All these variables except number 3 determine the amount and rate of transfer of energy through the skin to the thermal 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 choice of subjects further compounds the problem. In diabetic patients thermal thresholds and other parameters of nerve function vary with blood glucose levels,¹⁰ introducing another 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. Their 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

- 1 Levy D, Abraham R, Reid G. A comparison of two methods for measuring thermal thresholds in diabetic neuropathy. *J Neurol Neurosurg Psych* 1989;52:1072-7.
- 2 Lele PP. Relationship between cutaneous thermal thresholds, skin temperature and cross sectional area of the stimulus. *J Physiol (London)* 1954;126:191-205.
- 3 Kenshalo DR. Psychophysical studies of temperature sensitivity. In: Neff WD ed. *Contributions to sensory physiology*. Vol 4. New York, London: Academic Press, 1970:19-74.
- 4 Molinari HH, Greenspan JD, Kenshalo DR. The effects of rate of temperature change and adapting temperature on thermal sensitivity. *Sens Processes* 1977;1:354-62.
- 5 Hensel H. *Thermal sensations and thermoreceptors in man*. Illinois, Springfield: Thomas, 1982.
- 6 Jamal GA, Hansen S, Weir AI, Ballantyne JP. Reproducibility of thermal sensation threshold measurements. *J Clin Physiol Physiol Measurement* 1986;7:391-2.
- 7 Jamal GA. A quantitative study of thermal sensation in man. PhD thesis, University of Glasgow 1986.
- 8 Cohen ML. Measurement of the thermal properties of human skin. A review. *J Invest Dermatol* 1977;69:333-8.
- 9 Stoll AM. Thermal properties of human skin related to nondestructive measurement of epidermal thickness. *J Invest Dermatol* 1977;69:328-32.
- 10 Delaney C, Westerman RA, Horowitz M, Pratt A, Kent P. Effects of blood glucose on small nerve fibre function in diabetes mellitus. *Proc Aust Physiol Pharmacol Society* 1989;20(1):11.

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 that influence 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 commercially 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; this 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.¹ Our experience with the Glasgow thermal testing method (as used in the Medelec instrument) showed that it was no more reproducible than three other methods, a finding which is at variance with Dr Jamal's claim of "negligible" intraindividual variability.²

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 application pressure, and the fact that both methods involve application of uncontrolled tactile stimuli). As to the question of thermal neutrality, Kenshalo³ 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 stimulus is relevant to the testing of thermal sensation in untrained subjects in clinical settings.

DAVID LEVY
RALPH ABRAHAM
GORDON REID
Department of Diabetes and Endocrinology,
Central Middlesex Hospital,
London NW10 7NS

- 1 Fagius J, Wahren LK. Variability of sensory threshold determination in clinic use. *J Neurol Sci* 1981;51:11-27.
- 2 Levy DM, Abraham RR, Abraham RM. A comparison of four methods for measuring thermal thresholds in diabetes. *Diabetic Med* 1987;4:591A.
- 3 Kenshalo DR. Psychophysical studies of temperature sensitivity. In: Neff WD, ed. *Contributions to sensory physiology*. Vol 4. New York, London: Academic Press, 1970:19-74.

Responses to temperature in primary hypothyroidism

Using standard neurophysiological criteria Beghi *et al*¹ made a definite diagnosis of polyneuropathy in 72% of 39 consecutive outpatients with primary hypothyroidism. They took care to maintain skin temperature at 32-34°C throughout these studies, but do not comment upon core temperatures.

It is well recognised that hypothyroid patients may be hypothermic.² In 1983 we found similar abnormalities in peripheral nerve conduction in hypothyroid patients.³ 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 rapid 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 718 cases per 1000. Our 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 5WW

- 1 Beghi E, Delodovici M, Boglium G, *et al*. *J Neurol Neurosurg and Psychiatry* 1989;52:1420-3.
- 2 O'Malley BP, Davies TJ, Rosenthal FD. TSH responses to temperature in primary hypothyroidism. *Clinical Endocrinology* 1980;13:87-94.
- 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.

