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Efficacy of electrical stimulation of the zygomaticus muscle in complete facial paralysis: evidence from facial grading and automated image analysis

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Abstract

Surface Functional Electrical Stimulation (FES) is a well-studied intervention for multiple muscular disorders. However, it is still controversially discussed as a complementary therapy for complete facial paralysis. The aim of this intervention is to test a daily home-based ES concept as a pilot study regarding safety, feasibility, and effects on facial functionality and symmetry. In a prospective single-centre pilot study, 10 patients (median 61 years, denervation 130 d) with complete peripheral facial paralysis performed home-based FES of the affected lateral mouth region. Stimulation parameters, facial paralysis scores and standardised photographs were assessed in monthly follow-ups. No serious adverse events appeared. Stimulation parameters could be constantly increased indicating effective muscle training while subjectively perceived functionality of the face improved. Thus, smile angle of the paralysed side improved as well. FES is a safe therapy model for application in facial nerve paralysis patients. A feasible stimulation protocol could be applied, which improved the functionality and symmetry of the stimulated facial region. A future controlled, randomised and double-blind follow-up study is needed to investigate these initial results in a further evolved replicable setting.

Key Words: facial paralysis, electrical stimulation, denervated muscle.

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Surface Functional Electrical Stimulation (FES) of skeletal mucles is a well-observed procedure for the therapy of various nerval lesions. It is a non-invasive therapy approach that is used, for example, in the muscular rehabilitation of nerve diseases. It has a beneficial effect on blood circulation, increases muscular strength and can stop or even reverse atrophy behavior.[1-5] Amongst others, FES is already used in the treatment of paralytic disorders of the Central Nervous System (CNS) such as stroke, lumbar disc herniation, paraplegia and multiple sclerosis[5-8] as well as pathologies of the Peripheral Nervous System (PNS) as in recurrent laryngeal nerve palsy and plexus brachialis lesions.[9,10] A further paralysis disorder that would also benefit from FES application is peripheral facial paralysis, which is caused by lesions of the facial nerve resulting in a denervation of facial muscles. A key pathology associated with long lasting facial paralysis is the atrophy of facial muscles leading to restrictions of mimical functionality. Patients suffer from cosmetical and functional losses often accompanied by a negative perception of their own body and self-consciousness in social relationships.[11] This leads to distress and depression, culminating in the withdrawal from social interactions.[12] On a functional level, a complete loss of eye and mouth muscle tone results in severe constraints such as ulceration of the sclerae, eating or speaking impairments and reduced oral health.[13] Whereas surgical reinnervation procedures are the primary solution for most patients, even in these cases a supportive treatment is essential to bridge the time until reinnervation and reduce consequential damages. As patients experience suffering in the context of the disease, non-invasive approaches such as bridging FES need to be investigated in a way that complements surgical treatment options.

First studies suggest FES to be a suitable intervention in the

denervation atrophy of facial muscles and provide evidence of enhanced facial movements.[14-16] However, FES is still a subject of scientific controversy in terms of applicability and therapy adherence due to possible side effects such as deteriorating nerval regeneration and enhancing depression or hostility in patients undergoing the treatment.[17-19] Contrary to the still widespread assumption that FES could have a negative influence on the recovery of nerve lesions in the facial region, the safety of FES in the context of incomplete as well as complete facial palsy has been proven in several studies.[14,20,21]

A particularly suitable way for regular training of denervated muscles is the use of daily home-based FES. To date, it has mainly been established in the treatment of spinal cord injury as it enables effective rebuilding of muscle structure, mass and strength.[4,5,22,23] Furthermore, this method has already been used for studies in patients with facial palsy.[15,20] Yet, none of these studies have adapted the stimulation parameters to suit the individual FES training progress of the respective patient at regular intervals during a standardised study course.

The aim of this study is to test a daily home-based FES protocol with the goal of providing a conservative therapy supplement for patients with complete facial paralysis. It will therefore investigate the safety and feasibility as well as probable effects on facial functionality and symmetry.

Materials and Methods

Study design

This trial was conceived as a prospective single-center observational study. The study was registered in the German Clinical Trials Register (DRKS00015015). The local institutional ethics committee approved the study (no. 550503/18). All patients provided written informed consent prior to inclusion.

Requirements for study inclusion were patients with a unilateral total peripheral facial paralysis with no residual voluntary activity confirmed by needle electromyography (EMG),[24-26] minimum age of 18 years, mental and physical aptitude for homebased surface electrical stimulation as well as a high motivation to participate in the clinical study. Exclusion criteria were pregnancy or breastfeeding, signs of reinnervation in the EMG, conservative treatment procedures (e.g. botulinum toxin injections) or physiotherapy within the last three months, medical conditions that influence the results of the clinical investigations (e.g. general muscle diseases; epilepsy; skin diseases), known allergies or intolerances to materials used in the clinical trial, malignant or life-threatening diseases at the time of inclusion or bilateral or central facial paralysis. To solely investigate the effect of FES unaffected by nerval reinnervation, patients stopped FES and terminated the study as soon as they showed first signs of reinnervation in EMG. Furthermore, patients terminated the study if they showed voluntary muscle tone of the affected side of the face, visible voluntary movement, and visible synkinesis as well as serious adverse events, the occurrence of malignant and life-threatening diseases, or facial paralysis on the contralateral side as well as on their individual demand. Hence, the follow-up time varied between the participants. At the latest, the patients' follow-up was terminated after one year of study inclusion.

