Diabetes-associated cognitive decline

In this section, a panel of multidisciplinary team members give their opinions on a recently published diabetes paper. In this issue, the focus is on the proposal of a new term – 'diabetes-associated cognitive decline' – which describes a state of cognitive impairment in people with diabetes that is mild to moderate.

Clare Shaban, Chartered Clinical Psychologist, Royal Bournemouth Hospital, Bournemouth

The authors provide evidence from the literature that suggests the association between diabetes and cognitive decline is a valid concept, but one that is hampered by lack of definition and criteria for assessment.

It is timely to clarify the role of subtle complications that can have significant negative outcomes for people living with diabetes. Not only do we need to understand the barriers to care that result in poor glycaemic control and increased risk of complications, but it is also necessary to understand the extent to which more subtle complications can affect the individual's ability to self-manage his or her condition effectively.

The descriptive definition of research criteria suggested by the authors is a key step in contributing to the understanding of the nature and prevalence of diabetes-related cognitive decline. Prospective studies that track cognitive function from the time of diagnosis through the life span would be ideal.

Further research into the link between poor glycaemic control and microvascular complications will serve to further inform the treatment interventions available to patients in terms of both managing physical symptoms and psychosocial sequelae.

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Simon Croxson, Consultant Physician, Bristol General Hospital, Bristol

Good cognition is an attribute that people value most highly and fear losing.

We've all read papers and wondered if there was a disease-specific, hyperglycaemia-related impairment of cognition in diabetes.

This paper by the respected team of Mijnhout et al defines diabetes-associated cognitive decline succinctly and clearly, although a Gaussian distribution would normally have approximately 8% of people 1.5 times the standard deviation or greater below the mean.

This is a valuable concept: firstly it provides further reason, if needed, to obtain optimum glycaemic control; secondly it justifies longer consultations with some patients; thirdly it provides a start for further research.

However, the scale of this impairment in type 1 diabetes is dwarfed by the dementia associated predominantly with type 2 diabetes in older people, which is complicated and less amenable to study, as the authors state. There is also fair evidence already that marked cognitive decline in older people with diabetes is particularly related to hypertension (Hassing et al, 2004).

One aim of glycaemic control in older people is to improve cognitive function and wellbeing; this is based on several studies (e.g. Gradman et al, 1993; Testa and Simonson, 1998), but they are small and don't provide clear glycaemic targets. I feel that this is a more pressing research need.

Gradman TJ, Laws A, Thompson LW, Reaven GM (1993) Verbal learning and/or memory improves with glycemic control in older subjects with non-insulin-dependent diabetes mellitus. *Journal of the American Geriatric Society* **41**(12): 1305–12

Hassing LB, Hofer SM, Nilsson SE et al (2004) Comorbid type 2 diabetes mellitus and hypertension exacerbates cognitive decline: evidence from a longitudinal study. *Age and Ageing* **33**(4): 355–61

Testa MA, Simonson DC (1998) Health economic benefits and quality of life during improved glycemic control in patients with type 2 diabetes mellitus: a randomized, controlled, double-blind trial. *Journal of the American Medical Association* **280**(17): 1490–6

Diabetic encephalopathy: a concept in need of a definition

Mijnhout GS, Scheltens P, Diamant M et al (2006) *Diabetologia* **49**(6): 1447–8

DIABETOLOGIA

New term for cognitive impairment in diabetes proposed

1 Around 40% of people with poorly controlled or long-standing diabetes are reported to have cognitive dysfunction, although the prevalence depends on the method of assessment.

2 The cognitive domains with the most pronounced lowering of performance are flexibility and mental speed. While the impairment is typically of a mild-to-moderate nature, it can have a significant effect on daily functioning, with an accompanying adverse effect on individuals' quality of life.

3 The cognitive impairment witnessed in people with diabetes being treated with insulin has been largely attributed to hypoglycaemic episodes rather than hyperglycaemia, but there is little supporting research.

4 In 1950, the term 'diabetic encephalopathy' was introduced to denote cognitive decline as a complication of diabetes. Support was provided for the use of this term in 1965 when a set of pathological changes distinct from that of any →

→ other condition was identified in the brains of 16 people who had died from the vascular complications of diabetes.

5 The term 'diabetic encephalopathy' has not been widely adopted, however, in part because clear diagnostic criteria have not been established. The term's failure to enter the standard medical lexicon may also be associated with its strong negative connotations; the cognitive impairment seen in people with diabetes is typically mild, after all.

6 A new term – 'diabetes-associated cognitive decline' (DACD) – is proposed by the authors to facilitate research and to promote awareness of the disorder. It is explained that the term is not meant to describe a specific set of pathological changes, but instead to denote mild-to-moderate cognitive decline in people with diabetes that is not linked to other causes.

7 The authors state that initial research into the pathogenesis of DACD should focus on people with type 1 diabetes, because type 2 diabetes is associated with risk factors such as hypertension and hyperlipidaemia that may introduce bias.

8 Given the mild-to-moderate nature of cognitive dysfunction in type 1 diabetes, the lowering in performance that the authors use as a criterion for DACD is a drop relative to controls of 1.5 times the standard deviation or greater.

9 Three additional diagnostic criteria are provided to enable research aimed at refining the new term: the cognitive impairment is chronic; the impairment is normally accompanied by subjective complaints; the cause is not dementia or other plausible conditions, such as stroke.

10 The authors hope that their descriptive definition will stimulate research into the aetiology, consequences and treatment of DACD.

11 Another suggested area for research is the impact that DACD has on day-to-day functioning and self-care in people with diabetes.

Brian Frier, Consultant Physician and Honorary Professor, Royal Infirmary of Edinburgh, Edinburgh

Efforts to direct attention towards how diabetes affects the brain are long overdue. Like the eye and the kidney, the brain is probably a target organ for microangiopathy, but the clinical effects may be subtle and take longer to emerge. Increased life expectancy in type 1 diabetes may be accompanied in some people by premature cognitive decline becoming manifest in middle age, a condition that has been reported anecdotally.

Increasing sophistication in neuroimaging has permitted correlation of functional and structural changes in the brains of people with type 1 and (to a lesser extent) type 2 diabetes.

In type 1 diabetes, chronic hyperglycaemia (implied by the presence of established retinopathy) is associated with the co-existence of modest cognitive impairment in some domains and structural abnormalities in the brain that may represent the presence of microangiopathy (Ferguson et al, 2003).

Fortunately, the adult brain appears to be relatively resistant to recurrent exposure to severe hypoglycaemia, although hypoglycaemia may still have a contributory role to the development of a putative 'diabetic encephalopathy' in type 1 diabetes.

In type 2 diabetes, cognitive impairment certainly occurs. But in addition to the effect of ageing, per se, many other factors, such as hypertension and macrovascular disease, can influence cerebral function, so it is difficult to dissect the specific role of glycaemic derangement, and the term 'diabetic encephalopathy' may be inappropriate.

Although research on the effect of diabetes on the brain is difficult, it is vitally important to inform future clinical management.

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Ferguson SC, Blane A, Perros P et al (2003) Cognitive ability and brain structure in type 1 diabetes: relation to microangiopathy and preceding severe hypoglycemia. *Diabetes* **52**(1): 149–56

'In type 2 diabetes, cognitive impairment certainly occurs. But in addition to the effect of ageing, per se, many other factors, such as hypertension and macrovascular disease, can influence cerebral function, so it is difficult to dissect the specific role of glycaemic derangement, and the term 'diabetic encephalopathy' may be inappropriate.'

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