Applicability of Selective Electrical Surface Stimulation in Unilateral Vocal Fold Paralysis

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Objective: Selective electrical surface stimulation (SES) of the larynx is not yet routinely considered therapy option in treatment of unilateral vocal fold paralysis (UVFP). Goal of this monocentric feasibility study was to provide systematic data on applicability of SES of intrinsic laryngeal muscles in UVFP under consideration of sensitivity and discomfort thresholds and nonselective side effects.

Methods: Thirty-two UVFP patients were included in the study. Symmetric triangular-shape, charge-balanced pulse widths (PWs) of 1, 10, 25, 50, 100, 250, and 500 milliseconds (ms) were tested with increasing amplitudes (AMPs). The stimulation was delivered as a train of five pulses using square surface electrodes. Selective laryngeal responses were examined by flexible laryngoscopy. Nonselective side effects (swallowing reflex, coughing, different severity degrees of unspecific strap muscle/platysma response) were judged by observation.

Results: Selective laryngeal response could be triggered in 28/32 (87.5%) patients during respiration/rest and in 26/32 (81.3%) patients during phonation. The most effective PWs for the selective eliciting of selective bilateral vocal fold adduction are comprised between 50 and 100 ms in combination with an average AMP comprised between 7.1 and 7.2 mA.

Conclusion: Our results indicate that, in UVFP patients, PWs comprised between 50 and 100 ms in combination with a median AMP between 7.1 and 7.2 mA are expected to deliver in >75% of the cases a specific, effective, and safe bilateral adduction of the VF.

Key Words: Electrical laryngeal stimulation, vocal fold paralysis, atrophy, voice therapy. **Level of Evidence:** 3

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INTRODUCTION

Unilateral vocal fold paralysis (UVFP) treatment approaches generally aim to improve glottal closure during phonation and vocal function. Yet, the standard treatment for UVFP is based on surgical intervention, voice therapy (VT), or a combination of the two.¹ Voice exercises may help improving the voice quality (VQ); however, present studies lack objective evidence demonstrating the benefit of VT.² Surgical approaches include different techniques of injection laryngoplasty, external vocal fold (VF) medialization (thyroplasty type I), and reinnervation.

Although functional electrical stimulation (ES) has been often used for the therapy of paralyzed muscles, its

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Laryngoscope 131: September 2021 E2566 implementation in UVFP therapy is unconventional. So far, selective electrical surface stimulation (SES) has been applied for treating a number of benign laryngeal diseases, muscle tension disorders,^{3,4} benign VF lesion,⁵ and presbyphonia.⁶ Up to now, only few papers reported on its effectiveness for the treatment of UVFP.^{2,7,8} Concerning its use in UVFP patients, it is expected that SES helps preventing atrophy of denervated muscles and supports the nerval regeneration process.⁷ In 2008, Ptok and Strack reported on the results of 69/90 (after exclusion of 21 data sets for various reasons) UVFP patients (onset between 2 weeks and 6 months prior therapy) receiving 3 months traditional voice exercise treatment alone (VE) or accompanied by ES. In the ES group, VF irregularity decreased significantly more than in the VE group, whereas maximum phonation time (MPT) assessment failed to detect differences between the two groups.⁷ Perez et al. published on the therapeutic effects of synchronous ES in UVFP patients with paralysis onset between 10 and 24 months before therapy start.⁸ Twenty patients (7 men and 13 women) were recruited to this study, and 10 patients (3 men and 7 women) concluded the study. MPT, jitter, shimmer, and harmonics-to-noise ratio showed a significant improvement after 10 ES sessions of 30 minutes performed once per week for 10 consecutive weeks. No significance was observed for F0. No safety issues were reported.⁸ Although the results of the aforementioned studies are promising, the systematic use of SES in laryngeal diseases is currently very limited, most likely due to the complexity of the laryngeal physiology, which makes

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extremely difficult to determine a combination of parameters able to generate a therapeutic neuromuscular stimulation through superficial electrodes without causing undesirable side effects.

The goal of this monocentric study is to provide systematic data on the applicability of SES in UVFP therapy. The effects of SES have been assessed in terms of VF adduction at respiration/rest visually via laryngoscopy. In addition, sensitivity, discomfort thresholds, and any undesirable side effects (swallowing, coughing, unspecific strap muscle/platysma response) have been documented for the different combinations of amplitude (AMP) and pulse width (PW).