Study protocol

Ten patients were included in the pilot study and attended a baseline examination (T0). This included an EMG examination to verify complete unilateral peripheral facial paralysis. In order to classify the extent of the paralysis, the Sunnybrook Facial Grading Score (SFGS) and the Patient-reported Outcome Measures Scores (PROMs), consisting of the Facial Clinimetric Evaluation (FaCE) and the Facial Disability Index (FDI), were assessed during baseline and follow-up.[27-32] A standardised portrait photography was performed at baseline and during follow-up. In addition, ultrasound examinations of the facial muscles were performed.[33,34] The results of the ultrasound examination are published separately.[26] Subsequently, remote calls and follow-up visits were planned and carried out according to a standardised schedule (Table 5). During the remote telephone calls, the occurrence of undesired side effects was queried, and the PROMs were assessed. Follow-up visits took place in the hospital and according to the same procedures as during the baseline examination. There was a maximum of three remote calls and seven follow up visits after 2, 4, 6, 8, 10, 12, 16, 28, 40, up to at latest 52 weeks (T2 to T52). In every follow-up, EMG was conducted in order to detect potential signs of reinnervation. Patients terminated FES when EMG and clinical findings clearly indicated facial reinnervation.

Electrical stimulation protocol

During the baseline examination, the FES parameters were determined in a comfortable sitting position with STMISOLA stimulator (BIOPAC Systems Inc., Germany). For home training, STIWELL® med4 device (CE 0297; P/N 9001015) developed by MED-EL Elektromedizinische Geräte Gesellschaft m.b.H., Innsbruck, Austria) stimulation device was used. In each ES, two adhesive electrodes (PALS® Neurostimulation electrodes, oval 4 cm x 6.4 cm, Axelgaard Manufacturing Co., Ltd., Lystrup, Denmark, CE-certified, REF 896230) were placed superficially over the zygomaticus muscle on the affected side. The cranial electrode was used as the cathode and the caudal electrode as the anode. Both electrodes were positioned as close as necessary to the corner of the mouth to avoid stimulation of the surrounding muscles. Phase duration (PD) of 1, 2, 5, 10, 15, 25, 50, 100, 250, 500 and 1000 ms with increasing amplitudes in between 0.1 and 20 mA were then tested. Biphasic triangular and rectangular waveforms with a constant frequency of 1 Hz were used. Amplitudes were noted for each phase length at which the zygomaticus muscle contracted without pain and simultaneous stimulation of surrounding facial muscles.[35] The parameters at the point of the strongest possible contraction below the pain threshold were acquired and then used to program the FES devices. To test tolerance, patients were stimulated for 20 min under medical supervision. Only the investigators were able to change stimulation settings by entering a password. The pa-

tients would not accidentally stimulate incorrectly or harm themselves.

After the test stimulation, the patients were shown how to apply the electrodes correctly in front of a mirror and how to operate the FES device. Based on the clinically determined FES parameters, patients performed FES at home twice every day (both in the morning and evening with an in-between break of at least 6 hours) for 20 min. For home training, a two-phase stimulation in a triangular waveform with a stimulating pulse interval of 5 seconds and a pulse pause of 1 second was performed (Figure 1). At each follow-up visit, the parameters and electrode position were adjusted again to ensure optimal therapy success and patient safety. An increase of the stimulation intensity was tested during each follow-up during a 20-minute stimulation in the clinic and applied if no fatigue occurred as a sign of training effect. Vice versa, the stimulation parameters were decreased if fatigue was observed. Accordingly, on the day of the follow-up visit, only a single run of FES was performed at home, and the new stimulation parameters were applied until the next follow-up.

Facial electromyography and automated facial image analysis

Standardised needle-EMG on frontalis, zygomaticus, orbicularis oculi and oris muscle were performed using VIASYSY Synergy (version 15.0. VIASYS Healthcare UK Ltd. Warwick, United Kingdom).[25] The electrical activity of each muscle was monitored for denervation, synkinesis and reinnervation. SFGS was assessed by physicians of the ENT-Department of the University Hospital Jena. Patients self-completed the PROMs including FaCE and FDI to record the subjectively perceived status of disease progression under therapy. Portrait photography was performed using a Nikon D90 camera (NIKON Corp. Tokyo, Japan). Photographic analysis was performed with Emotrics, an automated machine-learning based programme.[36] Anatomical landmarks were automatically set by the software's algorithm and manually corrected by the examiner. These points were programmed to be set on the eyebrows, eyelid margins, bridge of the nose, lip margins and facial rim.[36,37] Following superficial parameters were assessed: Brow height (BH, distance between pupil and upper edge of the eyebrow), palpebral fissure height (PFH, distance between upper and lower edge of the eyelid), commissure height deviation (CHd, height distance between mouth angle of the affected side and the contralateral side), commissure excursion (CE, distance between mouth angle and intersection of midline and lower lip margin) and smile angle (SA, angle between midline and distance of commissure excursion). The automatically determined midline had to be corrected on the basis of anatomical parameters by moving the iris fixation points.[37] Accordingly, the surface parameters whose reference points are the iris and pupil were evaluated first (BH, PFH). Then the midline was adjusted and the parameters whose reference point was the corrected midline were calculated (CHd, CE, SA). Both the paralysed and contralateral sides of the face were analysed.

