GMF in wound healing in the brain. We previously applied GMF onto adult rat brains inflicted with a stab wound and observed marked gliosis in the wound area (Troy, Lim and Eng, unpublished). However, the interpretation was complicated by the presence of large amounts of endogenous GMF in the mature animal, which minimized the differential response between the GMF-treated and the untreated animals. In the current report, the experiment was conducted in neonatal rats, where the endogenous GMF level is low[14]. Since in newborn rats the blood-brain barrier is poorly developed, we chose to administer GMF by the i.p. route. In addition, the wound itself disrupted the barrier locally, making the site accessible from circulation. I.p. injection avoided the possibility of extending the size of the wound, which could have happened with local application of GMF sample to the wound.

At first glance, it may be difficult to reconcile the ability of GMF to minimize posttraumatic atrophy and the fact that GMF did not enhance the formation of glial scar in neonatal brains. The difficulty can be resolved, however, if we consider that the brain responds to injury in two major ways: the regenerative attempts of the cells to regain the normal histotypic organization, and the formation of a scar (gliosis) to fill up the wound. It is logical to assume that regeneration, which is possible in young animals, is the repair mechanism of choice. It is only when the regenerative ability is impaired, as in the adult brain, that a glial scar is inevitable.

Our data provided no clues as to whether this regenerative process involved neurons or glia, or the interaction between the two. Nor did it necessarily imply axonal regrowth or sprouting. Inasmuch as no direct effect of GMF on neurons has been reported so far, one can only postulate an indirect influence of GMF on neurons through glia. In view of our recent evidence that GMF stimulates astrocytes to secrete other growth factors[15,16], such a hypothesis may not be far off.

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Synkinesis in hemifacial spasm: results of recording intracranially from the facial nerve

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Summary. We show evidence that the motonucleus of the facial nerve is involved in producing the synkinesis in patients with hemifacial spasm. These results were obtained by recording from the intracranial portion of the facial nerve and from the orbicularis oculi muscle in patients operated upon for hemifacial spasm during electrical stimulation of the mandibular branch of the facial nerve. Also, the electromyographic response from the same muscle was recorded when the facial nerve was electrically stimulated at a location near the brainstem. The results show that it is unlikely that the symptoms of patients with hemifacial spasm can be explained on the basis of ephaptic transmission at the site of lesion of the facial nerve.
Key words. Facial nerve; hemifacial spasm; synkinesis; intraoperative recordings.

Hemifacial spasm (HFS) is a rare disorder that causes involuntary contractions of the mimic muscles of one side of the head. The contractions usually begin in the orbicularis oculi muscle, and unless treated, progress to all mimic muscles, including the platysma[1,2]. It has been shown in several studies that, in addition to the spasm, patients with HFS experience synkinesis, which implies that an attempt to contract one muscle group also involves other muscles[3,4]. In the great majority of patients with HFS, an artery or a vein is found to be compressing the root entry zone (REZ) of the facial nerve. Decompression of the nerve using microvascular techniques is an effective treatment with a rate of cure of over 95%[1,2]. There is evidence that vascular compression of the nerve causes damage to the myelin of the axons at the REZ,[5] and it has been hypothesized that the symptoms of HFS are the result of the formation of artificial synapses between nerve fibers of that local damage to the nerve causes sprouting, degeneration, and rerouting of connections in the nucleus[6]. Other hypotheses state that HFS is a disorder of the facial motonucleus[7,8].

Recent studies have demonstrated that ephaptic transmission, indeed, occurs between abnormally myelinated axons[8-10], as well as development of 'trigger zones' in the injured portion of a peripheral nerve causing spontaneous (ectopic) activation[11], and there is an increase in the nerve's sensitivity to mechanical deformation[12,13]. These abnormalities occur while the nerve maintains its ability to conduct nerve impulses.