METHODS

Study characteristics

The data presented in this article were generated between November 2018 and February 2020 at the Medical University of Vienna within an open-label, prospective, monocentric, case-seriesbased clinical investigation, approved by the ethics committee (EC number 2046/2017). The study is published on the German Clinical Trials Register (Deutsche Register Klinischer Studien).

Population

Thirty-two adult subjects diagnosed with UVFP were enrolled into the study (Table 1). At the time of enrollment, the UVFP mean duration from the first diagnosis was 15.4 (SD 57.3) months (mos). No clinically relevant coughing, sleeping, and/or respiratory problems were reported by the patients at the time of enrollment. No subjects reported more than mild swallowing problems based on the Sydney Swallow Questionnaire or the MD Anderson Dysphagia Inventory. Laryngeal electromyography (LEMG) was performed in 7/32 (22%) patients at enrollment.

Stimulation

Surface stimulation was performed using STMIsola (BIOPAC Systems, Inc. Germany). Symmetric triangular-shape, chargebalanced PW of 1, 10, 25, 50, 100, 250, and 500 ms were tested with increasing AMPs between 1 and 20 mA. We started by administering a PW of 100 and went down to 1 and performed thereafter the measurement at 250 and 500 ms to avoid that the administration of the longest PWs could cause a carry-over effect potentially biasing the results with shorter PWs. Generally, the administration of PWs lower than 25 was a rare event because, if we saw an unspecific strap muscle/platysma response, coughing and/or swallowing reflexes, or the patient-reported discomfort at 25 ms, we did not try shorter PWs to reduce the burden for the patient. The stimulation was delivered as a train of five pulses. Two wet surface square electrodes of 40×28 mm (anode and cathode, respectively) were placed by the principal investigator (B.S.-S.) on the region corresponding to each thyroarytenoid muscle by means of neck palpation, fixed in place with a neck brace and connected to the external stimulator. Initially, the sensitivity (the minimal AMP at which the patient perceives the stimulation) and the discomfort (the AMP at which the stimulation does trigger discomfort/pain) thresholds were detected. The sensitivity threshold describes for each administered PW the lowest AMP at which the patient felt the stimulation. It was exclusively assessed by means of patient's feedback, but it was generally repeated starting from 0 mA up and again from 5 mA down to 0, to confirm the first result. The stimulation parameters causing undesirable side effects were documented, such as those triggering the

means of flexible XION video laryngoscopes connected to the software DiVAS by XION Medical (version 2.8.3-build30, Berlin, Germany). In short, videos were taken to record the patient breathing normally at rest and during phonation of the vowel /i:/ in presence and in absence of ES. These videos were then used for offline assessment and confirmation of the online assessment performed by two medical doctors and one technician during the stimulation. The stimulation was considered successful only when it elicited bilateral VF adduction sufficient to cause their adduction at rest and/or during phonation. VQ during phonation in absence and in presence of stimulation was not assessed. The occurrence and, if so, the severity of unspecific strap muscle/platysma response, coughing, and/or swallowing reflexes were judged by observation.

unspecific strap muscle/platysma response (grade 1 = mild superfi-

Statistical Analysis

Data were analyzed using IBM SPSS statistics software (Version 25; IBM, New York) for medical statistics. Descriptive statistics were used to report demographic data. Due to the non-Gaussian distribution and limited sample size, nonparametric analysis was conducted. Distribution of continuous data was described using mean with standard deviation and median (min, max). Qualitative data are presented as absolute and relative frequencies. The Friedman's (Fr) test was used to determine overall significant differences across the PWs (ms). When the overall *P*-value indicated significant difference (P < .05), a post hoc Wilcoxon signed-rank test for paired data with Bonferroni correction was used to determine which pairs were significantly different. All tests were two-sided, with alpha = 5%.