Statistics

Linear mixed models were used to detect significance in stimulation parameters, SFGS, PROMs and photographic surface parameter value changes. The parameter "face side" was used for side comparison statistics and the parameter "visit number" was included for the longitudinal analysis of the stimulation parameters, scores and automated image analysis as fixed effects as well as a random intercept for patient in the model. Continuous values are summarised by

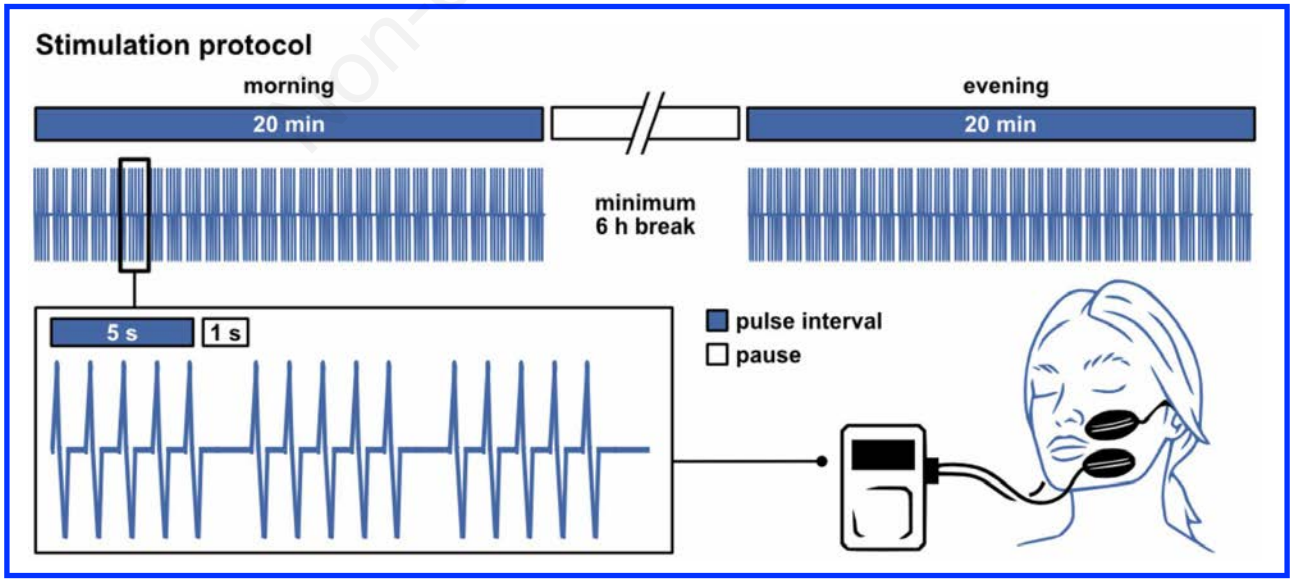

Figure 1. *Home-based electrical stimulation protocol; two-phase stimulation using 1 Hz impulse frequency as an example: five biphasic triangular waveform salvos followed by a pause period of 1 sec repeatedly form a 20-minute stimulation interval which is conducted twice a day by the patient at home. The first FES interval was performed in the morning with a subsequent break of a minimum break of 6 hours followed by a second FES interval in the evening.*

mean and standard deviation or median and 25th/75th percentile if the data was not normally distributed. All clinical visit values were analysed in pairwise comparison as well as using an overall test to detect significance for the whole period of investigation. The significance level was set to $p < 0.05$. The assessed data was documented in Microsoft Excel (Version 2308. Microsoft Corp. Redmond, Wahington, USA). The statistical analysis was performed in IBM SPSS Statistics for Windows (Version 27.0. IBM Corp. Armonk, New York, USA). Statistical graphs were designed using GraphPad Prism (Version 10.2.1, GraphPad Software Inc., Boston, Massachusetts, USA).

Results

Patient characteristics

10 patients (median 61 years, 25th to 75th percentile 38.3 – 71 years; 4 female, 6 male, median time of clinical onset of the facial paralysis 130 d) underwent FES for a mean of 95 days (min. 35, max. 301) (Table 1). None of the patients experienced any undesired severe side effects of the ES. Minor side effects were skin irritation caused by the adhesive electrodes (n=1) and an unpleasant feeling (n=1). After T 28 (28±2 weeks) all 10 patients had terminated the study either due to reinnervation (n=6) or other termination criteria: stroke (n=1), long-term rehabilitation after total hip arthroplasty (n=1), metastasis of parotid carcinoma (n=1) and personal reasons (moved away; n=1).

