Published in final edited form as:

J Neuroimaging. 2015 July ; 25(4): 564–570. doi:10.1111/jon.12269.

A PILOT STUDY OF DIAGNOSTIC NEUROMUSCULAR ULTRASOUND IN BELL'S PALSY

EMAN A. TAWFIK, MD^a, FRANCIS O. WALKER, MD^b, and MICHAEL S. CARTWRIGHT, MD, MS^b

^a Department of Physical Medicine & Rehabilitation., Faculty of Medicine, Ain Shams University, Cairo, Egypt.

^b Department of Neurology, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC, USA.

Abstract

Background and purpose—Neuromuscular ultrasound of the cranial nerves is an emerging field which may help in the assessment of cranial neuropathies. The aim of this study was to evaluate the role of neuromuscular ultrasound in Bell's palsy. A second objective was to assess the possibility of any associated vagus nerve abnormality.

Methods—Twenty healthy controls and 12 Bell's palsy patients were recruited. The bilateral facial nerves, vagus nerves, and frontalis muscles were scanned using an 18 MHz linear array transducer. Facial nerve diameter, vagus nerve cross-sectional area, and frontalis thickness were measured.

Results—Mean facial nerve diameter was 0.8 ± 0.2 mm in controls and 1.1 ± 0.3 mm in patients group. The facial nerve diameter was significantly larger in patients than controls ($p = 0.006$, 95% CI for the difference between groups of 0.12–0.48), with a significant side-to-side difference in patients as well ($p = 0.004$, 95% CI for side-to-side difference of 0.08–0.52). ROC curve analysis of the absolute facial nerve diameter revealed a sensitivity of 75 % and a specificity of 70 %. No significant differences in vagus nerve cross-sectional area or frontalis thickness were detected between patients and controls.

Conclusions—Ultrasound can detect facial nerve enlargement in Bell's palsy and may have a role in assessment, or follow-up, of Bell's palsy and other facial nerve disorders. The low sensitivity of the current technique precludes its routine use for diagnosis, however, this study demonstrates its validity and potential for future research.

Keywords

Facial nerve ultrasound; cranial nerves; Bell's palsy; cranial neuropathy, vagus nerve

Corresponding author: Eman A. Tawfik, MD, Address: Department of Physical medicine & Rehabilitation, Faculty of Medicine, Ain Shams, University, Cairo, Egypt. Postal code: 11591. Tel.: +2-01005078368, Fax: +2-26830729, Eman_Tawfik@med.asu.edu.eg..

Disclosure: The authors have nothing to disclose.

Financial conflicts-of-interest: The authors have no conflicts of interest to disclose.

INTRODUCTION

Assessment of neuromuscular disorders through imaging of nerves and muscles using high-resolution ultrasound has become a common diagnostic technique, yet a variety of possible uses remain unexplored. One emerging area is its use in the assessment of cranial nerves. Four out of the 12 cranial nerves can be readily imaged using ultrasound.¹ These are the optic, facial, vagus, and spinal accessory nerves. The least studied is the facial nerve, and we are aware of only one published study.² No reference data of the nerve's size as measured by ultrasound has been published, and the value of ultrasound in the assessment of facial nerve lesions has not been conclusively determined.

Bell's palsy is the most common facial nerve disorder. Its exact etiology and pathogenesis are not well understood. One of the postulated theories is that the nerve gets entrapped and compressed in its bony canal as a result of epineural edema.³ Facial nerve ultrasound may provide a tool to assess the anatomical aspects of the nerve, complementary to the functional aspects assessed by electrodiagnostic studies. One of the questions previously raised regarding Bell's palsy is whether the facial nerve lesion occurs alone or as a part of a more generalized cranial polyneuropathy process. Several studies have found clinical association of Bell's palsy with other cranial neuropathies.⁴⁻⁶ If this proves to be true, it may help in our current understanding of the pathogenesis of such a common mononeuropathy.

The aim of this study was to image the extra-cranial portions of the facial and vagus nerves using high-resolution ultrasound to determine their ultrasonographic features in Bell's palsy and healthy individuals.

METHODS

Participants

The study included 20 healthy volunteers and 12 Bell's palsy patients. The volunteers were recruited from the local community and personnel in the medical center. Bell's palsy patients were recruited from departments of neurology, internal medicine, family medicine, and otolaryngology. The study was approved by the Wake Forest School of Medicine Institutional Review Board and a written informed consent was obtained from all participants.

