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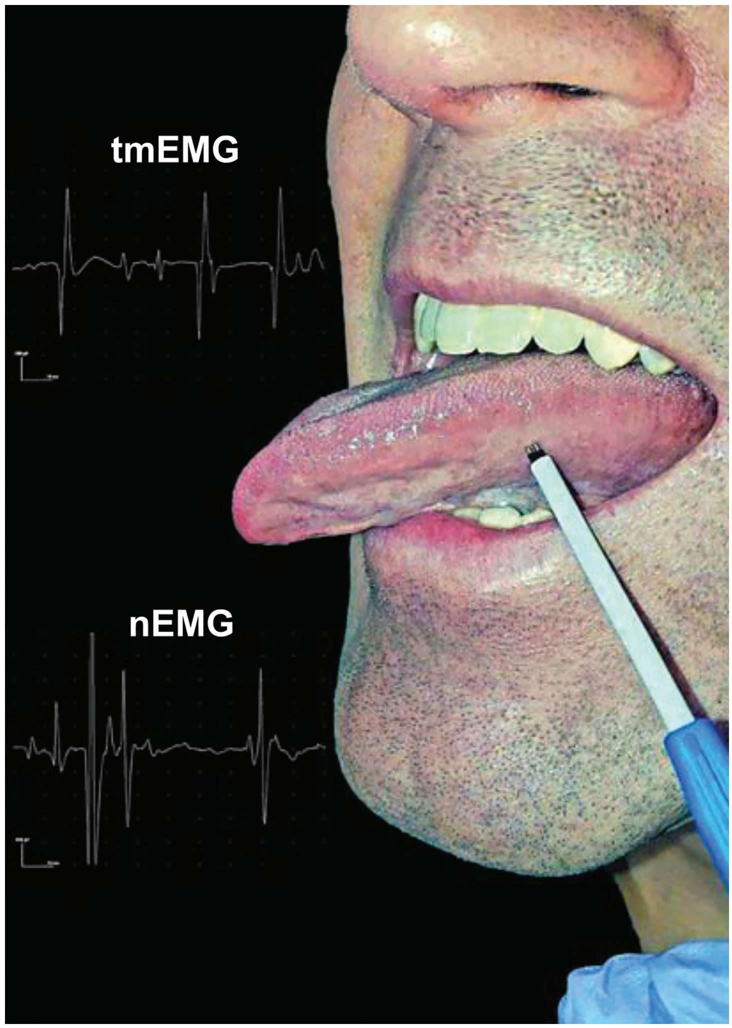

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Cover: EMG analysis of genioglossus using the transmembranous EMG (tm EMG) probe. For details, see Menon et al. A pilot study of a novel transmembranous electromyography device for assessment of oral cavity and oropharyngeal muscles, pages 303–310.

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CLINICAL RESEARCH ARTICLE

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Pilot study of a novel transmembranous electromyography device for assessment of oral cavity and oropharyngeal muscles

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Abstract

Introduction/Aims: Electromyography (EMG) can provide valuable insights into the pathophysiology of oropharyngeal muscles in various disease states, but the invasive nature of the conventional needle EMG (nEMG) has its limitations in this setting. We aimed to examine the inter-rater reliability (IRR) of a novel transmembranous EMG (tmEMG) sensor as a non-invasive technique for assessment of oral cavity and oropharyngeal muscles for neuromuscular pathology.

Methods: The study was a prospective, cohort, pilot study with blinded data analysis in healthy participants (n = 6), patients with moderate to severe obstructive sleep apnea (OSA) (n = 5) and bulbar amyotrophic lateral sclerosis (ALS) (n = 5). Each patient underwent sampling from bilateral palatoglossus (PG) and genioglossus (GG), using both tmEMG and nEMG. IRR was expressed as percentage agreement and prevalence-adjusted bias-adjusted kappa coefficient (PABAK).

Results: Substantial IRR was found for participants with ALS (81.6%, PABAK 0.63) and OSA (78.8%, PABAK 0.61), and in healthy participants (87.1%, PABAK 0.74). A better IRR was seen with tmEMG (95.7%, PABAK 0.92) than with nEMG (73.9%, PABAK 0.48) for healthy participants and also for those with OSA. Studies from GG had higher IRR than PG. Only one participant had a minor adverse event (sore throat).

