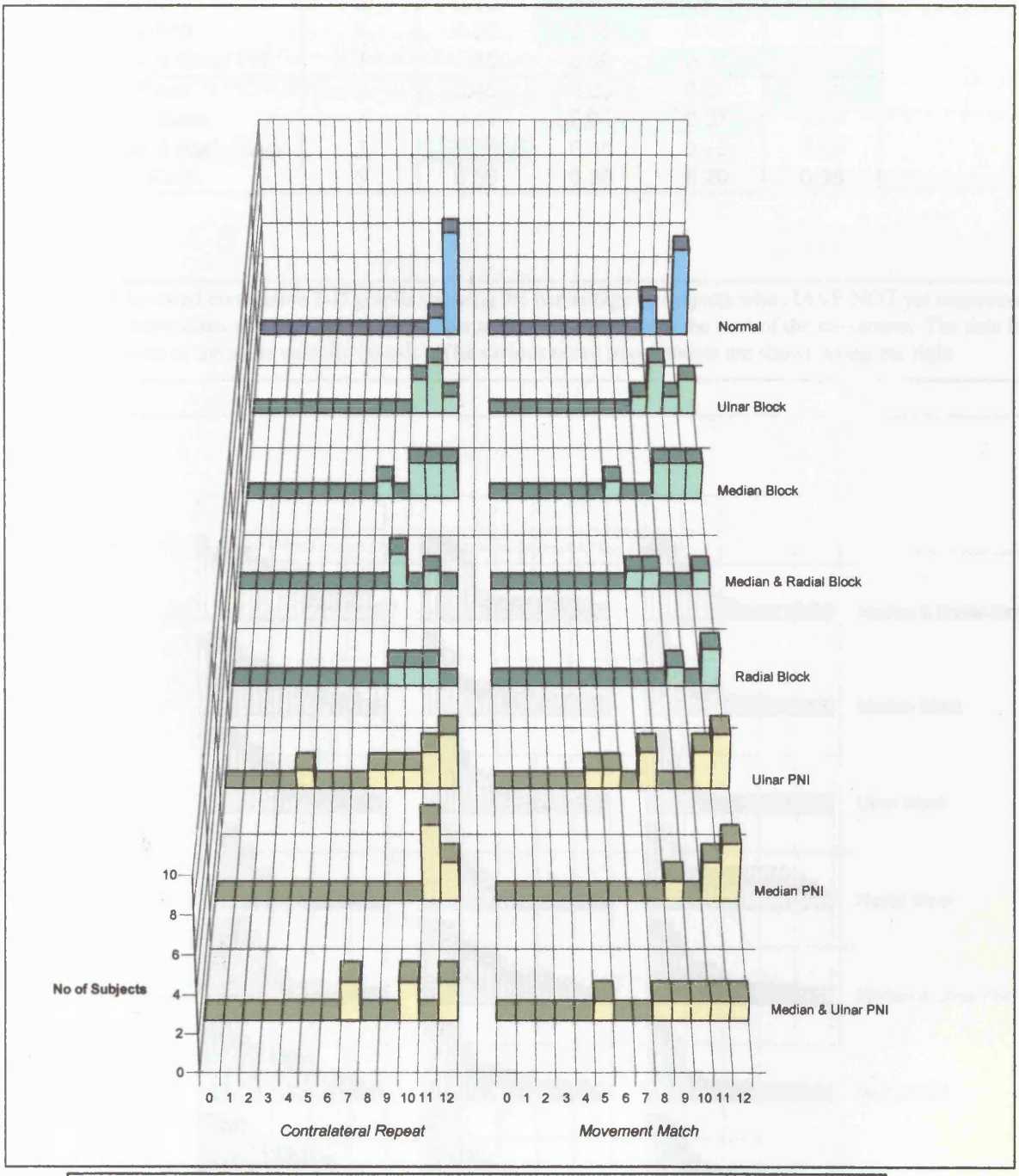


Table 4.11. Significant differences in response delays between ulnar nerve impairments and controls as given by 1-tailed MW test. Confidence values are given for mean delays at each velocity and for 0.5^{cutoff}. Confidence levels of <0.05 are highlighted in blue.

		Velocity			
ABDUCTION DELAY	*n*	*1.5°s^{-1}*	*3°s^{-1}*	*6°s^{-1}*	*0.5cutoff*
Ulnar PNI	10	0.02	0.01	0.008	0.0003
Median PNI	7	0.10	0.10	0.27	0.09
Median & Ulnar PNI	6	0.02	0.07	0.09	0.03
Ulnar Block	7	0.03	0.04	0.10	0.02
Median Block	7	0.02	0.05	0.02	0.04
Median & Rad. Block	3	0.20	0.10	0.10	0.05
Radial Block	3	0.20	0.20	0.10	0.35

		Velocity			
ADDUCTION DELAY	*n*	*1.5°s^{-1}*	*3°s^{-1}*	*6°s^{-1}*	*0.5cutoff*
Ulnar PNI	10	0.37	0.05	0.001	0.0002
Median PNI	7	0.36	0.05	0.19	0.07
Median & Ulnar PNI	6	0.35	0.09	0.01	0.01
Ulnar Block	7	0.45	0.23	0.10	0.01
Median Block	7	0.45	0.04	0.05	0.06
Median & Rad. Block	3	0.05	0.35	0.20	0.20
Radial Block	3	0.50	0.35	0.20	0.35

Figure 4.22. Inverted cumulative 3-D graphs showing the percentage of subjects who HAVE NOT yet responded to abduction movements applied to the index finger as time proceeds from the start of the movement. The data is pooled for moves of the same velocity (x-axis). The various nerve impairments are shown along the right

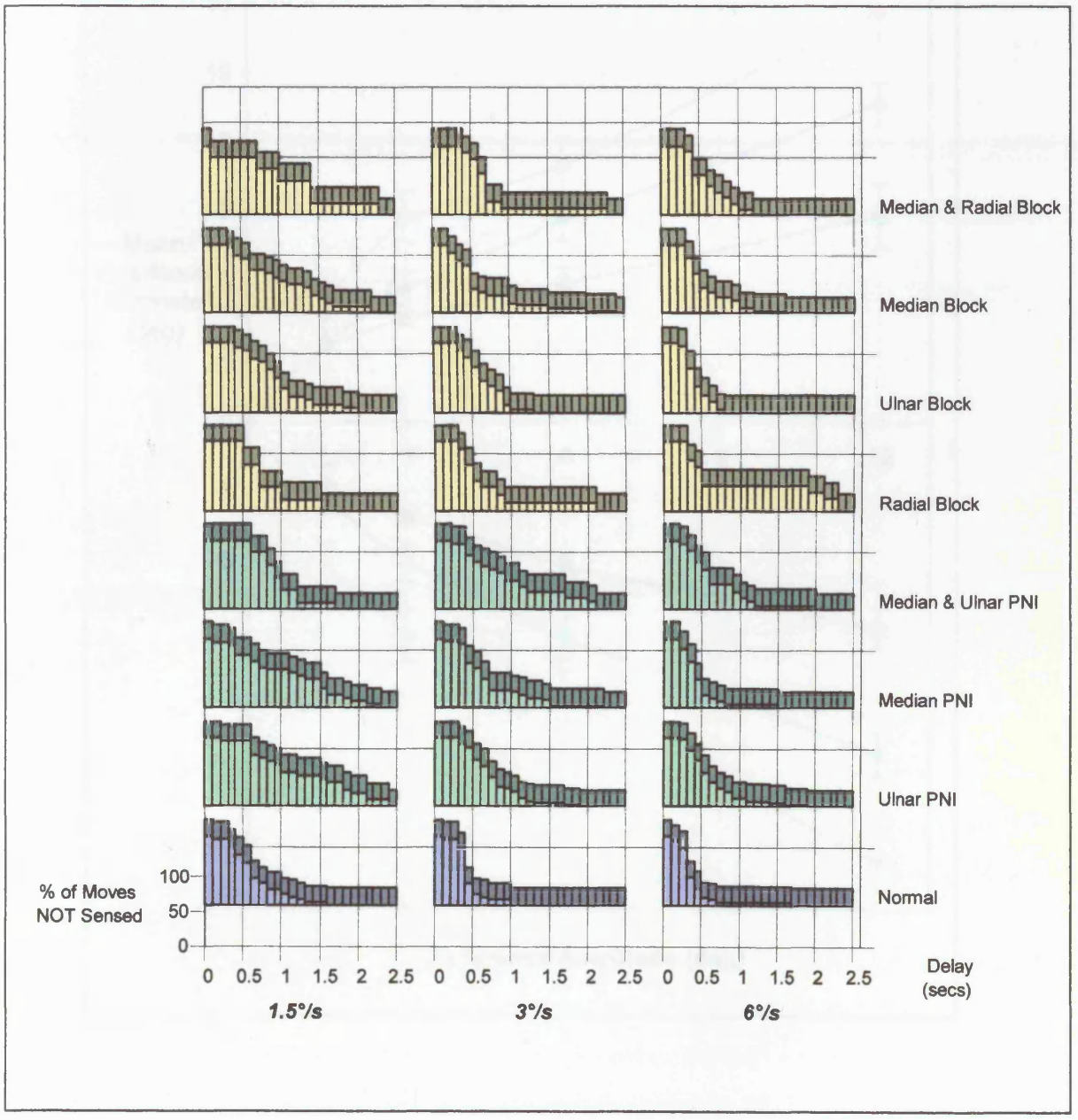


Figure 4.23. Mean estimates +/- standard errors of like-amplitude moves during CR tests in the index finger (model 3). Mean values of abduction moves are given above the x-axis and adduction values below. Values are given for normal hands, and various median (med.), radial (rad.) and ulnar nerve impairments caused by anaesthetic block or peripheral nerve injury

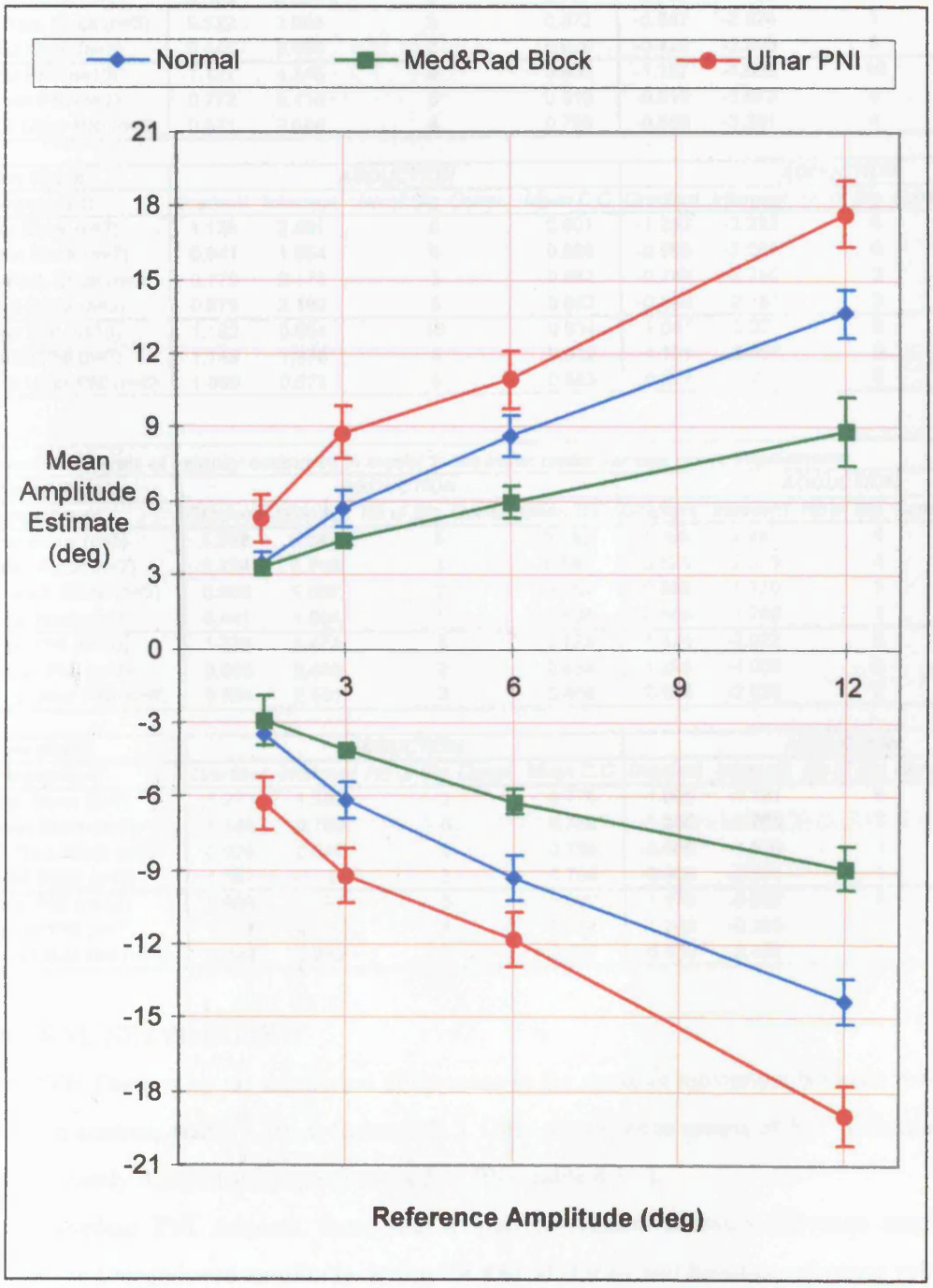


Table 4.12. Regression analysis of (A) amplitude and (B) velocity estimates in model 3: the index finger, under various nerve impairments. Gradients and intercepts are for pooled data. The proportion of subjects in which there was a significant correlation between reference and reproduced amplitudes and velocities is given in row *'No of Sig. Correl'*. Mean correlation coefficients are given in column *'Mean C.C'*.
1.5° moves were not included in the analysis of velocity estimates.

A. Regression analysis of amplitude estimates in model 3: the index under various nerve impairments.

Contralateral Repeat	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Ulnar Block (n=6)	1.011	3.234	6	0.880	-1.125	-3.850	6	-0.870
Median Block (n=7)	0.609	4.007	6	0.777	-0.739	-4.123	6	-0.802
Med. & Rad. Block (n=3)	0.522	2.684	3	0.872	-0.547	-2.524	3	-0.890
Radial Block (n=3)	0.445	3.465	3	0.926	-0.429	-3.696	3	-0.887
Ulnar PNI (n=10)	1.127	4.346	9	0.909	-1.187	-4.809	10	-0.910
Median PNI (n=7)	0.772	5.416	5	0.810	-0.919	-5.673	5	-0.828
Median & Ulnar PNI (n=6)	0.671	2.684	4	0.739	-0.558	-3.381	4	-0.636
Movement Match	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Ulnar Block (n=7)	1.125	2.491	6	0.901	-1.243	-2.232	6	-0.919
Median Block (n=7)	0.941	1.954	6	0.888	-0.985	-2.088	6	-0.901
Med. & Rad. Block (n=3)	0.779	2.173	3	0.862	-0.748	-2.295	3	-0.862
Radial Block (n=3)	0.879	2.180	3	0.883	-0.849	-2.183	3	-0.918
Ulnar PNI (n=10)	1.192	0.564	10	0.934	-1.047	-2.201	9	-0.878
Median PNI (n=7)	1.149	1.976	6	0.912	-1.111	-2.057	5	-0.822
Median & Ulnar PNI (n=6)	1.069	0.573	5	0.883	-0.871	-2.221	5	-0.876

B. Regression analysis of velocity estimates in model 3: the index under various nerve impairments.

Contralateral Repeat	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Ulnar Block (n=6)	1.298	2.546	5	0.742	-1.396	-2.487	4	-0.707
Median Block (n=7)	0.724	2.748	3	0.543	-0.825	-2.379	4	-0.665
Med. & Rad. Block (n=3)	0.586	1.052	2	0.764	-0.666	-1.170	1	-0.626
Radial Block (n=3)	0.441	1.804	1	0.608	-0.669	-1.268	1	-0.487
Ulnar PNI (n=10)	1.324	2.474	8	0.724	-1.474	-2.022	6	-0.632
Median PNI (n=7)	0.938	5.486	2	0.634	-1.295	-4.006	5	-0.799
Median & Ulnar PNI (n=6)	0.504	2.481	3	0.466	-0.596	-2.026	2	-0.513
Movement Match	***ABDUCTION***				***ADDUCTION***			
Impairment	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*	*Gradient*	*Intercept*	*No of Sig. Correl.*	*Mean C.C.*
Ulnar Block (n=7)	1.273	1.399	5	0.779	-1.069	-1.181	6	-0.749
Median Block (n=7)	1.198	0.782	6	0.764	-1.386	-0.065	7	-0.832
Med. & Rad. Block (n=3)	0.926	0.646	2	0.798	-0.600	-1.509	1	-0.642
Radial Block (n=3)	1.357	-0.153	3	0.788	-0.863	-0.671	1	-0.738
Ulnar PNI (n=10)	0.909	1.197	6	0.692	-1.170	-0.960	5	-0.668
Median PNI (n=7)	1.863	-0.277	6	0.784	-1.309	-0.285	7	-0.787
Median & Ulnar PNI (n=6)	0.899	0.929	3	0.597	-0.632	-2.425	3	-0.618

PERIPHERAL NERVE INJURY

Median PNI: There were no significant differences in the sense of movement between median PNI subjects and controls (table 4.10. & figure 4.21.). Only responses to means of $3°s^{-1}$ adduction moves were significantly delayed subsequent to median PNI (table 4.11.).

In median PNI subjects, there was a high correlation between reference amplitude of movements and reproduced amplitude during CR and MM tests and between reference velocity and reproduced velocity during MM tests (table 4.12.). However, regression equations for individual subjects made it clear that some subjects overestimated amplitudes and velocities whereas others

underestimated. The resultant large standard errors meant that there were no significant differences between median PNI subjects and normal subjects.

Ulnar PNI: Detection and grading of movements were more adversely affected following ulnar PNI compared to median PNI. Detection of movement subsequent to ulnar PNI was significantly impaired compared to the control digit during both CR and MM tests ($\alpha<0.05$) (figure 4.21. & table 4.10.). Response delays were prolonged throughout, subsequent to PNI, with significant differences between control and PNI data present for means of $1.5°s^{-1}$, $3°s^{-1}$ & $6°s^{-1}$ abduction moves and $3°s^{-1}$ and $6°s^{-1}$ adduction moves ($\alpha<0.05$) (table 4.11.).

Amplitude and velocity matching during CR tests was characterised by consistent overestimation. Means of 3°, 6° & 12° *like-amplitude* abduction moves and 6° & 12° like-amplitude adduction moves were all significantly higher subsequent to ulnar PNI ($\alpha<0.05$) (figure 4.23.). Mean estimates of $1.5°s^{-1}$ and $3°s^{-1}$ abduction and $1.5°s^{-1}$, $3°s^{-1}$ and $6°s^{-1}$ adduction *like-velocity* moves were also significantly different during CR tests because of overestimation by ulnar PNI subjects. Gradients and intercepts were also elevated. However, regression analysis also demonstrated that there was often significant correlations between reference and reproduced amplitudes and velocities (tables 4.12.A. & B.). There were no significant differences in amplitude matching or velocity matching during MM tests between normal and PNI subjects.

Median and Ulnar PNI: Detection of movement following median & ulnar PNI was significantly impaired compared to the control digit during both CR and MM tests ($\alpha<0.05$) (table 4.10.) (figure 4.21.). There were also significant differences in response delay for $1.5°s^{-1}$ & $3°s^{-1}$ abduction moves and $6°s^{-1}$ adduction moves as well as for 0.5^{cutoff} for abduction and adduction moves subsequent to median & ulnar PNI ($\alpha<0.05$) (figure 4.22. & table 4.11.).

Differences in amplitude matching were less obvious for median & ulnar PNI subjects compared to ulnar PNI subjects and only means estimates of 12° abduction moves performed during ***CR*** tests were significantly different because of underestimation by the PNI subject ($\alpha<0.05$). Correlation coefficients were high for four of the six subjects. There was no significant correlation between reference and matched amplitudes for the other two subjects (CR tests). Amplitude matching during ***MM*** tests tended to be better than during CR tests and was less sensitive to nerve impairment (table 4.12. A.). Velocity matching by median and ulnar PNI subjects produced variable responses with large standard errors.

CORRELATION TO CLINICAL MEASURES

In the majority of subjects, median nerve anaesthesia resulted in an absence of cutaneous sensation on radial and ulnar aspects of the index digit tip and on glabrous skin over the index MCP joint. Median nerve anaesthesia also resulted in slight reduction in motor power. The maximum voluntary contraction (± standard error) of the left 1DI muscle was reduced from 27.0 N (±2.9) in the normal hand to 19.7N (±3.8) by median nerve anaesthesia (appendix 4.11.). In contrast, ulnar nerve anaesthesia caused the mean MVC of the left IDI muscle to fall to 3.1N (± 0.7), whereas average Weinstein's sensitivities were all 3.7 or greater (where 0 = no sensitivity and 5 = able to sense the finest Weinstein's filament). Although one type of anaesthetic block resulted in profound motor loss and the other in sensory loss, proprioceptive scores were high under both conditions. Most movements were sensed following ulnar or median PNI although the ability to grade movement was often adversely affected.

Measuring cutaneous sensation at the three points around the MCP joint (i.e. dorsal, lateral and medial), reflected proprioceptive function better than measuring at the digit tip. This was best illustrated during combined median and radial nerve anaesthesia where low cutaneous sensation around the index MCP joint was accompanied by deterioration in kinaesthesia.