Age, sex, race, height, and weight were documented, and body mass index was calculated. A brief history was obtained with emphasis on the presence or absence of diabetes and/or other comorbidities, date of onset of Bell's palsy, the side affected, and the treatment received. Clinical grading of Bell's palsy was conducted using the facial nerve grading system.⁷ The scale is divided into 6 grades with level 1 representing normal function and level 6 representing total paralysis. Any patient or volunteer with significant peripheral nervous system diseases, traumatic facial nerve lesions and/or parotid gland disorders was excluded from the study.

Ultrasound Techniques

The facial and vagus nerves were scanned on both sides in patients and control groups. Additionally, the frontalis muscle, as one of the facial nerve innervated muscles, was scanned bilaterally. Given the difficulties of disguising a clinical diagnosis of Bell's palsy, the examiners were un-blinded to the patient's diagnosis and to the laterality of the lesion. All images were obtained by one author (E.T.) using an Esaote ultrasound system (Biosound MyLab25; Esaote Group, Genoa, Italy) and an 18 MHz linear array transducer. Depth was set at 3 cm for scanning the facial nerve, 4 cm for scanning the vagus nerve, and 2 cm for scanning the frontalis muscle.

The subject was asked to lie in the lateral decubitus position on the side opposite the scanned site. For facial nerve scanning, the probe was placed just under the ear lobule with the mark on the probe directed toward the examiner's left side to image the nerve along its longitudinal course inside the parotid gland, after its exit from the stylomastoid foramen. A cross-sectional view of the facial nerve is difficult to obtain because of the small caliber of the facial nerve. The probe was kept perpendicular to the skin at all times with minimal pressure by the probe, to ensure accurate measurements. The facial nerve diameter was measured at the site of maximum thickness with measurement marks placed on the border of the hyperechoic edges of the nerve.

The vagus nerve was imaged in the carotid sheath, at the mid-neck level with the transducer placed transversely first at the level of thyroid cartilage and then moved laterally to identify the vagus nerve as a small rounded hypoechoic/or honeycomb structure wedged between the carotid artery and jugular vein. The cross-sectional area of the vagus nerve was measured using the trace function on the ultrasound device.

For scanning of the frontalis muscle, the transducer was placed transversely just above the eyebrow. Muscle thickness was measured with the marks extending from frontal bone to the lower edge of the subcutaneous tissue overlying the muscle. One patient had facial synkinesis and was additionally scanned using ultrasound M-mode, where the probe is positioned on the orbicularis oris muscle and the patient was asked to blink the ipsilateral eye. In addition to size measurements, the echogenicity and vascularity of the facial nerve, vagus nerve, and frontalis muscle were also observed and documented.

Prior to the in-vivo scanning of the facial nerve, cadaveric scanning was performed for the purpose of anatomical validation. Two fresh cadavers were used. In the first cadaver, the facial nerve was scanned using the same procedure and the same machine adjustments of in vivo imaging. After identification of the nerve by ultrasound, the site of the probe was marked on the skin and dissection was performed until reaching the expected level of the nerve. A transverse section of the structure suspected to be the nerve was then examined under a magnifying lens. In the second cadaver, the same procedure was followed but before dissection, the nerve was injected with blue ink, guided by ultrasound (Figure 1A), and then dissection was conducted until the injected structure was identified (Figure 1B). A transverse section of the stained structure was examined under a magnifying lens to identify its anatomical pattern.

Statistical Analyses

Statistical analysis was performed using MedCalc software (version 14.12.0). Data were calculated, tabulated and analyzed. Means and standard deviations of facial nerve diameter, vagus nerve cross sectional area, and frontalis muscle thickness were determined, along with calculation of side-to-side differences in measurements.

The measurements obtained from the left side in controls, and from the diseased side in patients were used in comparison and correlation studies. Student unpaired t-test was used to compare the sonographic measurements in controls and patient groups, in side-to-side comparisons, and in different subgroups of patients. The test was considered statistically significant when the p-value was < 0.05 . For more quantitative analysis, the 95 % Confidence Intervals (CIs) for the differences in means were also calculated in comparative studies.

A receiver-operating characteristic (ROC) analysis was performed to determine the sensitivity and the specificity of the absolute facial nerve diameter and the side-to-side difference in diameter.