Discussion: The current study shows that analysis of PG and GG in both healthy and disease states using tmEMG has high IRR compared with nEMG analysis. Further validation studies can be undertaken to test its utility in analysis of oral cavity and oropharyngeal muscles.

KEYWORDS
ALS, oropharyngeal muscles, OSA, surface EMG, transmembranous EMG

Abbreviations: AHI, Apnea-Hypopnea Index; ALS, amyotrophic lateral sclerosis; BMI, body mass index; CI, confidence interval; EMG, electromyogram; ESS, Epworth sleepiness scale; FDA, Food and Drug Administration; FEES, fiberoptic endoscopic evaluation of swallowing; GG, genioglossus; IRR, inter-rater reliability; MUP, motor unit potential; nEMG, needle electromyogram; NSAID, nonsteroidal anti-inflammatory agents; OSA, obstructive sleep apnea; PABAK, prevalence-adjusted bias-adjusted kappa coefficient; PG, palatoglossus; PSG, polysomnogram; sEMG, surface electromyogram; tmEMG, transmembranous electromyogram; VFS, videofluoroscopy.

1 | INTRODUCTION

Neuromuscular disorders that affect the oropharyngeal muscles impair the upper aerodigestive tract and can lead to significant morbidity and mortality.[1,2] An accurate assessment of patients having oropharyngeal dysfunction is vital not only for prognostication and for choosing management strategies but also for determining the pathological process leading to the dysfunction. At present, the gold standard tools for oropharyngeal dysfunction evaluation are videofluoroscopy (VFS) and fiberoptic endoscopic evaluation of swallowing (FEES).[3] While both examine physiology and function of the oropharynx, they cannot reliably identify and distinguish between the different pathological processes that lead to dysfunction.

Electromyography (EMG) is a versatile electrophysiological technique that helps to confirm or exclude a neuromuscular diagnosis and has been used to analyze physiological and pathological processes affecting swallowing.[4–7] Dysfunction of the oropharyngeal musculature has also been implicated as a cause of obstructive sleep apnea (OSA). Evidence for local nerve and muscle pathologies as well as neurogenic EMG changes have been found in patients with OSA in whom no other clinical evidence for a neuromuscular disorder was apparent.[8–13] The EMG methods used to study motor control in dysphagia and OSA include the use of surface (skin), hooked wire, needle, and suction (mucosal) electrodes.[7] There are several technical disadvantages to the surface recordings, such as the distance from the muscle of interest and filtering effects of the intervening tissue; only needle electrodes inserted intramuscularly are presently considered suitable for diagnosis of neuromuscular pathology.[14–16] But, needle EMG (nEMG) has its own disadvantages, such as pain, potential for bleeding, infection, and tissue damage, especially when examining the oral cavity and oropharyngeal muscles where space is confined and the palatal and pharyngeal muscles are very thin.[17]

Since many muscles of interest in the oral cavity and oropharynx are covered with only a very thin mucous membrane, impediments of distance and intervening tissue could be sufficiently low to allow recording of signals from the membrane surface that might approximate those obtained from the invasive intramuscular nEMG. A probe configured with a bipolar sensor was designed and produced for use in the oral cavity and oropharynx to test the hypothesis that transmembranous surface EMG is a reliable and valid alternative to nEMG in the diagnosis of neuromuscular pathology.

This paper describes the inter-rater reliability (IRR) of the transmembranous EMG (tmEMG) probe as a non-invasive technique for the assessment of neuromuscular function in the oral cavity and oropharynx in comparison with conventional nEMG.

2 | METHODS

The study was a prospective, cohort, pilot study with blinded data analysis and two physician raters to assess the IRR of a tmEMG probe in healthy participants, patients with moderate to severe OSA, and patients with ALS having documented symptoms and signs of bulbar dysfunction. Each participant underwent EMG sampling from four muscles, bilateral palatoglossus (PG) and bilateral genioglossus (GG), using both tmEMG probe and conventional nEMG.

