The course of corticofacial projections in the human brainstem

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Summary

Transcranial magnetic stimulation was used to investigate the corticofacial projections in 53 patients with (n = 28) and without (n = 25) central facial paresis due to unifocal ischaemic lesions at different brainstem levels. Lesion topography documented by MRI studies was correlated with the electrophysiological findings. In the majority of patients the corticofacial fibres travel within the ventromedial base of the pons and cross the midline at the level of the facial nucleus. In some individuals, however, we found evidence that corticolingual fibres form an ‘aberrant bundle’ in a paralemniscal position at the dorsal edge of the pontine base. In other patients the corticofacial fibres loop down into the ventral part of the upper medulla, cross the midline and ascend in the dorsolateral medullary region ipsilaterally to the facial nucleus. The findings suggest that facial paresis due to a brainstem lesion may present as contralateral supranuclear facial paresis by a lesion of the cerebral peduncle, pontine base, the aberrant bundle and the ventral medulla. Supranuclear facial paresis ipsilateral to the lesion side may result from a lesion in the lateral medulla, and facial paresis of the supranuclear type may be imitated by a lesion of the peripheral facial nerve in the dorsolateral medulla with involvement of the lower pons.

Keywords: corticofacial projections; corticobulbar tract; facial nerve; brainstem; transcranial magnetic stimulation

Abbreviations: CMAP = compound muscle action potential; TMS = transcranial magnetic stimulation

Introduction

The anatomy and function of the facial nerve in man are well known, but there remains some uncertainty about the course of the corticofacial fibres within the human brainstem. Histological studies of human post-mortem material using the Marchi technique (Hoche, 1898; Barnes, 1901) described a fibre bundle (the ‘aberrant bundle’) which was branching off the main pyramidal tract at the midbrain and upper pontine level and running along the tegmental border. More recent studies using the Nauta–Gygax technique (Kuypers, 1958) and a modified Bielschowsky stain (Yamashita and Yamamoto, 2001) have confirmed these results.

With regard to the supranuclear facial fibres in the brainstem, it is still unclear (i) whether the corticofacial fibres branch off from the main ventral pyramidal tract within the pyramidal base (Sand, 1903) or if, together with other fibres, they form an aberrant bundle running more dorsally at the tegmental border near the medial lemniscus (Hoche, 1898; Barnes, 1901); (ii) at which level these fibres branch off from the main tract or aberrant bundle; (iii) at which level they cross the midline to reach the contralateral facial nucleus; and (iv) if the fibres form a loop into the medulla oblongata and then take an ascending course to the facial nucleus (Sacco et al., 1993).

Patients and methods

We studied 53 patients with (n = 28) and without (n = 25) central facial paresis due to unilocal ischaemic brainstem lesions. The localization was based on clinical findings and MRI studies. Patients with multiple lesions and vascular encephalopathy were excluded from the study. The corticofacial projections from either hemisphere to the contralateral orofacial subnucleus and the peripheral pathways were investigated by transcranial magnetic stimulation (TMS) (Urban et al., 1997a).

The histories of three patients participating in the present study have been published previously in the form of case reports (Urban et al., 1998b, 1999).
All patients gave their informed consent to participation in the study, which was approved by the local ethics committee (State Medical Council Rheinland-Palatinate).

**Transcranial magnetic stimulation**

The corticofacial projections were investigated by TMS and recordings of compound muscle action potentials (CMAPs) of the buccinator muscles on either side of the face. We used pairs of Ag–AgCl surface disc electrodes embedded at a distance of 18 mm in a specially designed fork-shaped metacrylate device, which was adapted to the oral vestibulum (Urban et al., 1997a). The electrodes were in contact with the insides of the cheeks. Slight contraction of the buccinator muscles was achieved by pursing the lips.

