

# The Corrugator Supercilii, Not the Orbicularis Oculi, Reflects Rocuronium Neuromuscular Blockade at the Laryngeal Adductor Muscles

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**Background:** Some studies suggest that the orbicularis oculi is resistant to neuromuscular blocking drugs and behaves like laryngeal muscles. Others report little or no difference between the orbicularis oculi and the adductor pollicis. These discrepancies could be related to the exact site of recording. The purpose of this study was to compare two monitoring sites around the eye with the adductor pollicis and the laryngeal adductor muscles.

**Methods:** After institutional approval and informed consent, the evoked response to train-of-four stimulation was measured in 12 patients by acceleromyography at the thumb (adductor pollicis), the eyelid (orbicularis oculi), and the superciliary arch (corrugator supercilii) after 0.5 mg/kg rocuronium during propofol–fentanyl–nitrous oxide anesthesia. In 12 other patients, laryngeal adductor neuromuscular blockade was assessed *via* the cuff of the tracheal tube and compared with the adductor pollicis and the corrugator supercilii after 0.6 mg/kg rocuronium.

**Results:** After 0.5 mg/kg, maximum blockade (%T1, mean  $\pm$  SD) was less at the corrugator supercilii ( $80 \pm 20\%$ ) than at the adductor pollicis ( $100 \pm 1\%$ ) and the orbicularis oculi ( $93 \pm 8\%$ ) ( $P < 0.01$ ). Clinical duration (25%T1) was shorter at the corrugator supercilii ( $12 \pm 7$  min) than at the adductor pollicis ( $25 \pm 4$  min) and orbicularis oculi ( $24 \pm 10$  min) ( $P < 0.01$ ). After 0.6 mg/kg, maximum blockade was similar at the corrugator supercilii ( $88 \pm 8\%$ ) and the laryngeal adductor muscles ( $89 \pm 11\%$ ). Clinical duration at the corrugator supercilii and the laryngeal adductors was  $17 \pm 7$  and  $17 \pm 10$  min, respectively.

**Conclusions:** Muscles around the eye vary in their response to rocuronium. The response of the superciliary arch (corrugator supercilii) reflects blockade of laryngeal adductor muscles. However, the eyelid (orbicularis oculi) and thumb (adductor pollicis) have similar sensitivities.

STIMULATION of the temporal branch of the facial nerve and inspection of the muscular response around the eye are performed frequently during anesthesia to assess the intensity of neuromuscular blockade. Despite technical difficulties in measuring the muscle response, it is generally agreed that muscles surrounding the eye and the

adductor pollicis have different responses to neuromuscular blocking drugs. Caffrey *et al.*<sup>1</sup> measured the mechanical response using a transducer attached to the superciliary arch and reported that recovery from atracurium neuromuscular blockade occurred earlier than at the adductor pollicis. When the electromyographic response was measured over the same area after vecuronium injection, onset occurred earlier, neuromuscular blockade was less intense, and duration of action was shorter than at the adductor pollicis.<sup>2</sup> The neuromuscular profile was similar to that of the diaphragm, which suggests that monitoring muscle movement near the superciliary arch might be indicated when deep blockade is desired. When the response of the superciliary arch was monitored visually, onset of atracurium neuromuscular blockade occurred earlier than at the adductor pollicis but at the same time as at the laryngeal adductor muscles.<sup>3</sup> Based on these data, visual estimation of the onset time of muscle relaxants at a muscle moving the eyebrow has been proposed to predict intubating conditions.<sup>4,5</sup> This muscle was presumed to be the orbicularis oculi.

However, other investigators did not measure resistance of the orbicularis oculi relative to the adductor pollicis. With acceleromyographic measurements over the eyelid and at the thumb, onset time and duration of action were found to be similar at both sites after injection of mivacurium, atracurium, or vecuronium,<sup>6</sup> suggesting that the adductor pollicis and orbicularis oculi had the same sensitivity to neuromuscular blocking drugs. These discrepancies could be attributed to the site of recording (superciliary arch *vs.* upper eyelid) or the method of measurement (mechanomyography, electromyography, and visual inspection *vs.* acceleromyography).