Jamar grip strength was adversely affected by both median and ulnar nerve anaesthesia. Interestingly, median nerve anaesthesia had a more detrimental affect on grip strength causing mean values to fall from 449 N (±30 N) in the normal hand (mean of positions II and III, ± standard error) to 197 N (±50 N) during median nerve anaesthesia compared to 239 N (±21 N) during ulnar nerve anaesthesia.

Anaesthesia of the skin was also accompanied by a rise in temperature, typically up to values of about 34-35°. Thus, median nerve anaesthesia caused temperatures to rise over the thenar eminence and lateral borders of the thumb and index. Ulnar nerve anaesthesia caused temperatures to rise over the hypothenar eminence and the lateral border of the little finger.

4.2. 8-10Hz PULSATILE OUTPUT

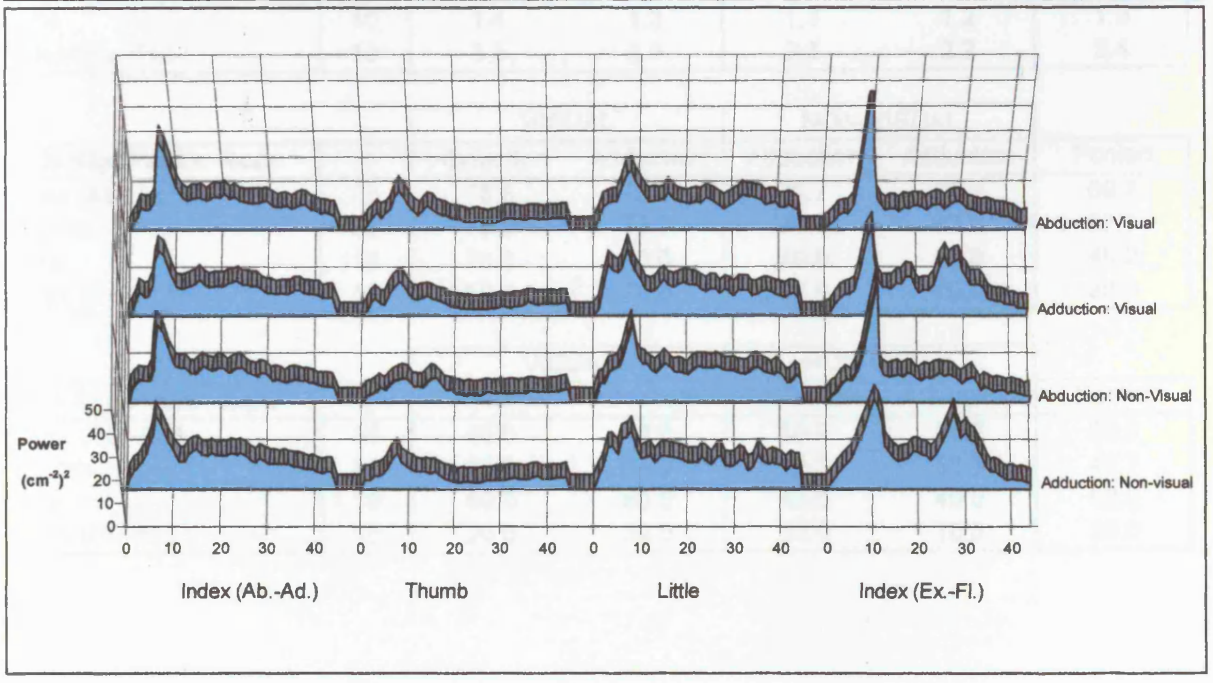
Two-tailed MW tests and Student's t-tests (heteroscedastic) were used to look for significant differences between medians and means, respectively. Unless stated, results from analysis by MW tests are quoted.

4.2.1. Normal Data

4.2.1.1. Intrinsic Hand Musculature

During slow movements, oscillations within the range of 7-11 Hz were evident in all three models with the highest occurrence of significant 8-10Hz peaks in order of the index, thumb and little finger (see figure 4.23. and table 4.18.). During all movements, the *absolute* power between 7-11 Hz, was significantly greater in the index compared to the thumb but not compared to the little finger ($\alpha<0.05$) (appendix 4.12.). The *normalised* power between 7-11 Hz was significantly larger in the index compared to both the thumb and little finger, but only during abduction-visual movements. There were no significant differences between the thumb and little finger ($\alpha<0.05$). There were no significant differences between abduction and adduction moves or between moves performed in the absence and presence of visual feedback (appendix 4.12.).

Figure 4.23. Averaged power spectra of acceleration traces during slow 5°/s velocity tracking movements in the thumb, index and little fingers. The recorded digit is given along the x-axis, and the movement phase along the right hand side. Recordings lasted 3 minutes resulting in 15 sweeps averaged for each subject. Sample sizes, significant peaks and absolute and normalised power in the 7-11Hz range are given in table 4.17.
Ab.-Ad = abduction: adduction, Ex.-Fl. = extension:flexion.



4.2.1.2. Comparison of Extrinsic and Intrinsic Hand Musculature

The 8-10Hz tremor peaks visible during index extension: flexion moves, predominantly under the control of extrinsic muscles, were compared with those seen during abduction: adduction moves, primarily controlled by intrinsic musculature (figure 4.23.). There were no significant differences between 8-10Hz tremor peaks evident during extension: flexion moves and abduction: adduction moves in the index as measured by either absolute or normalised power in the 7-11Hz range (appendix 4.12.).

There were some peaks evident at higher frequencies during extension movements of the digit. For example, in 50% of subjects, there were significant peaks in the 25-30 Hz range during extension movements.

Table 4.18. Three measures of the proportion of spectral power in the 7-11Hz range in power spectra of acceleration traces of slow movements in the thumb, index and little fingers.
This included absolute power, normalised power and percentage of subjects who showed significant peaks in the range 7-11Hz. Values are listed for index, thumb and little finger abduction: adduction moves and index extension: flexion moves.

		VISUAL		NON-VISUAL		
A. Absolute Power	n	Abduction	Adduction	Abduction	Adduction	Pooled
Index (Ab.-Ad.)	35	144.1	106.7	140.1	120.6	128.2
Thumb	31	65.9	60.0	49.7	62.1	59.5
Little	10	98.8	96.2	114.4	94.5	100.4
Index (Ex.-Fl.)	10	172.0	128.3	154.3	162.4	154.5

		VISUAL		NON-VISUAL		
B. Normalised Power	n	Abduction	Adduction	Abduction	Adduction	Pooled
Index (Ab.-Ad.)	35	2.2	1.8	1.7	1.6	1.8
Thumb	31	1.5	1.5	1.6	1.4	1.5
Little	10	1.4	1.3	1.3	1.2	1.3
Index (Ex.-Fl.)	10	3.3	2.3	2.3	2.2	2.4

		VISUAL		NON-VISUAL		
C. % Sig. Peaks: Accn	n	Abduction	Adduction	Abduction	Adduction	Pooled
Index (Ab.-Ad.)	35	78.8	75.8	72.7	69.7	69.7
Thumb	31	75.0	75.0	71.4	67.9	57.1
Little	10	70.0	40.0	40.0	50.0	40.0
Index (Ex.-Fl.)	10	90.0	70.0	80.0	70.0	80.0

		VISUAL		NON-VISUAL		
D. % Sig. Peaks: EMG	n	Abduction	Adduction	Abduction	Adduction	Pooled
Index (Ab.-Ad.)	35	46.6	40.0	50.0	56.7	60.0
Thumb	31	33.3	54.2	33.3	58.3	41.7
Little	10	60.0	60.0	40.0	40.0	60.0
Index (Ex.-Fl.)	10	20.0	30.0	30.0	10.0	30.0

4.2.1.3. Comparison of Pulsatile Output During Position Holding and Slow Movements

In all three digits, the *absolute power* between 7-11 Hz was significantly less during a position holding task in comparison to slow abduction: adduction movements ($\alpha<2x10^{-4}$). Significant differences in *normalised power* were not so apparent and only the index finger showed consistent significant differences in normalised power during position holding and slow movements. This was due to the presence of 8-10 Hz peaks during the position holding task as seen in power spectra of acceleration and rectified EMG traces. However, the incidence of 8-10 Hz peaks was not as common during position holding as during slow movements (table 4.19. and figure 4.24.). The amplitudes of 8-10 Hz peaks in acceleration power spectra were small in comparison to background noise at frequencies over 20 Hz (figure 4.24.).

There were no significant differences in absolute and normalised power between 7-11 Hz when position holding holding was performed in the absence or presence of visual feedback.

Figure 4.24. Averaged power spectra of acceleration traces during position holding in each digit. Recordings lasted 40 seconds with visual feedback provided.

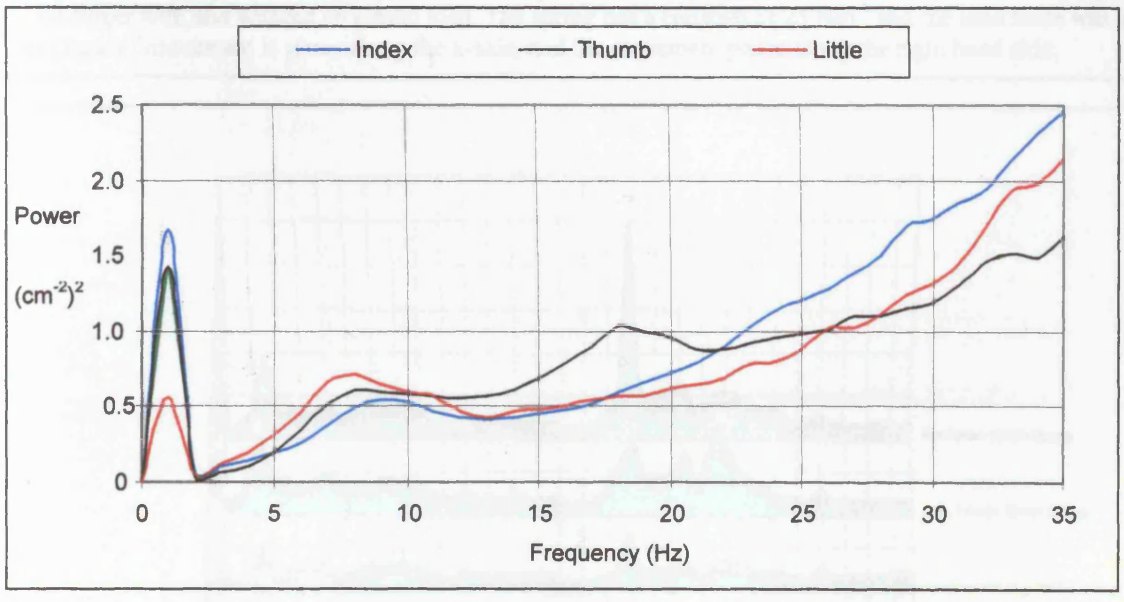


Table 4.19. The percentage of PNI and CTS subjects who showed significant peaks in the range 7-11Hz during position holding using power spectra from acceleration and rectified EMG traces. Values are listed for index, thumb and little fingers in an abducted position. Visual= with a visual target to maintain position, Non-visual=no visual target.

		Acceleration		*Rectified EMG*	
	n	Visual	Non-Visual	Visual	Non-Visual
Index (Ab.-Ad)	28	48.00	40.00	54.17	70.83
Thumb	29	30.77	23.08	38.46	38.46
Little	10	50.00	50.00	80.00	60.00

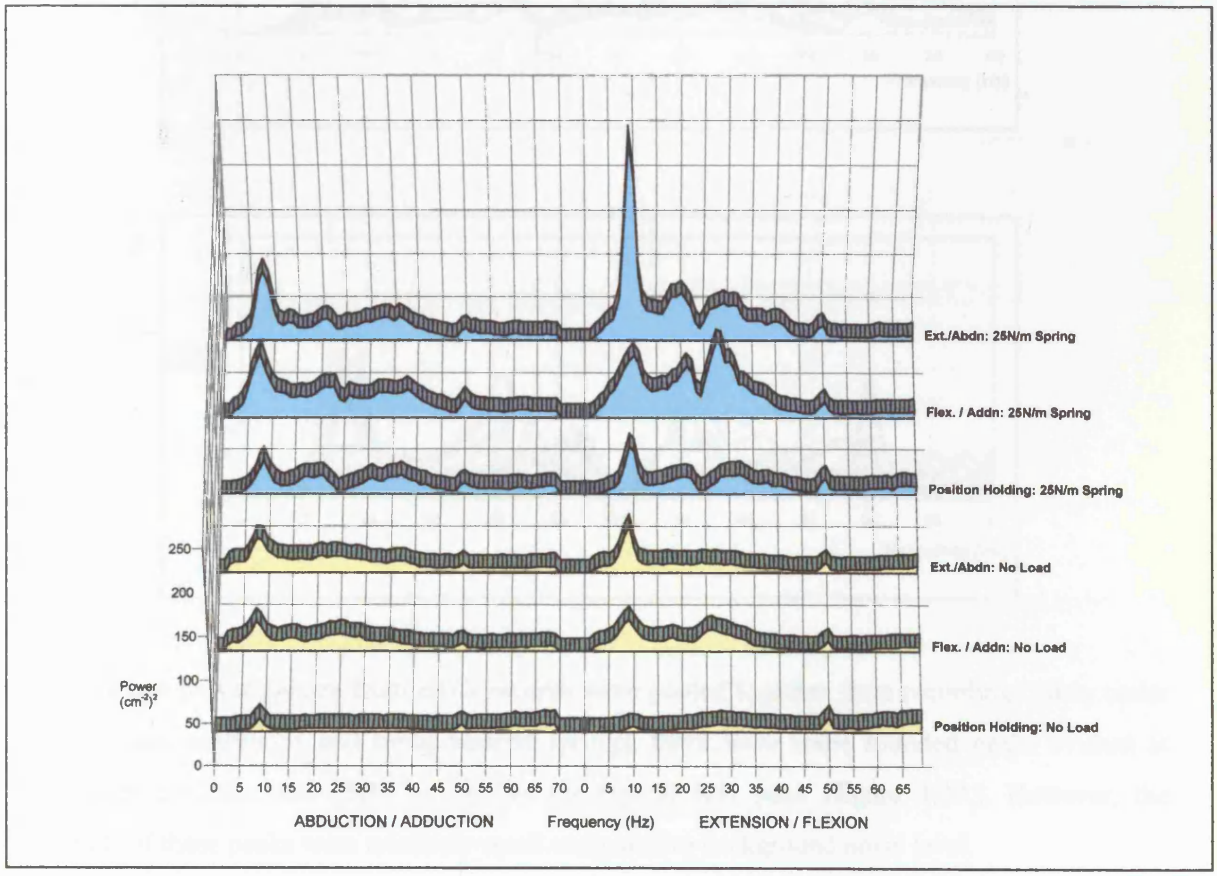
4.2.1.4. Resting Tremor

The presence of small but significant peaks in the range of 7-11Hz (i.e. the five most significant peaks) were evident in the velocity spectra of 34.3%, 17.2%, 50% and 50% of subjects for index, thumb and little finger abduction: adduction moves and for index extension: flexion moves, respectively. Other, higher, frequencies were also evident in spectra of displacement data. In approximately 20% of subjects there were significant peaks in the 22-25 Hz range during both index finger abduction: adduction and extension: flexion moves. In approximately a third of subjects there were significant peaks in the ranges of 15-20 Hz during thumb abduction: adduction moves.

4.2.1.5. Conditions of an Elastic Load

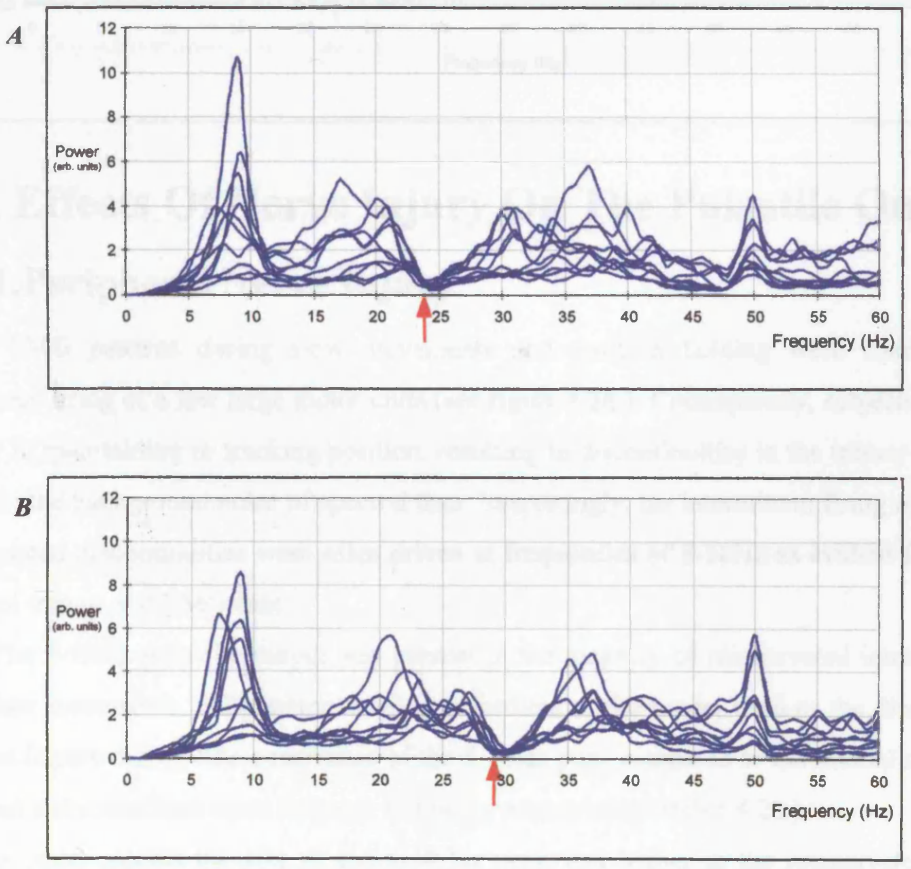
Appling an elastic load to the index finger accentuated 8-10Hz frequency amplitudes during both slow movements and a position holding tasks. Significant differences in *absolute power* were evident for the majority of position holding tasks and extension: flexion moves (appendix 4.12.) (figure 4.25.). These significant differences were not so obvious when using normalised power as a measure of 8-10Hz oscillations.

Figure 4.25. Averaged power spectra of acceleration traces during slow movements and position holding of the index finger with and without an elastic load. The spring has a constant of 25 Nm^{-1} and the load force was 2.5 N. The plane of movement is given along the x-axis, and the movement phase along the right hand side.



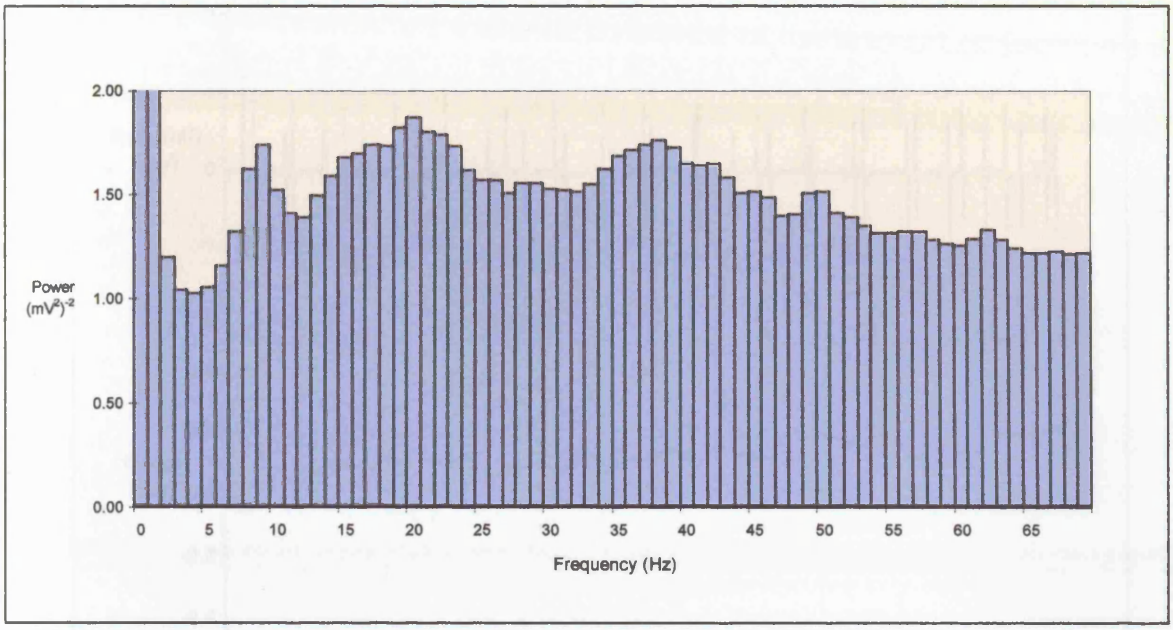
It became apparent, by varying the spring constant of the elastic load, that the spring absorbed a certain frequency equivalent to the longitudinal resonance frequency of the spring. Rather than there being discrete frequency peaks between 15-45 Hz, there seemed to be a broad band elevation of power between 15 and 45 Hz which was subject to the dampening effect of the spring at its resonance frequency (figures 4.26.). The spring would absorb at the resonance frequency irrespective of the force applied or whether the movement performed was abduction: adduction or extension: flexion.

Figure 4.26. Individual power spectra of acceleration traces during position holding of the index finger in abduction against two springs of different constants (i.e. 23.5 Nm^{-1} and 29 Nm^{-1}). The applied load was 2.5 N. The spring constant is indicated on the x-axis with a red arrow. Due to the amplification of higher frequencies in the acceleration spectra, 50 Hz noise is also greatly amplified. Each spectral curve has been normalised so that the sum of the values equals 100.