The proximal peripheral facial nerve was stimulated magnetically at the extra-axial intracranial segment. The circular coil was located ipsilaterally parieto-occipital to the facial nerve, the appropriate site for measuring the peripheral motor conduction time (Rösler et al., 1989; Urban et al., 1997a). For stimulation of the left (right) peripheral nerve, side B (A) was viewed from the outside. The distal nerve was also stimulated electrically at the stylomastoid foramen. All responses were recorded at least twice to ensure reproducibility. A detailed description of the recording technique has been published elsewhere (Urban et al., 1997a, b).

Filter settings for CMAP recordings were 20–2000 Hz. A Magstim 200S (Novametrix, Whitland, Dyfed, UK) and a circular coil (mean diameter 9 cm) with a peak magnetic field of 2.0 T were used for TMS recordings. The centre of the coil was positioned tangentially 2 cm (buccinator muscle) lateral to Cz. On stimulation of the left (right) hemisphere, side B (A) was viewed from above. Stimulation strength was increased stepwise during slight preinnervation until stable latencies were achieved. The shortest latency and the largest amplitude (peak-to-peak) out of four responses were measured.

An upper motor neurone lesion was assumed when (i) the cortical evoked response was absent, (ii) the TMS-evoked/M-wave amplitude ratio was reduced (to ≤10%), or (iii) the central motor conduction time or the interside difference in central motor conduction time was increased (by more than the mean plus 2.5 SD), the peripheral motor conduction time and absolute amplitude of the M-wave remaining within normal limits. Stimulation intensity was increased to 100% of the maximum output of the stimulator before a response was regarded as absent. The absence of a potential was defined as no reproducible response in four consecutive trials at a gain of 200 μV/division (Rösler et al., 1989; Urban et al., 1998a). Normative data for our laboratory have been reported previously (Urban et al., 1997a; Urban and Hopf, 1997).

**MRI**

All patients had biplanar high-resolution T2-weighted imaging of the brainstem to identify the location of the infarction.

**Table 1 Lesion sites of the patients with abnormal (n = 28) and normal (n = 25) corticofacial tract function on TMS using recordings from the buccinator muscle**

<table>
<thead>
<tr>
<th>Lesion site</th>
<th>Abnormal corticofacial trait function</th>
<th>Normal corticofacial trait function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midbrain</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Pontomesencephalic</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Pons</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Pontomedullar</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Medulla oblongata</td>
<td>5</td>
<td>5</td>
</tr>
</tbody>
</table>

Brain MRIs were obtained in each patient within the first 2 weeks according to a fixed protocol. (i) Echoplanar imaging T2-weighted imaging and echoplanar imaging diffusion-weighted imaging within 24 h after onset of symptoms (1.5 T Magnetom Vision; repetition time 4000 ms, echo time 103 ms, gradient strength 1150 s/mm²) was used to identify the acute brainstem infarction. Scanning time per slice was 250 ms. (ii) High-resolution T2-weighted imaging (slice thickness 3 mm) in the axial and sagittal planes and T1-weighted imaging was performed before and after intravenous administration of the contrast medium.

The slice orientation was parallel (sagittal sections) and perpendicular (axial sections) to the sagittal brainstem cuts of the Schaltenbrand atlas (Urban et al., 2001).

**Digital imaging postprocessing**

The area of infarction was identified by two neuroradiologists. The individual slices were normalized (according to their T2- and T1-weighted brainstem outlines) and projected on to 10 levels of the anatomical atlas of Schaltenbrand and Wahren (Schaltenbrand and Wahren, 1977). All right-sided lesions were mirrored to the left side for easier comparison. This enabled us to study each lesion at every level in relation to the anatomical structure determined by the Schaltenbrand atlas. Unix and NT workstations and Numaris (Siemens, Erlangen, Germany), Photoshop (Adobe, San Jose, USA), Photopaint (Correl, Ottawa, Canada) AFNI software (Cox, 1996) were used for postprocessing.