Because it is important to interpret correctly the response to facial nerve stimulation, this study was designed to (1) measure the onset, intensity, and recovery of rocuronium-induced neuromuscular blockade at two sites around the eye (upper eyelid and superciliary arch) (part 1), and (2) to verify which muscle around the eye is a good guide of laryngeal adductor muscles' neuromuscular blockade (part 2).

## Materials and Methods

The study was approved by the Centre Hospitalier de Montréal Scientific Review Committee and Research Ethics Committee (Montreal, Quebec, Canada). Twenty-four patients classified as American Society of Anesthesiologists physical status I or II, 18–60 yr old, were included

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**Fig. 1.** Position of the stimulating electrodes and acceleromyographic probes around the eye. To record the movement of the orbicularis oculi, the probe was positioned on the external half of the right upper eyelid. The position was the internal half of the left superciliary arch for the corrugator supercilii. To avoid signal contamination, surface electrodes were positioned close to the probe. Current intensity of 20 mA was sufficient to obtain a supramaximal stimulation and avoid direct muscle stimulation.

in the study after obtaining informed consent. Patients were scheduled for elective and nonhemorrhagic surgery (minor orthopedic procedures or diagnostic gynecological laparoscopies). All patients were free of cardiovascular, hepatic, renal, or neuromuscular disease. They were not taking any drugs suspected to interfere with neuromuscular transmission. Exclusion criteria included anticipated abnormal airway, suspected allergy to muscle relaxants, and body weight more than 20% of ideal.

At the time of arrival in the operating room, an intravenous catheter was placed in the left antecubital fossa to administer fluids and drugs. Pulse oximetry, electrocardiographic data, and arterial blood pressure were monitored noninvasively. Anesthesia was induced with 30–40  $\mu\text{g}/\text{kg}$  alfentanil, and 2.5 mg/kg propofol 30 s later.

In part 1 (12 patients), a laryngeal mask airway was inserted during deep anesthesia without the aid of neuromuscular blocking drugs. The lungs were ventilated mechanically to keep end-tidal carbon dioxide tension within the range of 35–40 mmHg. Core temperature was monitored and maintained at normal levels.<sup>7</sup> Anesthesia was maintained with 6–10 mg  $\cdot$  kg<sup>-1</sup>  $\cdot$  h<sup>-1</sup> propofol and 40/60% oxygen–nitrous oxide.

Surface electrodes were used for all sites of stimulation. The temporal branch of the facial nerve was stimulated at two different sites as shown in figure 1: near the orbit on the right side and over the external part of the superciliary arch on the left side. The ulnar nerve was stimulated at the left wrist. All nerves were stimulated supramaximally with train-of-four stimulation (four pulses 0.2 ms in duration, at a frequency of 2 Hz, 2 s in duration) every 15 s. Typical current intensity was 20 mA for the facial nerve and 40 mA for the ulnar nerve. The evoked responses at the thumb and near the eye

were measured by three TOF-Guard acceleromyographs (Organon-Teknika, Fresnes, France). One probe was positioned on the distal part of the thumb; another, as shown in figure 1, was positioned on the external half of the right upper eyelid (orbicularis oculi); and a third one was positioned on the internal half of the left superciliary arch (corrugator supercilii). Because of low response for both the orbicularis oculi and the corrugator supercilii, the signal from the acceleration transducer was amplified 5 times.

After 10 minutes' baseline measurement with the same mode of stimulation to obtain a variation of less than  $\pm 2\%$  of the control response for the last 3 min before administration of the muscle relaxant,<sup>8</sup> 0.5 mg/kg rocuronium was injected as a rapid bolus. After maximal neuromuscular blockade was reached, the interval between train-of-four stimulation was increased to 1 min. Neuromuscular monitoring was continued until at least 95% recovery of the first twitch (T1) for all muscles.

