Eye Exercises for Treatment of Idiopathic Cranial Nerve VII Paresis: Pilot Study

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ABSTRACT: ***Background:*** To determine if fine-motor eye exercises can be used for treatment of unilateral, idiopathic cranial nerve VII paresis to improve rate of recovery. ***Methods:*** In this prospective, randomized controlled trial, eligible patients were randomized to perform fine-motor eye exercises (n=18) or to do no exercise (n=9) for a period of four weeks. Orbicularis oculi muscle strength was measured in paretic and unaffected eyes at baseline, two weeks and four weeks using an Orbicularis Oculi Pressure Sensor. ***Results:*** The average initial strength of the paretic orbicularis oculi muscle was 34±10 mm Hg compared to the unaffected muscle which was 103±17 mm Hg at baseline (n=27). By four weeks, patients who performed eye exercises improved more than those who did not (74.4 versus 47.4 mm Hg, p=0.029). While there was some loss to follow-up, 63.8% of patients performing exercises (7/11) achieved functional recovery at four weeks compared to 12.5% (1/8) of those who did not (p=0.059). Steroids and antivirals were found to have independent positive effects on improving functional outcome. ***Conclusions:*** Eye exercises have a potential role in the treatment of idiopathic cranial nerve VII paresis and warrant consideration in the management of these patients.

RÉSUMÉ: Exercices oculaires dans le traitement de la paralysie idiopathique du VIIe nerf crânien : une étude pilote. ***Contexte :*** Le but de l'étude était de déterminer si les exercices oculaires de motricité fine peuvent être utilisés pour traiter la paralysie du VIIe nerf crânien afin d'améliorer le taux de guérison. ***Méthode :*** Les patients éligibles à cette étude prospective, randomisée et contrôlée, ont fait soit des exercices oculaires de motricité fine (n = 18) ou aucun exercice (n = 9) pendant quatre semaines. La force du muscle orbiculaire de l'œil a été mesurée au niveau de l'œil parétique et de l'œil normal avant l'intervention, après deux semaines et après quatre semaines au moyen du Orbicularis Oculi Pressure Sensor. ***Résultats :*** Avant l'intervention, la force initiale moyenne du muscle orbiculaire de l'œil parétique était de 34 ± 10 mm Hg par rapport à 103 ± 17 mm Hg (n = 27) pour le muscle non atteint. Quatre semaines plus tard, les patients qui avaient fait des exercices oculaires se sont améliorés plus que ceux qui n'en avaient pas faits (74,4 versus 47,4 mm Hg ; p = 0,029). Bien que certains patients aient été perdus de vue, 63,8% des patients qui ont fait les exercices (7/11) présentaient une récupération fonctionnelle après quatre semaines par rapport à 12,5% (1/8) de ceux qui n'avaient pas fait d'exercice (p = 0,059). Nous avons constaté que les stéroïdes et les antiviraux avaient des effets positifs indépendants sur l'amélioration fonctionnelle. ***Conclusions :*** Les exercices oculaires pourraient jouer un rôle dans le traitement de la paralysie idiopathique du VIIe nerf crânien et méritent d'être envisagés dans le traitement de ces patients.

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Idiopathic peripheral cranial nerve VII paresis was first described in 1821 by Sir Charles Bell and is sometimes also referred to as Bell's Palsy[1]. Loss of facial nerve function leads to facial disfigurement, increased salivation, alteration of taste as well as ocular complications. Decreased orbicularis oculi muscle strength can lead to ocular surface and eyelid problems such as epiphora, lagophthalmos, paralytic ectropion and exposure keratopathy. Loss of corneal protection can lead to corneal ulceration and potential blindness if treatment is delayed[2]. Treatment usually consists of a combination of eye lubrication, eyelid taping and, in severe cases, a tarsorrhaphy.

