Abnormalities of the balance between inhibition and excitation in the motor cortex of patients with cortical myoclonus

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Summary
Patients with cortical myoclonus may have purely focal or multifocal jerks, or they may have additional bilateral or generalized jerks, suggesting the spread of excitatory myoclonic activity between the cerebral hemispheres and across the sensorimotor cortex. The factors contributing to this spread of activity were investigated in 10 patients with multifocal cortical myoclonus and eight patients with multifocal and bilateral or generalized cortical myoclonus. The two groups were termed 'non-spreaders' and 'spreaders', respectively. Eight of the patients were also epileptic. Motor thresholds to single transcranial magnetic shocks at rest were higher in 'non-spreaders' (median 88%, range 45–100% of stimulator output) than either 'spreaders' (50%, range 26–90%, P = 0.023) or healthy subjects (38%, range 28–53%, P < 0.001). This pathological elevation in motor threshold was not simply an effect of treatment with antiepileptic drugs. Paired transcranial magnetic stimuli were used to investigate ipsilateral cortico-cortical and transcallosal inhibition. There was less (MANOVA, P < 0.05) ipsilateral inhibition at interstimulus intervals (ISIs) of 1–6 ms in 'spreaders' (mean 107±SEM 23% of control) compared with 'non-spreaders' (75±15%) or healthy subjects (59±10%). There was also less (P < 0.05) transcallosal inhibition across inhibitory timings (10, 12 and 14 ms) in the 'spreaders' (98±6% of control) compared with the 'non-spreaders' (64±8%) or healthy subjects (59±6%). There was no relationship between ipsilateral cortico-cortical and transcallosal inhibition and the presence or absence of epilepsy, although non-epileptic patients did have higher motor thresholds (median 85%, range 32–100% of stimulator output) than either epileptic patients (50%, range 26–90%, P < 0.001) or healthy controls (38%, range 28–53%, P = 0.002). Abnormalities in ipsilateral and transcallosal inhibition appear to facilitate the spread of the cortical myoclonic activity responsible for bilateral and generalized jerks. However, these abnormalities in inhibition do not play a major role in the development of generalized seizures in patients with cortical myoclonus.

Keywords: cortical myoclonus; motor threshold; cortico-cortical inhibition; transcallosal inhibition

Abbreviations: EMG = electromyography; FDI = first dorsal interosseous; ISI = interstimulus interval

Introduction
Cortical myoclonus is thought to involve the sensorimotor cortex and rapidly conducting pyramidial pathways (Kugelberg and Widen, 1954; Lhermitte et al., 1971; Pagni et al., 1971; Chauvel et al., 1978; Hallett et al., 1979). It may be elicited by peripheral stimuli or provoked by voluntary action. Such cortical reflex and action myoclonus is most commonly focal or multifocal, but in some patients bilateral or generalized jerks may also occur with stimulation or movement of a single limb (Lance and Adams, 1963; Shibasaki et al., 1978; Brown et al., 1991). We recently investigated these more extensive myoclonic jerks, and showed that myoclonic activity is able to spread relatively rapidly from an initial focus in one sensorimotor cortex to other ipsilateral sensorimotor cortical areas through cortico-cortical pathways, and to the opposite sensorimotor cortex through the corpus callosum. We suggested that similar processes might underlie the generalized seizures common in patients with cortical myoclonus (Brown et al., 1991).
Normally the spread of excitation within the cortex and between the two cerebral hemispheres is kept in check by inhibitory processes. It is now possible to examine some of these processes in man using the technique of transcranial magnetic stimulation. In healthy subjects magnetic stimulation of the sensorimotor cortex leads to local and transcallosal inhibition, as judged by the amplitude of the electromyographic (EMG) activity elicited by a test shock to the ipsilateral or contralateral sensorimotor cortex (Ferbert et al., 1992; Kujurai et al., 1993). Here we show that such cortical and transcallosal inhibition is reduced in patients with multifocal cortical myoclonus who also have bilateral or generalized jerks, compared with patients with multifocal cortical myoclonus alone, or normal subjects.