Attempts to determine experimentally which of these hypotheses about HFS is valid has been made by Auger[3], who found that the synkinesis observed when the blink reflex was elicited disappeared after microvascular decompression surgery to

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treat HFS. Electrical stimulation of one branch of the facial nerve has been shown to give rise to the contraction of muscles that are innervated by other branches of the facial nerve[14]. This was taken as an indication that 'crosstalk', similar to that which gives rise to synkinesis, was occurring. However, due to the fact that the latencies of responses of the afferent and efferent branches of the reflex are not known, it was not possible to determine the exact location of the 'crosstalk' on the nerve.

In order to find out if there is 'crosstalk' (ephaptic transmission) at the location of the lesion in the REZ of the facial nerve, which might explain the synkinesis seen in patients with hemifacial spasm, or whether the synkinesis was produced in the facial nucleus, we recorded the EMG responses of the orbicularis oculi muscle and the nerve action potentials from the intracranial portion of the facial nerve to electrical stimulation of a branch of the facial nerve (ramus marginalis mandibularis) in 13 patients with HFS who were undergoing microvascular decompression surgery, and we stimulated the intracranial portion of the facial nerve near the REZ in the same patients and recorded the EMG response from the orbicularis oculi muscle. In some patients we also stimulated the zygomatic branch of the facial nerve (fig. 1). The patients were operated upon under general endotracheal anesthesia using the method described by Jannetta[2] with Forane and nitrous oxide. Succinylcholine and 3 mg of tubocurarine were given prior to intubation. No other muscle relaxant agents were given. The effect of the initially administered muscle relaxants had vanished at the time of the recording, which was done at least one and a half hours after the administration of curare.

The mean latency of the earliest detectable EMG responses of the orbicularis oculi muscle to electrical stimulation of the distal part of the marginal mandibular branch of the facial nerve obtained in 13 patients was 10.72 msec (SD = 0.96) and the mean latency of the negative peak of the response from the facial nerve near the brainstem to the same antidromic stimulation of the facial nerve was 3.78 msec (SD = 0.41). The mean latency of the response from the orbicularis oculi muscle to electrical stimulation of the intracranial portion of the facial nerve was 4.45 msec (SD = 0.40). The sum of these two latter latencies is 8.23 msec, thus 2.49 msec shorter than that of the response from the orbicularis oculi muscle to stimulation of the mandibular nerve. These values were obtained prior to decompression of the facial nerve. The recording and stimulus sites on the intracranial portion of the facial nerve were close to the brainstem (fig. 1). We compared the responses obtained by stimulating and recording proximally and distally to the site of lesion and only found small differences in latencies that could be explained by the normal conduction velocity of the nerve. We thus did not see any sign of a slowing of the conduction in the lesioned part of the nerve. Our results thus indicate that ephaptic transmission in the injured part of the facial nerve is unlikely to cause the response from the oculi muscle

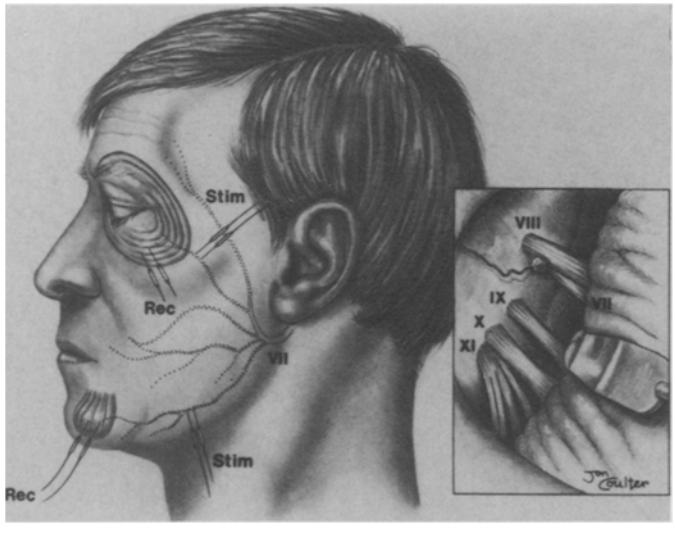

Figure 1. Schematic illustration of stimulation of two branches of the facial nerve and recording of EMG from two facial muscles. Insert: Illustration of recording from the intracranial portion of the facial nerve.

