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RECURRENT LARYNGEAL NERVE RECOVERY PATTERNS ASSESSED BY SERIAL ELECTROMYOGRAPHY

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Abstract

Introduction—Following acute injury to the recurrent laryngeal nerve (RLN), laryngeal electromyography (LEMG) is increasingly being used to determine prognosis for recovery. The LEMG findings change during the recovery process, but the timing of these changes is not well described. In this canine study, LEMGs were obtained serially following model RLN injuries.

Methods—36 canine RLNs underwent crush (n=6), complete transection with reanastomosis (n=6), half-transection-half-crush (n=5), cautery (n=5), stretch (n=5), inferior crush (n=4), or inferior transection with reanastomosis (n=5) injuries. Injuries were performed 5cm from cricoid, or were 5cm further inferior. Under light sedation, LEMG of thyroarytenoid muscles was performed monthly for 6 months following injury. At 6 months, spontaneous and induced vocal fold motion was assessed.

Results—Except for the stretch injury, the remaining groups showed very similar recovery patterns. Fibrillation potentials (FPs) and/or positive sharp waves (PSWs) (signs of “bad prognosis”) were seen in all cases at one month and lasted on average for 2.26 months (range 1–4). Motor unit potentials of at least 2+ (scale 0–4+) (signs of “good prognosis”) were seen beginning at 3.61 months (range 2–6). The stretch injury was less severe, with 3/5 showing no FPs/PSWs at one month; all recovered full mobility. Ten of the 36 TA muscles (27.8%) had one EMG showing both bad prognosis and good prognosis signs simultaneously, at 2–4 months post-injury.

Conclusion—LEMG can be used to predict RNL recovery, but timing is important and LEMG results earlier than 3 months may overestimate a negative prognosis.

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Keywords

Recurrent laryngeal nerve; electromyography; vocal cord paralysis

INTRODUCTION

Laryngeal electromyography (LEMG) is a minimally invasive means of obtaining information on the innervation status of the laryngeal muscles. Hillel has provided a comprehensive investigation of LEMG in normal volunteers as well as patients with laryngeal dystonia.{1} The role of LEMG in determining prognosis for recovery from unilateral vocal fold paralysis (UVFP) has been discussed in numerous papers over the last three decades, nicely summarized in a recent meta-analysis by Rickert et al.{2} This analysis found ten studies that compared LEMG data with clinical outcome data in patients. The conclusion was that LEMG is good predictor of poor recovery, but a much less reliable predictor of good recovery. An earlier evidence-based review of LEMG by the American Association of Electrodiagnostic Medicine concluded that LEMG had anecdotal support for use as a prognostic indicator of recovery from UVFP, but inadequate evidence.{3}

Part of the problem with LEMG is the qualitative nature of the data provided. The standard rating scale{4} used by neurophysiologists assigns a value from 0–4+ based on the frequency and locations of observations of motor unit potentials, polyphasic potentials, and fibrillations (Table 1). A more quantitative method of assessment may be the use of “turns analysis” as recently reported by Smith et al.{5} This method shows promise, but it requires software that is not currently available in many neurodiagnostic labs.

Rickert et al. summarized the prognostic criteria used in the ten studies analyzed, and found they were remarkably similar.{2} A good prognostic sign was the presence of motor unit potentials, to a “near-normal” extent in most of the studies. A bad prognostic finding was the presence of fibrillation potentials. We chose to use the criteria of 2+ for either of these to define good or bad prognosis for this study.

Two new approaches to early intervention for patients with UVFP have been proposed recently. Rosen et al.{6} reported the use of nimodipine in a series of patients, and found recovery rates higher than their historical controls. They recommend its use only in patients with poor-prognosis LEMGs. Paniello proposed that patients with UVFP undergo injection of the posterior cricoarytenoid muscle with vincristine, a microtubule inhibitor that blocks reinnervation of this muscle that antagonizes adduction.{7} However, vincristine blockade does not impair existing innervation,{8} and in a canine model, laryngeal adduction was not improved if vincristine was given more than 3 months post-injury.{9} Thus, a method for early, clear identification of which UVFP patients have a poor prognosis for recovery would be highly useful. An electrodiagnostic method is the logical choice.

