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Mis-reinnervation in Leprous Neuritis Affecting the Facial Nerve*†

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Evidence for misdirection of fibres in severe and well-established leprous neuritis of branches of the facial nerve is presented. In the present study blinkbursts, twitches, and voluntary co-contractions were abundantly seen. Fibrillation and giant polyphasic potentials were rare. Leprous neuritis is contrasted with Bell's palsy in terms of site of involvement, and the significance of this is discussed. Misdirection as a source of re-innervation is one of several factors influencing recovery.

Introduction

Leprosy is the commonest cause of peripheral neuropathy in the world today. Paralysis of facial muscles occurs in approximately 2% of patients afflicted with this disease. Although often compared with Bell's palsy, the pattern of paralysis seen is quite different. This is because in leprosy the site of pathological change is one or more of the peripheral branches of the facial nerve, and not the main trunk (Fig. 1). At this site there is a reduction in temperature which has been shown by Brand (1964) and confirmed by Job and Desikan (1968) to be an important factor in the development of nerve lesions. The leprosy bacilli proliferate more readily at reduced temperature. The presence of osseo-fibrous tunnels in the region of the zygoma have been implicated specifically in the facial nerve by Dastur *et al.* (1966) as selecting factors in determining this site of involvement. Hence, unlike Bell's palsy, lower facial palsy is less frequently seen and varying degrees of paresis of the upper facial musculature is a feature. A variable degree of recovery may take place, and a better understanding of the processes of recovery is of more than academic interest.

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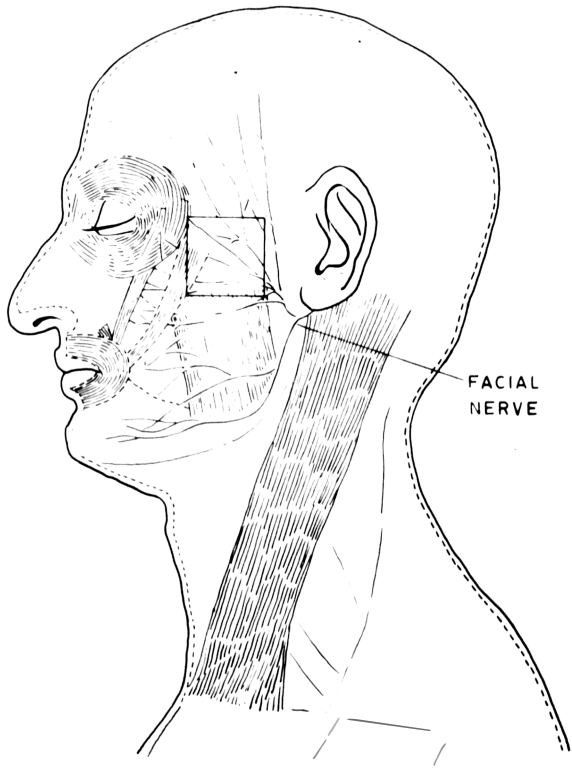

Fig. 1. Branches of the facial nerve. Any of these may be involved, either in isolation or together with other branches, but the commonest site of involvement is within the rectangular area shown in the diagram.

Materials and Methods

The frontalis, upper and lower halves of the orbicularis oculi (pars palpebralis) and levator labii superioris muscles were studied electromyographically, using a Medelec MS3R 2-channel model and concentric needle electrodes, in 22 patients as part of their postoperative assessment following temporalis transfer for lagophthalmos due to leprous neuritis. All had had, as prerequisites for surgery, severe established paralysis of 1 year's duration or more and medical control of the progress of the disease. In 5 of these cases bilateral operations had been performed so that 27 sites of the face affected by leprosy were studied. All cases were also studied in detail, clinically and by faradic stimulation, as part of a larger series to be reported elsewhere by Ranney and Furness (1973).

In addition to examining these 27 in detail, 1 patient with signs that resembled hemifacial spasm also had the other (normal) side examined for comparison, and in 2 other cases with visible contralateral co-contractions in the levator labii superioris muscle on the unparalysed opposite side the muscles concerned were also examined electromyographically. Also examined were the procerus and corrugator supercilii muscles in one patient and the levator anguli oris in another

when visible ipsilateral co-contractures were seen. Of the 22 patients 5 had lepromatous, 12 borderline, and 5 tuberculoid leprosy. Their ages ranged from 17 to 55, with an average of 38.7 years, and 20 were male and only 2 female.

Results

The general pattern of paralysis in the 4 muscles selected for study is shown in Table 1; it is not in any way related to the type of leprosy. Fibres of orbicularis oculi in the upper lid were the most severely affected. While the lower lid fibres were affected almost as often, partial paralysis was very much more common in this muscle. Consequently a remarkably larger number of incomplete patterns were seen in the lower lid as compared with the upper.

