Insulin (resistance) is unrelated to cognitive performance among individuals with type 2 diabetes – The Maastricht Study

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Background: Type 2 diabetes, hyperinsulinaemia, and insulin resistance are associated with cognitive impairment and dementia. Experimental studies indicate that insulin signalling in the brain is related to cognitive performance. Hence, it has been suggested that insulin levels and insulin resistance are determinants of cognitive performance among individuals with type 2 diabetes. In this study, we evaluated whether insulin-related variables indeed contribute to the heterogeneity in cognitive performance among individuals with type 2 diabetes.

Methods: In this cross-sectional study, 806 individuals with type 2 diabetes (mean age 62±8 years, 67% men, mean HbA1c 6.9±1.1 %, mean BMI 29.8±5.0 kg/m²) completed a neuropsychological test battery to determine memory function, information processing speed, and executive function and attention. Fasting plasma insulin and C-peptide were assessed, and insulin resistance was estimated using the Homeostasis Model Assessment (HOMA2-IR) in non-insulin treated individuals (n=641). The unadjusted coefficient of determination (R²),
obtained from multiple linear regression analyses, was used to estimate the proportion of variance explained by measures of insulin-related variables.

**Results:** Sex, age, and educational level together explained 18.0% ($R^2$) of the variance in memory function, 26.5% in information processing speed, and 22.8% in executive function and attention. Fasting insulin, C-peptide, or HOMA2-IR did not increase the explained variance (maximum $\Delta R^2$ 0.3%, $P \geq 0.14$). Similar results were obtained when insulin-related variables were added to models that additionally included glycaemic control, cardiovascular risk factors, and depression.

**Conclusions:** Our results show that measures of peripheral insulin resistance are unrelated to cognitive performance among individuals with type 2 diabetes.

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