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

The recent report by Osenbach *et al*¹ 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 mitral valve prolapse,² arterial aneurysms,³ gastrointestinal angiodysplasias,⁴ and telangiectasias.⁵

It has been suggested that this association represents an underlying mesenchymal disorder of von Willebrand's disease, resembling the heritable connective tissue disorders.^{2,4} Abnormalities of the mesenchym derived extracellular matrix may be the common ground of, among others, von Willebrand's disease, Ehlers-Danlos syndrome, polycystic

kidney disease, mitral valve prolapse, and certain (cerebro) vascular anomalies.⁶⁻¹⁰

The possibility that von Willebrand's disease is a mesenchymal or connective tissue disorder enforces the plea made by Dr Osenbach and his colleagues¹ 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.*'s¹ patient had successful surgical extirpation of the lesion after two weeks of cryoprecipitate therapy. 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-vessel 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 and other bleeding disorders.^{11,12} The drug is administered at doses of 0.3 to 0.4 µg/kg body weight by intravenous infusion 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 principal 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 as effective as exogenous vWF infused with plasma concentrates, allowing safe performance of surgical procedures.¹³ Moreover, prolonged bleeding time in patients with severe von Willebrand's disease can, after partial correction by infusion of cryoprecipitate, be further shortened by DDAVP administration.¹⁴

Treatment with DDAVP avoids the risks associated with the administration of plasma derived products, for example, viral transmission and allergic reactions. DDAVP administration is associated with very few adverse effects.¹⁵ Mild facial flushing, probably caused by vasodilatation of the skin, is most frequently encountered. Other less common side effects are mild and transient headaches, a 10% increase in heart rate, and minor 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 I SCHIEVINK
MARCEL M LEVI*
Department of Neurology and
Centre for Thrombosis, Haemostasis, and
Atherosclerosis Research,*
Academic Medical Centre,
1105 AZ Amsterdam, The Netherlands

1 Osenbach RK, Loftus CM, Menezes AH, *et al.* Management of intraventricular haemorrhage secondary to ruptured arteriovenous malformation in a child with von Willebrand's disease. *J Neurol Neurosurg Psychiatry* 1989;52:1452-4.

2 Pickering NJ, Brody JI, Barrett MJ. Von Willebrand syndromes and mitral-valve prolapse. Linked mesenchymal dysplasias. *N Engl J Med* 1981;305:131-4.

- 3 Wautier J-L, Fuscuardi J, Warnet A, *et al.* Syndrome de Willebrand acquis et angiodysplasie au cours d'une leucémie lymphoïde chronique. *Nouv Presse Med* 1977;6:3733-9.
- 4 Duray PH, Marcal JM, LiVolsi VA, *et al.* Gastrointestinal angiodysplasia: A possible component of von Willebrand's disease. *Hum Pathol* 1984;15:539-44.
- 5 Conlon CL, Weinger RS, Cimo PL, *et al.* Telangiectasia and von Willebrand disease in two families. *Ann Intern Med* 1978;89:921-4.
- 6 Andrews RJ. Collagen in cerebral aneurysms, mitral valve prolapse, and von Willebrand syndrome. *Stroke* 1984;15:917-8.
- 7 Schievink WI, Limburg M, Oorthuys JWE, *et al.* Cerebrovascular disease in Ehlers-Danlos syndrome type IV. *Stroke* 1990;21:(in press).
- 8 Brown RAP. Polycystic disease of the kidneys and intracranial aneurysms. The etiology and interrelationship of these conditions. Review of recent literature and report of seven cases in which both conditions coexisted. *Glasgow Med J* 1951;32:333-48.
- 9 Proesmans W, van Damme B, Casaer P, *et al.* Autosomal dominant polycystic kidney disease in the neonatal period. Association with a cerebral arteriovenous malformation. *Pediatrics* 1982;70:971-5.
- 10 Hossack KF, Leddy CL, Johnson AM, *et al.* Echocardiographic findings in autosomal dominant polycystic kidney disease. *N Engl J Med* 1988;319:907-12.
- 11 Manucci PM, Ruggeri ZM, Pareti FI, *et al.* 1-Deamino-8-D-arginine vasopressin: A new pharmacological approach to the management of haemophilia and von Willebrand's disease. *Lancet* 1977;i:869-72.
- 12 Kobrinsky NL, Israels ED, Gerrard JM, *et al.* Shortening of bleeding time by 1-deamino-8-D-arginine vasopressin in various bleeding disorders. *Lancet* 1984;i:1145-8.
- 13 Warrior AZ, Lusher JM. DDAVP: a useful alternative to blood components in moderate hemophilia A and von Willebrand's disease. *J Pediatr* 1983;102:228-33.
- 14 Cattenao M, Moia M, Della Valle P, *et al.* DDAVP shortens the prolonged bleeding times of patients with severe von Willebrand disease treated with cryoprecipitate. Evidence for a mechanism of action independent of released von Willebrand factor. *Blood* 1989;74:1972-5.
- 15 Bichet DG, Razi M, Lonergan M, *et al.* Hemodynamic and coagulation responses to 1-desamino [8-D-arginine] vasopressin in patients with congenital nephrogenic diabetes insipidus. *N Engl J Med* 1988;318:881-7.

