The staircase phenomenon at the corrugator supercilii muscle in comparison with the hand muscles

S. Deschamps, G. Trager, P. A. Mathieu and T. M. Hemmerling*

Neuromuscular Research Group, Department of Anesthesiology, Centre Hospitalier de l’Université de Montréal, Université de Montréal, Montréal, Canada

*Corresponding author. E-mail: thomashemmerling_2000@yahoo.com

Background. Phonomyography (PMG) is a novel method to monitor neuromuscular block. It is non-invasive and can be applied to any muscle. It can be used interchangeably with mechanomyography (MMG). The staircase phenomenon has not been investigated for this method or at the corrugator supercilii muscle. The purpose of this work was to determine the staircase effect at three different muscles using two different methods.

Methods. In 10 patients undergoing general anaesthesia with sevoflurane, using a laryngeal mask airway without the aid of neuromuscular block, one piezo-electric microphone each was applied to the corrugator supercilii muscle and the first dorsal interosseus muscle. In addition, a force transducer was attached to the tip of the thumb to determine the force of the adductor pollicis muscle. Supramaximal stimulation at 1 Hz was used at the ulnar and the facial nerve. All signals were simultaneously recorded for 30 min. Data are presented as means (SD).

Results. The staircase effect was significantly positive for the first dorsal interosseus muscle and the adductor pollicis muscle. The signal potentiation was not significantly different between the first dorsal interosseus muscle with a maximum increase at 148 (19)% using PMG, and the adductor pollicis muscle at 154 (22)% using MMG. The evoked signals reached a plateau after 15–18 min at both muscles. There was only a small initial increase in signal height at the corrugator supercilii to a maximum of 117 (20)% at 7 min, after which the signals decreased to reach a plateau at 25 min. In comparison with the signal height of 105 (25)% at 30 min, there was no significant difference of signal heights throughout the observation period.

Conclusions. A positive staircase phenomenon is found equally at the first dorsal interosseus muscle and the adductor pollicis muscle. There is no significant staircase effect at the corrugator supercilii muscle.

The staircase phenomenon describes the fact that repetitive stimulation of a motor nerve under anaesthesia evokes muscle contractions of increasing amplitude of the corresponding muscle. During repetitive stimulation, there is a significant increase in phosphorylation of the regulatory light chains of myosin, which is proportional to the degree of staircase phenomenon. This increases calcium sensitivity and the force of the muscle contraction.

The staircase effect is an important issue for pharmacodynamic studies as it defines the duration of control stimulation before a stable response is established. Previous studies have investigated the staircase effect for hand muscles, especially the adductor pollicis muscle. However, some animal studies have shown that the staircase effect is not uniform at all muscles. Van Lunteren and Vafaie found that force potentiation in rats is more pronounced at the sternohyoid muscles than at the diaphragm. It is additionally known that the method of monitoring has an influence on the degree or duration of the staircase effect. In addition to the traditional monitoring of the adductor pollicis muscle, monitoring of the corrugator supercilii muscle has become more popular as it reflects better the neuromuscular block at more centrally located muscles, such as the diaphragm or the adductor muscles in the larynx. No study so far has studied the staircase effect at the corrugator supercilii muscle nor has the staircase effect been evaluated via phonomyography.
The current study has as primary objective to investigate the staircase phenomenon at the corrugator superciliii muscle in comparison with the hand muscles and as secondary objective the detection of the staircase effect by phonometryography.

**Methods**

Ten patients undergoing general anaesthesia for routine surgery, using a laryngeal mask airway (LMA™ without aid of neuromuscular block agents, were included in this study after approval of the local ethics committee and written informed consent. Patients with neuromuscular disorders, presenting contraindications against the use of an LMA or on medications interfering with neuromuscular block were excluded from this study as well as pregnant women.

On arrival at the operating theatre, a standard monitoring of 5-lead ECG, pulse oxymetry, non-invasive arterial pressure and BIS monitoring (Aspect 2000 monitoring system, Aspect Medical Company, MN, USA) was applied. Anaesthesia was induced using remifentanil 0.25–0.5 μg kg⁻¹ min⁻¹, followed 2 min later by propofol 2.5 mg kg⁻¹. A flexible LMA (FLMA, Laryngeal Mask Company, size 4 for women, size 5 for men) was inserted by the same anaesthetist (T.H.) in all patients at first attempt. Intermittent positive pressure ventilation was started, adjusted to maintain an end-tidal P co₂ of 4.6–5.3 kPa. Anaesthesia was maintained with remifentanil 0.25–0.5 μg kg⁻¹ min⁻¹ and sevoflurane titrated to keep the value of BIS between 40 and 50.