In part 2 (12 patients), a 7.5 mm internal diameter tracheal tube was inserted under deep anesthesia without the aid of neuromuscular blocking drugs. The cuff of the tube was positioned between the vocal cords.<sup>9</sup> The lungs were ventilated mechanically to keep end-tidal carbon dioxide partial pressure within the range of 35–40 mmHg. Core temperature was monitored and maintained at normal levels.<sup>7</sup> Anesthesia was maintained with 6–10 mg  $\cdot$  kg<sup>-1</sup>  $\cdot$  h<sup>-1</sup> propofol and 50/50% oxygen–air. The temporal branch of the facial nerve was stimulated over the external part of the superciliary arch as in part 1. The ulnar nerve was stimulated at the left wrist, and the recurrent laryngeal nerve was stimulated at the notch of the thyroid cartilage.<sup>9</sup> Supramaximal train-of-four stimulation was applied at all three sites. Typical current intensity for the recurrent laryngeal nerve was 60 mA. Acceleromyographic data was recorded for the thumb (adductor pollicis) and the superciliary arch (corrugator supercilii) as in part 1. The response of the laryngeal adductors was measured by connecting the inflatable cuff pilot balloon of the tracheal tube to an air-filled pressure transducer as previously described.<sup>9</sup> After a 10-min baseline measurement with less than 2% variation in the last 3 min, 0.6 mg/kg rocuronium was injected as a rapid bolus. Recordings continued until at least 95% T1 recovery was seen in all muscles.

All neuromuscular parameters were defined according to the “good clinical research practice (GCRP) in pharmacodynamic studies of neuromuscular blocking agents.”<sup>8</sup> Lag time was the interval between injection of rocuronium and the first decrease of T1. If submaximal neuromuscular blockade (T1 < 95%) was reached, onset time was defined as the time elapsed between the beginning of the muscle relaxant injection and the first of three consecutive T1s with the same amplitude. If T1 maximum depression was from 95–100%, onset time was defined as the time until 95% T1 depression. The

**Table 1. Patient Characteristics**

	Part 1	Part 2
Age (yr)	36 ± 9 (25–50)	36 ± 15 (18–58)
Weight (kg)	71 ± 11 (57–100)	67 ± 9 (57–83)
Height (cm)	172 ± 8 (156–172)	169 ± 9 (157–188)
Sex (F/M)	6/6	6/6

Mean ± SD (range). No comparison was done between part 1 and part 2.

recovery times were defined as the time between the beginning of the muscle relaxant injection to 10, 25, and 90% T1 recoveries. The intervals between 25–75% T1 and 25% T1–train-of-four 90% were also measured when applicable.

The results are presented as mean ± SD with ranges and coefficient of variation (CV; SD/mean). Statistical analysis used one-way analysis of variance for repeated measures and a Bonferroni–Dunn test for pairwise multiple comparisons between muscles. The differences were considered to be statistically significant when  $P < 0.05$ .

