Direct Tongue Neurotization: The Effect on Speech Intelligibility in Patients with Möbius Syndrome

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Background: Möbius syndrome is a disorder characterized by developmental impairment of cranial nerve VII, VI, often XII, and other cranial nerves. Facial reanimation in such patients restores the ability of some motion and of limited emotional expression. In one-fourth of these patients, hypoglossal involvement results in severe speech impairment due to tongue atrophy and lack of voluntary mobility. Bilabial incompetence due to facial paralysis further deteriorates speech capability. Direct tongue neurotization has been used by the senior author (J.K.T) to improve tongue function and speech intelligibility in patients with Möbius syndrome. This study presents the senior author's experience with the technique as a component of multistage facial reanimation procedures.

Methods: Data collection was performed by retrospective review on six patients with Möbius syndrome who underwent direct tongue neurotization. In addition, each patient was videotaped for 30 minutes preoperatively and postoperatively according to a standardized protocol.

Results: Four independent investigators scored speech intelligibility in each patient using a standardized grading system. The results showed considerable improvement in speech intelligibility and articulation. Higher improvement was noted in patients with partial bilateral hypoglossal involvement than in patients with complete unilateral involvement of the hypoglossal nerve, as well as in younger ages. No difference was noted between sexes.

Conclusions: To the authors' knowledge, this is the first study presenting the effect of direct tongue neurotization on speech intelligibility in patients with Möbius syndrome. Tongue neurotization has therefore an important role in restoring the ability of these patients to communicate and obtain the potential to develop normal social skills. (*Plast. Reconstr. Surg.* 125: 150, 2010.)

Möbius syndrome is a rare disorder,[1–4] first described by van Graefe and Saemisch[5] in 1880. It was named, however, after the neurologist Paul Julius Möbius,[6] who defined its clinical characteristics in 1888. It is typically characterized by the abnormal development of VII and VI cranial nerves and consequently, unilateral[6] or bilateral[7] paralysis of these nerves. Other cranial nerves are also involved, with the hypoglossal (XII) being the third most frequently involved, the trigeminal (V), the glossopharyngeal (IX), and less frequently oculomotor (III), trochlear (IV), and cochlear (VIII). The number of reported cases in the literature does not exceed 300.[8] Most reports converge on an approximate prevalence of 0.002 percent of births.[9] Möbius syndrome appears to affect both genders equally.

Initial symptoms of patients with Möbius syndrome are problems with breast or bottle feeding, impaired swallowing, drooling, and diminished or absent facial expression when crying. Facial paralysis may be incomplete or asymmetric, but it is usually bilateral. When paralysis is complete, the

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Received for publication January 8, 2009; accepted June 23, 2009.

DOI: 10.1097/PRS.0b013e3181c59d60

Disclosures: *Neither of the authors has a financial interest or any commercial association related to the information presented in this article. There are no conflicts of interest or any funding sources that require disclosure.*

lower face is frequently spared. Anomalies of the lower extremities or other cranial nerves may be variably expressed.[10–14] Facial paralysis is often combined with the involvement of other cranial nerves. The abducens (cranial nerve VI) is frequently involved, while cranial nerves III and IV are less frequently involved,[15] resulting in the inability to perform and coordinate eye movement, severe strabismus, and amblyopia. Epicanthic folds, ocular hypertelorism, microstomia, external ear deformity with occasional hearing loss, and airway problems with aspiration may also be observed.[16–18] Cardiovascular anomalies are not commonly observed in Möbius syndrome patients.[19]

Musculoskeletal malformations, such as the absence of the sternal head of the pectoralis major muscle, rib defects, arthrogryposis, polydactyly, syndactyly, brachydactyly, aphalangia, and talipes equinovarus have also been reported. Möbius syndrome may also be associated with Klippel Feil anomaly, and Kallmann Poland and Hanhart syndromes.[17,20,21]

ETIOLOGY

The etiology of Möbius syndrome has not yet been clearly determined. It is often characterized as a congenital neurologic disorder, but no pathognomonic congenital factors have been identified. The multifactorial pathogenesis includes genetic, vascular, and toxic factors.

In studies of the karyotype of Möbius syndrome patients, it has been claimed that chromosomal translocation between chromosomes 1 and 13[22] or that segmental deletion of chromosome 13[23] takes place. Another study presented a family of Möbius syndrome patients with a localized gene in chromosome 3, supporting the idea of potential genetic heterogeneity of the syndrome.[24] The aforementioned anomalies indicate the existence of a genetic location responsible for Möbius syndrome, but further studies on genetic mapping are needed. In addition, patient families' studies have shown inconsistent inheritance patterns; thus, the role of genetic predisposition is yet controversial.[15,25]

Ischemia of the developing fetus due to vascular interruption has also been hypothesized. Intrauterine vascular injury following maternal trauma has been reported to be responsible for infarction of brainstem nuclei and chronic hypoxia, which leads to the clinical presentation of the syndrome.[26]

Toxic effect of certain pharmaceutical agents has also been suggested as a possible cause of the syndrome in several cases. Such agents and medications include the prenatal use of misoprostol for ulcer prevention, ergotamine for migraine treatment, and cocaine.[27–30]

AIMS

Restoration of tongue function in Möbius syndrome patients significantly improves communication ability and expression, which are prerequisites for harmonious mental development. This study evaluates the effect of direct tongue neurotization, a novel procedure, and its role in the reconstructive strategy toward improving speech ability and communication potential.