A small piezo-electric microphone (model 1010, UFI company, CA, USA; frequency response: 2.5–5 kHz) was attached using a standard glueing tape at the following muscle sites: the left first dorsal interosseus muscle (Fig. 1), and the left corrugator superciliii muscle (Fig. 2). The acoustic signals were amplified and bandpass filtered between 0.5 and 100 Hz using an AC/DC-amplifier (Model 15LT, Grass Instruments, Astra-Med, Inc., West Warwick, USA). The signals were continuously sampled at 100 Hz using the Polyview software package (Astra-Med). The single twitch signal was measured peak-to-peak. In addition, at the left hand, a force transducer was attached to the tip of the thumb and glued securely (Fig. 1), equipped with a preload of 250 g, to measure the force of contraction of the adductor pollicis muscle (MMG; Model 15LT, Grass Instruments, Astra-Med, Inc., West Warwick, USA; force transducer: FT 10, same manufacturer). The corresponding ulnar and facial nerves were stimulated using commercial nerve stimulators (Innervator®, Fisher Paykel Company, Auckland, New Zealand) at supramaximal stimulation thresholds at 1 Hz (pulse width: 0.2 ms) each. Stimulation was performed at all sites for 30 min.

The mean twitch response at 30 min in per cent of the initial twitch height was compared with all previous twitch values at 1 s intervals for each muscle site using bilateral paired t-test. In addition, the twitch values as a function of time were compared between all monitoring sites using ANOVA.

The sample size was calculated for Power of 80% to find at least a mean difference of 15 (SD, 15)% between the maximal increase of the signal amplitude for the first dorsal interosseus muscle vs the corrugator superciliii muscle during the observation period.

**Fig 1** The illustration shows the installation of the microphone for the first dorsal interosseus muscle and the attachment of the force transducer for mechanomyographic monitoring of the adductor pollicis muscle. The microphone is firmly attached using a hypoallergenic adhesive tape onto the skin overlying the groove between the index finger and the thumb; the force transducer with a preload of 250 g is attached to the tip of the thumb using a small plastic tube into which the thumb is placed and glued with the force transducer via a short metallic string. The arm is placed in a specially moulded cast and secured throughout the observation period.

**Fig 2** Placement of the microphone at the corrugator superciliii muscle using a standard medical glueing tape; care is taken to place the microphone at the lateral portion of the muscle thus creating the maximum acoustic signal.

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Results
For all 10 patients (four women, six men), mean age 43 (SD 20) yr and weight 81 (15) kg, neuromuscular measurements could be obtained. Mean stimulation currents for the ulnar nerve and the facial nerve were 55 (5) and 20 (5) mA, respectively.

There was no detachment of any microphone from the skin or force transducer from the tip of the thumb throughout the observation period. For the first dorsal interosseus muscle (PMG) and the adductor pollicis muscle (MMG), there was a progressive and significant increase of the evoked twitch height to an average of 148 (23) and 154 (22)% at 30 min, respectively. After 7 min, there was no significant difference between the mean signal height and the signal height at 30 min for the first dorsal interosseus muscle and adductor pollicis muscle (Fig. 3). The time course and degree of the staircase effect was not significantly different between first dorsal interosseus muscle and adductor pollicis muscle. Signals of both muscles reached a plateau at 15–18 min. In contrast, the evoked acoustic signals at the corrugator supercili muscles remained significantly more stable. After an initial moderate increase to a maximum of 117 (24)% at 7 min, they decreased towards a plateau with a mean signal height of 104 (27)% at 30 min. For the corrugator supercili muscle, the mean signal height was not significantly different from the signal height at 30 min at any time during the observation period (Table 1).

Based on the mean difference of the maximum increase of signal amplitude, we calculated a power of 0.99 for our study.

Discussion
The staircase phenomenon is significantly positive at both hand muscles in similar form, reaching a plateau after 15–18 min. There is a minimal initial increase of signal amplitude at the corrugator supercili muscle, followed by a slow signal decrease towards a plateau at 25 min. As the evoked signals at the corrugator supercili muscle are not different at any time in comparison with the amplitude at the end of the observation period, there is virtually no staircase effect at this muscle. Time frame and degree of the staircase effect are similar for the first dorsal interosseus muscle and the adductor pollicis muscle, measured using either PMG or MMG.

The term ‘staircase phenomenon’ was first mentioned in the medical literature in 1922. However, the fact that repetitive stimulation causes potentiation of evoked signals was first demonstrated in cardiac muscle by Bowditch and in skeletal muscle by Kronecker. More recent research found possible clues to the underlying physiology. The staircase phenomenon is caused by increased calcium sensitivity of the muscle cell due to phosphorylation of the regulatory light chains of myosin during repetitive electric stimulation.