When power spectra from *EMG records* were pooled together from recordings taken under different load conditions and using various springs, there were some rounded peaks evident at frequencies of 20Hz and 38Hz as well as the typical 9Hz peak (figure 4.27.). However, the amplitude of these peaks were relatively small compared to background noise level.

Figure 4.27. A power spectrum representing pooled data of EMG records taken during trials performed during the lifting of various loads of 2.5N, 5.0N and 10.0N using springs of two different spring constants. A large DC component is evident (bins 1 and 2 Hz are off scale). Some very broad frequency peaks are evident at 20Hz and 38Hz and a more discrete peak at 9Hz.



4.2.2. Effects Of Nerve Injury On The Pulsatile Output

4.2.2.1.Peripheral Nerve Injury

EMG patterns during slow movements and position holding were characterised by synchronous firing of a few large motor units (see figure 4.28.). Consequently, subjects often found difficulty in maintaining or tracking position, resulting in discontinuities in the tremor trace and an increase in the background noise of spectral data. Interestingly, the intermittent firing of motor units and associated discontinuities were often driven at frequencies of 8-10Hz as evident from spectral analysis of tremor and EMG data.

The 8-10Hz pulsatile output was present in the majority of reinnervated intrinsic muscles during slow movements and position holding regardless of the model used or the direction of the movement (figure 4.29.). The occurrence of the 8-10Hz peak compared to the normal situation was as frequent and sometimes more frequent following reinnervation (table 4.20.).

In some models the size of the 8-10 Hz peak was higher in the reinnervated hand. For example, during slow movements, absolute 7-11 Hz power was greater in the five median PNI hands compared to contralateral normal hands ($\alpha<0.05$). During position holding, absolute 7-11 Hz power was greater in ulnar PNI hands compared to control hands using both the models of the index and little fingers (n=12 and 9, respectively) (compare figures 4.24. and 4.30.).

Figure 2.28. Raw EMG data and tremor (displacement) evident during a position holding task by the little finger subsequent to ulnar PNI. Large asynchronous spikes are possibly manifestations of motor units which are larger in size but less frequent in number. (subject: DS)

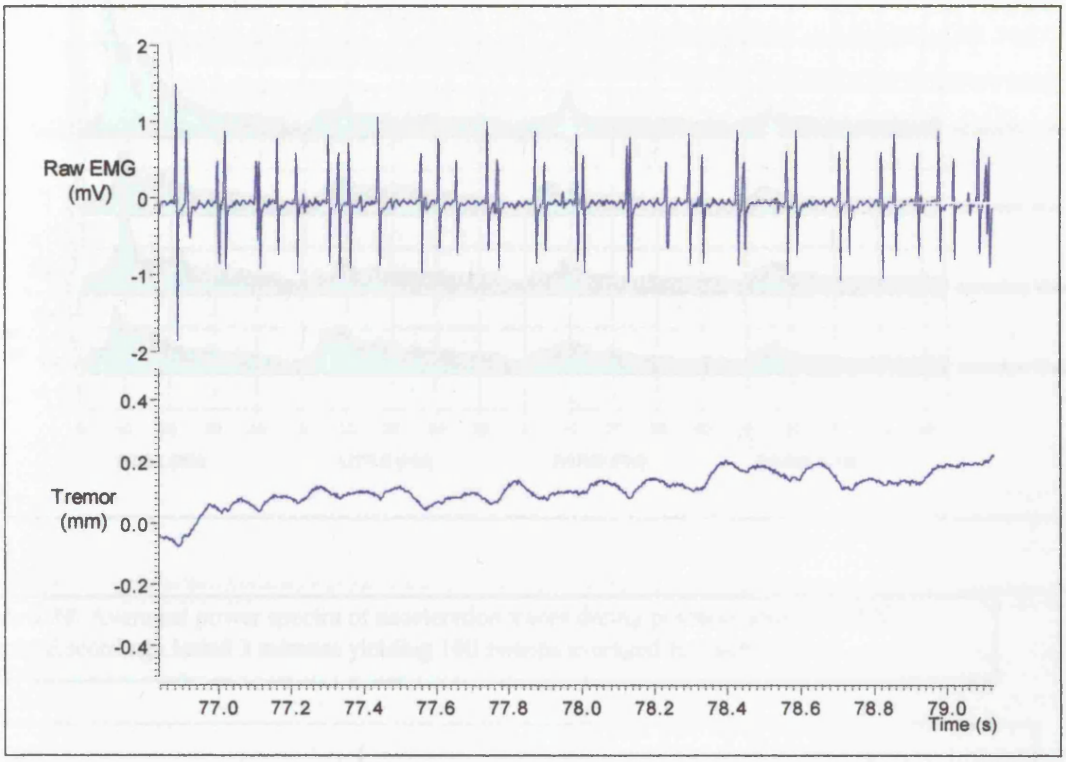


Table 4.20. The percentage of PNI and CTS subjects who showed significant peaks in the range 7-11Hz during slow movements and position holding. Values are listed for index, thumb and little finger abduction: adduction moves.
Abdn=abduction, addn=adduction. Vis= with a visual target to follow, Nvis=no visual target.

I. PNI		SLOW MOVEMENTS					POSITION HOLDING	
	n	Abdn: Vis.	Addn: Vis.	Abdn: Non-Vis.	Addn: Non-vis.	n	Visual	Non-Vis.
TREMOR								
Index	7	100.00	71.43	100.00	71.43	12	25.00	25.00
Thumb	5	80.00	80.00	60.00	80.00	5	60.00	60.00
Little	4	75.00	75.00	50.00	50.00	9	77.78	33.33
All	16	87.50	75.00	75.00	68.75	26	50.00	34.62
EMG								
Index	7	50.00	87.50	75.00	12.50	12	41.67	50.00
Thumb	5	50.00	50.00	50.00	50.00	5	20.00	40.00
Little	4	50.00	75.00	25.00	25.00	9	55.56	55.56
All	16	50.00	75.00	56.25	25.00	26	42.31	50.00

II. CTS		SLOW MOVEMENTS					POSITION HOLDING	
CTS	n	Abdn: Vis.	Addn: Vis.	Abdn: Non-Vis.	Addn: Non-vis.	n	Visual	Non-Vis.
TREMOR	17	64.71	76.47	47.06	64.71	16	18.75	18.75
EMG	17	46.67	53.33	33.33	66.67	16	64.29	42.86

Figure 4.29. Averaged power spectra of acceleration traces during slow 5°s^{-1} velocity tracking movements in PNI and CTS subjects. The recorded digit is given along the x-axis, and the movement phase along the right hand side. Recordings lasted 3 minutes resulting in 15 sweeps averaged for each subject.

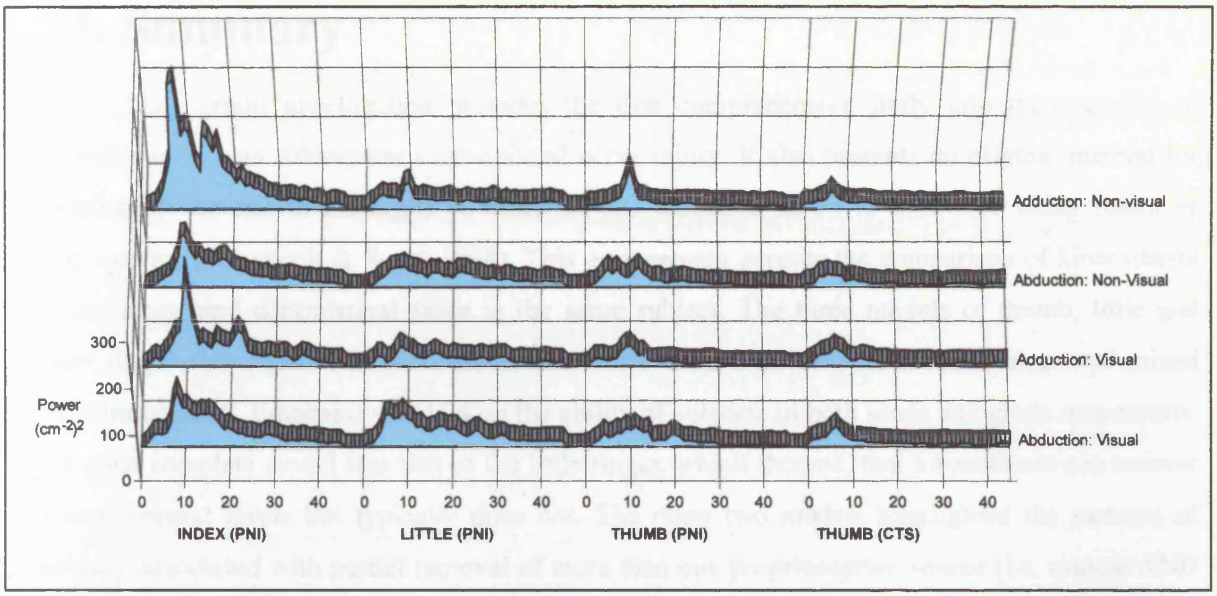
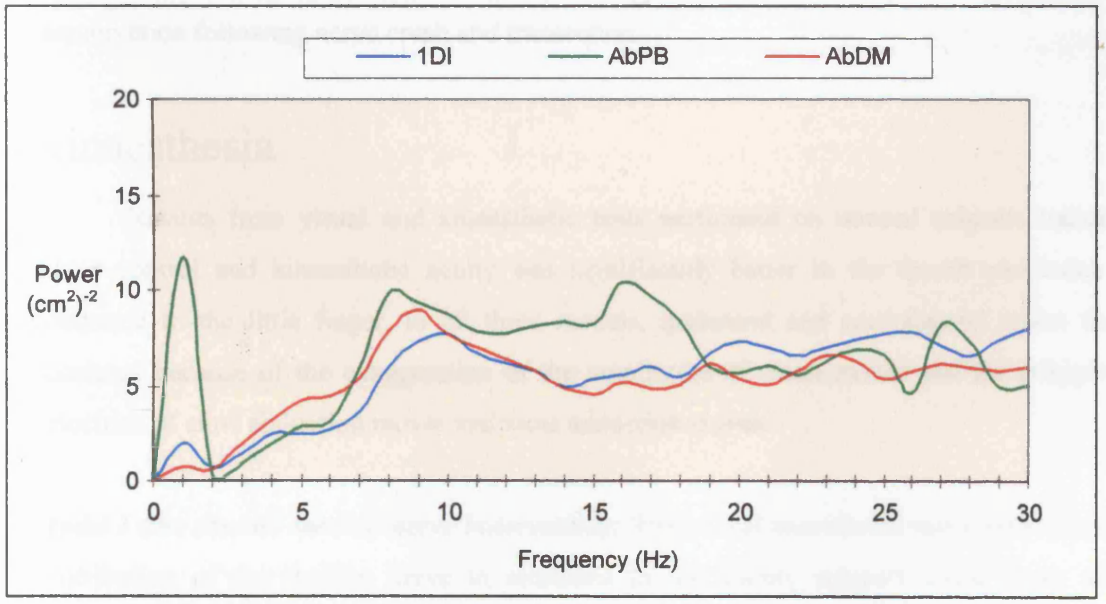


Figure 4.30. Averaged power spectra of acceleration traces during position holding in PNI subjects. Recordings lasted 3 minutes yielding 160 sweeps averaged for each subject.



4.2.2.2. Carpal Tunnel Syndrome

As with PNI, nerve compression of the median nerve did not reduce either the occurrence or size of 8-10 Hz tremor during slow movement or position holding tasks (figures 4.28. and appendix 4.12.). Indeed, absolute 7-11 Hz power was greater in CTS subjects tested compared to controls during most phases of slow movement.

CHAPTER 5: DISCUSSION

5.1. Summary

The current investigation provides the first comprehensive study into the recovery of kinaesthesia in man subsequent to peripheral nerve injury. It also presents an original method for applying movements to the digits in which an AC induction motor is controlled using vector or 'slip' control (Proudlock & Scott, 1998). This arrangement permits the comparison of kinaesthesia on ipsilateral and contralateral sides in the same subject. The three models of thumb, little and index finger abduction: adduction movements were used to investigate median, ulnar and mixed nerve innervation. Emphasis was laid on the ability of subjects to both sense and grade movements. The most complete model was that of the little finger, which showed, that kinaesthesia can recover to near normal levels but typically does not. The other two models highlighted the patterns of recovery associated with partial removal of more than one proprioceptive source (i.e. muscle AND skin/joint in the thumb) or of complete removal of a single proprioceptive source (i.e. muscle OR skin/joint in the index finger).

An additional study into the nature of 8-10Hz tremor in the digits indicated that these oscillations were generated by intrinsic musculature in normal hands and also subsequent to reinnervation following nerve crush and transection.

Kinaesthesia

Results from visual and kinaesthetic tests performed on normal subjects indicated that motor control and kinaesthetic acuity was significantly better in the thumb and index models compared to the little finger. In all three models, ipsilateral and contralateral repeat tests were restricted because of the exaggeration of the amplitudes of small moves and the exaggeration of velocities of slow abduction moves and most adduction moves.

Model 1 (the thumb: median nerve innervation): When local anaesthesia was used to eliminate the contribution of the median nerve to sensation in the thumb, subjects could sense and grade movements with a similar degree of accuracy to controls. These results highlighted how large but incomplete deprivations of sensory sources can still leave a surprising amount of residual kinaesthetic sensation. Additional trials in which both median and radial nerves were anaesthetised demonstrated that a significant contribution of the kinaesthetic sensation in the thumb subsequent to median nerve anaesthesia was due to skin and joint proprioceptors innervated by the radial nerve. The poor correlation between kinaesthetic acuity and standard clinical measures of sensorimotor function was largely due to the fact that cutaneous sensitivities were usually measured in areas not essential for kinaesthesia in the CMC joint of the thumb. An adequate model for assessing the

kinaesthetic contribution of the median nerve, possibly the most important proprioceptive nerve, is still lacking.

Model 2 (the little finger: ulnar nerve innervation): Ulnar nerve anaesthesia had a profound effect on kinaesthesia in the little finger, although even here, loss of sensation was not absolute. Four of the seven subjects could sense at least some of the movements, but subjects were unable grade amplitude and velocity. Sometimes, the moves were sensed in the extension: flexion plane rather than the abduction: adduction plane, which suggests that extrinsic muscles may provide the source for the residual sensation following anaesthesia. Although the normal little finger had poorer motor control and sensation than the thumb and index finger, the little finger model still provided the most complete model for investigating the recovery of proprioception following PNI, since muscle, skin and joint are all innervated by a single nerve.

The little finger model demonstrated that the recovery of kinaesthesia subsequent to long term ulnar PNI is highly variable, ranging from no sensation of movement to complete recovery, in which subjects could sense and grade movements to within normal values. Commonly, subjects could sense movements but showed deficits in the ability to grade amplitudes and velocities. The delay taken to respond to movements was also usually prolonged. These observations agree with animal receptor reinnervation studies that show that there is high variability in the functional restoration of connections and in the recovery of appropriate firing patterns in reinnervated proprioceptors (eg. Terzis & Dykes, 1980; Sanders & Zimmerman, 1986; Banks & Barker, 1989; Lewin & McMahon, 1991a & 1991b). Regression analysis demonstrated that measures of motor and sensory reinnervation correlated well with kinaesthetic recovery in the digit.

Model 3 (the index finger: mixed nerve innervation): Anaesthesia of skin and joint receptors, for example, during median and/or radial nerve anaesthesia in the index finger (and also the thumb), often resulted in range compression or diminution of the amplitudes of repeated or matched moves with the normal hand. This agrees with the observations of Ferrell and coworkers (Ferrell & Smith 1987, 1988, 1989; Ferrell & Milne, 1989). In addition, however, anaesthesia of muscle spindle receptors, as occurs during ulnar nerve anaesthesia of the index finger, resulted in range expansion or exaggeration of movements. This may suggest a difference in the role of muscle receptors compared to skin and joint receptors in kinaesthesia.

Following reinnervation of muscle receptors, index finger kinaesthesia (subsequent to ulnar PNI) was characterised by deterioration in the ability to sense movements and exaggeration when grading amplitudes and velocities. The effects of reinnervation of cutaneous and joint sensation in the index (subsequent to median PNI) were mixed. Typically, subjects were able to sense movements and there was a high correlation between reference and matched movement amplitudes and velocities, however, subjects often either underestimated or overestimated amplitudes and

velocities of movements. The possibility that these observations can be accounted for by differences in recovery patterns of muscle and skin or joint is discussed further.

In both the thumb and index finger models, the ability to grade amplitudes and velocities following median or ulnar PNI was frequently worse than during anaesthetic blocks of the same nerve. This implies that the sensation from reinnervated proprioceptors has the capacity to confound normal residual sensation. Mechanisms underlying this phenomenon are discussed along with programmes that may be used to improve recovery of proprioception.

Pulsatile Output

In the normal hand, 8-10 Hz discontinuities in the power spectra of velocity and acceleration records of slow movement traces were evident in all three models, although most obviously in the index finger. The 8-10 Hz discontinuities were also apparent under conditions of an elastic load, however, higher significant peaks in the range of 20-45 Hz seemed to be an artifact due to the absorption of a discrete frequency by the spring.

The 8-10Hz discontinuities were also evident following reinnervation subsequent to nerve trauma (PNI) and nerve compression (CTS). Indeed, the amplitude and occurrence of significant 8-10Hz peaks were more apparent during position holding than in the normal hand. These results confirm the central origin of the 8-10 Hz pulsatile output and are discussed further.

5.2. Equipment Design

The use of AC induction motor for applying movements to human digits provided many advantages over equivalent pneumatic, stepper or DC brushless motor systems and satisfied most requirements needed for applying physiological movements to limbs and digits (Proudlock & Scott, 1998). Ranges of motion could be set at 20°, 40°, 60°, 90° or 120° using three levels of safety features, i.e. software, electrical and mechanical stops. The resolution (32.4 seconds of arc) and velocity range ($0.009°s^{-1}$ to $90\ 000°s^{-1}$) exceeded original specifications. Monitoring of position could be set to right or left hands. Using digital input/outputs to trigger the motion control module, all trials could be managed from one PC. Problems with stiction in the system were overcome by replacing standard industrial lubricants with low viscocity clock oil. Although an equivalent brushless DC motor system was likely to provide higher dynamic response capabilities, the AC induction motor was significantly cheaper than its DC equivalent. The AC induction motor system was also much easier to configure for free movement of the digit, which was achieved by cutting power to the motor.

Some difficulties were encountered in attempting to reduce system vibration. This presented a serious problem because of the sensitivity of muscle and cutaneous proprioceptors to

vibration (Goodwin *et al.*, 1972; Johansson *et al.*, 1982a; Sittig *et al.*, 1987). A number of methods were used to effectively reduce vibration including replacing the existing optical encoder with a higher resolution encoder, tuning position and velocity loop gains, using a pneumatic cuff to attach the digit to the motor shaft and adding a custom-built antivibration coupling between the motor shaft and digit. There were also problems encountered in controlling torque using the AC induction motor system due to variations in the phase currents and the system compliance introduced with the addition of the antivibration coupling. Although phase currents could be tuned to minimise fluctuations in torque, nothing could be done to reduce the system compliance since this would adversely affect the vibration-reducing capacity of the antivibration coupling. Alternative methods were used to apply forces to the digits involving a mass and pulley arrangement to apply the force at the correct vector (see section 5.5. 'Sense of Force').

In all, the final specifications of the system met most of the original specifications of the system and in a number of cases exceeded them. Although the AC induction motor was used in this study for applying movements to digits, the system would be suitable for applying movements to a number of joints, including the wrist, knee or elbow.

5.3. Kinaesthesia

5.3.1. Normal Tests

The methods used in the present study placed a particular emphasis on the ability to grade the amplitude and velocity of movement. Contralateral movement repeats of applied moves have been used to investigate kinaesthesia in previous studies (Ferrell and Smith, 1987, 1988, 1989; Ferrell and Milne, 1989). However, the index finger PIP joint model used by Ferrell *et al.* was not ideal for investigating proprioception subsequent to PNI. In the current study, normal subjects were recruited to investigate accuracy and consistency in sensing and grading movements of the thumb CMC joint, the little finger MCP joint and index MCP joint, where all movements were applied in the abduction: adduction planes. Particular attention was paid to the motor ability of each digit in performing the movements, the effect of memory, and the loss of proprioceptive information during transfer to the contralateral side. In addition, differences between tensed and relaxed hands and dominant and non-dominant hands were also assessed.

For the majority of movements, normal subjects could accurately match amplitudes and velocities, indicating that the methods provided an adequate means for assessing the ability of subjects to grade movements. There were some areas of weakness. Subjects tended to exaggerate amplitudes of small movements when repeating visually tracked movements (VR) suggesting that the effects of memory limited the accuracy of repeats of small amplitude movements. The same patterns of overestimation were also evident in kinaesthetic IR and CR test results. Similarly, velocities of slow abduction and most adduction moves were also exaggerated during VR, IR and

CR tests. MM test results, however, were not marked by the same exaggeration of small amplitudes or velocities, which suggests that proprioceptive feedback is not the limiting factor in reproducing movements.

Subjects could visually track movements (VT) with a high degree of accuracy indicating that motor control was not the restricting factor upon the tests. Motor control and kinaesthesia were poorer in the little finger compared to the index and thumb.

