

## Physiology and Pathophysiology of the Swallowing Area of Human Motor Cortex

S. Hamdy,<sup>1</sup> Q. Aziz,<sup>1</sup> D.G. Thompson<sup>1</sup> and J.C. Rothwell<sup>2†</sup>

<sup>1</sup>*Department of Gastrointestinal Science, Hope Hospital, University of Manchester, Manchester, M6 8HD, UK;*

<sup>2</sup>*Sobell Department of Neurophysiology, Institute of Neurology Queen Square, London WC1N 3BG, UK*

### SUMMARY

**Swallowing problems can affect as many as one in three patients in the period immediately after stroke. Despite this, in the majority of cases, recovery usually occurs to a safe level after a month or two. In this review, we show how the organization of the cortical projections to swallowing muscles can account for many of the clinical observations on swallowing after stroke and explain why recovery is common in the long term. In addition, we examine approaches that may be useful in speeding up recovery of swallowing. Swallowing may be a useful model in which to study central nervous reorganization after injury.**

### INTRODUCTION

The principal problem after stroke is lack of voluntary control of muscles on the affected side. A pure motor lesion interrupts motor cortical output to brainstem and spinal centers, and this causes weakness and spasticity. The extent to which

recovery can take place depends on the ability of these projections to either regrow or have their influence replaced by activity in other systems. The systems controlling distal and proximal muscles provide an interesting contrast in the way the CNS reacts to stroke damage.

Cortical projections to distal hand muscles are dense and direct. Recovery of function after stroke is usually poor. Studies with transcranial magnetic stimulation show that in healthy subjects, projections from the undamaged hemisphere are small and do not, at least in most cases, seem to increase in efficacy after stroke (Turton & Lemon, 1999). Although functional imaging and EEG recordings show increased activity of the undamaged hemisphere during movements of the paretic side (Chollet et al., 1991), it seems likely that much of the improved function occurs because of recovery of damaged systems in the affected hemisphere.

The situation seems to be quite different for proximal muscles. The data presented in this paper illustrate the organization of cortical input to swallowing muscles and show how understanding the details of this input can yield insights into dysphagia after stroke and into possible ways of treating swallowing problems.

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†Corresponding author:  
fax: +44 20 7278 9836  
e-mail: j.rothwell@ion.ucl.ac.uk

### CNS CONTROL OF SWALLOWING

Swallowing is usually thought to be the result of local peristaltic mechanisms in the esophagus, combined with reflex involvement of swallowing centers in the brainstem. However, the cerebral cortex appears to play a critical role in the initiation of voluntary swallows. Indeed, repetitive electrical stimulation of appropriate regions of the cortex in anaesthetized animals or in humans undergoing neurological surgery can induce swallowing (Penfield & Boldrey, 1937).

Injury to swallowing motor areas and/or their connection to the brainstem will usually result in problems with swallowing (dysphagia). The most common cause of this is stroke. Up to half of all stroke patients experience dysphagia, and this is frequently associated with life threatening complications of pulmonary aspiration and malnutrition (Gordon et al., 1987).

### STUDIES OF DYSPHAGIA AFTER STROKE

Although much animal evidence suggests that both cerebral hemispheres have a role in the initiation of swallowing, other studies of brain damage in humans suggest that one or the other hemisphere may be dominant. In fact, one of the earliest observations of a unilateral cerebral lesion producing dysphagia was that of Bastian (1898). He reported a case of a man admitted to hospital with hemiplegia and aphasia, but who also had transient problems in swallowing. A later post-mortem revealed that apart from two limited lesions in the left hemisphere, the brain was healthy. More recently, Meadows (1973) reported six cases of dysphagia. All of them had confirmed unilateral lesions with the cerebral cortex, five of which affected the right hemisphere. Since then, a number of studies have confirmed that 40% or more of patients with unilateral hemispheric stroke

may have swallowing difficulty. There was an increased tendency for the pharynx to be involved if the damage was limited to the cortex of the right hemisphere.

### TMS STUDIES OF HUMAN SWALLOWING MOTOR CORTEX

In order to obtain more information about the organization of the cerebral projections to swallowing muscles, Hamdy et al. (1996) performed a series of experiments in which they used transcranial magnetic stimulation (TMS) to map the pattern of cortical projections to the pharynx, the striated portion of the oesophagus, and mylohyoid muscles.

