Materials

Study population

This study is based on the Finnish Health 2000 Examination Survey carried out in 2000–2001, its supplemental examinations on a subpopulation, and its follow-up survey, the Health 2011 study, all conducted by the Finnish National Institute for Health and Welfare. The Health 2000 survey was a comprehensive, nationwide, population-based survey. A subsample (n=1864, age 45–74) of the main study population (n=6770) was invited to take further examinations in 2001–2002 to study cardiovascular health and diabetes more thoroughly. Of the invited 82% (n=1526) attended the supplemental survey. In 2011 all the individuals who had attended the original Health 2000 Survey, were invited to attend the Health 2011 follow-up survey.

In total 961 individuals, who had attended all the three surveys, were included in the present study. Those who did not undergo an OGTT due to use of insulin (n=22) or other reasons (n=19) and those with missing cognitive test results at baseline (n=14) or follow-up (n=24) were excluded from this study. Altogether 111 individuals had died or were lost to follow-up. (Supplementary Figure 1).

The studies were approved by the Ethics Committee for epidemiology and public health in the hospital district of Helsinki and Uusimaa, Finland. Written informed consent was obtained from all of the participants before attending the studies.

Baseline measurements

In the supplemental cardiovascular examinations in 2001–2002 OGTT was performed according to international guidelines. Participants were given glucose solution of 300ml containing 75g of glucose and water, and 2-hour glucose value was determined 120 minutes after the glucose ingestion by the glucose dehydrogenase method (Diagnostica Merck, Darmstadt, Germany) in an automated clinical chemistry analyzer (Thermo Clinical Labsystems, Konelab, Vantaa, Finland). Blood pressure (BP) was measured in a sitting position from the right arm three times with the oscillometric OMRON M4 blood pressure measuring device (Omron Matsusaka Co, Japan,

OMRON Healthcare Europe B.V., Hoofddorp, The Netherlands). The mean of the three measurements was used. Information about the participants' medical history and medication was obtained by interviews and questionnaires.

Supplementary results

The possible modulating effects of type 2 diabetes, *APOEε4*, age, and sex on the associations between 2-hour glucose and the cognitive test scores as well as on the associations between 2-hour glucose and the change in the cognitive test scores from 2000 to 2001 were analyzed by testing for interactions in the age, sex, and education adjusted model. The interaction of '2-hour glucose x age' was significant for predicting the change in word-list learning (p=0.04). No other significant interactions were found (all p-values ≥ 0.06). None of the interactions were significant after Bonferroni correction.

The analysis predicting the change in word-list learning was stratified according to age group (<54 years (the median age) and ≥54 years adjusted for age, sex, and education. The association between 2-hour glucose and the change in word-list learning was statistically significant among participants ≥54 years but not among participants <54 years (for age group ≥54 years: slope -0.15, 95% CI -0.24 to -0.05, p=0.003; for age group <54 years: slope -0.03, 95% CI -0.14 to 0.08, p=0.55).

Supplementary Table 1: Characteristics of the study population at baseline and cognitive test scores at baseline and at follow-up.

	N=961
age	55.6 (7.4)
women, n (%)	536 (55.8)
years of education	11.6 (3.8)
APOEε4 genotype, n (%)	304 (33.0)
fasting glucose (mmol/l), median (Q1, Q3)	5.6 (5.2, 6.0)
2h glucose (mmol/l) in OGTT, median (Q1, Q3)	6.3 (5.1, 7.7)
serum total cholesterol (mmol/l)	5.6 (0.9)
systolic blood pressure (mmHg)	137 (21)
BMI (kg/m2)	27.0 (4.4)
BDI score, median (Q1, Q3)	5 (2, 10)
Current smoking, n (%)	86 (9.0)
verbal fluency in 2000	25.2 (6.9)
word-list learning in 2000	21.3 (3.7)
word-list delayed recall in 2000	7.2 (1.7)
verbal fluency in 2011	23.8 (7.1)
word-list learning in 2011	20.5 (4.4)
word-list delayed recall in 2011	6.9 (2.1)

The values are given as mean (SD), unless stated otherwise.

Supplementary Table 2. Adjusted coefficient of determination (r^2_{adj}) of the models predicting cognitive performance in 2011.

	verbal fluency	word-list learning	word-list delayed recall
2-hour glucose, unadjusted	0.01	0.04	0.04
adjusted for age, sex, and education	0.16	0.29	0.22
further adjusted for *APOEε4* genotype, type 2 diabetes, hypertension, hypercholesterolemia, BMI, BDI-score, and smoking	0.16	0.29	0.22

Supplementary Figure 1. Flow chart of the study population.