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HEAD AND NECK

Long-term electrophysiological assessment after hypoglossal-facial anastomosis

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Abstract

Purpose To investigate and provide objective documentation of the possible differences in the axonal reinnervation process of facial muscles after hypoglossal-facial nerve anastomosis. Then, to search for the presence of the trigemino-hypoglossal reflex and determine whether it indicates better peripheral recovery.

Methods Electrophysiological examination performed on 20 patients who had undergone VII–XII anastomosis, with follow-up periods of more than 2 years.

Results The mean follow-up time after surgery was 4.1 ± 1.3 years (range 2–8 years). The degrees of axonal reinnervation for the orbicularis oculi (OOc) and orbicularis oris (OOr) were 46.91 ± 19.77 and 32.65 ± 14.85, respectively. And the difference between these muscles was statistically significant ($p = 0.018$) in favor of the OOc. In addition, R1 blink reflexes that were not followed by R2 components were observed in 30% of the patients. However, these 6 patients with short-latency potential did not differ from the others in terms of latency, the amplitude of compound muscle action potential (CMAP), and degree of axonal reinnervation ($p > 0.05$) at both muscles (OOc and OOr).

Conclusion The recoveries of the lower face and upper face are different after VII–XII anastomosis, and in our patients the OOc healed better. In addition, R1 blink reflexes that were not followed by R2 components were observed in 30% of the patients. However, the patients with these blink reflexes did not have better peripheral healing in their neuromuscular units, which suggests that the blink reflex is not an indicator for peripheral recovery.

Keywords Facial paralysis · Facial reanimation · Hypoglossal nerve · Surgical anastomosis · Nerve repair · Muscle reinnervation · Electroneurography

Introduction

Among the surgical options for facial reanimation, hypoglossal-facial (VII–XII) anastomosis is the most commonly used and well-established nerve transfer technique [1]. Classical end-to-end anastomosis involves reconstructing the continuity of the facial nerve using the hypoglossal nerve, to stimulate the movements of the paretic facial muscles via newly formed motor units. This treatment is reported in the surgery literature to be quite effective. The clinical procedure used to evaluate the results of hypoglossal-facial nerve anastomosis often includes grading systems based on scoring by either the clinicians or the patients [2, 3]. These modalities provide a rough overview of the nerve healing process and clinical recovery. However, there may be incompatibilities in terms of clinical recovery between the physician's assessment and

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the patients' self-evaluation. In such situations, electrophysiological studies supply objective findings.

Electroneurography (ENoG) is used routinely as an objective method of evaluation at all stages of the healing process in patients with facial palsy. Assessment of compound muscle action potential (CMAP) yields information on both the degree of axonal loss and the reinnervation of the mimic muscles [4, 5]. Using side-to-side CMAP comparison is helpful for prognostic prediction in the early phase of nerve damage. Also, it shows the success of axonal sprouting after surgical repair. These electrophysiological findings can, at the same time, be supported by needle electromyography and blink reflex studies. However, there are few electrophysiological studies of patients with VII–XII anastomosis, and more than 10 years have passed since some of these studies [6–9].

In our study, we first aimed to identify possible differences and provide objective documentation of the axonal reinnervation process of facial muscles after hypoglossal-facial nerve anastomosis. We then looked for the presence of the trigemino-hypoglossal reflex, which may arise due to possible plastic changes in the brainstem.

Material and methods

The study was conducted in the Department of Otolaryngology and Neurology, at Gazi University, in Ankara, Turkey, and was approved by the local ethics committee. Patients who had complete facial paralysis after a retrosigmoid vestibular schwannoma removal and subsequently undergone VII–XII end-to-end anastomosis before 2013 in the Department of Otorhinolaryngology were included in the study. Patients who had follow-up periods of less than 2 years or had not agreed to electrophysiological examination were excluded. The restorative VII–XII anastomosis surgery was performed in a classic manner where the most distal hypoglossal nerve was cut and sutured end-to-end to the facial stump at the level of the stylomastoid foramen. Every participant signed an informed consent form. The electrophysiological examinations were carried out by an experienced neurology specialist.

Electrophysiological methods

The electrophysiological examinations were performed using the Nihon Kohden EMG instrument (Nihon-Kohden Neuropack MEB-5504 system, Tokyo, Japan). The bandpass frequency filter was set at 20–10.000 Hz. Surface recordings were made using standard silver/silver chloride (Ag–AgCl) surface electrodes and analyzed with a 5–10 ms/div sweep speed and 200–500 UV sensitivity. The onset latency and peak-peak amplitudes of the CMAP and blink reflex responses (R1 and R2) were determined through manual cursor marking of the beginnings and peaks of the potentials.

