

**INTRACORTICAL INHIBITION AND MOTOR CORTICAL  
CONTROL OF INTRINSIC HAND MUSCLES**

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*for the degree of*

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*by*

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*My deepest gratitude to  
my father & my mother  
for their love, support and  
encouragement*

*This thesis is dedicated to them.*

# INTRACORTICAL INHIBITION AND MOTOR CORTICAL CONTROL OF INTRINSIC HAND MUSCLES

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## **ABSTRACT**

Direct cortico-motoneuronal (CM) connections of corticospinal tract neurons are a distinctive feature of the primate motor system which are known to be important for the capacity to perform independent finger movements. However, it is still unclear how the appropriate combinations of CM cells are recruited to produce the selective (fractionated) control over muscles of the upper limb that is necessary for independent finger movements. I have investigated whether GABAergic intracortical inhibitory (ICI) circuits in human motor cortex contribute to the selection of the appropriate CM cells during a motor task requiring selective activation of one of several intrinsic hand muscles. Behaviour of ICI circuits during voluntary contraction was compared for the dominant and non-dominant hemisphere of right-handed subjects, as hemispheric differences in ICI may contribute to preferential use of the right hand for fine motor tasks. Finally, I investigated the range of forces over which ICI contributes to selective activation of a hand muscle.

Neurologically normal adult human subjects were recruited for all experiments. Surface electrodes recorded electromyographic activity of abductor pollicis brevis (APB), first dorsal interosseous and abductor digiti minimi muscles during controlled isometric contractions of APB at different force levels while subjects attempted to keep the other two muscles relaxed using visual feedback of EMG. Paired-pulse transcranial magnetic stimulation (TMS) was used to assess ICI at rest and during selective activation of a hand muscle. TMS intensity and interstimulus interval were varied in different trials.

Data were compared for two different directions of induced current in the brain; posteriorly directed current (PA stimulation) and anteriorly directed current (AP stimulation).

ICI is suppressed for corticospinal neurons controlling the muscle targeted for selective activation; no change in ICI was seen for corticospinal neurons controlling the muscles required to be relaxed. This indicates that differential modulation of ICI in human motor cortex contributes to selective activation of a hand muscle. The direction of current flow induced in the brain proved to be critical for demonstrating this effect. It was observed with AP stimulation but not PA stimulation. I argue that this is due to preferential activation by PA stimulation of interneurons producing  $I_1$  waves in corticospinal neurons. These interneurons are not acted upon by ICI circuits. This problem makes the conventional PA paired-pulse TMS technique unreliable for the assessment of ICI during voluntary contraction. With AP stimulation it was demonstrated that ICI is not modulated during weak selective activation of a hand muscle (<5% of maximal voluntary contraction), but ICI effects on CM cells controlling the target muscle are progressively suppressed at higher levels of activation. The present study is the first to examine hemispheric differences in ICI *during* selective isometric contraction of an intrinsic hand muscle. No hemispheric differences were observed. These studies have demonstrated a functional role for ICI in fractionation of hand muscle activity in normal subjects. It also provides an improved basis for investigating the changes in ICI with TMS in various neurological conditions in which it has been reported that GABAergic inhibition is abnormal.

## **DECLARATION**

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

Maryam Zoghi

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## **Aims and General Introduction**

The role of the motor cortex in the control of precision movements in muscles of the hand has been widely studied. It has been shown that corticospinal neurons in motor cortex with direct connections to spinal motoneurons are important neural structures for the capacity to perform independent finger movements. However, it is still unclear how the appropriate combinations of these corticomotoneuronal (CM) cells are recruited to produce selective control over muscles of the upper limb that is necessary for independent finger movements. It has also been shown that GABAergic intracortical inhibitory (ICI) circuits are less effective in some movement disorders such as focal task-specific dystonia. These patients are not able to overcome the overflow of motor commands to unwanted muscles during the performance of a fine and complex movement, like writing. It has been proposed that altered GABAergic inhibition contributes to the overflow by impairing the selection of corticospinal neurons for task performance. I have investigated in normal subjects whether ICI circuits in human motor cortex contribute to the selection of the appropriate CM cells during a motor task requiring selective activation of one of several intrinsic hand muscles. Paired-pulse transcranial magnetic stimulation is a powerful technique for studying the function of ICI circuits in human motor cortex. It is important to establish the function of GABAergic ICI circuits in normal subjects as a first step to understanding the pathophysiology of movement disorders, such as focal dystonia, in which this system is impaired.

The main aim of the experiments reported in Chapter 2 was to determine whether the suppression of ICI that accompanies voluntary activation of an intrinsic hand muscle is restricted to corticospinal neurons controlling the active muscle when it is activated independently of other intrinsic hand muscles. For this experimental series I used the paired-pulse TMS technique with the conventional posterior-anterior (PA) direction of current flow induced in the brain. It became apparent that there were significant problems with the conventional approach. This led me to adopt an improved technique to study the function of ICI in human motor cortex. In the next series of experiments I examined this issue using paired TMS with anterior-posterior (AP) stimulation, and I showed that ICI was differentially modulated for corticospinal neurons controlling the active muscle during a fractionated muscle activation of abductor pollicis brevis while other hand muscles were kept relaxed by the subject (Chapter 3).

To strengthen the case that differential modulation of ICI is a component of the voluntary command mediating selective activation of hand muscles, I addressed two further issues. First, I used another hand muscle, abductor digiti minimi (ADM) as the target muscle, to show that the result obtained with APB was not particular to activation of a thumb muscle. Second, modulation of ICI was explored during voluntary selective, and involuntary activation of ADM to comparable EMG levels to show that the voluntary nature of the task influenced the amount of ICI suppression for corticospinal neurons controlling the active muscle (Chapter 3).

Next I assessed whether the differential suppression of ICI with voluntary activation is a function of target force level. I directly compared paired-pulse TMS with PA or AP stimulation for assessment of ICI in the same subjects. The experiments demonstrate a force threshold for modulation of ICI with AP TMS, and further demonstrate differences between AP and PA TMS. I concluded that PA TMS is not suitable for assessment of ICI under circumstances in which motoneuron excitability may be altered. These results are presented in Chapter 4.

Using AP paired TMS, I investigated the possible contribution of ICI to hand preference by comparing the function of ICI circuits in dominant and non-dominant hemispheres at rest and during selective activation of hand muscles over a range of target forces. No hemispheric differences in ICI were observed. These findings are also presented in Chapter 4.

Finally, I conducted another series of experiments with a figure-8 coil to determine whether intracortical facilitatory circuits had any influence on the results obtained. ICF circuits are also potentially activated by the paired pulse TMS technique, but it is difficult to assess their contribution with AP paired TMS and a circular coil, because the longer interstimulating intervals required to test ICF allow the possibility of transcallosally mediated interactions from the opposite hemisphere which is preferentially activated by AP TMS. These studies show that ICF circuits are not activated by focal AP paired-pulse TMS, but also the figure of eight coil was less

reliable for use in assessing ICI with AP current flow than the circular coil. The results of these experiments are presented in Chapter 5.