5.3.1.1. Sensing Movements

Movement Detection

The ability to sense movement was primarily dependent upon amplitude (figure 4.16. p126). Under conditions in which the detection of movements was near threshold, subjects did not generally sense the initial change in velocity of the ramp move, but rather the change in position across the move as indicated by the time delays in response to movements. Accordingly, the tests predominantly discriminated between position sensitivity when kinaesthetic thresholds were approached. The kinaesthetic sensitivities of the thumb and index fingers were slightly higher than in the little finger. The majority of subjects could sense all 12 moves in the index finger and thumb, whereas in the little finger, most subjects could detect 10 or more of the moves (figure 4.3., p104).

Thresholds for 70% correct detection of ramp moves of varying velocities and amplitudes for the DIP joint of the middle finger are given by Gandevia *et al.* (1983). Above $10°s^{-1}$, subjects could sense amplitudes down to 0.8-1.2°, but thresholds increased to approximately 3° at $5°s^{-1}$, 4.5° at $2.5°s^{-1}$ and 8° at $1.25°s^{-1}$. Thus, during abduction and adduction moves in the thumb CMC joint, index finger MCP joint and little finger MCP joint, thresholds were much lower than those recorded for the DIP joint. For example the majority of $1.5°s^{-1}$ moves were sensed down to amplitudes of 1.5° in both the thumb and index fingers.

Differences in threshold may be explained by the more stringent regime used by Gandevia *et al.* in which subjects had to determine the direction of movement for correct detection. Alternatively, it is possible that differences in threshold reflect the variations between the relative changes in the length muscle fascicles during movement in each of the models. After comparing thresholds of muscles of different proximo-distal locations to changes in fascicle lengths in unembalmed cadavers, McCloskey and coworkers concluded that the change in muscle fascicle length determines kinaesthetic threshold (Hall & McCloskey, 1983; Refshauge *et al.* 1995).

Fascicle lengths of extrinsic muscles, which move the DIP joint, are longer than those of shorter intrinsic muscles, which move joints of the thumb, index and little fingers in abduction and adduction. For example, resting fibre lengths of the middle finger divisions of the flexor digitorum profundus and extensor digitorum communis muscles, controlling DIP joint extension and flexion have been estimated at 6.6 cm and 6.0 cm, respectively (Brand & Hollister, 1993). In comparison, estimations of resting fibre lengths of the 1DI and 2PI muscles, controlling index finger abduction:

adduction are 1.5 cm and 1.7 cm, respectively (Brand & Hollister, 1993). Other contributing factors, which will also affect proprioceptive acuity, include the differences in moment arm of each muscle at the relevant joint, which is determined by the anatomical arrangement of the tendon insertion. Also, the interossei and lumbricals have an additional contribution to long digit extension and flexion proprioception although this is likely to enhance acuity.

Response Delays

A number of studies have looked at the delay in response to an applied movement of slow velocity (eg. Barrack *et al.*, 1983; Taylor & McCloskey, 1992; Hall *et al.*, 1994). Typically, the velocity is less than $1°s^{-1}$ and the delay is expressed as an amplitude threshold. In this study, delays were compared for moves applied at a number of different velocities, all of which were above $1°s^{-1}$ and have been expressed in seconds rather than as amplitude.

Proprioceptive response delay (PRD) was principally dependent upon the velocity of the movement (figure 4.4, p105), presumably because the PRD is a measure of amplitude threshold and rate of change of amplitude varies with velocity. For most movements, the visual response delay (VRD) was significantly less than the PRD (table 4.1, p106) suggesting that subjects do not sense the initial change in velocity but rather the change in amplitude. The proportion of moves sensed within a 0.5s time period was used as a measure of how often subjects sensed the initial change in velocity, and consequently of the rapidly adapting proprioceptive system.

Overall, the PRD provided a more discriminative measure of kinaesthetic threshold than sense of movement, probably because delay is a continuous measure, whereas detection is discrete and restricted to only 12 moves. One limitation of the test, however, was that PRD gave a poor measure of adduction sensation because of the cue provided by the abduction move preceding it. Negative VRDs and PRDs observed during adduction moves confirmed that prediction of the movement frequently occured.

5.3.1.2. Grading Movements

Amplitudes

Regression analysis of amplitudes reproduced during motor and sensory tests demonstrated that the capabilities of the normal hand for estimating amplitudes were high. Correlation coefficients were above 0.97 for visual tracking tests and above 0.77 during kinaesthetic tests for abduction: adduction movements (table 4.43. p112). Overestimation of small moves was, however, a restricting factor during repeat tests.

VISUAL TRACKING

By tracking a visual target it could be shown that the motor capabilities of the three digits were not a limiting factor in estimating amplitudes (figure 4.5.A., p108). Mean errors were typically

down to fractions of a degree. Gradients and correlation coefficients of amplitude data were close to unity and intercepts near zero.

Adduction moves were consistently larger than abduction moves because of overshooting at the end of adduction movements. This may be explained by the fact that during abduction, elastic forces of the muscle and tendon would assist braking at the end of the move, whereas during adduction, elastic forces would resist braking. Also, differences may be due to poorer motor control mechanisms during adduction, which is the less important action in all three digits.

VISUAL REPEATS

Consistent patterns in amplitude reproduction emerged when visually tracked movements were repeated. Small 1.5° moves were consistently overestimated, with the error of overestimation decreasing as the amplitude increased (figure 4.5.B., p108). Thus, regression analysis gave intercepts that were high (greater than 2°) and gradients that were less than unity. Correlation coefficients were also high (0.90-0.94) indicating that the pattern of repeating was consistent.

The overestimation of 1.5° moves may be the result of an amplification of the movement amplitude during the memory process, or also because of an inability for sensory feedback to provide an accurate signal during the movement repeat. However, more accurate estimation of amplitudes during MM tests suggests that kinaesthetic acuity is not a limiting factor. Results from VT tests suggest that this error does not result from an insufficiency in motor control. This suggests that the memory process may cause deterioration in the reproduction of small amplitude moves.

During 3° and 6° moves, the degree of overestimation of amplitude increased for faster moves. This phenomenon was not apparent during the IR test, which differed only from the VR test in that the move was sensed through kinaesthesia rather than vision. The error may result from the transformation of the movements from visual coordinates into motor coordinates. Because of the sensitivity of the visual system to movement, it may be possible that the velocity of a move can distort the movement amplitude in the transformation from visual space into motor space.

Accurate estimation of 12° moves indicates that when the amplitude is sufficiently large, the effects of memory errors or the transformation from visual coordinates to motor coordinates become less significant.

IPSILATERAL REPEATS

Similar regression line equations of VR and IR test amplitude data signify that a similar pattern of overestimation of smaller amplitude moves is evident during both tests (figure 4.5., p108). The errors seen during repetition of 1.5° moves during IR tests are also likely to be due to the effects of memory and indicate that repeat tests are deficient at providing accurate measure of the ability to grade a small amplitude. In the methods used by Ferrell *et al.* (Ferrell & Smith, 1987, 1988, 1989; Ferrell & Milne, 1989; Ferrell & Craske, 1992), the joint was moved to one of four positions, each 25° apart, covering a range of 75°. The much larger range used may explain the

absence of errors seen in amplitude reproduction by the normal hand in the experiments of Ferrell and coworkers.

CONTRALATERAL REPEATS

Amplitude matching during IR and CR tests was very similar (figure 4.5., p108 & 4.6.A., p111) as was evident from the absence of significant differences between individual moves or like-amplitude means using the Student's t-test. This meant that IR tests performed by the normal hands of PNI subjects could be safely used as controls for CR tests performed on PNI hands.

MOVEMENT MATCH

The pattern of amplitude reproduction during MM tests differed slightly from those seen during visual and proprioceptive repeat tests (figure 4.6.B., p111). Amplitude estimates were better than those perfomed during repeat tests for small moves but slightly worse than repeat tests for larger moves. The reason for the differences between MM and repeat tests may be related to the effects of the memory component of the repeat tests, which is not evident during MM. It is possible that the memory process may amplify the amplitude of small movements causing a source of error in small amplitude estimates performed during IR and CR tests. Amplitude estimates made during MM tests are also derived differently from those of repeat tests, since they depend on the ability of the subject to grade the velocity of moves correctly to give an accurate measure of amplitude. It may be that this method of amplitude estimation could cause errors when matching larger amplitude moves.

Velocities

During both motor and sensory tests, subjects were less able to reproduce velocities of movements compared to amplitudes. Mean correlation coefficients were between 0.86-0.92 for VT tests and between 0.58-0.79 for kinaesthetic tests (abduction and adduction). Velocity is a much more difficult parameter to compute than amplitude since it depends on derivation with respect to time. Greater errors are likely to result from the more complex sensory processing and motor execution processes involved in reproducing velocity signals.

VISUAL TRACKING

Normal subjects could track visual targets of moves with a reasonable degree of accuracy, with some notable exceptions. Slow velocity moves of 1.5° amplitude were consistently overestimated (figure 4.7.A., p114), so that omitting 1.5° moves from the analysis significantly improved correlations between reference and matched velocities. There was also a slight exaggeration of abduction moves. Both observations could be explained by the effects of a delay in the response to the start of movement. This results in subjects trying to 'catch up' with the visual cue

resulting in exaggeration of the velocity. This effect is likely to be more significant for small moves where less time is available to follow the target once it has been reached and also for slow movements where the difference between reference and matched velocity estimates is likely to be more significant.

VISUAL REPEATS

Slow velocity, 1.5° amplitude moves were exaggerated during VR tests but not IR tests (figure 4.7.B., p114). This may suggest that the errors that resulted during visual tracking tests were being repeated during visual repeats.

Subjects tended to overestimate slow abduction moves and the majority of adduction moves. The effect of the memory process may worsen depending on how long the velocity signal has remained in the memory causing slow movements to be consistently exaggerated. In all models the position of the digits in the abducted position is away from the normal resting position. Adduction movements might be overestimated due to the rapid return of the digit to the resting position where the subject feels more at ease.

IPSILATERAL AND CONTRALATERAL REPEATS

Slow abduction moves and most adduction moves were also exaggerated during both IR and CR tests possibly for similar reasons as suggested for VR tests. Internal factors, such as 'impatience', or external factors, such as the pressure to perform tests as rapidly as possible, may also influence the accurate reproduction of velocity. Slow velocity, 1.5° moves were reproduced more consistently during proprioceptive repeats compared to visual repeats. This suggests that some of the errors in repeating slow velocity 1.5° moves during VR tests are related to problems associated with tracking visual targets. Correlation between reference and matched velocities were higher if 1.5° moves were omitted from analysis of IR and CR velocity estimates.

Velocity reproduction during IR and CR tests was again very similar with only minor significant differences between data sets (figures 4.7.C., p114 & 4.8.A., p116). As a result, velocity estimates performed during IR tests were used as control data for CR test velocity estimates.

MOVEMENT MATCH

Correlation of reference and matched velocities during MM tests yielded lower intercepts than during repeat tests indicating that the movement matching was a better test for measuring velocity estimation (figure 4.8.B, p116). It is likely that estimates of slow velocity and adduction moves are more accurate during MM tests because there is no memory element involved. Correlation coefficients and gradients were all closer to unity and intercepts closer to zero if 1.5° moves were omitted from analysis.

5.3.1.3. Effects Of Muscle Contraction

The degree of muscle contraction, measured by the number of moves during which muscles showed EMG activity, was highly variable even though subjects were instructed to remain relaxed throughout trials (figure 4.2. p103). The number of subjects maintaining relaxation was highest during the passive Dn test. This indicates that subjects found it particularly difficult to maintain relaxation during tests in which they actively had to reproduce movements. A number of authors have reported differences in proprioceptive sensitivity because of relaxation or tensing of muscles during tests (Paillard & Brouchon, 1968; Gandevia & McCloskey, 1976; Colebatch & McCloskey, 1987; Taylor & McCloskey, 1992). In particular, Gandevia and McCloskey (1976), mention that when joint and skin afferents are under local anaesthesia, variations in muscle contraction cause high variability in kinaesthesia in the DIP joint.

The degree of muscle contraction did not have a large effect upon the measures of kinaesthesia used on the three models in the normal hand. The only consistent differences were seen during adduction moves in the index finger where muscle contraction caused shorter response delays and a deterioration in the ability to match velocity during MM tests. However, it is possible that prediction of adduction moves, which was more marked in the index finger, may underlie these differences. Subjects who are more tense might have a tendency to anticipate movements more than relaxed subjects.

Alternatively, the differences might be explained by the effect of the fusimotor system upon the 1DI muscle, whose level of activity is recorded by EMG. In the relaxed muscle, stretching of muscle during adduction causes primary and secondary muscle spindles to fire in relation to the position and velocity of the movement (Vallbo, 1974a; Edin & Vallbo, 1990; Grill & Hallett, 1995). An increase in fusimotor drive, accompanying muscle contraction, causes spindle discharge rates to increase but the firing bears a much less consistent relationship to position and velocity (Vallbo, 1974b; Hulliger & Nordh, 1981; Hulliger, Nordh & Vallbo, 1982). Thus, increased firing rates at the commencement of movements may account for reduced delays, whereas more complex firing patterns may have a detrimental effect on the ability to grade movements, especially velocity.

It has been suggested that joint and skin afferents can provide cues by which the position and velocity can be derived independently of fusimotor activity. In the absence of these cues, muscle contraction can cause errors in position matching (Ferrell & Smith, 1989). Interestingly, the effects of muscle contraction in the index finger were not apparent in the thumb. It is possible that the much larger area of dorsal skin stretched during thumb abduction: adduction may account for differences in proprioceptive weighting between inputs from muscle afferents and joint/skin afferents during abduction and adduction movements in the thumb and index finger. These early observations could be pursued further in a more rigourous investigation.

5.3.1.4. Differences Between Dominant And Non-Dominant Hands

All three digits of dominant hands could track visual cues with a higher degree of accuracy than those of non-dominant hands because of the superior motor control in the dominant hand. These differences were minimal compared with the errors associated with sensation and memory. Thus, during VR tests, only a few moves in the index finger were significantly different between dominant and non-dominant hands, and there were no significant differences during IR tests. There were also no significant differences in detection and delay tests between dominant and non-dominant hands during visual or proprioceptive tests.

Dominant hands were consistently more accurate at matching velocity compared to non-dominant hands during VT tests. This emphasises the complex motor control mechanisms needed to match the velocity of a visual target and the superior control of the dominant hand.

Comparisons of dominant and non-dominant 1DI muscles have demonstrated that, although there may be no differences in maximal voluntary contraction (Tanaka, McDonagh & Davies, 1984; Adams, DeLuca & Erim, 1998), motor units in the dominant 1DI muscle are significantly lower with respect to recruitment threshold, initial firing rate, average firing rate at target force and discharge variability (Adams, DeLuca & Erim, 1998). Adams *et al.* (1998) suggest that differences in the proportion of slow twitch fibres in dominant and non-dominant 1DI muscles may underly these differences. It has also recently been shown that hemispheric differences also exist in the cortical somatosensory representation of dominant and non-dominant hands (Soros *et al.*, 1999).

5.3.2. Consequences Of Peripheral Nerve Impairment

5.3.2.1. Model 1: Median Nerve Innervation (Thumb)

The Normal Hand

Results from visual and kinaesthetic tests performed on 55 normal subjects demonstrated that the normal thumb is under powerful motor control and has a high degree of kinaesthetic acuity. The thumb performed better than the little finger for nearly all motor and sensory tests but had comparable kinaesthesia to the index finger. The thumb was worse at tracking visual targets compared to the index finger but more accurate at repeating visually tracked moves.

For the majority of motor and sensory tests, performance during thumb adduction moves was consistently poorer than during abduction moves. Delays were significantly worse during thumb adduction moves compared to index finger adduction moves. For example, mean delays (± standard error) of $1.5°s^{-1}$ like-velocity moves were 0.478s (±0.061) in the index and 0.716s (±0.089) in the thumb. Repeated adduction amplitudes and velocities were consistently overestimated particularly during VR and IR tests.

A number of reasons may explain these findings:

1. The anatomical arrangement of the thumb greatly differs from that of the long digits. In abduction: adduction, the thumb has a wide range of motion around the CMC joint (approximately 80° for passive movement, Pelastanga, Field & Soames, 1994). The resting position of the thumb is also in a midrange position permitting a greater range of error in adduction beyond the resting position. Conversely, the MCP joints of the long digits have smaller ranges in abduction: adduction (approximately 40-60° for passive movement) and adduction past the resting position is further obstructed by adjacent digits.
2. Thumb adduction is a much less significant action than thumb abduction with less specialised musculature. It is likely to have much poorer motor control mechanisms.
3. Kinaesthetic acuity may be higher during abduction compared to adduction. For example, the joint capsule and skin overlying the CMC joint are both stretched during the abduction movement.

Anaesthetic Models

MEDIAN NERVE ANAESTHESIA

Although many subjects reported a sense of deadness in the thumb, a surprisingly high degree of residual kinaesthetic sensation was present following median nerve anaesthesia. Anaesthetised subjects were as able to sense moves and reproduce amplitudes and velocities as under control conditions (figure 4.11., p120 & 4.13. p122). However, there were some significant differences between anaesthetised and control hands; delays were extended significantly in median nerve anaesthetised hands for both $3°s^{-1}$ and $6°s^{-1}$ abduction moves.

The median nerve is the major source of innervation in the thumb, innervating more of the intrinsic musculature, skin and joint than both the radial and ulnar nerves together. Following median nerve anaesthesia, the thumb still has remarkable kinaesthetic sense given that this primary sensory source has been removed. There are a number of sources of sensation remaining subsequent to anaesthesia of the median nerve, which may account for the residual kinaesthesia:

- Some intrinsic thumb muscles are innervated by the ulnar nerve, namely, adductor pollicis, first dorsal interosseus and sometimes flexor pollicis brevis, although none of these have a direct action in thumb abduction: adduction (figure 1.4., p29).
- The extrinsic muscles, extensor pollicis longus, abductor pollicis longus and extensor pollicis brevis also adduct and extend the thumb and are innervated by the posterior interosseous branch of the radial nerve. In particular, the extensor pollicis longus is the prime mover in the action described as adduction (more correctly adduction: extension) in the thumb model used.
- A large area of skin over dorsal surface of the MCP and CMC joint of the thumb is innervated by superficial terminal branch of the radial nerve (figure 1.5., p30).
- The innervation of the CMC thumb joint is uncertain. Most anatomical texts report that the anterior interosseus nerve (arising from the median nerve high up in the forearm), and the

posterior interosseus nerve (a deep branch of the radial nerve) supply the CMC joint of the thumb (eg. Grays anatomy, 1995; Palastanga, Fields & Soames, 1994). However, a recent study on wrist joint innervation by Fukumoto *et al.* (1993) reported that the dorsal aspect of the thumb CMC joint receives innervation from the superficial branch of the radial nerve, and the palmar aspect from the lateral (antebrachial) cutaneous nerve also derived from the radial nerve. Further complications are added by communicating branches between superficial radial nerve and the posterior and lateral cutaneous nerves. Which ever of these nerves innervates the CMC joint, however, it is of interest that the innervation of the thumb CMC joint is not significantly affected by median and ulnar nerve injury at wrist level.

The findings stress that high levels of proprioceptive acuity are possible even in the absence of major sources of normal proprioceptive sensation in the hand. Many authors have investigated the effect of removing a single proprioceptive source upon kinaesthesia in the hand, such as the contribution from all muscle receptors or all skin/joint receptors (eg. Provins, 1958; Gandevia & McCloskey, 1976; Clark *et al.*, 1979; 1985; Gandevia *et al.*, 1983; Ferrell, Gandevia & McCloskey, 1987; Ferrell & Smith, 1987, 1988, 1989; Ferrell & Milne, 1989; Clark, Grigg & Chapin, 1989; Taylor & McCloskey, 1990a, 1992; Ferrell & Craske, 1992; Edin & Johansson, 1995). Removal of a single proprioceptive source usually results in deterioration, but not complete loss of kinaesthesia. Under median nerve anaesthesia all proprioceptive sensory sources are partially removed, rather than complete removal of a single source. This scenario also results in deterioration but by no means a complete loss of proprioceptive acuity.

MEDIAN AND RADIAL NERVE ANAESTHESIA

During median nerve anaesthesia of the thumb, remaining sensation comes from two main sources. There is residual sensation from the radial nerve innervating dorsal skin and the CMC joint. There is also the contribution of musculature, either extrinsic to the hand, or intrinsic musculature innervated by the ulnar nerve. In order to further explore the contributions of each, combined anaesthesia of both median *and* radial nerves was performed on three subjects.

Detection

Median and radial nerve anaesthesia resulted in a profound loss in the ability to both sense and grade movements (figure 4.10. p120). Only 50% of the moves were sensed by two of the subjects (during the MM test). PRDs were dramatically increased by as much as two or threefold during abduction and adduction moves at velocities of $3°s^{-1}$ and $6°s^{-1}$.

The results suggest that the radial nerve provides a major source of proprioception following the impairment or loss of median nerve function. Microneurographical recordings have revealed that 90% of radial nerve cutaneous afferents respond during movements of the digits (Edin & Abbs, 1991) and that SA I and SA II afferents have high dynamic and static sensitivities to skin stretch (Edin, 1992). Radial nerve joint afferents display a unidirectional firing pattern, with

discharge increasing during flexion of the long digits (Edin, 1990). Both cutaneous and radial afferents appear to code adequately for digit movement and position. Evidence that kinaesthetic sensory input derived from the radial nerve reaches consciousness was provided by Edin and Johannson (1995) who found that illusions of movement could be produced by stretching radially innervated skin over the index MCP joint during digital blocks of the digit. The current findings strongly suggest that the radial nerve is an inportant kinaesthetic source during movements of the thumb also.