Nerve conduction study

The facial nerve was stimulated supramaximally at the anterior tragus directly in front of the lower ear on both sides; CMAPs were obtained simultaneously from the OOc and OOr muscles. The stimulus duration was 0.1 ms. The active electrode was placed over the middle part of the lower eyelid for the OOc muscle, and the reference electrode was taped onto the bridge of the nose. For the OOr muscle, the active electrode was placed 2 mm above the lip and midway between the midline and the corner of the mouth. The reference electrode was taped over the OOc muscle of the opposite side. The distal motor latency (DML) was measured from the initial negative deflection. The degree of axonal reinnervation was calculated from both the affected and unaffected muscles in this manner: the peak-peak CMAP amplitude of the affected side/the peak-peak CMAP amplitude of the unaffected side $\times$ 100. A degree of axonal reinnervation of over 30% was defined as the electrophysiological finding of effective reinnervation. This value is defined in the literature as being an indicator of a good prognosis for cases of facial paralysis.

Blink reflex

Electrical stimulation was applied to the supraorbital nerve in the supraorbital notch with a bipolar stimulating electrode, usually about 3 times the intensity of the R2 threshold. The stimulus duration was 0.2 ms. The active electrodes were placed on the midpoints of both inferior OOc muscles, and the references were taped laterally to the lateral canthus of the eyes. Five stimuli were randomly applied to each side at a minimum of 10–15 s intervals and the onset latency of the response of both sides (ipsilateral R1 and R2 and contralateral R2) was measured from the stimulus onset to the initial deflection of the potentials.

Statistical analysis

Statistical analysis was performed using SPSS software (SPSS version 22, Chicago, IL, US). The conformity of the data to normal distribution was assessed using the Kolmogorov–Smirnov test. Continuous variables were analyzed as mean $\pm$ standard deviation values and discrete variables as frequencies and percentages. The CMAP and blink reflex parameters were compared using a Student's two-tailed *t* test. A *p* value of 0.05 was considered statistically significant.

Results

A total of 20 patients with a mean age of 43.4 ± 12.8 years (range 24–67 years) participated in the study. All were patients who had complete facial paralysis after a retrosigmoid vestibular schwannoma removal and who had undergone VII–XII end-to-end anastomosis. The mean interval between the first operation and anastomoisis was 3.2 ± 2.1 months (range 1–8 months). The mean follow-up time after anastomosis surgery was 4.1 ± 1.3 years (range 2–8 years). Healing in fifteen patients (75%) was at HB Grade 3, and five patients (25%) healed with HB Grade 4. These demographic results are summarized in Table 1.

The electrophysiological evaluation results of the CMAPs for both sides (affected and unaffected) and both muscles (OOc and OOr) have been tabulated and are shown in Table 2. The statistical analyses of the affected and unaffected sides include a comparison of all parameters (latency and amplitude of the CMAPs for both the OOc and OOr muscles) and, as expected, showed statistical significance ($p < 0.05$). In addition, when the statistical analyses that were put forward of comparisons between OOc and OOr muscles at the affected sides, the degree of axonal reinnervation showed a statistical significance ($p = 0.018$) in favor of the OOc, and the effective reinnervation percentage was also higher for the OOc (45% for OOc; 30% for OOr). Despite the statistical significance in favor of OOc, four patient (20%) have shown the opposite where OOr axonal reinervation was better.

As had been expected, the electrical stimulation of the supraorbital nerve in the unaffected sides revealed ipsilateral R1 and R2 responses of the blink reflexes but the absence of contralateral R2 responses. In 6 of the 20 patients, the ipsilateral short-latency potential resembling the R1 reflexes through the stimulation of the affected side was observed but was not followed by the R2 components. The mean latency of the short-latency potential was prolonged in comparison to the R1 responses of the unaffected sides. Figure 1 provides an example of the blink reflex study of one patient. However, the 6 patients with short-latency potential did not differ from the others in terms of the latency, the amplitudes of the CMAPs at both muscles (OOc and OOr), and the degrees of axonal reinnervation ($p > 0.05$). The mean affected side R1-like latencies in these 6 patients were prolonged in comparison to the R1 latencies in the unaffected sides (11.56 ± 1 and 79; 9.18 ± 0.88, respectively; $p = 0.024$).