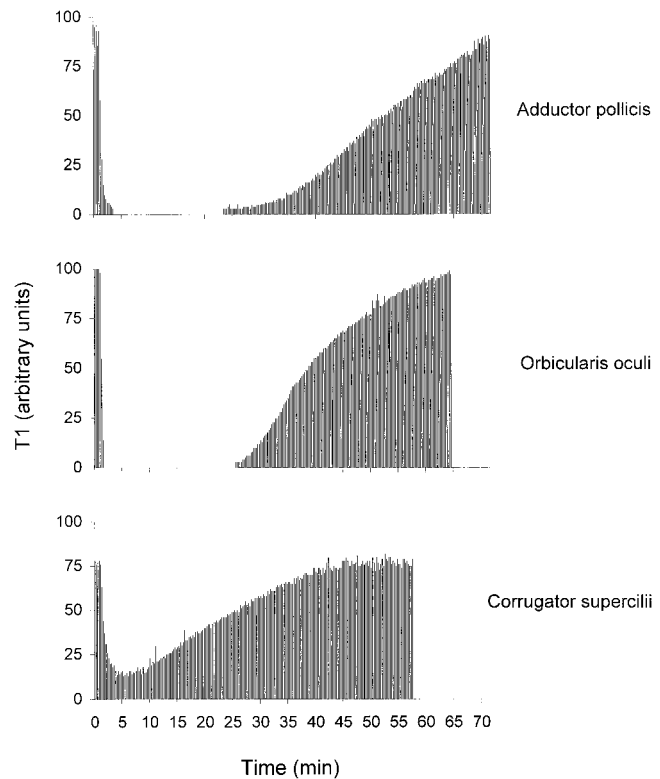
## Results

The patient characteristics are presented in table 1. There was an equal number of men and women in each of the two parts of the study. No comparisons were made between patients of part 1 and part 2.

A typical tracing of simultaneous recording at the adductor pollicis, the orbicularis oculi (eyelid), and the corrugator supercilii (superciliary arch) (part 1) is presented in figure 2. For the orbicularis oculi and the corrugator supercilii, twitch height baseline values ranged between 50 and 100 arbitrary units, and the train-of-four ratio was systematically greater than 100%. For the adductor pollicis, the twitch height control value was automatically set at 100. After injection of rocuronium, when no response was obtained at the orbicularis oculi (eyelid), movements of the superciliary arch were still visible. No visible response was observed at the superciliary arch when first twitch height at the corrugator supercilii was lower than 10%.

### *Part 1: Neuromuscular Effects of Rocuronium at the Adductor Pollicis, the Orbicularis Oculi, and the Corrugator Supercilii*

After 0.5 mg/kg rocuronium, time to reach maximum neuromuscular blockade was significantly longer at both the orbicularis oculi and the corrugator supercilii than at the adductor pollicis (table 2). Maximum blockade was significantly less at the corrugator supercilii than at either the orbicularis oculi or the adductor pollicis. No difference in maximum blockade was found between the orbicularis oculi and the adductor pollicis (table 2 and fig. 3). Recovery times were shorter at the corrugator supercilii than at the orbicularis oculi and the adduc-



**Fig. 2.** Simultaneous recording in one patient of the evoked response at the adductor pollicis, the orbicularis oculi, and the corrugator supercilii. Train-of-four stimulations were repeated every 15 s. Rocuronium, 0.5 mg/kg, was administered at time zero. For clarity of presentation, only the first twitch height (T1) response is displayed.

tor pollicis, both of which had similar time courses (table 2 and fig. 3).

### *Part 2: Neuromuscular Effects of Rocuronium at the Adductor Pollicis, the Corrugator Supercilii, and the Laryngeal Adductor Muscles*

After 0.6 mg/kg rocuronium, there was no statistically significant difference with respect to lag time, onset time, maximum block, or recovery profile between the corrugator supercilii and the laryngeal adductor muscles (table 3 and fig. 4). Both these muscles demonstrated a shorter lag time but a longer onset time than did the adductor pollicis (table 3 and fig. 4). Maximum blockade was less and recovery was more rapid at the corrugator supercilii and the laryngeal adductor muscles than at the adductor pollicis (table 3 and fig. 4).

## Discussion

This study shows that the neuromuscular responses to rocuronium recorded at the eyelid (orbicularis oculi) and the thumb (adductor pollicis) are very similar. Also, the superciliary arch (corrugator supercilii) and the laryngeal adductor muscles demonstrate virtually the same neuromuscular profile. The first two muscles (orbicularis



**Table 2. Part 1: Neuromuscular Effects of 0.5 mg/kg Rocuronium (with N<sub>2</sub>O) on the Adductor Pollicis (AP), the Orbicularis Oculi (OO), and the Corrugator Supercilii (CS)**