For acceptance of a participant in the healthy group, a subject had to meet strict criteria to exclude subjects with sleep disordered breathing or OSA (Supporting Information Figure S1, which is available online). This was necessary because the neurogenic hypothesis of OSA allowed for the possibility of apparently normal subjects with neurogenic EMG changes in the pre-symptomatic phase of OSA. These strict criteria proved exceedingly difficult to meet. For example, American Academy of Sleep Medicine gives guidance that an Apnea-Hypopnea Index (AHI) of 5 or less is normal. As seen in Figure S1, only 6 of 64 screened healthy volunteer candidates qualified to be enrolled in the study. It should be noted that falling outside these exceedingly strict parameters does not imply those subjects are abnormal. Moderate to severe OSA was diagnosed by in-laboratory polysomnography (PSG) with an AHI of 25 or higher. All participants with ALS had been previously diagnosed by the regional ALS center with clinical and electrodiagnostic evaluation. Each ALS subject had bulbar symptoms of varying degree and had either no upper motor neuron signs of bulbar ALS or had EMG or clinical evidence of lower motor neuron involvement of the tongue. The risks explained included induction of a gag reflex or feeling of nausea, minor irritation or bleeding at the testing site, mild allergic reactions to the topical anesthetic or to the probe tip itself, and infection at the needle insertion site. After risks were explained and questions answered, informed consent was obtained. Before testing the participants must have refrained from smoking for 10 days, NSAIDs for 2 wk, and anticoagulants for a time specified by the principal investigator. Inclusion and exclusion criteria were applied independently for each of the three cohorts, with some criteria common to all groups. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Advarra Institutional Review Board, Columbia, MD, USA.

For the testing, the participants were seated comfortably to allow the physician to adequately visualize the soft palate anatomy. The tmEMG probe is a disposable single-use bipolar tmEMG recording device with the sensor configured with two electrodes located at the distal end of the probe in a parallel orientation. The electrodes are made of stainless steel, and each electrode is 0.75 mm in diameter with an interelectrode distance of 0.75 mm. The electrodes are connected to a shielded multi-conductor single-pair cable with an integrated ground wire. The probe cable has two 1.5 mm DIN 42802 touch-proof connectors for each electrode and one crimp wire connector pin used to connect the cable to a conventional surface/skin ground electrode. The probe thus has a small recording surface, and the short inter-electrode distance between active and reference electrode and pressure can be applied with the probe to indent the tissue without penetration. The Transmembranous EMG or tmEMG Probe™ configured with a single Transmembranous EMG or tmEMG Sensor (Powell Mansfield, Inc., San Diego, USA) (Figure 1) was connected to a Sierra Summit™ EMG system (Cadwell, Kennewick, WA, USA) using standard DIN 42802 touchproof connectors. The Ambu Neuroline Ground Electrode (Ambu, Inc., Columbia, MD, USA) was placed over

