Letters to the editor

Cerebral function in a relatively young subset of NIDDM patients

Dear Sir,

Biessels et al. recently reviewed cerebral function in diabetes mellitus [1]. It is apparent that most studies evaluating the affliction to the central nervous system in this disease have been carried out on patients with insulin-dependent diabetes mellitus, where recurrent episodes of hypoglycaemia are a major determinant of the multitude of observed abnormalities. Whether the diabetic milieu itself can influence cerebral functions during the course of the disease is a frequently debated question, with obvious scientific and socio-economic implications.

We studied a small group of patients with non-insulin-dependent diabetes mellitus (NIDDM) using sensitive psychometric and electrophysiological methods in an attempt to closely scrutinize the cognitive functioning in these patients. The Mini Mental Status Examination (MMSE) is a brief screening test for dementia, with demonstrated reliability and validity [2]. The Neurobehavioural Cognitive Status Examination (NCSE) represents a new approach to rapid cognitive assessment [3]. This examination assesses multiple domains of cognitive functioning and provides a differentiated profile of the patient's cognitive status. Compared to the MMSE, the NCSE has a high sensitivity but low specificity [4]. Event-related brain potentials indicate the timing of sensory and cognitive processes. The P-300 wave component has been identified as a late cortical neurophysiological event reflecting the activity of cognitive and mnemonic functions in humans [5].

We randomly selected 15 patients (6 female, 9 male) with NIDDM of more than 5 years' duration (mean duration, 6.6 years), and between the ages of 40 and 55 years (mean age 48.6 years). Elderly diabetic patients were excluded to avoid confounding influences such as ageing or other chronic diseases (e.g. cerebrovascular disease). Patients with a history of clinically evident hypoglycaemic episodes or recurrent ketonuria or those requiring insulin for regular control of glycaemia at any time during the course of the disease, were excluded from the study. A history of recent good or acceptable blood glucose control was ensured by selecting patients with recent glycosylated haemoglobin value of less than 9%.

The average MMSE score was 27.73 out of a total score of 30. The NCSE revealed significant impairment in attention in 4/15 (26.6%), construction ability in 5/15 (33.3%), and short-term memory in 7/15 (46.6%) of the patients when compared

to five control subjects ($p < 0.01$). There was no notable impairment in calculation, language or reasoning ability. The P-300 latency was significantly delayed in all the patients, with an average latency of 365.6 ms, which was significantly longer as compared to that observed in the control subjects (mean P-300 latency, 301.6 ms), ($p < 0.001$).

Our study indicates, for the first time, that definite neurocognitive and electrophysiological dysfunction exists in a relatively younger subset of adult patients with NIDDM who have had no clinically obvious recurrent hypoglycaemic episodes.

Yours sincerely,

J. Dey, A. Misra, N. G. Desai, A. K. Mohapatra, M. V. Padma

References

1. Biessels GJ, Kappelle AC, Bravenboer B, Erkelens DW, Gispen WH (1994) Cerebral function in diabetes mellitus. *Diabetologia* 37: 643–650
2. Folstein MF, Folstein SE, McHugh PR (1975) "Mini Mental State": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 12: 189–198
3. Kiernan RJ, Muller J, Langston JW, Dyke CV (1987) The neurobehavioural cognitive status examination: a brief but differentiated approach to cognitive assessment. *Ann Intern Med* 107: 481–485
4. Schwamm LH, Dyke CV, Kiernan RJ, Merrin EL, Mueller J (1987) The neurobehavioural cognitive status examination: comparison with cognitive capacity screening examination in a neurosurgical population. *Ann Intern Med* 107: 486–491
5. Hillyard SA, Kulas M (1983) Electrophysiology of cognitive processing. *Ann Rev Psychol* 34: 33–61

Response from the authors

Dear Sir,

Jayant Dey et al. present new and interesting data concerning a small group of non-insulin-dependent diabetic patients of relatively young age and short history of diabetes. In line with the notion that diabetes might be accompanied by cerebral dysfunction [1]; they report cognitive impairment in 4–7 patients out of 15 as revealed by a Neurobehavioural Cognitive Status