TABLE 1

General pattern of electromyographic activity in 27 halves of the face in 22 patients

	Upper lid	Lower lid	Frontalis	Lev. lab. sup.	Total
Full interference pattern	1	2	14	16	33
Incomplete interference pattern	6	16	8	10	40
No voluntary activity	20	9	5	1	35
Total	27	27	27	27	108

While the mass movements sometimes described in Bell's palsy were *not* seen, blinkbursts and periodic twitches were often obvious at first sight. Clinically visible blinkbursts were seen and confirmed electromyographically in the pars orbitalis of the lower half of orbicularis oculi in 2 cases, and in the levator labii superioris in 5 patients. One of these 5 had unilateral upper and bilateral lower facial involvement, but blinkbursts in levator labii superioris occurred only on the side with a full interference pattern in orbicularis oculi. On the other side this patient had 10-μV twitches in the same muscle; these were out of phase with blinking but synchronous with rhythmical twitch activity in the lower half of the orbicularis oculi on that side. Single twitches of up to 75 μV in amplitude in the levator labii superioris occurred in another patient with gentle voluntary eye closure and are therefore also listed as co-contractions. Still another patient had continuous twitch-like activity which could not be controlled voluntarily but which spread to the opposite levator labii superioris on tight eye closure.

Voluntary co-contractions were seen 21 times in 16 of the 22 patients studied; all but one of these were on the same side (Table 2). This type of synkinesis was seen in 3 out of 5 patients with lepromatous leprosy, 9 out of 12 with borderline, and in 4 out of 5 with tuberculoid disease, so that again no relationship was seen to exist between the type of leprosy and the incidence of co-contraction. Five occurred in orbicularis oculi of the lower lid in 4 patients—3 in pars palpebralis and 2 in pars orbitalis, and all were associated with voluntary activation of the levator labii superioris muscle of the same side. Five occurred in the frontalis of 5 patients; 4 of these co-contractions were observed on attempted closure of the eye (Fig. 2) and in 3 of these 4 this was the only type of voluntary activity possible. Surprisingly, contraction of frontalis occurred in the 5th case on

TABLE 2

Electromyographic abnormalities seen in 27 halves of the face in 22 patients

	Upper lid	Lower lid	Frontalis	Lev. lab. sup.	Procerus corrugator	Lev. ang. oris.	Total
Blinkbursts		2 (in pars orbitalis)	0	5			7
Twitches	0	1	0	3			4
Voluntary co-contractions	0	3 (pars palpebralis) 2 (pars orbitalis)	5	9	1	1	21[a]
Fib. potentials		0	1	0			2
Giant polyphasics	0	1	1	0			2

[a]One of these was contralateral, associated with complete ipsilateral paralysis (see text).

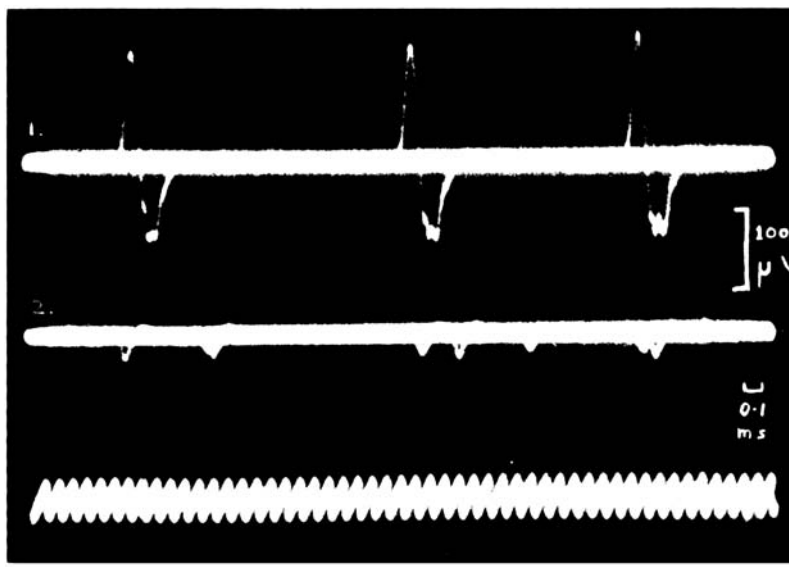

Fig. 2. Co-contraction in frontalis muscle (Lead 1) during spontaneous activity in lower lid orbicularis oculi (Lead 2).

activation of the ipsilateral levator labii superioris. Volitional activity was possible also in this particular case.

