MATTERS ARISING

Clinical evaluation of extracellular amino acids in severe head trauma by intracerebral in vivo microdialysis

The article by Kanthan and Shuaib[1] is a timely reminder of the potential importance of clinical applications of intracerebral microdialysis. However, there are several methodological and interpretive shortcomings in their case report. Firstly, the microdialysis probe used (Carnegie CMA-10) is one which is designed solely for experimental use in animals. It has no human product licence. Conventional techniques for sterilisation of products to be used in humans can damage the components of the probe, alter its microdialysis characteristics, and may even result in the release of toxic substances. There are also examples of the dialysis membrane becoming detached from the probe shaft and being left in situ (R Bullock, personal communication, 1995). These problems, compounded by the lack of a dialysis probe licensed for intracerebral use in humans, are the basis for the lengthy delay in extrapolating this exciting technique from experimental to clinical studies.[2]

The interpretation offered for the results of Kanthan *et al* is conjectural. High concentrations of all neurotransmitters analysed were found during a three hour period of microdialysis preceding brain death. Are these consequent to neuronal death or a cause of it? The authors did not describe any in vitro testing of probe recovery rate for the measured compounds on removal of the probe from the patient. Without this vital information and in the absence of any reported correlation between the measured neurotransmitter concentrations with either neuroradiological (CT or MR) findings or neuropathology their results provide information of questionable value. Other important information was lacking from their report—namely, details of probe position in either white or grey matter, the relation of the probe tip to any contusion or other macroscopic intracranial pathology, and the presence of hypoxia, pyrexia or hypotension all of which are "secondary insults", commonly found in patients with head injury, which aggravate brain damage. This type of information is crucial if we are to explain the large differences previously reported both between and within patients monitored by microdialysis.[3] The contribution of excitotoxic neurotransmitters to secondary brain injury is still controversial.[4] We agree with the authors that intracerebral microdialysis of patients with head injury may be a useful tool in understanding the pathogenesis of neuronal injury, but this monitoring method must be carefully assimilated into a multimodality patient monitoring system.[5] Speculative and poorly designed case reports do not contribute to scientific advancement in this field.

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Kanthan and Shuaib reply:

We thank Mr Whittle for his comments.

As regards the microdialysis probe CMA-10; we are aware that this product has not been marketed for human use. However, for research purposes these are being used in accordance with strict protocol regimes as followed in Professor Ungerstedt's laboratory. In our laboratory, extensive bench work has been carried out regarding presterilisation and post-sterilisation effects on the efficacy of the probe, concentrations of neurotransmitters, and on decay. The exact placement of the probe in the cortex of the frontal lobe was also done both in fresh necropsy and cadaveric brains before clinical use. These and other issues regarding the methodology have been published in our methods paper (*J Neurosci Methods* 1995;**60**: 151–6).

The issue regarding the exact interpretation of the high concentrations of neurotransmitters remains speculative. We agree with Mr Whittle that it is conjectural whether these are the result or the cause of neuronal death. We also agree that the exact role of excitotoxic neurotransmitters to "secondary brain injury" remains unclear. It is precisely with this in mind that other extraneous factors were not explored in our case. However for the record, our patient was not hypoxic, hypotensive, or febrile during the in vivo microdialysis. Nevertheless, earlier such insults may be contributing factors to the high concentrations noted. This remains a complex issue and we advocate intracerebral in vivo microdialysis as an additional monitoring tool in understanding and unravelling these and other related phenomena of the exact pathogenesis of head trauma.

Visually induced paroxysmal nausea and vomiting as presenting manifestations of multiple sclerosis

Khan *et al* reported an interesting patient with visually induced paroxysmal nausea and vomiting as a presenting manifestation of multiple sclerosis.[1] Their patient was able to suppress the nausea and vomiting by closing the eyes or avoiding visual motion stimuli. This case illustrates the potential for activation of vestibular and autonomic centres from visual pathways.

This patient seems to be an extreme case of what in neuro-otology clinics would be called "visual vertigo".[2] These patients report unsteadiness, dizziness, or "sickish" sensations in environments with confusing visual cues or excessive visual motion (for example, supermarkets, moving crowds, disco lights). A history of vestibular disease, abnormalities in the neuro-otological examination, and added oculomotor findings—for example, old squints—are common. Khan *et al* also stress the importance of considering multiple sclerosis in cases like theirs, particularly because the possibility of a psychogenic disorder may be raised if there are no other indicators of neurological disease.[1] The same consideration applies to "dizzy" patients. Symptoms triggered or exacerbated in supermarkets or by people or traffic moving around, not surprisingly can be taken as phobic. Although the name "postural phobic vertigo" has been coined to describe those patients with dizzy or postural symptoms with no vestibular history or findings *and* a psychogenic background,[3] both the report of Khan *et al* and our own report[2] emphasise the need for careful investigation in patients with visually induced vertigo, nausea, or postural imbalance.

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1 Khan OA, Sandoz GM, Olek MJ. Visually induced paroxysmal nausea and vomiting as presenting manifestations of multiple sclerosis [letter]. *J Neurol Neurosurg Psychiatry* 1995;**59**:342–3.
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Persistent vegetative state

The editorial of Kennard and Illingworth[1] notes, correctly, that the persistent vegetative state syndrome raises immense ethical and social dilemmas. It might be added, further, that the syndrome incites highly litigious questions. And the spotlight of scrutiny should properly remain focused on the contentious ethical, social, and legal dilemmas arising from this interdisciplinary matter.

The extraordinary litigiousness of American society has often been commented on, and the matter of the dilemma of the persistent vegetative state does not depart from this tradition. A body of case law, germane to end of life decision making, has actually grown over the course of the past 20 years or so in the United States, with primal roots extending to the landmark case in 1976 involving Karen Quinlan.[2] More recently, in 1990, the United States Supreme Court decided its first "right to die" case, in a matter involving Nancy Cruzan.[3] In this primordial case, decided by the highest court in the United States, it was held that the state of Missouri may require the continued treatment of a patient in a persistent vegetative state, in the absence of "clear and convincing" proof that the patient authorised explicitly the termination of treatment.

At least in American jurisprudence, the presumption, traditionally, has been that the patient in a persistent vegetative state would wish to be kept alive; and, in turn, the burden has fallen on those desiring to terminate the treatment of the patient in a persistent