Cognitive Function in Children and Subsequent Type 2 Diabetes

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OBJECTIVE — To assess whether a diagnosis of type 2 diabetes by age 42 years is associated with prior cognitive deficits in childhood.

RESEARCH DESIGN AND METHODS — Logistic regression estimated type 2 diabetes risk among 9,113 members of the 1958 British birth cohort of the National Child Development Study (NCDS). Associations with type 2 diabetes were estimated for general ability and reading comprehension assessments at age 11 years, modeled using SD units. Adjustment was for markers of early-life exposures, social and material family characteristics, sex, and disability, with further adjustment for BMI at age 7 years.

RESULTS — Adjusted odds ratios (95% CIs) for type 2 diabetes (n = 69) are 0.67 (0.51–0.87) for general ability and 0.58 (0.44–0.77) for reading comprehension. Neither additional adjustment for BMI, nor limiting the definition of type 2 diabetes to onset after age 33 years altered the associations substantially.

CONCLUSIONS — Impaired cognitive function may precede clinical onset of type 2 diabetes.

Type 2 diabetes is associated with decreased cognitive function in adults (1,2), particularly among elderly people (3). Less is known about cognitive function in children who will subsequently receive a diagnosis of type 2 diabetes in adulthood. We investigated the association of cognitive function at age 11 years with a subsequent type 2 diabetes diagnosis using British longitudinal data.

RESEARCH DESIGN AND METHODS — The National Child Development Study (NCDS) follows all individuals born between 3 and 9 March 1958 (~17,000 births) and living in the U.K. (4). At birth, midwives recorded information on sex, birth weight, gestational age, mother’s age, mother’s age at leaving school, smoking during pregnancy (after the 4th month), and the Registrar General’s social class based on occupation (5). All significant diagnoses, impairments, and disabilities and height and weight were recorded at the medical examination conducted at age 7 years. Diabetes in a first-degree relative was recorded at this time. Cognitive function was assessed at age 11 years with tests administered at school for general ability (comprising verbal and nonverbal components) with a range of 0–79 (6) and reading comprehension with a range of 0–35 (7). A medical examination and record review at age 16 years recorded confirmed or possible diagnoses of diabetes. Interviews at ages 33 and 42 years identified type 2 diabetes through a question about “diabetes that did not require insulin injections” and excluding diabetes only present during pregnancy (4). Ethnic origin was recorded at age 42 years.

Despite some attrition, the cohort remains generally representative, with 11,419 subjects participating at age 42 years (4). Those with a confirmed or suspected diagnosis of diabetes (type 1 or 2) by age 16 years, as well as those with type 1 diabetes or insufficient information on diabetes, were excluded from all analyses. Those with missing data for the main measures were also excluded, therefore information for 9,182 subjects was available for analysis.

A diagnosis of type 2 diabetes after age 16 years was the dependent variable in logistic regression analysis. The general ability and reading comprehension test scores were examined separately and modeled using SD units (Z scores). Adjustment was for sex, birth weight, gestational age (a separate category identified 835 without a valid value), parental social class, maternal smoking during pregnancy, age mother left school, mother’s age at delivery, presence of mild or severe mental retardation, disability, and ethnic origin (97% white British). Potential confounding factors were modeled as categorical variables, except birth weight. Separate models were adjusted for BMI (available for a subset of subjects) at age 7 years, modeled as a continuous variable. Further models examined type 2 diabetes diagnosed after age 33 years.

RESULTS — Cohort members with a diagnosis of type 2 diabetes after age 16 years had statistically significant lower assessment scores at age 11 years after adjustment for potential confounding factors (Table 1). The associations reflect a general shift in distribution, rather than because of a small number of outlying values. The odds ratios indicate the reduction in risk of later type 2 diabetes—associated with 1 SD increase in test score. Adjustment for BMI in childhood did not eliminate the significant association of lower test scores with increased type 2 diabetes risk. Exclusion of subjects with diabetes with onset before age 33 years reduced the sample size with valid data, but lower test scores at age 11 years was still significantly associated with increased type 2 diabetes risk. The associa-
tions were not notably altered by exclusion of cohort members with a first-degree relative with diabetes or by modeling gestational age in days as a continuous variable or birth weight as a categorical variable (data not shown).

