The Diabetes–Brain Connection: From Epidemiology to Therapeutic Perspectives at EASD 2026

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Conflicts of interest:	Meireles has declared support for travel to EASD 2026 from EASD; and funding from FCT/MCTES (PIDDAC): CIMO, UID/00690/2025 (10.54499/UID/00690/2025) and UID/PRR/00690/2025 (10.54499/UID/PRR/00690/2025), and SusTEC, LA/P/0007/2020 (DOI:10.54499/LA/P/0007/2020).
Keywords:	Brain health, cognitive impairment, dementia, diabetes, glucagon-like peptide-1 (GLP-1) receptor agonists.
Citation:	EMJ Diabet. 2026;14[1]:27-30. https://doi.org/10.33590/emjdiabet/YL709700

THE RELATIONSHIP between diabetes and brain health is receiving increasing attention. Cognitive impairment and dementia are not traditionally among the complications that first come to mind when discussing diabetes, yet evidence presented at the European Association for the Study of Diabetes (EASD) 2026 highlighted how closely metabolic health, vascular complications, inflammation, and brain function may be connected.

The session 'Protecting the Brain' brought together several aspects of this growing field. Looking across the wider programme, a broader picture also emerged: researchers are moving beyond asking whether diabetes is associated with cognitive decline and are beginning to ask how we can identify people at risk earlier, understand the mechanisms involved, and potentially modify the trajectory.

HOW IMPORTANT IS DIABETES AS A DEMENTIA RISK FACTOR?

One of the challenges in understanding the relationship between diabetes and dementia is that the two conditions share many risk factors. Wiggers et al.[1] addressed this issue using data from the USA All of Us Research Program, including 83,370 adults aged over 50 years without previous dementia. Over a median follow-up of 8.1 years, 2,327 participants developed dementia.[1]

After mutually adjusting for a range of risk factors, diabetes remained independently associated with incident dementia (hazard ratio [HR]: 1.42; 95% CI: 1.28–1.57). Several diabetes-related complications were also associated with increased risk, most notably stroke (HR: 2.22; 95% CI: 1.75–2.81), amputation (HR: 2.05; 95% CI: 1.43–2.95), and neuropathy (HR: 1.81; 95% CI: 1.52–2.15).[1] An interesting aspect of this analysis was its assessment of population attributable fractions. When the risk factors were considered together, the total adjusted population attributable fraction was 10.85%, with diabetes accounting for 1.56%.[1] This was considerably lower than estimates based on risk ratios from previous meta-analyses, illustrating how estimates of preventable

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dementia can change when overlapping risk factors are taken into account.

The findings also raise a clinically relevant point: cognitive health may be particularly important to consider in people who have already developed complications of diabetes, rather than viewing cognitive impairment as an entirely separate condition.

LOOKING BEYOND GLUCOSE

The mechanisms behind these associations are unlikely to be explained by hyperglycaemia alone. Findings from the Maastricht Study[2] added another piece to the picture by examining glycaemic dysregulation and peripheral inflammation together.

Among 1,745 participants with longitudinal cognitive data, Type 2 diabetes and higher peripheral inflammation were independently

associated with greater cognitive decline over 7–12 years. Prediabetes was not independently associated with cognitive decline. In the same analyses, HbA1c interacted with peripheral inflammation: higher HbA1c was associated with greater cognitive decline particularly among participants with lower inflammation.[2]

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The MRI findings were particularly interesting. Type 2 diabetes, HbA1c, and inflammation were independently associated with lower grey matter volume. Type 2 diabetes and prediabetes were associated with lower white matter volume, while Type 2 diabetes and higher HbA1c were associated with lower hippocampal volume.[2]

Importantly, the findings were not uniform across all outcomes, and no interactions were observed in the MRI analyses.[2] Nevertheless, they reinforce the idea that the relationship between diabetes and brain health is likely to involve several overlapping pathways, including metabolic and inflammatory processes.

