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Latency shift in compound muscle action potentials during electroneurography in facial palsy

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Abstract

Objective Electroneurography (ENoG) reliably predicts the prognosis of facial palsy. However, the results of ENoG are dependent on the location, where the wave is detected, as a compound muscle action potential (CMAP) arising from the facial muscles. To minimize errors in prognostic prediction, we analysed the latencies of facial CMAPs.

Materials and methods Fifty-seven patients with unilateral peripheral facial palsy and 24 healthy volunteers were enrolled. Amplitudes, negative peak latencies (NPL), and rise latencies (RL) of CMAPs were measured on the paralysed and healthy sides in patients and in healthy volunteers. The relationships of these latencies with ENoG values and the lowest House–Brackmann (H–B) scores were also analysed.

Results The amplitude of CMAP on the paralysed side was smaller, and NPL and RL were longer, than those on the healthy side in patients and healthy volunteers ($p < 0.01$). In patients, there was no difference in NPL between the ENoG < 40% group and the ENoG ≥ 40% group. Conversely, there was a significant difference in RL between the ENoG < 40% group and ENoG ≥ 40% group ($p = 0.03$). No relationships were observed between NPL or RL and the lowest H–B score.

Conclusions NPL and RL of CMAP on the paralysed side were equivalent or longer than those on the healthy side. During ENoG for facial palsy, CMAP should be measured on the healthy side first, and then detected (and the amplitude measured) on the paralysed side with reference to CMAP latency on the healthy side, to reduce errors in detecting facial CMAPs.

Keywords Facial palsy · Electroneurography · Compound muscle action potential · Latency

Introduction

The most serious concerns for patients with sudden-onset facial palsy are whether they can be cured, and if so, when. Therefore, the evaluation of the degree of facial nerve damage and the accurate prediction of the prognosis in facial palsy are extremely important to patients. Prognostic procedures include scoring facial movements, nerve excitability testing (NET), electromyography (EMG), electroneurography (ENoG), and stapedial reflex measurements. Each of these has advantages and limitations, and none alone provides a complete prognosis. Of these procedures, NET and ENoG are the most widely used.

ENoG, which was first described by Esslen in 1973 [1], is an electrophysiological test of facial palsy. The ENoG value, which is the ratio of the amplitude (from negative peak to positive peak) of the compound muscle action potential (CMAP) on the paralysed side to that on the healthy side, multiplied by 100, reflects the percentage of facial nerve degeneration on the paralysed side [1, 2]. In ENoG measurement, transcutaneous electrical stimulation is applied to the main trunk of the facial nerve close to the stylomastoid foramen [1, 3, 4]. The recording electrodes (cathode and anode) are generally applied to the nasolabial fold for CMAP recording (standard method) [1–3]. In contrast, we propose a midline ENoG measurement, in which the anode is placed on the mental protuberance and the cathode is placed on the

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philtrum over the orbicularis oris muscle [5, 6]. This midline method is simple and is not influenced by any resting asymmetry of the face in patients with unilateral facial palsy. The midline method has demonstrated larger CMAP amplitudes on both sides and shown a stronger correlation between the ENoG value and latency to full recovery from palsy than the standard method [6]. Therefore, we mainly use the midline method for prognostic diagnosis of facial palsy.

Certain details should be noted during ENoG, i.e., where the stimulating electrodes are placed, and the intensity of the stimulating current; the obtained CMAPs should also be measured. In particular, the ENoG value is easily influenced by where the examiners visually detect the negative and positive peaks in CMAPs, because facial muscle configurations are complex, and muscle movements exhibit mutual interference. In addition, other muscle action potentials generated from non-facial muscles are likely to be involved when strong supramaximal electrical stimulation is applied to the facial nerve. Thus, the CMAPs are intricate and measurement errors are possible.

In this study, we examined the latencies of bilateral CMAPs of the orbicularis oris muscle in patients with unilateral peripheral palsy and in healthy volunteers. This study was performed to explore differences in the latencies of CMAPs on the paralysed and healthy sides, and to minimize errors in CMAP measurements from the perspective of CMAP latency.

