

Effect of pulse waveforms on movement amplitudes and perceived discomfort in electric muscle stimulation in unresolved facial nerve palsy

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Abstract

Studies on the effects of the pulse waveform used in electrical muscle stimulation on the activations and perceived discomfort of the waveform have been mainly executed on limb muscles with variable results, however, knowledge of these effects on facial muscles is currently lacking.

We studied two waveforms, square wave and sinusoidal wavelet, for the activation of the frontalis muscle in 9 individuals with unresolved facial nerve palsy. Both waveforms produced a movement

that was greater in amplitude compared with the maximal voluntary movement of the affected side in 8 participants and at least as great as the healthy side's maximal voluntary movement in 4 participants. Both waveforms were equally successful in producing movements, and there was no significant difference in perceived discomfort ratings between the two waveforms. These findings will be useful for the future development of neuroprosthetic applications for reanimating facial muscles using electrical stimulation. Trial registration: ClinicalTrials.gov NCT03496025, registration date March 19, 2018.

Introduction

Facial nerve palsy has several consequences for the affected individual. For example, deficits in blinking and eye-closure predispose to corneal damage. Weakness in facial muscles also causes difficulties in eating, drinking and speaking because the mouth does not close properly.

Furthermore, loss of facial symmetry complicates social communication, which in turn may affect quality of life [1]. The most common form of facial nerve palsy, the Bell's palsy or idiopathic facial nerve palsy, accounts for more than half of all peripheral facial nerve palsies [2], and affects about 25 in 100,000 individuals annually [3]. The aetiology of Bell's palsy is unknown. Facial nerve palsy may also be caused by tumours or infections. The natural outcome of Bell's palsy is quite favourable with about 70 percent of patients recovering completely [2, 3]. Other aetiologies, however, have variable and often poorer prognoses. Prednisolone has been shown to improve the outcome and shorten the recovery time in Bell's palsy [4-7] and has become an established treatment modality in the acute phase. In a residual palsy, botulinum toxin can be used to improve rest symmetry and to treat synkinesis [8]. Different surgical interventions may be warranted in unresolved palsies to assist eye-closure and to improve rest and movement symmetry [9-12]. However, many of these surgical techniques are very demanding and are only performed in the most severe cases. Hence, other treatment options to improve the facial function in residual

palsies should be considered, especially in patients who are not candidates for the use of current surgical techniques.

The main indication for the use of functional electrical stimulation (FES) is in neuroprosthetics and rehabilitation in upper motor neurone lesions [13]. In lower motor neurone lesions, such as peripheral facial nerve palsy, the feasibility of FES is thought to be limited because the denervated muscle fibres undergo atrophy and lose their excitability. However, even in such cases, FES has shown potential for muscle regeneration and muscle fibre excitability [14, 15]. In a peripheral facial nerve palsy the denervation may not be complete even if the muscle appears clinically paralysed and in these cases it can be possible to produce movement by electrical stimulation [16]. Currently, there is no substantial evidence on the benefits of electrical stimulation for the rehabilitation of facial nerve palsy [17], although some studies have suggested that it might be beneficial [18]. A different approach to the use of electrical stimulation for the restoration of facial function is the idea of a neuroprosthesis, where muscle activation is measured from the healthy side of the face and this information is then used to stimulate the impaired side. This technique is referred to as facial or electrical pacing, and it has been studied in several animal models since the 1970's [19-26]. The principle of facial pacing has also been demonstrated in humans in an experimental paralysis of the frontalis muscle [27].

FES often causes experiences of discomfort at various levels, which is an important factor to consider when designing these systems. The discomfort caused by different types of stimulation pulses regarding pulse duration and pulse waveform has been studied quite extensively in limb muscles [28-32]. In these studies, longer (0.3 ms) symmetrical biphasic square pulse were preferred to the shorter (0.05 ms) asymmetrical biphasic square pulse [28]. Biphasic pulses were

evaluated to be more comfortable than monophasic pulses in upper and lower limb muscles [29]. A sine wave produced the desired activation of the quadriceps muscle in healthy individuals with the lowest current compared with the square wave and Russian wave stimulation [30]. In contrast, two other studies found no difference in discomfort levels when comparing sine, saw tooth and square waveforms or sine and square waveforms, respectively [31, 32]. In summary, findings vary between studies. The face has been shown to have a lower sensory threshold when compared with the limbs [33], which further underlines the importance of stimulation tolerability. Moreover, facial muscles have different fibre type compositions compared with limb muscles with a preponderance of fast type two fibres [34, 35], which may have an effect on their electrical stimulation characteristics.

