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ORIGINAL ARTICLE/ARTICLE ORIGINAL

Stimulus—response curve of human motor nerves: Multicenter assessment of various indexes

Évaluation multicentrique de différents indices de la courbe stimulus—réponse des nerfs moteurs chez l'homme

D. Boërio[a,b], J.-Y. Hogrel[b], J.-P. Lefaucheur[a,*], F.C. Wang[c], A. Verschueren[d], J. Pouget[d], E. Carrera[e], T. Kuntzer[e,*]

[a] *Service de physiologie—explorations fonctionnelles, hôpital Henri-Mondor, AP—HP, 94010 Créteil, France*
[b] *Institut de myologie, groupe hospitalier Pitié-Salpêtrière, 75013 Paris, France*
[c] *Département de neurophysiologie, CHU Sart-Tilman, 4000 Liège, Belgium*
[d] *Département de neurologie et maladies neuromusculaires, CHU La-Timone, 13005 Marseille, France*
[e] *Unité nerf—muscle, service de neurologie, centre hospitalier universitaire Vaudois, 1011 Lausanne, Switzerland*

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Summary The value of various indexes to characterize the stimulus—response curve of human motor nerves was assessed in 40 healthy subjects recruited from four European centers of investigation (Créteil, Lausanne, Liège, Marseille). Stimulus—response curves were established by stimulating the right median and ulnar motor nerves at the wrist, with stimulus durations of 0.05 and 0.5 ms. The following parameters were studied: the threshold intensity of stimulation to obtain 10% (I_{10}), 50% (I_{50}), and 90% (I_{90}) of the maximal compound muscle action potential, the ratios I_{10}/I_{50}, I_{90}/I_{50}, $(I_{90}-I_{10})/I_{10}$, $(I_{90}-I_{50})/I_{50}$, and $(I_{50}-I_{10})/I_{10}$, and the slopes of the stimulus—response curves with or without normalization to I_{50}. For each parameter, within-center variability and reproducibility (in a test—retest study) were assessed and between-center comparisons were made. For most of the parameters, the results varied significantly within and between the centers. Within the centers, only the ratios I_{10}/I_{50} and I_{90}/I_{50} were found constant and reproducible. Between the centers, the absolute intensity thresholds (I_{10}, I_{50}, I_{90}) and the ratio I_{90}/I_{50} did not show significant differences at stimulus duration of 0.5 ms, whatever the stimulated nerve. The reduced variability and good reproducibility of the ratios I_{10}/I_{50} and I_{90}/I_{50} open perspectives in neurophysiological practice for the use of these indexes of the stimulus—response curve, a rapid and noninvasive test.

* Corresponding authors.
E-mail addresses: jean-pascal.lefaucheur@hmn.aphp.fr (J.-P. Lefaucheur), thierry.kuntzer@chuv.ch (T. Kuntzer).

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Excitabilité nerveuse ;
Intensité de stimulation ;
Propriétés membranaires ;
Seuil d'intensité

Résumé La valeur de différents indices caractérisant la courbe stimulus—réponse des nerfs moteurs a été étudiée dans une population de 40 sujets sains recrutés dans quatre centres européens (Créteil, Lausanne, Liège, Marseille). Les courbes stimulus—réponse des nerfs médian et cubital ont été obtenues en délivrant des stimulations au poignet droit d'une durée de 0,05 et 0,5 millisecondes. Nous avons étudié les seuils d'intensité de stimulation permettant d'obtenir 10 % (I_{10}), 50 % (I_{50}) et 90 % (I_{90}) de la valeur maximale du potentiel d'action moteur global, les rapports I_{10}/I_{50}, I_{90}/I_{50}, $(I_{90}-I_{10})/I_{10}$, $(I_{90}-I_{50})/I_{50}$ et $(I_{50}-I_{10})/I_{10}$, ainsi que les pentes des courbes stimulus—réponse avec ou sans normalisation par I_{50}. Pour chaque paramètre, la variabilité et la reproductibilité (lors d'une étude test—retest) ont été évaluées dans les différents centres et des comparaisons ont été réalisées entre les centres. Pour la plupart des paramètres, les résultats variaient significativement aussi bien dans chaque centre qu'entre les centres. Seuls les rapports I_{10}/I_{50} et I_{90}/I_{50} furent trouvés constants et reproductibles dans chacun des centres. Par ailleurs, les seuils d'intensité absolus (I_{10}, I_{50}, I_{90}) et le rapport I_{90}/I_{50} ne montrèrent pas de différences significatives entre les centres pour une durée de stimulation de 0,5 millisecondes, quel que soit le nerf stimulé. La faible variabilité et la bonne reproductibilité des rapports I_{10}/I_{50} et I_{90}/I_{50} ouvrent des perspectives pour l'application en pratique neurophysiologique de ces indices qui caractérisent la courbe stimulus—réponse, un test rapide et non invasif.

