Advancing femoral nerve stimulation into the stage of science

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Transcutaneous electrical and, later, magnetic twitch stimulation of the femoral nerve have been introduced to quantify quadriceps muscle function. These techniques were developed in an attempt to overcome the drawbacks of measurements of maximal voluntary contraction force and tetanic stimulations. Maximal voluntary contractions are motivation-dependent maneuvers that can be marred by submaximal activation (1); tetanic stimulations are painful (6), and this is particularly problematic when assessing the elderly and frail.

It has been proposed that twitch stimulations of the femoral nerve are suitable for the quantification of quadriceps muscle dysfunction, if present, and for the quantification of quadriceps muscle fatigue. Using paired stimuli, twitch stimulation of the femoral nerve may allow quantifying the relative contribution of low and high frequencies to force output. Single and paired stimuli may also allow quantification of induction and recovery of contractile fatigue. It has also been reasoned that paired stimuli can improve the resolution of twitch interpolation, a technique used to quantify extent of voluntary recruitment and central fatigue (1, 7, 10).

Magnetic twitch stimulation of the femoral nerve and its electric counterpart (the less user friendly, less reproducible and the more painful of the two) have been used in many studies (2). Surprisingly, systematic comparison of these two techniques against each other and against a reference method is not available.

In this issue of the Journal of Applied Physiology, Vergès and colleagues (11) fill in this important gap in our technical knowledge. For the first time, they painstakingly assess the reliability of magnetic twitch stimulation of the femoral nerve against electrically evoked twitches. In addition, they compare the reliability of magnetic and electrical twitch stimulation against transcutaneous tetanic stimulations of the femoral nerve and of the quadriceps muscle. The reference technique against which all comparisons were performed was the submaximal transcutaneous stimulation of the quadriceps. The assessment was performed in healthy subjects both in the unfatigued and fatigued states.

With this investigation, Vergès and colleagues (11) make an important contribution to this challenging field. For the first time they show that single and paired magnetic twitch stimulation of the femoral nerve provide assessment of quadriceps function equivalent to that provided with single and paired electrical twitch stimulation. They also report that the ratio of total twitch force elicited by paired stimulation (electrical or magnetic) at 10 and 100 Hz (Fpaired_10:100) provides similar information to the standard low-to-high-frequency force ratio elicited by submaximal electrical tetanic stimulation of the muscle (Ftet_10:100). Contrary to their expectations, and in a departure from what has been reported for in vitro preparations of rat diaphragm (12), the ratio of the second twitch elicited by paired stimulation (electrical or magnetic) at 10 and 100 Hz (T2_10:100) was only weakly associated with the Ftet_10:100 ratio. The investigators reason that, for the human quadriceps in vivo, the fatigue-associated change in Fpaired_10:100 ratio is a better index of low-to-high-frequency fatigue than the fatigue-associated change of the T2_10:100 ratio.

Although technical in nature, this investigation raises some interesting biological questions. First, in addition to muscle length, mass, fatigue, and intensity of nerve stimulation, what other factors determine the amplitude of single or paired twitches? A portion of the contraction elicited by nerve stimulation could arise from a central mechanism through an evoked orthodromic sensory volley (3). In leg muscles, evoked sensory volleys require pulse widths lasting more than 0.05 ms (see Figs. 3A and B in Ref. 3), frequency of stimulation greater than 25 Hz (see Fig. 3C and D in Ref. 3), and trains of stimulation lasting more than 1.5–5 s (see Fig. 2 in Ref. 3). The duration of (supramaximal) magnetic twitch stimulation in the protocols of Vergès and colleagues (11) was 0.1 ms, and only paired twitches were used during electrical and magnetic twitch stimulation. Therefore, any central contribution to contractions evoked by (single and paired) twitch stimulations is unlikely to be operative in this study.

Second, does coactivation of muscles, other than the quadriceps, determine the amplitude of twitch force elicited by magnetic stimulation? Magnetic stimulation produces a wider field of stimulation than electrical stimulation. When performing magnetic stimulation of the phrenic nerves, particularly with the posterior cervical approach (5), the wider field of stimulation causes coactivation of extradiaphragmatic respiratory muscles (5). In contrast, Vergès and colleagues (11) report nearly absent coactivation of (antagonistic) muscles during magnetic stimulation. Nearly absent coactivation of antagonistic muscles (and supramaximality of the stimulus) during magnetic stimulation underscore the mechanism responsible for the equivalent twitch force and M-wave characteristics with the two twitch stimulating techniques.

Third, the investigators report exercise-associated decrease in the area and duration of the M wave, and a (nonsignificant) decrease in M-wave amplitude. These findings substantially confirm the observations of Piitulainen and colleagues (8), who recorded similar changes in M-wave parameters following eccentric exercise on the elbow flexors. Whether decreases in M-wave area, duration, and amplitude purport impaired sarcolemmal excitability, itself due to disturbed ion distribution and/or transport over the plasmalemma, remains to be determined (8). In addition, whether the decreased M-wave duration could also be related to increased muscle fiber conduction velocity secondary to a higher intramuscular temperature remains unknown.

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Lastly, is it possible to determine whether low-frequency fatigue is present with one-point-in-time determination of the T210:100 ratio as it has been suggested for the diaphragm muscle (12)? The great overlap in T210:100 ratios recorded during nonfatigued and fatigued conditions (see Fig. 8 in Ref. 11) suggests that the elusive quest for a measurement that may provide this answer will not be the T210:100 ratio.

Notwithstanding the important contribution of the study of Vergès and colleagues (11), some unanswered questions remain. The investigators acknowledge that supramaximal nerve tetanic stimulation is the reference technique to calculate the low- to high-frequency force ratio (Ftet10:100). They recognize that the technique is very painful when performed with electrical stimulation, and difficult to perform with magnetic stimulation. The investigators reasoned that it was appropriate to use the submaximal tetanic-transcutaneous stimulation of the quadriceps as the reference technique against which paired twitches were to be compared. The decision was based on the recent observation by the same group of investigators that submaximal tetanic stimulations are as effective as supramaximal stimulations in detecting quadriceps muscle fatigue elicited by eccentric muscle contractions (6).

This is a study in which only (young) healthy volunteers were recruited. Information on patients with sarcopenia or specific neuromuscular pathologies need to be gathered before recommending the routine use of magnetic twitch stimulation for the evaluation of quadriceps function in disease states. Obesity can affect the capacity of magnetic stimulation to obtain supramaximal stimuli. No obese subjects were recruited in the study.

The study of Vergès and colleagues (11) could have important clinical implications in a field in which the state of knowledge is rather rudimentary. Measurements of single and paired magnetic twitches could become important objective end points to assess the effects of interventional studies in stable patients (9) and in critically ill patients (4). Early identification of weakness in the intensive care unit (even in sedated patients) should facilitate the design and implementation of interventions intended to preserve or restore muscle function. Prospective measurements of muscle strength could provide new insight into the mechanism(s) of neuromuscular abnormalities in critically ill patients.

In conclusion, Vergès and colleagues (11) make a strong case for the use of magnetic twitch stimulation of the femoral nerve in nonfatigued and fatigued states. The challenge now is to demonstrate whether basing management decisions on noninvasive, noninvasive assessment of quadriceps dysfunction (itself a harbinger of poor patients’ outcome, see Ref. 9) can have true clinical impact. The challenge is formidable, but the accumulating data suggest that progress may be at hand.

**REFERENCES**