**Subjects**

Patients gave their informed consent to the neurophysiological studies and the procedures were approved by the local ethical committee. Details of the 18 cases studied are presented in Table 1. All the patients had cortical action myoclonus, with a short-latency time-locked cortical correlate preceding jerks during voluntary action. In addition, Cases 5, 6, 10, 13, 16, 17 and 18 had cortical reflex myoclonus, defined by giant cortical evoked potentials and C reflexes following electrical stimulation of the median nerve at the wrist. Cases 3 and 4 had giant cortical evoked potentials in the absence of a reflex EMG response. Cases 10, 11, 14 and 16 have been reported previously (Brown et al., 1991; their cases 6, 1, 9 and 5, respectively).

Eight of the cases were also epileptic, with a history of two or more seizures (see Table 1). Fifteen patients were tested while taking various combinations of clonazepam, carbamazepine, phenobarbital, phenytoin, piracetam, primidone or sodium valproate as shown in Table 1. Cases 9, 12 and 18 were investigated off drug treatment. Disability was assessed using the myoclonus disability rating scale (Brown et al., 1993).

Motor threshold to transcranial magnetic stimuli and cortico-cortical inhibition were measured in 12 healthy subjects, and transcallosal inhibition was measured in six healthy subjects. The age range of the normal subjects was 18–75 years. There was no significant change in resting motor threshold, ipsilateral inhibition or transcallosal inhibition with age amongst normal subjects or patients.

**Methods**

Electromyographic recordings were made using bipolar silver/silver chloride electrodes placed 2–3 cm apart longitudinally over the muscle bellies or, in the case of the first dorsal interosseous (FDI), over the muscle belly and the second metacarpophalangeal joint. The EEG was recorded from silver/silver chloride electrodes fixed to the scalp with collodion. Electromyography and EEG were band pass filtered at 3 kHz with time constants of 30 ms and 100 ms, respectively. The sampling rate was 5 kHz per channel. Trials were recorded onto a personal computer using a 1401 laboratory interface (Cambridge Electronic Design, Cambridge, UK), and analysed off-line.

**Sensory evoked potentials and backaveraging**

Sensory evoked potentials were recorded following stimulation of the median nerve at the wrist with a constant voltage rectangular pulse of 0.2 ms duration at intensities just above motor threshold. Sensory evoked potentials were the average of 512 stimuli. C3 and C4 were referred to linked ear-lobe electrodes. Sensory evoked potential amplitude was measured from the first major cortical positive peak (conventionally known as the P25) to the second major negative peak (the N33). It was considered giant if it exceeded 6.0 μV. In 14 healthy control subjects, aged 18–60 years, the mean somatosensory evoked potential amplitude was 1.8 μV (range 0.4–3.4 μV).

For backaveraging C3 was linked to F3, Cz to Fz and C4 to F4 in a bipolar montage. The patient sat supported comfortably, while moving one limb to command. The other limbs were relaxed. Electromyographic activity in the active limb was used to trigger the collection of EEG and electromyographic activity.

Surface EMG was recorded from at least FDI, forearm extensors and tibialis anterior bilaterally. The laterality and relative latencies to onset of EMG activity were measured in a minimum of 50 single trials recorded during voluntary movement, and 50 trials recorded during median nerve stimulation. Patients were considered ‘spreaders’ if at least 10% of the action or reflex jerks involved bilateral EMG activity, with the onset of EMG activity in homologous muscles separated by <15 ms on the two sides of the body. In bilateral jerks such EMG activity was only recorded in the stimulated or active limb, and its opposite counterpart. In generalized jerks, the same activity was recorded in all four limbs. In ‘non-spreaders’ action, and, if present, reflex jerks nearly always remained confined to the active or moved limb (Brown et al. 1991). In these patients <5% of jerks involved bilateral EMG activity with the onset of EMG in homologous muscles separated by <15 ms on the two sides of the body.

**Motor threshold, ipsilateral cortico-cortical and transcallosal inhibition**

Experiments were performed using a figure-of-eight stimulating coil (external loop diameters 9 cm) powered by a High power Magstim 200 magnetic stimulator (Magstim, Dyfed, UK), giving a maximum output of 2.2 Tesla. The coil was oriented in such a way that electric currents induced in the brain flowed in a posterior to anterior direction in the hand area of the motor cortex. Responses were recorded from the contralateral relaxed and active FDI. Motor threshold was
Table 1  Clinical details

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Cortical reflex myoclonus</th>
<th>Cortical action myoclonus</th>
<th>Seizures</th>
<th>Medication (daily dose)</th>
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<tr>
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<td>+</td>
<td>10/year</td>
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<td>5/year</td>
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*No underlying cause found, despite full investigation; †Cases 3 and 4 had giant evoked potentials but no reflex jerks; ‡total of six fits up to age 38, none since.

defined as the stimulus intensity producing a response in at least 50% of trials (with the stimulus delivered directly, and not through a Bistim module). In addition, motor threshold was measured in the contralateral active FDI using transcranial anodal electrical stimulation of the motor cortex (D180, Digitimer Ltd, UK) in two patients. The amplitude of the threshold response was ~50–100 μV.