Stimulation parameters

During the observation period of six months, the average stimulation frequency could be increased from 1.3 Hz±0.4 at baseline to 6.0 Hz±1.0 after 28±2 weeks ($p < 0.001$). At the same time, the individually adjusted phase duration was reduced from an average of 155.0 msec±11.7 to 63.8 msec±26.1 (p=0.004). The average voltage was increased from 16.2 V±1.4 to 25.6 V±3.1 (p=0.008). Overall tests were highly significant for each value ($p \leq 0.001$, Table 2).

Scores and questionnaires

During baseline, patients showed a mean SGFS total of 6.2±3.1, which increased non-significantly by 55 % to 9.6±6.9 by the end of the study interval in pairwise comparison (p=0.646). Over the entire duration of the study, overall tests showed no significant improvement or deterioration in either the SFGS total or the sub scores for resting state and voluntary movement. In contrast, the FDI body and FaCE oral function sub scores showed an overall significant improvement while FES being performed (p=0.031, Figure 2A). The FDI body increased from an initial average value of 53.0±4.7 to 66.0±6.8 (p=0.032) and FaCE oral function sub score from 50.0±9.9 to 69.9±13.9 (p=0.097) in pairwise comparison. On the other side, there was no significant improvement or deterioration of the FDI social or FaCE social function sub scores with initial baseline means of 58.4±8.5 and 52.5±11.6 over time (Table 2 and 6).

Table 1. *Patients' characteristics*

ID	Age (years)	Sex	Etiology	Palsy duration (days)[a]	Reinnervation after 1 year	Termination after	Nerval anastomosis surgery	Reason of termination
1	51	M	Vestibular schwannoma	118	Yes	T8	None	Reinnervation
2	24	F	Parotid cancer	188	No	T28	HFJA	Personal reasons
3	64	M	Chronic otitis media	48	No	T12	None	Stroke
4	77	F	Zoster oticus	141	Yes	T12		Reinnervation
5	61	F	Vestibular schwannoma	383	Yes	T28	HFJA	Reinnervation
6	61	M	Vestibular schwannoma	34	No	T12	None	Rehabilitation after THA
7	71	M	Temporal bone fracture	58	Yes	T4	None	Reinnervation
8	71	M	Parotid cancer	674	No	T8	None	Metastasis
9	30	M	Benign parotid tumor	3	Yes	T12	Great auricular nerve interposition	Reinnervation
10	41	F	Parotid cancer	1004	Yes	T12	HFJA	Reinnervation

[a]clinical onset upon baseline visit; HFJA, hypoglossal-facial nerve anastomosis; THA, total hip arthroplasty; M, male; F, female.

Table 2. *Surface electrical stimulation: stimulation parameters and scores at clinical visit*

Parametrer	Overall F	Overall p[a]	n	Baseline Mean±SD	n	T 4 Mean±SD	p[b]	n	T 8 Mean±SD	p[b]	n	T 12 Mean±SD	p[b]
Stimulation parameters													
Frequency [Hz]	6.84	**.000**	10	1.3±0.4	9	1.9±0.5	.345	6	3.2±0.6	**.013**	2	5.0±1.0	**.002**
Phase duration [msec]	6.07	**.001**	10	155.0±11.7	9	103.3±12.3	**.006**	6	78.1±15.1	**.000**	2	51.3±26.1	**.001**
Voltage [V]	5.73	**.001**	10	16.2±1.4	9	23.8±1.5	**.001**	6	24.5±1.8	**.001**	2	26.6±3.1	**.004**
SFGS and PROMs													
SFGS total	0.92	.498	10	6.2±3.1	9	10.8±3.3	.299	7	13.6±3.7	.122	4	12.9±4.9	.245
SFGS resting state	0.73	.628	10	3.8±0.3	9	3.0±0.3	.061	7	3.4±0.3	.405	4	3.3±0.4	.306
SFGS vol. movement	0.70	.651	10	6.3±0.7	9	6.4±0.7	.909	7	7.6±0.8	.147	4	6.8±1.0	.625
FDI body	2.36	**.031**	10	53.0±4.7	9	60.5±4.8	**.007**	7	58.0±5.0	**.026**	4	59.7±5.6	**.003**
FDI social	1.17	.342	10	58.4±8.5	9	65.1±8.5	.375	7	59.5±8.7	.121	4	61.2±9.1	.053
FaCE total	1.55	.165	10	43.7±6.2	9	46.7±6.2	.997	7	42.3±6.4	.104	4	39.0±6.9	.098
FaCE oral function	2.36	**.031**	10	50.0±9.9	9	52.9±10.0	.445	7	47.9±10.4	.325	4	69.5±11.6	.127
FaCE social function	1.73	.114	10	52.5±11.6	9	56.8±11.7	.669	7	55.8±12.1	**.007**	4	47.1±13.2	.051