The patients were subdivided according to gender, presence or absence of diabetes, severity, and chronicity into: females/males; diabetics/non-diabetics; grade 1-3/grade 4-6; and acute/chronic.

Pearson correlation coefficient was used to correlate facial nerve sonographic measurements with age, height, weight, body mass index, and disease duration. Again, a p-value < 0.05 was considered significant.

RESULTS

The study included 20 healthy volunteers and 12 Bell's palsy patients. Seven of the volunteers, and 8 of the patients were men. All the volunteers were Caucasians while the patients group included 8 Caucasians and 4 African Americans. The demographic data from both groups are shown in Table 1.

In the patient group, 2 out of the 12 patients were smokers and 4 had chronic diabetes. The disease onset ranged from 1 week to 6.9 years, with a mean duration of 12 months. Six were considered in the acute stage (onset ≤ 4 weeks) and 6 were in the chronic stage (onset > 4 weeks). Seven patients had left side paralysis and 5 had right side paralysis. Three patients had previous Bell's palsy attacks. All patients except 2 received steroid treatment for at least 2 weeks, and 2 of them received additional antiviral treatment. One patient had facial synkinesis.

Facial Nerve Results

Mean facial nerve diameter obtained from the left side in controls (20 facial nerves) was 0.8 ± 0.2 mm, while in patients the mean diameter of the diseased side (12 facial nerves) was 1.1 ± 0.3 mm, which was significantly larger than controls ($p = 0.006$, 95% CI = 0.12 - 0.48) (Table 2).

Side-to-side differences in diameter ranged from 0.0 to 0.7 mm with a mean of 0.2 ± 0.2 mm in controls, and ranged from 0.1 to 0.7 mm with a mean of 0.4 ± 0.2 mm in patients with a significant difference in means between controls and patients ($p = 0.030$, 95% $CI = 0.05 - 0.35$) (Table 2).

Side-to-side comparison of the diameter revealed non-significant differences in controls ($p = 0.777$, 95% $CI = -0.10 - 0.10$) (Table 3A), but revealed significant differences in patients ($p = 0.004$, 95% $CI = 0.08 - 0.52$) (Table 3B).

ROC curve analysis of the absolute facial nerve diameter revealed an area under the curve of 0.81. A cutoff value of 0.9 mm resulted in a sensitivity of 75 % and a specificity of 70 %. Using a cutoff value of 0.8 mm yielded higher sensitivity of 91.7 %, but reduced specificity to 50 %. (Figure 2A) For the side-to-side difference in diameter, the area under the curve was 0.72, a cutoff value of 0.2 mm yielded a sensitivity of 83.3 % and a specificity of 45 %. Using cutoff value of 0.3 mm raised the specificity to 70 % but, reduced sensitivity to 50 %. (Figure 2B).

Assessing variation in diameter in the different patients' subgroups (females/males; diabetics/non-diabetics; grade 1-3/grade 4-6; acute/chronic) revealed a non-significant difference in the 4 subgroups ($p > 0.05$).

Facial nerve sonographic features were consistent in all controls; it appeared as a thin tubular-like structure with a hypoechoic center and hyperechoic rim (Figure 3A). In patients, facial nerve echogenicity was normal in 7, hyperechoic in 4 (Figure 3B) and in 1 patient, the nerve's outer rim was blurred. Two out of the 4 patients in whom the nerve demonstrated increased echogenicity had disease duration > 1 year, the other 2 patients had disease duration 4 weeks, and 22 days respectively. The single patient with blurred outer nerve border was the only one in the very acute stage of the disease (1 week) among the 12 patients. No increase in Doppler signal of the facial nerve was noted in controls or patients.

Left side diameter in controls, and diameter of the diseased side in patients were not significantly correlated with age, height, weight, body mass index, or disease duration.

Vagus Verve Results

The mean cross-sectional area of the vagus nerve was larger in patients than in controls (5.5 ± 1.6 mm² in controls vs. 6.7 ± 2.3 mm² in patients) but the difference was not statistically different ($p = 0.122$, 95 % $CI = -0.21 - 2.61$) (Table 2). Side-to-side difference in cross-sectional area didn't significantly differ in patients compared to controls ($p = 0.364$, 95 % $CI = -0.54 - 1.54$) (Table 2). Also, side-to-side comparison of cross-sectional area in controls and patients revealed non-significant difference (Table 3A, 3B). Similar to facial nerve results, comparing the cross sectional area in different subgroups of patients revealed non-significant differences. The echogenicity of the vagus nerve was normal in all patients and controls, and no increased Doppler signal was detected.