The techniques of cortico-cortical inhibition (Kujirai et al., 1993) and transcallosal inhibition (Ferbert et al., 1992) have been described in detail elsewhere. In the former, conditioning followed by test magnetic stimuli were delivered through the same stimulating coil over the motor cortex, using a Bistim module. The intensity of the conditioning stimulus was 5% (of stimulator output) below active threshold, while the test shock was set to evoke a muscle response in relaxed FDI of ~1 mV peak-to-peak amplitude. Interstimulus intervals between 1 and 15 ms were investigated.

When testing transcallosal inhibition, conditioning and test magnetic stimuli were delivered over the motor cortex ipsilateral and contralateral to the examined FDI, respectively. Interstimulus intervals of 6–16 ms were investigated. Both conditioning and test stimulus intensities were adjusted so that when given alone they produced EMG responses of ~1 mV in the relaxed FDI contralateral to the stimulus.

Three blocks of 40 trials were recorded. Each block consisted of four different conditions delivered pseudo-randomly; test alone and test and conditioning at three different ISIs. All recordings were made at rest. The area of
Fig. 1 Electromyographic records of a focal action jerk in Case 3 (A), and a generalized action jerk in Case 14 (B). The jerks are provoked by voluntary movement of the right (R) arm. In A myoclonic EMG activity is confined to the active limb (e.g. R biceps and FDI). In B EMG activity is generalized, affecting muscles of the right and left (L) arms and legs. There is a latency difference of ~9 ms (see vertical lines) between homologous muscles on the right and left sides of the body, consistent with the transcallosal spread of myoclonic activity from the left to the right motor cortex (see Brown et al., 1991).

Results

Patients were divided into two groups on the basis of the polymyographic findings (Table 1). Myoclonic jerks were virtually confined to the stimulated or active limb (multifocal myoclonus) in Cases 1-10. An example of such an action jerk is shown for Case 3 in Fig. 1A. Jerks, at most, involved one limb and adjacent trunk. The cortical spread of excitatory activity responsible for the myoclonus was therefore limited in this group, which we term ‘non-spreaders’ (Brown et al., 1991).

Cases 11-18 showed frequent additional bilateral (both upper or both lower limbs involved) or generalized (all four limbs involved) action jerks as described by Brown et al. (1991). An example of a generalized action jerk is shown in Fig. 1B for Case 14. The reflex jerks in four of these patients (Cases 13, 16, 17 and 18) could similarly be extensive. Thus there was evidence of spread of activity across the sensorimotor cortex and between the two cerebral hemispheres. This group were termed ‘spreaders’. The difference in latency between forearm extensors or FDI between the two sides of the body was 3-10 ms (mean 6 ms) for bilateral action jerks in Cases 11-18, and 6-16 ms (mean 11 ms) for bilateral reflex jerks in Cases 13, 16, 17 and 18. [These differences are similar to those described by Brown et al. (1991).]

There was no difference between the range of aetiologies or
Inhibition in cortical myoclonus

Dijability

Fig. 2 The total disability scores in 'spreaders' and 'non-spreaders'. The median scores are represented by horizontal lines. 'Spreaders' were more disabled (P = 0.045, Mann-Whitney rank sum test).

drug treatments between the 'non-spreaders' and 'spreaders' (Table 1). However, 'spreaders' were more (P = 0.045) disabled than 'non-spreaders' (Fig. 2).