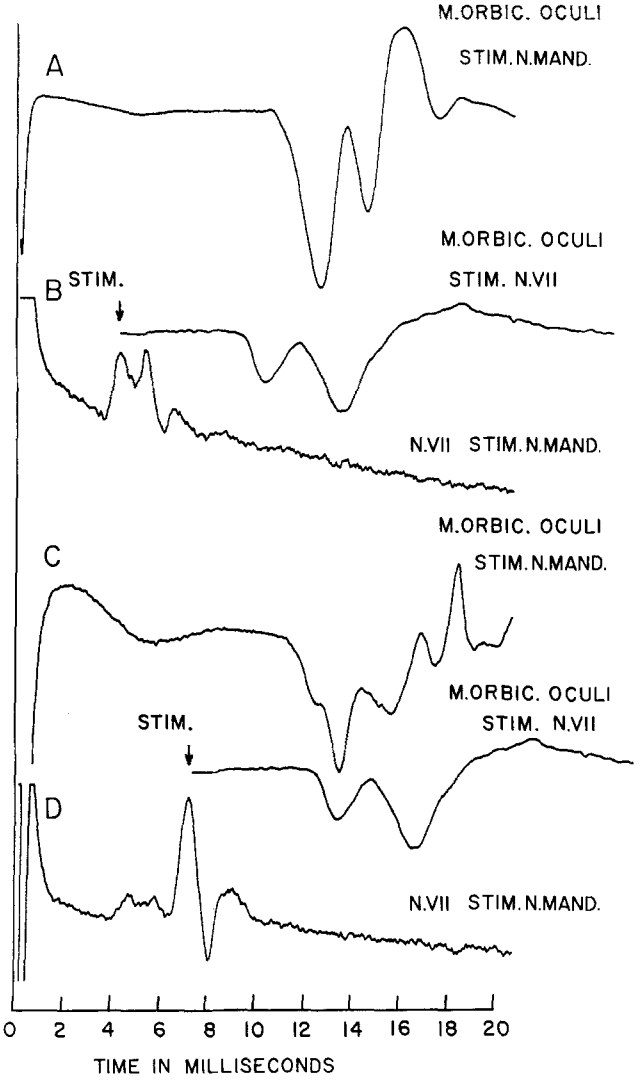

Figure 2. *A*: Recording from the orbicularis oculi muscle in response to electrical stimulation of the marginal mandibular branch of the facial nerve as illustrated in figure 1 (monopolar, 5 V, 140-μs duration, 10 pps). The recording was obtained during the operation prior to craniectomy. *B*: Recording from the facial nerve intracranially with the same stimulation of the marginal mandibular nerve at a time when there was no response from the orbicularis oculi muscle. One electrode was placed on the nerve near the brainstem and the other in the cerebrospinal fluid about 5 mm from the nerve (fig. 1). Also shown is the response from the orbicularis oculi muscle to electrical stimulation of the facial nerve near the brainstem (monopolar, 0.5 V, 140-μs duration, 10 pps). The recording is shifted in time so that the time of stimulation coincides with the maximal response from the facial nerve. *C*: Recording from the orbicularis oculi muscle in response to stimulation of the mandibular nerve similar to that shown in A, obtained a few seconds prior to the recording of the response from the facial nerve shown in B. *D*: Recording from the facial nerve made simultaneously with that seen in C. In all recordings the bandwidth was 0.3–3000 Hz.

upon stimulation of the mental branch of the facial nerve. The results indicate involvement of the facial nucleus in this response.