Cranial nerve VII (CN VII) paresis occurs with an incidence of approximately 20.2 cases per 100,000 people per year[3]. It can occur at any age but the highest incidence is in people between 15-45 years of age[4]. Cranial Nerve VII paresis typically has a sudden onset (i.e. within 24 hours) and its progression can be followed during the first seven to ten days. A large, observational study conducted in Copenhagen studied the natural history of 1,701 patients with CN VII paresis by examining patients weekly for the first six months and then monthly for the following six months. The CN VII paresis was diagnosed clinically and patients were followed over one year; if patients failed to return for follow-up visits they were questioned via telephone interview. They found that 71% of cases have complete, spontaneous recovery by six months after the onset[5]. Furthermore, they found that 85% of patients started to show signs of recovery within three weeks but only 3% recovered completely by two weeks and 27% by four weeks[5]. It is during this acute period, while the patient is not recovered, that ocular complications are more likely to occur.

One of the greatest limitations with treatment studies for CN VII paresis is that there is limited ability to measure and quantify

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facial nerve functions. Electromyography (EMG) testing, for example, can be done to monitor the blink reflex, facial compound muscle action potential and needle EMG evidence of denervation and reinnervation; but nerve degeneration can sometimes take 10-14 days to be detected[5]. Therefore, descriptive grading systems have been developed to monitor facial nerve paresis but these systems can produce inconsistent results. The House-Brackmann Grading System is the most commonly used grading scale. It was endorsed by the American Academy of Otolaryngology in 1985 and consists of six descriptive grading scales[2]. The Nottingham Scale incorporates linear measurements of facial asymmetry as a more objective measurement but requires several time consuming calculations. Recent treatment effect studies still use the House-Brackmann grading system or EMG as their primary outcome measure[6].

Although the etiology of idiopathic CN VII paresis is unknown, there have been several hypotheses proposed. There has been sporadic support for inflammation of the facial nerve being associated with paresis as well as HSV reactivation[2]. As CN VII paresis is a relatively rare disease and a large proportion of patients recover spontaneously, studies on treatment effects show varying results. Optimal treatment still remains controversial but has included observation, steroids alone, antivirals alone or combination of steroids and antivirals[6,7]. Dosages are typically Prednisone 1mg/kg for seven days and Acyclovir 800mg five times per day for seven to ten days or equivalent antiviral. As early as the 1940s, facial nerve exercises have been described and include gross-motor facial movements such as eyebrow raising, eyelid closure, whistling and blowing out of cheek done twice a day[8,9]. Recently, a renewed interest in neuroplasticity has re-ignited the idea of using facial exercises as a means of enhancing the neural output of the facial nerve.

Methods & Materials

The study protocol was approved by the Research Ethics Board at Queen's University and enrollment began in September 2007. All patients with unilateral, idiopathic CN VII paresis were identified from the Emergency Departments at Kingston General and Hotel Dieu Hospitals in Kingston, Ontario. Patients were required to be greater than 16 years-of-age and within seven days of onset of the CN VII paresis. Exclusion criteria were previous CN VII palsy, bilateral idiopathic CN VII palsy, complicated or post-surgical CN VII palsy.

Informed consent was obtained from all study participants and examinations were performed at Hotel Dieu Hospital Eye Centre. The initial study visit included a full ophthalmic exam, baseline orbicularis oculi muscle strength measurements and randomization into treatment or control group.

The ocular examination included visual acuity, tonometry, confrontation visual fields, extraocular movement examinations, anterior segment and posterior segment examinations of both eyes. This included inspection for exposure keratopathy, corneal ulceration and lagophthalmos. Patients were treated with lubrication therapy as necessary. A full cranial nerve exam was also performed to rule out any other cranial neuropathies.

Orbicularis oculi muscle function was then quantified using a novel instrument developed at Queen's University[10]. This instrument, referred to as the OOPS (Orbicularis Oculi Pressure Sensor) consists of a surgical eyelid speculum that has been modified to forcibly open by means of a "frictionless" hydraulic cylinder (Figure 1). The cylinder is pressurized by a standard clinic sphygmomanometer placed in series with a damping chamber (Figure 2). The OOPS meter can measure the orbicularis oculi muscle strength during maximum volitional eyelid closure in millimeters of mercury (mm Hg) upon bilateral forced eyelid closure.