Besides safety and tolerability issues, the development of facial pacing technology also has technical requirements. It should be possible to filter off the stimulus signal possibly coupled to the electromyography (EMG), which is the most common method used to detect the muscle activation of the healthy side [36]. From this aspect, a stimulation signal whose power is focused on a narrow frequency band would be ideal [37].

The aim of this study was to electrically stimulate the frontalis muscle of individuals with an unresolved facial nerve palsy with two different pulse waveforms, square pulse and enveloped sine pulse (sinusoidal wavelet), and investigate their effects on the muscle activation and the perceived discomfort. Due to its anatomical location, the activation of the frontalis muscle is easy to measure, and its stimulation does not significantly spread to other facial muscles [16, 38] which makes it an ideal target muscle to study the effects of the stimulation.

Methods

Participants

We recruited 11 participants (7 females, 4 males), aged 24 to 62 years ($M = 46$, $SD = 11$) from a pool of 14 people from our previous study investigating electrical stimulation for unresolved peripheral facial nerve palsy [16]. Three individuals from the original pool who had had either a symmetrical function of the frontalis muscle ($n=2$) or showed no movement response to electrical stimulation ($n=1$) were excluded from the study. The grade of the palsy was assessed with the Sunnybrook facial grading system (SB) [39]. SB is a composite score that evaluates the rest symmetry, symmetry of the movements and synkinesis ranging from zero (total paralysis) to one hundred (symmetrical facial function) and the symmetry of different voluntary movements is evaluated on a five-grade scale where 1 corresponds to no movement and 5 corresponds to complete (symmetrical) movement. The participants' SB score ranged from 25 to 63 ($M = 43$ $SD = 15$). Among the 11 participants, two showed a symmetrical function of the frontalis muscle (SB subscore 5) and were excluded from the analysis. For the nine participants that were included in the study, the SB subscore for frontalis muscle ranged from 1 to 4 ($M = 2.3$, $SD = 0.9$). The study was approved by the Ethics Committee of Pirkanmaa Hospital District. The participants signed a written consent form concerning the participation and a separate consent form for the subsequent use of the video material.

Equipment

The stimulator used in the experiment was developed and manufactured at the Faculty of Medicine and Health Technology, Tampere University [37]. The safety of the stimulation hardware complies with the standard IEC 60601-2-10 "Particular requirements for the basic safety and essential performance of nerve and muscle stimulators". The maximal stimulus current amplitude was limited to 48 mA, and the voltage amplitude was limited to 100 V. The pulse duration was

controlled so that the energy of the single pulse did not exceed what was set in the standard. Two pulse waveforms were used: a square wave and a sine wave with eight periods and a sinusoidal envelope (sinusoidal wavelet) (Fig. 1). The waveform of the Nth sinusoidal wavelet pulse x_N as a function of time t is described in Equation (1), where A is the pulse amplitude, f_c is the high carrier frequency, T_d is the pulse duration, and f_p is the pulse repetition frequency.

$$\begin{aligned}
 x_N(t) &= c(t)m_N(t) \\
 c(t) &= A \sin(2\pi f_c t) \\
 m_N(t) &= \begin{cases} \sin(2\pi f_m t), & (N-1)T_p \leq t < (N-1)T_p + T_d \\ 0, & (N-1)T_p + T_d \leq t < NT_p \end{cases} \quad (1) \\
 f_m &= \frac{1}{2T_d}, \quad T_p = \frac{1}{f_p}
 \end{aligned}$$