The remaining sensation which exists following median and radial nerve anaesthesia, however, demonstrates that the radial nerve is not the only proprioceptive source following median nerve anaesthesia but that extrinsic and ulnar nerve innervated intrinsic musculature also contributes to thumb kinaesthesia.

Grading Movements

Amplitudes and velocities were greatly underestimated particularly during CR tests performed under median and radial nerve anaesthesia (figure 4.13. p122). Ferrell et al. have also described the underestimation of movements, or range compression, seen during anaesthesia of skin/joint during digital nerve blocks of the PIP joint of the index finger (Ferrell & Smith, 1987, 1988, 1989; Ferrell & Milne, 1989). It has been suggested that joint receptors and possibly also slowly adapting skin receptors have a bias towards firing at extremes of the range of motion. (Burke *et al.*, 1988; Ferrell and Smith, 1988; Clark, Grigg and Chapin, 1989; Ferrell and Smith, 1989). When these two sources are removed, the subject does not sense the joint moving out of midrange positions with the result that amplitudes are reduced when repeated.

RADIAL NERVE ANAESTHESIA

The effects of anaesthetising the radial nerve alone were not as dramatic as when both median and radial nerves were blocked. Radial nerve anaesthesia caused a reduction in the ability to sense moves during CR tests but not MM tests. Ferrell and Milne (1989) noted that subjects under digital nerve anaesthesia did not report any sense of movement or change in position during slow movements of the index PIP joint, but invariably moved the digit in the correct direction when asked to do so. Possibly, the absence of facilitation during anaesthesia of the skin causes the conscious appreciation of a movement to diminish. Since muscle spindle input requires summation to reach conscious levels (Vallbo *et al.*, 1984; Macefield, Gandevia and Burke, 1990) it is possible that subconsciously movement is still sensed through muscles spindles input and other remaining sources. The CR test differs from the MM test in that definite affirmation of sense of movement is required from the subject. The two tests may, therefore, operate at different levels of consciousness.

Radial nerve anaesthesia did not result in any significant differences in PRD, amplitude or velocity estimation compared to the normal hand. However, patterns of grading abduction movements varied for the three subjects. This may be an indication that subjects may use different

means in trying to reproduce abnormal sensation resulting from partial sensory deprivation. Alternatively, this may be the result of normal subject variability. More data would be required to make any firm conclusions.

Regression analysis indicates that during both radial nerve anaesthesia and median & radial nerve anaesthesia there is a poor correlation during *adduction* between reference and matched amplitudes and velocities. This observation is opposite to expectation since the areas of skin and joint innervated by the radial nerve are activated by stretching during abduction rather than adduction. The results may indicate that poor mechanisms of kinaesthetic acuity during adduction in the normal thumb are further impaired by removal of radial nerve sensation in the thumb.

Peripheral Nerve Injury

No differences were apparent between controls and median or median & ulnar nerve injured subjects in the detection of movement, although PRDs were prolonged in PNI subjects, especially during faster movements. Significant correlations between reference and matched amplitudes performed by median or median & ulnar PNI subjects were high but were often characterised by underestimation or overestimation. In particular, median nerve subjects tended to overestimate amplitudes during CR tests and underestimate amplitudes during MM tests. Mean correlation coefficients between reference and matched velocities were much lower than correlations between amplitudes (table 4.7.A. & B., pp122-123) highlighting that velocity matching is a more complex task requiring optimal sensory feedback. The small sample sizes of median and median & ulnar PNI groups (n=8 and 6, respectively), high variability with respect to the time since injury, and insufficiencies of the model used for investigating median nerve injury caused difficulties in reaching solid conclusions regarding the effect of median nerve injury in the hand.

The median nerve is a mixed nerve supplying thenar and lumbrical muscles, an estimated 17,000 tactile units in the glabrous skin (Johansson & Vallbo, 1979a), as well as numerous joints in at least three digits. The potential for inappropriate innervation following median nerve injury is high. In particular, spindles of thenar and lumbrical muscles stand a significant chance of being reinnervated by the large number of cutaneous afferents supplying the palmar skin. Numerous authors have reported the poor recovery following sectioning and resuturing of mixed nerves (Collins, Medell & Munson, 1986; Gregory, Luff & Proske, 1982; Ip, Luff & Proske, 1988; Banks & Barker, 1989, 1991; Lewin & McMahon, 1991a & 1991b). Lewin & McMahon (1991a) have shown that cutaneous afferents only poorly reinnervate muscle spindles and do not exhibit the normal slowly adapting response to muscle stretch. The number of stretch sensitive units falls to 41%, compared to 88% in the normal muscle and 67% in muscle reinnervated by muscle afferents. Nearly all of the reinnervated spindles exhibit rapidly adapting responses. Thus, inappropriate reinnervation may account for poor performance with respect to grading movements, following median and median & ulnar PNI.

Since the ability to grade moves was worse following long term median PNI than subsequent to median nerve anaesthesia, it is possible that abnormal firing patterns in reinnervated receptors may confound the normal sensation provided by radial and ulnar nerves and extrinsic musculature. A number of authors have demonstrated from animal models that abnormal firing patterns such as elevated thresholds and absence of static discharge persist in the muscle spindles (Gregory, Luff & Proske, 1982; Banks & Barker, 1989, 1991), Golgi tendon organs (Scott, Davies & Petit, 1995; Scott, Petit & Davies, 1996) and cutaneous receptors (Terzis & Dykes, 1980). Abnormalities are even worse following inappropriate reinnervation and many receptors exhibit properties corresponding to the reinnervating axon rather than the target structure (Lewin & McMahon, 1991a, 1991b). Neglect of the injured hand may also contribute to deterioration in kinaesthesia. Both the effects of abnormal firing of reinnervated receptors and hand neglect are likely to be improved by sensory re-education (Dellon, 1981).

Correlation to Clinical Assessments

During median nerve anaesthesia and PNI, standard clinical measures of thumb sensorimotor function, i.e. MRC grading of the abduction action and Weinstein's filament cutaneous sensitivities at the digit tip, indicated that both sensory and motor function was usually impaired or even absent. However, a high degree of kinaesthetic acuity was present in the thumb when expressed in terms of the ability to sense and grade movements. This discrepancy was, in part, due to the fact that thumb adduction MRC gradings were not taken into account. More importantly, cutaneous sensitivities were recorded in inappropriate areas since the skin is particular sensitive to movement induced stretch (Knibestöl, 1975; Johansson, 1978; Edin & Johannson, 1995).

A more accurate measure of sensation relating to kinaesthesia was that of cutaneous sensory thresholds at the three points around the CMC thumb joint (i.e. dorsal CMC joint, dorsal web space and thenar eminence, figure 3.7., p101). Sensation was high at these three points during median nerve anaesthesia, but much poorer during combined median and radial nerve anaesthesia. This correlated well with the impaired ability of the median and radial nerve anaesthetised subjects to sense and grade movements in the thumb.

5.3.2.2. Model 2: Ulnar Nerve Innervation (Little Finger)

Normal Hand

The potential of the little finger as a model for investigating peripheral nerve injury was restricted by poor motor and sensory function in the normal hand. Compared to the index finger and thumb, the little finger had poorer sense of movement, delays were consistently longer, and amplitude and velocity estimates were significantly worse for the majority of motor and sensory

tests. Accurate tracking of amplitude and velocity during VT tests showed that deficits were primarily due to the effects of memory and poorer kinaesthesia in the little finger.

Differences between the little finger and the index finger or thumb can be explained by considering the functional zones of the hand. Tubiana (1981) describes three zones:

- ***Zone 1: the thumb:*** a highly mobile digit which flexes at right angles to the other digits to allow thumb opposition.
- ***Zone 2: the index and middle fingers:*** which act together with the thumb to form the dynamic tripod which performs precision grip and tasks of fine manipulation.
- ***Zone 3: the ring and little fingers:*** which provide a very strong flexion action important in power grip and also provide a stable base upon which the dynamic tripod can function.

Kinaesthesia is of prime importance in the three radially situated digits because of their role in fine manipulatory tasks. The need for intricate proprioceptive mechanisms of feedback in zone 3 digits is not so great. Thus, kinaesthetic acuity in the little finger is likely to be less compared to the index and thumb. The importance of the abduction: adduction action of the little finger is to position the digit ready for grasping objects. This crude action is not likely to be under as powerful mechanisms of motor control as those that exert influence over actions such as thumb and index abduction: adduction.

Anaesthesia

Anaesthesia of the ulnar nerve had a profound, but predictable, effect upon kinaesthesia in the little finger since most if not all the skin, muscles and joints in the medial third of the hand are innervated by the ulnar nerve. However, in more than half of the anaesthetised subjects, anaesthesia did not completely abolish sensation of abduction: adduction movements. In the movements that were detected, delays were greatly prolonged and subjects could neither grade amplitude or velocity of the movements.

It is possible that the residual sensation in the little finger following ulnar nerve anaesthesia may be the result of incomplete anaesthesia or from sensation arising from more distant areas of skin that are stretched during movements (Edin & Abbs, 1991). In one subject, aberrant cutaneous innervation patterns meant that some sensation was remaining towards the ulnar border of the dorsum of the hand which might detect movement. However, the fact that the majority of subjects sensed movements in the flexion-extension plane, rather than in the abduction: adduction plane, suggests that extrinsic muscles may provide the source of sensation following anaesthesia. Brand & Hollister (1993) mention that the extensor digiti minimi tendon has a tendency to deviate to the ulnar side of the little finger MCP joint causing it to have a extensor: abductor action. This muscle is, therefore, a good candidate for the source of residual sensation in the little finger subsequent to ulnar nerve anaesthesia.

Compared to the index finger and thumb models, the little finger provides the most complete model for investigating recovery of proprioception following PNI. Of the three paradigms, it came closest to providing a system that is wholly innervated by a single nerve. The model is, however, restricted by the poorer sensation of the normal little finger and the unanticipated possible contribution of the extrinsic muscles as an additional proprioceptive source.

Peripheral Nerve Injury

The little finger model was used in 16 long term ulnar nerve injured subjects to demonstrate that recovery of proprioception subsequent to nerve injury is extremely variable. The degree of recovery of movement sense varied from no sensation to full recovery. Two subjects sensed no movements at all. At the opposite end of the spectrum, two subjects sensed over 10 out of the 12 movements (figure 4.15., p126). For the majority of subjects the number of moves detected was few, delays were abnormally prolonged, and amplitude and velocity estimations were extremely poor. There was a significant correlation between reference and matched amplitudes in 6 subjects (MM test) and between reference and matched velocities in 3 subjects (MM test) (see tables 4.9.A. & B, p128). However, a small number of the subjects could grade movements with the same degree of accuracy as controls.

Animal studies have demonstrated that there are a number of factors that can cause variability in functional reinnervation of proprioceptors:

1. ***The Effects of Prolonged Denervation:*** This can lead to atrophy and degeneration of target structures. Muscles undergo a rapid reduction in mass due to loss of protein content as mediated by myogenic regulatory factors (Davis & Kiernan, 1981; Adams *et al.*, 1995). Kobayashi *et al.* (1997) have shown that in rats, denervation periods of more than one month result in a profound loss of muscle mass following reinnervation. Fu and Gordon (1995a, 1995b) have shown that prolonged denervation resulted in less than 50% of nerve fibres reinnervating muscle.

   Muscle spindles (Boyd, 1962; Poppele, 1993; Zelená, 1994), Meissner corpuscles (Dellon, Witebsky & Terrill, 1975) and Merkel cell receptors (Nurse, Macintyre & Diamond, 1984; Mills, Nurse & Diamond, 1989) all undergo a significant degree of atrophy following denervation. However, Golgi tendon organs (Zelená, 1994), Pacinian corpuscles and joint Ruffini endings (Sasamura, 1986), do not atrophy to any great degree following denervation.

2. ***Number of Fibres Reaching End Organs:*** Transection of a peripheral nerve can result in impaired reinnervation because axons may also be lost into foreign tissue and commonly result in neuroma formation. Epineural and perineural primary repair or delayed secondary repair of the transected nerve are performed to ensure the largest number of axons enter into the distal stump (Sunderland, 1978; Scott, 1986; Shaw, Wilgis & Brushart, 1993; Barker, Berry & Scott,

1990). However, the condition of the nerve following trauma and successfulness of the repair influence the degree of recovery.

The mixed content of a nerve, which affects the proportion of available targets for reinnervating axons, also affects the degree of successful reinnervation (Banks and Barker, 1989, 1991). The location of receptors further from reinnervating axons may result in poor innervation. For example, Golgi tendon organs are located further from the nerve entry point compared to the spindles and subsequently receive less innervation subsequent to nerve trauma (Collins, Mendell & Munsen, 1986).

3. ***Inappropriate Reinnervation of Receptors:*** Following nerve crush, appropriate reinnervation of target organs results in excellent sensory and motor recovery (Hyde & Scott, 1983; Barker, Scott & Stacey, 1985; 1986; 1988; Sanders & Zimmerman, 1986; Scott, Davies & Petit 1995; Scott, 1996; Scott, Petit & Davies, 1996). Following nerve trauma and resuturing, there is the potential for reinnervation of incorrect structures.

   When muscle afferents reinnervate muscle sensory structures, functional abnormalities often persist in spindle and GTO responses, such as the absence of resting or maintained discharge (Gregory, Luff & Proske, 1982; Banks, Barker & Brown, 1985; Banks & Barker, 1989, 1991; Scott, Davies & Petit 1995; Scott, Petit & Davies, 1996). However, all three types of muscle afferents, Ia, II and Ib, appear to be able to establish functional connections with all three sites (Collins, Mendell & Munson, 1986; Banks & Barker, 1989). Also, when cutaneous afferents reinnervate skin, tuning curves for Meissner corpuscles and Merkel cells are often elevated but return to normal over ensuing months (Terzis & Dykes, 1980; Mackel *et al.*, 1983). In the human, Meissner corpuscles and Merkel cells recover successfully whereas Pacinian corpuscles appear to be poorly reinnervated (Dellon, 1981). Little data exists concerning the reinnervation of Ruffini endings.

   Cross reinnervation experiments of muscle and cutaneous nerves in the rat demonstrate that many muscle afferents form low threshold connections with cutaneous targets but that a high percentage of these responses are slowly adapting (Lewin & McMahon, 1991b). Conversely, when skin reinnervates muscle, the number of stretch sensitive units falls to half of the proportion of units in the normal muscle (Lewin & McMahon, 1991a). Nearly all of the responses are rapidly adapting.

Results from kinaesthetic tests showed that PNI subjects could often sense movements but could not grade amplitudes and velocities. The probabilty of axons reaching a target structure and displaying some kind of mechanoreceptive response is much higher than the probability of those target structures exhibiting responses appropriate to the type of receptor reinnervated. The ability to grade movements relies on appropriate slowly and rapidly adapting responses in response to movement. The poor recovery of the ability to grade movements following reinnervation is likely to

be due to the abnormal tonic and phasic afferent firing patterns in response to movement (Terzis & Dykes, 1980; Sanders & Zimmerman, 1986; Banks & Barker, 1989; Lewin & McMahon , 1991a & 1991b; Scott, Petit & Davies; Scott, 1996).

Correlation to Clinical Assessments

The wide spread in the degree of kinaesthetic sensation in normal, ulnar anaesthetised and ulnar PNI hands permitted a comparison of measures of sensorimotor function to kinaesthetic sense (figure 4.18., p130). The highest correlations between data sets were evident when cutaneous sensitivity around the MCP joint (Weinstein's filaments) and measures of motor recovery (MRC testing) were combined additively. This stresses again that kinaesthetic acuity is dependent upon the combined sensation derived from the sources of both muscle and skin/joint (Gandevia & McCloskey, 1976; Gandevia *et al.*, 1983; Ferrell, Gandevia & McCloskey, 1987).

5.3.2.3. Model 3: Mixed Innervation (Index Finger)

Normal Hand

The normal index finger was able to perform motor and sensory tasks with a similar degree of accuracy as the thumb but a higher degree of accuracy than the little finger.

Adduction PRDs were consistently less than abduction PRDs in the index finger. This may be due to higher kinaesthetic sensitivity during index finger adduction in comparison to the thumb and little finger. Alternatively, the restricted range of motion in index finger (approximately 50°, compared to 80° and 57°, for the thumb and little fingers, respectively; Palastanga, Field & Soames, 1994) may cause subjects to initiate adduction moves more rapidly.

Anaesthesia

The different anaesthetic models applied to the index finger allowed comparison to be made between the contribution of muscle receptors whose effects are removed by ulnar nerve anaesthesia, to the contribution of skin and joint receptors, whose effects are removed by median and/or radial nerve anaesthesia. In the case of ulnar nerve anaesthesia, the contribution of the dorsal and palmar interosseus muscles are removed but not the median innervated lumbrical muscles (LUM1 & LUM2). Median and radial nerve anaesthesia completely removes the contribution of receptors in dorsal and palmar skin and of the receptors in the underlying joints.

DETECTION AND DELAY

Deficits in sense of movement and PRD resulted from all four paradigms of median, ulnar, median & radial and radial nerve anaesthesia. (where $\alpha<0.1$ for median & radial and radial nerve anaesthesia) (see figure 4.21., p133).

These findings are in agreement with those of Gandevia, McCloskey and coworkers (Gandevia & McCloskey, 1976; Gandevia *et al.*, 1983; Ferrell, Gandevia & McCloskey, 1987) who compared detection thresholds in the DIP joint of the middle finger when the contribution of muscle, skin and/or joint receptors were selectively removed by muscle disengagement or anaesthesia. They found that acuity was highest when all the proprioceptive machinery was intact. Removal of any single proprioceptive source caused a deficit to a greater or lesser extent.

The model of index finger MCP joint abduction: adduction differed from that used by Gandevia and McCloskey in that extension: flexion of the middle finger DIP joint is mainly controlled by long muscles whose tendons cross a series of articulations before reaching the distal phalanges. It could be argued that the contribution of cutaneous and joint receptors in and around the DIP joint may have a particular significance because of this complicated arrangement of muscles and tendons controlling the joint. The results from this study show that skin and joint innervation are also important where musculature controlling the joint is in the form of shorter intrinsic muscles, which only principally act upon one articulation.

AMPLITUDE

A consistent pattern emerged during tests of amplitude estimation performed under anaesthesia. During anaesthesia of the skin and joint, i.e. median & radial nerve anaesthesia, larger amplitude moves tended to be underestimated during CR tests (figure 4.23., p135). This was similar to the pattern seen during median & radial anaesthesia in the thumb. During anaesthesia of musculature, i.e. ulnar nerve anaesthesia, smaller moves tended to be overestimated by subjects during MM tests.

Ferrell *et al.* found that anaesthesia of the skin and joint receptors in and around the PIP joint of the index finger produced a characteristic pattern of amplitude reproduction (Ferrell & Smith, 1989; Ferrell & Milne, 1989). Matching the position of an anaesthetised finger with an unanaesthetised finger resulted in range compression, i.e. the moves were underestimated, whereas matching the position of an unanaesthetised finger with an anaesthetised finger gave rise to exaggeration of movements, or range expansion. In both cases the moves were sensed as being underestimated when the digit was under anaesthesia. The current study adds a further scenario in which removal of the contribution of muscle afferent input results in range expansion during anaesthesia, the opposite of the pattern seen during anaesthesia of skin. The reason this phenomenon can only be observed during the MM test is probably because of the defiencies in the repeat tests for measuring small amplitude estimation which tended to be exaggerated during the repeat process.

It has been well documented that joint receptors fire when a joint is under stress, which occurs towards the extremes of the range of motion (eg. Grigg & Hoffman, 1982; Burke *et al.*, 1988; Clark, Grigg & Chapin, 1989; Grigg & Hoffmann, 1991; Grigg, 1994). When Ferrell *et al.* anaesthetised the index finger PIP joint capsule in one subject, this resulted in errors in amplitude

reproduction towards the extremities of the range of motion but not in the midrange (Ferrell & Smith, 1988, 1989). Similarly, FA II cutaneous receptors are selectively responsive to skin stretching (Knibestöl, 1975; Johansson, 1978; Edin & Abbs, 1991; Edin & Johansson, 1995) which is optimal at extreme joint positions, especially during flexion. It is possible, therefore, that joint and skin receptors may have a bias towards coding positions towards the extremities of the range of joint motion, whereas muscle spindle receptors are biased toward firing in the midrange of motion. The patterns of range compression or underestimation of amplitude seen during anaesthesia of skin and joint receptors could be explained by the fact that subjects do not perceive that the joint moves out of midrange positions. Commonly, subjects report a sense of the anaesthetised digit being 'wrapped in cotton wool' (Ferrell & Milne, 1989). This may be due to the resulting conflict between the efference copy signal and sensory feedback.

The overestimation of small amplitudes seen during the MM test may be the reverse effect of what is observed during skin and joint anaesthesia, i.e. a deterioration in the ability to grade midrange moves when muscle is anaesthetised. Alternatively, it is possible that because the removal of the contribution of muscle receptors eliminates position sense (Horch, Clark & Burgess, 1975; Clark *et al.*, 1985, 1986, 1989; Taylor & McCloskey, 1990) subjects find it much more difficult to grade small amplitude moves. During large amplitude moves subjects may be able to derive an accurate position signal from the velocity of the move.

VELOCITY

During median or ulnar nerve anaesthesia, medium velocity moves ($3°s^{-1}$) were consistently overestimated during abduction moves in both CR and MM tests. During median and median & radial nerve anaesthesia, there were also some deficits in the ability to reproduce velocities. Grill and Hallett (1995) have recently demonstrated that both secondary spindle afferents and SA II cutaneous receptors fire in relation to velocity of $5\text{-}80°s^{-1}$ moves at the MCP joint. It is conceivable that removing either source could have a detrimental effect on estimating velocity.