Materials and methods

Patients and healthy volunteers

The study population consisted of 57 patients (36 males, 21 females; mean age 55.6 years [range 18–88 years]) with unilateral peripheral facial palsy (45 Bell's palsy, 12 Ramsay–Hunt syndrome) and 24 healthy volunteers (6 males, 18 females; mean age 40.0 years [range 21–76 years]). No patients had a history of facial palsy on the contralateral side and none of the healthy volunteers had episodes of facial palsy on either side. All of the patients were treated with intravenous prednisolone (starting at 80 or 120 mg) and oral intake of antiviral medicine within 5 days after the onset of palsy, and continued to undergo this treatment for 8 days (total prednisolone dose 400 or 480 mg; total valacyclovir dose 21,000 mg). The facial movement of patients was assessed using the House–Brackmann (H–B) facial nerve grading scale score [7]. ENoG is typically applied to patients with complete facial palsy for prognostic diagnosis; the prognosis of patients with incomplete palsy is good and ENoG is needless. However, the CMAPs in severe palsy patients are often small, undetectable, and immeasurable. To examine the change in CMAP latency corresponding to the degree of palsy, this study also enrolled patients with incomplete facial palsy who had detectable CMAPs. Approval for this study was obtained from the appropriate institutional ethical review board.

CMAP measurements

For patients with facial palsy, CMAPs were measured 10–14 days after the onset of facial palsy. For the recording electrode setting, we chose the midline method; the anode was fixed to the mental protuberance and the cathode was placed on the philtrum [5, 6]. This midline method records CMAPs of the orbicularis oris muscle innervated by bilateral facial nerves.

The recording electrodes (6 mm in diameter) were filled with electrode paste and taped firmly to the skin. Moist hook-and-loop tape with a ground electrode was wound around one wrist. Percutaneous stimulation was produced with bipolar metal electrodes that were enclosed in a plastic block. One electrode was placed in front of the tragus and the other was placed between the ascending ramus of the mandible and the mastoid process, as close as possible to the stylomastoid foramen, to stimulate the main trunk of the facial nerve [1, 3, 4]. Stimulation was produced with rectangular impulses at 1 Hz and 0.2 ms, and the current intensity was increased from zero to a level at which the amplitude of the summation potential observed on the screen did not increase any further. Then, the current intensity was increased by an additional 10% (supramaximal stimulation). Nerve stimulation and CMAP recordings were performed using the evoked EMG mode (four channels) on an MEB-9100 system (Nihon Kohden, Tokyo, Japan).

The greatest peak-to-peak amplitude was measured and expressed as the CMAP (mV). The negative peak latency (NPL) (the latency from stimulus pulse onset to the negative peak) and rise latency (RL; the latency from stimulation pulse onset to the rise time) of CMAPs were measured (Fig. 1) and compared between the healthy volunteers and the patients with facial palsy. The ENoG value was also calculated for each patient.

Statistical analyses

The amplitudes of CMAPs evoked on the paralysed and healthy sides in patients and healthy volunteers were compared using Wilcoxon's signed-rank test. The NPL and RL in these three groups were also compared using Wilcoxon's signed-rank test. In patients, the correlations of RT and NPL with ENoG values and the lowest H–B score were examined using Spearman's rank correlation coefficient. Statistical analyses were performed using JMP Pro software (ver. 13.2.1; SAS Institute, Cary, NC, USA). In all analyses, $p < 0.05$ was taken to indicate statistical significance.

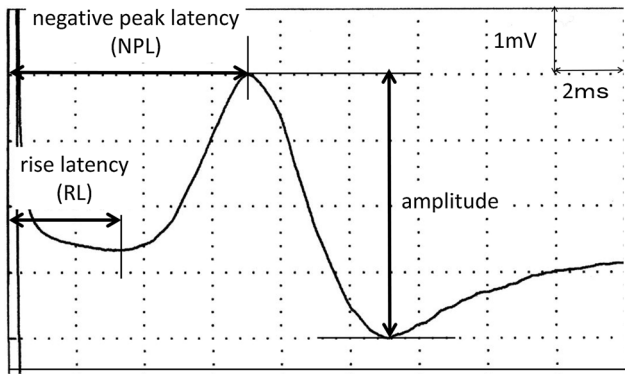

Fig. 1 Parameters of compound muscle action potential (CMAP) measurement

Results

Amplitude of CMAP and ENoG values

The CMAP amplitudes on the paralysed side of patients ranged from 0.07 to 4.74 mV (median 1.46 mV), while those on the healthy side ranged from 0.56 to 8.33 mV (median 4.26 mV). The mean ENoG value was 39.4% (1 SD = 23.7%). In 24 healthy controls, the CMAP amplitudes of 48 sides ranged from 1.53 to 7.02 mV (median 4.6 mV). There were significant differences in CMAPs between the paralysed and healthy sides in patients ($p < 0.01$), and between the paralysed side and equivalent side of healthy volunteers ($p < 0.01$). Conversely, there was no difference in CMAP amplitude between the healthy side of patients and the equivalent side of healthy volunteers ($p = 0.12$) (Fig. 2).