	n	T 16 Mean±SD	p[b]	n	T 20 Mean±SD	p[b]	n	T 28 Mean±SD	p[b]
Stimulation parameters									
Frequency [Hz]	2	5.0±1.0	**.002**	2	5.5±1.0	**.001**	2	6.0±1.0	**.000**
Phase duration [msec]	2	51.3±26.1	**.001**	2	48.8±26.1	**.001**	2	63.8±26.1	**.004**
Voltage [V]	2	27.1±3.1	**.003**	2	29.6±3.1	**.000**	2	25.6±3.1	**.008**
SFGS and PROMS									
SFGS total	2	15.6±6.9	.215	2	20.1±6.9	.072	2	9.6±6.9	.646
SFGS resting state	2	3.5±0.6	.667	2	3.0±0.6	.256	2	3.5±0.6	.667
SFGS vol. movement	2	7.4±1.4	.451	2	7.9±1.4	.276	2	5.9±1.4	.783
FDI body	2	53.5±6.8	.932	2	48.5±6.8	.446	2	66.0±6.8	**.032**
FDI social	2	56.7±10.1	.805	2	56.7±10.1	.805	2	50.7±10.1	.258
FaCE total	2	36.2±7.9	.206	2	37.8±7.9	.322	2	37.9±7.9	.326
FaCE oral function	2	63.7±13.9	.250	2	76.2±13.9	**.031**	2	69.9±13.9	.097
FaCE social function	2	49.3±15.6	.795	2	46.2±15.6	.611	2	43.0±15.6	.448

FaCE, Facial Clinimetric Evaluation; FDI, Facial Disability Index; PROMs, Patient-reported Outcome Measures; SFGS, Sunnybrook Facial Grading Score, [a]overall significance; [b]significance of the mean value differences in relation to baseline mean value.

Table 3. *Surface electrical stimulation: photographic surface parameters at clinical visits*

Parameter	Side	Side comparison Mean diff.	p[a]	Overall F	p[b]	Baseline n	Baseline Mean±SD	T 4 n	T 4 Mean±SD	p[c]	T 8 n	T 8 Mean±SD	p[c]
BH [mm]	palsy	16.51	<0.001	0.38	.885	10	16.5±0.9	9	16.8±0.9	.738	7	16.7±1.0	.869
	contra.	20.97		2.66	**.046**	10	21.0±1.6	9	20.3±1.6	.482	7	21.4±1.6	.723
PFH [mm]	palsy	8.86	.459	2.75	**.041**	10	8.6±0.4	9	8.9±0.5	.334	7	9.6±0.5	**.003**
	contra.	8.66		2.11	.097	10	8.3±0.4	9	8.2±0.4	.731	7	9.2±0.5	**.025**
CE [mm]	palsy	21.66	<0.001	0.81	.571	10	21.9±1.5	9	22.1±1.5	.666	7	21.5±1.5	.604
	contra.	24.00		0.77	.600	10	23.9±0.9	9	23.8±1.0	.904	7	23.9±1.0	.971
ChDev [mm]		0.89			.824	10	4.8±1.0	9	4.6±1.1	.758	7	4.4±1.1	.528
SA [°]	palsy	89.46	<0.001	2.11	.098	10	87.8±3.9	9	89.3±4.0	.053	7	90.0±4.0	**.012**
	contra.	98.92		0.57	.753	10	98.5±3.7	9	99.5±3.7	.544	7	99.4±3.8	.592

Parameter	Side	T 12 n	T 12 Mean±SD	p[c]	T 16 n	T 16 Mean±SD	p[c]	T 20 n	T 20 Mean±SD	p[c]	T 28 n	T 28 Mean±SD	p[c]
BH [mm]	palsy	4	16.0±1.1	.612	2	17.4±1.4	.509	2	17.2±1.4	.605	2	15.7±1.4	.504
	contra.	4	19.6±1.8	.295	2	20.3±2.1	.681	2	25.8±2.1	**.009**	2	19.4±2.1	.356
PFH [mm]	palsy	4	8.9±0.5	.467	2	9.6±0.6	.053	2	8.8±0.6	.724	2	9.7±0.6	**.034**
	contra.	4	8.4±0.6	.870	2	8.7±0.7	.496	2	9.5±0.7	.077	2	9.4±0.7	.099
CE [mm]	palsy	4	21.6±1.6	.799	2	23.0±1.7	.279	2	22.7±1.7	.435	2	20.8±1.7	.350
	contra.	4	22.8±1.1	.189	2	25.1±1.3	.252	2	24.1±1.3	.796	2	23.8±1.3	.944
ChDev [mm]		4	4.6±1.2	.777	2	5.9±1.3	.250	2	4.5±1.3	.806	2	4.6±1.3	.826
SA [°]	palsy	4	89.3±4.0	.157	2	90.0±4.1	.109	2	91.4±4.1	**.014**	2	90.5±4.1	.054
	contra.	4	99.9±4.0	.517	2	103.6±4.4	.087	2	100.9±4.4	.404	2	100.9±4.4	.414

BH, brow height; contra., contralateral side; CE, commissure excursion; ChDev, commissure height deviation; PFH, palpebral fissure height; SA, smile angle; SFGS, Sunnybrook Facial Grading Score; [a]mean difference significance between paralysed and contralateral side; [b]overall significance; [c]significance of the mean value differences in relation to baseline mean value.