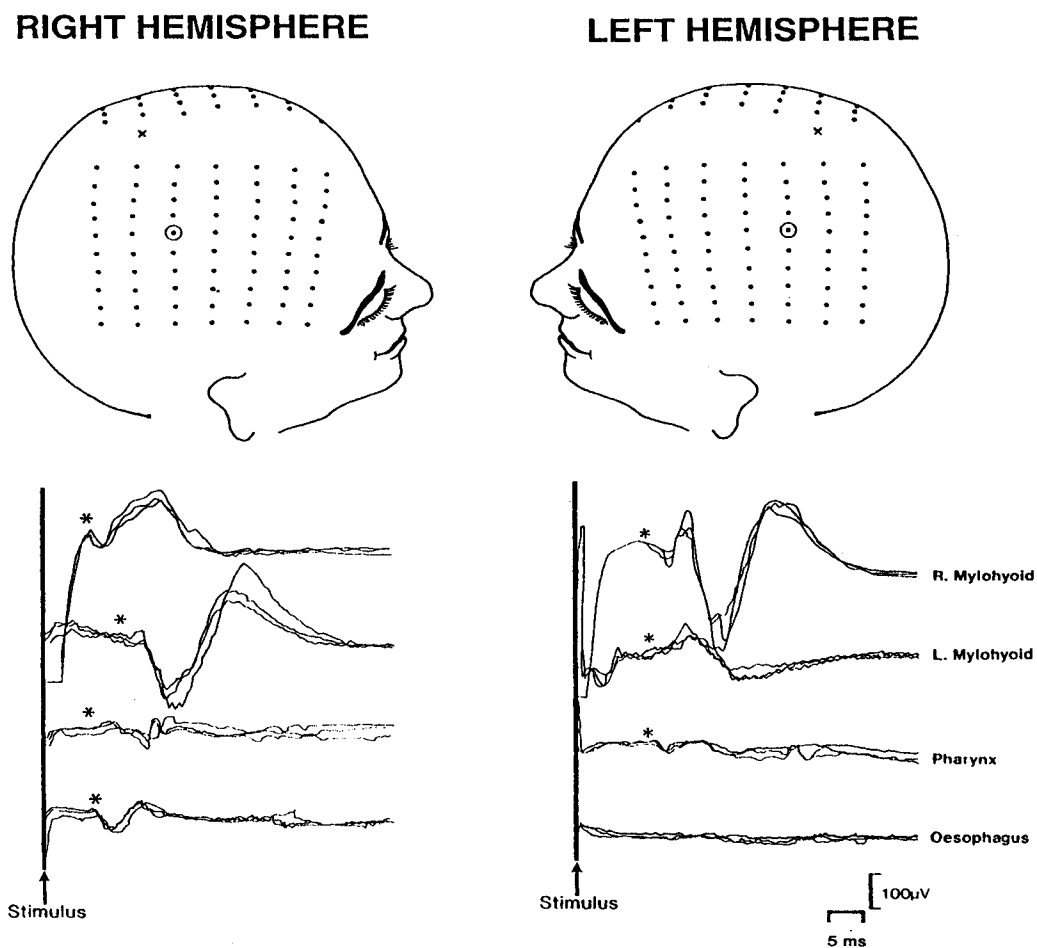
Figure 1 gives a typical example of the type of results that were obtained. The subject's scalp was marked out with a 1 cm group of points and each point stimulated 3 times at a fixed intensity. Stimulation over the upper central portion of either hemisphere could provoke EMG responses at short latency in mylohyoid, pharynx, and oesophageal muscles. The latency of these responses was short (about 8 to 10 ms), compatible with a very direct and rapidly conducting pathway from cortex via brainstem to the muscle. It is important to note that since only single stimuli were used to activate the cortex, the responses were simple muscle twitches rather than a full swallowing sequence of the sort that is seen during surgery when the brain is stimulated with a train of several hundred stimuli at a rate of 50 to 60 Hz.

Mapping the projection from each hemisphere shows that the various swallowing muscles are arranged somatotopically, with the mylohyoid lateral and the pharynx and esophagus more medial. However, the most important finding from a large group of individuals was that stimulation of one hemisphere tended to evoke larger responses in the pharynx and the esophagus than that from the homologous part of the opposite hemisphere.