RESULTS

Population

Because LEMG was performed only in 7/32 (22%) patients, the potential effects of different types of nerve injuries on the stimulation results could not be verified. We could not determine whether different etiologies could affect the stimulation outcomes because, as depicted in Table 1, in the majority (17/32; i.e., 53.1%) of the cases, the UVFP was caused by iatrogenic injury during thyroid surgery, whereas patients suffering from UVFP with other etiologies were present in relative percentage of 6% or lower. This great imbalance among the etiology groups would have severely biased any comparisons.

Sensitivity Threshold

The AMP values for the sensitivity threshold assessed at the various PWs are shown in Table 2. Independently from the applied PW, the median sensitivity threshold was below 5 mA. Fr analysis detected a significant decrease in the AMP required to reach the sensitivity threshold when a PW of 1 ms was compared respectively with PW of 10, 25, 50, 100, 250, and 500 ms (Fr = 59.9, df = 6, P < .0001).

| TABLE 1. | | | | | | |
|---|-----------------------|----------------------|------------------------|-----------------|--|--|
| Patients' Characteristics. | | | | | | |
| Parameter | Absolute No. of pts.* | Relative No. of pts. | Mean ± SD [†] | Median (Min-Max | | |
| Gender | | | | | | |
| Female | 16 | 50% | | | | |
| Male | 16 | 50% | | | | |
| UVFP | | | | | | |
| Right | 12 | 37.5% | | | | |
| Left | 20 | 62.5% | | | | |
| UVFP etiology | | | | | | |
| latrogenic, thyroid surgery | 17 | 53.1% | | | | |
| latrogenic, other surgeries | 6 | 18.8% | | | | |
| Idiopathic | 6 | 18.8% | | | | |
| Cancer | 1 | 3.1% | | | | |
| Traumatic | 1 | 3.1% | | | | |
| Acute respiratory infection | 1 | 3.1% | | | | |
| Regular alcohol consumption | | | | | | |
| None | 12 | 37.5% | | | | |
| Currently | 20 | 62.5% | | | | |
| Smoking | | | | | | |
| Never | 15 | 46.9% | | | | |
| Formerly | 9 | 28.1% | | | | |
| Currently | 8 | 25.0% | | | | |
| Age (yr) | | | 54.0 ± 14.3 | 55.5 (25–78) | | |
| Body mass index (BMI; kg/m [†]) | | | 26.2 ± 5.7 | 26.0 (18–46) | | |
| Duration of UVFP (mo) | | | 15.4 ± 57.3 | 1.7 (0–314) | | |

Absolute frequencies for each parameter are given for all the patients and in brackets for the patients suffering from UVFP. *Total no. of patients (N = 32) for which the stimulation was assessed.

[†]Standard deviation.

Discomfort Threshold

The AMP values for the discomfort threshold assessed at the various PWs are shown in Table 3. Independently from the applied PW, the median discomfort threshold was below 17 mA.

Unspecific Responses to SES

SES triggered a swallow reflex in 41% and 44% of the assessed patients when a PW of 250 or 500 ms, respectively, was used (Table 4). Swallow reflex was triggered by SES in 22% of the patients at a PW of 50 ms and in $\leq 6\%$ of the patients tested with a PW of 100 ms or ≤ 25 ms.

A total 34.3% of the patients tested with a PW of 100 ms experienced a SES-elicited coughing reflex within an AMP range of 5 to 19 mA.

Grade 1 platysma response occurred in 34% of the patients assessed with a PW of 500 ms; in 44% with a PW of 250 ms; in 66% with a PW of 100 ms; and in a percentage above 70% in patients assessed with shorter PWs (Table 5). In general, the use of shorter PWs was accompanied by an increased percentage of unspecific strap/platysma muscle responses.

Grade 2 platysma response occurred in 19% of the patients assessed with a PW of 500 ms; in 25% with a PW of 250 ms; in 50% with a PW of 100 ms; and in a

| TABLE 2. |
|---|
| Sensitivity Threshold: Amplitudes (AMPs) (Mean ± SD) for All Pulse Widths (PWs) Measured for All Patients. |

| | | All Patients* | |
|----------|------------------|-----------------------|------------------|
| PW in ms | No. of Pts.* (%) | $Mean \pm SD^\dagger$ | Median (Min–Max) |
| 500 | 32/32 (100%) | 1.8 ± 1.1 | 1.0 (0.5–5.0) |
| 250 | 32/32 (100%) | 2.2 ± 1.9 | 2.0 (1.0–10.0) |
| 100 | 32/32 (100%) | 2.1 ± 1.6 | 2.0 (1.0–7.0) |
| 50 | 32/32 (100%) | 2.3 ± 1.7 | 2.0 (1.0-8.0) |
| 25 | 27/32 (84%) | 2.4 ± 2.1 | 2.0 (1.0–10.0) |
| 10 | 31/32 (97%) | 2.5 ± 2.0 | 2.0 (1.0–10.0) |
| 1 | 30/32 (94%) | 3.7 ± 1.8 | 3.0 (2.0–10.0) |