This study was undertaken in order to plot LEMG findings as they change over time, with the goal of identifying LEMG criteria for a good or bad prognosis by 3 months post-injury. The canine model was used due to its long track record in laryngeal research and to its similarity to human neuromuscular anatomy and physiology. A similar study was reported

by Mu and Yang in canines,{10} and they concluded that patients with new-onset UVFP should undergo LEMG at three time intervals: 1 week, 4–5 weeks, and 10–12 weeks, in order to determine prognosis for recovery. But many patients do not present for diagnosis in time to follow this algorithm.{11} In this project we sought to develop additional insights that could be clinically applicable.

METHODS & MATERIALS

Nineteen purpose-bred, conditioned, 20–25kg hound-type female mongrel dogs were used. They were maintained in an AAALAC-approved facility, and their care guidelines were followed strictly. The study protocol was approved by the Institutional Animal Care and Use Committee (IACUC) of Washington University in St. Louis. Prior studies have showed that the left- and right- sided results are independent of one another, so each dog provides two experiments.

Initial Surgical Procedure

Each dog was given a general anesthetic and intubated. The neck was explored and the recurrent laryngeal nerves (RLNs) identified. A tracheostomy was performed as previously described. Pretreatment (baseline) laryngeal adductor pressures were measured as previously described. Laryngeal electromyography (LEMG) was performed as described below. Controlled RLN injuries were randomly selected for each side and performed as described below. The stoma was matured and the wound closed, and the animal was allowed to recover and heal.

Laryngeal EMG

A four-channel Nicolet Viking-IV EMG machine was used. Direct laryngoscopy was performed, and monopolar electrodes were inserted percutaneously through the cricothyroid membrane and into each thyroarytenoid (TA) muscle. A pair of hook-wire electrodes was inserted transorally into the posterior cricoarytenoid (PCA) muscles. Ground and reference electrodes were placed. The anesthetic was lightened by dialing back the inhalant, and spontaneous activity of the laryngeal muscles followed. The TA electrode positions were adjusted several times in order to sample a wide area of the muscle. If needed, a glottic closure reflex was stimulated by gentle touching of the supraglottis with a cotton swab. The presence of fibrillation potentials, positive sharp waves, polyphasic action potentials, and motor unit potentials was determined by an electrophysiologist (MA-L) and recorded using a standard 0–4+ rating scale (Table 1). In some cases, compound motor action potentials (CMAPs) were obtained using the stimulator function of the Viking-IV, yielding a latency, amplitude and duration.

RLN Injuries

These were performed 5 cm inferior to the cricothyroid joint. Left and right sided experiments were randomly assigned from the following groups:

- A. Crush injury – a small hemostat was applied to the RLN at one click for 15 seconds. N=6.

- B.** Transection/repair – the RLN was completely transected, then reanastomosed using 9-0 nylon sutures. N=6.
- C.** “Half-half” injury – the RLN was crushed as in group A; then, approximately 50% of the nerve diameter was transected (not repaired). This group is intended to represent an injury severity that is intermediate between crush and transection. N=5.
- D.** Cautery – a bipolar cautery tip was applied across the RLN, and activated at 20 watts until the nerve just started to change color (0.3–0.5 seconds). N=5.
- E.** Stretch – the CMAP setup was prepared. A set of three 9-0 nylon sutures were placed through the perineurium, spaced about 120° apart around the circumference of the nerve, and left long for grasping. A second similar set of sutures was placed about 1.5 cm caudal to the first set. The RLN was stimulated at 10–12 volts, manually at approximately 3 Hz, and the CMAP observed on the monitor. The sutures were gently pulled away from one another, stretching the RLN, until the CMAP signal just disappeared to zero. N=5.
- F.** Inferior crush – like group A, but the injury was applied 5 cm more inferiorly (10 cm from the cricothyroid joint). N=4.
- G.** Inferior transection/repair – like group B, but the injury and repair were carried out 5 cm more inferiorly (10 cm from the cricothyroid joint). N=5.
- H.** Control – no nerve injury. N=2.

