

Cognitive impairment and dementia in Type 2 diabetes



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Introduction

Recent research highlighting the adverse effects of diabetes on the brain poses many difficulties for clinical staff. Older patients with Type 2 diabetes have an increased risk of developing dementia and adults with Type 1 or Type 2 diabetes may have an increased risk of cognitive impairment. This information is at best worrying and at worst psychologically devastating to informed patients given that many fear dementia more than death itself. The situation is not helped by the dearth of research on the impact of cognitive impairment or on treatment options or how to prevent dementia.

What do we know about dementia in diabetes?

To date, most research has focused on Type 2 diabetes. The dementia that occurs in Type 2 diabetes is similar in nature to that seen in the general population with an adverse impact on cognitive abilities sufficient to cause impairment in functional abilities and often accompanied by a number of troubling behavioral and psychological symptoms. The majority of affected individuals have late-onset dementia that is

due to either Alzheimer's disease, vascular dementia or commonly a combination of both conditions. The risk of developing dementia is approximately 1.5–2-times the risk in the general population, which translates into an estimated 6–8% of all cases of dementia being attributable to diabetes [1]. In epidemiology, any increased disease risk has several possible explanations. It can mean that more people with the risk factor will develop the disease but it can also mean that they will develop the disease at an earlier age. In a recent study of over 25,000 patients diagnosed with dementia in Western Australia, we found that the latter was the case. The average age when patients with diabetes developed dementia was 78.5 years for men and 81.0 years for women, which was just over 2 years younger than where dementia was not associated with diabetes [2]. These results could help put the problem in context when discussing with patients.

As diabetes is an established risk factor for cerebrovascular disease, it is not surprising that vascular explanations are relevant. In many cases, ischemic infarcts and microvascular ischemic changes in the brain interact, possibly synergistically,



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with the neurodegenerative processes that cause Alzheimer's disease and lower the threshold for clinical dementia. It is possible that Type 2 diabetes may promote Alzheimer's neuropathology directly but this remains unproven. Many common medical conditions that often coexist with diabetes also appear to be causally related to dementia. These include hypertension, atrial fibrillation and chronic lung diseases, emphasizing that careful clinical management of diverse medical problems may be vital in preventing late-onset dementia.

Many diabetes-related risk factors have been implicated but the evidence is conflicting on most of them. The risk of dementia may be greatest in people with long-duration diabetes and risk factor control in middle age may be especially important. Studies have reported associations with hyperglycemia and with specific anti-diabetic agents including insulin and metformin but the available evidence is weak and insufficient to alter standard therapeutic guidelines. The few clinical trials that included cognitive measures have been short-lived and did not measure dementia as a study end point. The largest of these, the ACCORD MIND study, demonstrated no benefit from tight glycemic control on performance with cognitive function tasks [3]. There is stronger evidence that hypoglycemic episodes severe enough to require hospital admission may increase the risk of dementia [4], although again there are negative studies linking hypoglycemia with cognitive disorders. This may be partly explained by the fact that cognitive impairment and dementia are also at risk factors for severe hypoglycemia [5], which can be the first indication of an emerging dementia. Recent concerns about diabetes overtreatment and its potential for harm in older patients and have led to calls for developing individual glycemic targets for vulnerable patients [6] and avoidance of hypoglycemia appears to be a particularly important concern.

What about cognition in younger adults?

A number of studies have demonstrated that adults with Type 2 diabetes may have reduced cognitive abilities compared with nondiabetic adults with reported deficits in tasks of memory and executive function and with slower cognitive processing speeds. There are several important points to emphasize about these findings. Cognitive abilities decline in everyone as part of normal aging commencing from around

40 years of age. Peak cognitive abilities are strongly influenced by childhood social factors including education and this influence persists long into old age [7]. Several cardiovascular risk factors, including smoking, hypertension and hyperlipidemia, have been linked to faster rates of age-related cognitive decline so the impact of diabetes may not be unique. The reported extent of the reduction in cognitive abilities due to diabetes is generally small, often within the normal range with no loss of functional ability. Whilst a greater extent of age-related cognitive decline could theoretically alter the threshold for clinical expression of dementia-causing pathologies, this has not been established in diabetes or other conditions. There is a language problem in the research literature in that the terms cognitive impairment and cognitive decline are used interchangeably in studies of normal aging and studies of clinical cognitive disorders.

How does this alter clinical management?

The present state of knowledge gives little concrete guidance for clinicians in how to prevent or treat dementia in diabetes but there is considerable evidence to support a range of practical interventions. The lifestyle factors known to prevent and help manage diabetes are also recommended for the prevention of the common types of dementia. The evidence base is strengthening for healthy diets, in particular the Mediterranean diet, and for increased physical activity levels via exercise programs of conventional frequency and intensity. Cardiovascular risk factor management is especially important from middle age with conventional targets for patients with diabetes. Consequently, and happily, managing dementia risk in patients with Type 2 diabetes is remarkably similar to optimal management of diabetes and cardiovascular risk factors. The available evidence supports standard targets for glycemia, blood pressure and lipid control but optimal dementia prevention may require meticulous risk factor control from middle age onwards. Careful avoidance of hypoglycemia, especially severe episodes, appears to be vital for all and glycemic targets and medication regimens need to be carefully tailored for frail older patients or those with a heavy burden of diabetic complications.

Screening for cognitive impairment in older patients with diabetes should probably occur in certain situations. This would include where patients appear to be less able to manage their diabetes; for example, where new problems

emerge with glycemic control or adherence to therapy. Cognitive screening would also be reasonable before escalating treatment or introducing new educational or motivational strategies. Cognitive screening in people aged over 75 years is now standard in many clinical settings, simple to do and is generally well accepted by this age group.

There are many reasons for optimism in this situation. National cohort studies have demonstrated reductions in the incidence of late-life dementia in many western countries, apparently due to improvements in education and public health early in the 20th century [8]. Clinical outcomes for patients with diabetes have also improved with modern management and there is every reason to expect that improvements in cardiovascular health will also translate into improved cognitive outcomes.

To conclude, the problem of cognitive impairment and dementia in Type 2 diabetes is an

important topic for clinicians to consider and discuss with their patients. Current evidence suggests that the way to cognitive health in Type 2 diabetes is remarkably similar to good clinical management of the diabetes. This potentially daunting topic can be readily reframed as an opportunity to focus preventive efforts and motivate and empower patients into a healthier lifestyle that is likely to confer long-lasting benefits.

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