^{*}No. of responsive patients for which the stimulation was assessed. [†]Standard deviation.

percentage above 59% in patients assessed with shorter PWs (Table 5). The use of shorter PWs was accompanied by an increased percentage of unspecific strap/platysma muscle responses.

Grade 3 platysma response occurred in 6% of the patients assessed with a PW of 500 ms; in 13% with a PW of 250 ms; in 34% with a PW of 100 ms; and in a percentage above 38% in patients assessed with shorter PWs (Table 5). The use of shorter PWs was accompanied by an

increased percentage of unspecific strap/platysma muscle responses.

Selective Laryngeal Responses During SES

At respiration/rest, the stimulation was delivered in burst of five pulses for 2 seconds followed by 2-second

| TABLE 3. Discomfort Threshold: Amplitudes (AMPs) (Mean ± SD) for All Pulse Widths (PWs) Measured for All Patients. | | | | |
|--|------------------|---------------------------------------|------------------|--|
| | All Patients* | | | |
| PW in ms | No. of Pts.* (%) | $\text{Mean} \pm \text{SD}^{\dagger}$ | Median (Min-Max) | |
| 500 | 15/32 (47%) | 8.8 ± 5.2 | 8.0 (3.0–20.0) | |
| 250 | 18/32 (56%) | 9.7 ± 6.1 | 8.5 (3.0–30.0) | |
| 100 | 18/32 (56%) | 10.7 ± 6.3 | 10.0 (3.0–28.0) | |
| 50 | 20/32 (63%) | 9.8 ± 4.9 | 9.0 (4.0–24.0) | |
| 25 | 14/32 (44%) | 9.3 ± 5.3 | 8.0 (4.0-21.0) | |
| 10 | 14/32 (44%) | 11.2 ± 4.7 | 9.0 (5.0–20.0) | |
| 1 | 10/32 (31%) | 15.2 ± 6.2 | 14.0 (7.0–24.0) | |

 $^*\text{No.}$ of responsive patients for which the stimulation was assessed. $^{\dagger}\text{Standard}$ deviation.

| TABLE 4. |
|---|
| Undesirable Swallowing Reflex: Amplitudes (AMPs) (Mean ± SD) for All Pulse Widths (PWs) Measured for All Patients. |
| |

| | | All Patients* | | |
|----------|------------------|----------------------------|------------------|--|
| PW in ms | No. of pts.* (%) | Mean \pm SD [†] | Median (Min-Max) | |
| 500 | 14/32 (44%) | 6.9 ± 1.7 | 3.0 (5.0–10.0) | |
| 250 | 13/32 (41%) | 8.5 ± 5.9 | 3.0 (3.0–26.0) | |
| 100 | 1/32 (3%) | n.a. | n.a. | |
| 50 | 7/32 (22%) | 10.1 ± 7.2 | 3.0 (5.0–24.0) | |
| 25 | 1/32 (3%) | n.a. | n.a. | |
| 10 | 2/32 (6%) | n.a. | n.a. | |
| 1 | 2/32 (6%) | n.a. | n.a. | |

^{*}No. of responsive patients for which the stimulation was assessed. [†]Standard deviation. pause to cause VF adduction within the duration of a single inspiration cycle of about 0.5 and 2 seconds, not to cause any potential respiratory distress to the patients. During phonation, the stimulation was delivered continuously for a maximum of 3 seconds. We observed that it did not prevent the physiological minimal opening of the posterior third of the VFs that normally occur during phonation and was well tolerated by all patients.

