Figure 1 Binding of gangliosides with serum IgMs from a patient with Guillain-Barré syndrome subsequent to acute cytomegalovirus hepatitis. Lane 1: bovine brain gangliosides GM1, GD1a, GD1b, and GT1b. Lane 2: purified GM2 and GalNAc-GD1a. (A) Thin layer chromatography plate stained with orcinol. (B) Chromatogram immunostained after overlaying it with serum from the patient (1:100) then with peroxidase conjugated antihuman IgM (Dako, Denmark; 1:1000). The chromatography plates were developed in a solvent system of chloroform/methanol/ 12mM magnesium chloride in water (5:4:1, volume). The IgMs from the patient reacted specifically with the GM2 and GalNAc-GD1a.

bind to N-acetylgalactosaminyl GD1a (GalNAc-GD1a), a terminal trisaccharide identical to that of GM2. Jacobs *et al*² did not test whether IgM anti-GM2 antibodies react with GalNAc-GD1a. By contrast, Kusunoki *et al*³ reported that a patient with Guillain-Barré syndrome had IgM antibody activity against both GalNAc-GD1a and GM2, but in whom no result of anti-CMV antibody was shown. We had a patient with Guillain-Barré syndrome subsequent to acute cytomegalovirus hepatitis who had IgM antibodies both to GM2 and GalNAc-GD1a. We investigated whether the IgM anti-GM2 antibodies cross react with GalNAc-GD1a.

Three days after an episode of stomatitis, a 32 year old man noticed left sided facial weakness and dysaesthesia distally in his feet. Over a day, the facial weakness extended to the right side and dysaesthesia progressed to the limbs. He developed progressive weakness of the limbs on day 4, and the next day was unable to stand. On day 5, the patient presented with facial diplegia, severe limb weakness, and moderate reduction of superficial sensation distally in all four limbs. The respiratory muscles were slightly affected. Deep tendon reflexes were absent. Liver enzyme concentrations were raised slightly. Protein concentration in CSF was 109 mg/dl and cellularity was normal. High IgM anti-CMV antibody titres were found in both serum and CSF by enzyme linked immunosorbent assay (ELISA). An electrophysiological study suggested that the predominant process was demyelination involving the motor nerves. Right ulnar sensory nerve action potential was absent. Visser *et al*⁴ reported that patients with Guillain-Barré syndrome with associated cytomegalovirus were young and often developed severe sensory loss with facial nerve involvement and respiratory insufficiency. They also reported a strong correlation between cytomegalovirus infection and severe sensory loss. The clinical manifestations in our patient were similar to those reported by Visser *et al*.

Thin layer chromatography with immunostaining showed that the serum IgM from our patient reacted strongly with GM2 and

GalNAc-GD1a, but not with GM1, GD1a, GD1b, or GT1b (fig 1). ELISA confirmed that his serum had high titres of IgM antibodies to GM2 (1:25 600) and to GalNAc-GD1a (1:12 800) on day 4. Plasmapheresis was performed on days 5, 8, 24, 27, and 29, he was able to walk without assistance on day 60, but his facial diplegia showed slow improvement. The IgM anti-GM2 (1:800) and anti-GalNAc-GD1a (1:400) titres in this patient were significantly reduced on day 39. In the absorption study his serum was added to separate wells coated with individual ganglioside antigens (GM2, GalNAc-GD1a, GM1, and GD1a). The absorption rate was calculated from (1-(optical density at 492 nm in the well with serum with absorption treatment)/(optical density in the reference well with serum without absorption treatment)). No IgM anti-GM2 antibody was absorbed by GM1 or GD1a (fig 2). By

Figure 2 Absorption study of serum IgM anti-GM2 antibody from the patient carried out with GM2, GalNAc-GD1a, GM1, and GD1a. Serum samples were diluted serially from 1:250 to 1:8000 and added to wells coated with 5 pmol portions of each ganglioside antigen. The absorption rate was calculated from (1-(optical density at 492 nm in the well with serum with absorption treatment)/(optical density in the reference well with serum without absorption treatment)). The IgM anti-GM2 antibody in our patient was not absorbed by GM1 and GD1a but was by GM2 and GalNAc-GD1a.

contrast, IgM anti-GM2 antibody was absorbed by GalNAc-GD1a. Larger studies are needed to confirm whether (1) some patients with Guillain-Barré syndrome after CMV infection have IgM anti-GalNAc-GD1a antibody and (2) that the anti-GalNAc-GD1a antibodies cross react with GM2.

