Denervation in Hemiplegic Muscles

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This study examined the frequency of denervation activity in hemiplegic muscles in relation to the size and location of the central lesion. We studied 20 patients, 14 with major unilateral cerebral infarctions in the middle cerebral or internal carotid territories; four with a single lacune in the pons, internal capsule, or thalamus; and two with precentral infarcts. Using somatosensory evoked potentials, motor conduction studies, and assessments of conduction across the plexus and roots, we detected no conduction abnormalities on the affected side. Fibrillation was common in both groups, especially in distal and intermediate muscles. The distribution of the fibrillation and the normal conduction studies suggested that trauma of peripheral nerves was not a factor. Although the normal conduction studies and pattern of fibrillation activity do not exclude peripheral nerve trauma as the cause of the fibrillation, we suggest that transsynaptic degeneration is a reasonable alternative explanation. (Stroke 1990;21:1700-1704)
ment: 1) The surface recorded maximum "compound muscle action" potential (M potential) size (peak-to-peak amplitude and negative peak area) of the thenar and hypothenar muscles, representing distal muscles, was measured; as well as the extensor digitorum communis, representing an intermediate muscle; and the biceps and triceps, representing proximal muscles for the arm. For the leg, the extensor digitorum brevis and plantar foot muscles represented distal muscles; the gastrocnemius and anterior and lateral compartment muscles represented intermediate; and quadriceps and hamstring muscles represented proximal muscles. 2) Maximum motor conduction velocities were measured in the median nerve between the axilla and wrist, and in the common peroneal nerve between the popliteal fossa and ankle. In all cases, the temperatures on the affected and unaffected sides were within 1°C of each other. 3) Fibrillation activity was graded using a scheme modified from Miller et al.13 Fibrillation potentials and positive sharp waves were graded from 0 to +++ as 0, no abnormal activity; +, persistent single trains in at least two areas within the muscle; ++, moderate numbers in three or more areas; and ++++, many in all areas. 4) To exclude lesions of the brachial plexus, somatosensory evoked potential and motor conduction studies were carried out. The former were conducted for the median nerve by stimulation of this nerve at the wrist with sufficient intensity to evoke a maximum antidromic nerve action potential from the combined second and third digits while recording from the axilla (deltoid reference), cervical region (C=6 spine with Fz reference), and contralateral primary sensory area for the arm (Fz reference). Motor conduction across the spinal roots and adjacent brachial plexus was studied by percutaneous stimulation of the spinal roots using a Devices D-180 stimulator (Digiter Ltd., Welwyn Garden City, Hertfordshire, U.K.) while recording the hypothenar maximum M potential. These same hypothenar motor fibers were stimulated in the axilla, 2–3 cm proximal to the medial epicondyle, 2–3 cm distal to the cubital tunnel, and at the wrist. This method and the sensory evoked potential studies provided measures of conduction across C-8–T-1 roots, the lower trunk, the medial cord, and the ulnar nerve. 5) In the cases with precentral infarction, magnetic stimulation of the motor cortex was carried out as well using a Cadwell MES-10 stimulator (Cadwell Laboratories, Kennewick, Wash.).

Results

Figure 1 shows the reduction of the maximum M potentials of proximal, intermediate, and distal muscles in both the arm and the leg, which were significantly reduced on the paralyzed side (p<0.01). These reductions in M potential size were already evident by the third and fourth weeks and persisted through the seventh week. There were no significant differences in the reductions in M potential sizes of those patients with massive as compared to smaller infarctions. There were also no significant differences in maximum sensory and motor conduction velocities, including the most proximal segment between the spinal cord and axilla, between the affected and unaffected sides (Figure 2).

Fibrillation was present in six of eight patients with massive cerebral infarctions examined between 18 and 30 days (Figure 3). It was greatest in distal and intermediate muscles as compared to proximal muscles, and in the arm compared to the leg. The shortest interval at which any of these studies were carried out was 18 days, and this patient had fibrillation in distal and intermediate muscles. There were, however, two patients examined between the
third and fifth weeks in whom no fibrillation was seen in the arm or leg despite a massive unilateral cerebral infarction. In all five patients examined for the first time between 50 and 90 days, fibrillation was found, which again was more pronounced in distal and intermediate as compared to proximal muscles, and more in the arm than in the leg. The patient examined for the first time at 181 days after a previous massive cerebral infarction had no fibrillation.

The most extraordinary cases were those with the small infarcts (Figure 4). Here, five of the six cases had fibrillation, and the pattern was similar to that in the cases with massive infarctions. The earliest case studied, one of the patients with a small precentral cortical infarct, already had fibrillation at 10 days. In two cases followed serially, one had more pronounced fibrillation on second examination, whereas the other had no significant changes on the 20th and 27th days as compared to the initial study on the 12th day.