Motor thresholds to transcutaneous stimulation of the motor cortex

'Motor thresholds to transcutaneous stimulation of the motor cortex'

'Non-spreaders' in general had higher thresholds than either 'spreaders' (P = 0.023) or healthy controls (P < 0.001). The distribution of motor thresholds within the three groups of subjects is shown in Fig. 3, in which each tested cerebral hemisphere is plotted. One striking feature amongst the patients was the number with relaxed motor thresholds in excess of 80% of stimulator output: two 'spreaders' and four 'non-spreaders' (four and seven tested hemispheres, respectively). The highest motor threshold recorded in healthy subjects was 53%. The pathologically increased thresholds in some of the patients did not simply reflect drug effects: Cases 9 and 18 showed greatly elevated thresholds without antmyoclonic treatment (see inverted unfilled triangles in Fig. 3).

The pathological elevation in motor threshold may be cortical in origin. In Case 18 the relaxed and active thresholds to magnetic stimulation were 85% (cf. median 38%, range 28–53% in healthy subjects) and 50% (cf. median 28%, range 20–38% in healthy subjects), respectively. However, when transcranial electrical stimulation of the motor cortex was used in the same subject, motor threshold in active FDI was 40%, which is the average active motor threshold in normal subjects (Rothwell et al., 1987). Similar findings were evident in Case 8.

Ipsilateral cortico-cortical inhibition

Ipsilateral cortico-cortical inhibition was measured in Cases 1–6 and 11–16. Thresholds were too high to allow this measurement in all but one of the remaining patients. There was significantly less (MANOVA, P < 0.05) ipsilateral inhibition at ISIs of 1–6 ms in the 'spreaders' (107±23% of control) compared with the 'non-spreaders' (75±15% of control) or healthy subjects (59±10% of control). The difference between 'non-spreaders' and healthy subjects did not reach statistical significance. Figure 4A compares the ipsilateral cortico-cortical inhibition in a healthy subject with that in a 'spreader' (Case 13) at an ISI of 3 ms. The results from all the subjects are summarized in Fig. 5. The difference between 'spreaders' and 'non-spreaders' did not seem to be due to variations in motor threshold as it persisted in those 'spreaders' (Cases 12 and 14) and 'non-spreaders' (Cases 2, 3 and 6) with similar motor thresholds (of 45–60%). In four 'spreaders' (Cases 12, 13, 14 and 16), including one patient tested off medication (Case 12), inhibition at conditioning-test intervals of 6 ms was replaced by net excitation (Fig. 6A). There was no correlation between ipsilateral cortico-cortical inhibition and resting motor threshold or the amplitude of the cortical somatosensory evoked potential.

Transcallosal inhibition

Transcallosal inhibition was measured in Cases 1–3, 6, 7 and 11–16. All but two of the remaining subjects had relaxed motor thresholds that were too high to allow assessment
using the double shock technique. There was significantly less (MANOVA, \( P < 0.05 \)) transcallosal inhibition across inhibitory timings (10, 12 and 14 ms) in the ‘spreaders’ (98±6% of control) compared with ‘non-spreaders’ (64±86% of control). Inhibition in the ‘non-spreaders’ was the same as that in healthy subjects (59±6% of control). Figure 4B compares the transcallosal inhibition in a healthy subject with that in a ‘spreader’ (Case 13) at an ISI of 10 ms. The results from all the subjects are summarized in Fig. 7. The difference between ‘spreaders’ and ‘non-spreaders’ did not seem to be a threshold effect as it persisted in those ‘spreaders’ (Cases 12 and 14) and ‘non-spreaders’ (Cases 2, 3 and 6) with similar motor thresholds. Inhibition was replaced by net excitation at intervals of 10, 12 and 14 ms in two patients

Fig. 5 The pattern of cortico-cortical inhibition in 12 healthy controls, six ‘spreaders’ and six ‘non-spreaders’. The inhibition of the test shock produced by the conditioning shock is expressed as the percentage of the size of the test, when this is delivered alone. Error bars show the SEM. Cortico-cortical inhibition was reduced in ‘spreaders’ over 1–6 ms (MANOVA, \( P < 0.05 \)) compared with controls and ‘non-spreaders’. Open triangles = controls; open circles = ‘spreaders’; closed triangles = ‘non-spreaders’.

