should be mentioned at the outset that the accuracy of the applied method is limited’ (Panayiotopoulos and Scarpalezos, 1975).

Problem 2 The factors of error involved in the motor axon counting technique would affect disproportionately the results in health, denervation, and muscular dystrophy, thus precluding comparative studies between them.

1. In denervation, although the ‘alternating’ phenomenon (McComas et al., 1971) is less troublesome (Panayiotopoulos and Scarpalezos, 1975), the additive summation of newly recruited MUP is less satisfactory than in control subjects (McComas et al., 1971b; Panayiotopoulos and Scarpalezos, 1975). Moreover, ephaptic activation of degenerated motor axons cannot be totally excluded.

2. In Duchenne muscular dystrophy the factors of error contributing to an underestimation of the number of motor axons are much greater than in healthy subjects and denervation (a detailed discussion can be found in Panayiotopoulos (1976) as well as in previous reports: Scarpalezos and Panayiotopoulos, 1973; Panayiotopoulos et al., 1974). It would be also impossible with the ‘new methods’ to determine ‘the firing levels of ‘small MU (which) could make an undetectable contribution to the surface EMG’ (Brown et al., 1976). One might ask why we applied the method in neuromuscular diseases despite our awareness of the above several problems. Our purposes were (a) to point out the fundamental difficulties of the original technique, results from which were considered the strongest evidence to support the neurogenic hypothesis, and (b) to show that by approximately equalising the factors of error between health and muscular dystrophy there is in fact no loss of motor axons in muscular dystrophy and that ‘the neurogenic hypothesis is based on poor and vulnerable evidence’ (Panayiotopoulos and Scarpalezos, 1975; Panayiotopoulos et al., 1976). McComas has recently participated in an experimental ‘study which provides direct evidence against a neuropathogenesis for murine dystrophy’ (Law et al., 1976).

In the results of the ‘new methods’ (Milner-Brown and Brown, 1976) two out of four cases of muscular dystrophy have numbers of motor units below the lowest normal value. In view of the recent work (Law et al., 1976) the above findings may be an indirect evidence that the ‘new methods’ do not equalise the factors of error between health and muscular dystrophy.

In conclusion, we believe that the above main and other problems of the motor axon counting technology should be vigorously discussed and tested if ‘new methods’ and ‘new results’ are to be presented in the future.

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SIR.—Our intention in the papers (Brown and Milner-Brown, 1976; Milner-Brown and Brown, 1976) has been to highlight errors in the method originally proposed to estimate motor unit numbers (McComas et al., 1971a), and report modifications that can correct for one of the most important errors: the fluctuation in the electrical excitability and overlap in the firing levels of motor axons. The modifications are part of a continuing programme to develop a method, acceptable to patients, and capable of providing accurate quantitative estimates of the number of motor units (MU) in muscles.

Differences in the latencies from the stimulus shock to maximum voltage(s) in MU can partially, indeed completely, hide the voltage contribution of MU to the incremental sum, particularly if the range in latencies of the single MU is large. Precisely for that reason we have stated that MU isolated using isometric contraction, F discharge, or multiple point stimulation cannot be used directly to calculate a mean MU potential voltage (Feasby and Brown, 1974; Milner-Brown and Brown, 1976). These methods were, however, used to isolate single MU in order to indicate the presence of large MU in the muscle and to emphasize how unrepresentative the sample of MU used in calculating the mean motor unit potential (MMUP) are.

In ‘problem 1’, Dr Panayiotopoulos states that ‘The most essential requirement is that the MUP be summated in a precisely additive manner’. The lack of temporal coincidence of the potential maxima of individual MU is evident, and has been quantitatively illustrated by comparing the mean amplitudes of MUP obtained directly from incremental responses with MUP isolated using graphical subtraction (Panayiotopoulos et al., 1974), or computer methods (Ballantyne and Hansen, 1974; Brown et al., unpublished). However, in the original method (McComas et al., 1971a) and our modified methods (Milner-Brown and Brown, 1976), the probable ‘error’, due to the lack of temporal coincidence of potential maxima of individual MU, is inherent in the summation of the compound potential (CP) of the first 10 MU used in calculating the MMUP as well as the maximum CP. As there is no obvious reason to suggest that the algebraic summations are not the same in both CPs, the probable ‘errors’ should cancel out when the maximum CP is divided by the MMUP. Therefore, the relative importance of the pattern of summation in the overall MUP seems to have been overemphasised by Dr. Panayiotopoulos.

Panayiotopoulos and colleagues seemed to imply that their modified method was an improvement on the original method, because in their method ‘an effort was made to minimise the possibility of missing small amplitude MUAP’ (Panayiotopoulos et al., 1974; Panayiotopoulos and Scarpalezos, 1975). In a recent study we showed that motor units are excited in order from small to large by graded increases in the stimulus intensity (Kadrie et al., 1976). Therefore, the case for exclusion of the very small MU by the
original method has been overstated, the methods and observations on which it has been based being incorrect. The recognition of the voltage contribution of single MU to the surface record depends on the potential steps occurring in an all-or-nothing manner, the ‘all’ responses being clearly reproduceable in configuration and beyond the possible errors introduced by noise, stimulus artefact, and the inclusion of out of order summation ‘alternation’ potentials. In our opinion, none of the above conditions is met by the methods reported by Panayiotopoulos et al. (1974).

In conclusion, we would like to add that, even though no method for estimating MU numbers has been found to date that is entirely acceptable, the two modified methods incorporating an important correction should help to make the method of estimating MU numbers more accurate. However, it is premature in our opinion to hypothesise on the aetiology of neuromuscular disorders based on data obtained from motor unit estimates alone.

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