Monthly LEMGs were obtained exactly as described above for 6 months post-operative. The dog underwent a brief general anesthetic to allow electrode placement, then lightened and EMG data obtained. Data collection continued as the dog was awakened to observe additional spontaneous volitional activity.

Infraglottic exam was performed at 6 months to determine range of motion of the vocal folds. With the dog awake and seated, a rigid or flexible laryngoscope was introduced through the stoma and directly to the underside of the vocal folds. A small bolus of water was introduced into the pharynx to induce swallowing and glottic closure. A videocamera was used and the output recorded digitally. The movement of each vocal fold was evaluated independently by three otolaryngologists and scored using the rating scale in Table 2, and the median scores comprised the data.

RESULTS

All animals completed the planned experiments, resulting in 228 LEMGs (19 dogs x 2 hemilarynges x 6 time points). There were no intraoperative complications. Three dogs developed seromas in their neck wounds during the first week postoperative; these were managed successfully with drainage and antibiotics.

The LEMG data is given in Table 3. It can be seen that the pattern and timing of the LEMG findings was similar for all injury groups except E (stretch): the first 2–3 months have predominantly spontaneous activity (fibrillation potentials and positive sharp waves);

polyphasic potentials (a sign of recovery-in-progress) rise in middle months, then fall again as they are replaced by mature motor unit potentials. This is a typical pattern for any muscle undergoing denervation-reinnervation, but these serial EMGs help define the timeline in the larynx. The data from the non-stretch groups was averaged (bottom of Table 3) and plotted in Figure 1 (top) to show this pattern more clearly.

The stretch group apparently had a less severe injury than the others, as evidenced by a much quicker recovery (Figure 1, bottom). The nerves were stretched until the CMAP signal was lost, but acute loss of CMAP might indicate some other conduction deficit besides axonal disruption. The mean distance between the indicator sutures increased from 1.3 cm to 2.2 cm, for a mean strain of 70%. This lesser injury also accounts for the higher MUP ratings in the stretch group (Table 1). Some MUPs were seen even in the first month, suggesting some axons were not traumatized by the stretch injury.

It is interesting to compare the recovery patterns for the crush group with the inferior crush group, and the transection/repair group with the inferior transection/repair. At the generally accepted nerve growth rate of 1 mm/day, we might expect the “inferior” groups, with the injury performed 5 cm more caudal, would require perhaps 50 more days to recover. But the first appearance of positive prognostic signs occurs at essentially the same time in both groups. This suggests that the 1 mm/day rule may not apply to RLN regeneration.

Using ratings of 2+ or more for fibrillation potentials as signs of a “bad prognosis,” and ratings of 2+ or more for motor unit potentials as indicators of a “good prognosis,” some additional findings are given in Table 4. It can be seen that fibrillation potentials disappear on average by 2 or 3 months, but can last up to 4 months; while motor unit potentials appear on average in just under 4 months, but can appear as early as 1–2 months in all injury groups, earlier than expected. This suggests that there may be muscles that simultaneously have EMG findings of both good and bad prognosis, or of neither. Among all 228 EMGs, there were 10 instances (4.4%) that simultaneously showed good prognosis and bad prognosis, although no experiments showed this more than one month ($10/36 = 27.8\%$). There were 22 EMGs (9.6% of 228) that had neither good nor bad prognoses, which occurred in 14 experiments (38.9% of 36), most often in month 3 ($13/14 = 92.9\%$). These were randomly distributed among all injury types with no detectable pattern. Examples are shown in Figure 2. Clearly these results would vary if the criteria for good or bad prognosis were changed to 3+, although the changes would be small due to the low number of 2+ ratings of either type.

The final MUP rating was 4+ in 17 experiments, 3+ in 20, and 2+ in only one (from the half-half group). Infraglottic exams showed movement rated at 3+ in 33% and 4+ in 47% of cases, excluding the stretch group (which all had 4+ or 5+ movement). The experiments that resulted in better movement had good-prognosis EMGs at an earlier time: an average of 3.3 months for those that had 4+ movement at the 6 month terminal date, vs. 4.4 months for those that finished with 3+ movement. Of note, among the experiments that finished with 3+ or 4+ movement, 50% had good prognostic EMGs at 2 or 3 months, while 50% did not show good prognostic signs until the 4th or 5th month post-injury.