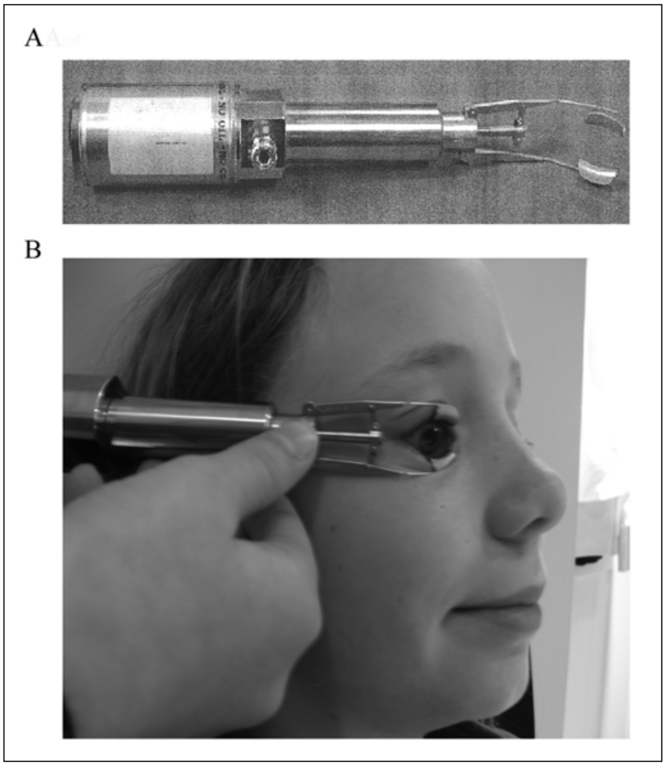

Figure 1: *(A) Surgical Eyelid Speculum of the Orbicularis Oculi Pressure Sensor (B) Speculum placed in a subject's eye.*

Figure 2: *Orbicularis Oculi Pressure Sensor (OOPS).*

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Table 1: Steps of Eye Exercises

Eye Targeting	Eyelid Peeking	Eyelid Press
1. Look down at target (e.g. thumbnail close to torso) for 5 sec 2. Close eyes gently for 5 sec 3. Repeat above 10 times	1. Close eyes gently for 3 sec 2. Open eyes slightly "to peek" for 3 sec 3. Repeat above 10 times	1. Close eyelids gently for 3 secs 2. Press eyelids "inward" and hold contraction for 3 sec 3. Repeat above 10 times

The patients' eyes were each anaesthetized with 1 drop of tetracaine 0.5%. Orbicularis oculi muscle strength was then measured three times during forced eyelid closure in both paretic and unaffected eyes using the OOPS meter. All six measurements were recorded.

At the end of the first visit, participants were asked to select an envelope that would assign them a study number and explain to them which arm of the study they were in. They were asked to not disclose that information on subsequent visits so that examiners would remain blinded to patient assignment. Those who were randomized to no exercises were provided with a copy of the informed consent and asked to comply with follow-up visits but not given any specific information on eye exercises.

Patients who were randomized to the eye exercise group received an instructional DVD and a daily log in their envelope. The DVD described and demonstrated exactly the same method of performing the eye exercises. It could be watched as many times as necessary in the convenience of their own homes. The daily log was used to record compliance with eye exercises and included a text version of the exercises as a daily reminder.

The eye exercise patients were asked to perform three sets of fine-motor eye exercises twice a day for a total of four weeks. The eye exercises included ten repetitions of eye targeting, eyelid peeking and eyelid press (see Table 1). These eye exercises take approximately three to four minutes to perform.

All patients were re-examined at two weeks and four weeks following baseline measurements. Orbicularis oculi strength measurement was repeated in the paretic and unaffected eyes on each visit. Using the same methodology as the baseline assessment, each was measured three times and all six measurements were recorded. Primary endpoint of complete recovery was proposed as 75% strength of unaffected eye as this corresponds with House-Brackmann recovery of 75-100%.

Data analysis was performed using IBM SPSS Statistics software (version 17 for Windows). Intraclass correlation coefficients were calculated to assess the repeatability of OOPS measurements within the same session; if repeatability was high, the three values would be averaged into one value for analysis. Paired samples t-tests were used to assess change in OOPS measurements of the control and paretic eye from baseline to two weeks, baseline to four weeks, and two weeks to four weeks. Repeated measures ANOVA was also performed but due to loss to follow-up the sample was small. Thus, the paired samples t-tests allowed us to maximize the comparisons between each of two time points. Change scores were calculated for both groups, and independent samples t-tests were used to compare the change in exercise and no exercise patients. Finally, linear regression analysis was used to test the independent contribution of eye exercises versus medication regimen. Data shown are Means±SD and were considered statistically significant if $p<0.05$.

