HUMAN MOTOR CORTICAL PLASTICITY AND UPPER LIMB PERFORMANCE

A thesis submitted for the Degree of

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by

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Abstract

The capacity of the adult human nervous system to alter the strength of connections between neurons and between networks of neurons is an exciting area of research providing novel insights into the mechanisms involved in learning, memory and recovery following brain damage. In recent years, it has become clear that both afferent input into the motor cortex and the learning of a new motor task can drive cortical reorganisation. This thesis is concerned with the functional significance of this plasticity, in both normal subjects and stroke patients, and with the question of whether stimulation-induced plasticity can lead to improved fine motor performance.

My initial experiments were conducted to determine the optimal method of analysing responses to transcranial magnetic stimulation (TMS), and to investigate aspects of motor performance as the hand performs a precision task to grasp and lift an object. Studies on normal subjects showed that there is little difference between the dominant and non-dominant hands performing this task, but the type of grip used influences grip-force control. An investigation of stroke patients performing this task demonstrated that certain parameters were sensitive to differences between the affected and unaffected hands and these parameters were highly correlated with stroke-specific functional outcome measures.

The induction of plastic change in the human motor cortex can be induced by repetition of movements, performing a complex motor task or stimulation of the peripheral afferents and/or the motor cortex itself. I observed that the application of so-called "associative stimulation" to two hand muscles in normal subjects increased the excitability of the corticospinal projection to those muscles, and improved performance times on a subsequent motor task to a greater extent than subjects receiving a control intervention. I then applied associative stimulation to

the affected hand of stroke patients in conjunction with rehabilitation, which improved their ability to perform the dextrous grip-lift task. This is the first study to show that this method of inducing motor cortical plasticity can also lead to functional improvements in stroke patients.

These studies confirm that using afferent stimulation to drive cortical reorganisation is associated with improved function and fine motor performance in both normal subjects and stroke patients.

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.

SIGNED……………………………… DATE…………………..………..

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Aims and general introduction

Reorganisation of the human motor cortex can be induced by manipulation of afferent inputs reaching the cortex. This can be achieved with motor training, or stimulation of peripheral nerves and/or muscles to increase the excitability of corticospinal projections, which supports the hypothesis that afferent input can drive cortical reorganisation. While this short-term reorganisation of the motor cortex has been demonstrated using various experimental paradigms, evidence for an associated functional effect is lacking. This is particularly pertinent as we (McKay et al., 2002; Ridding et al., 2000) and subsequently others (Bütefisch et al., 2004) have proposed that techniques to induce cortical plasticity may enhance the effectiveness of rehabilitation following brain damage such as stroke.

Cortical reorganisation can be demonstrated using transcranial magnetic stimulation (TMS). Stimulation of the motor cortex can induce descending volleys in the corticospinal tract and, in turn, muscle responses which are termed motor evoked potentials (MEPs). Changes in the amplitude of MEPs indicate changes in the strength of the corticospinal projection to the target muscles. Alternate methods of analysing MEPs had been reported in the literature and my first series of experiments was designed to determine the optimal method of analysing these potentials. The results of this study, detailed in Chapter 2, confirmed that measuring the individual peak-to-peak amplitude for each response, and then taking the mean over a number of trials, was the most appropriate method for analysing MEPs from small hand muscles and this method was thus used for the remainder of the studies detailed in this thesis.

The potential for afferent stimulation to improve motor performance was investigated in Chapter 3. I used a period of stimulation of the motor points of two hand muscles to increase the excitability of the corticospinal projection, in accordance with previous reports, and I contrasted the effect of this type of stimulation with a control group who received no intervention, and another group of subjects who received a period of non-associative stimulation that does not increase excitability. Following this, all subjects performed a complex motor task a number of times. All subjects improved their performance times, but only subjects in the associative stimulation group also demonstrated an increase in MEP amplitude. This was not associated with an increased level of performance at the commencement of task, but during the task their performance improved more rapidly than the other groups, suggesting that the preconditioning stimulation which increased excitability also conferred a functional benefit.

A possible limitation of previous studies that describe changes in excitability but lack evidence of functional effect is the difficulty in detecting subtle changes in performance of the hand in healthy subjects. Common tools to assess manual dexterity, such as the Purdue Pegboard Test, may not be sensitive enough to detect improved performance in normal subjects who are already performing at a high level. In order to investigate aspects of a precision task in more detail, I used a grip-lift apparatus for the assessment of fine motor performance of the hand. This enabled quantitative assessment of differences between the dominant and non-dominant hands of normal subjects, as well as the effect of alternate postures of the hand when performing the precision grip-lift task. These studies are described in Chapter 4.

Few researchers have examined the precision grip-lift task in stroke patients, and none have included poorly-recovered patients, or have compared the affected hand with the non-hemiplegic, supposedly unaffected upper limb. I addressed these issues in experiments outlined in Chapter 5, in order to ascertain the usefulness of the grip-lift apparatus in detecting change in the upper limb following stroke over a period of time or as a result of an intervention. Rather than comparing aspects of the task to age-matched controls, I considered that if the task were sensitive enough to detect a difference between the hands of individual stroke patients then it should be a useful measure of changes in dexterity following stroke. Results indicated not only which parameters were useful to detect a change between the hands, but also that these same parameters, when compared with basic speed and strength tests, explained a large proportion of the variance of standard stroke-specific tests of function.

Finally, I combined the findings from the above experiments to explore the potential of afferent stimulation to increase the excitability of the motor cortex and to induce functional changes in a group of subacute stroke patients. This longitudinal study involved two groups of ten stroke patients, randomly allocated to be given stimulation of two muscles of the paretic hand, or sham stimulation. All patients participated in a standardised rehabilitation program based on task-specific physiotherapy, to test the hypothesis that increased excitability of the motor cortex would make it more responsive to motor learning. At the end of the intervention, all patients improved their functional abilities, but the stimulation group also increased their ability to perform aspects of the precision grip-lift task. This study, presented in Chapter 6, confirms that methods that induce cortical plasticity can enhance the effect of rehabilitative strategies and may become a useful adjunct in the restoration of function following brain injury.