SURGICAL ANATOMY

The tongue is composed of muscle tissue covered by oral mucosa that contains sensors for taste, heat, pain, and tactile information on its dorsal surface. The intrinsic muscles that constitute most of the mass and are responsible for the shape and movement of the tongue are the inferior, superior, transverse, and vertical lingualis.[31] Extrinsic muscles of the tongue have an external origin, while their terminal fibers are contained within the tongue. Styloglossus, hyoglossus, palatoglossus, geniohyoglossus, and pharyngoglossus are the extrinsic muscles.[31,32]

The tongue consists of symmetrical halves separated in the midline by a fibrous septum. Muscle fibers arranged in various directions, fat, and connective tissue compose the substance of each half. The terminating branches of the extrinsic muscles are inserted in the submucosal membranous layer, immediately under the mucosal surface. The orientation and the blending of the muscular fibers from both intrinsic and extrinsic muscles offer the unique ability of movement toward all directions. Furthermore, they control and modify the shape of the tongue, which is critical for the production of phonemes and speech. Data obtained by electropalatography, diagnostic cineradiography, magnetic resonance imaging, and digital morphometry have greatly contributed to the investigation of tongue

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kinesiology during speech and aided the approach of restoring effective tongue motion.[33]

Tongue atrophy is observed in cases with cranial nerve XII involvement. The extent of the atrophy and the resulting asymmetry of the tongue depend on which side is affected and whether cranial nerve XII involvement is partial or complete. Hemi-glossal atrophy, fatty replacement, and asymmetry are noted in cases of unilateral involvement.[34] Pronounced atrophy is observed in bilateral cranial nerve XII involvement.[35–37]

SURGICAL TECHNIQUE

Restoration of tongue movement, bulk, and shape has been achieved in our center with the use of a direct tongue neurotization procedure. The surgical technique involves identification of the motor donor first.[37] Cranial nerve XI or the cervical plexus motor donors or the ipsilateral C7 root is identified by an incision along the posterior border of the sternocleidomastoid (Figs. 1 and 2). Intraoperative microstimulation and inspection of resulting contractions confirms the identity of the nerve. The sural nerve graft, which was previously harvested, is brought in the operating field. The proximal part of the nerve graft is brought in opposition to the respective donor. The distance from the coaptation to the tip of the ipsilateral side of the tongue is measured, and about 3 to 4 cm of extra graft length is allowed to take care of the movements of the neck. By using a malleable metal tunneler placed from the neck incision and progressing to the base of the tongue intraorally, a subcutaneous tunnel is created. At the posterior and inferior part of the tongue, the tunnel assumes a submucosal plane posteriorly proceeding between hyoglossus and the genioglossus anteriorly. The roof of the tunnel consists of the fibers of the inferior lingualis. The tunnel follows the normal path of the hypoglossal nerve along the nerve ending at its tip. Through a stab incision, the metal tunneler is expressed at the tip of the ipsilateral tongue. The distal end of the sural nerve is sutured to the hole at the end of the tunneler at the neck incision (Fig. 3). While using saline irrigation, the nerve graft is tunneled from the neck incision to the tip of the tongue. Its distal end is divided in two to three fascicles, which are then implanted to the tip of the tongue and allowed to ramify. The stab incision is closed with 7-0 polydioxanone suture. The operating microscope is then brought over the neck incision. An end-to-side coaptation through a perineurial window and partial neurectomy are performed with the accessory nerve or the C7 root (Fig. 4). An end-to-end coaptation is carried out with the cervical motor donors. At the completion of the neurorrhaphy, the neck incision is closed in two layers.

Fig. 1. Intraoperative view of a child with Möbius syndrome undergoing the direct tongue neurotization procedure. Note the incision along the posterior border of the sternocleidomastoid (*arrow*) that was used to identify ipsilateral motor donors.

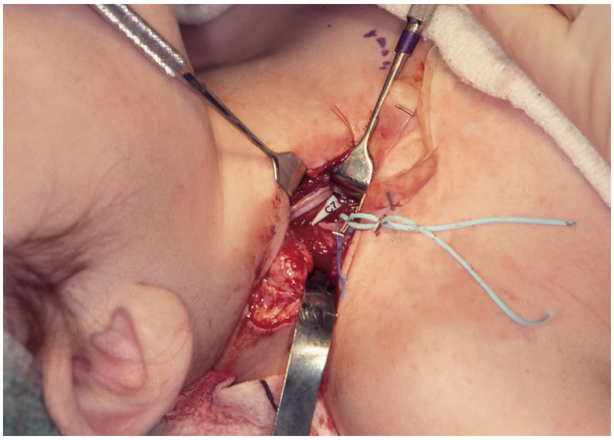


Fig. 2. Intraoperative view of the child in Figure 1 depicting the exploration of the right C7 root, which is going to be used as the motor donor for the direct tongue neurotization procedure.

PATIENTS AND METHODS

Data collection was performed by retrospective analysis of the charts of six patients with Möbius syndrome who underwent direct tongue neurotization at some point of their multi-staged facial reanimation procedures between January of 1981 and January of 2007. In this study, only patients with complete obstetric, medical, and surgical history were included. In addition, meticulous preoperative physical, neurological, and electrophysiological examination, detailed examination of the facial musculature and follow-up period of 18

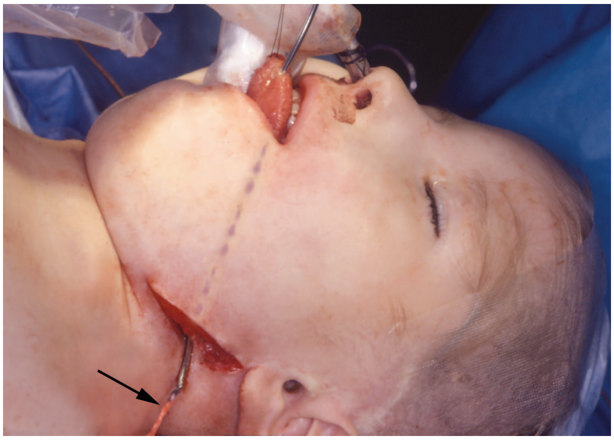


Fig. 3. Intraoperative view of a child with Möbius syndrome undergoing the direct tongue neurotization procedure. The metal tunneler is clearly seen entering from the left submandibular incision and emerging from the tip of the ipsilateral tongue. The distal end of a sural nerve graft is attached to the distal end of the metal tunneler with 6-0 Prolene suture (*arrow*). In this case, the donor nerve was the ipsilateral accessory nerve (cranial nerve XI). After the nerve passed from the left neck to the tip of the left tongue, the proximal part of the sural nerve was coapted in an end-to-side manner to the left accessory nerve through a perineurial window. This allows for neurotization of the ipsilateral tongue without downgrading the function of the left sternocleidomastoid and left trapezius muscles. The distal end of the sural nerve is divided into several fascicles, which are then implanted to the tip of the tongue and allowed to ramify. The stab incision in the tongue is closed with 7-0 polydioxanone suture.