EMG from PCA muscles was obtained inconsistently. When it was available, two interesting findings emerged: 1) evidence of reinnervation (polyphasic or motor unit potentials) in the TA muscle always preceded such findings in the PCA muscle; and 2) synkinesis, of PCA fibers reinnervating the TA muscle, was always seen when the nerve injury involved transection of axons. Figure 3 shows significant TA activity with every breath following a transection/repair injury, but not following a crush injury. The amplitude of the synkinetic TA signal is much higher than the small TA respirator activity that is occasionally seen in normal controls.

The control group had normal MUPs at all six monthly EMGs, and never had any evidence of fibrillation potentials or positive sharp waves or polyphasic potentials.

DISCUSSION

The canine larynx is an excellent model in which to study injuries to the RLN, as the neuromuscular anatomy is highly analogous to the human. The nerve injuries in this study were intended to model typical injuries that might occur during thyroidectomy, the most common cause of unilateral vocal fold paralysis.{11,12} It would be expected that more inferior injuries, such as those that occur within the chest, would require longer recovery time given the longer distance the nerve needs to regenerate. The similar recovery patterns seen in the “inferior crush” and “inferior transection/repair” groups raises questions about the traditional notion of nerves growing back at the rate of 1 mm/day. Perhaps the RLN differs from other peripheral motor nerves in this regard.

The presence of MUPs as early as 2 months in most of these experiments was earlier than expected. Absence of MUPs at 1 month indicates these are not coming from some secondary nerve source. Instead, it is testimony that the RLN has a strong tendency to regenerate. The recovery of at least some vocal fold motion in most of the dogs in this study, despite some severe RLN injuries, suggests that this tendency may be stronger in the canine model than in humans, where recovery of mobility after transection injuries is uncommon.

This study was motivated by a desire to determine whether LEMG can be used in the early months following injury to identify patients with a poor prognosis for spontaneous recovery, to aid in selection of patients most appropriate for early intervention such as nimodipine therapy{6} or PCA blockade with vincristine {7}. The latter strategy has been shown to be effective in a canine model only if administered within 3–4 months of nerve injury.{9} The present study shows that LEMG can be used to screen out patients with a high likelihood of recovery; half of the dogs that recovered mobility had a good-prognostic EMG by 3 months. However, the other half developed their positive prognostic EMG at a later date and would not be screened out at the 3 month interval.

Thus, negative prognostic EMG findings at 3 months are problematic. A full 25% of dogs with a negative prognostic EMG at 3 months later developed movement ratings of 3 or better. Thirteen of the 36 experiments (36.1%) had neither positive nor negative prognostic EMG findings at 3 months. The EMG findings at 3 months can identify cases with good prognosis, but negative prognostic findings need to be interpreted carefully. One option

would be to repeat the EMG at a later time, but doing so runs the risk of missing the therapeutic window of the early intervention.

This study confirms previous findings regarding the differential recovery of the adductor and abductor divisions of the RLN, that the adductor axons recover first. This is compatible with Semon's law, which basically states that the abductor axons are more susceptible to injury than the adductors.^{ 13 } It also confirmed that synkinesis is very common when the RLN axons have been injured.

CONCLUSIONS

The time course of RLN recovery following a variety of injuries has been elucidated by serial EMGs. Positive-prognostic signs are likely valid, but negative-prognostic findings need to be interpreted carefully. The canine RLN has a strong tendency to regenerate, and first signs of reinnervation can be seen as early as 2 months after injury. Synkinesis can be expected whenever the RLN axons have been transected.

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Figure 1. EMG rating pattern over 6 months. Ratings on scale of 0–4+. Fibrillation potentials, a negative prognostic indicator, are plotted as negative values. Left, mean ratings for all study groups except for stretch injury; Right, mean ratings for stretch group. FP, fibrillation potentials; PSW, positive sharp waves; Poly, polyphasic potentials; MUP, motor unit potentials.