**Results**

Clinically, 28 out of the 53 patients showed both central facial paresis and a lesion of the central corticofacial motor pathway on MRI and by TMS. The remaining 25 patients had normal facial movements and no TMS abnormalities. The level of lesions in the brainstem is shown in Table 1 for both groups. Figure 1 demonstrates one exemplary patient with contralateral central facial paresis due to a lesion of the left base of the pons (Fig. 1, top), in whom TMS of the left motor cortex (ipsilateral to the pontine lesion) evoked no...
Superposition of the lesion sites of the patients with central facial paresis demonstrated that the cerebral peduncles were affected mainly in the central portion at the midbrain and pontomesencephalic junction levels (Fig. 2A and B). However, more precise lesion localization was not possible because of the small number of patients with midbrain and pontomesencephalic lesions (n = 3). The common lesion area at the upper and middle pontine levels was spread across the centre of the pontine base (Fig. 2C–F). At the lower third of the pons (Fig. 2G and H), the lesion sites were shifted to a more ventromedial position close to the midline.

MRI demonstrated a small lesion in the dorsal base of the pons at the border to the tegmental region in three patients presenting with isolated contralateral volitional central facial paresis. Figure 3 demonstrates one exemplary patient with isolated contralateral central facial paresis due to a lesion of the right dorsal base of the pons near the medial lemniscus (Fig. 3, top), in whom TMS of the facial motor cortex (ipsilateral to the pontine lesion) evoked no response in the contralateral buccinator muscle (Fig. 3, bottom).

Central facial paresis was further observed in patients with upper medullary infarctions (Fig. 2I and J). One patient with left ventral medullary infarction (Fig. 4) also showed contralateral central facial paresis. Two patients with lateral medullary infarctions had a central-type facial paresis ipsilateral to the lesion with a supranuclear lesion pattern on TMS (Fig. 5). Two additional patients with dorsolateral medullary infarction also presented with facial paresis of the central type. However, a comparison with the unaffected side showed that these patients had a nuclear/infranuclear facial nerve lesion, indicated by an amplitude reduction of 90–95% on distal electrical stimulation of the peripheral facial nerve on Days 11–13 after onset of symptoms (Fig. 6).

The superimposed lesion areas in the patients with normal corticofacial tract function largely spared the cerebral peduncle and the pontine base and affected mainly the tegmental part of the brainstem (Fig. 7A–I). However, in 44% of patients the pontine base and the ventral medulla were also affected.

Discussion

Data on the course of corticobulbar fibres in the brainstem that connect the motor cortex with the facial nucleus are
Fig. 2 (A–I) Superposition of infarction areas leading to central facial paresis and abnormal corticofacial tract function on TMS. Projection of the infarction areas into axial brainstem slices from the midbrain to the medulla oblongata.
Fig. 4 Top: MRI (axial section) of a patient with left-sided ventral medullary infarction. Bottom: TMS of the facial motor cortex and stimulation of the proximal and distal facial nerve with recordings from the buccinator muscles (Day 10 after onset of symptoms). Stimulation of the left motor cortex (ipsilateral to the medullary lesion) evoked no response in the contralateral buccinator muscle.

Fig. 3 Top: MRI (axial and sagittal views) of a patient with isolated contralateral central facial paresis due to a lesion of the right dorsal base of the pons near the medial lemniscus. Bottom: TMS of the facial motor cortex and stimulation of the proximal and distal facial nerve with recordings from the buccinator muscles (Day 12 after onset of symptoms). Stimulation of the right motor cortex (ipsilateral to the pontine lesion) evoked no response in the contralateral buccinator muscle.
The classical localization postulates that ventral brainstem lesions rostral to the lower pons result in contralateral central-type facial paresis, whereas the ipsilateral peripheral type of facial weakness results from lesions of the lower dorsolateral portion of the pons. The facial corticobulbar tract in the rhesus monkey provides strongly unilateral innervation to the contralateral lower face muscles (Morecraft et al., 2001). The lateral subnucleus, innervating the peri-oral muscles, primarily receives contralateral projections from the primary motor cortex, while the upper face muscles receive bilateral input from the supplementary and rostral cingulate cortex. These histological findings correspond to TMS findings in the buccinator muscle, where predominantly contralateral responses but inconsistent ipsilateral responses with longer latencies and smaller amplitudes have been observed (Urban et al., 1997a). The buccinator muscle is therefore especially suitable for the investigation of central type facial paresis (Urban et al., 1998b, 1999a). Further advantages of buccinator muscle recordings compared with recordings from other lower face muscles are the high CMAP amplitude due to the large muscle volume, the low stimulation artefact with intra-oral recording, lack of relevant volume conducted activity from the contralateral side and the well-defined motor point, which, in most instances, leads to a clear negative onset of the CMAP.