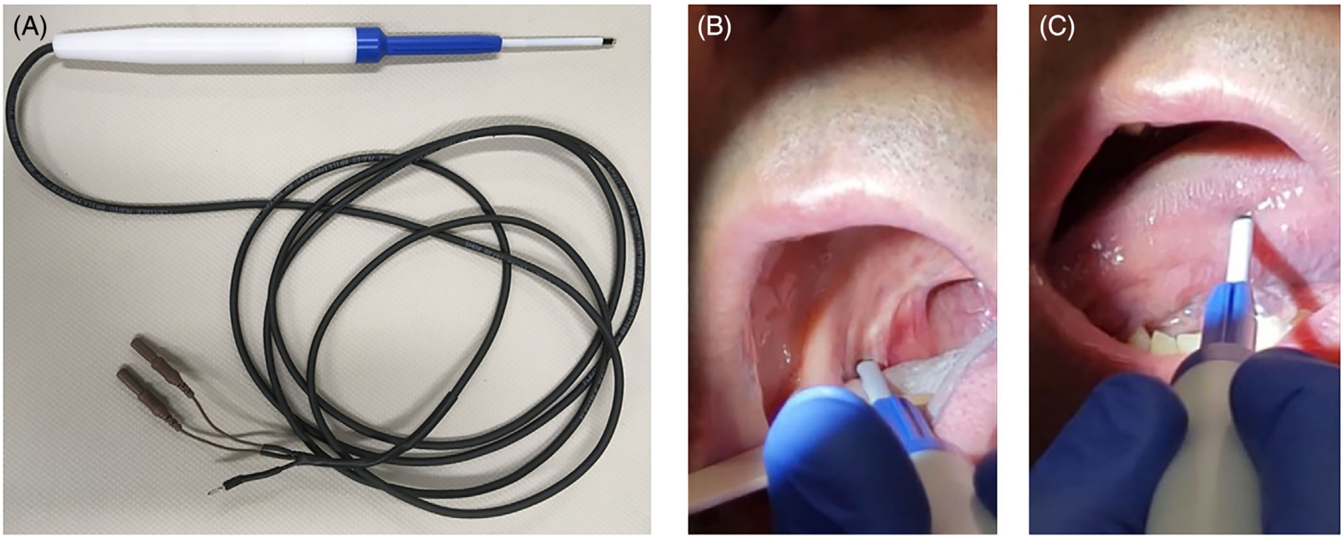

FIGURE 1 A, The tmEMG probe with connectors for standard EMG machine. B, The tmEMG probe placed on the right PG in a healthy participant. C, The tmEMG probe placed on the left GG (lateral aspect of left side of tongue with tongue positioned to right side) in a healthy participant

the cheek on the zygomatic arch. Filter settings were 10 Hz–10 kHz for tmEMG and nEMG recordings. Topical 20% benzocaine was applied on the mucosal surface overlying the muscle to be examined. The tmEMG probe was positioned on the mucosal surface correlating to the expected midpoint of right and left palatoglossi and genioglossi (Figure 1). This was followed by nEMG using a Food and Drug Administration (FDA)-approved very fine concentric needle electrode (Ambu, Inc., Columbia, MD, USA Neuroline 25 mm × 30G) inserted in a straight line through the mucosal surface, at the same location tested by tmEMG probe, and introduced to a depth sufficient to obtain a diagnostic quality EMG tracing from each muscle. EMG was performed on each subject by two otolaryngologists: P.M. examined all subjects, and M.O.L. examined all except one subject, when another otolaryngologist joined P.M.. Each of the four muscles was studied twice with the probe, once by each of the two examiners present, but only one examiner (P.M.) performed the needle examination. The protocol was to record a minimum of at least two free run epochs of 10 s or more to obtain an optimal tmEMG tracing and a minimum of one epoch of 10 s or more of adequate nEMG tracing. For each participant, there were a minimum of 12 recorded tracings: 8 with tmEMG probe, and 4 using nEMG. The aim was to obtain 192 tracings recorded from 16 subjects, with four muscles per subject and three examinations each (two tmEMG, one by P.M. and M.O.L. each, and one nEMG by P.M. only).

Voluntary motor activation was executed by asking participants to deviate and press the tongue against the cheek for GG and to perform deep nasal breathing for PG with progressively increasing effort. The recordings were stored off-line and then analyzed in the Sierra Summit EMG software. All participants were observed at the conclusion of the EMG procedures for excessive bleeding or swelling and were given written instructions on how to contact the research staff should any adverse events arise, such as a sore throat, fever, testing site irritation, or any other study-related concerns. The research staff contacted the participants 1 and 7 days after completion of the EMG test to document any adverse events.

Once the final subject had been studied, the EMG recordings were then analyzed. Both EMG raters (V.B. and G.S.) are experts in clinical electrophysiology. Nonetheless, because tmEMG is a new technique and the muscles studied are uncommonly examined by needle, both raters familiarized themselves with the nEMG and tmEMG recordings by an unblinded review of healthy subject tracings. All tmEMG and nEMG data, including that of the healthy subjects, was then de-identified and randomized before analysis by the two raters (V.B. and G.S.). This meant that, although a rater might have been present during the EMG acquisition, at the time of analysis, they were blind to the subject source of the recordings, the examiner, and to the EMG technique used, probe or needle. Only the muscle side and name were revealed. The recordings were analyzed semi-quantitatively and included spontaneous activity (fibrillation potentials and positive sharp waves), motor unit potential (MUP) morphology (number phases, duration, and amplitude), and recruitment pattern. Each recording was then classified as normal, neurogenic, or myogenic .