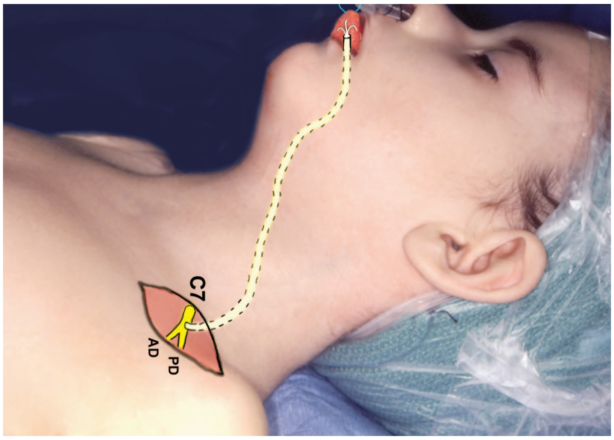


Fig. 4. Diagrammatic depiction of the direct tongue neurotization procedure in a child with Möbius. The proximal part of the sural nerve graft is brought in apposition to the ipsilateral C7 root that was previously exposed. The sural nerve using a malleable metal tunneler has been tunneled to the tip of the tongue. Its distal end is divided in two to three fascicles, which are then implanted to the tip of the tongue and allowed to ramify. Under the operating microscope, an end-to-side coaptation through a perineurial window and partial neurectomy is carried out with the ipsilateral C7 root.

months or longer were prerequisites for patient inclusion. All patients underwent the appropriate at their age speech therapy.[38–40] Patient demographics are shown in Table 1. The type and the degree of cranial nerve involvement in each patient are also shown.

Speech Evaluation

The speech protocol was standardized to contain a wide range of words and phrases, the same for each patient. Scoring was based on the degree of intelligibility of phonemes and on the number of omitted and compensatory[38,39] phonemes. For patients under the age of six, speech intelligibility was compared with the normally anticipated speech milestones for the corresponding age.[40] Preoperative and postoperative videotapes of each patient were reviewed by four unblinded independent investigators, using the grading system shown in Table 2. The senior author (J.K.T.) did not participate in the scoring process. Intraclass correlation and intrarater reliability coefficients were almost equal to 1. The videotapes were identical and the conditions of reviewing were the same for all reviewers. An inherent limitation of reliability studies, however, is that each rater's subsequent ratings are contaminated by the knowledge of previous ratings. Preoperative and postoperative scores for each patient comprise the median scores obtained from the four investigators. Descriptive statistics were used to organize and present the results in this study.

RESULTS

Preoperative and postoperative intelligibility scores were obtained and are listed in Table 3. The neurotized affected sides of the tongue and the corresponding motor donors are also shown. In three patients, intelligibility was improved by two grades (Table 3) and in three patients by one. The mean age in patients with two-grade improvement was 6.1 years and in the patients with the one-point improvement was 14.4 years. In addition, two patients with partial bilateral cranial nerve XII involvement had two-grade improvement versus one with complete unilateral cranial nerve XII involvement. Similarly, among those patients with the one-grade improvement, two had complete unilateral and one partial bilateral cranial nerve XII involvement. There was no difference in improvement among patients who underwent additional procedures addressing bilabial competence be-

Table 1. Patient Demographics and Description of the Type and Degree of Cranial Nerve Involvement

Patient	Sex	Diagnosis	Age (yr)	Type and Degree of Cranial Nerve Involvement
A	M	Ms	4	cbCNVII, cbCNVI, pbCNXII
B	M	Ms	9	cbCNVII, pbCNVI, pbCNVIII, pbCNIX, pbCNX, puCNXI, pbCNXII
C	F	Ms	5.5	pRCNVII, cLCNVII, puCNV, cbCNVI, puCNIX, puCNX, puCNXI, cuCNXII
D	M	Ms, Poland	12	cRCNVII, pLCNVII, cbCNVI, cuCNXII
E	F	Ms	4.3	pbCNVII, cbCNVI, pbCNXII
F	M	HFM, Ms	27	cuCNVII, puCNV, cbCNVI, cuCNVIII, cuCNXII

M, male; F, female; B/L, bilateral; L, left; R, right; Ms, Möbius syndrome; HFM, hemi-facial microsomia; p, partial; c, complete; b, bilateral; u, unilateral; CNV, trigeminal nerve; CNVI, abducent nerve; CNVII, facial nerve; CNVIII, vestibulocochlear nerve; CNIX, glossopharyngeal nerve; CNX, vagus nerve; CNXI, accessory nerve; CNXII, hypoglossal nerve.

