Electrical and Transcranial Magnetic Stimulation of the Facial Nerve: Diagnostic Relevance in Acute Isolated Facial Nerve Palsy

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Key Words
Facial palsy • Transcranial magnetic stimulation • Electrical stimulation

Abstract
Unilateral facial weakness is common. Transcranial magnetic stimulation (TMS) allows identification of a conduction failure at the level of the canalicular portion of the facial nerve and may help to confirm the diagnosis. Methods: We retrospectively analyzed 216 patients with the diagnosis of peripheral facial palsy. The electrophysiological investigations included the blink reflex, preauricular electrical stimulation and the response to TMS at the labyrinthine part of the canalicular proportion of the facial nerve within 3 days after symptom onset. Results: A similar reduction or loss of the TMS amplitude (p < 0.005) of the affected side was seen in each patient group. Of the 216 patients (107 female, mean age 49.7 ± 18.0 years), 193 were diagnosed with Bell’s palsy. Test results of the remaining patients led to the diagnosis of infectious [including herpes simplex, varicella zoster infection and borrelia (n = 13)] and noninfectious [including diabetes and neoplasma (n = 10)] etiology. Conclusions: A conduction block in TMS supports the diagnosis of peripheral facial palsy without being specific for Bell’s palsy. Significance: These data shed light on the TMS-based diagnosis of peripheral facial palsy, an ability to localize the site of lesion within the Fallopian channel regardless of the underlying pathology.

Introduction
Unilateral facial weakness is a common neurological symptom and in 60–75% of cases, it is due to idiopathic peripheral facial nerve palsy, also known as Bell’s palsy [1]. The annual incidence of Bell’s palsy is about 20–30 per 100,000 inhabitants [1, 2]. Other causes include acute viral infections, borrelia, diabetes, pregnancy, trauma, tumors of the parotic gland and other systemic diseases. In at least 85% of affected cases, a complete or nearly complete recovery without treatment can occur within 5 months [1]. Therapeutic decisions vary depending on the etiology. To avoid unnecessary diagnostic procedures and overtreatment, tools for early diagnosis are desirable.

Cerebral imaging with magnetic resonance imaging (MRI) can be used for a detailed analysis of the posterior fossa. It is used in patients with hearing loss, progressive facial weakness, otorrhea or other progressive neurological signs [3]. The preferred imaging modality in patients with suspected osseous lesions is computed tomography.
(CT). For ruling out infectious diseases, the analysis of cerebrospinal fluid is usually performed in most cases. However, in Bell’s palsy, all these diagnostic tests show no pathology. A conduction block of the facial nerve within the canalicular portion is considered typical for Bell’s palsy when investigated within 3 days after the onset of symptoms. Therefore, neurophysiological methods such as transcranial magnetic stimulation (TMS) and electrical stimulation of the facial nerve are presumed to be of relevance to confirm the diagnosis and obtain information concerning the prognosis of the palsy at the onset of symptoms [4–8]. TMS allows identification of a conduction failure at the level of the canalicular portion of the facial nerve which is not accessible by electrical stimulation, and thus helps to identify the location of the lesion [9]. However, all electrophysiological investigations of the facial nerve need to be performed within the first few days after the onset of facial palsy in order to detect focal hypoexcitability before the onset of significant axonotmesis [5, 6, 10, 11].

The aim of this study was to investigate whether the conduction block of the facial nerve within its canalicular portion as part of a diagnostic work-up is typical for Bell’s palsy and to show a better sensitivity of TMS in combination with electrical stimulation compared to electrical stimulation alone in a large group of patients when investigated within 3 days of symptom onset. The study included a larger number of patients than previous studies [4–8].

Patients and Methods

Patients and Diagnostic Work-Up

The clinical and electrophysiological data of 216 patients presenting with a first-time unilateral peripheral facial nerve palsy (ICD 10: G 51.0), who were admitted to the Department of Neurology, Klinikum Bremen-Ost, Germany between January 2000 and December 2005, were analyzed retrospectively. Only patients who underwent full electrophysiological investigation within the first 3 days after onset of symptoms were included. None of the patients had contraindications for TMS such as epilepsy, pregnancy or a cardiac pacemaker.

Individual diagnosis was based on clinical work-up as described below. The clinical classification was made by experienced neurologists who were blinded to the electrophysiological results. The clinical severity of the facial palsy was described as complete or incomplete. Routine blood tests and an analysis of the cerebrospinal fluid were part of the diagnostic work-up, including blood serologies or immunological assays for Borrelia burgdorferi, varicella zoster virus (VZV) and herpes simplex virus type I (HSV 1). MRI or CT as well as otorhinolaryngological and ophthalmological examinations were also performed to complete clinical work-up for individual diagnosis whenever available.