BOOK REVIEWS

Neurobiology of Disease. Edited by A L PEARLMAN AND R C COLLINS. (Pp 482; Price: £25.00.) ISBN 0-19-505319-2 (Pbk). 1990. Oxford University Press.

We doctors love names, and the more confusing and meaningless the better. In the past we could keep patients, lay people, junior staff and even the press in place but now names have taken on a totally new life. Speaking as a Consultant Neurological Pathophysiologist with neuroanatomical undertones and an interest in neurological rehabilitation and a working day of neuro-epileptology, neuropsychiatry, neuro-genetics, neuro-dynia and neuro-everything else, I wish this excellent book—which was originally called (or, as the editors charmingly put it “described by the appellation”) “Neurological Pathophysiology” and is now called “Neurobiology of Disease” and has first class introductions of normal functioning systems—was called “Neurology” (ie that branch of science and

medicine which deals with the nervous system, both normal and in disease), or is this wish an early manifestation of neuro-dementia representing a loss of neuro-adaptive behaviour, and neuro-intelligence?

The Editors of this book have brought together 28 eminent contributors who have, together with the 2 editors, produced one of the most readable and worthwhile introductions to neurology on sale today.

The book, in 2 sections, dealing with functional and anatomical systems, and disease processes, is successful in its aims of providing both an introduction to “the scientific basis of neurology” for medical students and “the expression of fundamental mechanisms” for scientists in neurobiology, (ie it provides an introduction—an excellent introduction—to the study of neurology). The first part, entitled “Functional and Anatomical Systems” consists of 12 chapters dealing with normal and demyelinated axons, peripheral nerve, neuromuscular junction, muscle, the somato-sensory system and pain, the auditory system, the visual system, eye movements and vestibular system, motor system, hypothalamus, cerebral cortex, memory and amnesia. The second part, “Disease Processes” deals with the genetic disorders (almost entirely about Huntington's disease), seizures and epilepsy, aging and dementia, demyelinating disease, stroke, metabolic encephalopathy, cerebrospinal fluid, blood brain barrier, and brain oedema, brain tumours, infections and Parkinsonism.

The separation into “functional and anatomical systems”, and “disease processes”, is not entirely satisfactory. For example, muscle is dealt with in the first section on “function and anatomical systems” where there is an excellent introductory section. Disorders of muscle are also described in this basic section, where there are 4 or 5 pages on inherited muscle disorders, half a page on inflammatory muscle disease, a couple of pages on motor neurone diseases (most of which is on spinal muscular atrophy), and non-dystrophic muscle disease is difficult to find either in the text or in the index. Muscle disease doesn't feature in the section on disease processes which seems to be almost entirely devoted to the brain. Similar criticisms pertain to peripheral nerve. “Memory and Amnesia” comes into the section on Functional and Anatomical Systems and includes herpes simplex encephalitis which also comes in the section on Disease Processes. It seems rather pointless to divide neurology in this way and to separate disease processes from functional and anatomical systems, particularly since the avowed purpose is to “describe the expression of fundamental mechanisms gone awry, and thereby . . . provide clues for elucidating those mechanisms”. There are other places where there is a markedly noticeable lack of balance. For example, acupuncture is given some 19 lines, whereas half that space is given to Melzack and Wall's contribution which has had such a profound effect on the interest and the understanding of pain. There are several, relatively minor errors, which in themselves are perhaps of no great importance. However, the book is intended for medical students and the errors should not really have arisen. For example, spinal shock is described as following brain stem lesions or transection of the human cervical spinal cord. In fact, spinal shock occurs at any level of transection below the mid-pons. Above this level a transection produces decerebrate rigidity, which is dealt with in much greater detail and more accurately.