Table 2. Scoring System Used for the Evaluation of Speech Intelligibility in Patients with Möbius Syndrome

Score	Description
1	No intelligibility, inarticulate sounds
2	Minimal intelligibility, most phonemes omitted or distorted, no compensation
3	Some intelligibility, many phonemes distorted, good compensation
4	Good intelligibility, a few distorted phonemes, excellent compensation
5	Maximum intelligibility, comprehensible speech

fore and those who did so after direct tongue neurotization. The aforementioned procedures were not performed at the same stage with direct tongue neurotization. No difference between sexes was noted. In addition to speech intelligibility evaluation, in every follow-up visit, needle electromyography and nerve conduction studies were performed and provided evidence of axonal regeneration in the implanted nerve grafts, in all cases. Needle electromyographies showed improvement in tongue motor units in all cases. Preoperative and postoperative motor units are shown in Figure 5. No complications related to the procedure of direct tongue neurotization were observed. Exemplary cases demonstrating restoration of tongue movement, bulk, and shape are shown in Figures 6 through 9. These cases are accompanied by audiovisual clips so that the reader can appreciate the difference in speech intelligibility in these patients [see **Videos, Supplemental Digital Content 1 through 8,** which demonstrate the preoperative and postoperative results of patients 1 through 4 (featured in Figs. 6 through 9); patient 1 preoperatively, ***http://links.lww.com/PRS/A111***, and postoperatively, ***http://links.lww.com/PRS/A112***; patient 2 preoperatively, ***http://links.lww.com/PRS/A113***, and postoperatively, ***http://links.lww.com/PRS/A114***; patient 3 preoperatively, ***http://links.lww.com/PRS/A115***, and postoperatively, ***http://links.lww.com/PRS/A116***; patient 4 preoperatively, ***http://links.lww.com/PRS/A117***, and postoperatively, ***http://links.lww.com/PRS/A118***].

DISCUSSION

The pathology of speech impairment in Möbius syndrome patients is closely associated with the degree of cranial nerve involvement, the orofacial anomalies, and the process of learning. Partial or complete cranial nerve VII involvement determines the degree of facial muscles' functional impairment. Lip approximation and control, cheek motility that controls the intraoral air

Table 3. Preoperative and Postoperative Scores of Speech Intelligibility in Patients with Möbius Syndrome; Motor Donors, Degree of Hypoglossal Involvement, and Neurotized Sides of the Tongue Are Also Shown

Patient	Preoperative Score	Postoperative Score	Motor Donor	Hypoglossal Involvement	Target
A	2	4	R C7, L C7	pbCNXII	R tongue
B	1	3	R CNXI (st), L CNXI (st)	pbCNXII	R tongue, L tongue
C	2	4	L C4, L CNXI (tr)	cuCNXII	L tongue
D	3	4	L (mb)	cuCNXII	L tongue
E	1	2	L C7, R C8-T1,	pbCNXII	L tongue, R tongue
F	3	4	R (mb)	cuCNXII	L tongue

L, left; R, right; CNXI, accessory nerve; CNXII, hypoglossal nerve; (st), branch for sternocleidomastoid; (tr), branch for trapezius; (mb), mandibular branch of facial nerve, C7, C8, T1, corresponding cervical plexus and thoracic roots; p, partial; c, complete; b, bilateral; u, unilateral.

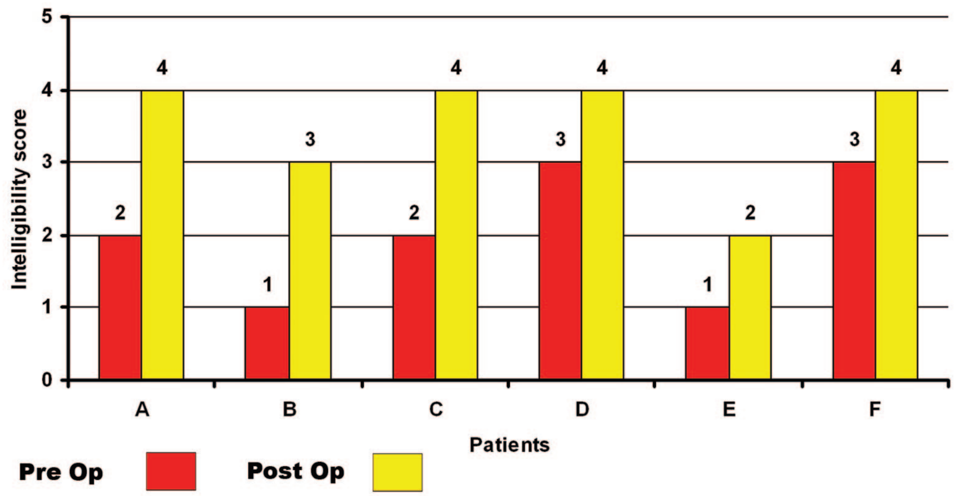


Fig. 5. Preoperative and postoperative electromyographic scores (motor units) of the tongue in patients with Möbius syndrome (0 corresponds to complete denervation, and 5 signifies complete electrogenesis).

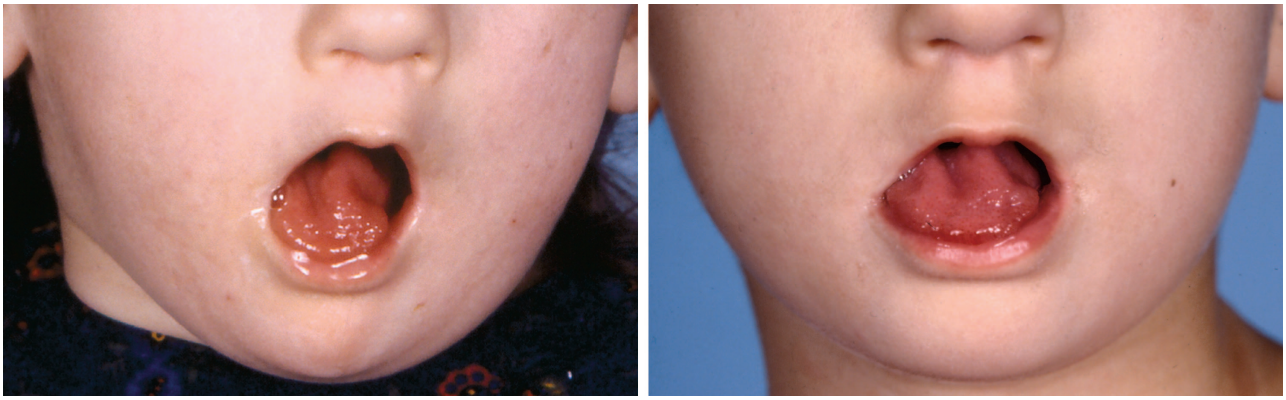


Fig. 6. A 4-year-old girl presented to our center with a diagnosis of Möbius syndrome, micrognathia, microglossia, and focomelia of the right upper extremity. She had bilateral cranial nerve VII palsy, complete bilateral cranial nerve VI palsy, and bilateral cranial nerve XII palsy (patient E in Table 1). The tongue appeared denervated and shriveled (*left*), and her speech was inarticulate and incomprehensible. By using nerve grafts, the left side of the tongue had direct neurotization from the posterior division of the left C7 root, while the right side of the tongue was directly neurotized from the right C8 and T1 roots. (*Left*) The tongue of the patient 2 years after the tongue neurotization procedure. Note increased bulk and improved shape.