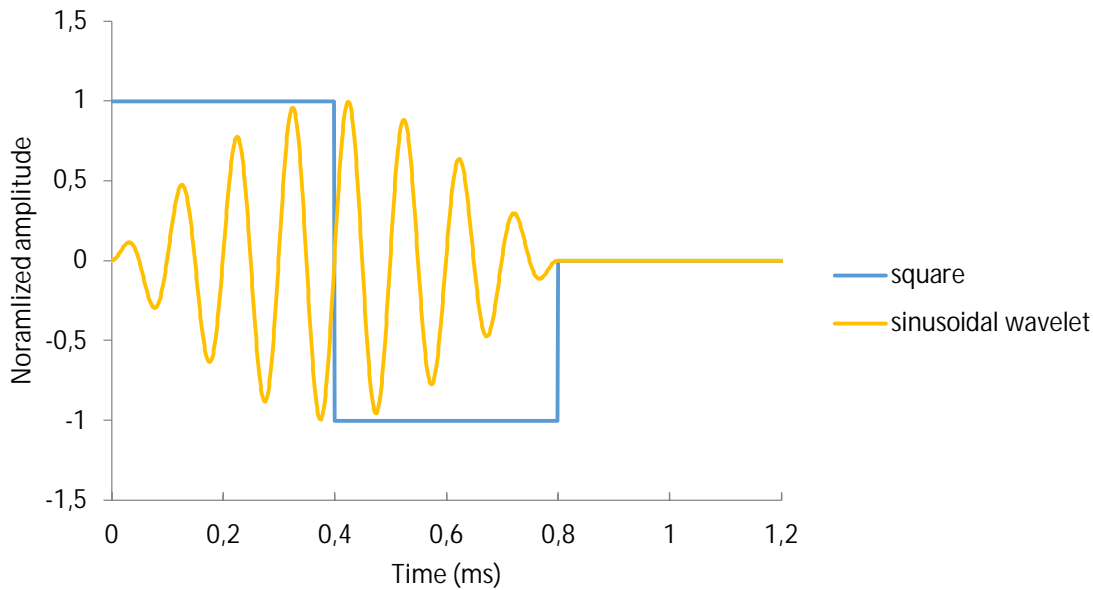


Figure 1. Illustration of the waveforms used.

The duration of a single stimulus pulse (the positive and negative phases combined for square waves or the duration of the envelope pulse for the sinusoidal wavelet) was 0.8 ms, which was repeated with a frequency of 250 Hz to produce a 1000 ms long stimulus pulse train. These

stimulation parameters were chosen on the basis of explorative pilot testing in which we studied the effects of stimulation pulse frequencies between 100-250 Hz on perceived discomfort. We found that the high frequency stimulation was experienced as more comfortable than lower frequencies, and thus chose to use 250 Hz pulse repetition frequency. Commercial adhesive pre-gelled electrodes (Quirumed®, GMDASZ Manufacturing Co., Ltd., Shenzhen, China) were used for the stimulation. The surface area of the electrodes was manually trimmed to 1.5 cm². The skin was prepared with an alcohol swab before the adhesion of the electrodes.

Procedure

Two surface electrodes were attached on the frontalis muscle with 1 cm inter-electrode distance (Fig. 2) in accordance with previously described guidelines for EMG measurements [40]. Two surface EMG electrodes were attached on the healthy side to corresponding sites and their reference electrode was placed on the ipsilateral mastoid process for the purpose of another study. For measurement purposes, to calibrate the actual distances to the video recording, four ticks were marked with a skin marker pen on the participant's face, one on the forehead medially to the electrodes, and the other ipsilateral to the side of stimulation on the cheek below the eye, with a distance of 70 mm, on both sides of the face. Before the stimulation, the participant performed five maximal voluntary eyebrow raises. The frontalis muscle was then stimulated with the two previously described waveforms in separate sets in a counterbalanced order. The stimulation was repeated three times at each amplitude level, with approximately 1-second inter-stimulus intervals. The stimulation was started at a 1.0 mA amplitude level for the square pulse and at a 2.0 mA amplitude level for the sinusoidal wavelet pulse. The amplitude was increased in 0.5 mA and 2.0 mA steps, respectively, until the participant wanted to discontinue the stimulation (e.g., because of discomfort), or the maximal stimulation amplitude (24 mA for the square wave and 48 mA for the sinusoidal wavelet) was reached. As the intensity of muscle activation is

dependent not only on the current amplitude, but also on the amount of charge injected into the muscle, the amplitudes have to be different for the two waveforms of the stimulus to achieve the same stimulation result. After reaching the sensory threshold level (i.e., the lowest amplitude level at which the participant felt the stimulus), the participant rated the level of discomfort caused by the stimulation on a scale ranging from 0 (not at all uncomfortable) to 10 (extremely uncomfortable) after each stimulation amplitude level. The voluntary and stimulated movements were recorded with a Panasonic V750 digital video camera with 50 frames per second.