Table 2: Demographic characteristics of patients (n=27)

Characteristic		Total patients (n=27)	No eye exercises (n=9)	Eye Exercises (n=18)
Age (Years)	Mean (SD)	48 (15.7)	49 (13.9)	47 (16.9)
	Range	16-75	29-64	16-75
Sex	Female	13 (48%)	4 (44%)	9 (50%)
	Male	14 (52%)	5 (56%)	9 (50%)
Medication	Steroid	11 (41%)	4 (44%)	7 (39%)
	Steroid+Antiviral	16 (59%)	5 (56%)	11 (61%)

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Table 3: Intraclass correlation coefficient of patients with CN VII paresis at baseline presentation

		Intraclass Correlation Coefficient	95% Confidence Interval	Significance (p-value)
No Exercise Subjects	Control Eye	0.83	0.58-0.96	<0.001
(n=9)	Paretic Eye	0.87	0.65-0.97	<0.001
Exercise Subjects	Control Eye	0.91	0.81-0.96	<0.001
(n=18)	Paretic Eye	0.96	0.92-0.98	<0.001
Total Subjects	Control Eye	0.89	0.80-0.94	<0.001
(n=27)	Paretic Eye	0.95	0.90-0.97	<0.001

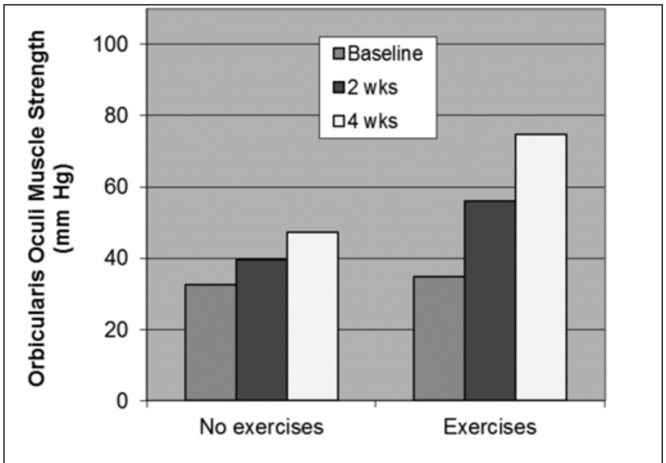
RESULTS

Twenty-seven patients met our inclusion criteria and were recruited for the study between September 2007 and March 2009. Eighteen patients were randomized to perform specific eye exercises and nine patients were randomized to no eye exercises. Participant demographics are shown in Table 2.

Measurements of Orbicularis oculi muscle strength were repeated three times to test for reliability of the orbicularis oculi pressure sensor (OOPS) measurements. The intraclass correlation coefficient (ICC) of control and paretic eyes was calculated at baseline, two and four weeks. Table 3 shows that all ICCs were very high at baseline; results were similar for the other time points and therefore not shown. The sets of three values were therefore averaged for each eye at each of the time points. The ICCs were very close regardless of whether the assessment was of the exercise, no exercise or combined groups. Therefore the reliability of the OOPS is high irrespective of which eye is being measured (control vs. paretic) and which group the patient was assigned to.

Orbicularis oculi muscles from control eyes were analyzed to quantify average otherwise healthy muscle strength and to test for repeatability of measurements over time. The average strength of the unaffected orbicularis oculi muscle was 102.7 ± 16.8 mm Hg at baseline (all patients, n=27). Using paired samples t-tests, no statistically significant differences were found between average orbicularis strength in the control eye from baseline to Week 2 (p=0.66) or from Week 2 to Week 4 (p=0.11). Therefore, measurements of the control eye muscles were stable and repeatable throughout the study period.