capacity during sound formation, and nasal wall motility affecting the role of the nose as a resonator are the main functions that cranial nerve VII involvement affects.[41]

It is difficult to separate the complex process of articulation and formation of meaningful phrases into parts. Linguistic analysis, however, uses phonemes as the minimal sound units that serve to distinguish between meanings of words. One primary requirement for the production of such phonemes is the coordinated function of the orofacial musculature. When this function is impaired, phonemes cannot be produced or are distorted during speech. Cranial nerve VII involvement primarily concerns the expression of vowels and the bilabial phonemes /p/, /b/, and /m/.[42]

Cranial nerve XII involvement (25 percent of the cases)[7,10,42] affects the movement of the tongue, which has a primary role in the production of the alveolar /t/, /d/, /n/, /r/, /z/, /l/, the dental /th/, /θ/, the velar /k/, /g/, and their uvular counterparts /q/ and /G/ phonemes. Furthermore, even the passive position of the tongue contributes to the production of all the phonemes by regulating intraoral space and resonance. Misarticulations may also be the result of imprecise

Fig. 7. A 12-year-old white boy was born with multiple congenital anomalies that included complete cleft palate, Möbius syndrome with complete right cranial nerve VII palsy, complete bilateral cranial nerve VI palsy, and complete unilateral cranial nerve XII palsy (patient D, in Table 1). He also had Poland syndrome on the right side, difficulty speaking, difficulty swallowing, and failure to thrive. The cleft palate was repaired at 18 months of age. (*Left*) He had a denervated tongue with some deviation to the right, and he demonstrated slurred speech. The left side of the tongue was directly neurotized from the left mandibular branches of cranial nerve VII. The patient's tongue is displayed here (*right*) 2 years after the direct tongue neurotization procedure. Note the improvement in bulk and shape.

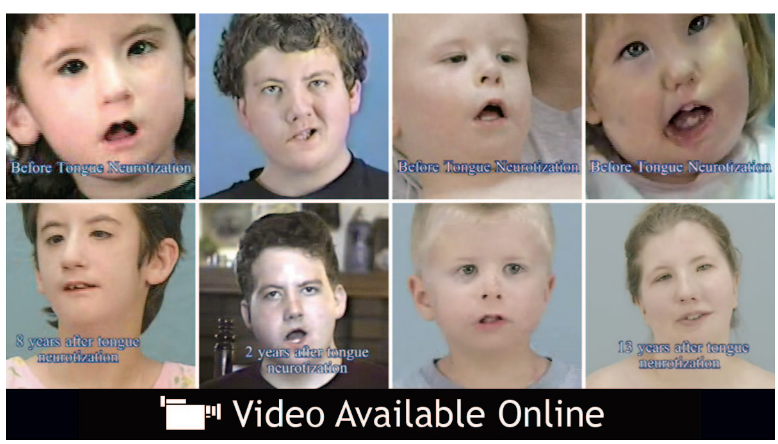
Fig. 8. A 2-year-old child born at 39 weeks of gestation. The delivery was vaginal and lasted 5 hours. No forceps or suction was used. Deficit in facial movements were noted at the time of delivery. A neurologist made a diagnosis of Möbius syndrome soon after birth. The child presented to our center with complete cranial nerve VII paralysis bilaterally, complete cranial nerve VI paralysis bilaterally, and partial bilateral cranial nerve XII palsy. (*Left*) A denervated tongue with minimal movement. The patient had direct bilateral tongue neurotization procedures from the right and left C7 roots. Two segments of sural nerve grafts were used for these procedures. (*Right*) The patient's tongue 4 years later. Note improved shape and bulk.

tongue contact and position during production of phonemes that are not directly associated with tongue movement. Consequently, lingual muscles atrophy, and tongue movement diminution results in the omission or distortion of practically all phonemes as well as vowels.[38]

Involvement of cranial nerve IX has been estimated to be in 10 percent of the cases and increases the incidence of velopharyngeal incompetence, hypernasality, and further speech impairment due to increased diversion of air through the nose. Cranial nerve V palsy is rare, but when present, the resulting inability to close the mouth deteriorates significantly the ability for speech. In addition, in cranial nerve V palsy, oral cavity floor position and relative movement are impaired due to digastric, stylohyoid, mylohyoid, and geniohyoid denervation. Cochlear nerve impairment and chronic otitis media affects hearing ability and may even lead to hearing loss. Audiological disorders interfere with effective learning and increase speech development problems.[17]

Orofacial anomalies are also responsible for a part of speech disorders and articulation inability,

Fig. 9. A 4-year-old child who was born by an unassisted delivery, vertex presentation. At birth, a left-sided facial paralysis was noted. The baby had difficulty in sucking and feeding, and on two occasions she suffered from aspiration pneumonia when she was 4 and 12 months. She was referred to our center when she was 2 years old, where she was diagnosed with a right partial seventh palsy, a left complete facial palsy, a bilateral cranial nerve VI palsy, a partial cranial nerve IX , X, and XI palsy, and a left complete cranial nerve XII paresis (patient C, Table 1). (*Left*) The patient's tongue when she was 4 years of age. Note denervation atrophy on the left side. She had two direct neurotizations to her left side of her tongue through two nerve grafts from the left cranial nerve XI (via end-to-side coaptation) and from the left C4 motor. (*Right*) The tongue of the patient 13 years after the tongue neurotization procedure. Note the nearly normal bulk and shape. The patient also had excellent speech.