The corticospinal and corticobulbar pathways are phylogenetically relatively new tracts and are characterized by greater interindividual and interspecies variation of their position within the central nervous system. Such variation has been demonstrated for the corticofacial fibres (Hoche, 1898; Barnes, 1901; Dejerine, 1914). In post-mortem studies of the human brainstem, a fibre bundle (the ‘aberrant bundle’) was described as branching off the main pyramidal tract at the midbrain and upper pontine level. This fibre bundle runs along the border of the tegmentum in a paralemniscal position and contributes fibres to the trigeminal and facial nuclei. Whether the hypoglossal nucleus also receives such ‘aberrant’ fibres has not been demonstrated conclusively. The existence of the aberrant bundle has been denied by others (Sand, 1903), although more recent findings (Kuypers, 1958; Puvanendran, 1978; Yamashita and Yamamoto, 2001) have supported its presence. Assuming the existence of the aberrant bundle, there should be at least some patients with paralemniscal pontine lesions who present with isolated central facial paresis. The latter was identified in three of our patients with isolated contralateral central facial paresis. The lesions were located in the middle (and upper) pons, indicating that the

Fig. 5 Top: MRI (axial and sagittal views) of a patient with left-sided lateral medullary infarction. Bottom: TMS of the facial motor cortex and stimulation of the proximal and distal facial nerve with recordings from the buccinator muscles (Day 10). Stimulation of the right motor cortex (contralateral to the lesion) evoked no response in the left buccinator muscle.
Fig. 6 Top: MRI (axial and sagittal views) of a patient with right-sided dorsolateral pontomedullary infarction. Bottom: TMS of the facial motor cortex and stimulation of the proximal and distal facial nerve with recordings from the buccinator muscles (Days 2 and 13 after onset of symptoms). On Day 2, stimulation of the left motor cortex evoked a prolonged and amplitude-reduced response in the contralateral buccinator muscle, while the peripheral responses were in the normal range, suggesting a supranuclear lesion. On Day 13, however, the CMAP amplitudes following right peripheral nerve stimulation were also diminished, demonstrating that the amplitude reduction on cortical stimulation is due to a peripheral nerve lesion.

aberrant fibres run ipsilateral to the main ventral pyramidal tract and do not cross the midline before reaching the lower pons level (Fig. 8). The use of TMS demonstrated that, in these patients, the corticolingual and corticospinal projections were not affected either clinically or electrophysiologically by the lesion (data not shown). This finding is supported by results of previous findings on the course of the corticolingual tract fibres in the human brainstem, which showed no evidence that the corticolingual fibres travel within the aberrant fibre bundle (Urban et al., 1996). However, because of the small number of patients investigated, we cannot draw any final conclusions on the frequency of the presence of an aberrant bundle.

Superposition of the lesion areas demonstrated that contralateral central facial paresis is associated with lesions of the cerebral peduncle and the ventral base of the pons, which is in agreement with current knowledge (Brodal, 1981). The responsible lesion areas in the upper and middle pons were spread over a larger area around the centre of the pontine base and shifted ventromedially in the lower third of the pons. This finding may indicate convergence of the corticofacial fibres before they cross the midline and reach the contralateral facial nucleus. More precise localization was not possible because of the large infarction size in most patients. We cannot exclude the possibility that the corticofacial fibres are split into a number of small dispersed fascicles and do not form a compact bundle within the base of the pons. This point awaits further clarification following the analysis of small lesions and selective involvement of the corticofacial projection, which apparently occur in only a very small number of patients.