When comparing the strength of the paretic orbicularis oculi muscle, there was an overall increase muscle strength over time as measured by the OOPS. The average initial strength of the paretic muscle was 32.6±6.8mm Hg in the group randomized to no exercises and 34.9±11.7mm Hg in the exercise group. There were no significant differences in initial strength between the two groups. Using an independent samples t-test, muscle strength between the exercise versus no exercise group at two weeks trended towards an improvement (p=0.14). This trend attained statistical significance at four weeks (p= 0.029). At four weeks, the exercise group showed an increase in muscle strength by 27.3mmHg (~155%; Figure 3). A repeated measures ANOVA was also performed on these data and this pattern of change was statistically significant for the exercise group (n=11, p=<0.001) but not significant for the no exercise group (n=8, p=0.241). Although the sample was small for this analysis, the results do confirm the results of the independent samples t-tests.



	No Exercises (mm Hg ± SD) n=9	Exercises (mm Hg ± SD) n=18	Significance (p-value)
Paretic Eye:			
Baseline	32.6 ± 6.8	34.9 ± 11.7	0.585
2 wks	39.6 ± 17.6	56.1 ± 27.0	0.142
4 wks	47.4 ± 20.8	74.7 ± 27.0	0.029

Figure 3: *Average Orbicularis Oculi Muscle Strength in Paretic Eye over four weeks.*

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Table 4: Results of Linear Regression Analysis (Medications & Exercises)

Baseline to Two Weeks	Coefficient	95% CI	p-value
Constant			
Steroids + Antivirals (Reference Steroids Only)	16.4	1.7, 31.1	0.031
Exercise Group (Reference No Exercise)	13.7	-1.3, 28.7	0.071
Two to Four Weeks			
Constant			
Steroids + Antivirals (Reference Steroids Only)	-3.4	-15.6, 8.8	0.568
Exercise Group (Reference No Exercise)	11.7	-0.5, 23.9	0.058
Baseline to Four Weeks			
Constant			
Steroids + Antivirals (Reference Steroids Only)	11.2	-9.7, 32.0	0.275
Exercise Group (Reference No Exercise)	25.3	4.4, 46.1	0.021

Reference groups are coded as 0; comparison groups are coded as 1.

Finally, total muscle function over the unaffected eye was also compared and shown in Figure 4. Seventy five percent of total muscle function was determined to be clinically significant and consistent with functional recovery. At baseline, initial strength of the paretic orbicularis muscle was 32% and 34% of normal for the no exercise and exercise patients respectively. At four weeks, the strength of the paretic muscle had increased to 47% and 76% of muscle function for the no exercise and exercise patients, respectively. In absolute numbers, 1 out of 8 (12.5%) patients in the no exercise group and 7 out of 11 (63.8%) in the exercise group regained 75% of orbicularis muscle function at four weeks. While falling short of achieving statistical significance, this is likely due to the small sample size at Week 4 (p=0.059).