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because these are not uncommon and include microstomia, microglossia hypodontia, cleft palate, cleft lip, bifid uvula, and dental malocclusion.

Speech development depends on both the stimuli that the patient receives and learning potential. The cognitive process of learning requires normal mental abilities. The characteristic mask-like face due to facial diplegia and the resulting inability of the patients to express emotions and communicate has led in the past to the belief[43] that a certain degree of mental retardation affects patients with Möbius syndrome. Current studies[9,41,44] report that there is no significant difference in intelligence quotient and behavior in patients with Möbius syndrome compared with the average normal one. Nevertheless, almost one-third of patients with Möbius syndrome present with autistic behavior.[45]

Consequently, phonation disorders comprise a heterogeneous group, including functional dysphonia, flaccid dysarthria, omission or distortion, and compensation of phonemes and speech signals.[42] Audiovisual perception and development has a substantial role in speech ability. Several studies describe speech compensation strategies of Möbius syndrome patients who supplement the verbal output.[46–53]

Although the heterogeneity of speech impairment etiology in Möbius syndrome patients is considerable, the role of severe cranial nerve XII involvement remains one of the most important. To our knowledge, there are no present studies addressing the effect of tongue restoration procedures in speech improvement for patients with Möbius syndrome. Furthermore, this study is the first to investigate the effect of direct tongue neurotization and provide results that justify the role of the procedure in the reconstructive strategy. These results are based on speech intelligibility evaluation.

Segmental evaluation methods, such as the Articulation Index or Speech Transmission Index, have been developed to evaluate speech quality, but they are not suitable for evaluating speech synthesis in general.[54–56] Diagnostic Rhyme Tests use a set of isolated words to test for consonant intelligibility, and results from participants are summarized by averaging the error rates from answer sheets. The Cluster Identification Test is based on a statistical approach. The test vocabulary, including all phoneme components, is not predefined, and it is generated for each test sequence separately.[54–56]

Sentence level tests have been developed to evaluate the comprehension of synthetic speech. The occurrence frequency of words is modeled in prechosen sentences. Unlike in segmental tests, some items may be missed, and the given answer may still be correct, especially if meaningful sentences are used.[54–56]

In comprehension tests, participants hear sentences or paragraphs and answer to the questions about the content of the text. Other tests evaluate pronunciation and intelligibility of common proper names (e.g., city names).[54–56]

Several methods have been developed to evaluate speech overall quality, such as the Mean Opinion Score, which is probably the most widely used method to evaluate speech quality in general, using a five-level scale from bad (1) to excellent (5).[54–56] The scoring system in this study is of this type.

Direct tongue neurotization comprised a part of multistage facial reanimation procedures that aim at restoring voluntary expression and augment mental and psychological development, as well as social and interpersonal skills.[57] Facial reanimation was addressed by free gracilis transfer for smile restoration in four cases, free pectoralis minor transfer for smile restoration in one, digastric transfer for depressor complex substitution in one, and direct neurotization of depressor complex in one. Bilabial competence and speech intelligibility are improved by all of the aforementioned procedures. None of these procedures, however, was performed at the same stage with direct tongue neurotization. Consequently, speech evaluation concerned the effect of direct tongue neurotization alone. In addition, the phonemes that primarily depend on tongue movement (the alveolar /t/, /d/, /n/, /r/, /z/, /l/, the dental /th/, /θ/, the velar /k/, and /g/) were evaluated in the scoring according to the grading system in Table 2.

The procedure yielded a relatively higher improvement in speech intelligibility in patients with partial bilateral involvement of cranial nerve XII than in those with complete unilateral involvement, but this was not statistically significant. Furthermore, mean preoperative electromyography score (motor units) in patients with partial bilateral involvement was 1+ versus 2+ in complete unilateral involvement, whereas the corresponding postoperative scores were 2.3+ and 3+, respectively. This shows that the procedure resulted in an improvement of 1.3 motor units in the former group of patients and in only 1 motor unit in the later. Consequently, when both sides of the tongue retain a partial motor unit activity, the procedure results in a combined functional improvement. This improvement is higher than the one in cases of unilateral complete hypoglossal involvement, however, not in a statistically significant way.

Some, but not the only, reasons why higher improvement was observed in younger ages could be due to differences in the formation of new neuromuscular junctions[58,59] and in nerve regeneration process.[60,61] Improved electromyography motor unit scores in the bilateral patients was due to increased axonal input provided by the two nerve grafts, as opposed to the single nerve graft in the unilateral cases. The lesser improvement in the unilateral complete was due to denervation atrophy of the hemi-tongue.

If the child presented with somewhat understandable speech, intensive speech therapy alone was applied. Continuous feedback and cooperation with the speech therapists were always integral parts of the process. If with intensive three time a week speech therapy there were signs of speech improvement, no tongue neurotization took place.

In cases of children presenting with incomprehensible speech (only gurgling sounds), they were offered the tongue neurotization procedure. It may be considered by some a flaw to not have a control group of untreated patients, as without a control group, the possibility exists that the noted improvement might have occurred for other unexplained reasons other than the tongue neurotization procedure. It is important, however, to mention that the introduction of the tongue neurotization procedure was attempted after lengthy follow-ups of these patients with observation and conservative treatment that yielded no improvement. There are very limited alternatives in these kids: there are no available motor donors for cross-innervation, as these kids have multiple cranial nerve lesions. In addition, cortical learning takes place if there is a muscle target that the brain can work with. If the target is denervated and gone, brain plasticity cannot make an atrophic tongue speak legibly. Speech therapy improves targets that have some muscle in them but can do nothing for denervated targets. Tongue neurotization may restore muscle function up to the point that speech therapy can have optimal results.

