All these variables except number 3 determine the amount and rate of transfer of energy through the skin to the neural receptors. The standardisation of this energy transfer is a basic prerequisite for techniques of thermal threshold measurement. Their failure to control these variables invalidates any conclusions on the reliability or otherwise of a single component, namely the psychophysical aspect, of the techniques.

In addition to the technical difficulty the authors choose of subjects further compounds the problem. In diabetic patients thermal thresholds and other parameters of nerve function vary with blood glucose levels, influencing an even greater variable.

Their definition of "static" and "dynamic" methods of application of thermal stimulation is misconceived; dynamic stimuli are applied in both techniques (for example, in the Sensortek method, the temperature of the thermal receptors will alter with time when a thermode of different temperature is applied to the skin surface). The authors' statement, in the discussion, that differences between these two techniques are due to the nature of the stimulus (static versus dynamic) has no conceptual or rational basis.

In conclusion, the authors have not assessed the merit of the two psychophysical procedures, rather they have compared two techniques for thermal threshold testing, which incorporate among many other variables, two different psychophysical procedures. This conclusion as to the efficiency or otherwise of the psychophysical aspect of the two techniques is invalid.

GORAN A JAMAL
Department of Neurology
STIG HANSEN
West of Scotland Health Boards,
Department of Clinical Physics and Bioengineering
JOHN P BALLANTYNE
Department of Neurology,
Institute of Neurological Sciences,
Glasgow

2 Lile PP. Relationship between cutaneous thermal thresholds, skin temperature and the measurement of areas of the stimulus. Physiol London 1954;126:191-205.

Levy et al reply: Dr Jamal and his colleagues argue that we are unable to comment on the relative advantages of the two algorithms used for testing thermal sensation as we did not control for a number of confounding variables: influence of the rate of heat transfer through skin. This was not the aim of our study; we set out to compare, in a routine clinical setting, two technically available methods. The algorithms used were one of many differences between the two methods. We simply made the point that in screening studies the choice of a suitable apparatus need not be determined by the psychophysical basis of the test; it is evident from the similar coefficients of variation of all comparable methods.

Dr Jamal's long excursion into the factors influencing transfer of thermal energy is irrelevant since control of stimulus-related factors other than skin temperature and site would have materially altered the methods from those which are commercially available, and does not affect our proposition that precision and reproducibility are related neither to the choice of apparatus nor to the algorithm used. It is our contention that the high variability of all clinical psychophysical methods owes more to "central processing" than to the standardised presentation of the stimulus. Our experience with the Glasgow thermal testing method (as used in the Medelec instrument) showed that it was no more reproducible than the other methods, a finding which is at variance with Dr Jamal's claim of "negligible" intrindividual variability.

Some of the technical points raised by Dr Jamal apply equally to both methods, so we are unclear how they would affect a comparative study (for example, the surface skin temperature, the lack of calibration of heat transfer at the thermode, the thermode's application pressure, and the fact that both methods involve application of uncontrolled tactile stimuli). As to the question of thermal neutrality, Kenshalo found that it could be achieved over a wide range of temperatures, 29-37°C; Dr Jamal's advocacy of the use of a basal temperature of 35°C is therefore arbitrary and in addition quite impractical and time-consuming to achieve in diabetic patients, many of whom have peripheral small- and large- vessel disease. The criticism of our use of diabetic patients on the basis of the known effects of ambient blood glucose levels on nerve function is misplaced in a paper devoted specifically to a clinical study of diabetic patients. In addition, in a large group comparison, the effects of blood glucose variation can also be discounted.

A study comparing algorithms alone with control of all stimulus-related factors has yet to be done and remains a formidable challenge. We are yet to be convinced that strict attention to details of presentation of the thermal stimuli is relevant to the testing of thermal sensation in untrained subjects in clinical settings.

D AVID LEVY
RALPH ABRAMAH
GORDON REID
Department of Diabetes and Endocrinology,
Central Middlesex Hospital,
London NW10 7NS

Responses to temperature in primary hypothyroidism

Using standard neurophysiological criteria Beghi et al made a definite diagnosis of hypothyroidism in 72% of 39 consecutive patients with primary hypothyroidism. They took care to maintain the temperature at 32-34°C throughout these studies, but do not comment upon core temperatures. It was well recognised that hypothyroid patients may be hypothermic.1 In 1983 we found similar abnormal peripheral nerve conduction in hypothyroid patients.2 We also corrected skin temperature in these studies. Central conduction velocity in the visual pathways, represented by latency of the visual evoked potential, was also slow. These abnormalities were reversed by thyroxine. However, we also demonstrated that correction of hypothermia by central warming led to a remarkable improvement of both of these neurophysiological parameters in untreated patients.