Electrophysiological Studies

The electrophysiological investigations within 3 days of symptom onset included the R1 and R2 response of the blink reflex, preauricular electrical stimulation and the response after TMS at the labyrinthine part of the canalicular proportion of the facial nerve regarding latencies and amplitudes, as described previously [6, 12, 13]. All recordings were performed bilaterally to enable side-to-side comparison. We used the orbicularis oculi muscle to record facial motor neurography compound muscle action potentials (CMAP), placing the electrode directly under the eye and the indifferent electrode on the side of the nose. Filter settings were set to 2–10,000 Hz. To excite the facial nerve at the stylomastoid foramen, a supramaximal electrical stimulus was used. Latencies were measured to the onset of the initial negative deflection, or, if an initial negative deflection was not obtained, from the point when CMAP left the baseline level.

The MagStim 200 magnetic stimulator was used to investigate the labyrinthine segment of the facial nerve prior to its entry in the Fallopian channel. The diameter of the stimulation coil was 90 mm and it was positioned parieto-occipitally on the skull with a clockwise current orientation on the right side and vice versa [coming from the vertex (Cz in the 10–20 system) 7 cm from the ear and 4 cm from the occiput]. The output of the stimulator was increased stepwise until a maximal response was obtained or the output of the stimulator reached the maximum of 60%. In some cases, the increased stimulator output let to potentials with such a conspicuously short latency, similar to extracranial stimulation. In these cases, it can be presumed that a stimulation of the facial nerve prior to entering the Fallopian channel was not successful and could not be obtained. These data were excluded from the further analysis. The healthy side was stimulated first in order to determine the stimulation intensity required to achieve a maximal response. Figure 1 illustrates original TMS waveforms in a patient with Bell’s palsy.

![Graph showing mean relative amplitudes of the CMAP evoked by magnetic and electrical stimulation of the affected facial nerve as compared to the unaffected side.](image-url)
Amplitudes evoked by electrical and magnetic stimulation of both facial nerves as measured from baseline to the negative peak were used for quantification of the CMAP. Individual CMAP amplitudes of the affected side were calculated as percentage of the amplitudes evoked at the healthy side.

**Statistics**

We used the Mann-Whitney U test for nonparametric parameters between 2 groups, the Kruskal-Wallis test for nonparametric parameters between more than 2 groups and the χ² test/Fisher’s exact test for the qualitative parameters gender and severity of the facial palsy.

**Results**

**Clinical Characteristics and Demographics**

Altogether, 216 patients [49.7 ± 18.0 years, 107 females, median for duration of the disease 1 day (1–3 days)] were included in this study. Out of these, 208 patients obtained an analysis of their cerebrospinal fluid, 171 had a CCT scan, 106 had an MRI scan, 89 had an otorhinolaryngological examination and 11 had an ophthalmological examination. Altogether, 193 were diagnosed with Bell’s palsy after elimination of other causes based on typical clinical work-up. Thirteen patients had an infectious etiology (5 had VZV infection, 3 had borreliosis, 2 had HSV I infection, 2 had unknown viral etiology and 1 had otitis media). Ten patients had a noninfectious etiology (6 had diabetes, 1 had sarcoidosis, 1 had metastasis, 1 had acoustical neurinoma and 1 had nuclear facial palsy because of multiple sclerosis). Oral steroids were started in 186 patients, 3 patients were treated with acyclovir, 6 with antibiotics, the patient with the acoustical neurinoma underwent surgical therapy, 7 were advised how to live with diabetes, 3 received physiotherapy without other treatment and 8 received no treatment at all because they left the hospital shortly after admission of their own accord. Physiotherapy with special exercises for facial palsy were started for 213 patients during their stay in the hospital. For detailed clinical and demographic data, see tables 1 and 2.

**Electrophysiological Investigations**

TMS of both facial nerves, electrical stimulation and blink reflexes were performed in each patient within 3...
days of the onset of symptoms. All examinations were tolerated well and no adverse effects were observed. The earliest examinations were performed on the day of symptom onset (n = 88), the last examination was performed on day 3 after symptom onset (n = 29).

All patients with idiopathic facial palsy were examined with electrophysiological investigations on average 2.9 ± 0.9 days after symptom onset, all patients with infectious etiology 3.4 ± 0.4 days after and the patients with a noninfectious etiology 2.6 ± 1.1 days after i.e. not significantly different (p = 0.114). Blink-reflex studies showed typical patterns for facial palsy in each case (data not shown).

Table 3 shows electrophysiological data and figures 1 and 2 summarize relative and absolute amplitudes of the CMAP evoked by magnetic and electrical stimulation of the affected facial nerve compared to the unaffected side. There are no statistical differences between the groups.

Correlation Analysis

In all patient groups, there were no correlations between (the percentage of) amplitude decrease in transcranial cisternal or electrical stimulation and age, duration of symptoms or degree of facial palsy (total vs. subtotal).