Photographic surface parameters

BH, CE and SA of the paralysed side where significantly lower than of the contralateral side ($p < 0.001$). However, PFH did not show a significant difference between the mean values of the affected and unaffected sides (Table 3). Overall testing showed and PFH of the paralysed side ($p=0.041$). Interestingly, there was a significant increas for BH of the contralateral side ($p=0.046$) as well. In pairwise comparison, the mean BH of the contralateral side increased from 21.0 mm±1.6 to 25.8 mm±2.1 20±2 weeks after baseline ($p=0.009$) but decreased non-significantly to 19.4 mm±2.1 after 28±2 weeks ($p=0.356$). Meanwhile BH of the paralysed side presented a non-significant decrease from 16.5 mm±0.9 at the baseline to 15.7 mm±1.4 after 28±2 weeks ($p=0.504$). During the same interval, PFH of the contralateral side increased non-significantly from 8.3 mm±0.4 to 9.4 mm±0.7 ($p=0.099$) in pairwise comparison, while PFH on the paralysed side increased significantly from 8.6 mm±0.4 to 9.7 mm±0.6 ($p=0.034$, Figure 2B). For CE, ChDev and SA no significance was detected in overall testing. However, pairwise comparisons showed individual, significant increases in SA of the paralysed side from 87.8°±3.9 at baseline to 90.0°±4.0 after 8±2 weeks ($p=0.012$) and 91.4°±4.1 after 20±2 weeks ($p=0.014$).

Discussion

In line with a variety of prior FES studies, there was no evidence of any harmful effect of FES on the facial muscles over the entire course of the study.[14,20,21] In particular, on a functional level, several effects could be observed: the minimum phase duration, which triggered a significant contraction of the stimulated zygomaticus muscle, could be continuously reduced. Depending on the length of the phase duration, the number of recruited muscle fibres can increase.[1] If, as in this case, a constantly visible contraction of the stimulated muscles can be triggered despite continuously reducing the phase duration, the threshold for triggering a contraction might be lowered as a sign of effective muscle training. Likewise, the stimulation voltage and