Frontalis Muscle Results

Frontalis muscle thickness didn't significantly differ between patients and controls ($p = 0.558$, 95 % $CI = -0.49 - 1.09$) (Table 2). In patients, muscle thickness on the diseased side was minimally decreased compared to the healthy side, but the difference was not significant ($p = 0.753$, 95 % $CI = -1.24 - 1.04$) (Table 3B).

Other Findings

Results of scanning of 2 facial nerves in 2 cadavers demonstrated a tubular thin structure on dissection, with evidence of a focal stained area of the explored structure after ultrasound-guided ink injection in the second cadaver (Figure. 1B). Examination of a transverse section of the dissected structure from the 2 cadavers under a magnifying lens revealed the typical fascicular pattern of a nerve, denoting accurate localization of the facial nerve by ultrasound.

Other incidental ultrasound findings were observed during our study in 3 different patients. In 1 patient, the vagus nerve was identified in the anterior part of carotid sheath between the carotid artery and jugular vein instead of its usual posterior location, and in another patient, a lymph node was identified next to the left vagus nerve. M-mode ultrasound scanning in 1 patient with facial synkinesis demonstrated simultaneous contraction and relaxation of orbicularis oris with contraction and relaxation of orbicularis oculi (Figure 4).

DISCUSSION

In our study, facial nerve diameter and side-to-side difference in diameter was significantly larger in patients compared to controls. Also, the diameter of the affected side was significantly larger than that of the healthy side in patients group. These findings may reflect part of the pathogenesis of Bell's palsy. In Bell's palsy, the facial nerve is usually entrapped at the facial canal.⁸ Operative findings and contrast-enhanced magnetic resonance imaging have demonstrated nerve swelling and enhancement at /or proximal to the facial canal rather than distally.^{9,10} However, in our study, we detected enlargement of the facial nerve inside the parotid gland using ultrasound. Our findings are quite similar to previous results reported by Lo² and colleagues, who detected enlargement of the facial nerve in Bell's palsy, but their scanning site was more proximal than our site. They scanned the nerve at the mastoid region, and we scanned it inside the parotid gland. We think it is the main trunk of the nerve that is enlarged, and smaller branches are too thin to be visualized via ultrasound. Also, the two cadaveric dissections we performed confirmed that the nerve trunk is the captured part in the ultrasound image. Tracing the nerve more distally in the face was not possible because of the small size of distal branches. We think that our findings may reflect diffuse nerve inflammation and edema, rather than reflecting focal swelling from the entrapment.

The area under the ROC curve was 0.81 for the absolute diameter and 0.72 for the side-to-side difference in diameter denoting that facial nerve ultrasound can fairly discriminate between patients and controls. In ROC curve analysis, we chose cutoff values which yielded a relatively balanced sensitivity and specificity (0.9 mm for the absolute facial nerve diameter, and 0.2 mm for the side-to-side difference in diameter). These cutoff values are less than the "mean + 1SD" of the control values. Of note, Cutoff values = mean + 2SD of

the control values is associated with very low sensitivity (25 % for the absolute diameter, and 8.33 % for the side-side difference in diameter). These findings denote an overall low sensitivity of facial nerve ultrasound. The low sensitivity may be related to the small number of recruited patients or related to the fact that most of our patients especially the acute cases were scanned after they finished a steroid treatment course which might decreased the degree of nerve swelling. These findings suggest that this facial nerve ultrasound technique may be of limited usefulness for confirming a diagnosis, of Bell's palsy, but it remains possible that it may be useful for prognostication² and evaluation of other facial nerve disorders.

The nerve echo-texture in patients was similar to that in controls except in 5 patients. The increased nerve echogenicity noticed in 4 out of those 5 patients may be caused by inflammation or fibrosis, especially since two cases had disease duration >1.5 years. In 1 patient, the normal hyperechoic rim of the nerve was difficult to visualize and appeared blurred. This patient had the shortest disease duration among our patients (1 week). We believe this possibly may have been caused by epineural edema, which masked the nerve's outer border.