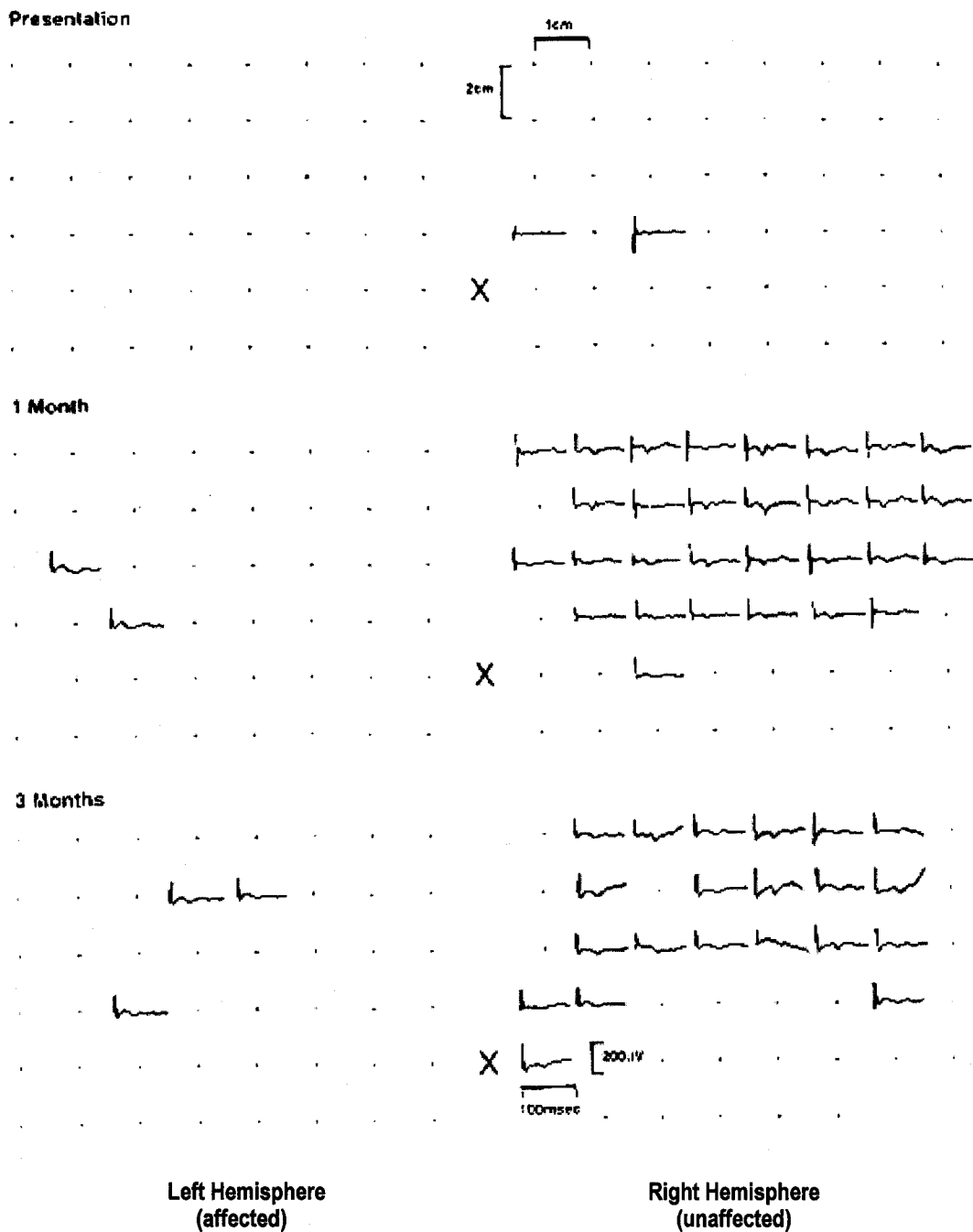
Thus, as in the subject illustrated in Fig. 1, the responses in the pharynx and the esophagus from stimulation of the right hemisphere are larger than those from stimulation of the left hemisphere. This difference in projection was independent of handedness and was even seen in a pair of identical right-handed twins, suggesting little genetic contribution to its development.