Negative peak latency of CMAPs

In the 57 patients, the NPL on the paralysed side ranged from 6.04 to 10.6 ms (median 7.68 ms), while that on the healthy side ranged from 5.72 to 9.94 ms (median 7.06 ms). Intrasubject differences in NPL (paralysed side–healthy side) ranged from − 0.06 to 2.18 ms (median 0.66 ms). Six patients had shorter NPL on the paralysed side than the healthy side, but all differences were within 0.06 ms. In healthy volunteers, NPL ranged from 6.02 to 8.94 ms (median 6.84 ms). There were significant differences in NPL between the paralysed side and healthy side in patients ($p < 0.01$), and between the paralysed side and equivalent side of healthy volunteers ($p < 0.01$). In contrast, there was no difference between the healthy side of patients and the equivalent side of healthy volunteers ($p = 0.35$) (Fig. 3).

Rise latency of CMAPs

In the 57 patients, the RL on the paralysed side ranged from 2.96 to 6.44 ms (median 4.02 ms, while that on the healthy side ranged from 2.44 to 4.82 ms (median 3.56 ms). Intrasubject differences in RL (paralysed side–healthy side) ranged from − 0.06 to 2.78 ms (median 0.52 ms). Two patients had shorter RL on the paralysed side than the healthy side, but all differences were within 0.06 ms. In healthy volunteers, RL ranged from 2.14 to 4.84 ms (median 3.49 ms). There were significant differences in RL between the paralysed side and healthy side in patients ($p < 0.01$), and between the paralysed side and equivalent side of healthy volunteers ($p < 0.01$). There was no difference between the healthy side of patients and the equivalent side of healthy volunteers ($p = 0.62$) (Fig. 4).

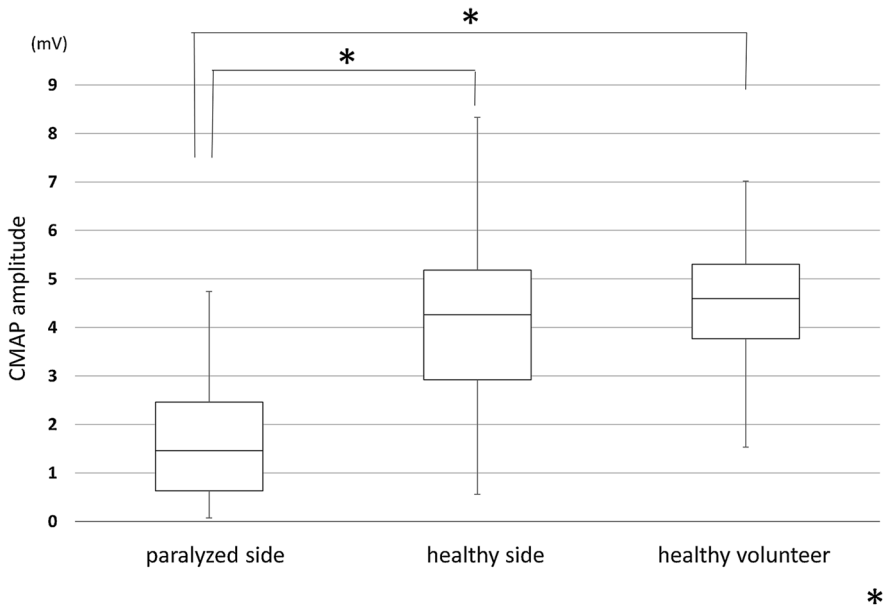

Fig. 2 Box plots of CMAP amplitude, on the paralysed and healthy sides, of patients with facial palsy and healthy volunteers. Significant differences are indicated with asterisks

