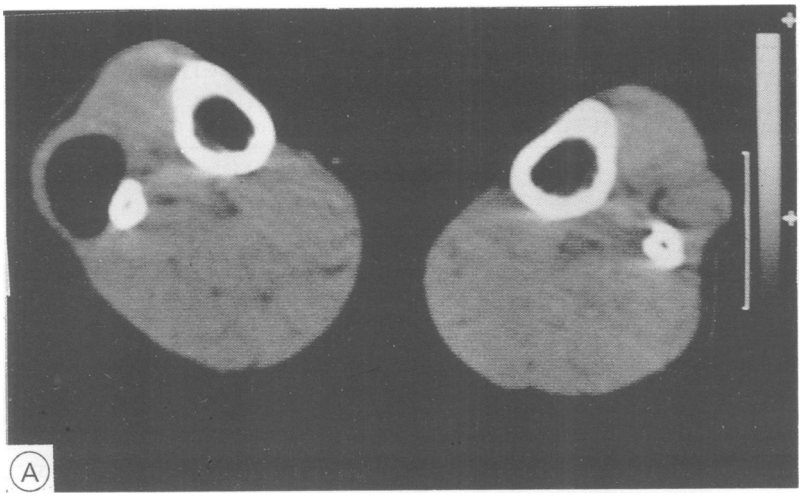

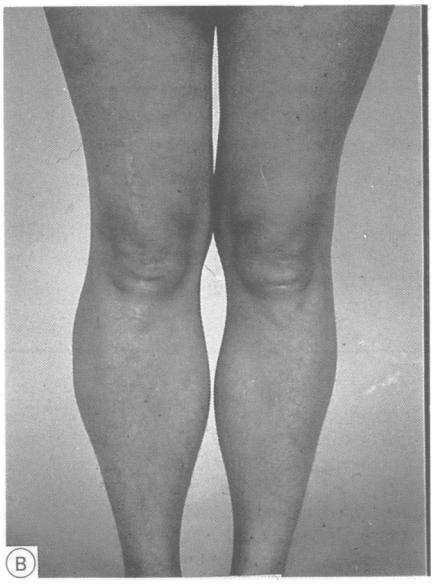

Figure A) Case 1. CT scan of the calves just below the fibular head. B) Case 2. Ventral aspect of the calves.

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 × 3 × 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 denervation hypertrophy.[2-4] Focal myositis or muscle neoplasms, if invading the terminal nerve branches, might induce "profuse spontaneous activity".

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1 Mattle HP, Hess CW, Ludin H-P, Mumenthaler M. Isolated muscle hypertrophy as sign radicular or peripheral nerve injury. *J Neurol Neurosurg Psychiatry* 1991;54:325–9.
2 Kindblom L-G, Angervall L, Stener B, Wickbom I. Intermuscular and intramuscular lipomas and hibernomas. *Cancer* 1974;33:754–62.
3 Booher RJ. Lipoblastic tumors of the hands and feet. *J Bone Joint Surg.* 1965;47:727- 40.
4 Fettell MR, Duffy PE, Rowland PE. Infiltrating lipoma: a cause of monomelic hypertrophy. *Muscle Nerve* 1978;1:75–80.

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 associated 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 differic 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 homoeostatic 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 models[12] 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 Mazurek[13] 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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1 O'Loughlin V, Dickie AC, Ebmeier KP. Serum iron and transferrin in acute neuroleptic induced akathisia. *J Neurol Neurosurg Psychiatry* 1991;54:363–4.
2 Sachdev P, Loneragan C. Acute drug-induced akathisia is not associated with low serum iron status. *Psychopharmacol* 1991;103: 138–9.
3 Brown KW, Glen SE, White T. Low serum iron status and akathisia. *Lancet* 1987;I:1234–6.

4 Barnes TRE, Halstead SM, Little P. Akathisia variants: Prevalence and iron status in an inpatient population with chronic schizophrenia. *Schizophr Res* 1990;3:79 (abst).
5 Barton A, Bowie J, Ebmeier K. Low plasma iron status and akathisia. *J Neurol Neurosurg Psychiatry* 1990;53:671–4.
6 Nemes ZC, Rotrosen J, Angrist B, *et al.* Serum iron levels and akathisia. *Biol Psychiatry* 1991;29:411–3.
7 Sachdev P, Loneragan C. The present status of akathisia. *J Nerv Ment Dis* 1991;179: 381–91.
8 Finch CA, Huebers H. Perspectives in iron metabolism. *N Engl J Med* 1982;306: 1520-8.
9 Pollitt E, Leibel RL. *Iron deficiency: brain biochemistry and behaviour* New York: Raven Press, 1982.
10 Ben-Shachar D, Youdim MBH. Neuroleptic induced dopamine receptor supersensitivity and tardive dyskinesia may involve altered brain iron metabolism. (abst) *Br J Pharmacol* 1987;90:95.
11 Rutledge JN, Hilal SK, Silver AJ, *et al.* Study of movement disorders and brain iron by MR. *Am J Neuroradiol* 1987;8:397–411.
12 Emerich DF, Sanberg PR. Neuroleptic dysphoria. *Biol Psychiatry* 1991;29:210–3.
13 Rosebush PI, Mazurek MF. Letter. *Am J Psychiatry* 1991;148:148–9.