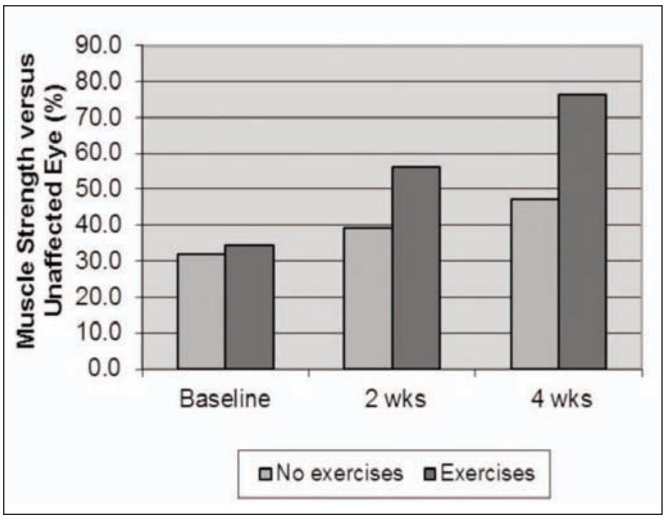

Figure 4: *Percentage of paretic orbicularis muscle function over time.*

Since all study patients had been treated with steroids and some with a combination of steroids and antivirals, there were two potential factors that could affect the final recovery of muscle strength. Linear regression analysis was therefore performed to evaluate whether medications versus exercises had a stronger or more important effect (Table 4). For the change from baseline to two weeks, combined steroid and antiviral treatment contributed to 16.4 mm Hg of muscle strength improvement compared to steroids alone (p=0.03), and exercise contributed 13.7 mm Hg as compared to no exercise (p=0.07). For change between two and four weeks, there is little effect of the medication (p=0.57) but a borderline significant effect of the exercises (p=0.06). For the change from baseline to four weeks, treatment with combined steroid and antiviral treatment contributed 11.2 mm Hg of muscle strength improvement compared to steroids alone (p=0.28), and exercise contributes 25.3 mm Hg as compared to no exercise (p=0.02), suggesting that overall, the exercise had the greater benefit.

Conclusions

The findings show that the Orbicularis Oculi Pressure Sensor (OOPS meter) is a novel instrument that can be used to perform quantifiable and reproducible measurements of orbicularis oculi muscle strength. It has previously been used in patients with myasthenia gravis and has been shown here to be an innovative tool for evaluation of patients with CN VII paresis. It can potentially be used to measure disease progression or recovery as well as to monitor efficacy of therapy. It is portable, safe and

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easy to use. In this study, we have evaluated its repeatability and it has been shown to produce consistent measurements during one session as well as over time.

Cranial nerve VII paresis can be a disfiguring disease and can lead to ocular complications. As patients are often healthy and high-functioning individuals, they are motivated to recover quickly. Oral medications such as antivirals are often prescribed, although their effect on the course of the disease remains controversial. In this study population, all patients were prescribed either a course of steroids or a course of steroids and antivirals. This is the preferred practice pattern amongst emergency department physicians in the Kingston area. Eye exercises have been recommended in the past as an adjuvant therapy but have not been formally studied.

In this study, orbicularis oculi muscle function was quantified in a population of patients with acute onset CN VII paresis using the Orbicularis Oculi Pressure Sensor. Due to the unilateral presentation of this disease, comparison of the paretic eye muscle strength to the unaffected eye muscle strength was used to calculate percentage of total muscle strength at different time points. At baseline, the average strength of the unaffected orbicularis oculi muscle was 102.7±16.8 mm Hg and of the paretic muscle was 34±10 mm Hg. Therefore the muscle strength in the paretic eye at baseline was on average 33.1% of its total muscle strength.

Recovery of orbicularis oculi muscle function was also studied over time and compared between patients performing fine-motor exercises to those that were not performing exercises. The orbicularis oculi muscle is innervated by CN VII and can be extrapolated as an indicator of CN VII recovery. Eye exercises are easy to perform and patients do not incur any additional cost. As shown in Figure 4, patients performing eye exercises did regain a greater amount of muscle function at two and four weeks compared to patients not performing eye exercises. It is during these initial few weeks that functional recovery is critical. The regression analysis suggested that there was substantial benefit of both exercise and medication in the first two weeks, but that over the following two weeks, the exercise continued to provide benefit while the medication did not. Over the four week period, the exercise had the greater positive effect on muscle strength.

The mechanism underlying the success of facial exercise in Bell's Palsy is not known. Facial weakness is the result of conduction block, axonal degeneration, or both. It is theoretically possible that exercise is a physiologic form of direct nerve stimulation that might stimulate axonal growth and /or remyelination through release of trophic factors. Alternatively the effect of exercise seen in this study may simply reflect the hypertrophy of existing intact muscle units. Serial MUNE (Motor Unit Estimate) testing would help to determine which of these proposed mechanisms is correct.

As CN VII paresis occurs in a small subset of the population, we were limited in the number of patients that we were able to enroll and therefore this study is still limited as a pilot study. We cannot confirm that patients in the no exercises group refrained from any type of eye exercises but it is unlikely that they would have performed specialized fine-motor exercises as prescribed in our treatment group. Patients in the treatment group were compliant with exercises until they recovered and then stopped. The concurrent usage of steroids and/or antivirals also added another confounding variable but we did not change patient's oral medications. Our linear regression analysis helps to interpret the relative contribution of medications versus exercise to the overall recovery rate. Each was found to have an independent positive contribution.

The findings ultimately demonstrate that there is a potential role for fine-motor eye exercises in the treatment of CN VII paresis. A larger study is warranted.

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