Examination and in all patients by a P-300 analysis. From this study it would appear that relatively complex tasks are affected, which is in line with the literature we reviewed. However, suggestive as they are, the data should be treated with caution as the experimental and control group differ in size and both are relatively small. Furthermore, one would like to know how metabolic control was achieved (diet and/or oral hypoglycaemic drugs). As it stands the results seem to be of a preliminary nature but point to the possibility that careful analysis will reveal cognitive dysfunction also in younger patients suffering from NIDDM.

Sincerely yours,
G.J. Biessels, B. Bravenboer, W.H. Gispen

References

1. Biessels GJ, Kappelle AC, Bravenboer B, Erkelens DW, Gispen WH (1994) Cerebral function in diabetes mellitus. *Diabetologia* 37: 643–650

Monitoring kidney function in diabetic nephropathy

Dear Sir,

Dr. P. Rossing and colleagues [1] have once again highlighted the imprecision of derived measurements of the glomerular filtration rate (GFR) when compared to the plasma clearance of $^{51}\text{CrEDTA}$. In clinical practice creatinine clearance is the usual method of assessing GFR despite the well-known disadvantages of this measurement [2]. Blood pressure reduction and dietary protein intake restriction have been shown to retard the rate of decline of GFR in diabetic nephropathy [3, 4] but the effects of these interventions are heterogeneous and in the latter intervention those gaining no benefit should not continue with this difficult dietary modification. Assessing whether a low protein diet (LPD) is retarding the rate of decline of GFR in an individual patient cannot be achieved using creatinine clearance as the data below demonstrate.

Nineteen insulin-dependent diabetic patients with nephropathy were studied prospectively for 29 (12–39) months on a normal protein diet (NPD) and subsequently for 33 (12–49) months on an LPD [4]. The creatinine clearance and the plasma clearance of $^{51}\text{CrEDTA}$ were performed within 8 h of each other in each patient on four (1–7) occasions on NPD and five (2–8) occasions on LPD. Creatinine clearance overestimated the plasma clearance of $^{51}\text{CrEDTA}$ by a mean of $5.8 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ on NPD (Fig. 1) and $5.3 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$ on LPD (Fig. 2). The limits of agreements were wider on NPD (28 to $-40 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$) than on LPD (19 to $-30 \text{ ml} \cdot \text{min}^{-1} \cdot 1.73 \text{ m}^{-2}$).

These data reinforce the points made by Dr. Rossing. Derived measures of GFR are imprecise and unacceptable for monitoring response to a therapeutic intervention in an individual patient. Thus, in both the clinical and experimental setting isotopic clearance methods should be employed in the measurement of this important clinical parameter.

Corresponding author: Dr. J.D. Walker, Department of Diabetes, Royal Infirmary of Edinburgh, Lauriston Place, Edinburgh EH3 9YW, UK

Fig. 1. (see text)

Fig. 2. (see text)

Yours sincerely,

J.D. Walker, R. A. Dodds, J.J. Bending, G. C. Viberti

References

1. Rossing P, Astrup A-S, Smidt UM, Parving H-H (1994) Monitoring kidney function in diabetic nephropathy. *Diabetologia* 37: 708–712
2. Payne RB (1986) Creatinine clearance: a redundant clinical investigation. *Ann Clin Biochem* 23: 243–250
3. Parving H-H, Andersen AR, Smidt UM, Hommel E, Mathiesen ER, Svendsen PA (1987) Effect of antihypertensive treatment on kidney function in diabetic nephropathy. *BMJ* 294: 1443–1447
4. Walker JD, Bending JJ, Dodds RA, Mattock MB, Murrells TJ, Keen H, Viberti GC (1989) Restriction of dietary protein and progression of renal failure in diabetic nephropathy. *Lancet* ii: 1411–1414