Study: Diabetes Complications in Young Children Target the Brain

Detectable and persistent differences in brain development of children with Type 1 Diabetes are associated with hyperglycemia

(February 10, 2021) – Brain volume, verbal IQ, and overall IQ are lower in children with Type 1 diabetes (T1D) than in children without diabetes, according to a new longitudinal study published in *Diabetes Care* (https://doi.org/10.2337 /dc20-2125), a journal of the American Diabetes Association. The nearly eight-year study, led by Nelly Mauras, MD, a clinical research scientist at Nemours Children's Health System in Jacksonville, Florida, and Allan Reiss MD, a Professor at the Stanford University School of Medicine in California, compared brain scans of young children who have T1D with those of non-diabetic children to assess the extent to which glycemic exposure may adversely affect the developing brain.

"Our findings indicate that, despite improved glycemic control now possible with emerging technologies, individuals with T1D are at risk for cognitive dysfunction," said Mauras, principal investigator of the study, and Chief of the Division of Endocrinology, Diabetes & Metabolism at the Nemours Children's Health System in Jacksonville, Florida, and Professor of Pediatrics at the Mayo College of Medicine. "Our longitudinal data support the hypothesis that the brain is a target of diabetes complications in young children. Whether these changes can be reversed with scrupulous diabetes control requires further study."

The research team – from the ***Diabetes Research in Children Network (DirecNet***), a multicenter National Institutes of Health-funded consortium – studied 144 children with T1D and 72 children without diabetes. Participating children had a median age of 7 years and average disease duration of 2.4 years when the study began. All study participants underwent structural magnetic resonance imaging (MRI) studies, as well as age-appropriate cognitive testing. In those with T1D, metabolic control was assessed using continuous glucose monitors (CGM) and hemoglobin A1C (HbA1C) testing. Over the eight-year study period, up to four MRIs were performed measuring white- and gray-matter volumes in various brain regions for all participants. In the T1D group, the research team assessed total cumulative hyperglycemic exposure since diagnosis.

The researchers found that total brain volume, gray- and white-matter volumes, overall IQ, and verbal IQ were lower in the diabetes group at 6, 8, 10, and 12 years, compared to controls. Differences at baseline persisted or increased over time, and brain volumes and cognitive scores declined as lifetime HbA1C index and higher sensor glucose rose. "Although differences in cognition were mild – around 4 IQ points – this magnitude is similar to other conditions that affect the brain," said Mauras. "We know that T1D can cause complications in multiple organ systems, and our study adds knowledge to earlier research which suggested that glucose level variation in T1D can negatively affect brain development, beginning in childhood."

"It is truly important to follow-up on these results in two ways. The first is to study this and other populations of individuals with T1D into young adulthood to see if and how brain and cognitive issues affect long-term educational and vocational outcome. The second is to see if more rigorous early control of blood sugars can stop or even reverse the brain and

cognitive effects we have observed in this study," said Reiss, co-principal investigator of the study and Robbins Professor and director, Division of Interdisciplinary Brain Sciences at the Stanford University School of Medicine. Future research should examine whether improved diabetes control could possibly reverse the observed brain changes, and such studies also might follow individuals with T1D into young adulthood to see whether and how brain and cognitive issues affect long-term education and vocational outcomes.

The DirecNet (https://public.jaeb.org/direcnet/view/home) consortium includes Nemours Children's Health System Jacksonville, Fla.; the Stanford University School of Medicine; Washington University, St Louis; University of Iowa; and Yale University.

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