For pharmacodynamic studies in anaesthetic neuromuscular research, it is important to consider the staircase effect for any given monitoring method as it defines the time of control stimulation before a signal height plateau is reached. It is generally agreed for pharmacodynamic studies to at least stimulate for 5 min before the application of a neuromuscular blocking agent. It is interesting to note that there are, however, very few studies that have investigated the staircase effect for different monitoring methods in anaesthesia, and none for different muscles.

One study used acceleromyography to measure the staircase effect at the adductor pollicis muscle and found a twitch potentiation to 150–180% of the control twitch height.
Table 1 Mean (sd) of signal height at the corrugator supercilii muscle (CS), first dorsal interosseus muscle (FDI) and the adductor pollicis muscle (AP), measured every 1 min up to 10 min, at 20 and 30 min. P-value calculated for difference of means at the three monitoring sites at the same time.

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depending on the frequency of repetitive stimulation. By using data from this study, Eleveld and colleagues designed a two-exponential model to describe the twitch potentiation for acceleromyographic neuromuscular monitoring. Similar potenciations are found when MMG is used for neuromuscular monitoring. In contrast, Krarup and colleagues did not find the phenomenon of potentiation when electromyography was used for monitoring the platysma and the adductor pollicis muscle after tetanic stimulation and hypothesize that this might be because of supramaximal stimulation of all muscle fibres. In another study, Duchateau and Hainut compared the force potentiation and the potentiation of electromyographic signals at the adductor pollicis muscle and also did not find a positive staircase effect with EMG. Phonomyographic signals, as shown in the present study, show a positive staircase effect in the same way as mechanomyography or acceleromyography.

In our study, sevoflurane was used to maintain anasthesia. Sevoflurane is known to potentiate the effect of neuromuscular blocking agents. However, there is no study showing that the use of volatile anaesthetics changes directly the amplitude of the evoked contraction. In addition, this effect would be uniform for all muscles.

Phonomyography is a new method of neuromuscular monitoring, which agrees well with mechanomyography at the larynx, adductor pollicis muscle and corrugator supercilii muscle. Its ability to monitor neuromuscular block does not rely on the fact that a given preload is attached.

In comparison with one earlier study, potentiation of the signals of the first dorsal interosseus muscle and the adductor pollicis muscle reached a plateau in the current study. As the degree and time course of the staircase effect is related to the frequency of motor nerve stimulation, higher stimulation frequencies cause higher degrees of signal amplitude potentiation. In comparison with Kopman and colleagues, we used a higher stimulation frequency (1 Hz) for a longer period (30 min). Kopman and colleagues only stimulated the ulnar nerve for 10 min at 1 Hz, followed by train-of-four stimulation every 15 s for another 10–15 min. They stated that at 10 min, there was no plateau of the signal height reached. In our study, signals reached a plateau at the first dorsal interosseus muscle and the adductor pollicis muscle at 15–18 min. For both muscles, twitch heights after 7 min were no longer significantly different from the twitch heights at 30 min.

Twitch heights for the corrugator supercilii muscle initially increased; however, far less pronounced than at the adductor pollicis muscle and the first dorsal interosseus muscle, then, after 7 min, gradually decreased to a mean signal height at 30 min which was not significantly different from the initial control twitch height. There is no simple morphological explanation for this difference. It has been deduced from earlier studies that the staircase effect is proportional to the percentage of fast twitch muscle fibres in a given muscle; this would mean that the corrugator supercilii muscle, with its higher content of fast twitch fibres than the adductor pollicis muscle should show a distinct staircase effect—which it does not. However, fast twitch fibres are known to be more prone to fatigue than slow twitch fibres; therefore, the slow decrease of the signal height after an initial increase could be explained by the arrival of fatigue, especially with the high stimulation frequency—chosen in our study. However, our finding that the first dorsal interosseus muscle and the adductor pollicis muscle react in the same way contradicts this hypothesis of differences solely based on the content of fast twitch fibres. Johnson and colleagues have examined post-mortem the content of fast twitch fibres in 31 muscles. The content of fast twitch fibres in the first dorsal interosseus muscle was found to be on average at 57%; Goodmurphy and Ovalle found a very similar percentage of fast twitch fibres in the corrugator supercilii muscle, on average at 51%. Therefore, the content of fast twitch fibres cannot explain our findings.
In summary, our study of the staircase phenomenon at different muscles and using different methods has produced the following results: the staircase effect is similar at the adductor pollicis muscle when monitored using MMG and the first dorsal interosseus muscle when monitored using PMG. Both muscles, regardless of the monitoring method, show a positive staircase effect towards a plateau after 15–18 min during single twitch stimulation at 1 Hz. The staircase phenomenon is absent at the corrugator supercilii muscle. This cannot be explained with current morphological theories of the staircase effect.

References