Figure A) Case 1. CT scan of the calves just below the fibular head. B) Case 2. Ventral aspect of the calves.

was a 48 year old man who presented with the history and clinical signs of L5 and S1 radiculopathy including fibrillations, positive sharp waves, and bizarre low-frequency discharges in all peroneal, and some in the gluteal muscles, associated with unilateral calf enlargement. Distal motor latencies to the peroneal muscles were mildly prolonged. CT scans showed a $9 \times 3 \times 3$ cm lipoma, which was excised, (fig A) compressing both the deep and superficial peroneal nerves, and a homolateral S1 root compression by a slipped disc. Case 2, a 33 year old housewife, noted progressive painless calf enlargement over several years. Eventually, the circumference of the right calf exceeded that of the left one by 9 cm (fig B). Her neurological status was normal. Electromyography revealed dense fasciculations, bizarre low-frequency discharges, and chronic neurogenic alteration of motor unit potentials exclusively in the right triceps surae muscle. On surgery, diffuse lipomatosis was found and confirmed by microscopical examination. In both cases intramuscular areas with "silent" EMG—close to areas with profuse spontaneous activity—were indicative of a non-myogenic nature of the calf enlargements.

Large series suggest that intramuscular tumours are far more common than denerva-

tion hypertrophy.²⁻⁴ Focal myositis or muscle neoplasms, if invading the terminal nerve branches, might induce "profuse spontaneous activity".

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Mattle 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 profuse 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*¹ on the serum iron status of patients with acute neuroleptic-induced akathisia is of interest to us as our own similar investigation revealed no association between the two.² 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.³⁻⁶ 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,⁷ 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 make 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,⁷ 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.⁸ While transferrin is important for the exchange of iron between tissues, its saturation in the serum fluctuates between 20-50% in normal subjects (due to mono- and diferric 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,⁸ 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 depletion,⁹ 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,¹⁰ 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,¹¹ but only good animal models¹² 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 Mazurek¹³ 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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