The IRR between the two examiners was estimated by percent agreement and Cohen's kappa statistics with 95% confidence interval (CI). An inter-rater percentage agreement of more than 75% was considered acceptable and more than 90% optimal. A kappa coefficient of 0 or less was considered poor agreement, 0.01 to 0.2 slight agreement, 0.21 to 0.40 fair agreement, 0.41 to 0.60 moderate agreement, 0.61 to 0.80 substantial agreement, and 0.81 to 1.0 almost perfect agreement.[18] Cohen's kappa is strongly dependent on the prevalence of the response and is less meaningful in situations where the raters' coding is very high or very low in favor of a particular category.[19] Also, in situations where one rater's response falls completely into one category or when both raters agree completely in one category,

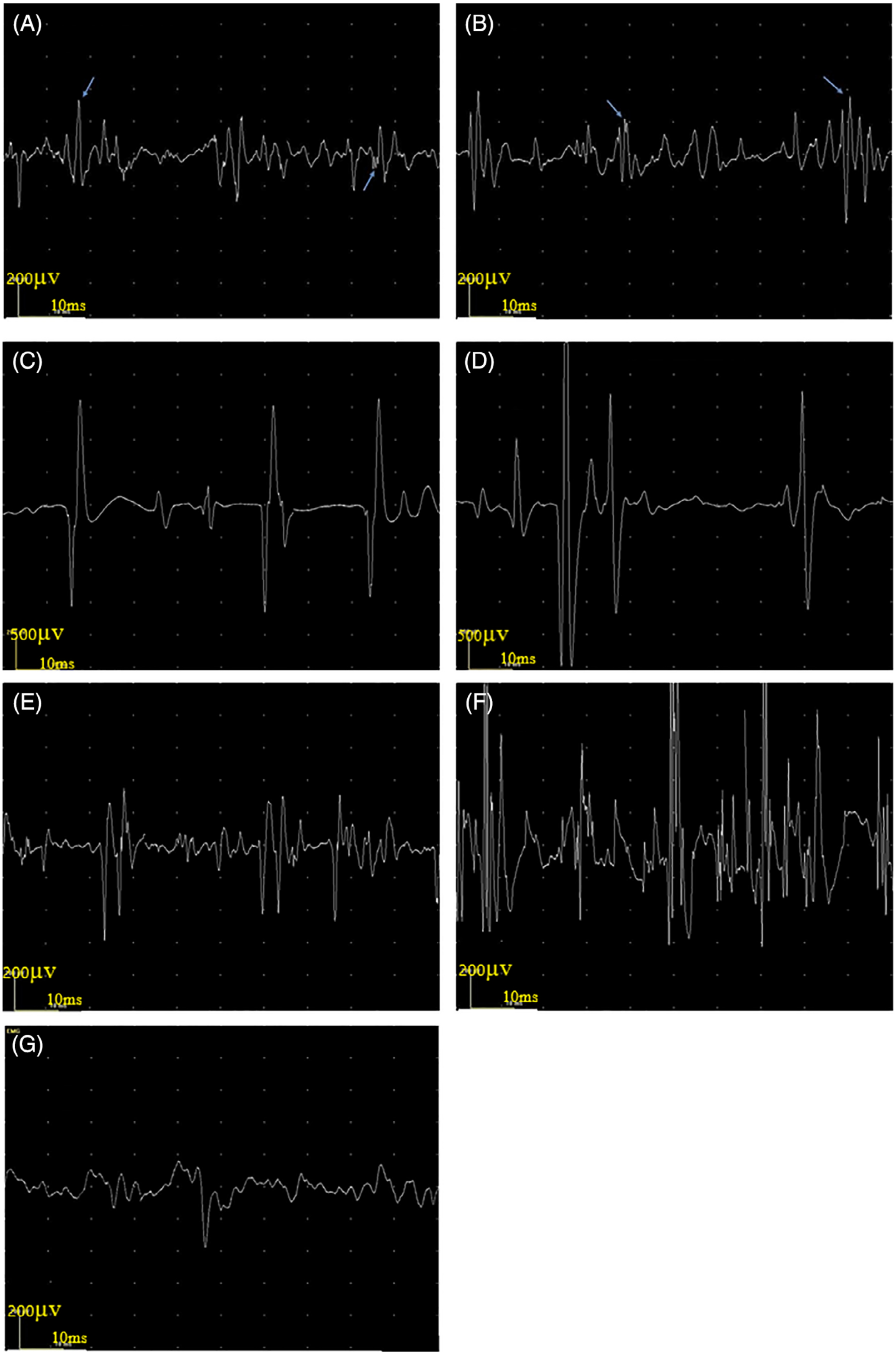

FIGURE 2 Comparison between tmEMG and nEMG recordings in healthy participants, and participants with ALS and OSA. EMG recordings from healthy subject PG using the probe (tmEMG) (A) and healthy subject PG using a concentric needle electrode (nEMG) (B). Note the similarity of amplitude and morphology in the transmembranous and needle recordings, including the amplitude, sharp rise time, high frequency components, and well-defined, low-amplitude turns in the MUPs (arrows). Next are recordings from the GG of two participants with ALS using the tmEMG (C) and nEMG (D) showing a neurogenic pattern. Next are recordings from the PG of two OSA subjects using the tmEMG (E) and nEMG (F). G, Last, EMG recording from abductor pollicis brevis using conventional skin surface electrodes (sEMG) for comparison with tmEMG recordings. As represented by the scale markings, all recording segments in this figure are shown with 200 µV gain and 10 ms sweep speed, except for nEMG of GG for ALS subject, which is shown at 500 µV gain and 10 ms sweep speed

TABLE 1 Inter-rater comparison between tmEMG probe and nEMG in healthy subjects, and subjects with OSA and ALS

Groups or methods		Tracings	Percentage agreement between raters	Kappa (Confidence interval)	PABAK	*P*-Value
Overall		171	82.5	0.508 (0.358, 0.658)	.66	.000
Healthy participants		70	87.1	0.127 (-0.182, 0.436)	0.74	.223
	tmEMG	47	95.7	-0.22 (-0.051, 0.01)	0.92	.882
	nEMG	23	73.9	0.137 (-0.26, 0.534)	0.48	.420
OSA		52	78.8	0.178 (-0.104, 0.362)	0.61	.117
	tmEMG	32	90	0.439 (-0.007,0.885)	0.8	.005
	nEMG	20	63.1	-0.099 (-0.275, 0.077)	0.26	.485