On closure or attempted closure of the eyes co-contractions were seen in the levator labii superioris in 9 patients; in 8 of them these were on the same side, but one, in which the ipsilateral lip musculature was also paralysed, occurred on the opposite side. In all cases the co-contractions occurred on gentle eye closure, and therefore were not a manifestation of attempts to "screw up" the face in order to facilitate closure of the eye in the presence of lagophthalmos. In one case, resembling hemifacial spasm, there was also spread of the ipsilateral co-contraction to the other side on tight closure of the eye.

Although it was not planned to study other facial muscles in so much detail, a careful inspection of all muscles, lasting 30 min, was made. During the course of this examination associated movements were also noted in the corrugator and procerus muscles in one patient and in the levator anguli oris in another, both on attempting gentle eye closure. The clinical impression of co-contraction in these muscles was confirmed electromyographically.

Fibrillation potentials and giant polyphasic potentials were uncommon. It is of interest, but possibly of no significance, that both were found only in patients with tuberculoid leprosy. Fibrillation potentials were seen on only two occasions: in the upper lid of one patient in whom no spontaneous activity was present, and in frontalis of the same patient where giant polyphasic M.U.P's of 3500 μV were also seen on voluntary activity. It should be noted in this case that 31 months previously i.e., 1 year after the onset of paralysis, frontalis was recorded as not responding to faradic stimulation. Two months later there was a slight response, and now there is a normal response.

Discussion

Following facial paralysis due to Bell's palsy, associated movement in physiologically unrelated muscles, clinically discernible blinkburst activity, and spontaneous twitching have been observed. Taverner (1955) has postulated that some, if not all, of these phenomena can be explained by misdirection of regenerating axons. Good support for this theory has recently been put forward by Teasdall and Salman (1971), who demonstrated by means of evoked muscle potentials that in 5 out of 8 cases of Bell's palsy with associated movements "during facial nerve regeneration some of the most rapidly conducting nerve fibres which originally innervated orbicularis oculi subsequently supplied orbicularis oris". Mis-reinnervation has also been reported in the forearm by Satoyoshi *et al.* (1971) following cervical nerve root trauma and has also been cited by Ford and Woodhall (1938) as occurring during recovery of certain cranial, spinal and autonomic nerves from trauma and from infection. So far it has not been reported in leprosy.

In leprous neuritis of the facial nerve the evidence here presented indicates that misdirection of regenerating nerve fibres occurs in this condition also, and often leads to a loss of regenerating axons which would otherwise innervate the orbicularis oculi. The blinkbursts activity seen in the levator labii superioris can best be explained on the basis of misdirection. Regenerating fibres originally destined for some part of orbicularis oculi seem to have been misdirected to levator labii superioris instead. A similar misdirection could explain the co-contraction of levator labii superioris seen on voluntary gentle eye closure. Similarly, axons which normally innervated orbicularis oculi but were misdirected to frontalis would explain the associated movement in this muscle. In 3 cases they were the only source of innervation, so that the patients could only raise the eyebrows when told to close the eye, while in a 4th case the frontalis muscle received some of its original axons also. In another case the source of re-innervation of frontalis appears to have been the nerve to the levator labii superioris. When this investigation was initiated it was felt that there might be some evidence of axon sprouting at the intramuscular level, for Dastur (1956) reported such an occurrence in leprosy in other muscles, although to a limited degree. But bridging of the gap between so widely separated muscles as frontalis

and levator labii superioris by axon sprouting at the sub-terminal level is incredible, and the rarity of giant polyphasic potentials also renders such a possibility even less likely. The concept of re-innervation by fibres misdirected at a more proximal level would seem to be the only rational explanation for the associated movements seen so abundantly in these cases.

It is possible that in Bell's palsy misdirection of axons occurs at the site of the lesion, since there, there is close proximity of all nerve fibres. However, in leprosy the site of involvement is almost always more peripherally situated, where the individual branches are exposed to low temperatures and possibly enclosed in osseo-fibrous tunnels. Where the branches are so isolated from each other re-innervation by misdirection seems hardly possible—yet it does seem to occur. Sullivan in 1939 showed that in experimental division of the facial nerve in monkeys there could be retrograde degeneration which would leave the neurolemmal tubes proximal to the site of the lesion open and receptive to in-growth from healthy axons, at least for a short distance. Antia *et al.* (1966) demonstrated at operative explorations that the facial nerve does not consist of a simple system of branches, but rather of a network or plexus of branching and re-anastomosing fibres. Is it not possible then that in some cases retrograde degeneration, or even the disease process itself, extends back at least to the level where it is in contact with such a branch? In some cases it need not extend very far.