CAN WE DETECT COGNITIVE IMPAIRMENT EARLIER?

Recognising the problem is one step; identifying it early enough to intervene is another. Wu et al.[3] presented a blood-based proteomic panel specifically developed for



detecting cognitive impairment in people with Type 2 diabetes.[3] Using data from 240 participants in the DECODE cohort, the investigators identified candidate proteins associated with cognitive impairment and subsequently developed a six-protein panel incorporating extracellular-matrix-related and metabolic proteins. The panel achieved an area under the curve of 0.84 in the internal assessment, compared with 0.52–0.66 for established biomarkers, and showed an area under the curve of 0.77 in external validation using the UK Biobank.[3] This remains an area for further validation before such biomarkers can be considered for routine use. However, the study illustrates a potentially important shift in the field: rather than waiting for clinically evident cognitive impairment, researchers are looking for measurable biological signals that might identify people at an earlier stage.

CAN TREATMENT CHANGE THE TRAJECTORY?

Perhaps the most clinically provocative question raised at EASD 2026 was whether the choice of glucose-lowering therapy might influence cognitive outcomes. The LIGHT-MCI trial provided randomised comparative evidence in this area.[4] The multicentre study included 396 people with Type 2 diabetes and mild cognitive impairment who were randomised to liraglutide, empagliflozin, or linagliptin, added to metformin, for 48 weeks. At Week 48, reversion of mild cognitive impairment occurred in 49.5% of participants receiving liraglutide, compared with 28.6% receiving empagliflozin and 20.4% receiving linagliptin. Liraglutide was associated with improvements in global cognition, multidomain cognitive performance, and instrumental activities of daily living, while the effects observed with empagliflozin were more limited.

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For a field in which much of the previous evidence has been observational or derived from secondary analyses, these randomised data are particularly noteworthy. They do not establish that liraglutide is neuroprotective, but they do provide evidence that deserves further investigation and raise the possibility that treatment choice could become relevant when cognitive impairment is already present.

Other studies presented at the meeting extended this question to newer therapeutic combinations. In multicentre emulated target trials using data from the TriNetX™ network (TriNetX, LLC, Cambridge, Massachusetts, USA), combined glucagon-like peptide-1 (GLP-1) receptor agonist and sodium-glucose co-transporter 2 (SGLT2) inhibitor therapy was associated with a lower risk of all-cause dementia, Alzheimer's disease, vascular dementia, and mortality than either treatment alone.[5] The size of the dataset and consistency of the findings are striking, although the observational design means that these results cannot establish causality.



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A much smaller randomised pilot study offered a different perspective. Among 20 people with Type 2 diabetes, 52 weeks of tirzepatide was associated with a greater reduction in MRI-measured perivascular space volume than insulin glargine.[6] The study was not powered to establish a clinical effect on cognition, but it raises an intriguing question about whether metabolic therapies might also influence markers related to brain structure and glymphatic function.

FROM DIABETES CONTROL TO BRAIN HEALTH

Taken together, the studies presented at EASD 2026 suggest that the conversation around diabetes and the brain is becoming more clinically focused. The field is moving from describing an association with cognitive decline towards identifying those at risk, exploring the biological pathways involved, and testing whether interventions can change the course of cognitive impairment. There is still considerable work to do. Biomarkers need validation in different populations; observational associations between glucose-lowering therapies and dementia need confirmation in adequately designed randomised trials; and changes in imaging or cognitive measures ultimately need to translate into outcomes that matter to patients.

For now, however, one message from EASD 2026 was clear: brain health deserves a place in the wider discussion of diabetes complications. Protecting the brain may not depend on a single intervention or pathway. Instead, it may require attention to glycaemic control, vascular and metabolic risk, inflammation, complications, early recognition, and potentially, the choice of therapy itself.

As the evidence develops, cognitive health may increasingly become part of what we mean by comprehensive diabetes care.

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