ALS		49	81.6	0.632 (0.417, 0.847)	0.63	.000
	tmEMG	32	78.1	0.559 (0.271, 0.847)	0.56	.002
	nEMG	17	82.3	0.658 (0.327, 0.989)	0.65	.004
EMG methods	tmEMG	110	88.1	0.639 (.461, 0.817)	0.78	.000
	nEMG	61	72.9	0.348 (0.117, .579)	0.46	.002

the kappa becomes equal to zero or undefined, regardless of the level of agreement between the raters, a result known as the kappa paradox. In such situations, the percentage agreement more reliably measures the IRR, especially when the raters are highly trained and little guessing is involved.[19,20] We also used the prevalence-adjusted bias-adjusted kappa (PABAK) instead of Cohen's kappa when the marginal distribution of values indicated a prevalence problem.[21-23] All statistical analyses were performed with SPSS Version 20 (SPSS Inc, Armonk, NY).

3 | RESULTS

The study was conducted in six healthy participants, five participants with moderate to severe OSA, and five patients with ALS having bulbar symptoms. After excluding those tracings that could not be completed due to participant intolerance, a total of 177 tracings were examined off-line. The tracings that could not be completed were 13 tmEMG probe and 2 nEMG recordings, but this difference was not statistically significant (χ^2 2.9, $P = 0.087$). Nine were from participants with ALS and due to difficulties with patient positioning, a strong gag reflex, or excessive saliva; four from participants with OSA, and two from healthy controls. Six of the recordings (four in OSA [three tmEMG and one nEMG], two in ALS [one tmEMG and one nEMG]) were classified as indeterminate by one of the raters. These were excluded from the analysis. Spontaneous activity was not noted accurately with either tmEMG or nEMG, given the inability to fully relax palatoglossus; and of 70 recordings in healthy participants, neurogenic changes were noted by at least one of the raters on 10 (14.3%) occasions (Supporting Information Tables S1 and S2). For 52 OSA recordings, abnormalities were noted by at least one rater in 13 (25%; 12 [23.1%] neurogenic and 1 [0.02%] myogenic changes) (Supporting Information Tables S3 and S4). In 49 ALS recordings, 31 (63.2%) were deemed neurogenic by at least one of the raters (Supporting Information Tables S5 and S6). EMG signals acquired with the tmEMG probe had visual and auditory characteristics very similar to those obtained with needle EMG (Figure 2; Supporting InformationVideos S1–S7).