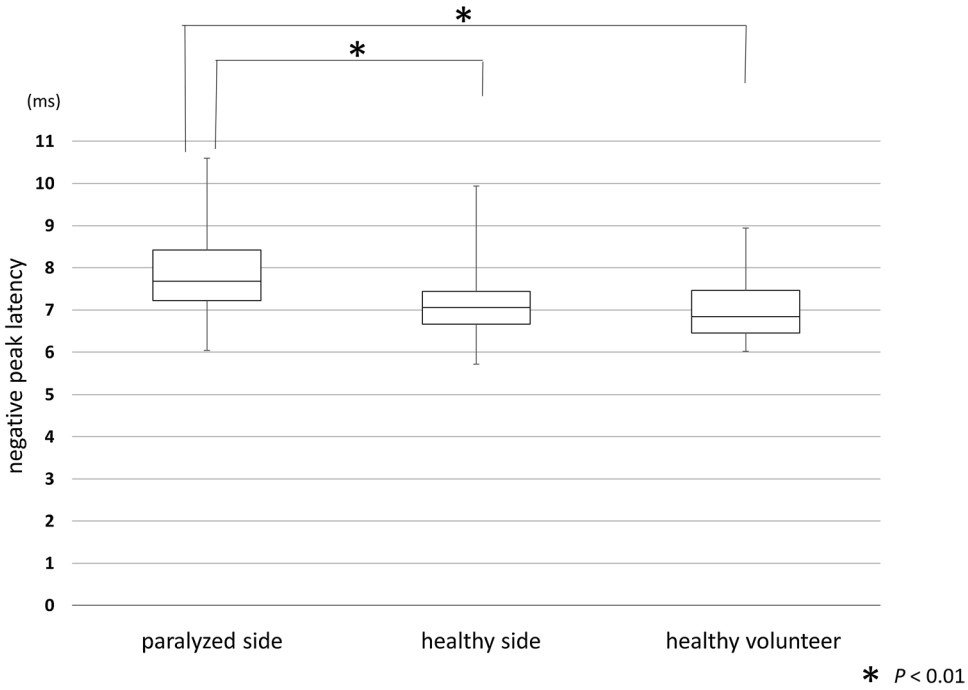

Fig. 3 Box plots of negative peak latency (NPL) of CMAP, on the paralysed and healthy sides, of patients with facial palsy and healthy volunteers. Significant differences are indicated with asterisks

Relationships of NPL and RL with ENoG value

The ENoG value in patients ranged from 2.9 to 94.2% (mean 39.3 ± 23.7%). There was no significant relationship between NPL and the ENoG value (rs = 0.07, $p = 0.59$) or between RL and the ENoG value (rs = − 0.25, $p = 0.06$). The patients were divided into two groups according to ENoG value (ENoG < 40%, $n = 29$ patients; ENoG ≥ 40%, $n = 28$ patients). There was no difference in NPL between the ENoG < 40% group (median 7.61 ms) and ENoG ≥ 40% group (median 7.84 ms) ($p = 0.86$). Conversely, there was a significant difference in RL between the ENoG < 40% group (median 4.16 ms) and ENoG ≥ 40% group (median 3.87 ms) ($p = 0.03$).

Relationships of NPL and RL with lowest H–B score

The lowest H–B scores were as follows: Grade II, $n = 2$; Grade IV, $n = 17$; Grade V, $n = 23$; and Grade VI, $n = 15$. Statistical analysis indicated no relationships of NPL and RL with lowest H–B score ($p = 0.83$ and $p = 0.66$, respectively).