Peripheral Nerve Injury

Ulnar PNI: Ulnar nerve injury had a more detrimental effect upon kinaesthesia in index finger abduction: adduction than median nerve injury causing deficits in both detection and PRD. Correlations between amplitudes and velocities of reference and reproduced moves were high but abduction and adduction moves were also consistently overestimated during CR tests performed on ulnar nerve injured subjects (figure 4.23., p135).

A number of suggestions may be submitted to explain the kinaesthetic deficits apparent in the index finger subsequent to ulnar nerve injury.

1. The intrinsic musculature controlling index finger abduction: adduction, i.e. the 1DI and 2PI muscles are innervated by the deep terminal branch of the ulnar nerve. This nerve branch follows a course through the ulnar aspect of the hand supplying muscles of the hypothenar

eminence before it crosses the hand to supply lumbrical and interosseii muscles. Towards the terminal end of the branch, it supplies the 2DI and 1DI muscles, along with AP and occasionally FPB. This means that following transection and reinnervation there are many different routes by which nerve fibres can be misdirected before reaching the 1DI and 2PI muscles.

2. Increased denervation periods, resulting from the longer route, reduce the likelihood of appropriate reinnervation (Fu & Gordon, 1995a, 1995b; Kobayashi *et al.*, 1997).
3. Another reason why ulnar nerve injury may have such a profound effect on kinaesthesia is because of the possibility that muscle receptors may be the primary sensory source of position sense (Horch, Clark & Burgess, 1975; Clark *et al.*, 1985, 1986, 1989; Taylor & McCloskey, 1990a). The slowly adapting responses of muscle spindles recover more slowly than rapidly adapting responses following nerve crush (Gregory, Luff & Proske, 1982; Banks, Barker & Brown, 1985; Banks & Barker, 1989, 1991, Scott, 1996). Following transection, recovery of tonic responses may be absent if reinnervation is by inappropriate nerve fibres (Banks & Barker, 1989; Lewin & McMahon, 1991b; Scott, 1996). This suggests that recovery of position sense might be poor or even absent following PNI. Further investigation of the recovery of position sense following reinnervation of muscle could easily be achieved using techniques similar to Clark *et al.* by applying very slow velocity moves to determine the presence or absence of absolute position sense in the index.

The results suggest that kinaesthesia subsequent to ulnar PNI is worse than during ulnar anaesthesia. This could be because inappropriate innervation may confound the normal sensation provided by skin and joint receptors. Misinterpretation of incoming signals may also result from a discrepancy between the efference copy signal and the motor output because of defective motor reinnervation. Improvements might be made by adapting current techniques of sensory reeducation, used to improve cutaneous sensation for developing the recovery of proprioception (Parry, 1976; Dellon, 1981).

Median and Median & Ulnar PNI: In the case of median PNI only, movement sense was similar to control values and differences in delays were only evident during $3°s^{-1}$ adduction movements. Animal studies have shown that reinnervation of FA I and SA I receptors following PNI is very good and regeneration or even neoformation of the receptors is possible (Burgess *et al.*, 1974; Terzis & Dykes, 1980; Dellon, 1981; Nurse, Macintyre & Diamond, 1984; Mackel *et al.*, 1983). Recovery of FAII receptors is much poorer (Terzis & Dykes, 1980; Dellon, 1981; Carlstet, Lugnegard & Andersson, 1986). Information concerning the functional recovery of SA II cutaneous receptors and joint receptors is sadly lacking. The versatile nature of the recovery of FA I and SA I receptors following PNI may indicate that cutaneous sensation has a greater potential for recovery compared to muscle sensation, accounting for the better levels of recovery of sense of movement following median PNI.

Following both median or median & ulnar nerve injury the ability to reproduce amplitudes and velocities was often highly correlated to reference moves, but patterns of amplitude and velocity reproduction were highly variable due to consistent overestimation or underestimation of movements. Following reinnervation of cutaneous receptors, a number of authors have recorded that thresholds are originally elevated but fall with time (Terzis & Dykes, 1980; Sanders & Zimmerman, 1986). Slowly adapting responses take much longer than rapidly adapting responses to recover. For example in the SA I receptor, Sanders & Zimmerman (1986) record that the slowly adapting response returns to normal values after six months following a nerve crush in the rat. Following transection in the monkey, rates of adaption can take as long as 10 months to return to normal values (Terzis & Dykes, 1980). Differences in recovery of receptor responses as well as misdirection of axons to different areas of skin may account for the mixed patterns of recovery of the ability to grade movements in both median and median and ulnar nerve injured subjects. The inputs from single cutaneous afferents are sufficient to reach consciousness (Vallbo *et al.*, 1984) in contrast to muscle afferents which require summation (Vallbo *et al.*, 1984; Gandevia, 1985; Schady, 1985; Macefield, Gandevia & Burke, 1990). This increases the likelihood of aberrant cutaneous afferent responses reaching conscious levels.

Correlation to Clinical Assessments

Discrepancies between standard measures of sensorimotor function and kinaesthetic acuity were not so obvious compared to the thumb model. This was due to the fact that Weinstein's filament sensitivities at the digit tip were similar to sensitivities on the glabrous surface of the MCP joint. Also, MRC grading of abduction movement of the index reflected motor innervation of adduction movements due to the close proximity of the 1DI and 2PI muscles, both innervated by the ulnar nerve. However, it was apparent during median & radial nerve anaesthesia of the index finger, that Weinstein's filament sensitivities at the three locations around the index MCP joint gave a more representative measure of kinaesthetic function than at the digit tips, which do not account for the radial innervation of the dorsal surface of the joint.

5.3.2.4. Summary

Model 1: Median Nerve Innervation (the thumb): Motor control and kinaesthesia in the normal thumb were good, but thumb abduction: adduction offered a poor model for investigating median nerve innervation due to the high degree of kinaesthetic sense remaining following median nerve anaesthesia. This was due to the contribution of extrinsic and ulnar-innervated intrinsic musculature and joint and skin innervated by the radial nerve.

A marked deterioration in the ability to sense and grade movements following combined median and radial nerve anaesthesia (n=3) demonstrated that the radial nerve provided an important source for thumb kinaesthesia. This is in agreement with other studies, which have emphasised the

importance of the radial nerve for kinaesthesia, during long digit flexion and extension moves (Edin, 1990; Edin & Abbs, 1991; Edin, 1992; Edin and Johannson, 1995).

Median PNI and median & ulnar PNI subjects could sense the majority of movements but showed variability when grading amplitudes and velocities of movements. This suggests that abnormal sensation resulting from reinnervation has the ability to confound the normal residual sensation.

Measuring cutaneous sensation around the thumb CMC joint provided a more accurate measure of sensation in relation to kinaesthesia compared to sensation at the digit tip.

Model 2: Ulnar Nerve Innervation (the little finger): Although the little finger showed the poorest motor control and kinaesthesia of the three digits, the profound effect of ulnar nerve anaesthesia upon sensation in the little finger demonstrated that it provided the best model for investigating recovery of kinaesthesia subsequent to PNI. A number of subjects could still sense some movements in the little finger during ulnar nerve anaesthesia, possibly due to the contribution of extrinsic musculature.

Recovery of the little finger following ulnar PNI was highly variable and ranged from no sensation to a recovery of kinaesthetic acuity, which approached that in the normal hand. The majority of subjects exhibited a degree of recovery that was somewhere between the two extremes. Clinical measures of sensorimotor function showed a good correlation to the detection of movement when combining motor strength and cutaneous sensitivity in an additive manner.

Variability in recovery is likely to be caused by the differences in the extent of the injury and success of subsequent repair (Scott, 1986), denervation period (Kobayashi *et al.*, 1997; Fu and Gordon, 1995a, 1995b), effects of inappropriate reinnervation of proprioceptors of the same modality (Banks and Barker, 1989, 1991) and of a different modality (Lewin & McMahon, 1991a, 1991b) and the amount of reeducation of the hand to utilise peripheral and central mechanisms of plasticity (Dellon, 1981).

Model 3: Mixed Nerve Innervation (the index finger): Ulnar nerve anaesthesia and/or median and/or radial nerve anaesthesia was used to remove the contribution of muscle afferents and joint/cutaneous afferents, respectively. Removal of either proprioceptive source caused deterioration in the detection of movement, in accordance with the findings of Gandevia, McCloskey and coworkers (Gandevia & McCloskey, 1976; Gandevia *et al.*, 1983; Ferrell, Gandevia & McCloskey, 1987) who found that kinaesthetic acuity was highest when all the proprioceptive machinery was in tact.

Grading of the amplitudes of movements seemed to be differentially affected by anaesthesia of the muscle and skin/joint. Subjects tended to underestimate large moves during median and radial nerve anaesthesia and exaggerate small moves during ulnar nerve anaesthesia (MM tests). This suggests that the contributions of muscle and skin/joint may have a bias towards coding for

movements in mid ranges and at joint extremities, respectively. Minor deficits in the ability to grade velocity were evident during anaesthesia of skin/joint or muscle. This is in agreement with the observations of Grill and Hallett (1995) that both secondary spindle afferents and SAII cutaneous receptors fire in relation to velocities of movements.

Ulnar nerve PNI had a more detrimental affect than median nerve PNI causing deficits in detection of movements and exaggeration of matched amplitudes. The locations of the 1DI and 2PI muscles at the most distal end of the ulnar nerve, poor recovery of tonic responses subsequent to reiinervation (Banks & Barker, 1989, 1991, Scott, 1996), and importance of muscle receptors to position sense (Clark *et al.*, 1985) may account for the defiencies in recovery of index finger kinaesthesia subsequent to ulnar PNI.

Detection of movements subsequent to median PNI was high but the ability to grade movements was often variable. This might highlight the relative success with which sensory axons can reinnervate skin (Dellon, 1981; Terzis & Dykes, 1980; Nurse, Macintyre & Diamond, 1984; Sanders & Zimmerman, 1986). However, since inputs from single cutaneous afferents reach consciousness (Vallbo *et al.*, 1984) it is possible that abnormal sensation resulting from reinnervation has a high capacity to confound normal sensation remaining in the digit.

5.4. Pulsatile Output

5.4.1. Normal Intrinsic Musculature

Spectral analysis of acceleration records revealed 8-10 Hz oscillations during slow abduction: adduction movements in the thumb, index and little fingers of normal hands (figure 4.23., p139). The 8-10 Hz pulsatile output was most obvious during both abduction: adduction moves and extension: flexion moves in the index finger. A number of reasons may explain this observation:

- Differences between the thumb and index may be due to there being fewer muscles controlling the index finger, particularly during abduction: adduction. When more muscles control a digit there is a greater possibility for desynchronisation of the 8-10 Hz output through the more diffuse motor unit pool controlling the movement of the digit. This is especially true when muscles controlling the thumb are a mixture of intrinsic and extrinsic muscles.
- Motor control over the little finger is poor and subjects had difficulty in visually tracking slow movements using this digit. Power spectra contained high levels of background noise associated with discontinuous steps performed when tracking movements. Both the procedures used to find significant peaks and calculate normalised power depended on levels of background noise.
- Reitsma (1993) has recorded 13Hz oscillations from the brachoradialis muscle. We also found significant 8-10 Hz oscillations in the index finger extension: flexion plane during rest, in half

of the ten subjects. It is possible that mechanical resonance of forearm muscles controlling extension: flexion of the index may exaggerate 8-10 Hz oscillations.

5.4.2. Task Related Differences In Pulsatile Output

SLOW MOVEMENTS COMPARED TO POSITION HOLDING

The 8-10 Hz tremor, expressed in terms of the absolute power (sum of the values in the range of 7-11 Hz), was significantly greater during slow moving tasks than during position holding (appendix 4.11.). The difference, however, was not so obvious when the absolute power was normalised with respect to the power of the frequencies immediately adjacent to 7-11 Hz. Small, but significant 8-10 Hz peaks, evident during position holding accounted for this effect (table 4.19. p141). These data suggest that the difference between manifestations of 8-10 Hz output during the two tasks is related to the size of the signal generated by the CNS. In other words, the 8-10 Hz tremor is still evident during position holding but is less obvious because of the relatively higher level of backgound noise level and due to the effects of system damping (figure 4.24., p141).

UNDER AN ELASTIC LOAD

Applying an elastic load against extension or abduction of the index finger accentuated frequencies in the 8-10 Hz range both during position holding and during slow movements (figure 4.25. p142). In particular, the addition of an elastic load dramatically increased the absolute power in the 7-11 Hz range during position holding (appendix 4.11.). This suggests that pulsatile output is not just a phenomenon associated with slow movements (McAuley, Rothwell and Marsden, 1998).

Vallbo & Wessberg suggested that pulsatile output may be a mechanism for generating slow movements. An 8-10 Hz clock would drive a double pulse generator producing an agonist burst followed by an antagonist burst. A pulse height controller would then provide the means of controlling the velocity of the move (Vallbo & Wessberg, 1993, 1996; Wessberg, 1995). In addition, since spindle afferent feedback is highly correlated to the pulsatile output, it was also suggested that pulsatile output might aid the integration of afferent information arriving at different times due to peripheral and central conduction times (Wessberg & Vallbo, 1995). However, the existence of 8-10 Hz discontinuities during a position holding task confirms that pulsatile output is not only a slow movement associated phenomenon.

A simple linear system with one degree of freedom can be described in terms of the inertial (m), viscous (c) and elastic (k) components of the system using the equation:

$$\gamma = \frac{c}{2\sqrt{k.m}}$$

Where γ = the damping ratio

m = mass

c = viscosity

k = spring constant

If the damping ratio is less than 1 then the system is underdamped and will be oscillatory. If γ is greater than 1 then the system is overdamped and will not be oscillatory. Thus, increasing the elasticity of the system changes the damping characteristics of the system and converts an overdamped or critically damped system into an oscillatory underdamped system. The small 8-10 Hz oscillations apparent during position holding are damped out by the system mechanics of the digit but become evident under conditions of an elastic load.

The existence of the 8-10Hz pulsatile output during a task which is not associated with macromovements prompts the question as to whether the pulsatile output is evident during all motor tasks but is not visible due to the damping characteristics of muscle and the inertia of mass components. It would also be of interest to examine whether the 8-10 Hz output are present in different areas of the motor system, such as in more proximal musculature which is subject to different descending control mechanisms than hand intrinsic muscles. Using an elastic load would enable the study of 8-10 Hz tremor in actions such as that of elbow flexion which are subject to the heavy damping of the inertia of the forearm.

5.4.3. Significant Peaks At Higher Frequencies

With the index finger abduction action under an elastic load, McAuley, Rothwell and Marsden (1998) found consistent oscillatory frequencies in acceleration, EMG and muscle vibration sound recordings at frequencies of 10Hz, 20Hz and 40Hz. When repeating experiments using springs of two different constants (i.e. 25 Nm^{-1} and 45 Nm^{-1}) we found it possible to show that a certain frequency was absorbed by the spring, equivalent to the longitudinal resonating frequency of the spring. Thus, rather than there being discrete peaks at 20 and 40 Hz, a wide band elevation in spectral power between 15 Hz and 45 Hz appeared to be 'cut into' by the notch filter characteristics of the spring (figures 4.26.A. and 4.26.B., p143).

McAuley, Rothwell and Marsden (1998) also observed 20 Hz and 40 Hz oscillations in EMG and muscle vibration sound recordings. We also found some 20 Hz and 40 Hz peaks in EMG records pooled across all trials performed on subjects (figure 4.27., page 144). However, the peaks were not as obvious as those given by McAuley *et al.* (1998). Interestingly, there were also significant peaks in the 25-30 Hz range in 50% of subjects during position holding of the index finger in extension.

The issue of higher frequency peaks as evidence of higher frequency central oscillatory devices needs to be addressed further. Applying an elastic load during elbow flexion would allow EMG recordings from the large biceps brachii muscle providing a much clearer and higher temporal EMG resolution than that given by the small intrinsic hand muscles.

5.4.4. The Effects Of Peripheral Nerve Impairment

Oscillations in the 8-10 Hz range were evident following reinnervation subsequent to median nerve compression (CTS) and nerve trauma (PNI) (figure 4.29. p146). Significant peaks were present in power spectra taken from both acceleration and rectified EMG traces and during both position holding and slow movements. Interestingly, the occurrence and amplitude of 8-10Hz tremor was significantly higher during position holding following ulnar nerve reinnervation of 1DI and AbDM muscles (figure 4.30., p146). Normal EMG patterns exhibit continuous asynchronous firing of numerous motor units. However, reinnervated muscle was often characterised by the synchronous firing of a few large motor units.

The existence of 8-10 Hz oscillations following such severe alterations in peripheral circuitry further suggests that the pulsatile output is of central origin. It is of interest that the modification in motor unit structure following reinnervation appears to exaggerate 8-10 Hz discontinuities. A number of authors have described the presence of enlarged motor units following reinnervation (Chan *et al.*, 1982; Dum *et al.*, 1986; Gordon & Stein, 1982, Fu & Gordon, 1995). It is possible that the infrequent firing of a few large motor units are more powerful at generating 8-10 Hz discontinuities than asynchronous activity of the many smaller motor units found in normal intrinsic hand muscles.

5.4.5. Summary

In normal position holding of the digits 8-10 Hz can be correctly described as a small localised peak amidst a broad range of frequencies. Yet a number of senarios can result in an increase in spectral power in the 8-10Hz range:

1. *An increase in central drive*, which results when performing slow movements or when resisting an elastic load.
2. *Alterations in peripheral circuitry* such as occur following reinnervation in which enlarged units generate larger 8-10 Hz oscillations.
3. *Reducing mechanical damping of the system* by using an elastic load.

5.5. Sense of Effort

Considerable difficulties were encountered when attempting to measure sense of force in PNI subjects. Muscle strength following nerve transection was usually significantly lower than the original strength of the muscle even after long recovery periods. For example in the PNI subject pool used in the current study, maximal voluntary contractions for actions of the thumb, index and little finger abduction were 15.3N (±2.7), 10.1N (±1.6) and 5.9N (±1.0), respectively, following PNI compared to 29.9N (±3.4), 24.8N (±2.6) and 14.8N (±1.7), respectively, in normal hands (n = 13, 12 and 13, respectively). This not only severely reduced the proportion of PNI subjects who

were capable of performing repeated lifting tasks, but comparisons between sense of effort in the nerve injured and normal hands may be inappropriate because of the large differences in maximal voluntary contraction between the two groups. Weight matching, the most commonly used method for investigating sense of effort, involves matching a reference weight with a mass applied on the contralateral side and thus requires lifting the two masses many times until a match is made (Kilbreath & Gandevia, 1992; 1995; reviewed in Gandevia & Kilbreath, 1995). This could cause fatiguing and even discomfort to subjects with nerve impairments.

Although these difficulties discourage investigation there are a number of factors, which strongly suggest that there are both central and peripheral components to the sense of effort, and thus make its recovery subsequent to reinnervation of interest:

1. Perceived heaviness is always greater in conditions of muscle weakness (McCloskey, Ebeling & Goodwing, 1974; Gandevia & McCloskey, 1977; McCloskey, 1981; Gandevia, 1987; Jones, 1988). The loss in strength associated with PNI may have the result of increasing perceived heaviness.
2. Positive and negative modification of afferent input by tendon vibration or cutaneous anaesthesia can influence perceptions of heaviness (McCloskey, Ebeling & Goodwin, 1974; Gandevia & McCloskey, 1977; Gandevia, McCloskey & Potter, 1980; Kilbreath *et al.*, 1995; Gandevia et al, 1990). Abnormal sensation associated with reinnervation of sensory receptors may influence perception of heaviness
3. A number of observations indicate that peripheral receptors may have a more direct role in evoking sensations of heaviness, in which case a dramatic changes in connectivity and firing patterns of sensory receptors subsequent to reinnervation could directly influence the sense of force:

- Under isotonic conditions, output from the Golgi tendon organ is linearly related to the contractile force as generated by either individual motor units or groups of motor units (Petit, Scott & Reynolds, 1997). It is difficult to imagine that a transducer so efficient at coding contractile tension does not have a significant contribution to sense of effort. Thompson *et al.*, (1990) record that desensitisation of GTO's using maximal voluntary contractions causes an increase in perceived heaviness. McIntyre, Proske & Rawson (1985) have also recorded evoked cortical discharges in area 3b as a direct result of Golgi tendon organ stimulation.
- Investigations by Johansson and co-workers have shown that sophisticated mechanisms control load and grip forces when lifting objects between the finger tips. These act to maintain sufficient grip force to prevent slip during steady or dramatic variations in load force (Johansson & Westling, 1984; 1987; Kinoshita *et al.*, 1997; Wing, 1996; reviewed in Johansson, 1996a, 1996b). Microneurographical recordings and local anaesthesia have demonstrated that this highly sophisticated control of force is mediated by sensory feedback provided by cutaneous receptors at the digit tips (Johansson & Westling, 1984,1987; Westling & Johansson, 1984).

- Henningsen, Knecht and Henningsen (1997) have shown that afferent feedback has a role in controlling fine forces. In the absence of visual feedback, the ability to produce the smallest possible increment of force was reduced when either muscle /and or cutaneous afferent feedback was removed. Muscle afferent feedback was more efficient than cutaneous feedback for providing control of fine force.

In an attempt to overcome some of the pitfalls associated with measuring sense of effort subsequent to PNI, the method of 'force matching' was implemented in the form of a pilot study to investigate force estimation. Rather than matching weights applied bilaterally, the method was based on the subject reproducing applied forces applied unilaterally. Subjects could then reproduce forces on either the ipsilateral or contralateral sides. Force matching has been previously used by matching compression forces applied using springs (Roland & Ladegaard-Pedersen, 1977). Also, Cafarelli (1982) used force matching to compare forces applied to the ipsilateral and contralateral adductor pollicis. The technique has the advantage that a single lift can be used to give an estimate of applied force. This reduces the number of lifts needed to investigate sense of effort.