Misdirection, being haphazard, might be expected to occur not only away from the external eye musculature but also in the reverse direction. Though less frequent, it did seem to occur in those patients in whom the lower half of the orbicularis oculi showed co-contraction on activation of the levator labii superioris. As a source of re-innervation of a paralysed orbicularis oculi a few branches of nerve fibres normally supplying muscles of the lower half of the face would account for the preponderance of incomplete interference patterns seen in the lower lid. This possibility deserves serious consideration, because Magora *et al.* (1965), Antia *et al.* (1966), and Margaret Brand in a personal communication, have expressed the view that the lower lid, not the upper, is more obviously denervated in leprosy, and yet in our series, while the frequency of involvement was almost identical, it was the upper lid that was the more completely paralysed. Perhaps some of the lower lids paralysed had partially recovered due to mis-reinnervation—although axon sprouting at the intramuscular level could also be a factor. It may also be that in the upper lid the axonal pathway is so completely blocked by the destructive process going on that sprouts originating proximally find their way into nerves destined for frontalis, levator labii superioris, and even orbicularis oculi of the lower lid to a much greater extent than can occur in the reverse direction.

The extent of recovery due to misdirection cannot be assessed on the basis of this study and may be less than these data would indicate. It is important to realize that the cases here reported represent a special group, and that there are other factors responsible for recovery of paralysed facial muscles which play an important rôle. The patients studied were those who had required a temporalis transfer operation for lagophthalmos, which in our series was never done until the paralysis had been present for 1 year, and the minimum follow-up period was 1 year; hence they all had established paralysis and of a severe degree, at least a far as the orbicularis oculi was concerned. Furthermore, clinical evidence of associated movements was not so frequent in those patients in the post-operative

study who were not also studied electromyographically. So the point being made here is, not that misdirection of fibres occurs often and is important as a source of re-innervation, but rather that it *does* in fact occur and may be one of several factors influencing recovery.

The mechanisms important in recovery of muscle function may be briefly summarized as follows:

(a) Recovery of the original nerve lesion may occur. In leprosy, as shown by Job and Desikan (1968), there may be segmental demyelination or axonal degeneration in funiculi invaded by the bacillus or there may be oedema of the nerves resulting from destruction of a few axons, causing neuropraxia in the adjacent non-infected funiculi. The view expressed by Ranney (1970) is commonly held, namely that there is often a combination of neuropraxia, segmental demyelination and axonal destruction, and that the spontaneous recovery frequently seen, especially in cases of lepra reaction, is often due to the recovery of the nerve lesion itself, particularly if it is neuropraxic in origin.

(b) Axon sprouting, whether at the sub-terminal level or, as described above, at a much more proximal level which can lead to misdirection of nerve fibres, is certainly a factor.

(c) Hypertrophy of muscle fibres in remaining motor units may occur following exercise. This has been commonly observed clinically in orbicularis oculi by the authors and by others such as Brand (1965) and Karat (1969, personal communication), and has been demonstrated in other muscles experimentally by Harreveld (1945). Edgerton (1967) has stated that over-stretching induces muscle atrophy, and therefore hypertrophy of surviving motor units can be facilitated by surgical means which prevent over-stretching of partially denervated muscles, e.g., the myofacial and static slings usually performed for treatment of lagophthalmos.

(d) Increased central excitation or recruitment is seen in hemifacial spasm, and in the cases here reported it seemed evident in one patient who showed also contralateral activity of levator labii superioris on tight eye closure but only ipsilateral co-contraction on gentle closure.

(e) The possibility of re-innervation through branches of other cranial nerves, especially of the 5th, as suggested by Martin and Helsper (1957), must not be forgotten. The possibility that this occurs through a direct take-over by motor neurons of the trigeminal nerve is excluded by the lack of associated movements in facial muscles on mastication. Conley (1964) has suggested that after resection of segments of facial nerve, regeneration into the terminal branches may occur from the intrapetrous portion of the facial nerve by way of the geniculate ganglion and superficial petrosal nerve. This could account for recovery of muscles in the area supplied by the maxillary division of the trigeminal nerve, notably the lower half of orbicularis oculi. However, it seems unlikely that the frontalis muscle could be re-innervated in this way. The same author (1971) has pointed out that such re-innervation is "smooth, has emotional control, and is often forceful in degree". While not denying this as a possible means of recovery in leprous neuritis, in general the blinkbursts and voluntary associated movements seen resemble more closely the phenomena seen in Bell's palsy, which have been attributed by Taverner (1955) to mis-reinnervation from other branches of the facial nerve.

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