	Lag Time (s)	Onset Time (s)	Maximum Block (% T1)	10% T1 (min)	25% T1 (min)	90% T1 (min)	RI (min)	25% T1-TOF 90 (min)
AP	33 ± 14 (15–60) 42	83 ± 28 (45–135) 34	100 ± 1 (97–100) 1	22 ± 4 (17–29) 17	25 ± 4 (19–33) 17	41 ± 8 (32–66) 18	10 ± 3 (6–16) 28	18 ± 6 (11–27) 30
OO	28 ± 11 (15–45) 39	218 ± 78* (60–330) 36	93 ± 8 (77–100) 8	15 ± 10* (3–35) 64	24 ± 10 (6–41) 43	42 ± 13 (24–67) 31	15 ± 6 (9–23) 42	25 ± 7* (19–40) 28
CS	39 ± 22 (15–75) 56	194 ± 59* (75–285) 31	80 ± 20*† (37–96) 25	7 ± 4*† (2–17) 68	12 ± 7*† (4–22) 53	30 ± 9*† (15–49) 31	13 ± 5 (8–22) 37	22 ± 7† (13–34) 32

Mean ± SD (range) and coefficient of variation (SD/mean). See text for definition of neuromuscular parameters.

\*  $P < 0.05$  versus AP. †  $P < 0.05$  versus OO.

N<sub>2</sub>O = nitrous oxide; TOF = train-of-four.

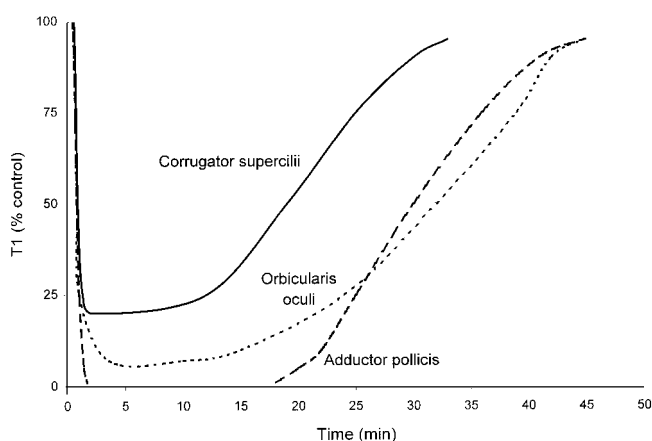
oculi and adductor pollicis) can be described as sensitive, with greater maximum blockade and longer duration of action, than the other two (corrugator supercilii and laryngeal adductors), which can be considered resistant, with less maximum blockade and shorter duration of effect.

The response clearly depends on the site of recording around the eye. The orbicularis oculi is a thin muscle that surrounds the eye. Its upper section is divided into a palpebral part, which covers the eyelid, and an orbital part, which lies under the eyebrow.<sup>10</sup> In previous studies,<sup>1,2</sup> movements recorded over the superciliary arch were attributed to the orbicularis oculi, but close inspection of the response to facial nerve stimulation suggests that the movements observed over the superciliary arch (fig. 1) corresponded to the action corrugator supercilii because the contraction involves mainly the medial part of the eyebrow. The corrugator supercilii is a small pyramidal muscle located at the medial end of each eyebrow, deep to the frontalis and orbicularis oculi. Attached to the medial end of the superciliary arch, it passes superolaterally through the overlying muscles, to the skin of the eyebrow near its mid point. It pulls the

eyebrows toward the nose and receives, like the orbicularis oculi, facial nerve innervation.<sup>10</sup> This close anatomic location between the corrugator supercilii and the orbicularis oculi could explain in part the conflicting data regarding the sensitivity of muscles around the eye to neuromuscular blocking drugs. Caffrey *et al.*<sup>1</sup> and Donati *et al.*<sup>2</sup> positioned a force transducer and electromyographic electrodes, respectively, over the superciliary arch, which anatomically corresponds to the location of the corrugator supercilii.<sup>10</sup> Both of these studies concluded that the “orbicularis oculi” was more resistant than the adductor pollicis after atracurium<sup>1</sup> or vecuronium<sup>2</sup>-induced neuromuscular blockade. On the contrary, with acceleromyographic measurements over the eyelid, Rimaniol *et al.*<sup>6</sup> suggested that onset time at the orbicularis oculi and the adductor pollicis were similar. It is likely that data was recorded from the corrugator supercilii in the first two studies and from the orbicularis oculi in the last.