VF Adduction at Respiration/Rest

Only in 4/32 (12.5%) assessed patients, no stimulation parameter combination could be found, able to stimulate a bilateral adduction of the VFs at respiration/rest. Of the 28/32 (87.5%) responsive patients, 71% responded with a PW of 50 ms and 75% with a PW of 100 ms within a median AMP range of 6 to 7 mA (Table 6). The response strongly decreased with shorter PWs (26% with 25 ms, 4% with 1 ms, and 14% with 10 ms) and moderately decreased with longer PWs (64% with 250 ms and 46% with 500 ms).

VF Adduction at Phonation

Only in 6/32 (18.8%) assessed patients no stimulation parameter combination could be found able to stimulate a bilateral adduction of the VFs at respiration/rest. Of the 26/32 (81.2%) responsive patients, 77% responded with a PW of 50 ms and 88% with a PW of 100 ms within a median AMP range of 6 to 7 mA (Table 7). The response strongly decreased with shorter PWs (27% with 25 ms, 15% with 10 ms, and 0% with 1 ms) and with longer PWs (50% with 250 ms and 35% with 500 ms). Independently from the applied PW, the median AMP range remained stable between 5 and 7.5 mA.

DISCUSSION

This study has been designed to assess the most effective stimulation parameter to obtain SES-induced bilateral adduction of the VFs in absence of or in combination with limited side effects/unspecific laryngeal muscle activation and discomfort.

TABLE 5.

Undesirable Nonselective Strap Muscle/Platysma Response Reflex Threshold: Amplitudes (AMPs) (Mean ± SD) for All Measured Pulse Widths (PWs) for All Patients.

| PW in ms | | Grade 1 | | | Grade 2 | | | Grade 3 | | |
|----------|-----------------------------------|---------------|---------------------|-----------------------------------|---------------|------------------|-----------------------------------|----------------|------------------|--|
| | No. of Responsive Patients (%) | Mean ± SD* | Median (Min–Max) | No. of Responsive Patients (%) | Mean ± SD* | Median (Min–Max) | No. of Responsive Patients (%) | Mean ± SD* | Median (Min–Max) | |
| 500 | _ 11/32 (34%) | 8.3 ± 1.9 | 9.0 (4.0–11.0) | 6/32 (19%) | 10.0 ± 2.3 | 9.5 (8.0–13.0) | 2/32 (6%) | n.a. | n.a. | |
| 250 | 14/32 (44%) | 7.1 ± 1.6 | 7.0 (4.0–10.0) | 8/32 (25%) | 8.4 ± 2.2 | 8.0 (6.0–13.0) | 4/32 (13%) | 15.7 ± 10.1 | 12.5 (8.0–30.0) | |
| 100 | 21/32 (66%) | 6.6 ± 2.7 | 5.0 (3.0–13.0) | 16/32 (50%) | 7.9 ± 2.9 | 7.0 (5.0–16.0) | 11/32 (34%) | 11.4 ± 6.4 | 10.0 (4.0–28.0) | |
| 50 | 23/32 (72%) | 6.3 ± 3.7 | 5.0 (3.0–20.0) | 19/32 (59%) | 8.1 ± 4.3 | 7.0 (4.0–22.0) | 16/32 (50%) | 9.4 ±4.8 | 8.5 (5.0–24.0) | |
| 25 | 24/32 (75%) | 5.6 ± 3.7 | 5.0 (2.0–18.0) | 19/32 (59%) | 6.9 ± 3.6 | 6.0 (3.0–20.0) | 14/32 (44%) | 8.3 ± 4.3 | 7.5 (5.0–21.0) | |
| 10 | 29/32 (91%) | 6.2 ± 3.7 | 5.0 (3.0–19.0) | 23/32 (72%) | 7.8 ± 3.0 | 7.0 (4.0–18.0) | 17/32 (53%) | 9.2 ± 4.2 | 8.0 (5.0–20.0) | |
| 1 | 27/32 (84%) | 9.1 ± 5.6 | 7.0 (2.0–30.0) | 20/32 (63%) | 11.2 ± 5.0 | 10.0 (6.0–26.0) | 12/32 (38%) | 13.4 ± 5.6 | 11.0 (7.0–24.0) | |

*Standard deviation.

TABLE 6.