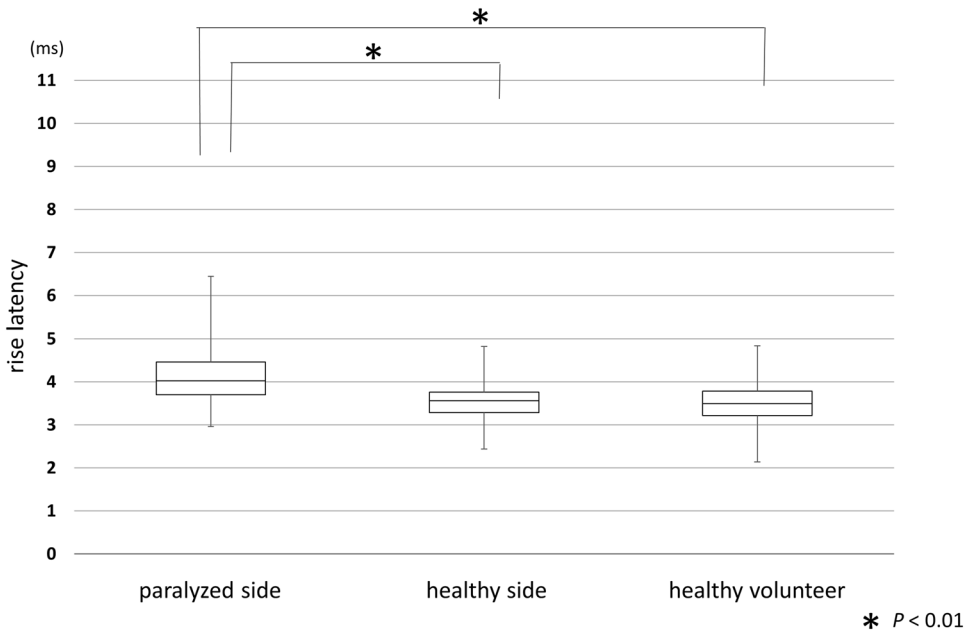

Fig. 4 Box plots of rise latency (RL) of CMAP, on the paralysed and healthy sides, of patients with facial palsy and healthy volunteers. Significant differences are indicated by asterisks

Discussion

In 1943, Seddon classified peripheral nerve injury into three categories according to severity, i.e., neuropraxia, axonotmesis, and neurotmesis [8]. The low ENoG value indicates facial nerve axonotomesis and/or neurotomesis on the paralysed side. Recovery from facial palsy requires at least 4 months; in the worst cases, recovery may be incomplete if the midline ENoG value is < 20% [6]. Moreover, facial palsy patients with ENoG values of approximately < 40% develop synkinesis [9, 10]. Therefore, ENoG is useful for evaluating facial palsy prognosis. However, it is sometimes difficult to detect both negative and positive CMAP peaks, because patients with severe facial palsy exhibit both low-amplitude CMAPs and artefacts from other muscles on strong electrical stimulation. In addition, the action potentials of non-facial muscles, such as masseter muscle, can contaminate the waveform under strong electrical stimulation, thus leading to errors. A new index is required for error-free measurement of CMAPs.

In the present study, we noticed CMAP latencies (NPL and RL) and found that, on the paralysed side, these were equivalent to or prolonged compared to the healthy side; in addition, CMAP amplitude was smaller on the paralysed side than the healthy side. We presume that these results may be common between midline and standard methods. Oedema and ischemia of the facial nerve associated with inflammation increase pressure in the facial canal, resulting in nerve "self-strangulation" and thus leading to facial nerve paralysis in patients with Bell's palsy and Ramsay–Hunt syndrome. Large-diameter nerve fibres with high conduction velocity are more susceptible to compression than thin nerve fibres in the early phase of nerve self-strangulation [11, 12]. As a result, the apparent conduction velocity of the entire facial nerve is reduced, and the CMAP latency thus increased, to a degree corresponding to the severity of nerve damage. If facial palsy patients have equivalent NPL and/or RL of CMAPs on the paralysed side, compared to the healthy side, neuropraxia (mild nerve injury and partial damage to the myelin sheath without Wallerian degeneration) may occur, and nerve conduction velocity is likely to be normal.

The present study confirmed that the relationship between CMAP latency on the paralysed and healthy sides is important when detecting CMAPs during ENoG. Figure 5 shows an example of the CMAPs of a complete palsy patient; if we select the obvious biphasic wave encircled by the dotted line on the paralysed side, the ENoG value is calculated as 22%, indicating good prognosis i.e., recovery from palsy within 4 months [6]. However, NPL and RL of this wave were shorter than those on the healthy side, suggesting that the wave did not originate from the orbicularis oris belonging to the facial muscles and probably reflected contamination by