Beghi et al state that using physiological criteria the prevalence of polyneuropathy in hypothyroidism is 71%. However, the data suggest, however, that these abnormal conduction velocities are, in many cases, appropriate physiological responses to a reduced core temperature rather than due to pathology of the peripheral nerves.

RJ ABBOTT
BP O'MALLEY
Leicester Royal Infirmary,
Leicester LE1 SWW

Management of intraventricular haemorrhage secondary to ruptured arteriovenous malformation in a child with von Willebrand's disease

The recent report by Osenbach et al about a 13 year old girl with von Willebrand's disease and an intracranial arteriovenous malformation raises some important issues.

Their patient developed intraventricular and subarachnoid haemorrhage following minor trauma. Although a bleeding diathesis was diagnosed, a structural vascular lesion was suspected and subsequently confirmed by angiography. The occurrence of an arteriovenous malformation in a patient with von Willebrand's disease is of interest in view of the possible association of this bleeding disorder with various cardiovascular abnormalities, including mural valve prolongation,3 arterial aneurysms,4 gastrointestinal angiodysplasias,5 and telangiectasias.6

It has been suggested that this association represents an underlying congenital disorder of von Willebrand's disease, resembling the heritable connective tissue disorders.7 Abnormalities of the mesenchymal extracellular matrix may be the common ground of, among others, von Willebrand's disease, Ehlers-Danlos syndrome, polycystic


3 Abbott RJ, O'Malley BP, Barnett DB, Timson L, Rosenthal FD. Central and peripheral nerve conduction in thyroid dysfunction: the influence of L thyroxine therapy compared with warming upon the conduction abnormalities of primary hypothyroidism. Clinical Science 1983;64:617-22.

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The possibility that von Willebrand's disease is a myocardial or connective tissue disorder enforces the plea made by Dr. Osenbach and his colleagues that structural vascular lesions should be ruled out in all patients with von Willebrand's disease who develop intracerebral haemorrhage upon minor trauma.

Osenbach et al's patient had successful surgical extirpation of the lesion after two weeks of severe bleeding. Administration of the synthetic vasopressin analogue 1-desamino [8-D-arginine] vasopressin (DDAVP) may have been considered in their patient with type I von Willebrand's disease. This type of von Willebrand's disease is characterised by decreased plasma levels of qualitatively normal von Willebrand factor: antigen (vWF:Ag), vWF:Ag strongly promotes platelet-vascular wall interaction. DDAVP has been shown to stimulate the release of factor VIII and vWF:Ag, shorten or completely normalise bleeding time, and provide surgical haemostasis in patients with von Willebrand's disease. Moreover, the drug is administered at doses of 0.3 to 0.4 μg/kg body weight by intravenous injection over 20 minutes. DDAVP was approved by the United States Food and Drug Administration in 1984 for the treatment of the haemostatic defect of von Willebrand's disease. After an adequate response to the drug has been shown before surgery, DDAVP is considered the primary therapy for patients with type I von Willebrand's disease undergoing surgery. Endogenous vWF:Ag released by DDAVP into plasma has been shown to be haemostatically active as exogenous vWF infused with plasma concentrates, allowing safe performance of surgical procedures. Moreover, prolonged bleeding time in patients with severe von Willebrand's disease can be partially corrected by infusion of cryoprecipitate, be further shortened by DDAVP administration.

Treatment with DDAVP avoids the risks associated with administration of plasma derived products, for example, viral transmission and allergic reactions. DDAVP administration is associated with very few adverse effects. Mild facial flushing, probably caused by the stimulation of the sympathetic nervous system, is most frequently encountered. Other less common side effects are mild and transient headaches, a 10% increase in heart rate, and mild decreases in blood pressure. These reactions can easily be attenuated by slowing the rate of DDAVP infusion. DDAVP administration can be repeated at intervals of 12 to 24 hours although some patients treated with this drug at closely spaced intervals may become progressively unresponsive over a period of approximately five days.

Wouter J. Schievink, Marcel M. Liefveld. Department of Neurology and Centre for Thrombosis, Haemostasis, and Atherosclerosis Research, Academic Medical Centre, 1105 AZ Amsterdam, The Netherlands.

Matters arising

Kidney disease, mitral valve prolapse, and certain (cerebro) vascular anomalies.