The following section contains details of the methods, results and conclusions that were drawn from a pilot study investigating the sense of effort in a small number of subjects. Force matching was used to estimate sense of effort in PNI subjects and weight matching was used in the current study to investigate the effects of CTS upon sense of force in the thumb.

5.5.1. Equipment

Stands consisting of two straddled parallel steel uprights were constructed for use in weight and force matching experiments (figure 5.1.). A perspex tray with a layer of foam rubber provided the base from which the masses could be lifted. Low friction pulleys and protractors ensured the correct vector of force was applied to the digit. The masses were lifted via a 15mm polyester strap fitted over the digit just proximal to the finger nail. Two strain gauges were used to record applied forces on ipsilateral and contralateral sides. They both showed near perfect linearity up to torques of $1Nm^{-1}$. During force matching, the optical laser also used to record tremor, provided feedback of the position of the digit to the subject so that movement of the digit was minimised during the application of force.

5.5.2. Protocol

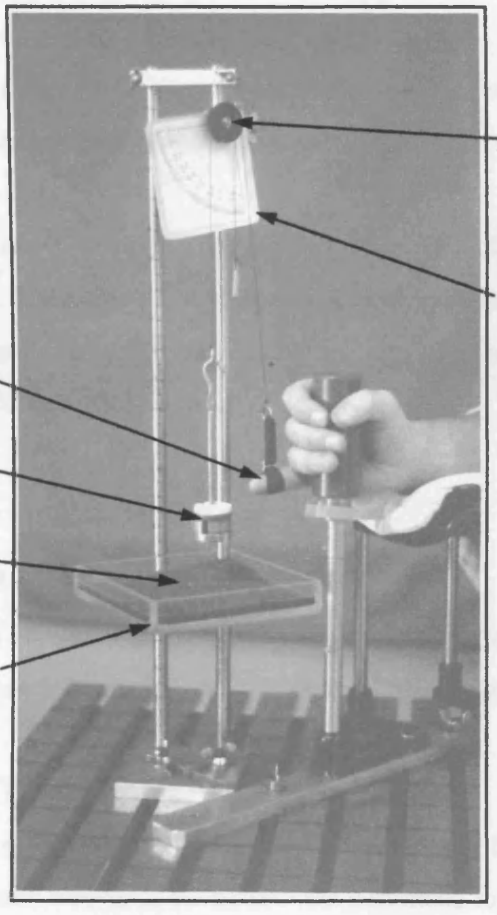
The three earlier mentioned models were used to assess sense of force, using the vectors of actions of the muscles AbPB, AbDM and 1DI (section 1.7.2. and diagrams 1.8.- 1.10., pp 51-53).

WEIGHT MATCHING

The protocol was loosely based on that used by Gandevia and Kilbreath (1995), but with two main differences. First, the number of lifts was reduced to minimise fatigue and subsequent discomfort to CTS subjects. Secondly, the masses used represented 3% and 15% of the MVC of each subject individually rather than collectively. This was important, to take account of the variation in strength of muscles. The protocol was as follows:

1. Maximal voluntary contractions were recorded for each subject using strain gauge equipment (see section 2.4., p62), and light and heavy reference weights were set at 3% and 15% of the MVC, respectively.
2. A reference weight was applied to the non-dominant side of normal subjects, and the injured hand of CTS subjects.
3. A variable weight was applied to the opposite hand. The weight could either be larger or smaller.
4. Subjects had to match the variable weight by asking for more or less mass to be added to the variable weight. There was no restriction to the number of lifts or in the manner in which the subject could lift the weight. All trials were performed without vision of the hands.
5. Five heavy and five light matching tasks were performed randomly.

Figure 5.1. Apparatus Used To Measure Sense Of Force (see text for explanation).



FORCE MATCHING

The same equipment was used as for weight matching tests (figure 5.1.) but the mass was replaced with a strain gauge when matching forces. Protocols bore a similarity to those used for grading movements during tests of kinaesthesia:

- ***Visual Tests:*** Visual feedback from the gauge was provided to the subject using the visual display (see section 2.3., p61). The subject pulled against the gauge to match a force level represented by a visual cue created using the sequence language of Spike 2.21 for Windows® (VM). The visual display was covered and the subjects reproduced the same force on the ipsilateral side (VR).

  The validity of visual tests during force matching proved to be deficient because feedback of the force applied in the form of a movement cue often gave the impression that the subject was pulling against an elastic load. This resulted in a small but consistent overestimation of repeats of visually matched forces.
- ***Ipsilateral and Contralateral Repeats:*** The force was applied to the digit by gently lowering a weight connected to the digit by the strap-line-pulley arrangement (figure 5.1.). Feedback of the digit position was provided using the optical displacement laser output and visual display so that the subject could minimise movement during the application of force. Following the application of the weight, the subject repeated the applied force by pulling on strain gauges situated on either the ipsilateral (IR) or contralateral (CR) sides. The visual display was covered during the repeat so that the subject concentrated upon accurate reproduction of the force.
- ***Force Matching (FM):*** This was identical to the contralateral repeat test, but force applied to the ipsilateral side was simultaneously matched on the contralateral side.

The forces used throughout the trials were 0.2N, 0.5N, 1.0N, 1.5N, 2.0N, 2.5N, 3.0N, 5.0N and when possible 7.0N and 10.0N. The forces were applied in a pseudorandom sequence. Triggers marked the point at which the subject perceived that he/she had correctly reproduced the torque. Surface EMG recordings were also taken during the tests.

5.5.3. Results

CTS SUBJECTS AND WEIGHT MATCHING

Comparison of the ability of 15 CTS subjects and 15 control subjects to match weight at 3% and 15% of MVC did not reveal any significant differences between the two groups.

PNI SUBJECTS AND FORCE MATCHING

Force matching tests were perfomed on a small number of normal (n=8) and PNI (n=5) subjects. In addition, two subjects under median nerve anaesthesia performed force matching with the

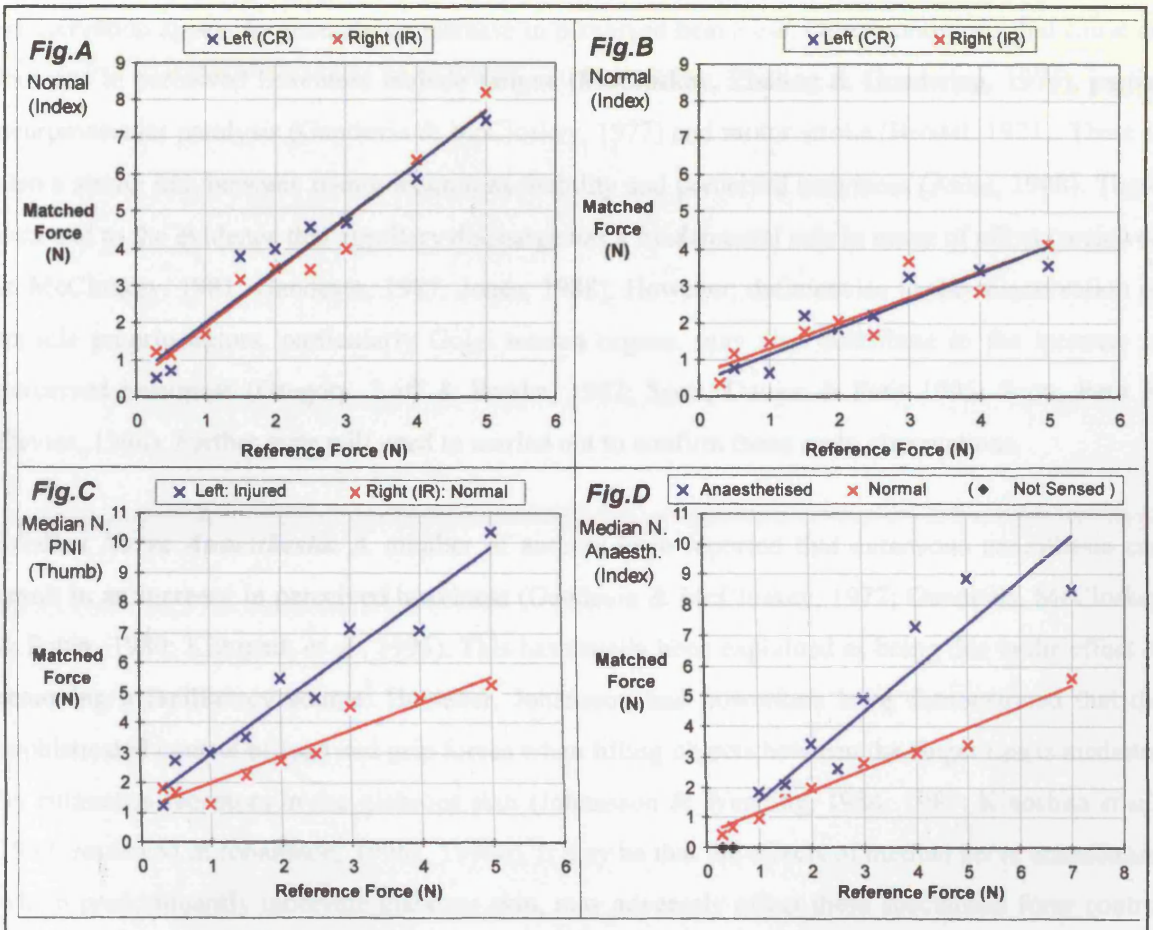
index finger. Regression analysis revealed that in all groups there was a high correlation between reference and matched forces regardless of the test.

Normals: Although there was consistency in the way individual subjects reproduced forces on ipsilateral and contralateral sides, there was variability between subjects. Figures 5.3.A. and 5.3.B. illustrate that patterns of repeating during IR and CR tests performed with the index for two normal subjects (subjects: FP and SK). Regression equations of CR and IR tests for each subject were similar. However, regression equations between the two subjects were quite different due to overestimation by one subject and underestimation by the other subject.

PNI: Figure 5.3.C. illustrates the difference between force estimation in normal and injured hands for one long-term median & ulnar PNI subject (subject: DS, 9 years post operative) when repeating movements applied to the thumb. Maximal voluntary contractions were reduced from 30N in the normal hand to 14N in the injured hand. Weinstein's filament sensitivities at the point of application of the force were similar on the injured and normal hands due to radial innervation of the application site. Figure 5.3.C. illustrates the consistent overestimation of forces applied to the injured hand.

Median Nerve Anaesthesia: Two subjects, under long-term marcaine local anaesthesia of the median nerve, were used to observe the effects of removing cutaneous inputs to sense of force. In one subject (EH), both normal and anaesthetised hands were characterised by consistent overestimation yielding little difference in force matching between normal and anaesthetised hands. In the second subject (FP), there were two observable effects of local anaesthesia (figure 5.3.D.). Firstly, the subject could not sense the lighter weights, equivalent to 0.3 N and 0.5 N. Secondly, when forces were detected by the index finger, the subject tended to exaggerate force repeats. The gradients of reproduced: reference force in the anaesthetised hand were double those in the normal hand.

Figure 5.2. The ability of individual subjects to match and repeat applied forces in the normal hand and subsequent to various nerve impairments. Figures A and B illustrate the close correlation between forces repeated by ipsilateral (IR) and contralateral (CR) hands in normal subjects. However, one subject tended to overestimate forces whereas the other subject tended to underestimate. In contrast, figure C shows a long term median PNI subject who tended to overestimate forces applied to the thumb of injured side compared to the normal hand. Likewise, following median nerve anaesthesia, the subject tended to match forces (FM tests) with the index finger in comparison to control conditions. Small forces where not sensed by the anaesthetised digit.
Regression analysis corroborates these observations (see table)



Regression Analysis

Figure A	Gradient	Intercept	R^2
Left (CR)	1.43	0.55	0.94
Right (IR)	1.46	0.43	0.96

Figure B	Gradient	Intercept	R^2
Left (CR)	0.73	0.40	0.88
Right (IR)	0.7	0.60	0.83

Figure C	Gradient	Intercept	R^2
Left (CR)	1.72	1.26	0.94
Right (IR)	0.89	1.1	0.91

Figure D	Gradient	Intercept	R^2
Normal	1.47	0.02	0.90
Anaesth.	0.70	0.45	0.86

5.5.4. Conclusions

Normals: The technique of force matching is likely to provide a useful means of assessing sense of force in conditions of muscle weakness where techniques requiring large numbers of lifts may cause discomfort. In particular, using force ipsilateral and contralateral repeats may well be of use in taking account for intersubject variability which seems to be apparent in normal subjects. The use of visual tests to identify components of motor control and memory are restricted by the creation of an illusion in which the subject senses that they are lifting against an elastic load.

CTS: Because of the restricted number of lifts used during weight matching in CTS subjects (n=5 for light and heavy weights) it is difficult to say conclusively whether the absence of significant differences between normal and CTS subject data was due to defiencies in the technique or because CTS caused no significant impairments in sense of effort.

PNI: Preliminary studies suggest that conditions of muscle weakness following nerve trauma and reinnervation appear to generate an increase in perceived heaviness. Other conditions that cause an increase in perceived heaviness include fatigue (McCloskey, Ebeling & Goodwing, 1974), partial neuromuscular paralysis (Gandevia & McCloskey, 1977) and motor stroke (Brodal, 1973). There is also a strong link between α-motoneuron excitability and perceived heaviness (Aniss, 1988). These data add to the evidence that corollary discharge has a fundamental role in sense of effort (reviewed in McCloskey, 1981; Gandevia, 1987; Jones, 1988). However, deficiencies in the reinnervation of muscle proprioceptors, particularly Golgi tendon organs, may also contribute to the increase in perceived heaviness (Gregory, Luff & Proske, 1982; Scott, Davies & Petit 1995; Scott, Petit & Davies, 1996). Further tests will need to carried out to confirm these early observations.

Median Nerve Anaesthesia: A number of authors have reported that cutaneous anaesthesia can result in an increase in perceived heaviness (Gandevia & McCloskey, 1977; Gandevia, McCloskey & Potter, 1980; Kilbreath *et al.*, 1995). This has usually been explained as being due to the effect of removing a facilitatory source. However, Johansson and coworkers have demonstrated that the sophisticated control of load and grip forces when lifting objects between the finger tips is mediated by cutaneous receptors in the glabrous skin (Johansson & Westling, 1984; 1987; Kinoshita *et al.*, 1997; reviewed in Johansson, 1996a, 1996b). It may be that the effects of median nerve anaesthesia, which predominantly innervate glabrous skin, may adversely affect these specialised force control mechanisms.

Interestingly, lighter forces applied to the index finger were often not sensed during median nerve anaesthesia. Henningsen, Knecht and Henningsen (1997) showed that in the absence of visual feedback, the resolution of control of fine forces is improved when either muscle or cutaneous afferent feedback is present. Cutaneous and muscle sensory feedback may have a particular role in the sensation of fine forces.

5.6. Future Areas of Research

5.6.1. Improving Actuator Design

The use of an AC induction motor proved to be a reliable method for applying movements to fingers (Proudlock & Scott, 1998) and might find use in a range of physiological applications. An antivibration coupling and inflatable cuff were successfully used to reduce vibration produced by the system, but also introduced compliance between the motor and digit. This meant that there were considerable difficulties encountered when attempting to configure the system for controlling force since an error resulted between the digit position and optical encoder reading whenever the digit opposed the force of the motor. System vibration could, however, be alternatively reduced by using a toothed rubber belt and pulley arrangement to scale down movements, without the need to introduce compliance into the system. A smaller motor could be used to apply movements, reducing the increased inertia of the system resulting from using a belt and pulley arrangement. Forces could be applied using simple mass and spring arrangements attached to the second shaft, driven by the belt and pulley arrangement.

Another possibility for investigating force sense is to modify the position encoder attached to the contralateral hand so that it can be used to apply forces. Ferrell and Smith (1989) looked at the effects of an isotonic load upon amplitude reproduction following anaesthesia of skin and joint in the PIP joint of the middle finger. Consistent errors resulted when a force was applied to the ipsilateral anaesthetised digit when trying to match moves applied to the contralateral normal digit. This highlights the importance of skin and joint afferents in providing independent proprioceptive cues when under load conditions. A similar protocol could easily be implemented using the current equipment by modifying the contralateral position encoder so that a mass could be applied when repeating movements. Attachment of the digit to the shaft would require a much more rigid arrangement than the inflatable cuff used. Micropore™ tape could be used to strap the digit to a stainless steel appendage fixed to the shaft.

5.6.2. Further Studies Into Kinaesthesia Subsequent to PNI

The methods used for measuring kinaesthesia in the current study were deficient in a number of different areas:

1. Sample sizes were often small for PNI groups and for radial nerve anaesthesia studies
2. The degree of muscle contraction during the study was highly variable even though subjects were instructed to remain relaxed throughout trials. Passive tests might be used as a means to eliminate muscle tensing during tests. This would require the development of a system able to apply bilateral movements for assessing the ability to grade amplitudes and velocities without the need for active movement by the subject.

3. Because single moves consisted of a symmetrical clockwise and anticlockwise rotation, the tests were deficient at discriminating between abduction and adduction sensation. It is very possible that anaesthesia or PNI may have a different effect on abduction and adduction kinaesthesia. This is particularly true in a digit such as the thumb where intrinsic and extrinsic muscles control abduction and adduction moves, respectively. Positioning the digit in midrange positions and looking at the sensitivity to moves applied in both abduction and adduction directions could easily be implemented to solve this problem
4. The limited range of amplitudes and velocities of applied movements meant that many subjects sensed all 12 moves, including some PNI and anaesthetised subjects. Determination of a sensory threshold would be a more discriminative method for investigating kinaesthesia rather than applying a series of moves of fixed amplitudes and velocities.
5. The trials did not discriminate between rapidly and slowly adapting proprioceptive systems.

5.6.2.1. Increasing Sample Sizes

Certain trials were inconclusive because of high inter-subject variability in PNI subjects and because of the small sample sizes used. Inter-subject variability was particularly high in the median PNI and combined median and ulnar PNI groups (n=8 and 6, respectively). To a certain degree, anaesthesia of median and ulnar nerves, performed on 7 subjects helped in making sense of the variable patterns evident in grading movements by PNI subjects. Larger numbers of nerve injured subjects might be recruited by setting up equipment in a larger population centre.

Pilot studies in which radial and combined median and radial nerve anaesthesia was applied proved to be fruitful even for the sample sizes used (n=3), and would merit further exploration by incorporating more subjects into the study.

5.6.2.2. Methods for Studying the *SA* and *RA* Proprioceptive Systems

SLOWLY ADAPTING SYSTEM

Clark *et al.* and others (Horch, Clark & Burgess, 1975; Clark *et al.*, 1985, 1986, 1989; Taylor & McCloskey, 1990) have applied very slow velocity movements to demonstrate that certain joints have an independent position sense. Using local anaesthesia of the ulnar nerve, Clark *et al.* (1985) have also shown that this position sense is probably mediated by muscle spindles, since anaesthesia abolishes position sense in abduction: adduction moves of the index finger MCP joint. The same model could be used in long-term ulnar PNI subjects to determine whether position sense recovers subsequent to nerve injury. If the position sense does recover, then looking at amplitude thresholds to slow velocity moves might test differences in the acuity of position sense between the normal and reinnervated hand.

RAPIDLY ADAPTING SYSTEM

Very few studies have investigated the sensitivity of the RA system independently from the SA system. Gandevia *et al.* (1983), have plotted amplitude thresholds for ramp movements applied at different velocities in the DIP joint of the middle finger. The SB1091 controller can be configured to perform point to point movements which have a specific acceleration and deceleration. It would be therefore, possible to investigate acceleration thresholds for moves of constant amplitude and velocity. Alternatively, sinusoidal moves could be applied to plot kinaesthetic threshold tuning curves similar to those plotted for cutaneous thresholds (LaMotte & Mountcastle, 1975, Johansson, *et al.*, 1982a). The SB1091 motion control module can be configured to perform sinusoidal moves using the arbitrary path generation mode.

5.6.2.3. Kinaesthesia in Different Areas of the Joint Range of Motion

The findings of this study, along with those others (eg. Grigg & Hoffman, 1982; Burke *et al.*, 1988; Ferrell & Smith, 1988, 1989; Clark, Grigg & Chapin, 1989; Grigg & Hoffmann, 1991; Grigg, 1994) suggest that joint receptors, in particular, may have a bias towards firing at extremes of the joint range. It is, therefore, possible that kinaesthetic thresholds may be affected in a differential manner in different areas of the range of joint motion subsequent to anaesthesia or PNI. Amplitude thresholds for either slow velocity or sinusoidal moves could be measured at different areas of the joint range of motion to explore this further.

5.6.2.4. Other Models for Investigating Kinaesthesia Subsequent to PNI

THE EFFECT OF PNI UPON JOINT AND CUTANEOUS AFFERENT SENSATION

The DIP joint of the middle finger has been used extensively by researchers to investigate kinaesthesia since the contribution of muscle sensation can be effectively removed by arranging the joint so that the muscle is functionally disengaged. (Gandevia & McCloskey, 1976; Gandevia *et al.*, 1983; Ferrell, Gandevia & McCloskey, 1987; Clark, Grigg & Chapin, 1989). The DIP joint model could also be used in median PNI subjects, to compare the sensation resulting from reinnervated cutaneous and joint innervation, when normal muscle sense *does* and *does not* contribute. Kinaesthaesia is variable in the index finger and thumb subsequent to long term median PNI subjects and is often worse than during anaesthesia of the nerve. It is possible that inappropriate reinnervation resulting from mislocation of axons may confound normal sensation. The three paradigms commonly used in the DIP joint model would provide a means of exploring the effects of abnormal sensation:

- ***Disengagement of muscles:*** the abnormal sensation arising from reinnervated joint and reinnervated cutaneous receptors alone.
- ***Engagement of muscles:*** the effect of abnormal sensation from reinnervated skin and joint upon normal sensation derived from muscle receptors.