Fig. 6 The pattern of cortico-cortical (A) and transcallosal (B) inhibition in Case 14. The inhibition normally seen at short latencies has been replaced by net excitation (cf. healthy subjects in Figs 5 and 7). Error bars show the SEM.
between and within the sensorimotor cortices, and those in initial focus. The former have multifocal, bilateral and whom there is little spread of myoclonic activity beyond the in whom there is frequent spread of myoclonic activity both in whom myoclonus is strictly multifocal or in normal controls. In addition, ‘spreaders’ have lower thresholds to transcranial magnetic stimulation than ‘non-spreaders’. In any one subject, the degree of ipsilateral and transcallosal inhibition, and the threshold to transcranial magnetic stimulation will be determined by pathological processes and drug treatment. For example, it is our experience that antimyoclonic drug treatment may reduce the number of bilateral and generalized jerks, changing a ‘spreader’ to a ‘non-spreader’, although it is unknown whether such changes are accompanied by alterations in ipsilateral and transcallosal inhibition. Nevertheless, in the present study it seems reasonable to conclude that the general pattern of changes seen were not solely due to drug effects. The range of drug treatments was broadly similar in the two patient groups. In addition, one ‘spreader’ tested ‘off’ medication had severely reduced ipsilateral and transcallosal inhibition, and a further two untreated patients had pathologically increased motor thresholds.

**Changes in epileptic patients**
The patients were also divided into those with epilepsy and those without. Non-epileptic patients had higher motor thresholds (median 85%, range 32–100%) than either epileptic patients (50%, range 26–90%, P = 0.014) or healthy controls (38%, range 28–53%, P < 0.001). This elevation of motor thresholds in non-epileptic patients was unlikely to be due to drug treatment as all three of the untreated patients were within this group (see Table 1). There was no difference in cortico-cortical inhibition (at timings of 1–6 ms) between patients with epilepsy (89±9% of control) and those without (89±14% of control). Similarly, there was no difference in transcallosal inhibition (at timings of 10, 12 and 14 ms) between patients with epilepsy (81±14% of control) and those without (85±8% of control). Strikingly, one patient (Case 14) in whom both cortico-cortical and transcallosal were replaced by net excitation had never had a seizure. The results from this case are shown in Fig. 6.

**Discussion**
Patients with cortical myoclonus may be divided into those in whom there is frequent spread of myoclonic activity both between and within the sensorimotor cortices, and those in whom there is little spread of myoclonic activity beyond the initial focus. The former have multifocal, bilateral and generalized jerks, whilst the latter have multifocal myoclonus (Brown et al., 1991). This broad physiological distinction is of clinical importance as ‘spreaders’ are more disabled than ‘non-spreaders’.

Here we define the processes contributing to cortical spread more exactly. Ipsilateral and transcallosal inhibition measured by transcranial magnetic stimulation are reduced in those patients with bilateral or generalized jerks compared with those in whom myoclonus is strictly multifocal or in normal controls. In addition, ‘spreaders’ have lower thresholds to transcranial magnetic stimulation than ‘non-spreaders’. In any one subject, the degree of ipsilateral and transcallosal inhibition, and the threshold to transcranial magnetic stimulation will be determined by pathological processes and drug treatment. For example, it is our experience that antimyoclonic drug treatment may reduce the number of bilateral and generalized jerks, changing a ‘spreader’ to a ‘non-spreader’, although it is unknown whether such changes are accompanied by alterations in ipsilateral and transcallosal inhibition. Nevertheless, in the present study it seems reasonable to conclude that the general pattern of changes seen were not solely due to drug effects. The range of drug treatments was broadly similar in the two patient groups. In addition, one ‘spreader’ tested ‘off’ medication had severely reduced ipsilateral and transcallosal inhibition, and a further two untreated patients had pathologically increased motor thresholds.

**Intrahemispheric inhibition**
Ipsilateral cortico-cortical inhibition was diminished in ‘spreaders’ relative to ‘non-spreaders’ at conditioning-test intervals of 1–6 ms. This would favour the intrahemispheric spread of cortical myoclonic activity known to occur in patients with generalized jerks (Brown et al., 1991). A similar deficiency in ipsilateral inhibition has been reported in patients with focal epilepsy (Fong et al., 1993).

**Interhemispheric inhibition**
Transcallosal inhibition was reduced in ‘spreaders’ between conditioning-test intervals of 10–14 ms. These intervals are similar to the interhemispheric delay recorded in the bilateral reflex jerks. Shorter intervals of 3–10 ms were recorded in bilateral action jerks, but these measurements are likely to underestimate the true interhemispheric delay (Brown et al., 1991). Thus transcallosal inhibition is reduced in these patients with bilateral or generalized jerks during the critical period when excitation reaches the ipsilateral cerebral cortex following stimulation or voluntary movement of one limb.