Introduction

Excitability properties of human peripheral nerves can be assessed by various neurophysiological methods [3,5]. One of these methods aims at measuring the stimulus intensities that are required for eliciting compound muscle action potentials (CMAPs) of given amplitudes, corresponding to various percentages of the maximal CMAP area or amplitude (M_{max}). The resulting ''stimulus—response'' curve is classically established for stimulus durations of 0.2 and 1 ms. This method, first developed by Brismar [2] to study metabolic neuropathies, was then applied by Meulstee et al. [10] in patients with demyelinating neuropathies. Various parameters have been proposed to characterize the stimulus—response curve, like the threshold intensities to obtain 10% (I_{10}), 50% (I_{50}) and 90% (I_{90}) of M_{max}, the ratio $(I_{90}-I_{10})/I_{10}$ [2] and the slope of the curve. Later, Kiernan et al. [5] proposed to analyze the curves by normalizing threshold intensities as percentages of I_{50}.

Altered intensity thresholds reflect various pathophysiological processes, that is, modification of nodal properties, increase in nerve capacitance (owing to the presence of endoneural edema or demyelination), or selective loss of the largest nerve fibers. Abnormalities of the stimulus—response curve have been reported in patients with diabetic or uremic neuropathy [2], acute or chronic inflammatory demyelinating neuropathy [4,9,10], motor multifocal neuropathy [7], or amyotrophic lateral sclerosis [12]. Nevertheless, the methodology of this test has been rarely questioned.

The present study was conducted in four European laboratories of clinical neurophysiology (Créteil, Lausanne, Liège, Marseille) and included 10 healthy subjects per center. The stimulus—response curves were established for the median and ulnar motor nerves in all subjects at two stimulus durations (0.05 and 0.5 ms). Our goal was to appraise the respective value of various indexes (previously used or original ones) that characterize the stimulus—response curve of human motor nerves with a focus on within- and between-center variability and on test—retest reproducibility.

Methods

Subjects

Forty healthy volunteers participated to the study. Ten subjects were recruited from each of the following centers: Créteil, Lausanne, Liège, and Marseille. They were 16 women aged from 20 to 50 years (mean $\pm$ S.D. = 34.0 $\pm$ 10.1) and 24 men aged from 22 to 49 years (mean $\pm$ S.D. = 34.1 $\pm$ 8.5). None of these subjects presented any clinical or electrophysiological sign of peripheral nerve disorder, either diffuse or focal, including entrapment neuropathy (carpal tunnel syndrome or ulnar nerve lesion at elbow). In addition, they did not present any risk factor for peripheral neuropathy, including diabetes, alcohol abuse or neurotoxic drug intake.

Investigation technique

Electrophysiological testing was performed with a Keypoint EMG machine (Medtronic Functional Diagnostics, Skovlunde, Denmark) in Créteil and a Viking IV EMG machine (Nicolet, Viasys Healthcare Inc., Conshohocken, PA, USA) in Lausanne, Liège and Marseille. Electrical stimuli were delivered at a frequency of 0.5 Hz. The cathode was placed over the median or ulnar nerve at the right wrist, approximately 1 cm proximal to the most distal crease, where the maximal CMAP could be obtained at minimal stimulus intensity. The anode was placed 4 cm more proximally at the dorsal aspect of the forearm. To ensure a maximal depolarization of the nerve fibers and to minimize the effects of phase cancellation, monopolar stimulation at a single distal site was preferred to bipolar stimulation and multiple stimulation sites. In response to such monopolar stimulation of the median or ulnar nerve, CMAPs were recorded from the abductor pollicis brevis (APB) or the adductor digiti minimi (ADM) muscle with a belly-tendon montage (the active electrode at the motor point and the reference at the proximal phalanx).