Table 1 Demographic data of the study population

Group size	20
Gender	
Male	13
Female	7
Mean age (year)	43.4 ± 12.8
Mean follow up time (year)	4.1 ± 1.3

Discussion

The present study, conducted with a large series and long follow-up times in patients who had undergone VII–XII anastomosis, revealed that the healing process differs between the OOc and OOr. The results indicate that in general the OOc has a better recovery after VII–XII anastomosis, but in some patients OOr may recover better. In addition, ipsilateral R1-like responses that were not followed by R2 components were seen in 30% of the patients, although this is possibly related more to the central neuronal reorganization or axon reflexes and ephapses rather than reflecting better peripheral healing in the neuromuscular units.

There are different grading systems for clinical examination and patient-based life quality questionnaires that detect the severity of facial palsy levels [2, 3]. These methods are widely used because they are available, easy to use, and

Table 2 Electrophysiological assessment results of compound muscle action potentials

	(*n*)	Orbicularis Oculi	(*n*)	Orbicularis oris	*p* values
Affected side					
Latency (msn)	(20)	3.77 ± 0.91	(20)	3.93 ± 95	0.220
Amplitude (mV)	(20)	1251.57 ± 463.46	(20)	1186.66 ± 727.80	0.176
Un-affected side					
Latency (msn)	(19)	2.46 ± 0.48	(18)	2.68 ± 0.62	0.609
Amplitude (mV)	(19)	2953.00 ± 1194.19	(18)	3545.00 ± 1502.22	0.750
Degree of axonal reinnervation (%)	(19)	46.91 ± 19.77	(18)	32.65 ± 14.85	**0.018**

(Degree of axonal reinnervation: CMAP amplitude of affected side/CMAP amplitude of unaffected side × 100)

The *p* value that was statistically significant was in bold

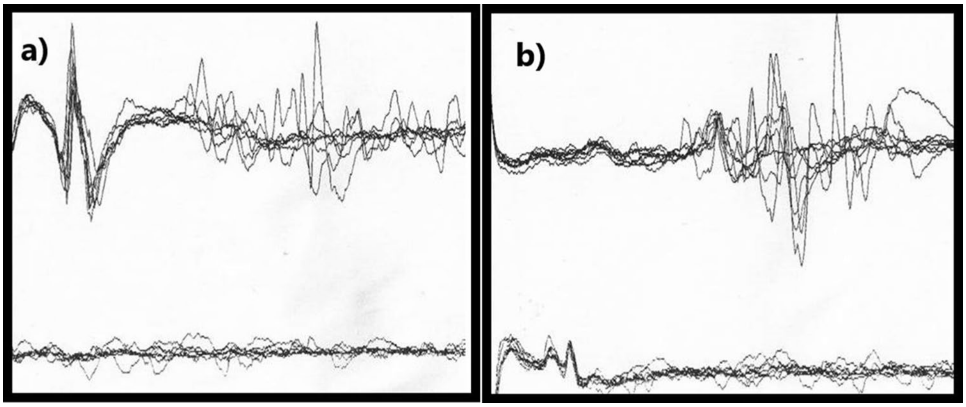

Fig. 1 An example of blink reflex responses after stimulation of supraorbital nerve at the affected side (lower traces) and un-affected side (upper traces), demonstrating the short-latency R1-like potential (V–XII), similar to the R1 response but not followed by the R2 component. **a** While ipsilateral R1 (IR1), R2 (IR2) response was obtained by supraorbital nerve stimulation of unaffected side, contralateral R2 (CR2) response was absent. **b** IR1 response and CR2 response were obtained by supraorbital nerve stimulation of the affected side, but no significant IR2 response was obtained

not time-consuming, and there is no need for any tools and devices. However, these methods give subjective results and do not offer predictions or more detailed information. Along with these subjective methods, we have used ENoG, which shows us the newly established neuromuscular units objectively and gives more detailed information. ENoG is also more sensitive than the clinical grading systems, it detects the recovery earlier, and it offers a chance to predict the surgical results [10]. In our study, we have recorded CMAPs from previous studies to give more detailed information about comparisons between the remodeled motor units after nerve reinnervation and the motor unit potentials (MUPs) [11, 12].