Figure 2.

EMG ratings for two individual animals. Left, a dog from the Inferior Crush group that has both good prognosis (2+ motor unit potentials) and bad prognosis (2+ fibrillation potentials) during month 2 (box). Right, a dog from the “Half-Half” group that has neither good nor bad prognostic findings (less than 2+) during months 3 and 4 (box).

Figure 3.

4-channel EMG at 5 months post-RLN injury during quiet respiration. Sweep speed = 20 sec/screen; each burst is one breath. Left side had transection/repair; note significant activity in TA muscle during breathing (synkinesis). Right side had crush injury with good recovery but no synkinesis.

Table 1

EMG rating scale, used to score fibrillation potentials, positive sharp waves, polyphasic potentials, and motor unit potentials. From Ref. 4.

0+	None
1+	Persistent single trains of potentials (>2–3 sec) in at least 2 areas
2+	Moderate # of potentials in 3 or more areas
3+	Many potentials in all areas (but not full)
4+	Full interference pattern of potentials

Table 2

Movement rating scale.

0	No movement
1	Brief twitch
2	Slight adduction
3	Adducts but does not reach midline
4	Adducts to midline
5	Adducts and abducts completely

Table 3

LEMG findings at each month. Mean values for each subgroup shown, on a scale of 0–4+, for fibrillations or positive sharp waves (F/PSW), polyphasic action potentials (Poly), and motor unit potentials (MUP).

Month		1	2	3	4	5	6
Crush	F/PSW	4.0	3.0	0.8	0.8	0.5	0.2
	Poly	0.0	0.3	0.8	1.5	1.5	1.0
	MUP	0.0	0.8	1.2	1.7	2.7	3.3
Trans/rep	F/PSW	4.0	3.2	1.2	0.0	0.0	0.0
	Poly	0.0	0.3	1.5	2.4	2.0	1.6
	MUP	0.0	0.3	1.8	3.2	3.2	3.3
Cautery	F/PSW	4.0	3.2	1.4	0.0	0.0	0.0
	Poly	0.0	0.4	1.8	1.6	1.8	1.5
	MUP	0.0	0.0	1.4	2.2	3.0	3.2
1/2-1/2	F/PSW	4.0	2.6	1.0	0.0	0.0	0.0
	Poly	0.0	0.8	1.6	1.8	1.6	0.4
	MUP	0.0	0.5	1.4	1.4	2.6	3.4
Inf. crush	F/PSW	4.0	3.0	1.0	0.3	0.3	0.0
	Poly	0.0	0.5	2.5	1.5	1.8	1.5
	MUP	0.0	0.5	1.8	2.3	2.5	3.3
Inf. trans/rep	F/PSW	4.0	3.8	2.0	0.4	0.0	0.0
	Poly	0.0	0.4	1.2	1.4	1.0	0.8
	MUP	0.0	0.4	1.1	3.2	3.6	3.6
Mean, grps 1–6	F/PSW	4.0	3.1	1.2	0.2	0.1	0.0
	Poly	0.0	0.5	1.6	1.7	1.6	1.1
	MUP	0.0	0.4	1.4	2.3	2.9	3.4
Stretch	F/PSW	2.0	1.2	0.6	0.0	0.0	0.0
	Poly	0.2	0.8	0.8	0.4	0.0	0.0
	MUP	1.0	1.4	2.3	3.6	3.8	3.8

Table 4

Timing of LEMG prognostic indicators of 2+ or more. Mean and maximum duration of poor prognostic indicators, and mean and earliest times of appearance of positive prognostic indicators, are shown.

Injury group	N	Poor Prognostic EMG		Good Prognostic EMG	
		Mean	Latest	Mean	Earliest
Crush	6	2.00	2	3.67	2
Inf. Crush	4	2.25	3	3.50	2
Trans/rep	6	2.17	3	3.33	2
Inf. Trans/rep	5	3.00	4	3.60	2
Cautery	5	2.20	3	3.80	3
Half-half	5	2.00	3	3.80	2
Stretch	5	0.60	2	2.20	1