Matters Arising

was the sharp difference of the homolateral scans CT over Figure 48 revealed alteration of the exclusively spontaneous and focal myositis or muscle neoplasms, if invading the terminal nerve branches, might induce "profuse spontaneous activity".

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Matte H et al reply: We thank Dr Meinck for his comments and the presentation of two additional cases of isolated muscle hypertrophy. However, comparing his and our cases, the EMG results were substantially different. As Dr Meinck states, both his patients showed intramuscular areas which were silent on EMG close to areas with diffuse spontaneous activity. Silent EMG areas were not present in our patients. We intended our cases to make a contribution to the understanding of the pathophysiology of isolated muscle hypertrophy after peripheral nerve or root lesions. We showed that this phenomenon is not restricted to the calves and may affect other muscles as well, where the stretch hypothesis for generation of muscle hypertrophy might not be true and profuse spontaneous activity of the muscle fibres might have caused hypertrophy. We agree that tumours are much more common causes of muscle masses and might cause spontaneous activity on EMG when invading terminal nerve branches. However, as stated, there are silent EMG areas within tumours. In these and doubtful cases we also perform MRI.

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Iron and Akathisia

The report by O'Loughlin et al. on the serum iron status of patients with acute neuroleptic-induced akathisia is of interest to us as our own initial investigation revealed no associated between the two. Since the publica-

tion hypertrophy. Focal myositis or muscle neoplasms, if invading the terminal nerve branches, might induce "profuse spontaneous activity".

Since the publication of our findings, we have repeated the study on a further 50 patients recently started on neuroleptic medication, with further negative results (unpublished). Studies of serum iron status in "chronic akathisia" have reported similarly conflicting findings. 3,4 It would therefore be worthwhile at this stage to re-examine the rationale and the methodology of the studies. We commend Dr O'Loughlin and colleagues for their attention to detail, except for the following points: 1) The definition of akathisia used in their study was based on scale scores. 3 Not only have the psychometric properties of this scale not been published, it was also designed to rate and not "diagnose" akathisia. As we point out elsewhere, 3 the issue of appropriately defining akathisia is of paramount importance. 2) The small number of patients with akathisia involved; 3) The failure of the authors to report the differential neuroleptic doses of the two groups. The dose can be an overriding factor that can skew the contribution of any other factors difficult to determine; 4) The lack of any correlation between Simpson and Angus scores and akathisia scores is surprising, suggesting that their patients may not have typical acute akathisia.

There are some important theoretical considerations. What constitutes iron deficiency, and whether serum biochemical measures accurately reflect the state of brain iron, is debatable. 4 While transferrin is important for the exchange of iron between tissues, its saturation in the serum fluctuations between 20-50% in normal subjects (due to mono- dieric forms), and small variations in saturation as seen in the above study are unlikely to affect iron delivery. The most important determinant of tissue iron delivery is the total number of transferrin receptors, and an efficient homeostatic mechanism exists to maintain the rate of iron transported to the tissues. The turnover of iron in the brain is low, and it has a tendency to resist iron depleton, raising further doubts about the pathophysiological significance of the reported findings. It is also possible that neuroleptic drugs either mobilise iron from peripheral tissues into the brain, or decrease iron turnover in the brain,4 making peripheral measures of iron status even more suspect in revealing the iron status in the brain. MRI may be one method of overcoming this problem, 3 but only good animal models 3 are likely to provide the final answer.

Despite these objections, we feel that there are compelling reasons to study the interaction of iron and neuroleptic drugs. The fall in serum iron and transferrin in the patients with akathisia reported by O'Loughlin et al. is intriguing, even though its significance for the development of akathisia is questionable. Rosebush and Mazureck 3 reported somewhat similar findings for patients who developed neuroleptic malignant syndrome. Little is known about the effect of neuroleptics on ferrokinetics. Clearly this area needs further informed investigation.