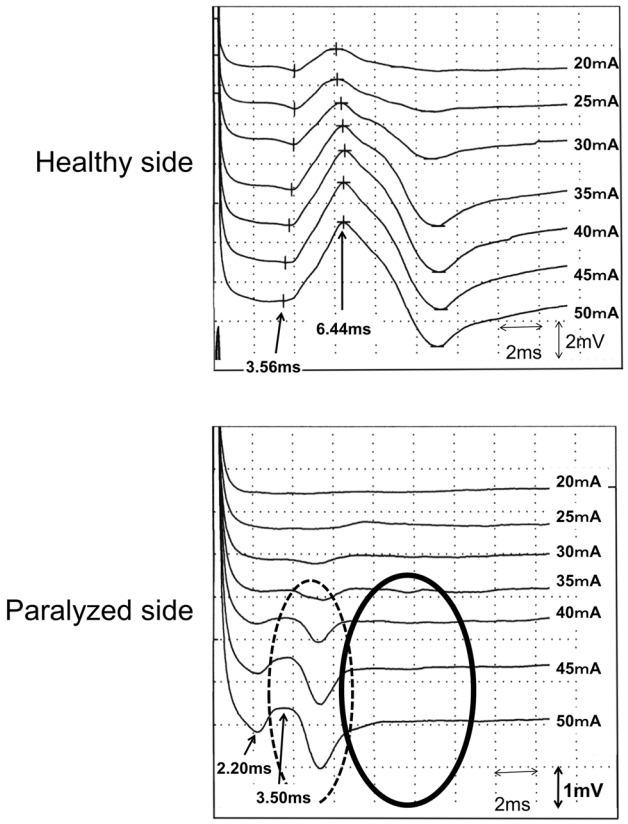

Fig. 5 CMAPs in a patient with severe facial palsy. On the paralysed side, a short-latency biphasic wave appeared with electrical stimulation of ≥ 35 mA (dotted-line circle). If we adopt this wave as a CMAP from the orbicularis oris muscle, the calculated electroneurography (ENoG) value (22%) indicated a good prognosis. However, the NPL and RL of this wave (3.50 ms and 2.20 ms, respectively) with stimulation at 50 mA were shorter than those on the healthy side (6.44 ms and 3.56 ms, respectively). It is necessary for the examiner to detect the CMAP of the orbicularis oris muscle shown in the solid-line circle from the viewpoint of CMAP latency (the true ENoG value was 0%)

artefacts originating from other muscles, such as the masseter muscle, the evoked EMG latency of which during facial nerve stimulation is shorter than those of facial CMAPs [13]. Such a shortened biphasic wave is frequently observed during ENoG in patients with severe palsy under supramaximal stimulation of the facial nerve. The true CMAP of the orbicularis oris muscle is that encircled by the solid line, which shows prolonged latency, no biphasic wave, and an ENoG value of 0%, indicating poor prognosis. In fact, the patient whose CMAPs are shown in Fig. 5 did not achieve complete recovery by 1 year after the onset of facial palsy. Thus, waves on the paralysed side that exhibit shorter latencies than those of CMAPs on the healthy side should not be regarded as facial CMAPs when calculating ENoG values.

In this study, in terms of intrasubject differences, NPL (paralysed side–healthy side) and RL (paralysed side−healthy side) ranged from − 0.06 to 2.18 ms and − 0.06 to 2.78 ms, respectively; no patients showed NPL or RL on the paralysed side that were markedly shorter (> 0.1 ms) than those on the healthy side. As shown in Figs. 3 and 4, it is necessary to determine whether NPL and RL on the paralysed side are equivalent to or longer than those on the healthy side in individuals when we detect CMAPs.

There was no significant relationship between NPL and the ENoG value in this study. In cases with a low amplitude of CMAP, it is not easy to detect the rise time and peaks of the CMAP visually because of the faint biphasic wave of CMAP. This may be one reason why we could not find a correlation between NPL and ENoG value. In addition, no relationship was observed between RL and the ENoG value. However, RL in the group with ENoG value < 40% (median 4.16 ms) was delayed compared to the other group with ENoG value ≥ 40% (median 3.87 ms). Tojima reported that the MCV was still normal when the ENoG value was ≥ 40% [11]. In patients with facial palsy, an ENoG value ≥ 40% suggests that Wallerian degeneration has not occurred in the facial nerve [11] and RL should not be markedly delayed compared to the healthy side, or to healthy controls (3.56 and 3.49 ms, respectively, in this study).

There was no significant relationship between NPL or RL and the lowest H–B score in this study. The H–B grading system is used worldwide and is useful to estimate the degree of facial palsy without any requirement for expensive apparatus. However, it is a subjective evaluation and is subject to unavoidable interindividual variation. This may be one reason why no correlations were observed between the CMAP latency and H–B score in this study.

In conclusion, the present study confirmed that NPL and RL of CMAP on the paralysed side were equivalent to or longer than those on the healthy side in patients with facial palsy. Accordingly, it is necessary to measure CMAPs on the healthy side first, and then detect negative and positive peaks in CMAPs and measure their amplitudes on the paralysed side (with reference to the CMAP latencies in the healthy side) for precise prediction of prognosis according to ENoG; waves on the paralysed side exhibiting shorter latencies than those of CMAPs on the healthy side should not be regarded as facial CMAPs when calculating ENoG values.

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Compliance with ethical standards

Conflict of interest The present authors have no financial relationship to disclose.

Ethical approval Approval for this study was obtained from the Institutional Ethical Review Board of Osaka Medical College (Approval #0484 and RIN375).

Informed consent Informed consent was obtained from all individual participants (patients and volunteers) included in the study.

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