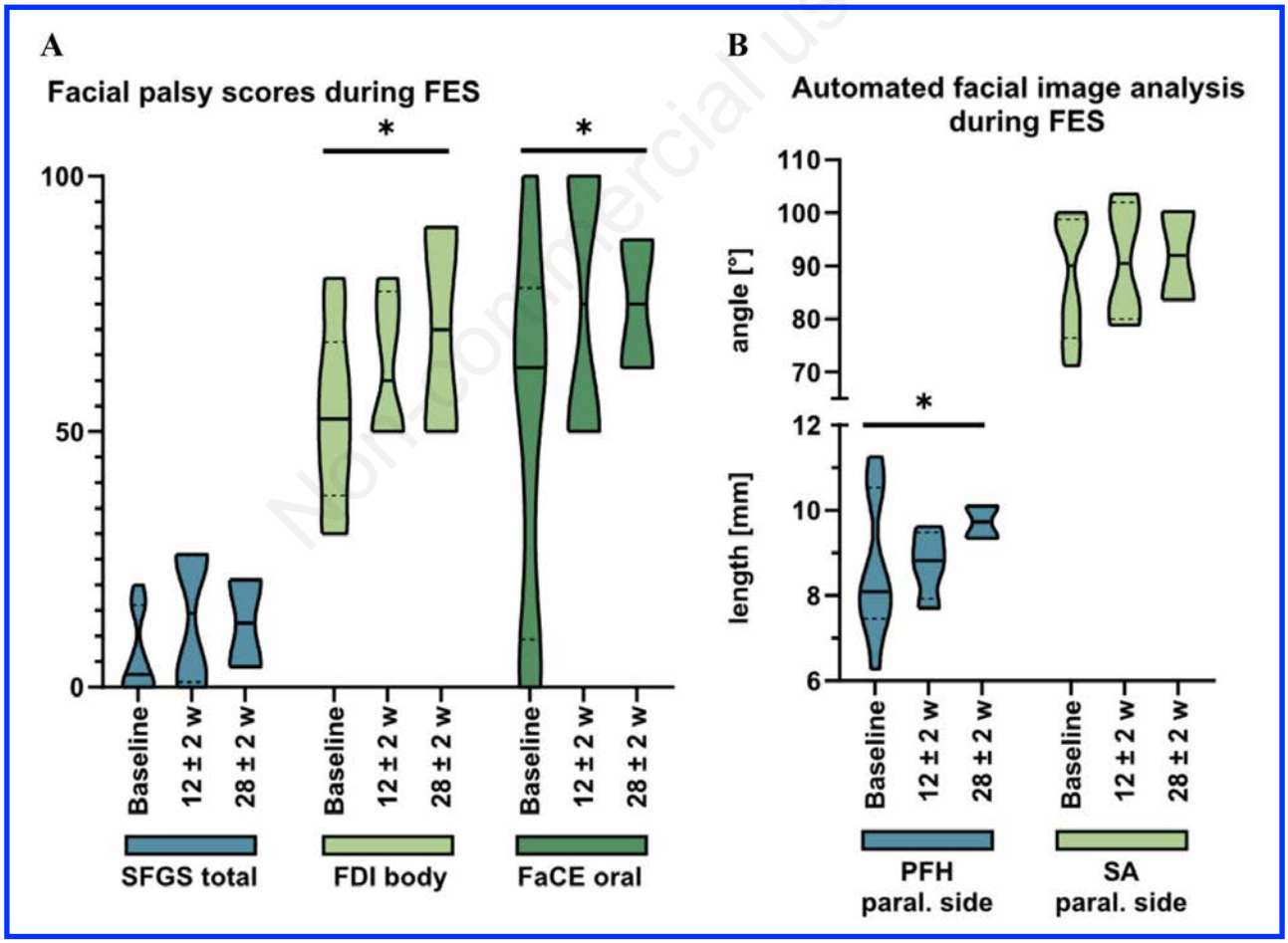

Figure 2. *Effect of electrical stimulation on function and symmetry of the face as well as quality of life; truncated violin plots displaying median as continuous line and quartiles as dashed line. A) Facial palsy scores during FES; FaCE, Facial Clinimetric Evaluation; FDI, Facial Disability Index; SGFS, Sunnybrook Facial Grading Score; * overall significance ($p < 0.05$). B) Automated facial image analysis during FES of the paralysed side of the face; PFH, palpebral fissure height; SA, smile angle; *overall significance ($p < 0.05$).*

frequency could be continuously increased during the clinical visits without fatigue occurring within the stimulation interval. As a result, the stimulated zygomaticus muscle showed an increase in training capacity. Similarly, several studies investigating FES of muscles remote from the face[5,38,39] and facial muscles[15,16] showed an increase in strength and function of the trained muscles.

Puls et al. examined the SFGS subscores for resting state and voluntary movement of seven patients with complete peripheral facial nerve paralysis who received ES, which also showed no significant increase or decrease in size.[20] Expectedly, voluntary movement of completely denervated muscles would not improve until reinnervation, as the affected muscles cannot contract voluntarily. On the one hand,

Table 5. *Schedule of visits and remote calls according to study protocol.*

Visit	Remote call	T.	Time after baselinein weeks*	EMG	SFGS	PROMs	Photos	US
Baseline		T 0		Yes	Yes	Yes	Yes	Yes
	1	T 2R	2			Yes		
FU 1		T 4	4	Yes	Yes	Yes	Yes	Yes
	2	T 6R	6			Yes		
FU 2		T 8	8	Yes	Yes	Yes	Yes	Yes
	3	T 10R	10			Yes		
FU 3		T 12	12	Yes	Yes	Yes	Yes	Yes
FU 4		T 16	16	Yes	Yes	Yes	Yes	Yes
FU 5		T 20	20	Yes	Yes	Yes	Yes	Yes
FU 6		T 28	28	Yes	Yes	Yes	Yes	Yes
FU 7		T 40	40	Yes	Yes	Yes	Yes	Yes
FU 8		T 52	52	Yes	Yes	Yes	Yes	Yes

**At T2R and T4 a deviation ±1 week and from T6 to T52 of ±2 weeks were allowed. FU, follow up; EMG, needle electromyography; SFGS, Sunnybrook Facial Grading Score; PROMs, Patient Reported Outcome Measures; T, visit number; US, ultrasound.*

Table 6. *Surface electrical stimulation: scores during remote calls.*

Parameter	n	Baseline Mean±SD	n	T 2R* Mean±SD	p	n	T 6R* Mean±SD	p	n	T 10R* Mean±SD	p
PROMS											
FDI body	10	53.0±4.7	9	62.4±4.8	**.007**	7	61.3±5.0	**.026**	6	65.1±5.1	**.003**
FDI social	10	58.4±8.5	9	61.8±8.5	.375	7	64.9±8.7	.121	6	67.0±8.8	.053
FaCE total	10	43.7±6.2	9	43.7±6.2	.997	7	49.6±6.4	.104	6	50.0±6.5	.098
FaCE oral function	10	50.0±9.9	9	44.9±10.0	.445	7	42.8±10.4	.325	6	38.2±10.7	.127
FaCE social function	10	52.5±11.6	9	55.5±11.7	.669	7	74.1±12.1	**.007**	6	68.7±12.4	.051

FaCE, Facial Clinimetric Evaluation; FDI, Facial Disability Index; PROMs, Patient-reported Outcome Measures; SFGS, Sunnybrook Facial Grading Score; p, significance of the mean value differences in relation to baseline mean value; R, remote call.*

both studies, Puls et al. and the present study show no further deterioration of the score from the start of FES, which declined immensely towards baseline. FES could therefore prevent a further deterioration in resting symmetry. In this case, patients could psychologically and socially benefit of a potential preservation of facial symmetry.[11,12] On the other hand, including a comparatively small amount of patients in both studies, increasing trends as for SFGS would have probably gained significance with a larger number of subjects.