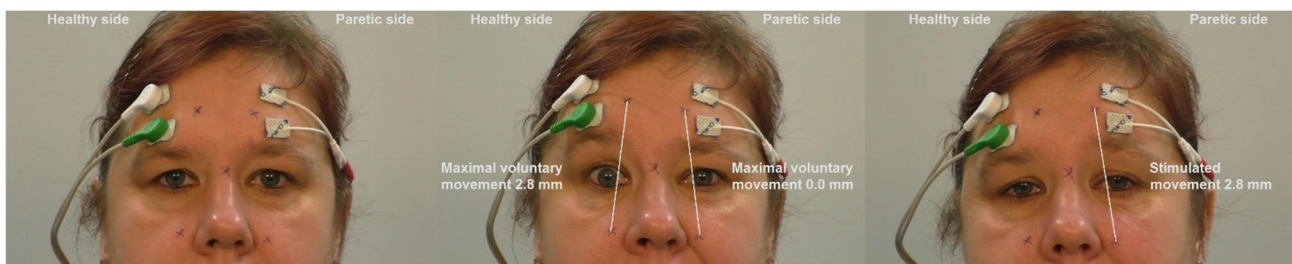


Figure 2. Participant's face at rest (left), showing maximal voluntary eyebrow raise (middle) and maximal eyebrow raise by electrical stimulation (right). EMG electrodes were attached on the healthy side of the face in order to measure EMG signals with stimulation artefact for another study. Photographs published with permission.

Data analysis

The voluntary and stimulated movements were evaluated offline from the video recordings. The amplitude of the maximal voluntary movement (MVM) of both sides and the stimulated movement was measured with a digital ruler using the ticks, when applicable, or anatomical landmarks. The MVM was defined as the average of five maximal voluntary eyebrow raises. The stimulated movements were compared to both healthy and to paralysed side's MVM. As the MVM varies among individuals, the movement used for the analysis was the percentage proportion of

the stimulated movement compared to the MVM. Data analyses were done using SPSS® statistical software, version 22.0 (SPSS Inc., Chicago, IL, USA) and Matlab®, version R2016a (The MathWorks, Inc., Natick, MA, USA). Wilcoxon signed-rank test was used for statistical analysis. The linear regression of the movement response to stimulation was computed by first extracting the linear range for each participant and each waveform separately by only including the data points between 10% and 90% of the maximum movement range achieved by the stimulation. Linear regression was used to fit a line to the data points, and the R^2 statistic and p-value of the regression were computed.

Results

The MVM of the frontalis muscle of the unaffected side ranged from 2.8 mm to 8.4 mm (Mean±SD 5.0 mm±1.9 mm). The MVM of the paralysed side ranged from 0.0 mm to 5.7 mm (Mean±SD 1.4 mm±2.3 mm), or 0% to 87% of the healthy side's MVM (Mean±SD 31%±30%).

The stimulation with both square wave and sinusoidal wavelet produced a better movement compared with the affected side's MVM in all but one participant. In 4 out of 9 participants, both square pulse and sine wavelet pulse produced a movement that was at least of the same amplitude as the MVM of the unaffected side (Table 1). The maximal stimulated movement amplitudes and the corresponding discomfort ratings are presented in Table 1.

Table 1. Maximal voluntary and stimulated movements of the paralysed side presented as the percentage of the healthy side's maximal voluntary movement (MVM) together with the discomfort ratings and stimulation amplitudes at these levels. The grey background indicates movements greater than the paralysed side's MVM.

Participant	Voluntary movement of the affected side	Stimulated movement of the affected side		Discomfort rating		mA	
		Square wave	Sinusoidal wavelet	Square wave	Sinusoidal wavelet	Square wave	Sinusoidal wavelet
1	0%	≥ 100%	≥ 100%	2	1	7	34
2	68%	68%	54%	4	7	5	20
3	18%	76%	85%	7	6	5.5	32
4	8%	58%	57%	8	8	6	36
5	24%	92%	80%	6	9	4.5	22
6	5%	≥ 100%	≥ 100%	2	2	3.5	14
7	44%	70%	59%	5	5	5.5	24
8	87%	≥ 100%	≥ 100%	7	8	3.5	20
9	24%	≥ 100%	≥ 100%	5	7	6	20

The movement produced by the stimulation was at least 50% of the healthy side's MVM in all participants with both waveforms. Figure 3 shows the number of participants in which the stimulation of the affected side reached 50% to 100% movement from the MVM of the unaffected side with the given waveform. The Wilcoxon signed-rank test showed no statistically significant differences in movement amplitude between the stimulation waveforms.