Because the pattern and duration of nerve stimulation can influence onset time at the adductor pollicis,<sup>11</sup> both of these variables were the same (train-of-four every 15 s) for all the muscles studied in both parts of the study. Neuromuscular response can also be modified by the duration of stabilization of control responses, so this time period was kept the same in all experiments.<sup>12,13</sup>

The hemodynamic effects of intravenous anesthetic agents influence the onset time.<sup>14</sup> Therefore, the same anesthetic induction and maintenance techniques were used in both parts of the study. Inhalational agents were avoided because of their possible interaction with rocuronium.<sup>15</sup> The effect of nitrous oxide on neuromuscular blockade is uncertain.<sup>8</sup> The influence on the current results was probably low, because duration of action of 0.5 mg/kg rocuronium with nitrous oxide was 25 min at the adductor pollicis (part I), shorter than a slightly larger dose (0.6 mg/kg, 33 min) without nitrous oxide (Part II). If significant potentiation had been present, the duration of the smaller dose would have been similar if



**Fig. 3.** Mean first twitch height (T1) against time after 0.5 mg/kg rocuronium.

**Table 3. Part 2: Neuromuscular Effects of 0.6 mg/kg Rocuronium (without N<sub>2</sub>O) on the Adductor Pollicis (AP), the Corrugator Supercilii (CS), and the Laryngeal Adductor Muscles (AL)**

	Lag Time (s)	Onset Time (s)	Maximum Block (% T1)	10% T1 (min)	25% T1 (min)	90% T1 (min)	RI (min)	25% T1-TOF 90 (min)
AP	42 ± 12 (30–75) 30	90 ± 35 (45–150) 38	100 — —	29 ± 10 (17–50) 34	33 ± 12 (20–57) 35	47 ± 15 (33–90) 32	10 ± 5 (5–26) 52	20 ± 9 (12–44) 45
CS	29 ± 15* (15–60) 52	206 ± 72* (90–330) 35	88 ± 8* (75–97) 9	8 ± 6* (2–24) 76	17 ± 7* (8–29) 40	34 ± 7* (24–44) 24	12 ± 4 (5–20) 36	22 ± 10 (13–45) 47
AL	25 ± 9* (10–40) 36	181 ± 70* (72–300) 39	89 ± 11* (75–100) 12	11 ± 8* (2–23) 72	17 ± 10* (2–30) 56	33 ± 10* (19–52) 34	10 ± 3 (6–13) 25	NM†

Mean ± SD (range) and coefficient of variation (SD/mean). See text for definition of neuromuscular parameters.

\*  $P < 0.05$  versus AP. † Not measured at the AL.

N<sub>2</sub>O = nitrous oxide; TOF = train-of-four.

not longer than that of the larger dose. The reason to avoid nitrous oxide in the second part of the study was because its diffusion into the inflatable cuff of the tracheal tube could alter pressure measurements.<sup>9</sup>

A dose of 0.5 mg/kg was chosen for part 1 because it was expected to yield approximately 95–100% neuromuscular blockade at the adductor pollicis.<sup>16,17</sup> For part 2, 0.6 mg/kg was used because it is the recommended dose to facilitate tracheal intubation.<sup>5</sup>

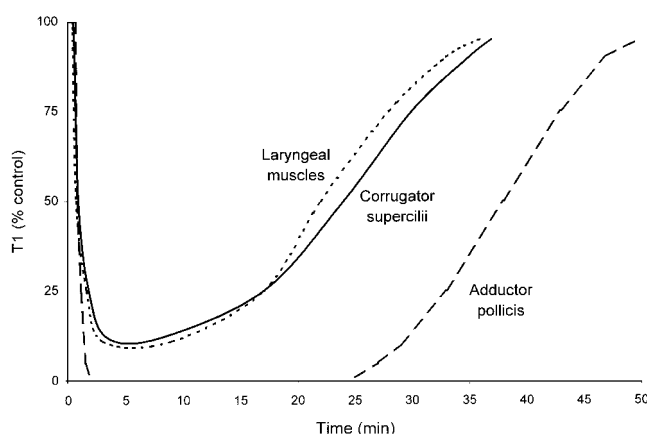
Except for the laryngeal adductor muscles, all muscles (adductor pollicis, orbicularis oculi, and corrugator supercilii) were monitored by acceleromyography. It is often not possible to use the same method of measurement to compare different muscles in humans.<sup>2,18</sup> In the current study, the same method for neuromuscular monitoring (e.g., acceleromyography) was used for the three muscles used for monitoring (adductor pollicis, orbicularis oculi, and corrugator supercilii), and a standard method was used for laryngeal muscles.<sup>9</sup>