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Electrophysiological recordings in bilateral hemifacial spasm

Hemifacial spasm typically consists of unilateral involuntary spasms of the mimic muscles innervated by either facial nerve. There is some controversy whether mechanical irritation of the facial nerve entry zone by vessels in the cerebellopontine angle or hyperexcitability of the facial nerve nucleus is the main cause of this problem.^{1,2} To our knowledge, only two cases of bilateral hemifacial spasm have been described in some clinical detail but without electrophysiological recordings.^{3,4} The mechanism underlying the bilateral occurrence of spasms has not been investigated so far: either hyperexcitability of a facial nerve nucleus spreading to the contralateral side or independent mechanical irritation of both nerves might be involved. We report a patient with predominantly left sided spasms, electrophysiological diagnosis of bilateral facial spasm, the clinical course after surgical treatment according to MR evidence of elongated vertebral and basilar arteries, and implications of electrophysiological recordings on the pathogenesis of bilateral hemifacial spasm.

This 60 year old male patient presented with a history of gradually increasing left eye twitching over the past few years. He did not notice involvement of other facial muscles or of associated symptoms such as hearing deficits, vertigo, or headache. Visual inspection showed frequent clonic involuntary synchronous contractions of his left orbicularis oculi and left orbicularis oris muscles. On voluntary contraction of the orbicularis oculi muscle, there was some synkinesis of the left orbicularis oris

muscle and vice versa. There was no weakness of facial muscles or other neurological deficit. Four channel surface EMG recording from facial muscles was performed to ascertain the suspected diagnosis of left hemifacial spasm. Recordings gave evidence of irregular and asynchronous spasms of left and right facial muscles with higher frequency, amplitude, and longer duration on the symptomatic left side (fig 1A). Blink reflex recordings with stimulation of either supraorbital nerve showed bilateral R2 components also involving the orbicularis oris muscles of both sides (fig 1B); latencies of R1 and R2 components were in the normal range. Magnetic resonance imaging showed a grossly distended vertebral and basilar artery approaching first the right cerebellopontine angle and later in its course also the left cerebellopontine angle before taking its normal median position in its rostral segment (fig 2). This extraordinary course suggested a

possible mechanical irritation of both facial nerves.

The patient thus had a neurovascular decompression on the symptomatic left side. During surgery, close contact of the basilar artery with nerve entry zones of the left facial and vestibulocochlear nerve was found. After interposition of a piece of ivalon sponge, spasms of the left facial muscles disappeared almost completely leaving a slight left facial nerve paresis which cleared completely over the next months without functional deficit. There was a partial hearing loss on the operated side. Electrophysiological control recordings 4 months after surgery showed a reduction of the amplitude of compound muscle action potentials recorded from the left orbicularis oculi muscle. There was also a loss of facial synkinesis on the operated side, whereas spontaneous spasms and synkineses of the right facial muscles remained un-

changed or even slightly increased (fig 1A). Right sided spasms have become more prominent also during clinical investigation; they have, however, so far not bothered the patient enough to warrant an additional contralateral operation.

Bilateral twitching of facial muscles most commonly occurs in blepharospasm; this focal dystonia may occasionally mainly present by contractions of the orbicularis oculi muscle of only one side as experienced by our patient. Even more so, in patients with bilateral hemifacial spasm a dystonic aetiology may be erroneously attributed and lead to unsuccessful treatment.³ Needle EMG recordings can be helpful in discriminating these diseases by showing unphysiologically high frequent discharges of motor units in hemifacial spasm.⁵ With surface electrodes, simultaneous electrophysiological recording from facial muscles of both sides can differentiate this disorder from