However, our view is supported by the finding that, in the patients with normal corticofacial tract function, the superimposed lesion areas showed a tendency to spare the pontine base and affect mainly the tegmental region of the brainstem. In 44% of these patients, however, the pontine
Fig. 7 (A–I) Superposition of infarction areas without central facial paresis and normal corticofacial tract function on TMS.
Fig. 8 Schematic drawing of the voluntary corticofacial projections in the human brainstem as indicated by our results (see text). 1 = main ventral pyramidal tract; 2 = ‘aberrant bundle’ in a paralemniscal position at the dorsal base of the pons; 3 = fibre loop into the ventral medullary region, crossing the midline and ascending in the dorsolateral medullary region to the facial nucleus from below. (A) Sagittal view; (B) coronal view.

base also showed MRI signal abnormalities, even though infarction does not necessarily impair the function of tracts running through the infarcted area (Hömgberg et al., 1991; Ferbert et al., 1992). In some of these patients with pontine base infarction and normal corticofacial tract function, the corticofacial tract fibres might travel outside the pontine base in an aberrant fibre bundle. Furthermore, lesions were also observed in the ventral and lateral medullary region, which suggests that the corticofacial fibres do not form a loop projecting into the upper medulla in every individual. An additional point regarding the pontomedullary region remains open to question. Contralateral facial paresis has been reported in ~50% of the small number of patients with ventral medullary infarctions (Table 2). It has been hypothesized that in these individuals the corticofacial fibres form a loop in the upper medulla, supplying the facial nucleus from below (Currier et al., 1961). To date, there is no conclusive histological evidence of such fibres. Supporting this hypothesis, we observed one patient with ventral medullary infarction on the left side who had contralateral facial paresis due to a supranuclear lesion confirmed by TMS (Fig. 7). Moreover, a mild and transitory central-type facial paresis is not uncommon in lateral medullary infarctions and can be observed in ~40% of patients (Table 3). In contrast to ventral medullary infarctions, facial paresis occurs ipsilaterally to the lesion side in these patients.

Four of our patients with upper medullary infarctions exhibited central facial paresis ipsilateral to the lesion side. Electrophysiological examination disclosed different mechanisms. In two patients with infarction of the lateral medulla, cortical TMS on Days 1 and 4 after onset of symptoms showed absent responses to the contralateral buccinator muscle, while magnetically and electrically evoked responses of both peripheral nerves were normal in both the acute stage and at follow-up 2 weeks later. These findings may indicate that supranuclear fibres form a loop in the medulla before reaching the facial nucleus and that the fibres were affected ipsilaterally to paresis after crossing the midline. Another electrophysiological pattern was found in two other patients who also presented with central facial paresis. MRI showed an infarction of the dorsolateral medulla oblongata. TMS of the facial motor cortex on Days 1–3 demonstrated an amplitude reduction in the contralateral buccinator muscle response, which was <30% of that recorded on the unaffected side, while the peripheral evoked responses of both facial nerves were normal. On Days 11–13, however, the buccinator muscle response following ipsilateral distal electrical stimulation was virtually absent. Clinically, the weakness was more pronounced peri-orally with relative sparing of the upper face muscles, but TMS indicated an axonal lesion of the infranuclear facial nerve. This can only be explained by an extension of the medullary lesion into the lower pons, either involving the intra-axial infranuclear nerve fibres
or affecting the corresponding facial subnucleus. A lesion extending caudally to rostrally would cause primarily peri-oral weakness imitating central-type facial paresis, since the peri-oral muscles are represented at the lower lateral pole of the facial nucleus (Jenny and Saper, 1987; Morecraft et al., 2001). Electrophysiological follow-up investigations including TMS are useful in differentiating supranuclear from nuclear or infranuclear intra-axial facial nerve lesions in lateral medullary infarctions.

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### References


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