In both parts of the study, time to maximum blockade was shorter at the adductor pollicis than at the corrugator supercilii, the orbicularis oculi, and the laryngeal adductor muscles (tables 2 and 3). This seems to contradict a previous study in which after 0.5 mg/kg rocuronium, onset time at the adductor pollicis was longer than

at the laryngeal adductor muscles.<sup>17</sup> The shorter onset time at the adductor pollicis in the current study is probably related to the fact that 100% blockade was observed in all patients, a situation which tends to shorten measured onset time.<sup>19</sup> This hypothesis is supported by the results of another study comparing the neuromuscular blocking effects of different doses of rocuronium on the adductor pollicis and laryngeal adductors. With small doses of the drug (0.4 mg/kg), maximum block was less than 100% at both muscles, and onset at the adductor pollicis was slower than at the larynx. Doubling the dose to 0.8 mg/kg produced complete block at the adductor pollicis and a faster onset at that muscle, whereas laryngeal block was still incomplete and onset time was unchanged compared with the 0.4 mg/kg dose.<sup>20</sup>

The current study demonstrates that there are important differences between muscles around the eye with respect to their response to rocuronium. The orbicularis oculi and the adductor pollicis have similar sensitivities, with comparable maximum effects, and similar recovery times (table 2). On the other hand, the corrugator supercilii seems to be more resistant than the adductor pollicis and the orbicularis oculi both in terms of maximum blockade and recovery times (table 2 and fig. 3). Its sensitivity is similar to that of the laryngeal adductor muscles because maximum blockade and recovery times of both muscles were comparable (table 3 and fig. 4). The results reported here are in accordance with those of previous studies reporting resistance of the laryngeal adductor muscles after vecuronium,<sup>21</sup> rocuronium,<sup>17</sup> or mivacurium<sup>22</sup> administration.

Onset time of laryngeal adductor blockade was found to correlate well with disappearance of visible muscle response after facial nerve stimulation.<sup>3</sup> For this reason, visual evaluation of train-of-four stimulation at the orbicularis oculi has been proposed and verified to predict intubating conditions.<sup>4,5</sup> The current study indicates that the response that was assessed visually in these studies



**Fig. 4.** Mean first twitch height (T1) against time after 0.6 mg/kg rocuronium.

was that of the corrugator supercilii and not the orbicularis oculi. The confusion about the muscle that was monitored does not invalidate the findings of the intubation studies. The current investigation does not provide data on the intensity of laryngeal (or corrugator supercilii) blockade required to obtain adequate intubating conditions. Many factors, including the depth of anesthesia, determine these conditions. However, the results of this study are in accordance with reports that intubating conditions are better after 1.0 mg/kg than 0.6 mg/kg rocuronium<sup>23</sup> because laryngeal block is incomplete with the lower dose.

## Conclusion

It is concluded that the discrepancies reported about muscle relaxant effects registered around the eye are related to the site of measurement. After rocuronium, the corrugator supercilii and not the orbicularis oculi has a sensitivity similar to that of the laryngeal adductor muscles. Quantitative neuromuscular monitoring based on acceleromyographic measurements is feasible at the corrugator supercilii, allowing assessment of resistant muscles, such as the laryngeal adductors. Measurement of corrugator supercilii response by acceleromyography, which is noninvasive and easy to perform, could be used as a surrogate measure of laryngeal adductor muscle blockade, which is invasive and difficult to set up.

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