Tuncay *et al.* investigated the effect of FES in 32 patients with acute facial nerve palsy over a period of three weeks. In parallel to our findings, Tuncay *et al.* also detected significant increases in the FDI body but also in the FDI social subscore.[14] The larger patient collective, compared to our study, likely reduced data scattering and increased significance. Moreover, Tuncay et al. also included patients with incomplete paresis and thus partially innervated facial muscles on the affected side. Thus, their participants might have experienced a noticeable improvement in functionality within a shorter period of time. In both studies, however, there was neither a deterioration in the social subscores, which were already severely reduced at baseline, nor a subjectively perceived improvement in the functionality of the patient's face during and after FES.[14]

Kim *et al.* evaluated automated image analysis with Emotrics to be suitable for evaluating the course of facial nerve palsy.[40] Their study showed both high interrater and intrarater reliability as well as significant intrasubject reliability between the paralysed and contralateral side for most of the investigated parameters. Interestingly, their study was not significant for neither BH nor PFH in side by side comparison. The latter did not show significance side differences in our study either. Contrastingly to our study Kim *et al.* also included patients with central as well as incomplete facial nerve palsy. Given that their patients might have had higher functionality of brow elevation on the palsy side, the lack of significance of BH between both sides of the face seems plausible.

Mastryukova *et al.* analysed the effects of FES on the zygomaticus muscle using MRI segmentation. The authors could detect an increase in muscular volume of the stimulated zygomaticus muscle in patients with complete denervation. However, most likely due to a small number of included patients, these results were not significant.[41]

Meincke *et al.* investigated the influence of FES on the CSA of the paralysed facial muscles using ultrasound imaging within the same pilot study.[26] In pairwise comparison, the CSA of the stimulated zygomaticus muscle increased, while other non-stimulated muscles, including the orbicularis oculi muscle, decreased significantly. In parallel, our findings suggest that PFH of the paralysed side worsened in the sense of an increasing eyelid difference while SA of the paralysed side improved. Since atrophy of the orbicularis oris muscle is essentially involved in the loss of tightness of the lower eyelid,[42] the results of Meincke et al. are consistent with the increase in PFH in our findings. Likewise, the increase in the CSA of the zygomaticus muscle as a functional muscle for smile movement may be related to the enlargement of SA. It is questionable why the BH of the unaffected side increased significantly. Guerreschi et al. describe common hyperactivity of the frontalis muscle of the unaffected side in patients with unilateral facial paralysis which could be responsible for increased brow elevation even in resting state.[11]

The recruitment of patients with complete peripheral facial nerve paralysis allowed us to study the isolated effect of FES without additional neural activity in the affected muscles. However, this strict inclusion criterion also means a smaller number of participants, making it difficult to draw conclusions about a larger collective. In addition, this pilot study design focused on the feasibility and tolerability of ES, which is why no control group or double blinding was planned. In order to prove unequivocal causality of FES on improvement of functionality and quality of life by means of score assessment, such steps are inevitably necessary. It is also probable that by stimulating not only the zygomaticus muscle but also a variety of additional affected facial muscles, general functionality and subjectively perceived training effects might improve even more.

Conclusions

To conclude, an FES protocol was applied that could be easily performed daily at home by the patients and confirmed its therapeutic safety. In addition, there were signs of an improvement in functionality and facial symmetry during the therapy. Based on these results, future controlled, randomised and double-blinded follow-up studies with a larger number of subjects are needed to continue investigation of FES in patients with facial nerve paralysis and confirm its potential effects based on our findings.

List of acronyms

BH, brow height
CE, commissure excursion
CNS, central nervous system
CSA, cross sectional area
ChDev, commissure height deviation
EMG, electromyography
FES, surface electrical stimulation
FaCE, Facial Clinimetric Evaluation
FDI, Facial Disability Index
PD, phase duration
PFH, palpebral fissure height
PNS, peripheral nervous system
PROMs, Patient-reported Outcome Measures
SA, smile angle
SFGS, Sunnybrook Facial Grading Score

Contributions

GFV, DA and WM were responsible for the study planning and design. OGL provided help with study financing and data interpretation. Patient recruitment, collection of gradings and scores, EMG and adjustment of the stimulation parameters during the clinical visits were mainly carried out by MG, AMK, JB, DA, GFV, OGL, JK and GM. Photographies were taken by AMK, JK, GM and JB. Data collection and ditisation was conducted by MG, AMK, JB, JK

and GM. Statistics were compiled by JK, GM and TL. JK designed the following digital graphics and wrote the article in close consultation with all co-authors.

Conflict of interest

JK, GM, MG, AMK, DA, JB, OGL and GFV have received stimulation devices and financial support for travel costs from MED-El, Innsbruck, Austria. OGL was supported by a grant from the DFG (GU-463/12-1) and MG received a grant by the Interdisciplinary Center for Clinical Research. The remaining authors have no conflicts of interest.

Ethics approval and consent to participate

The study was registered in the German Clinical Trials Register (DRKS00015015). The local institutional ethics committee approved the study (no. 550503/18). All patients provided written informed consent prior to inclusion.

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