A substantial IRR and percentage agreement was found for participants with ALS, OSA, and healthy participants (Table 1). Subsequently, separate comparisons of IRR were made for the tmEMG probe and nEMG for each group. A better IRR was seen with the tmEMG probe than with nEMG for healthy participants and also for participants with OSA (Table 1). In participants with ALS, the IRR for nEMG was marginally better than with tmEMG probe. In all the three groups, the IRR (PABAK score) for the tmEMG probe was substantial to almost perfect. This was also reflected when IRR was compared between the tmEMG probe and nEMG for the entire cohort, with the

TABLE 2 Inter-rater comparison between tmEMG and nEMG among PG and GG muscles

		Tracings	Percentage agreement between raters	Kappa (CI)	PABAK	*P*-Value*
Overall PG		54	75	0.378 (0.175, 0.581)	0.50	.000
	PG tmEMG	27	86.8	0.621 (.388,.854)	0.74	.000
	PG nEMG	27	51.9	0.011 (–.263, 0.285)	.04	.936
Overall GG		88	89	0.648 (.437, .859)	.79	.000
	GG tmEMG	56	91.1	0.617 (.316, .918)	.82	.000
	GG nEMG	32	87.5	0.668 (0.373, 0.963)	.75	.000

*For Cohen's kappa.

TABLE 3 Inter rater comparison between tmEMG and nEMG in the three patient groups (healthy subjects, subjects with OSA and ALS)

Variable	Tracing	Percentage agreement between raters	Cohen's kappa	PABAK	P*
Healthy palatoglossus probe	23	95.6	0.000	.91	
Healthy palatoglossus needle	11	63.6	-0.158	.27	0.521
Healthy genioglossus probe	24	95.8	0.000	.92	
Healthy genioglossus needle	12	75.0	0.308	0.5	0.140
OSA palatoglossus probe	14	76.9	0.341	.54	0.132
OSA palatoglossus needle	11	33.3	0.000	-.34	
OSA genioglossus probe	17	100	0.000	1	
OSA genioglossus needle	10	90	0.000	0.8	
ALS palatoglossus probe	17	82.3	0.643	.65	0.008
ALS palatoglossus needle (7)	7	57.1	0.160	0.14	0.659
ALS genioglossus probe (15)	15	73.3	0.474	.46	0.057
ALS genioglossus needle (10)	10	100	1	1	0.002

*For Cohen's kappa, CI- confidence interval, PABAK- prevalence-adjusted-bias-adjusted kappa, OSA- obstructive sleep apnea, ALS- amyotrophic lateral sclerosis

former having a substantial agreement while the latter had a moderate agreement.

The IRR was then examined for the recordings obtained from PG and GG separately. Taken collectively, studies from GG had a higher percent agreement and substantial IRR compared with PG. Further analysis revealed that, both in PG and in GG, the tmEMG probe had a better IRR than nEMG, and the latter had a poor IRR when recorded from PG (Table 2).

We also examined the IRR for PG and GG recordings from the three subgroups. An optimal percentage agreement and almost perfect IRR was seen with tmEMG probe in healthy participants for both PG and GG; 95.6%, PABAK 0.91 and 95.8%, PABAK 0.92, respectively. A similar pattern was seen for PG and GG in OSA, where the IRR for the tmEMG probe was better than nEMG. The exception was ALS, where the nEMG recording from GG performed better than the tmEMG probe. The tmEMG recording from PG had a better IRR than nEMG in ALS (Table 3).

There were no major adverse events in the study. One healthy control reported a mild sore throat on the first day after the procedure, which resolved by day 2 with saline and soda gargles.