In our study, we found no evidence of vagus nerve pathology by ultrasound scanning in Bell's palsy patients. The lack of vagus nerve abnormalities may be from study size, timing, inability of ultrasound to detect involvement of the vagus nerve, or true lack of vagus nerve involvement.

Frontalis muscle thickness was not significantly different in patients compared with controls. Facial muscle atrophy is expected to occur as a result of axonal degeneration. We did not find such changes in our patients. This may be related to the fact that the frontalis muscle is a very thin muscle and atrophy may not be evident in ultrasound images. Similar results were obtained in a study by Volk et al¹¹ who evaluated the frontalis muscle using ultrasound, in addition to five other facial muscles in chronic Bell's palsy. Volk and his colleagues found evidence of muscle atrophy of all studied muscles on the paralyzed side, except for the frontalis and orbicularis oculi muscles.

The cadaveric portion of our study was essential because of the nearby structures which can potentially be confused with the facial nerve during scanning. Our results showed accurate identification of the facial nerve by ultrasound, and thus validate the scanning technique used.

We noticed other incidental ultrasound findings during our study, including a different anatomical location of the vagus nerve inside the carotid sheath, a cervical lymph node next to a vagus nerve, and involuntary simultaneous contraction of orbicularis oris with orbicularis oculi muscle (synkinesis). Although these findings were observed in only a few patients, they emphasize the additional value ultrasound can provide such as identification of anatomical variants, evaluation of structures surround affected nerves, and dynamic muscle assessment.

The study has some limitations including lack of blinding of the authors to the patient's diagnosis, small number of recruited patients. The small number of recruited patients is

attributed to the nature of the study, as we aimed to conduct a pilot study over 3 months prior to the application of the technique on a wider scale.

We did not test the reliability of facial nerve ultrasound. However, previous studies have examined the inter- and intra-rater reliability of nerve ultrasound in general and found it to be high, though this study did not include the facial nerve.¹² Another limitation is that we did not conduct electrodiagnostic studies, which perhaps would have provided important and correlating information for comparing the sonographic appearance of the nerve in axonal versus demyelinating lesions. It is worth noting, however, that in general, axonal neuropathies do not cause large ultrasonographic changes to nerves^{13,14}

In conclusion, this study demonstrates the ability of ultrasound to identify facial nerve enlargement in Bell's palsy. Although the sensitivity of facial nerve ultrasound demonstrated in our study is potentially a limiting factor for its use as a diagnostic tool, the significant difference in absolute diameter and side-to-side difference in diameter between patients and controls denotes the ability of ultrasound to detect facial nerve enlargement which may be useful in both Bell's palsy and potentially other conditions affecting the facial nerve. We recommend further validation of our results in large scale studies with the inclusion of a larger number of acute cases. Serial sonographic scanning of the nerve from disease onset until recovery, and assessment of inter- and intra-rater reliability, would also help advance this promising technique. Our study provides additional value as it establishes a starting point for reference values of facial nerve diameter and side-to-side difference in diameter in healthy individuals. Also, the study is the first to anatomically validate facial nerve scanning technique. These results may provide the basis for ultrasound use in the evaluation of the facial nerve in Bell's palsy and in other diseases affecting facial nerve.

Acknowledgments

None.

Funding sources: Dr. Cartwright has funding from NIH/NINDS (1K23NS062892) to study neuromuscular ultrasound.

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FIGURE 1. Facial nerve scanning in a cadaver

A) Ultrasound image of the facial nerve during ultrasound-guided ink injection. The needle (2 small black arrows) is advanced and directed toward the facial nerve (white arrow). B) Cadaver image after ultrasound guided ink injection and dissection. The explored structure is stained with the ink at a focal point (blue arrow). Subsequent examination of the stained structure revealed the typical fascicular pattern of a nerve.

FIGURE 2. ROC curves for facial nerve diameter and side-to-side difference in diameter

(A) ROC curve for facial nerve diameter. Cut off value of 0.9 mm for the absolute facial nerve diameter resulted in 75 % sensitivity, and 70 %, specificity. Area under the curve is 0.81.

(B) ROC curve for side-to-side difference in diameter. Cutoff value of 0.2 mm for the side-to-side difference in diameter resulted in 83.3 % sensitivity, and 45 % specificity. Area under the curve is 0.72.

ROC = receiver-operator characteristics.