Table 3. Electrophysiological data of all investigated patients with facial palsy, differentiated by idiopathic, infectious and noninfectious etiology

|                  | Idiopathic (n = 193) | Infectious (n = 13) | Noninfectious (n = 10) | p value |
|------------------|----------------------|---------------------|------------------------|---------|
| TMS amplitude-affected side, mV | 0.15 ± 0.55          | 0.01 ± 0.01         | 0.29 ± 0.50            | 0.071   |
| TMS amplitude-unaffected side, mV | 2.06 ± 1.11***       | 3.40 ± 1.65***      | 2.15 ± 0.57**          | 0.199   |
| Electric amplitude-affected side, mV | 2.34 ± 1.30          | 2.12 ± 0.84         | 1.94 ± 1.21            | 0.577   |
| Electric amplitude-unaffected side, mV | 2.58 ± 1.18***       | 2.29 ± 0.76         | 2.25 ± 0.67            | 0.580   |
| TMS latency-affected side, ms* | 3.90 ± 1.02          | n.a.                | 2.83 ± 1.3             | 0.156   |
| TMS latency-unaffected side, ms | 4.27 ± 0.61          | 4.24 ± 0.78         | 4.34 ± 1.21            | 0.300   |
| Electric latency-affected side, ms | 2.32 ± 0.49          | 2.46 ± 0.60         | 2.21 ± 0.70            | 0.175   |
| Electric latency-unaffected side, ms | 2.27 ± 0.45          | 2.19 ± 0.28*        | 2.21 ± 0.50            | 0.500   |

Values are given as mean ± standard deviation unless otherwise specified. p values are according to the Kruskal-Wallis test for unrelated parameters and the Wilcoxon test for related parameters. n.a. = Not applicable.

*** p = 0.001; ** p = 0.005; * p = 0.029 as compared to affected side.

* In those patients with maintained potential: idiopathic n = 20, infectious n = 0, noninfectious n = 3.
Discussion

It has been suggested that a significant reduction or complete absence of the muscle response to cisternal TMS early in the course of the disease is typical and may be specific for Bell’s palsy [10, 11]. Our data, however, suggest that this is not the case, and demonstrates a conduction block in facial TMS in all patients with facial palsy regardless of the etiology. Hypoexcitability of the labyrinthine segment of the facial nerve to early TMS was also evident in patients with infectious (e.g. borreliosis and zoster oticus) as well as noninfectious etiology. Our data, including a larger number of patients, are in line with two previous studies [7, 8].

In general, the degree of neurapraxia is optimally measured by comparing the muscle response to stimulation proximal and distal to the conduction block. In facial nerve palsy, however, direct stimulation of the facial nerve proximal to the conduction block is not possible, as the site of the lesion is inaccessible within the temporal bone [14, 15]. The labyrinthine segment of the facial nerve can be excited by TMS [4–6]. It has been demonstrated that hypoexcitability of the facial nerve to TMS occurs within a few hours of symptom onset and may last several months [4–6].

Although TMS is highly sensitive in detecting the site of the lesion within the Fallopian channel, it seems to not be specific to the etiology of facial nerve palsy.

After preauricular electrical stimulation there was a reduction of amplitudes of the affected side in each patient group with significance in patients with idiopathic facial palsy; this suggests a more pronounced axonal degeneration in this latter group. In a previous study [7], however, there was a similar result in patients with zoster oticus. The number of patients with infectious etiologies (n = 13) in our study and with zoster oticus (n = 5) in the study by Nowak et al. [7] was small; further studies with a greater number of patients are thus needed to come to a final conclusion. The peculiar result of shorter electric latencies on the affected side after TMS, compared to the unaffected side in patients with infectious facial palsy, may be due to a technical problem caused by overstimulation. This means, as discussed earlier, that the labyrinthine segment of the facial nerve was not stimulated and that a peripheral stimulation occurred instead, caused either by special anatomic conditions and/or the higher output of the stimulator.

We found no correlation between the percentage of amplitude decrease in transcranial or electrical stimulation and age, duration of symptoms or the clinical degree of facial palsy (total vs. subtotal) in any of our patient groups. Nowak et al. [7] described a correlation of the amount of CMAP amplitude reduction to electrical stimulation with the clinical degree of palsy. We might have lost this correlation, because due to retrospective analysis we could set the severity of the facial palsy only as complete or incomplete, compared to the 6 clinical grades of facial palsy according to the scale proposed by House and Brackmann [16] used by Nowak et al. [7].

Concerning prognosis of the facial nerve lesion, Fisch [17] worked out a helpful algorithm: 80–100% of patients with a grade of I or II according to the House and Brackmann scale [16] have a favorable outcome if axonal loss, assessed by electrical stimulation, does not exceed a 90% amplitude decrease compared to the healthy side within the first 3 weeks. In contrast, only 50% of these patients have a favorable outcome if 90% or more axonal degeneration is present [17]. As this is a retrospective study, one limitation is that we cannot comment on the possible prognostic factors of TMS.

Summarizing our findings, TMS is capable of localizing the site of lesion within the Fallopian channel, regardless of the underlying pathology. It is therefore a helpful diagnostic tool for early diagnosis of facial palsy in general. It is not specific for Bell’s palsy but does have specific relevance in facial palsy diagnosis, especially regarding other diagnostic procedures such as electrical stimulation.

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