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Figure A) Case 1. CT scan of the calves just below the fibular head. B) Case 2. Ventral aspect of the calves.
Disturbances of C-fibre-mediated sensibility in lumbosacral disc disease

I was interested to read the communication by F Strian et al.1 There is difficulty, however, in accepting that heat pain threshold is lowered in the foot contralateral to the sciatic root compression, rather than raised in the foot ipsilateral to the lesion (as is the warmth threshold).

With JA Campbell, AW Chan, G Lejon and T Nurmiko, thresholds to most somatosensory modalities have been measured using the method of limits, at five body sites on each side in a large number of volunteers, as well as in patients with neuropenic pain conditions. In the case of the foot, a Marstock-Peltier thermo stimulator measuring 25.0 × 50.0 mm (12.5 cm²) was applied just below the medial malleolus, where the skin is neither thickened nor hairy. Our results for warmth and heat pain in (1) the normal foot; (2) the diabetic foot; (3) postherpetic neuralgia; and (4) central post-stroke pain ("thalamic syndrome") are shown in table 1. In cases 3 and 4, comparison is made (paired r test) between expected normal measurements on the other side of the body, while in (2) age-matched normal subjects were used (unpaired r test). Our results suggest that while there is a large rise in the warmth threshold (average about 6°C), or twice this, for the warm-cold limen, on the affected side, there is only a very small (average about 2°C) but significant, rise in the heat pain threshold, also on the affected side.

Strian et al used a thermode measuring 6 cm². With J Giewald, we have performed experiments using both large (12.5 cm²) and small (1.3 cm²) thermodes, and found that while warmth thresholds vary according to the surface area of the thermode, heat pain thresholds do not. We find the ipsilateral mean (SD) heat pain threshold of 48.1 (1.6°C) to be significantly lower than that of the unaffected side, and this finding is confirmed when comparing our normal thresholds (see table 2) and those found by others, and would suggest that the ipsilateral heat pain threshold in the patients of Strian et al may be raised.

We would like to know how many of their 9 patients had L5 root lesions and how many S1; where on the foot they measured heat pain thresholds for the two roots; and whether there is any difference according to site, in both patient population and control subjects—although it must be admitted that our own results are somewhat lower than theirs. Further, the postherpetic neuralgia patients suggest that site makes little difference.

Table 1 Mean warmth and heat pain thresholds (°C) in normal feet

| Age (mean) | 17-30 (22-1) | 31-45 (35-1) | 46-60 (54-1) | 61-74 (68-7) |
| Number | 28 | 28 | 28 | 28 |
| Warmth threshold (SD) | 36-75 (3-22) | 37-65 (2-89) | 37-75 (2-88) | 39-4 (4-03) |
| Heat pain threshold (SD) | 41-5 (2-7) | 41-75 (2-4) | 43-0 (3-3) | 43-1 (2-5) |

Table 2 Mean (SD) warm thresholds, warm-cold limens, and heat pain thresholds (°C) in neuropenic pain conditions

| Warm-cold Limen (SD) | 40-8 (6-9) | 40-8 (6-9) | Paired t test p = 0.000001 | Warm pain threshold 46-6 (2-6) |
| Painful diabetic neuropathy | Warm-cold Limen (SD) | 40-8 (6-9) | Paired t test p = 0.000001 | Warm pain threshold 46-6 (2-6) |
| Postherpetic neuralgia | Pain Threshold (SD) | 35-4 (0-3) | Paired t test p = 0.00003 | Pain threshold 45-8 (0-5) |
| Central post-stroke pain | Pain Threshold (SD) | 35-4 (0-3) | Paired t test p = 0.002 | Pain threshold 42-7 (0-45) |
| Painful diabetic neuropathy | Warm-cold Limen (SD) | 40-8 (6-9) | Paired t test p = 0.000001 | Warm pain threshold 46-6 (2-6) |
| Postherpetic neuralgia | Pain Threshold (SD) | 35-4 (0-3) | Paired t test p = 0.00003 | Pain threshold 45-8 (0-5) |
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References