The two precentral cases were the only cases studied with magnetic stimulation. In both, the hypothenar maximum M potential was nearly the same in response to spinal root and wrist stimulation, but

**Figure 2.** Top panel: Somatosensory evoked potential study of a subject with a precentral infarction. As in all other cases, peripheral sensory conduction between the hand and spinal cord was normal and, in this particular case, was normal between the spinal cord and contralateral primary sensory area in the presence of an infarct apparently restricted to the precentral hand area. Bottom panel: Motor conduction study in the above case. Surface recordings from the hypothenar muscle group in response to supramaximal stimulation of the C-8–T-1 spinal roots and the ulnar nerve at the axillary, above the elbow, below the elbow, and at wrist levels. Motor conduction velocities were normal across all segments. The motor cortex was stimulated by means of a Cadwell MES-10 stimulator, but no consistent response was detectable from the hypothenar muscles.

**Figure 3.** Plots of the quantity of fibrillation as modified from Miller et al. in representative distal, intermediate (INTER), and proximal (PROX) muscles in the upper (U.E.) and lower (L.E.) extremities in cases with major internal carotid artery (ICA) and middle cerebral artery (MCA) infarctions. Top panel: Eight cases examined at intervals shorter than 35 days after infarction. Bottom panel: Cases examined after 50 but before 90 days after infarction (o). On case was examined at 181 days (●), but no fibrillation was found.
were ablated or the pyramidal tract was sectioned in subhuman primates. McComas et al. reported losses of about half the normal numbers of motor units in spinal motor neurons was carried out in earlier anatomical studies in which areas of motor cortex are evident with both small and massive lesions. Fibrillation was seen as early as the second and third weeks, and was accompanied by reduced maximum M potential sizes, and lasted many weeks thereafter. Fibrillation was observed in muscles contralateral to cerebral lesions as early as the second week and lasted many weeks thereafter. Fibrillation was accompanied by reduced maximum M potential sizes, seen as early as the second and third weeks, and was as evident with both small and massive lesions.

Atrophy of muscles contralateral to cerebral lesions or pyramidal tract sections is well-documented in subhuman primates, and hemiplegic atrophy in humans is a long-established observation. Charcot in 1879 described degenerative changes in motor neurons after contralateral intracerebral hemorrhage. Charcot's and others' descriptions of degenerative changes in spinal motor neurons contralateral to lesions in the cerebral hemisphere and in lumbosacral motor neurons after lesions of the cervical cord, as well as the abundant clinical reports of fibrillation in hemiplegic and paraplegic muscles, suggest that transsynaptic degeneration of motor neurons may explain the development of fibrillation and possibly contribute to the development of atrophy contralateral to cerebral lesions.

Unfortunately, neither needle electromyography of paretic or atrophic muscles nor an examination of spinal motor neurons was carried out in earlier anatomical studies in which areas of motor cortex were ablated or the pyramidal tract was sectioned in subhuman primates. McComas et al. reported losses of about half the normal numbers of motor units in hemiplegic muscles, but curiously, these losses were not apparent within the first 8 weeks even though fibrillation in previous and later studies was often evident as early as the second week.

That transsynaptic degeneration does occur in the central nervous system is well known. Previously, we showed that hemisection of the macaque spinal cord in the thoracic region resulted in loss of about 20% of ventral motor neurons many levels below the hemisection. Hemisection could be expected to interrupt all descending projections to motoneurons, both direct and indirect, and cortical and noncortical, and as a consequence to be more likely to induce transsynaptic degeneration of motor neurons than lesions of the motor cortex. The latter indeed turned out to be the case, as ablation of areas 4 and 6 failed to induce any detectable loss of motor neurons.

Based on the above prior study, we expected greater and more extensive fibrillation in cases of massive cerebral infarction as compared to the smaller cortical and lacunar infarctions reported here. To our surprise, such was not the case. Small cortical lesions and lacunes induced fibrillation as regularly as did the massive lesions, especially when account is taken of the earlier times at which studies on the smaller lesions were carried out as compared to the massive lesions.

The fact that smaller lesions seemed as productive of fibrillation as massive lesions suggests that certain pathways may be especially important and that interruption may be the primary cause of the fibrillation. There is evidence that the direct corticomotoneuronal projection, already more pronounced in chimpanzees as compared to lower primates, may be even more prominent in humans and especially dense in its connections to distal and perhaps intermediate muscles. Whether the direct corticomotoneuronal projections have any special significance with respect to the appearance of fibrillation in humans remains unproved.

Our studies suggest that peripheral nerve trauma was not the basis for the fibrillation. Not only was the fibrillation too widespread to be explained by trauma to one or even two peripheral nerves, but conduction, both sensory and motor, across the brachial plexus and roots was in all cases normal and the same as on the unaffected side. With one exception, previous studies of fibrillation in hemiplegic and paraplegic muscles were not designed to exclude peripheral nerve trauma as a cause of the fibrillation activity. In the one study in which peripheral nerve trauma was judged to be excluded, not only was extensive fibrillation present but it was accompanied by fiber type grouping in the muscle biopsy. Other histologic studies of hemiplegic muscles in humans have shown type II muscle fiber atrophy and increased complexity of endplates, suggestive of collateral sprouting. In some instances, type I fiber hypertrophy also was seen.

We conclude that fibrillation activity is common in muscles rendered hemiparetic or hemiplegic after contralateral cerebral lesions and that transsynaptic degeneration.
degeneration of motor neurons is the most likely hypothesis. Peripheral nerve trauma seems an unlikely explanation for the development of fibrillation activity except in those cases in which evidence of trauma can be clearly demonstrated.

References

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