

letters to the editor

The following is the abstract of the article that generated Letters to the Editor in the November 2000 issue of the *Journal of Applied Physiology* (*J Appl Physiol* 89: 2105–2106, 2000). A follow-up letter by Dr. Bodor to the reply by Drs. Ng and colleagues appears below.

Ng, A. V., H. T. Dao, R. G. Miller, D. F. Gelinas, and J. A. Kent-Braun. Blunted pressor and intramuscular metabolic responses to voluntary isometric exercise in multiple sclerosis. *J. Appl. Physiol.* 88: 871–880, 2000.—To test the hypothesis that a lower mean arterial pressure (MAP) response during voluntary isometric exercise in multiple sclerosis (MS) is related to a dampened muscle metabolic signal, 9 MS and 11 control subjects performed an isometric dorsi-flexor contraction at 30% maximal voluntary contraction until target failure (endurance time). We made continuous and noninvasive measurements of heart rate and MAP (Finapres) and of intramuscular pH and P_i (phosphorus magnetic resonance spectroscopy) in a subset of 6 MS and 10 control subjects. Endurance times and change in heart rate were similar in MS and control subjects. The decrease in pH and increase in P_i were less throughout exercise in MS compared with control subjects, as was the change in MAP response. Differences in muscle strength accounted for some of the difference in MAP response between groups. Cardiovascular responses during Valsalva and cold pressor tests were similar in MS and control subjects, suggesting that the blunted MAP response during exercise in MS was not due to a generalized dysautonomia. The dampened metabolic response in MS subjects was not explained by inadequate central muscle activation. These data suggest that the blunted pressor response to exercise in MS subjects may be largely appropriate to a blunted muscle metabolic response and differences in contracting muscle mass.

Central Neuronal Fatigue in Multiple Sclerosis

To the Editor: Many thanks to Drs. Ng and colleagues for their response to my analysis and alternate interpretation (1) of their data on intramuscular responses to voluntary isometric exercise in multiple sclerosis (MS).

In their response, Drs. Ng and colleagues reported that they performed additional calculations showing that the electromyographic (EMG)-to-force ratios at end exercise increased threefold in both the MS and control groups, arguing against my central neuronal fatigue hypothesis for MS (see reply in Ref. 1).

On the contrary, my central neuronal fatigue hypothesis for MS holds that, during muscle contraction to fatigue, a number of central neurons fail as a result of cellular fatigue caused by the increased energy demands of neurotransmission through high-resistance demyelinated neural pathways.

At the end of exercise, those corticomotoneurons that did not fail as a result of central neuronal fatigue continue to innervate normal muscle fibers, which pro-

duce normal EMG signal, force, and EMG-to-force ratios. It is thus expected that no difference would be found in the rise of EMG-to-force ratios at end exercise in the MS and control groups, which is exactly what Drs. Ng and colleagues found in their additional calculations (see reply in Ref. 1). Furthermore, these findings argue against the presence of a muscle disorder in the MS group.

As Drs. Ng and colleagues correctly pointed out in their reply, my central neuronal fatigue hypothesis is largely based on the findings of a substantial difference in residual EMG vs. residual strength ratios between the MS and control groups (1). However, Drs. Ng and colleagues argue that, because their end-exercise EMG and postexercise maximal voluntary contraction (MVC) measurements were not made simultaneously, the two measurements do not correspond to each other, an assertion with which I disagree.

Because both the MS and control groups experienced the same time interval (1.5 min) between end-exercise EMG and postexercise MVC measurements, there is no reason why a ratio of these two independent variables cannot be made. If instead end-exercise EMG and MVC measurements are taken simultaneously (see reply in Ref. 1), then by definition these two variables cannot be considered to be independent, since end exercise was defined as the moment at which muscle force declined to 30% preexercise MVC in both groups.

The fact that a time interval (1.5 min) was present between end-exercise EMG and postexercise MVC measurements, allowing for the recovery of fatigued central neurons to occur in the MS group, is precisely why a substantial difference in the residual EMG vs. residual MVC ratios between groups can be detected.

With regard to residual EMG as an indicator of central neuronal fatigue, end-exercise residual EMG was 58% in the MS group and 69% in the normal group, arguing for central neuronal fatigue, but with $P = 0.32$ this did not reach statistical significance. Because both the MS and control groups overlap in terms of normal physiology, it may not be possible to use the single variable of residual EMG to definitively detect or refute the presence of central neuronal fatigue.

Analysis of a combination of variables may be necessary to do so, thus my calculation of the residual EMG vs. residual MVC ratio. It would be interesting if Drs. Ng and colleagues were to calculate this ratio on individual data points and determine whether the findings of a 0.8 ratio in the MS group and a 1.2 ratio in the normal group reach statistical significance. Nevertheless, depending on the degree of demyelination present, some individuals in the MS group may have ratios closer to the normal group, making it particularly

difficult to demonstrate a statistically significant difference between groups, especially given the small size of the MS group (nine subjects) in the current study (2).

REFERENCES

1. **Bodor M, Ng AV, Miller RG, and Kent-Braun JA.** Intramuscular metabolic responses to voluntary isometric exercise in multiple sclerosis are consistent with central neuronal fatigue. *J Appl Physiol* 89: 2105–2106, 2000.
2. **Ng AV, Dao HT, Miller RG, Gelinas DF, and Kent-Braun JA.** Blunted pressor and intramuscular metabolic responses to voluntary isometric exercise in multiple sclerosis. *J Appl Physiol* 88: 871–880, 2000.

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