FIGURE 3. Normal and abnormal sonographic features of the facial nerve in the longitudinal view

A) Normal facial nerve in a healthy volunteer: the nerve appears in as thin tubular structure with hypoechoic center and hyperechoic outer border (arrow) inside the homogenous parotid gland. The diameter measured 0.8 mm. B) Facial nerve in a patient: the nerve is enlarged and hyperechoic (arrow). The diameter measured 1.6 mm.

S.C. = subcutaneous.

FIGURE 4. M-mode ultrasound of orbicularis oris muscle in a patient with synkinesis

The image was captured while the patient blinked her eye. Top of the figure shows B-mode image of the transverse view of the orbicularis oris muscle with the position of the M-mode beam (vertical line) over the muscle. M-mode trace at the bottom of the figure shows contraction of the orbicularis oris (white arrows) during eye blinking.

Table 1

Demographic data of controls and patients.

Parameter	Controls (n=20)			Patients (n=12)		
	Min	Max	Mean	Min	Max	Mean
Age (years)	25	60	46	19	59	45
Height (cm)	157.5	210.8	172	154.9	177.8	165.5
Weight (Kg)	60.0	97.7	78.9	54.5	134.8	85.5
Body mass index	21.0	39.4	26.9	22.7	52.7	31.2

Table 2

Variation in sonographic measurements^a, and side-to-side difference in measurements in controls and patients.

Parameter	Controls (n=20)			Patients (n=12)			<i>P</i>	95 % <i>CI</i> ^b
	Min	Max	Mean±SD	Min	Max	Mean±SD		
FN diameter (mm)	0.5	1.3	0.8±0.2	0.7	1.6	1.1±0.3	0.006	0.12-0.48
VN CSA (mm ²)	2.0	9.0	5.5±1.6	4.0	10	6.7±2.3	0.122	-0.21-2.61
FT thickness (mm)	1.9	5.0	3.6±0.8	1.9	6.7	3.9±1.4	0.558	-0.49-1.09
FN diameter side-side difference (mm)	0.0	0.7	0.2±0.2	0.1	0.7	0.4±0.2	0.030	0.05-0.35
VN CSA side-side difference (mm ²)	0	3	1.0±1.0	0	6	1.5±1.9	0.364	-0.54-1.54

FN = facial nerve, VN = vagus nerve, CSA = cross sectional area, FT = frontalis, SD = standard deviation, CI = confidence intervals. Significant values are in bold.

^aMeasurements from the left side in controls were compared with measurements from the diseased side in patients.

^bThe 95 % *CI*s are the confidence of intervals for the differences in means between controls and patients.

Table 3A

Side-to-side comparison in control group.

Parameter	Right side (n=20)			Left side (n=20)			<i>P</i>	95 % <i>CI</i> ^a
	Min	Max	Mean±SD	Min	Max	Mean±SD		
FN diameter (mm)	0.6	1.0	0.8±0.1	0.5	1.3	0.8±0.2	0.777	-0.10-0.10
VN CSA (mm ²)	4.0	8.0	5.8±1.3	2.0	9.0	5.5±1.6	0.462	-1.23-0.63
FT thickness (mm)	2.0	5.2	3.4±0.8	1.9	5.0	3.6±0.8	0.372	-0.31-0.71

FN = facial nerve, VN = vagus nerve, CSA = cross sectional area, FT = frontalis, SD = standard deviation, CI = confidence intervals.

^aThe 95 % *CI*s are the confidence of intervals for the differences in means between the right and the left side.

Table 3B

Side-to-side comparison in patients group.

Parameter	Healthy side (n=12)			Diseased side (n=12)			<i>P</i>	95 % <i>CI</i> ^a
	Min	Max	Mean±SD	Min	Max	Mean±SD		
FN diameter (mm)	0.4	1.0	0.8±0.2	0.7	1.6	1.1±0.3	0.004	0.08-0.52
VN CSA (mm ²)	4.0	10.0	5.8±1.9	4.0	10.0	6.7±2.3	0.340	-0.89-2.69
FT thickness (mm)	2.1	5.8	4.0±1.3	1.9	6.7	3.9±1.4	0.753	-1.24-1.04

FN = facial nerve, VN = vagus nerve, CSA = cross sectional area, FT = frontalis, SD = standard deviation, CI = confidence intervals. Significant value is in bold.

^aThe 95 % *CI*s are the confidence of intervals for the differences in means between the healthy and the diseased sides.