#### DYSPHAGIA AFTER UNILATERAL CEREBRAL STROKE

The findings above in normal subjects only show that in most normal subjects, there is an asymmetry in the size of responses evoked by a constant stimulus to each hemisphere. However, whether this relates to a functional asymmetry in



**Fig. 1:** EMG responses recorded from swallowing muscles following TMS of motor cortex. The upper panels show a grid of stimulation sites marked out on the scalp. In the lower panels are superimposed EMG responses after stimulation of the right and left hemispheres at the sites marked with  $\odot$ . The vertex of the scalp is marked by a 'x'. An initial stimulus artifact can be seen in all traces, particularly in that from the mylohyoid muscles. This is followed after 8–10ms by a short latency response with an onset marked by \* above each trace. Note that the responses evoked in pharynx and esophagus are larger following stimulation of the right than the left hemisphere. (From Hamdy et al., 1996).



**Fig. 2:** Changes in the excitability of cortical projections to pharynx following recovery after a dysphagic stroke. The EMG responses are shown after stimulation of each point on the scalp in a single patient at presentation (top), and then 1 month (middle) and 3 months (bottom) after stroke affecting the left hemisphere. An 'X' marks the vertex of the scalp. Over the period of study, the patient progressed from severe dysphagia to controlled swallowing. Note how the size of responses evoked from the unaffected hemisphere increases in size over the same period. There was little change in the size of responses evoked from the affected hemisphere. (From Hamdy et al., 1998.)

the strength of the cortical projections from each hemisphere or is simply a result of anatomical differences (for example the distance of the cortex from the scalp surface) in each hemisphere is unclear. Results from patients with dysphagia tend to suggest that the former hypothesis is likely to be true. Hamdy et al. (1997a; 1998) measured the size of responses evoked by TMS from both hemispheres in pharynx and esophageal muscles in a large series of pure unilateral stroke patients. Half the patients had dysphagia, whereas the other half did not. The authors reasoned that if there were true functional asymmetry of swallowing projections from each hemisphere, then perhaps subjects who developed dysphagia after stroke had damaged the side of the brain with the largest (most dominant) projection to their swallowing muscles. If this were the case, then it would be expected that in dysphagic subjects, stimulation of the undamaged hemisphere would produce, on average, smaller responses in pharynx and the esophagus than stimulation of the undamaged hemisphere in non-dysphagic patients. Indeed, this proved to be the case, and therefore the size of the hemispheric projection to swallowing muscles may well have determined the presence or absence of dysphagia.