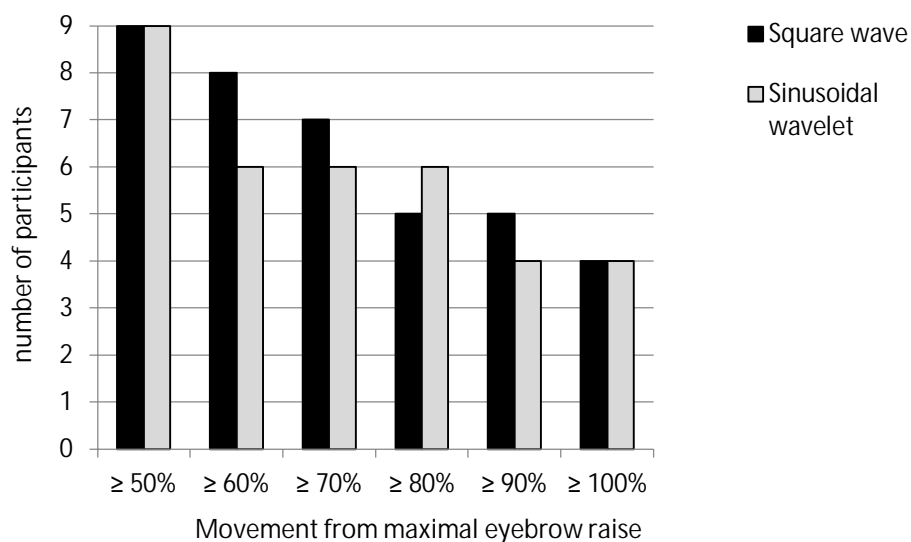


Figure 3. Number of the participants in whom the stimulated movement of the paralysed side reached the given percentage of the healthy side's maximal voluntary movement.

The discomfort rating at the level of the stimulated movement that was the individual's maximum (5 participants) or $\geq 100\%$ of the healthy side's MVM (4 participants) ranged from 2 to 8 (Mean \pm SD 5.1 \pm 2.1) for the square wave and from 1 to 9 (Mean \pm SD 5.9 \pm 2.8) for the sinusoidal wavelet (Table 1). The Wilcoxon signed rank test showed that the discomfort evaluations were not significantly different between the two waveforms at the level that produced either the individual's maximal movement or $\geq 100\%$ of the healthy side's MVM ($Z = 1.4, p = 0.167$). The discomfort ratings at each movement amplitude level are presented in Figure 4. To test the effects of the presentation order of the waveforms on the discomfort ratings, discomfort scores were categorised according to the order the waveforms were presented. The Wilcoxon signed rank test showed that the presentation order had a statistically significant effect on the discomfort ratings, $Z = 2.2, p < 0.05$.