The use of ENoG in facial palsy for monitoring and predicting recovery is a more established tool [13]. However, the electrophysiological data are limited because of the lack of electrophysiological studies and the small number of centers that perform these facial reanimation operations [4, 5, 10]. The electrophysiological studies of follow-ups after VII–XII anastomosis have shown that the reinnervations started about 4 months after surgery, reached their maximum improvements at the 18-month postoperative period, and then remained stable [14, 15]. In the ENoG results, higher CMAP amplitudes indicate better motor recovery, and one previous study revealed that after VII–XII anastomosis the axonal regeneration and muscular reinnervation proceeded better in the lower facial area than in the upper facial area [8]. However, this study has some limitations since the results have not undergone a statistical analysis and the CMAP amplitude of the normal side has not been taken into consideration; the CMAP amplitude for each muscle of the operated side was not proportioned to that of the normal side. In contrast, our results have shown that the OOc was healing better than the OOr. This supports the subjective results of our previous study, where we showed that the lacrimal control scores were higher than the oral function scores according to the Facial Clinimetric Evaluation scale for the patients who had undergone the VII–XII anastomosis [16]. This may, then, have decreased the ocular dryness and related complications in such patients. Nevertheless, in some of our patient healing process went different (in four of our study patient) and OOr recovered better. The differences in the reinnervations between issues regarding the lower face and upper face are controversial and require more studies with larger patient numbers in detailed assessments.

In facial reanimation, many factors can affect the outcomes, such as the surgical methods that are used, the repair times following injury, age, and other comorbidities. Since the surgical technique, age, other comorbidities and repair times following injury do not differ for lower and upper faces in the patients of present study, the probable differences between branches of facial nerve become the main issue and the differences in the reinnervations. As stated in previous studies, both the axonal counts and the diameters of the nerves affect the final success at nerve anastomosis [17, 18]. Therefore the most reasonable explanation for the different healing levels might be derived from the axonal difference in the branches, and this may vary between patients because the anatomy of the facial nerves and their branches have many variations [19].

In addition, with respect to the reinnervation of the facial nerves with the hypoglossal nerves, there is another interesting issue regarding the V–XII cranial nerves after anastomosis. Willer et al. [6] showed for the first time that some patients had R1 component blink reflexes that were not followed by R2 components at the OOc muscle on the operated side after anastomosis. These are referred to as trigemino-hypoglossal reflexes by many authors and have been attributed to the central neural plasticity and heterotopic sprouting of trigeminal afferents toward the hypoglossal motor neurons. Another study showed the same R1 responses after a peripheral spinal accessory nerve-facial anastomosis in one patient [9]. These results indicated that peripheral change has a remodeling effect on the central nervous system. Although Willer et al., noted the reflex in all patients who had recovered after VII–XII anastomosis (6 patients out of 8 patients; the other 2 did not show any clinical and electrophysiological recovery), we observed this in 6 of the 20 patients in our study. A subsequent study by the same author found that the stimulation of the ipsilateral operated side suggests both the R1-like and R2-like responses in some patients with good reinnervation in their OOc muscles [7]. We observed only an R1-like response, and the operated side supraorbital stimulation did not reveal any ipsilateral R2 component. We looked at whether the R1-like response can be an indicator of good recovery and compared the 6 patients who had R1 blink reflexes that were not followed by R2 components with the remaining 14 patients, in terms of the degrees of axonal reinnervation. We did not find any differences between these groups, which suggests that the R1-like response is only a central remodeling process rather than an indicator of the peripheral recovery level. Montero et al. suggest that these responses were due to re-excitation at a branching point of a regenerated motor axon or ephaptic transmission between two motor axons [20]. In our opinion, it may not be sufficient to explain the formation of these potentials by a trigeminal hypoglossal reflex that arises through the reorganization of neuronal connections, when taking into consideration the slower conduction velocity of the regenerated axon, even though the R1-like responses occurred later than the R1 responses.

The studies and information about this topic are scarce because there are few studies, and these have mainly been conducted and produced at one center [6–9, 14, 15, 21]. Therefore, our findings contribute to the topic by providing the largest series of VII–XII anastomosis to evaluate the electroneurography results and the R1 blink reflexes. In spite of these strong points, our present study has several limitations. We did not evaluate additional facial muscles (such as the mentalis, corrugator superficial muscles) and did not determine the thresholds.

Conclusion

In conclusion, the results of our study showed that lower face and upper face recovery are different after VII–XII anastomosis, and in our patients the OOc healed better. In addition, R1 blink reflexes that were not followed by the R2 components were observed in 30% of the patients. However, the patients with these blink reflexes did not have better peripheral healing in their neuromuscular units, which suggests that the blink reflex is not an indicator of peripheral recovery.

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Compliance with ethical standards

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