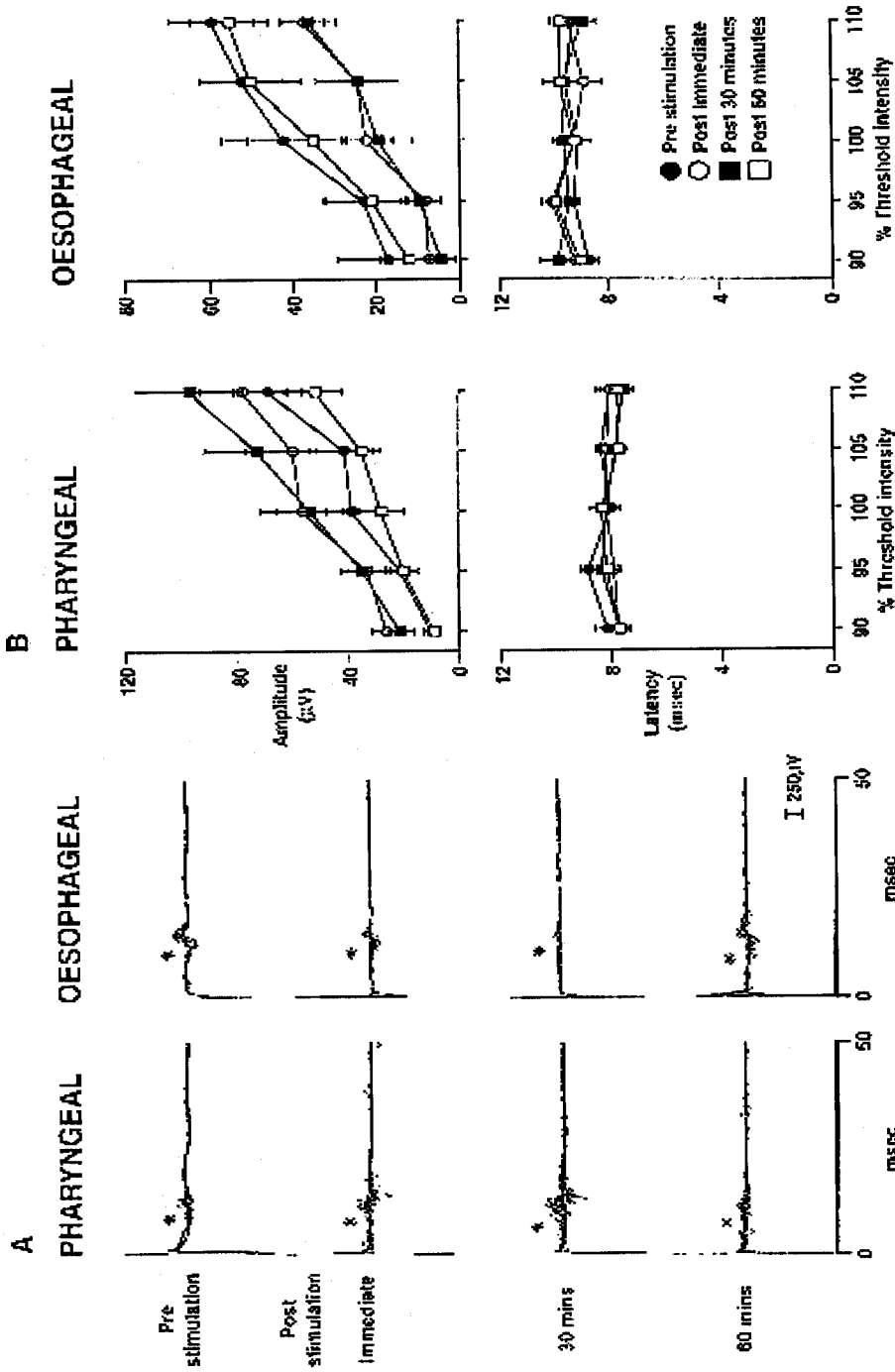
#### **RECOVERY OF SWALLOWING FUNCTION AFTER STROKE**

A large proportion of initially dysphagic patients eventually recover their ability to swallow. However, the mechanism responsible for this recovery is unclear. In a detailed study of stroke patients using TMS, Hamdy et al. (1998) mapped the cortical projections to the pharynx and esophagus in a series of dysphagic and non-dysphagic patients over a period of several months. Many initially dysphagic patients had recovered over this period, and it was possible to document the changes in the motor evoked potentials (MEPs) evoked by TMS in

swallowing muscles over that period. The study showed that responses evoked by stimulation of the pharyngeal representation in the undamaged hemisphere increased markedly in patients who recovered (Fig. 2). There was no change in patients who had persistent dysphagia nor in patients who were initially non-dysphagic. No changes were seen at all in the damaged hemisphere of any of these patients. The implication is that over a period of weeks, the undamaged hemisphere is capable of increasing the excitability of its projections to swallowing musculature in initially dysphagic patients. This is paralleled by an improvement in clinical swallowing function. Hamdy et al. therefore have suggested that the good recovery of swallowing function of the throat depends on compensatory reorganization of the undamaged hemisphere. The situation appears to differ from that of distal limb muscles, where some TMS studies have indicated that limb recovery after hemiparesis is more likely to result from an increase in the activity of remaining viable cortex in the damaged hemisphere. In such cases, the scope for expansion of a normal connection from the undamaged part of the brain may be a limiting factor in recovery.

