



Letter to the Editor

Reply to “Stimulus, response and excitability – What is new?”



We thank Burke and Kiernan for their interesting and constructive comments (Burke and Kiernan, 2018) on our recent Letter to the Editor (Milants et al., 2017). We agree with most of these comments. It is absolutely correct that by considering only iMAX, we lose valuable information related to the stimulus-response curve, particularly the curve slope or discontinuities in the curve as it can be seen in amyotrophic lateral sclerosis. Nevertheless, the delta between iMAX and motor threshold values might contain a similar information to the curve slope. Moreover, we wanted an as fast and simple procedure as possible without data importation and analysis in a spreadsheet data.

The Cappelen-Smith et al.'s paper (Cappelen-Smith et al., 2001) is of major importance in the field of excitability and was crucial in our choice to develop iMAX. In their Fig. 1, mentioned by Burke and Kiernan (2018), the relationship between compound muscle action potential (CMAP) amplitude (% maximum) and current (A) or normalized current (B), the greatest differences between healthy controls and patients with chronic inflammatory demyelinating polyneuropathy were for the highest CMAP amplitudes (CMAP 90% of maximum amplitude). Therefore, we postulated that it would be of interest to measure the amount of current for a CMAP 100% of maximum amplitude. iMAX was easily derived in healthy controls for the median nerve at the wrist and we are convinced that the 7.0 mA value is a reliable upper limit of normal. As indicated by Burke and Kiernan (2017), it may be trickier to precisely measure iMAX in patients with a severe motor axonal hypoexcitability. However, in the daily practice, if iMAX is clearly increased, even if the precise iMAX value is tricky to obtain, the clinician gets, in a couple of minutes, the valuable information that there is a significant motor axonal hypoexcitability, which is of major importance from a clinical point of view. Burke and Kiernan (2018) suggest that the current for a 40–50% CMAP might prove to be more reliable than iMAX. On one hand, prior to measure the current for a 40–50% CMAP, a CMAP 100% of maximum amplitude has to be evoked as precisely as possible, which in some way brings us back to iMAX. On the other hand, we wanted measuring the motor axons with the highest threshold of all axons including aberrant axons of a very high threshold.

The stimulus-response curve methodology and the computerized threshold tracking procedure (Bostock et al., 1998; Kiernan et al., 2000; Burke et al., 2001; Cappelen-Smith et al., 2001) are not without limitations. As already said, these methods are time consuming and they require a specific collection system and software (Milants et al., 2017). Moreover, in a multicenter study using a stimulus-response procedure, the variability of results was high, for most of the parameters, not only between the centers, but also within the centers as indicated by the test-retest evaluation (for

instance, coefficients of variation for slope estimates and for normalized slope estimates, respectively, ranged from 19.28% to 34.73% and from 15.12% to 27.91%) (Boërio et al., 2007). In a very recent abstract, Bostock himself wrote “However, nerve excitability testing remains a specialized technique: it is not possible on regular EMG machines, it is not required for any common diagnostic test, and abnormal recordings are often difficult to interpret.” (Bostock, 2017)

To answer the question asked by Burke and Kiernan (2018) more directly, what is really new with iMAX?: (1) look at a particular, usually neglected, point of the stimulus-response curve (the amount of current for a CMAP 100% of maximum amplitude); (2) develop an up-down-up stimulus intensity procedure to measure the more precisely as possible iMAX; and (3) allow everyone, in the daily practice and whatever the EMG machine, to answer the question very quickly if there is, or not, a motor axonal hypoexcitability.

At last, the present study is preliminary. We wish to measure iMAX to other points of the peripheral nervous system, as at the elbow (median and ulnar nerves) and at the fossa polpatea (fibular nerve), in healthy controls and in large cohorts of patients with hereditary or acquired axonal and demyelinating neuropathies. A multicenter study will be soon started in order to evaluate, at least in healthy controls, the variability of iMAX within and between centers.

Conflict of interest

François C. Wang has no conflict of interest to declare.

References

- Boërio D, Hogrel JY, Lefaucheur JP, Wang FC, Verschuren A, Pouget J, et al. Stimulus-response curve of human motor nerves: Multicenter assessment of various indexes. *Neurophysiol Clin* 2007;38:31–8.
- Bostock H. S117 Excitability testing in the 21st century. *Clin Neurophysiol* 2017;128:e216.
- Bostock H, Cikurel K, Burke D. Threshold tracking techniques in the study of human peripheral nerve. *Muscle Nerve* 1998;21:137–58.
- Burke D, Kiernan MC, Bostock H. Excitability of human axons. *Clin Neurophysiol* 2001;112:1575.
- Burke D, Kiernan MC. Stimulus, response and excitability – what is new?. *Clin Neurophysiol* 2018;129(1):333–4.
- Cappelen-Smith C, Kuwabara S, Lin CS-Y, Mogyoros I, Burke D. Membrane properties in chronic inflammatory demyelinating polyneuropathy. *Brain* 2001;124:2439–47.
- Kiernan MC, Burke D, Andersen KV, Bostock H. Multiple measures of axonal excitability: a new approach in clinical testing. *Muscle Nerve* 2000;23:399–409.
- Milants C, Benmouna K, Wang FC. IMAX: a new tool to assess peripheral axonal motor hypoexcitability. *Clin Neurophysiol* 2017;128(12):2382–3.

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