

## MATTERS ARISING

### Single fibre EMG studies in chronic fatigue syndrome: a reappraisal

We were interested in the short report from Roberts and Byrne concerning single fibre EMG studies in chronic fatigue syndrome.<sup>1</sup> They concluded that there was no evidence of abnormality at the terminal axon, neuromuscular junction, or muscle membrane in patients with chronic fatigue syndrome—a finding that concurs with our own of essentially normal jitter in 34 of 35 patients with chronic unexplained fatigue.<sup>2</sup> We did detect some evidence of raised fibre density in a small subgroup of patients with pronounced myalgia who also had mild abnormalities on muscle biopsy.

Raised fibre density is usually a result of collateral sprouting after reinnervation, but can also be due to fibre splitting as can occur in some myopathic states.<sup>3</sup> Therefore we believe that fibre density estimation performed in addition to jitter measurement adds considerably to the information obtained from single fibre EMG studies.

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- 1 Roberts L, Byrne E. Single fibre EMG studies in chronic fatigue syndrome: a reappraisal. *J Neurol Neurosurg Psychiatry* 1994;57:375-6.
- 2 Connolly S, Smith DG, Doyle D, Fowler CJ. Chronic fatigue: electromyographic and neuropathological evaluation. *J Neurol* 1993;240:435-8.
- 3 Stålberg E, Trontelj JV. *Single fibre electromyography*. Surrey: The Mirvalle Press Ltd, 1979:67-70.

#### Roberts and Byrne reply:

The findings of Connolly and Fowler are noted with interest. We were unable to find any significant differences in the fibre density of our patients with chronic fatigue syndrome (mean 1.57 (SD 0.20)) when compared with controls (mean 1.57 (SD 0.22)). In addition, the fibre density results could not be correlated with the clinical symptoms. In our laboratory, fibre density studies did not provide any evidence of a peripheral nerve or muscle abnormality.

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### Diencephalic amnesia: possible role of white matter structures

We wish to comment on certain aspects of the paper by Clarke *et al*,<sup>1</sup> who report a case of acute global amnesia occurring in a patient with cerebral infarct involving the

left anterior thalamic nuclei, the adjacent mammillothalamic tract, and the anterior part of the internal medullary lamina. They stress the specific role of the anterior thalamic regions in memory dysfunction and conclude that longlasting amnesia from a thalamic lesion can occur without structural damage to the dorsomedial nucleus.

The authors attributed the amnesia to the lesion of the anterior thalamic nucleus and did not consider the damage to the white matter.

Recently, amnesia as a "disconnection syndrome" has been attributed to selective damage to the mammillothalamic tract that connects the mammillary body to the anterior thalamic nucleus and to the anterior part of the internal medullary lamina that in turn connects the amygdala to the dorsomedial thalamic nucleus.<sup>2-4</sup>

The damage to the internal medullary lamina is mentioned by the authors only to underline that the dorsomedial nucleus could have been spared. Nothing is said about the lesion of the mammillothalamic tract.

We believe that, in the presented patient, dysfunction of the white matter structures could be involved in amnesia and this should have been considered and discussed.

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- 1 Clarke S, Assal G, Bogousslavsky J, *et al*. Pure amnesia after unilateral left polar thalamic infarct: topographical and sequential neuropsychological and metabolic (PET) correlations. *J Neurol Neurosurg Psychiatry* 1994; 57:27-34.
- 2 Aggleton JP, Mishkin M. Memory impairments following restricted medial thalamic lesions in monkeys. *Exp Brain Res* 1983;52: 199-209.
- 3 von Cramon DY, Hebel N, Schuri U. A contribution to the anatomical basis of thalamic amnesia. *Brain* 1985;108:993-1008.
- 4 Graff-Radford N, Tranel D, Van Hoesen GW, Brandt JP. Diencephalic amnesia. *Brain* 1990;113:1-25.

#### Clarke *et al* reply:

De Marinis' and Argenta's wish for a more detailed discussion of the possible role of white matter in the symptomatology of our patient is welcome. Our patient had a small infarction limited to the left anterior thalamic nuclei, the incoming mammillothalamic tract, and the anterior part of the internal medullary lamina. As we have already stated in our paper,<sup>1</sup> the dorsomedial nucleus was mostly spared, but was probably partially deafferented. Tracing studies in macaque monkeys<sup>2</sup> and partial evidence from human material<sup>3</sup> indicate that the pathway from the amygdala to the dorsomedial nucleus is close to the mammillothalamic tract, which is believed to convey fibres from the mammillary body to the anterior thalamic nuclei.<sup>3</sup> The internal medullary lamina is believed to contain fibres from the amygdala and from the orbitofrontal, anterior cingulate, insular and temporal cortices to the dorsomedial nucleus.<sup>4,5</sup> Thus as stated in our paper, the lesion of the mammillothalamic tract merely deafferented the

anterior thalamic nuclei that were in any case damaged.

We believe that the lesion of the anterior thalamic nuclei, and not the partial deafferentation of the dorsomedial nucleus, played the predominant part in the amnesia in our patient. Three lines of evidence support this view. Firstly, the lesion of the anterior thalamic nuclei, but not the deafferentation of the dorsomedial nucleus, produced observable metabolic changes in target territories. Indeed, we have found a relative decrease in the deoxyglucose uptake in the posterior cingulate cortex, which is known to receive input from the anterior thalamic nuclei, but not in any part of the frontal cortex. Lesions of the dorsomedial nucleus have been reported to decrease frontal cortex metabolism (for references see Clarke *et al*).<sup>1</sup> Secondly, macaque behavioural studies support this conclusion. Indeed, complete lesions of the anterior thalamic nuclei and mammillothalamic tract associated with degeneration in the dorsomedial nucleus produced a less severe amnesia than large mediotthalamic lesions.<sup>6</sup> Thirdly, neurotoxic lesions of anterior nuclei (destruction of the neuronal somata but not of fibres of passage) have been shown to produce memory deficits in rats.<sup>7</sup>

The role of white and grey matter structures in diencephalic amnesia is an interesting issue, but with each case report more problems tend to appear than to be solved. In many cases the precise extent of the lesion and its relation to anatomical structures are difficult to establish. Few of such studies have been combined with metabolic investigations. But by far the greatest problem is the lack of data on the connectivity of this region in humans. Our knowledge is an extrapolation of studies done mainly in non-human primates and in rodents. A relatively precise tracing technique (a modification of the Nauta method for anterogradely degenerating axons) can be used in humans and it has contributed to better understanding of functional organisation in other systems.<sup>8</sup> This technique allows efferent connections to be traced from a damaged area in post-mortem tissue, but its use requires experience and it is extremely tedious for analysis. Nevertheless, it is routinely used for research purposes in the laboratory of one of us (SC) and we could envisage collaboration for chosen cases.

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- 1 Clarke S, Assal G, Bogousslavsky J, *et al*. Pure amnesia after unilateral left polar thalamic infarct: topographical and sequential neuropsychological and metabolic (PET) correlations. *J Neurol Neurosurg Psychiatry* 1994; 57:27-34.
- 2 Graff-Radford NR, Tranel D, Van Hoesen GW, Brandt JP. Diencephalic amnesia. *Brain* 1990;113:1-25.
- 3 Van Buren JM, Borke RC. *Variations and connections of the human thalamus*. 1. The nuclei and cerebral connections of the human thalamus. Berlin: Springer Verlag, 1972: 55-74.