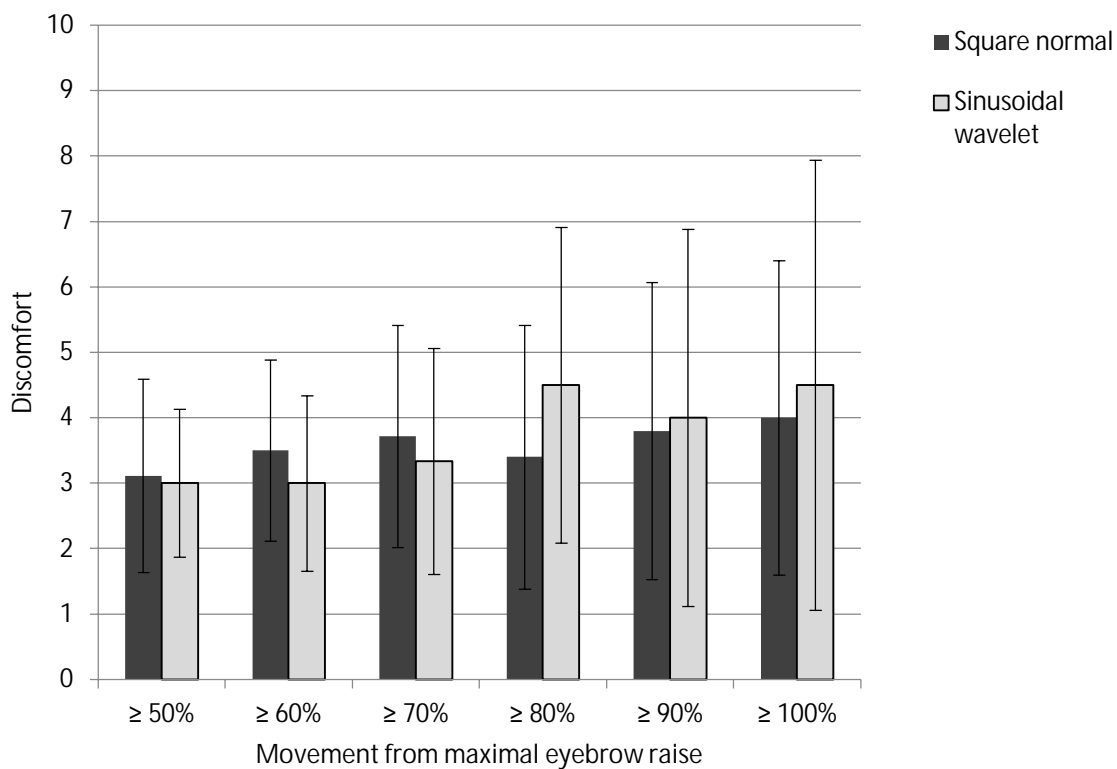


Figure 4. Mean discomfort ratings at each movement amplitude level.

The current amplitude at the level of the stimulated movement that was the individual's maximum (5 participants) or $\geq 100\%$ of the healthy side's MVM (4 participants) ranged from 3.5 to 7.0 mA (Mean \pm SD 5.2 mA \pm 1.2 mA) for the square pulse and from 14 mA to 36 mA (Mean \pm SD 24.7 mA \pm 7.5 mA) for the sinusoidal wavelet pulse. In those four participants whose maximal stimulated movement reached $\geq 100\%$ of the healthy side's MVM, the current amplitude needed to produce this activation ranged from 3.5 mA to 7 mA (Mean \pm SD 5.0 mA \pm 1.8 mA) for the square pulse and from 14 mA to 34 mA (Mean \pm SD 22.0 mA \pm 8.5 mA) for the sinusoidal wavelet pulse (Table 1).

A linear regression analysis was performed to study the relationship between the movement amplitude and the stimulation amplitude. The linear regression was statistically significant ($p \leq 0.05$) with all but a single participant for both waveforms. The R^2 values and levels of statistical significance of the regression are presented in Table 2. A typical response curve for the sinusoidal wavelet (participant 9) between the stimulation waveform amplitude and the range of introduced movement is presented in Figure 5.

Table 2. Linear regression R^2 statistics for the pulse waveforms with the participants. The level of statistical significance of the regression is denoted with asterisks (* for $p \leq 0.05$, ** for $p \leq 0.01$, and *** for $p \leq 0.001$).

	square	sinusoidal wavelet
1	0.92**	0.99***
2	0.98***	0.97*
3	0.88*	0.81
4	0.87	0.93**
5	1.00*	0.84*

6	0.93*	0.85*
7	0.92**	0.94*
8	0.90*	0.92**
9	0.99***	0.97*
\bar{x}	0.93	0.91
SD	0.05	0.06