**Thresholds**
On the average ‘non-spreaders’ had higher motor thresholds than ‘spreaders’ or healthy subjects. However, individual patients with normal and pathologically elevated motor
thresholds were found in both patient groups. Anticonvulsant medication may elevate motor threshold (Huftonel et al., 1990; Reutens et al., 1993). This may account for the higher thresholds in patients relative to healthy subjects, but it seems unlikely that it explains the difference seen between the two similarly treated patient groups. Moreover, two subjects with pathologically high motor thresholds were tested ‘off’ all medication.

Motor threshold was also higher in non-epileptic patients as opposed to epileptic patients or healthy subjects. Reutens et al. (1993) have reported that lower thresholds than normal are found in patients with idiopathic generalized epilepsy. Here we have found the corollary, that a pathologically elevated threshold is associated with relatively fewer seizures and less spread of myoclonic activity at the level of the cortex. Such increases in motor threshold may reflect adaptive processes within these patients, aimed at compensating for existing deficiencies of inhibition, including ipsilateral and transcallosal inhibition. The level at which the elevation of motor threshold occurs is unclear. In two patients, large threshold changes were apparent with magnetic shocks, which probably stimulate pyramidal neurons transynaptically, but were not seen with electrical shocks, which stimulate pyramidal axons directly (Day et al., 1989; Berardelli et al., 1990). These preliminary findings suggest that the elevation of the motor threshold occurs at the level of the cerebral cortex and depends on transynaptic input to pyramidal neurons.

The difference in threshold between the different patient groups necessitates caution in the interpretation of the inhibition results. It is possible that motor threshold changes without commensurate change in the threshold for inhibition with a conditioning magnetic shock. If this were the case then the differing intensity of stimulation between 'spreaders' and 'non-spreaders' might be important. However, this is unlikely to account for the increased cortico-cortical inhibition in the 'non-spreaders' as these patients were tested at higher stimulus intensities (had higher thresholds) and cortico-cortical inhibition decreases as stimulus intensity is increased (Kujirai et al., 1993). In addition, the difference persisted when those individual patients with similar thresholds from the two groups were considered. Transcallosal inhibition does tend to increase with increasing stimulus intensity, but differences were again preserved in patients with similar thresholds.

**Epilepsy**

We have previously speculated that the abnormal spread of excitatory activity within and between the two sensorimotor cortices may contribute to seizure generalization in patients with cortical myoclonus (Brown et al., 1991). Here we found no difference between cortico-cortical or transcallosal inhibition between patients with cortical myoclonus and epilepsy, and those with cortical myoclonus but no epilepsy. It therefore seems unlikely that deficiencies in these particular inhibitory processes within the sensorimotor cortex play a major part in the epileptic process in this patient group.

The normal motor cortex is not concerned with holding epileptic processes in check, but in orchestrating movement, and it is likely that cortico-cortical and transcallosal inhibition normally act to transform elemental mass movements as seen in cortical myoclonus into a meaningful pattern of synergistic activities. Given this perspective, it is easier to understand the relationship between the present findings and other instances of deficient inhibition. Recently, we have examined cortical inhibition in patients with other disorders of movement and have demonstrated abnormalities in Parkinson’s disease (Ridding et al., 1995) and writer’s cramp (Ridding et al., 1994). In both of these conditions there is a deficiency of motor cortical inhibition, but neither disease causes seizures. Results from animal experiments with local injections of bicuculline (Matsumura et al., 1992) suggest that one role of inhibitory connections within the motor cortex is to focus activity onto appropriate groups of neurons. Therefore, it seems probable that under normal conditions the role of this inhibition is to 'set' the motor cortex so that upon receiving the movement command from higher centres the appropriate output is produced, and inappropriate movement is suppressed.

In conclusion, both transcallosal and ipsilateral cortical inhibition are reduced in those patients with cortical myoclonus who have more extensive jerks. This lack of inhibition will facilitate the transcallosal and cortical spread of myoclonic activity responsible for bilateral and generalized myoclonic jerks. However, deficiencies in transcallosal and cortico-cortical inhibition within the motor cortex areas of the cerebral cortex are not major factors determining the presence or absence of generalized seizures in patients with cortical myoclonus.

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**References**


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