Simultaneous Adduction of Both Vocal Folds (VFs) at Respiration/ Rest: Amplitudes (AMPs) (Mean ± SD) for All Pulse Widths (PWs) Measured for All Patients.

| | | All Patients* | | | |
|----------|------------------|---------------------------------------|------------------|--|--|
| PW in ms | No. of Pts.* (%) | $\text{Mean} \pm \text{SD}^{\dagger}$ | Median (Min-Max) | | |
| 500 | 13/28 (46%) | 8.5 ± 6.6 | 7.0 (3.0–28.0) | | |
| 250 | 18/28 (64%) | 7.5 ± 4.8 | 7.0 (3.0–25.0) | | |
| 100 | 21/28 (75%) | 7.2 ± 4.9 | 6.0 (3.0–27.0) | | |
| 50 | 20/28 (71%) | 7.1 ± 2.5 | 7.0 (3.0–15.0) | | |
| 25 | 8/28 (28%) | 7.6 ± 4.5 | 6.0 (3.0–17.0) | | |
| 10 | 4/28 (14%) | 7.5 ± 1.0 | 7.0 (7.0–9.0) | | |
| 1 | 1/28 (4%) | n.a. | n.a. | | |

^{*}No of responsive patients for which the stimulation was assessed. [†]Standard deviation.

| TABLE 7. |
|--|
| Simultaneous Adduction of Both Vocal Folds (VFs) at Phonation: Amplitudes (AMPs) (Mean ± SD) for All Pulse Widths (PWs) Measured for All Patients. |

| | | All Patients* | | | |
|----------|------------------|-----------------------|------------------|--|--|
| PW in ms | No. of Pts.* (%) | $Mean \pm SD^\dagger$ | Median (Min–Max) | | |
| 500 | 9/26 (35%) | 8.3 ± 7.7 | 7.0 (3.0–28.0) | | |
| 250 | 13/26 (50%) | 6.2 ± 1.8 | 7.0 (3.0–10.0) | | |
| 100 | 23/26 (88%) | 6.5 ± 1.7 | 6.0 (3.0–9.0) | | |
| 50 | 20/26 (77%) | 6.9 ± 1.7 | 7.0 (3.0–10.0) | | |
| 25 | 7/26 (27%) | 6.4 ± 2.4 | 5.0 (4.0–11.0) | | |
| 10 | 4/26 (15%) | 7.7 ± 1.0 | 7.5 (7.0–9.0) | | |
| 1 | 0/26 (0%) | n.a. | n.a. | | |

^{*}No. of responsive patients for which the stimulation was assessed. [†]Standard deviation. The assessment of both discomfort threshold and side effect/unspecific laryngeal muscle activation occurrence showed that SES is a safe procedure within a relatively large range of PW (1–500 ms) and AMP (1–20 mA).

In agreement with the findings of previous studies,^{2,7,8} we showed that the use of a PW of 50 or 100 ms in combination with a median AMP comprised between 5 and 10 mA delivers the best results in terms of bilateral adduction of the VFs, while ensuring the lowest rate of side effects and/or discomfort (Fig. 1).

The discomfort threshold up to 20 mA was reached only in about 50% to 60% of the assessed patients with PWs \geq 50 ms and in 30% to 40% with PWs below this value (Table 3); these data may be misleading because we stopped the stimulation whenever it causes a side effect, and this occurred in the majority of the cases before the stimulation became truly uncomfortable for the patients.

We showed that SES-induced coughing reflex did not represent a serious problem for the stimulation within the applied setting. On the contrary, we showed that swallowing reflex can be easily induced in about 40% of the patients when using a PW of 250 or 500 ms, suggesting that these PWs could be clinically relevant for the treatment of diseases for which the induction of swallowing reflex may be beneficial.⁹ Because the swallow induction was obtained with a mean AMP range comprised between 6 and 8 mA, it is expected to be safe and below the discomfort threshold for most of the patients. In addition, at least the PW of 250 ms was able to induce the bilateral adduction of the VFs at respiration/rest or during phonation in more than 50% of the responsive patients and this may be a further advantage for stroke patients.