CONCLUSIONS

After years of observation and conservative treatment, the lack of improvement in severe cases due to the lack of any intervention was apparent, and it was exactly why the tongue neurotization procedure was introduced. In this study, direct tongue neurotization improved tongue function in patients with Möbius syndrome and cranial nerve XII involvement, as shown by speech intelligibility evaluation. This improvement is due to the restoration of voluntary tongue movement in these patients, as well as to the recovery of the spatial and morphological characteristics of the tongue that contribute to phoneme production. Speech improvement is extremely desirable in such patients, as it comprises the cornerstone of normal psychological, mental, and social development.

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REFERENCES

1. Terzis JK, Noah EM. *Restoration of Dynamic Movement in Möbius Syndrome.* San Diego, Calif.: American Society for Reconstructive Microsurgery; 1995.
2. Rubin LR. The Moebius syndrome: Bilateral facial diplegia: A discourse on the symptoms, pathology, and a surgical dynamic animation of the paralyzed face. *Clin Plast Surg.* 1976; 3:625.
3. Puckett CL, Beg SA. Facial reanimation in Möbius syndrome. *South Med J.* 1978;71:1498.
4. Zuker RM, Manktelow RT. A smile for the Möbius' syndrome patient. *Ann Plast Surg.* 1989;22:188.
5. Von Graefe A, Saemisch T. *Handbuch der gesamten Augenheilkunde.* Leipzig: W Engelman; 1880;6:60.
6. Möbius PJ. Uber angeborenen doppelseitige Abducens-Facialis-Lähmung. *Münch Med Wochenschr.* 1888;35:91–108.
7. Henderson JL. The congenital facial diplegia syndrome: Clinical features, pathology and etiology: A review of sixty-one cases. *Brain* 1939;62:381–403.
8. Orphanet. Prevalence of rare diseases by alphabetical list, 2008. Available at: http://www.orpha.net//consor/cgi-bin/Education_Home.php?lng=EN. Accessed June 22, 2008.
9. Verzijl HT, van der Zwaag B, Cruysberg JR, Padberg GW. Möbius syndrome redefined: A syndrome of rhombencephalic maldevelopment. *Neurology* 2003 61:327–333.
10. Kumar D. Moebius syndrome. *J Med Genet.* 1990;27:122–126.
11. Towfighi J, Marks K, Palmer E, et al. Möbius syndrome: Neuropathologic observations. *Acta Neuropathol (Berl).* 1979; 48:11–17.
12. Journel H, Roussey M, Le Marec BW. MCA/MR syndrome with oligodactyly and Möbius anomaly in first cousins: New syndrome or familial facial-limb disruption sequence? *Am J Med Genet.* 1989;34:506–510.
13. Larrandaburu M, Schüler L, Ehlers JA, MacDonalds Reis A, Lemos Silveira E. The occurrence of Poland and Poland-Moebius syndromes in the same family: Further evidence of their genetic component. *Clin. Dysmorphol.* 1999;8:93–99.
14. Carr MM, Ross DA, Zuker RM. Cranial nerve effects in congenital facial palsy. *J Otolaryngol.* 1997;26:80.
15. Traboulsi EI. Congenital abnormalities of cranial nerve development: Overview, molecular mechanisms, and further evidence of heterogeneity and complexity of syndromes with congenital limitation of eye movements. *Trans Am Ophthalmol Soc.* 2004;102:373–389.
16. Rogers GL, Hatch GF Jr, Gray I. Möbius syndrome and limb abnormalities. *J Pediatr Ophthalmol.* 1977;14:134–138.
17. Griz S, Cabral M, Azevedo G, Ventura L. Audiologic results in patients with Moebiüs sequence. *Int J Pediatr Otorhinolaryngol.* 2007;71:1457–1463.
18. Bamiou DE, Worth S, Phelps P, Sirimanna T, Rajput K. Eighth nerve aplasia and hypoplasia in cochlear implant candidates: The clinical perspective *Otol Neurotol.* 2001;22: 492–496.
19. Suvarna J, Bagnawar M, Deshmukh CT. Moebius syndrome with total anomalous pulmonary venous connection. *Indian J Pediatr.* 2006;73:427–429.
20. Bavinck JN, Weaver DD. Subclavian artery supply disruption sequence: Hypothesis of a vascular etiology for Poland, Klippel-Feil, and Möbius anomalies. *Am J Med Genet.* 1986;23: 903–918.
21. Jennings JE, Costigan C, Reardon W. Moebius sequence and hypogonadotrophic hypogonadism. *Am J Med Genet A.* 2003; 123A:107–110.