Figure 2 shows examples of such recordings when the pressure on the nerve from the offending artery is eliminated and the response of the orbicularis oculi muscle vanishes suddenly; however, it often reappears, for example when a Teflon felt implant is put into place between the artery and the nerve. (These patients also show spontaneous contractions of the facial muscles during the operation which vanish after pressure is released, although not necessarily at the same time that the response to stimulation disappears.) We take this as an indication that the mechanisms behind this response are dependent upon the facial nerve being under pressure from the offending vessel. An example of a recording from the facial nerve when there is no response of the orbicularis oculi muscle upon stimulation of the distal end of the marginal mandibular nerve is seen in figure 2, B, together with a recording of the response of the orbicularis oculi muscle upon intracranial stimulation of the facial nerve near the REZ. This recording is shown with the stimulus occurring at the time of the first peak in the response from the facial nerve.

As may be seen from figure 2, B, the EMG response from the orbicularis oculi muscle in these two situations does not match in time as would have been the case if the response to stimulation of the distal part of the facial nerve was caused by ephaptic transmission in the facial nerve near the brainstem. A recording made a few seconds earlier than those seen in figure 2, B using the same stimulation of the marginal mandibular nerve elicited a second and later response from the facial nerve, the latency of which was 7.84 msec (fig. 2, D).

When the time of intracranial electrical stimulation of the facial nerve is aligned with the peak of the response from the facial nerve recorded when the mandibular nerve is stimulated, it becomes obvious that the response of the orbicularis oculi muscle coincides with the large and late response from that muscle obtained by stimulating the mandibular nerve. The latency of this response, together with the fact that this large response is labile in nature and it appears concomitantly with the response from the orbicularis oculi muscle, indicates that the response is generated in the facial nucleus and that it is directly related to the synkinesis seen when the mandibular nerve is electrically stimulated. It is thus assumed that it is this large response from the intracranial portion of the facial nerve that gives rise to the response from the orbicularis oculi muscle and not the smaller early response.

These results thus indicate that the facial motonucleus is involved in HFS. How this activity is generated in the motonucleus, however, is not obvious. It may be that the trigger zones developed in the injured part of the nerve give rise to unnatural neural activity that propagates in both directions from the trigger zone, and which is conducted antidromically by the facial nerve to the motonucleus. This bombardment of the facial motonucleus by such unnatural neural activity may give rise to changes in the motonucleus which are similar to 'kindling'[15,16]. After the facial motonucleus has been exposed to this unnatural stimulation, nerve activation such as electrical stimulation may trigger reverberant activity in the nucleus. This activity engages the entire nucleus, and thus all facial muscles are activated together (synkinesis). The same mechanism may be the cause of spontaneous spastic contraction of the facial muscles.

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Comparison of diurnal and nocturnal rates of 5-hydroxytryptamine turnover in the rat mediobasal hypothalamus[1]

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Summary. Rates of 5-hydroxytryptamine (5-HT) turnover in the mediobasal hypothalamus of male rats were estimated using pharmacological methods during the daytime and at night. Concentrations of 5-HT in this hypothalamic area were higher nocturnally than diurnally; this was apparently due to increased 5-HT synthesis and decreased 5-HT catabolism at night.
Key words. Rat hypothalamus; hypothalamus, rat; 5-hydroxytryptamine turnover, diurnal; 5-hydroxytryptamine turnover, nocturnal.

The hypothalamus contains relatively high concentrations of 5-hydroxytryptamine (5-HT; serotonin), and this indolamine plays a key role in the regulation of numerous hypothalamic functions, including that of modulating cyclic anterior pituitary secretions[2]. This modulatory role may be related, at least in part, to cyclicity in 5-HT metabolism within the hypothalamus. Although several other studies have reported apparent cyclicity in 5-HT concentrations in the hypothalamus of various species including rats[3-6], gerbils[7] and humans[8], changes in 5-HT concentrations may not accurately reflect neuronal activity associated with that neurotransmitter, as pointed out by Neff and Tozer[9]. Day-night differences in 5-HT metabolism estimated by the rate of formation of radioactively labeled 5-hydroxyindole acetic acid either from tritiated tryptophan[10] or