We observed that the administration of ES with a PW of 50 ms is capable to effectively induce a bilateral adduction of the VFs at respiration/rest or during phonation in 71% and 77% of the responsive patients,



Fig 1. Bilateral adduction of the vocal folds (VFs) while ensuring the lowest rate of side effects and/or discomfort.

respectively (Table 6). However, this property is lost by stimulations delivered at lower PWs. For instance, for PWs ≤ 25 ms, grade 1 platysma response occurred between 64% and 91%, grade 2 between 59% and 72%, and grade 3 between 38 and 53% of the assessed patients.

For stimulations delivered within a PW range between 50 and 250 ms, the median sensitivity threshold is found between 1.0 and 2.0 mA, whereas relevant unspecific laryngeal muscle response is observed with a median AMP between 8 and 11.5. We showed that with stimulations delivered within this PW range, the most effective bilateral adduction of the VFs either at respiration/rest or during phonation can be elicited with a median AMP between 6 and 7.5 mA effectiveness point of view. This finding strongly suggests that it is possible to use SES to induce VF adduction within an AMP range below the discomfort threshold of the majority of the patients suffering from UVFP.

Based on our results, it should be concluded that the use of PWs shorter than 50 ms is mostly ineffective and accompanied by relevant side effects. The use of 500 ms too is expected to have a low efficacy and be consistently accompanied by increased swallowing reflex. On the contrary, the use of a PW comprised between 50 and 250 ms has shown the highest effectiveness accompanied with the lowest rate of side effects for the patients. The choice of the PW within this range should be taken considering the characteristics of the single patients and the presence of comorbidities for which, for instance, the induction of a swallowing reflex may be of use.

Although we showed that the success of SES-induced bilateral adduction of the VFs at respiration/rest or during phonation in absence or in presence of limited unspecific reactions is strictly related to applied PW and AMP, it also depends on the used electrodes and their correct placement and size. For this study, we used 40×28 -mm surface electrodes accurately placed cranially to the thyroid cartilages to avoid unspecific stimulation of the surrounding strap muscles and unspecific stimulation of either swallowing or coughing reflex.¹⁰

The major limitation of the study is the limited sample size in which it has been conducted, which, in particular, prevented us to systematically assess the effects of potential biases on the results of the stimulation, such as the UVFP etiology or duration. Concerning the potential effects of smoking, alcohol consumption, or a cumulative effect of both on the stimulation results, we could not draw statistically relevant conclusions because of the limited sample size, although our preliminary results seem to indicate that abstemious patients are less sensitive to the stimulation than patients drinking alcohol at least occasionally. At the same way, smokers seem to show readier strap muscle response at PWs ≤50 ms than nonsmoker patients (data not shown). Still, these preliminary findings require confirmation in a larger cohort to be generalized.

Our results support the possibility to selectively induce bilateral adduction of the VFs via surface electrodes if the following conditions are met:

• The chosen electrodes have a surface sufficiently large to deliver the stimulation without causing damages to

the tissue but sufficiently small to reduce the occurrence of unspecific activation of other laryngeal muscles beside the adductor muscles.

- The electrodes are accurately placed to promote the selective activation of the adductor muscles.
- The applied PW and AMP combination are precisely assessed to avoid discomfort or unspecific stimulation of the laryngeal muscles, while inducing synchronous adduction of both VFs.

The long-term effect of SES regarding the influence on the nerval regeneration and UVFP outcome needs to be investigated in future studies.

CONCLUSION

SES can be used to selectively induce bilateral adduction of the VFs in UVFP patients both at respiration/rest and phonation. Careful preassessment of the applied combination (PW, AMP) is necessary to avoid the unspecific activation of strap muscles rather than intrinsic laryngeal muscles or the occurrence of swallow reflex.

Our results indicate that, in patients suffering from UVFP, PWs comprised between 50 and 100 ms in combination with a median AMP between 7.1 and 7.2 mA are expected to deliver in >75% of the cases a specific, effective, and safe bilateral adduction of the VF.

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AUTHOR CONTRIBUTIONS

Annabella Kurz contributed to data analysis, literature research, and preparation of the manuscript. Matthias Leonhard and Guan-Yuh Ho performed the SES and educated the patients about the treatment. Ines Kansy also educated the patients about the treatment. Berit Schneider-Stickler performed the SES, educated the patients about the treatment, and performed literature research and study supervision.

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