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 Leijon and T Nurmikko, thresholds to most somatosensory modalities have been measured, by the method of limits, at five body sites on each side in a large number of volunteers, as well as in patients with neurogenic pain conditions. In the case of the foot, a Marstock Peltier thermode measuring 25·0 × 50·0 mm (12·5 cm^2) 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 *t* test) with the unaffected mirror-image area on the other side of the body, while in (2) age-matched normal subjects were used (unpaired *t* 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 cm^2. With J Giewald, we have performed experiments using both large (12·5 cm^2) and small (1·3 cm^2) 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[1] unaccountably high compared with 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.

It would be helpful 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 on the unaffected side of postherpetic neuralgia patients suggest that site makes little difference.

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1 Strain F, Lautenbacher S, Karlbauer G, Galfe G. Disturbances of C-fibre-mediated sensibility in lumbrosacral disc disease. *J Neurol Neurosurg Psychiatry* 1991;54:1013–14.

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 limen, and heat pain thresholds (°C) in neurogenic pain conditions

	Painful diabetic neuropathy	
64 Patients:	Warm-cold Limen (SD): 19·0 (8·8)	Heat pain threshold 46·6 (2·6)
Median age: 54	unpaired *t* test: $p < 0.000001$	$p < 0.00001$
28 Controls:	Warm-cold Limen (SD): 6·1 (2·65)	Heat Pain Threshold: 43·0 (3·3)
	Postherpetic neuralgia	
39 Patients:	Warm Threshold (SD): 40·8 (0·9)	Heat Pain Threshold (SD): 45·8 (0·5)
Median age: 69·5	paired *t* test: $p < 0.000001$	$p < 0.00003$
39 Controls:	Warm Threshold (SD): 35·4 (0·3)	Heat Pain Threshold (SD): 43·1 (0·5)
	Central post-stroke pain	
38 Patients:	Warm Threshold (SD): 40·5 (0·8)	Heat Pain Threshold (SD): 43·8 (0·4)
Median age: 64	paired *t* test: $p < 0.000001$	$p = 0.02$
38 Controls:	Warm Threshold (SD): 33·5 (0·4)	Heat Pain Threshold (SD): 42·7 (0·45)
	Painful diabetic neuropathy	
64 Patients:	Warm-cold Difference (SD): 19·0 (8·8)	Heat Pain Threshold: 46·4 (2·6)
Median age: 54	unpaired *t* test: $p < 0.000001$	$p < 0.00001$
28 Controls:	Warm-cold Difference (SD): 6·1 (2·65)	Heat Pain Threshold: 43·0 (3·3)
	Postherpetic neuralgia	
39 Patients:	Warm Threshold (SD): 40·8 (0·9)	Heat Pain Threshold (SD): 45·8 (0·5)
Median age: 69·5	paired *t* test: $p < 0.000001$	$p < 0.00003$
39 Controls:	Warm Threshold (SD): 35·4 (0·3)	Heat Pain Threshold (SD): 43·1 (0·5)
	Central post-stroke pain	
39 Patients:	Warm Threshold (SD): 40·5 (0·8)	Heat Pain Threshold (SD): 43·8 (0·4)
Median age: 64	paired *t* test: $p < 0.000001$	$p = 0.02$
38 Controls:	Warm Threshold (SD): 33·5 (0·4)	Heat Pain Threshold (SD): 42·7 (0·45)

Strain et al reply:

We found the comments of Dr Bowsher on our article very informative, and a suitable starting point for a discussion on the diagnostic value of heat pain sensitivity testing. His main concern was that the mean heat pain threshold in the dermatome ipsilateral to the chronic nerve root compression was 48·1°C, which he found unaccountably high. We wish to point out that our controls' value was 47·3°C in this study and that we had obtained a value of 46·5°C at the same sites in a much younger group of healthy subjects.[1] We therefore think the question is why are our values consistently higher than those reported by Bowsher, which are in the range of 41°C to 43°C.

Even with contact thermodes, the heat pain threshold cannot be considered as a physiological constant given in °C. It is clearly dependent on the physical characteristics of the thermode and the measurement procedures. We will give some examples of our experience. We recently changed from Marstock type thermodes (used also in the study under discussion) to a more advanced model with the same surface area (6 cm^2). Because of the different characteristics of these thermodes that is, the isolation layer between the Peltier elements and the thermode surface) an average lowering of the thresholds of about 1·5°C occurred.[2] The heat pain thresholds of three age groups measured at the lateral dorsum pedis were 44·9(1·5)°C (17–29 years), 44·8(1·9)°C (30–44 years) and 45·7(1·2)°C (45–63 years). These values are still considerably higher than those given by Bowsher. We think that there may be two reasons.

First, threshold estimates in the early trials were lower and more variable than in the later ones. For example, the difference between the first and the eighth trial with measurements on the foot was found to be −1·3°C.[3] We therefore disregard the first three trials in evaluation. Second, with the traditional Marstock procedures the temperature increases start from temperatures around 30°C and may lead to what we would call "premature pain responses" at temperatures well below 40°C. This can again be clearly seen in a very recent study by Jensen *et al.*[4] To avoid this, we set the base temperatures to 38°C or 40°C, which are levels that have not been felt painfully by any of our patients or control subjects.

Considering these factors, we think that the pain threshold values we reported, although different from those of Bowsher, should be considered valid and that it is very unlikely that the difference between the pain thresholds measured ipsi-and contralaterally to the nerve root compression is the consequence of an ipsilateral threshold increase rather than a contralateral threshold decrease. (As a reminder, the contralateral value was 45·8°C and significantly smaller than the value of the health controls).

We read the findings of Bowsher on heat pain and warmth sensitivity in different patient groups with interest and have no difficulty agreeing with them. However, hypalgesic phenomena in diabetic, postherpatic and post-stroke patients do not exclude the possibility of hyperalgesic phenomena in