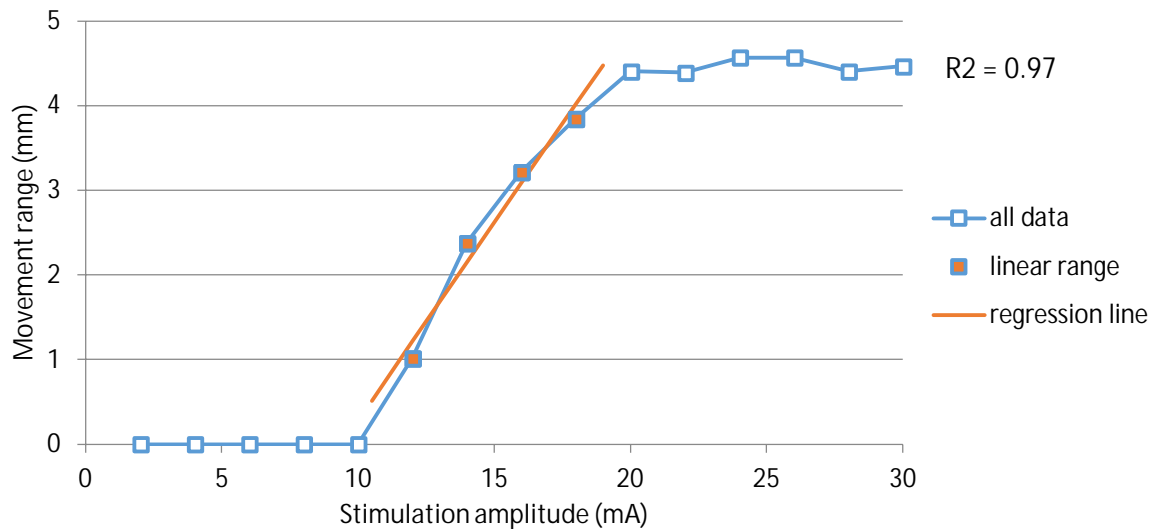


Figure 5. An example of the linear regression for the movement response to the sinusoidal wavelet stimulation waveform comprising pulses of a sine wave with eight periods and a sinusoidal envelope.

Discussion

The results show that stimulation with both waveforms produced a movement that was greater in amplitude compared with the maximal voluntarily produced movement of the affected side in 8 participants and at least as great as the healthy side's maximal voluntary movement in 4 participants. Both waveforms were equally successful in producing movements and there was no significant difference in perceived discomfort ratings between the two waveforms. As facial expressions are most often subtle, aiming for a maximal stimulated activation may not be necessary or even desired. Further, the stimulation produced a greater movement of the

paralysed side compared with the voluntary effort in 8 out of 9 participants. This suggests that the symmetry of the facial expression could be improved with the aid of electrical stimulation.

In this study, we investigated the activation of the frontalis muscle by electrical stimulation in individuals with an unresolved facial nerve palsy in which the stimulation had earlier been proved to produce movement. Consequently, it is noteworthy that activating facial muscles with electrical stimulation is not always feasible, specifically in cases where the muscle has no nerve supply [16].

Restricting the study to one muscle may be considered as a limitation since we do not know whether these results can be generalised to other facial muscles. This requires further investigation.

Tolerability is also an important issue in FES, especially in applications concerning peripheral facial nerve palsy, which is not associated with sensory loss. It is therefore crucial that the stimulation causes as little discomfort as possible. Previous studies on the effects of the stimulation waveform on the subjective discomfort ratings in limb muscles have had variable results [28-32]. To the best of our knowledge, the current study is the first to investigate the differences in tolerability of different pulse waveforms on the face in individuals with a peripheral facial nerve palsy. We found that the two waveforms did not differ significantly regarding the given discomfort ratings.

However, the order in which the waveforms were presented affected the discomfort ratings significantly in that the waveform presented first was perceived as being more uncomfortable.

This finding suggests that the stimulation felt more comfortable when the participants got used to the stimulation.

When comparing the muscle activations, both waveforms also performed equally well. The movement amplitude of at least 100% of the healthy side's MVM was reached in 4 out of 9 participants and reached at least 50% in all participants.

In addition to tolerability and safety, there are also technical requirements that need to be considered in the development of facial pacing technology. The technology should recognise the muscle activation of the healthy side with a very short delay. EMG is the most commonly used method for this [36]. One important concern is the artefact that the electrical stimulation inevitably creates to the EMG. Hence, the stimulation artefact should be easily filtered so that it does not corrupt the EMG. Our finding that neither of the waveforms studied was superior to the other with regard to tolerability and the capacity to produce movement is an important one since it suggests that these issues do not limit the choice of the waveform, and therefore technical factors can be more freely considered. From the studied waveforms, the artefact caused by the sinusoidal wavelet is significantly easier to filter as its power is focused on a narrow frequency band [37].

Furthermore, in prosthetic applications it is essential to develop a stimulation paradigm that functions predictably. In our study, the linearity of the produced movement of a reinnervated muscle in relation to the stimulation intensity proved to be very good, corresponding to the recruitment curves of a muscle with a normal innervation [41]. This is also a favourable finding when considering facial pacing technology.

Conclusion

Regarding the perceived discomfort, the capacity to produce movement and the linearity between the stimulation intensity and the elicited movement, the two waveforms studied were comparable. Thus, we conclude that the two waveforms would be equally suitable to be used in facial pacing technology and the choice of the waveform could be made by the technical requirements.

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