Figure 1 Four channel surface EMG recording from orbicularis oculi and oris muscles. (A) Spontaneously occurring spasms of facial muscles. EMG bursts are synchronous on each side (representing synkinesis) but asynchronous with regard to the contralateral side. Before surgery, bursts are more frequent, of higher amplitude and duration on the clinically symptomatic left side. After surgery, spasms occurred only on the right side at increased frequency. (B) Blink reflex with electrical stimulation of the right supraorbital nerve. Before surgery, R1 components appear in both muscles on the stimulated side, R2 components are seen synchronously on both sides thus also involving the contralateral orbicularis oris muscle (same phenomenon also with stimulation on the left side). After surgery, synkinesis of the orbicularis oris muscles has disappeared. Arrow=time of stimulation.

Figure 2 Axial T2 weighted MR sections and MR angiography (lower right panel) of brain stem and vertebrobasilar arteries. The left vertebral artery is hypoplastic (upper left and lower right). The larger right vertebral artery turns left over the midline and the caudal basilar artery (arrow) lies in the left cerebellopontine angle in close proximity to cranial nerves VII and VIII. A small vessel crosses these cranial nerves in the right cerebellopontine angle (upper right). At the midpontine level, the basilar artery turns back to midline (lower left).

the rare bilateral hemifacial spasm by showing synchronous twitching of the muscles innervated by each facial nerve but asynchrony of muscle twitching between right and left facial muscles. In normal subjects and on the unaffected side of patients with unilateral hemifacial spasm R2 components of the electrical blink reflex are restricted to both orbicularis oculi muscles, but additional facial muscles are usually involved in patients with hemifacial spasm. This synkinesis of other muscles, which was found in this patient bilaterally, could be due to ephaptic transmission at the nerve entry zone or to facial nerve nucleus hyperexcitability; the immediate postoperative disappearance of synkinesis and abnormal R2 spread found in this case would thus be compatible with either suppression of ephaptic transmission at the nerve entry root or reduction of secondary facial nerve nucleus hyperexcitability. Both the asynchrony of spontaneous muscle bursts and the persistence or even increase of spasms on the less affected side after contralateral successful surgery in our case suggest independent trigger mechanisms on both sides most probably due to bilateral nerve entry zone irritation by aberrant vessels. Even with irritation of the nerve entry root being the probable primary cause, hyperexcitability of brain stem nuclei may also play a part; the reduced contralateral R2 component of the orbicularis oris muscle of the side contralateral to surgery (fig 1B) might be due to a loss of facilitatory effect of the operated side on the generation of this response.

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CORRESPONDENCE

Depression and its relation to lesion location after stroke

The documentation of a 20% prevalence of depression after stroke¹ has important therapeutic implications for patients with significant ischaemic heart disease and/or cardiac arrhythmia coexisting, either coincidentally or in an aetiopathogenetic role, with stroke illness. In such patients therapeutic choices

now need to be governed by the recognition that, despite comparable therapeutic benefit, adverse cardiac events such as sinus tachycardia, severe angina, and ventricular ectopy, are more likely to occur after tricyclic drugs such as nortriptyline, than after selective serotonin reuptake inhibitors such as paroxetine ($p < 0.03$).² Whereas nortriptyline causes a sustained increase in heart rate and a reduction in heart rate variability,² the second being a marker of increased cardiac mortality risk,³ no such sequelae occur after paroxetine.²

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MacHale replies:

We wholeheartedly agree with Jolobe's comments on the need to treat depressive illness after stroke with appropriate antidepressant drugs that have a low risk of cardiovascular side effects. Other studies using trazodone¹ and other selective serotonin reuptake inhibitors such as citalopram² have shown that these are safe and effective in the treatment of this condition. Unfortunately, the problem remains that the vast majority of patients with depressive illness after stroke remain untreated. Despite clear evidence of negative effects on recovery in functional status and cognitive performance³ it has been shown that inadequate and insufficient efforts at treatment had not influenced the prevalence of depression up to 5 years after stroke.⁴ The first important step therefore seems to be to encourage clinicians to recognise and treat depression after stroke, the second being to educate them about which are the appropriate medications to prescribe.

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BOOK REVIEWS

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