

Beta-cell function in twins and siblings

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Background and Aims: In type 2 diabetes mellitus two pathogenic factors play a crucial role in the development of hyperglycaemia: impaired insulin secretion and insulin resistance. Remarkably, only a few studies have addressed the heritability of beta-cell function. The aim of our study is to determine the genetic and environmental contribution to inter-individual variation in β -cell function in twin families.

Material and methods: 76 healthy same sex twin pairs, aged 20 to 45 years, and additional same sex siblings were selected from the Netherlands Twin Register.

Protocol : a home visit for an Oral Glucose Tolerance Test (OGTT) after a 12-h overnight fast. We measured the blood glucose with the hemocue before and 2 hours after a 75 grams glucose load. Questionnaires about general health and food intake were completed. When diabetes was excluded, the participants visited the clinic twice after a 12-h overnight fast.

Visit 1 : physical examination, anthropometric measurements and blood sampling for haematological, biochemical and hormonal investigations. Next a standardized mixed meal (energy % 50 CH, 37 fat ,13 protein, men total 3000 kJ, woman total 2400 KJ) was given and followed by 4 hours of frequent blood sampling for blood glucose (by Yellow Spring) and hormonal levels.

Visit 2 : A combined euglycaemic/hyperglycaemic clamp test modified with additional GLP-1 and arginine stimulation, to assess several aspects of beta-cell function in relation to the ambient insulin sensitivity.

Analyses : ANOVA was used to test differences in characteristics between the groups and to obtain intra-class correlations .

Genetic relationship	MONOZYGOOT	DIZYGOOT	SIBS
Number	102	45	41
Sex: (male/female)	43/59	18/27	21/20
Age	30.8 (4.1)	29.2 (4.7)	*34.6 (8.1)
OGTT fasting bgll (mmol/l)	4.68 (0.460)	4.50 (0.42)	4.62 (0.48)
OGTT 2 hours bgll (mmol/l)	5.59(1.19)	*5.03 (0.97)	5.33 (1.13)
Meal fasting bgll (mmol/l)	4.40 (0.42)	4.30 (0.39)	4.42 (0.41)
Meal 2 hours bgll (mmol/l)	5.44 (0.72)	*5.13 (0.50)	5.42 (0.52)
HbA1c (%)	5.27 (0.27)	5.20 (0.24)	5.26 (0.26)
Total Cholesterol (mmol/l)	4.105 (0.76)	4.05 (0.78)	4.38 (0.81)
Weight (kg)	72.5 (10.6)	70.9 (12.9)	*78.5 (14.0)
Length (m)	1.748 (0.083)	1,770 (0.091)	1.771 (0.083)
BMI (kg / meter ²)	23.74 (3.29)	22.52 (2.92)	*25.01 (3.95)
Waist (cm)	85.2 (10.10)	81.56 (10.06)	*89.6 (10.95)
Waist Hip ratio	0.84 (0.07)	0.82 (0.07)	*0.87 (0.07)

Table 1: **CHARACTERISTICS** : Data as means (SD); bgll = bloodglucose ;BMI = body mass index. * : p <0.05

Results: MZ twins, DZ twins and siblings were comparable in most variables (Table 1). The higher weight, BMI, waist circumference and waist/hip ratio of the sibs are mainly due to their higher age. The DZ twin pairs were the youngest group, with the lowest blood glucoses, HbA1c, cholesterol and anthropometric measurements. In all groups, the fasting blood glucose before the OGTT was higher than the fasting blood glucose before the meal.

We found an estimation of the additive genetic component for the fasting blood glucose of 44% and 47 % respectively in OGTT and meal test. (see table 2 and Figure 1). The 2 hours OGTT blood glucose seemed independent of genetic influences. Our results show a remarkable difference between the components for 2 hours OGTT and 2 hours meal blood glucose levels. With regard to the glucose-metabolism measures, narrow sense heritability was largest for HbA1c.

Table 2 : Intra-class-correlations

MZ PAIRS	1st DEGREE RELATIVES	INTRAC-CLASS CORRELATION	Figure 1: Estimates of genetic and environmental variance components		
0,655	0,434	OGTT fasting bgll (mmol/l)	44%	21%	35%
0,349	0,375	OGTT 2 hours bgll (mmol/l)	40%		60%
0,624	0,387	Meal fasting bgll (mmol/l)	47%	15%	38%
0,571	0,148	Meal 2 hours bgll (mmol/l)	43%		57%
0,750	0,387	HbA1c (%)	73%		27%
0,712	0,473	total cholesterol (mmol/l)	48%	23%	29%
0,970	0,650	Length (m)	64%	33%	3%
0,632	0,234	BMI (kg/m ²)	37%		63%
0,669	0,355	Waist (cm)	63%	4%	33%
0,781	0,493	Waist Hip ratio	58%	20%	22%

■ heritability narrow-sense
■ unique environment
■ common environment
■ broad sense heritability

Discussion and conclusion :

The preliminary data of our study in 76 twin families show that HbA1c has a strong genetic component, while fasting glucose and 2 hours post OGTT/meal suggest a more environmental influence. The further data of the study (with hormonal levels) will reveal more information about the genetic and environmental contribution to inter-individual differences of B-cell funtion.

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