- ***Digital nerve anaesthesia (of normal subjects):*** the normal sensation arising from muscle receptors alone.

THE EFFECT OF PNI UPON MUSCLE AFFERENT SENSATION

The only model available in the hand for investigating the sensation resulting from reinnervated muscle alone is the model of index finger abduction: adduction movement in ulnar nerve injured subjects. However, to remove the sensation from cutaneous and joint afferents would require anaesthesia of median and radial nerve in the PNI subjects. Apart from the difficulty in finding willing volunteers, the ethical issues relating to performing anaesthetic blocks in areas that have been previously traumatised are questionable.

A TEST FOR INVESTIGATING MEDIAN NERVE INNERVATION
(A FUNCTIONAL MEASURE OF PROPRIOCEPTIVE RECOVERY)

The median nerve is possibly the most important nerve in the hand for proprioception. It innervates the lumbrical and thenar muscles, which of prime importance in sensing movements within the dynamic tripod. The glabrous skin innervated by the median nerve has some of the lowest thresholds and highest two-point discriminative capacities in the whole of the body (Johansson & Vallbo, 1980; Vallbo & Johansson, 1984). Median nerve anaesthesia results in a profound loss in the ability to perform fine manipulatory tasks with the hands. For example, in the current study subjects often took minutes to recognise objects in Moberg's pick-up tests in comparison to the few seconds taken by the normal hand. However, the effect of median nerve anaesthesia upon kinaesthesia during thumb abduction: adduction moves was only minor. Subjects could sense and detect movements with a high degree of acuity. Accordingly, simple measures of kinaesthesia were generally very poorly correlated to clinical measures of hand function. The results of the current study highlight the deficiencies of current models in providing an accurate measure of functional proprioception in the hand

Deficiencies of Current Tests

For future development in the investigation of proprioceptive recovery subsequent to PNI, a functional yet quantitative method of assessing kinaesthesia in the hand still needs to be developed. Current methods are restricted in three areas:

- The majority of proprioceptive studies in the hand have tended to focus on simple models involving a single joint, so that one or more sources of proprioception can be easily removed. However, these simple measures do not correlate well with functional proprioception in the hand.
- Most methods focus on the slowly adapting proprioceptive system rather than the rapidly adapting system primarily because the SA system is easier to measure. Yet, the slowly adapting

system is functionally less important than the rapidly adapting system since most physiological movements are faster than $5°s^{-1}$ (Dellon, 1981).

- Current methods do not measure kinaesthesia in the area which is of greatest importance in hand function, that is, in the dynamic tripod between the first three digits. Most of the tasks which involve fine control of movement are performed between the thumb and the first two fingers.

A Solution

The pantograph, once commonly used in architectural and engineering drawing offices for scaling diagrams, is a series of four levers arranged in a lattice to amplify or reduce movements. Usually, a diagram would be traced with one end of the framework, and a pen would reproduce a scaled picture at the other end of the framework. The pantograph could be easily modified to apply scaled movements to the digit tips. By attaching one end of pantograph to an x-y plotter or similar device and replacing the pen with a handle which can be grasped by the first three digits (figure 5.3.), a range of 2-dimensional moves could be applied to the hand to look at kinaesthesia within the dynamic tripod.

The range of movements used to assess kinaesthesia might include:

- The ability to sense a range of circles of different diameters applied at different rates of rotation. Since a circle is composed of two sinusoidal moves applied at right angles and 90° out of phase, this is the 2-dimensional equivalent of the sinusoidal threshold test mentioned earlier.
- The ability to sense a series of shapes applied at linear velocities including a circle, octagon, hexagon, pentagon, square, triangle and line. Here, the ability to detect changes in direction is under analysis. In each case the change in direction is either continuous or 45°, 60°, 72°, 90°, 120° and 180°, respectively. The velocity of the movement or size of the shape could also be varied.
- The ability to recognise letters and numbers. The letters of the alphabet can be grouped according to how they are drawn. For example, lower case letters can be grouped:

1) c, e, o, s: circular moves without a reversal in direction

2) a, d, g, q: circular moves including a reversal in direction

3) h, m, n, r, u: up and down moves with rounded ends

4) v, w, z: linear point to point moves

Varing the size of the letters would provide a simple means of determining the sensitivity threshold in the similar way in which the Snellen chart is used to determine visual acuity.

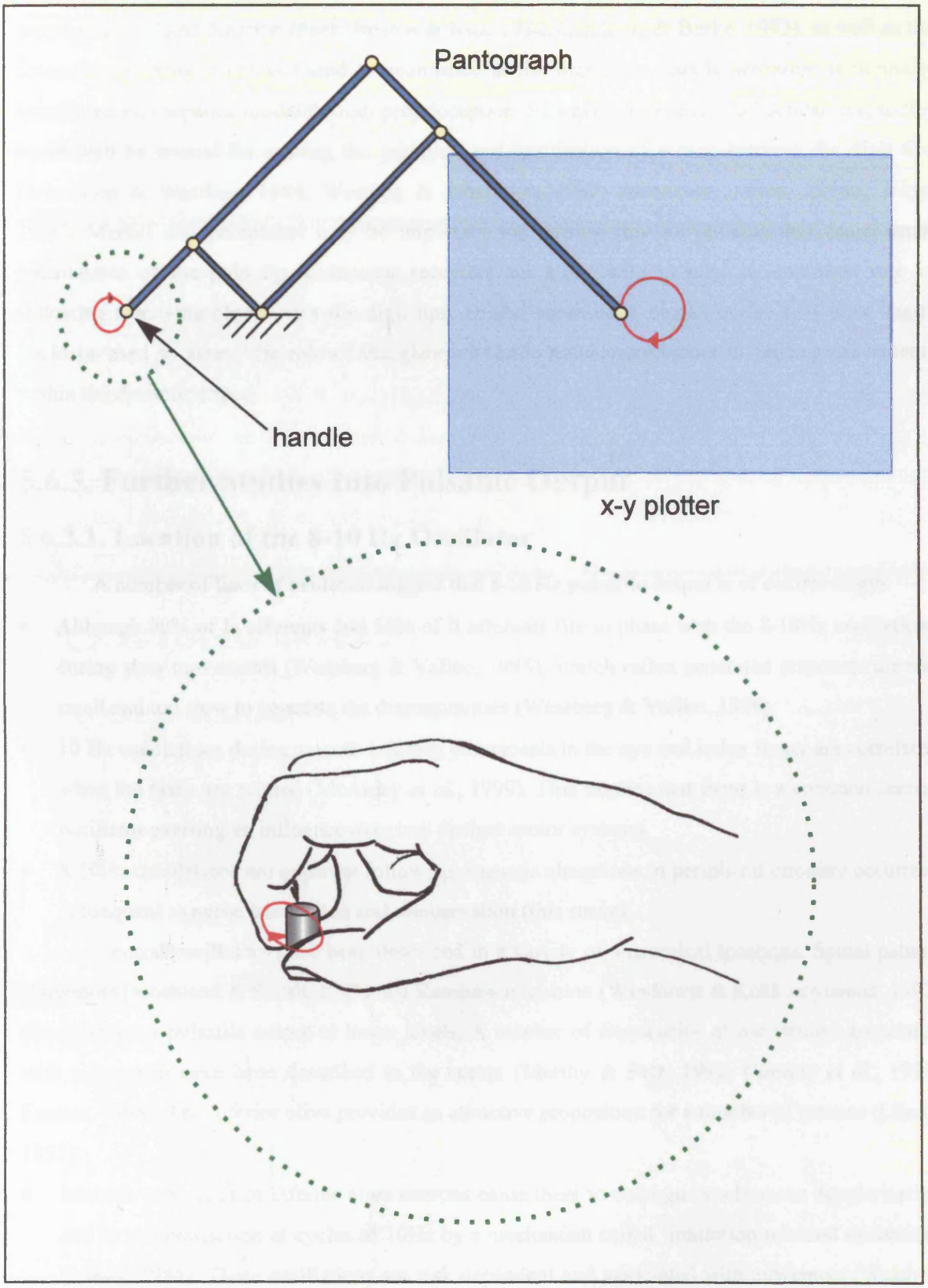


Figure 5.3. A method for applying 2-dimensional movements to the digit tips. A pantograph scales down movements generated using an x-y plotter. The subject senses movements through a handle attached to the end of the pantograph.

The importance of a test such as the pantograph sensory test is that it includes the contribution of specialised muscles such as the lumbricals, which have been implicated in proprioceptive hand function (Peck, Buxton & Nitz, 1984; Gandevia & Burke, 1992), as well as the cutaneous mechanoreceptors found in abundance at the digit tips. Tactile sensation is normally considered as a separate modality from proprioception. However, Meissner and Pacinian corpuscles could well be crucial for sensing the initiation and termination of moves between the digit tips (Johansson & Westling, 1984; Westling & Johansson, 1987; Johansson, 1996a, 1996b; Wing, 1996). Merkel cell complexes may be important for sensing tiny movements that cause small indentations of the pulp tip. Cutaneous receptors are also likely to play an important role in following a moving object with the digit tips. Digital anaesthetic blocks of the first three digits could be used to assess the role of the glabrous tactile mechanoreceptors in sensing movements within the dynamic tripod.

5.6.3. Further Studies Into Pulsatile Output

5.6.3.1. Location of the 8-10 Hz Oscillator

A number of lines of evidence suggest that 8-10 Hz pulsatile output is of central origin:

- Although 90% of Ia afferents and 50% of II afferents fire in phase with the 8-10Hz oscillations during slow movements (Wessberg & Vallbo, 1995), stretch reflex generated responses are too small and too slow to generate the discontinuities (Wessberg & Vallbo, 1996).
- 10 Hz oscillations during smooth tracking movements in the eye and index finger are correlated when the tasks are related (McAuley *et al.*, 1999). This implies that there is a common central oscillator exerting an influence over two distinct motor systems.
- 8-10Hz oscillations are apparent following dramatic alterations in peripheral circuitry occurring subsequent to nerve transection and reinnervation (this study).

Central oscillators have been described in a variety of anatomical locations. Spinal pattern generators (Koshland & Smith, 1989) and Renshaw inhibition (Windhorst & Kokkoroyiannis, 1992) can generate a pulsatile output at lower levels. A number of frequencies of oscillations associated with movement have been described in the cortex (Murthy & Fetz, 1992; Conway *et al.*, 1995; Farmer, 1998). The inferior olive provides an attractive proposition for a number of reasons (Llinás, 1991):

- Intrinsic properties of inferior olive neurons cause them to undergo synchronous depolarisation and hyperpolarisation at cycles of 10Hz by a mechanism called 'inhibition rebound excitation' (Llinás, 1984). These oscillations are task dependent and associated with movement (Welsh & Llinás, 1997).
- Harmaline induced tremor enhances the activity of the cells in the inferior olive (LaMarre & Weiss, 1973).

- The output of the inferior olive through climbing fibre input into Purkinje cells of the cerebellum has been suggested as a mechanism for providing control of coordinated motor activities (Llinás, 1991).
- The activity of the cerebellum is associated with the control of both eye and finger movements (Glickstein, 1998; Miall, 1998).

The location of the central generator of 8-10 Hz pulsatile output is still uncertain. However, since different kind of movements are generated from different neural substrates it may be possible to gain clues concerning the origin of the pulsatile output from the character of the 8-10Hz oscillations during different types of movement. For example, in the control of eye movements, the vestibular ocular reflex, smooth pursuit and visual fixation are three smooth eye movements, generated from different anatomical locations (Leigh & Zee, 1999). The addition of optical prisms into the subject's field of view would bring into effect adaptive responses, which are mediated by the inferior olive (Ito, 1982). The amplitude and frequency of occurrence of 8-10 Hz oscillations could be recorded during these various movements to see if there are any situations in which they are particularly prominent. Functional MRI may provide an additional means of tying in anatomically active areas that correlate to the generation of 8-10Hz pulsatile output.

ROLE OF THE 8-10 Hz PULSATILE OUTPUT

It has been postulated that the 8-10 Hz oscillations may act as a central timing device for the coordination of neuronal activities of various conduction delays (Bernstein, 1967; Llinás & Yarom, 1986). If movements are clocked at 8-10 Hz then this may be evident from the timing of rapid voluntary movments in the body. However, even the inertial components of the digits are likely to be sufficiently large to slow down movements and prevent comparison of the timing of rapid voluntary movements to the phase of 8-10 Hz oscillations.

Saccadic movements of the eyes are possibly the only voluntary movements rapid enough in the human motor system to allow comparison of the phase of 8-10 Hz oscillations with movement onset. Using a device with powerful temporal and spatial resolution to record horizontal and vertical eye movements, the timing of the initiation of a saccade could be compared to the phase of a sequence of 8-10 Hz discontinuities measured using a fast Fourier transform.

5.6.4. Recovery Of Proprioception Subsequent to PNI

There are two areas that might be exploited in the future to improve the recovery of proprioception subsequent to PNI:

1. Mechanisms of plasticity could be brought into play using re-education programs.
2. The degree and specificity of recovery following nerve trauma could be improved using developments in neurotrophic and conduit technologies.

5.6.4.1. Re-education programs

Mechanisms of plasticity exist in the spinal cord and cortex, such as collateral sprouting and short and long term changes in synaptic efficiency as mediated by excitatory amino acids, peptides and neurotrophins (King & Thompson, 1995; Woolf *et al.*, 1995) (Florence *et al.*, 1993, 1994; Koerber *et al.*, 1994). These mechanisms are appropriated fully by repeated re-establishment of sensory and motor neural paths during use. This principle underlies the basis of re-education.

A number of sensory re-education programs have successfully developed, although emphasis has been placed on the rehabilitation of tactile sensation (Parry, 1976; Dellon, 1981; Imai, Tajima & Natsumi, 1991). A comprehensive sensory re-education programmes was developed by Dellon (1981) in which the subject originally tries to distinguish between constant touch and movement until vibration sense of 256 Hz returns to the finger tips, indicating that all the modalities of tactile fibres have returned. Then the subject can begin to manipulate and identify household objects. The tests are made more difficult by using smaller objects or by placing them in media such as coffee beans or rice.

We suggest following a similar protocol to that of Dellon (1981) in charting sensory reinnervation. In addition, MRC grading can be used to follow motor reinnervation in the AbPB action for median PNI, and 1DI and AbDM muscle actions for ulnar PNI, until grades 3 to 5 are reached. Then we recommend a series of exercises to improve motor strength, which are performed in parallel with exercises designed to improve active touch and proprioception.

CHARTING REINNERVATION

Sensory Reinnervation: The subject tries to distinguish between constant touch and movement in the denervated digits until vibration sense of 256 Hz returns to the finger tips. This indicates that the modalities of FA I, FA II and SA I cutaneous units have reappeared (see Dellon, 1981).

Motor Reinnervation: Manual MRC testing of AbPB action for median PNI, and 1DI and AbDM actions for ulnar PNI are performed until grades 3 to 5 are reached.

IMPROVING MOTOR CONTROL

Early Recovery Exercises

Median PNI: Move the tip of the thumb to the tip of each of the four fingers in turn.

Ulnar PNI: Rapidly alternate between spreading the fingers as far apart as possible and pulling them together.

Muscle Strength Exercises

1. Squeeze a soft rubber ball between the thumb and digit tips
2. A key should be held between the pad of the thumb and the side of the index finger and pinched as hard as possible

3. A disk approximately 120mm dia. should be positioned flat against the palm of the hand and gripped as tightly as possible

IMPROVING ACTIVE TOUCH / PROPRIOCEPTION

1. ***Moberg's Picking-Up Test:*** Arrange a series of 10 different objects in a tray. Pick and identify each in turn without looking.
2. ***Peg Test:*** Arrange 10 pegs in a pegboard. Move each peg from one side of the board using the first three digits.
3. ***Buttons:*** Do up and undo a series of buttons as rapidly as possible. The size of the buttons can be varied to control the difficulty of the test.
4. ***Knots:*** Tie and untie knots in a piece of cord. The diameter of the cord can be varied to control the difficulty of the test.

5.6.4.2. Improving the Degree and Specificity of Recovery

Unlike the CNS, axons in the PNS possess a powerful potential for regrowth because of a number of favourable conditions that exist in the distal segment of peripheral nerve. These influences are able to affect both the degree and specificity of reinnervation.

1. ***The Basal Lamina Layer:*** The Schwann cell basal lamina layer provides a surface on which regenerating axons vigourously grow (Ide, Osawa & Tohyama, 1990). Adhesion molecules, the most notable being laminin, provides a surface on which cytosketal components can be built up during axonal extension (Letourneau, Condic & Snow, 1994; Ide, 1996). The basal lamina of other cell types such as skeletal muscle, endothelium and renal tubules have also been successfully used as scaffolds for regenerating axons (Ide, 1996).
2. ***Expression of Adhesion molecules by Schwann Cells:*** Schwann cells provide a supportive role in the regrowth of axons by expressing two groups of cell adhesion molecules. The immunoglobulin superfamily and the cadherin superfamily both promote neurite outgrowth (reviewed in Bixby and Harris, 1991; Ide, 1996). In contrast, oligodendrocytes of the CNS express proteins which inhibit the outgrowth of neurites (Caroni, Savio & Schwabb, 1988).
3. ***Production of Neurotrophins by Schwann Cells and Target Structures:*** The discovery of nerve growth factor (NGF) and its effects led to the development of one of the most important theories in neuroscience, namely the trophic theory of neuronal connections (reviewed in Barde, 1989; De La Cruz, Pastor & Delgado Garcia, 1996; Levi-Moltancini, 1982; Purves, Hadley & Voyvodic, 1986). The underlying principle behind the theory is that neurons are dependent upon target structures, neuronal or non-neuronal, due to the production of some trophic factor synthesised by a target and carried retrogradely to the cell body where it influences the activity and even survival of that neuron. The trophic theory bears great relevance to axonal degeneration and regeneration since axotomy interrupts trophic sources derived from target

structures. Disruption of neurotrophic sources initiates the chromolytic sequence of events. Further deprivation because of unsuccessful reinnervation leads to atrophy and even death of the neuron.

A number of neurotrophins have been implicated in peripheral nerve injury. NGF is produced at high levels by Schwann cells 24 hours after axotomy and is associated with sympathetic and sensory neurons (Heumann, 1987). Brain derived growth factor (BDNF), found in motor, sensory and sympathetic neurons reaches a maximum expression up to four weeks after axotomy (Meyer *et al.*, 1992). More recently, neurotrophin-3 (NT-3) has been recognised as being important for trophic interactions in proprioceptive and tactile fibres (Snider & Wright, 1996; Airaksinen & Meyer, 1996).

As the various factors influencing the degree and specificity of neurite outgrowth are being elucidated through techniques of molecular and cellular biology so the exciting prospect of generating artificial environments favourable to axon regeneration becomes more of a reality. Acellular nerve grafts have already been use with some successful in nerve reconstruction surgery (Ide, Osawa & Tohyama, 1990; Ide, 1996; Feneley, Fawcett & Keynes, 1991; Fujimoto, Miki & Ide,1992; Brunelli Vigasio & Brunelli, 1994). It is very likely that further progress in the quality of recovery of peripherally nerve injured subjects will come from the advancements in conduit technology and neurotrophism.

5.7. Concluding Remarks

The current study presents the first major clinical study into the recovery of kinaesthesia subsequent to PNI. It also includes a novel approach for applying movements to the digits using an AC induction motor. Of the three proposed models of thumb CMC joint, little finger MCP joint and index finger MCP joint abduction: adduction, the little finger provided the most complete model for studying reinnervation. Results from the little finger model indicated that recovery of the ability to sense and grade movement is extremely variable, varying from no sensation to normal sensation. Mechanisms underlying this variability are discussed at length.

The models of thumb and index abduction: adduction permitted comparison of the contributions of cutaneous/joint innervation and muscle innervation as proprioceptive sources. Results from these models indicate that each may have a different role in kinaesthesia and may also exhibit distinctive patterns of recovery subsequent to PNI. These two models also demonstrated that high levels of kinaesthetic acuity in a digit were often accompanied by severe deficits in sensorimotor function according to standard clinical measures. This discrepancy highlights the inadequacies of current methods for measuring kinaesthesic sensation, particularly that derived from median nerve innervation. Ways of improving methods for measuring kinaesthesia and sense

of force have been suggested, including a new design that focuses on sensitivity in the areas of the hand which are specialised with regard to sensation of movement and force.

The current study has also provided further evidence that 8-10 Hz pulsatile output is of central origin. It is evident in numerous intrinsic and extrinsic muscles in the hand. It is also present following the dramatic alterations in peripheral connectivity that result from peripheral nerve trauma.

A number of issues relating to the recovery of proprioception in the human hand subsequent to PNI have been addressed and some new light has been provided in this otherwise unexplored field. Deficiencies of current methods in providing measures of functional proprioception in the hand have also been suggested. As clinicians and physiologists look to the exploits of cellular and molecular biology to lead the way in providing new strategies for improving recovery subsequent to nerve trauma so the need for an accurate measure of functional proprioception in the hand intensifies. The present study has provided the first step in the development of models to assess the recovery of kinaesthesia in the human hand following peripheral nerve trauma. It has also proposed a number of different stategies that might be taken to further explore this new and exciting field.

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