22. Ziter FA, Wiser WC, Robinson A. Three-generation pedigree of a Möbius syndrome variant with chromosome translocation. *Arch Neurol.* 1977;34:437–442.
23. Slee JJ, Smart RD, Viljoen DL. Deletion of chromosome 13 in Möbius syndrome. *J Med Genet.* 1991;28:413–414.
24. Kremer H, Kuyt LP, van den Helm B, et al. Localization of a gene for Möbius syndrome to chromosome 3q by linkage analysis in a Dutch family. *Hum Mol Genet.* 1996;5:1367–1371.
25. Nishikawa M, Ichiyama T, Hayashi T, Furukawa S. Möbius-like syndrome associated with a 1;2 chromosome translocation. *Clin Genet.* 51:122–123.
26. Leong S, Ashwell KW. Is there a zone of vascular vulnerability in the fetal brain stem? *Neurotoxicol Teratol.* 1997;19:265–275.
27. Tfelt-Hansen P, Saxena PR, Dahlof C, et al. Ergotamine in the acute treatment of migraine: A review and European consensus. *Brain* 2000;123:9–18.
28. Bos-Thompson MA, Hillaire-Buys D, Roux C, Faillie JL, Amram D. Möbius syndrome in a neonate after mifepristone and misoprostol elective abortion failure. *Ann Pharmacother.* 2008;42:888–892.
29. Pastuszak AL, Schüler L, Speck-Martins CE, et al. Use of misoprostol during pregnancy and Möbius' syndrome in infants. *N Engl J Med.* 1998;338:1881–1885.
30. Puvabanditsin S, Garrow E, Augustin G, Titapiwatanakul R, Kuniyoshi KM. Poland-Möbius syndrome and cocaine abuse: A relook at vascular etiology. *Pediatr Neurol.* 2005;32:285–287.
31. Saito H, Itoh I. Three-dimensional architecture of the intrinsic tongue muscles, particularly the longitudinal muscle, by the chemical-maceration method. *Anat Sci Int.* 78:168–176, 2003.
32. Touré G, Vacher C. Anatomic study of tongue architecture based on fetal histological sections. *Surg Radiol Anat.* 2006; 28:547–552.
33. Hiiemae KM, Palmer JB. Tongue movements in feeding and speech. *Crit Rev Oral Biol Med.* 2003;14:413–429, review.
34. Dion JE, Fox AJ, Pelz D, Viñuela F. CT demonstration of hemiatrophy and fatty replacement of the tongue. *J Can Assoc Radiol.* 1984;35:395–396.
35. Rontal E, Rontal M. Lesions of the hypoglossal nerve: Diagnosis, treatment and rehabilitation. *Laryngoscope* 1982;92:927–937.
36. Strömland K, Sjögreen L, Miller M, et al. Mobius sequence: A Swedish multidiscipline study. *Eur J Paediatr Neurol.* 2002; 6:35–45.
37. Terzis JK, Karypidis D. Outcomes of direct muscle neurotization in pediatric patients with facial paralysis. *Plast Reconstr Surg.* 2009;124(5):1486–1498.
38. Kahane JC. Pathophysiological effects of Möbius syndrome on speech and hearing. *Arch Otolaryngol.* 1979;105:29–34.
39. Chester CH, Zuker RM. Complexities of speech in the Moebius syndrome patient. In Hinderer UT, ed. *Plastic Surgery*, Vol. II. New York: Elsevier Science; 1992.
40. Singh L, Singh NC. The development of articulatory signatures in children. *Dev Sci.* 2008;11:467–473.
41. Terzis JK, Noah EM. Dynamic restoration in Möbius and Möbius-like patients. *Plast Reconstr Surg.* 2003;111:40–55.
42. Goldberg C, DeLorie R, Zuker RM, Manktelow RT. The effects of gracilis muscle transplantation on speech in children with Moebius syndrome. *J Craniofac Surg.* 2003;14:687–690.
43. Briegel W. Neuropsychiatric findings of Mobius sequence: A review. *Clin Genet.* 2006;70:91–97.
44. Giannini AJ, Tamulonis D, Giannini MC, Loiselle RH, Spirtos G. Defective response to social cues in Möbius' syndrome. *J Nerv Ment Dis.* 1984;172:174–175.
45. Williams DL, Goldstein G, Kojkowski N, Minshew NJ. Do individuals with high functioning autism have the IQ profile associated with nonverbal learning disability? *Res Autism Spectr Discord.* 2008;2:353–361.
46. Von Berg S, McColl D, Brancamp T. Moebius syndrome: Measures of observer intelligibility with versus without visual cues in bilateral facial paralysis. *Cleft Palate Craniofac J.* 2007; 44:518–522.
47. Zeine L, Brandt JF. The Lombard effect on alaryngeal speech. *J Commun Disord.* 1988;21:373–383.
48. McColl D, Fucci D, Petrosino L, Martin D, McCaffrey P. Listener ratings of the intelligibility of tracheoesophageal speech in noise. *J Commun Disord.* 1998;31:279–289.
49. Holley SC, Lerman J, Randolph K. A comparison of the intelligibility of esophageal, electrolarynx, and normal speech in quiet and in noise. *J Commun Disord.* 1983;16:143–155.
50. Skipper JI, van Wassenhove V, Nusbaum HC, Small SL. Hearing lips and seeing voices: How cortical areas supporting speech production mediate audiovisual speech perception. *Cereb Cortex* 2007;17:2387–2399.
51. Schorr EA, Fox NA, van Wassenhove V, Knudsen EI. Auditory-visual fusion in speech perception in children with cochlear implants. *Proc Natl Acad Sci USA.* 2005;102:18748–18750.
52. van Wassenhove V, Grant KW, Poeppel D. Visual speech speeds up the neural processing of auditory speech. *Proc Natl Acad Sci USA.* 2005;102:1181–1186.
53. De Feo AB, Schaefer CM. Bilateral facial paralysis in a preschool child: Oralfacial and articulatory characteristics. In Berry W, ed. *Clinical Dysarthria.* San Diego, Calif.: College-Hill Press; 1983:165–190.
54. Allen DV, Bliss LS, Timmons J. Language evaluation: Science of art? *J Speech Hear Disord.* 1981;46:66–68.
55. De Bodt MS, Van de Heyning PH, Wuyts FL, Lambrechts L. The perceptual evaluation of voice disorders. *Acta Otorhinolaryngol Belg.* 1996;50:283–291, review
56. Kreiman J, Gerratt BR, Kempster GB, Erman A, Berke GS. Perceptual evaluation of voice quality: Review, tutorial, and a framework for future research. *J Speech Hear Res.* 1993;36: 21–40.
57. Terzis JK, Noah EM. Möbius and Möbius-like patients: Etiology, diagnosis and treatment options. *Clin Plast Surg.* 2002; 29:497–414.
58. Kurz MJ, Stergiou N. The aging human neuromuscular system expresses less certainty for selecting joint kinematics during gait. *Neurosci Lett.* 2003;348:155–158.
59. Vandervoort AA. Aging of the human neuromuscular system. *Muscle Nerve* 2002;25:17–25.
60. Cafferty WB, McGee AW, Strittmatter SM. Axonal growth therapeutics: Regeneration or sprouting or plasticity? *Trends Neurosci.* 2008;31:215–220.
61. Navarro X, Vivó M, Valero-Cabré A. Neural plasticity after peripheral nerve injury and regeneration *Prog Neurobiol.* 2007;82:163–201.