4 | DISCUSSION

The current study showed an almost perfect IRR for tmEMG readings in healthy participants and substantial IRR when used in patients with OSA and ALS. The IRR was higher with tmEMG for the entire cohort and within the three subgroups except when recording from GG in ALS. A better concordance was noted for recordings from GG than from PG. There might be several factors that could explain the IRR discrepancy between the two muscles. Anatomically, PG is a thin muscle that originates from the soft palate and palatine aponeurosis and forms part of the faucial pillar, while GG is a larger muscle more easily accessible to conventional nEMG.[24,25] Needle insertion and maintenance of position in PG would thus be more technically demanding. With a suboptimal needle position, the morphology of the MUPs and recruitment pattern would not be ideally characterized, which may result in greater inter-rater and intra-rater differences.[26,27] Due to the limited subcutaneous tissue, the tmEMG probe is close to the source of the MUPs, thus minimizing cross-talk and internal noise and overcoming one of the major limitations when recording from skin surface.[28] Except for GG, where the nEMG had a better IRR in ALS, in all subgroups the two raters had a better agreement with recordings obtained using the tmEMG probe than with conventional nEMG.

Due to the exploratory nature of the study, we chose OSA and ALS as disease models along with healthy controls for evaluating the tmEMG probe. The existing techniques, such as fine-needle EMG and surface EMG, have their own limitations in this setting.[7,29] In this regard, the current novel device has several advantages: providing good access to submucosal muscles, stability with movement, and very little discomfort.[30] We found neurogenic changes in 25% of the recordings obtained in participants with OSA and 66% of participants with ALS. PG has not been frequently examined in OSA, likely because of the difficulty in examining this muscle adequately through nEMG. In contrast, tmEMG of PG is relatively easy and may offer future avenues of research in OSA.

Among the three groups, the maximum concordance between the blinded raters was found in healthy participants, but a substantial concordance was found in patients with OSA and ALS as well. Interestingly, the two raters agreed substantially more with the tmEMG probe than with the conventional nEMG in almost all situations except in examination of GG in ALS. The lowest PABAK coefficient when using the probe was 0.46 when recording from GG in ALS. This should be seen in the context that the inter-rater agreement for nEMG in cervical and lumbosacral radiculopathies is around 0.5 to 0.6, despite being one of the most common nEMG studies in clinical practice.[31,32]

The strong similarity in the sound and appearance of tmEMG compared with nEMG stands in contrast to skin surface EMG and is likely responsible for the high IRR.

Recording from these oral cavity and oropharyngeal muscles was, overall, well tolerated by the participants, and there was no statistically significant difference in intolerance between tmEMG and nEMG. A difference in IRR between the muscles probably means that the tmEMG probe may be better suited to analyze muscles such as PG, which might be difficult to evaluate using nEMG. Among six tracings that were categorized as indeterminate by one of the raters, four were when using tmEMG probe, thus indicating suboptimal quality, but only in a small minority. Additional training could help mitigate tracing quality issues by building up expertise in correctly identifying, placing, and recording the tmEMG probe with minimal participant discomfort.

There are several caveats that mandate further evaluations. While the tmEMG probe appears to be precise as evidenced by the IRR, its accuracy remains to be confirmed. GG recording in bulbar ALS would be expected to be the most abnormal recording in the entire cohort. Here, the nEMG recording had a 100% agreement with kappa of 1 whereas the tmEMG probe had a 73.3% agreement and PABAK of 0.46, which indicates moderate agreement. The nEMG is the gold standard evaluation for diagnosis of neuromuscular pathology, and evidence supporting validity of tmEMG by that standard will be the subject of a subsequent paper. This pilot study did not include participants with myopathy, so it also remains to be seen whether tmEMG probe recordings would be adequate in identifying a myogenic process, such as oculopharyngeal muscular dystrophy, inclusion body myositis, or other inflammatory myopathies that cause oropharyngeal dysphagia.

5 | CONCLUSIONS

The current study provides evidence that analysis of PG and GG in both healthy and disease states using tmEMG probe has an overall high percentage agreement and IRR compared with conventional nEMG analysis. Our findings support a consideration of tmEMG as a clinically useful diagnostic test for neuromuscular pathology in examination of oral cavity and oropharyngeal muscles. Further validation studies are required before considering its broader application in clinical and research avenues.

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CONFLICTS OF INTEREST

Dr. Mansfield, Dr. Bril, and Mr. Studer have equity ownership in Powell Mansfield, Inc. Dr. Sheean, Dr. O'Leary, and Mr. Cordice serve or have served as consultants to Powell Mansfield, Inc.

ETHICAL PUBLICATION STATEMENT

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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