**CONCLUSIONS** — Poorer cognitive function at age 11 years was associated with an increased risk of type 2 diabetes by age 42 years. Although “diabetes that does not require insulin injections” is a somewhat imprecise definition of type 2 diabetes, we minimized the risk of confounding by other forms of diabetes by excluding all cohort members with a diagnosis of any form of diabetes by age 16 years (as well as those with insufficient information). The association of poorer childhood cognitive function with type 2 diabetes with onset after age 33 years provides additional control for relevant lifestyle factors and obesity risk.

It is possible that cognitive deficits present in childhood influence lifestyle factors that increase the risk of type 2 diabetes. Alternatively, poorer glycemic control or other shared risk factors may influence both cognitive development and the risk of type 2 diabetes. Insulin resistance is proposed as a possible mediator between dietary intake and cognitive deficits, and there is some evidence of altered β-cell function preceding the development of clinical hyperglycemia (8,9). Chronically elevated blood glucose levels have been linked to decreased cerebral blood flow in type 2 diabetes, and animal models suggest that myelin production is impeded by high blood glucose levels (10). It is possible that such mechanisms, even before overt clinical hypoglycemia, could impair cognitive development in childhood, thus helping to explain the lower levels of cognitive function in type 2 diabetic patients and greater susceptibility to risks for cognitive decline. This suggests that very early detection of subclinical disease and treatment may be of value in protecting against cognitive deficits.

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**Table 1—Test scores at age 11 years and the risk of subsequent type 2 diabetes diagnosed between 16 and 42 years of age**

|                      | Subjects without type 2 diabetes | Subjects with type 2 diabetes | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|----------------------|---------------------------------|-----------------------------|------------------------|-----------------------|
| Cohort members without a diagnosis of diabetes by age 16 years* |                                |                             |                        |                       |
| n                    | 9,113                           | 69                          | 0.63 (0.49–0.79)       | 0.67 (0.51–0.87)      |
| General ability      | 45 ± 16                         | 37 ± 17                     | 0.56 (0.44–0.72)       | 0.58 (0.44–0.76)      |
| Reading comprehension| 17 ± 6                          | 13 ± 6                      | 0.56 (0.44–0.72)       | 0.58 (0.44–0.76)      |
| Cohort members without a diagnosis of diabetes by age 16 years and with information on BMI at age 7 years† |                                |                             |                        |                       |
| n                    | 7,701                           | 59                          | 0.66 (0.51–0.85)       | 0.70 (0.53–0.93)      |
| General ability      | 45 ± 15                         | 39 ± 18                     | 0.58 (0.45–0.76)       | 0.60 (0.44–0.80)      |
| Reading comprehension| 17 ± 6                          | 13 ± 7                      | 0.58 (0.43–0.78)       | 0.63 (0.43–0.86)      |
| Cohort members without a diagnosis of diabetes by age 33 years* |                                |                             |                        |                       |
| n                    | 7,878                           | 48                          | 0.61 (0.46–0.81)       | 0.68 (0.50–0.93)      |
| General ability      | 45 ± 15                         | 37 ± 18                     | 0.58 (0.43–0.78)       | 0.63 (0.43–0.86)      |
| Reading comprehension| 17 ± 6                          | 14 ± 7                      | 0.58 (0.43–0.78)       | 0.63 (0.43–0.86)      |

Data are means ± SD and OR (95% CI). ORs are calculated using logistic regression and estimate the risk of subsequent type 2 diabetes for each SD change in test score. *OR (95% CI) values adjusted for sex, mental retardation (mild or severe), disability, family social class at birth (seven categories), birth weight in ounces, gestational age (<35, 35–36, 37–42, and ≥42 weeks and gestational age unavailable), ethnic origin (white British, Irish, white other, white and black Caribbean, white and black African, white and Asian, other mixed race, Indian, other Asian, Caribbean, African, other black, other ethnic group), smoking during pregnancy, age mother left school, and mother’s age at delivery. †OR (95% CI) values adjusted for characteristics listed above* and also for BMI at age 7 years.
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