#### **EFFECT OF PERIPHERAL SENSORY INPUT ON REORGANIZATION OF CORTICAL PROJECTION TO SWALLOWING MUSCLES**

Given that recovery from dysphagia may depend upon plastic changes in the function of projections from the undamaged hemisphere, we then wondered whether or not it might be possible to speed up the process of recovery by other interventions. One potential candidate for such a therapy might be a manipulation of sensory input to the cortex. Sensory input from the gut not only has a major influence on the activity of brainstem swallowing centers but also converges onto cortical sensory and motor areas. Furthermore, it has been



**Fig. 3:** Sensory driven changes in the excitability of cortical swallowing motor pathways. On the left are the responses evoked in pharynx and esophagus by TMS at threshold intensity in one individual before and after electrical stimulation of the pharynx at 10Hz for 10 min. Ten responses are superimposed. The \* indicates the onset of the response in each muscle. The graphs on the right show the data from 5 subjects combined at a range of different stimulus intensities. Note that both immediately and 30 min after stimulation, responses in the pharynx have increased in amplitude, whereas those in the esophagus have decreased. After 60 min, the responses in both muscles have returned to baseline values. There is no change in the latency of the responses. (From Hamdy et al., 1998.)

shown that the excitability of cortical projections to swallowing muscles can be influenced by the stimulation of afferent fibers in the vagal and trigeminal nerves (Hamdy et al., 1997b). In those studies, single stimuli were used but had only a very short-lasting effect. More recently, Hamdy et al. (1998) have gone on to show that prolonged electrical stimulation of the pharynx for up to 15 minutes can induce changes in motor cortical excitability that outlasts the stimulus by up to 30 minutes (Fig. 3). If this approach could be adopted in dysphagic stroke patients, then it could prove to be a potential mechanism for speeding recovery of function from the intact representation of the undamaged hemisphere. Such studies are now in progress.

### CONCLUSIONS

These studies indicate that it is possible to study the cortical projections to swallowing musculature in intact human subjects. Unexpectedly, they show that there is often an asymmetry in the connections from each hemisphere, and we have speculated that this may have two important consequences. First, damage to the 'dominant' hemisphere for swallowing may partially explain why some patients with apparently similar unilateral hemispheric strokes become more dysphagic than others. Second, the usual recovery from dysphagia may depend on increasing involvement of the projections from the remaining undamaged hemisphere. Finally, it appears that techniques involving the stimulation of afferent input from the pharynx may help to speed the process of recovery by promoting faster reorganization of corticobulbar projections.

### REFERENCES

- Bastian HC. 1898. A treatise on aphasia and other speech deficits. London, UK: Lewis.
- Chollet F, DiPiero V, Wise RJ, Brooks DJ, Dolan RJ, Frackowiak RS. 1999. The functional anatomy of motor recovery after stroke in humans: A study with positron emission tomography. *Ann Neurol* 29: 63–71.
- Gordon C, Langton Hower, R., Wade DT. 1987. Dysphagia in acute stroke. *Br Med J* 295: 411–414.
- Hamdy S, Aziz Q, Rothwell JC, Crone R, Hughes D, Tallis RC, Thompson DG. 1997a. Explaining oropharyngeal dysphagia after unilateral hemispheric stroke. *Lancet* 350: 686–692.
- Hamdy S, Aziz Q, Rothwell JC, Hobson A, Barlow J, Thompson DG. 1997b. Cranial nerve modulation of human cortical swallowing motor pathways. *Am J Physiol* 272: G802–G808.
- Hamdy S, Aziz Q, Rothwell JC, Power M, Singh KD, Nicholson DA, et al. 1998. Recovery of swallowing after dysphagic stroke relates to functional reorganization in the intact motor cortex. *Gastroenterology* 115: 1104–1112.
- Hamdy S, Aziz Q, Rothwell JC, Singh KD, Barlow J, Hughes DG, et al. 1996. The cortical topography of human swallowing musculature in health and disease [see comments]. *Nature Med* 2: 1217–1224.
- Hamdy S, Rothwell JC, Aziz Q, Singh KD, Thompson DG. 1998. Long-term reorganization of human motor cortex driven by short-term sensory stimulation. *Nature Neurosci* 1: 64–68.
- Meadows JC. 1973. Dysphagia in unilateral cerebral lesions. *J Neurol Neurosurg Psychiatry* 36, 853–860.
- Penfield W, Boldrey E. 1937. Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. *Brain* 60, 389–443.
- Turton A, Lemon RN. 1999. The contribution of fast cortico-spinal input to the voluntary activation of proximal muscles in normal subjects and in stroke patients. *Exp Brain Res* 129: 559–572.