

TWIN RESEARCH AND HUMAN GENETICS

SUPPLEMENTARY MATERIAL

A comparison of heritability estimates by classical twin modelling and based on genome-wide genetic relatedness for cardiac conduction traits

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Supplementary Table S1. Subject characteristics for MZ and DZ twins separately for the ECG diagnostic categories, based on maximally 2 402 twins for which ECG codes were provided by the ECG machine and including 137 women that met our exclusion criteria for the heritability analyses.

	MZ (n=880)	DZ (n=1522)	p-value
Atrial fibrillation ^a	17 (1.9 %)	25 (1.6 %)	n.s.
AV block ^b	37 (4.2 %)	50 (3.3 %)	n.s.
LVH total ^c	14 (1.6 %)	32 (2.1 %)	n.s.
Abnormal T-axis ^d	18 (2.2 %)	31 (2.1 %)	n.s.
RBBB ^e	19 (2.2 %)	29 (1.9 %)	n.s.
LBBB ^f	8 (0.9 %)	6 (0.4 %)	n.s.

^aDefined when a p-wave was not present and RR interval deviation $> 0.125 \times$ mean RR interval or a random RR interval; ^bFirst-degree atrioventricular block defined as a PR-interval > 210 ms; ^cLeft ventricular hypertrophy defined as the sum of the R amplitude in lead V5 and SV1 > 3.8 mV, or a computer algorithm was used including the following point score calculation: two points for a R amplitude > 1.1 mV in lead aVL and one point added at every $+0.1$ mV, two points for a S amplitude in lead V1 or R amplitude in V5 > 3 mV and one point added at every $+0.2$ mV, two points when the sum of the S amplitude in V1 and the R amplitude in V5 or V6 > 3 mV and one point added at every 0.3 mV. LVH was defined when ≥ 5 points or ≥ 2 points in combination with the presence of left atrial enlargement, repolarization abnormality or maximum change point of inclination-QRS start point > 68 ms in lead V5; ^dThe T-wave axis on the frontal plane was estimated automatically by the ECG reading software (ECAPS 12C, Nihon-Kohden), using a computer algorithm that considers integrated T-wave areas in each lead. This was classified, in accordance with previous studies(44), as abnormally deviated if at least -180 through -15 or 105 through 180 degrees; ^e $n_{MZ}=833$, $n_{DZ}=1 454$; ^e(Incomplete) right bundle branch block; ^f(Incomplete) left bundle branch block.

Supplementary Table S2. Pairwise Pearson correlation coefficients between ECG variables and with age. Above the diagonal pairwise correlations between the uncorrected ECG variables and of the uncorrected ECG variables with age are shown; below the diagonal pairwise correlation coefficients between ECG variables that are corrected for age and ECG machine (QT interval also corrected for RR interval), are shown.

	Heart rate	PR interval	QRS duration	QTc interval	RV5+SV1	SL product	C product	age
Heart rate	--	-0.08 ^{***}	-0.08 ^{***}	-0.78 ^{***}	-0.09 ^{***}	-0.10 ^{***}	n.s.	0.04 [*]
PR interval	-0.09 ^{***}	--	n.s.	0.10 ^{***}	n.s.	n.s.	0.09 ^{***}	0.19 ^{***}
QRS duration	-0.09 ^{***}	n.s.	--	0.22 ^{***}	0.08 ^{***}	0.28 ^{***}	0.36 ^{***}	0.06 [*]
QTc interval	n.s.	n.s.	0.21 ^{***}	--	0.11 ^{***}	0.12 ^{***}	0.09 ^{***}	-0.09 ^{***}
RV5+SV1	-0.08 ^{***}	n.s.	0.08 ^{***}	0.09 ^{***}	--	0.87 ^{***}	n.s.	0.11 ^{***}
SL product	-0.09 ^{***}	n.s.	0.30 ^{***}	0.11 ^{***}	0.87 ^{***}	--	0.15 ^{***}	-0.08 ^{***}
C product	n.s.	0.05 [*]	0.37 ^{***}	n.s.	0.12 ^{***}	0.16 ^{***}	--	0.23 ^{***}

^{***} p<0.001, ^{**} p<0.01; ^{*} p<0.05. n.s.= not significant, p-value ≥ 0.05.
SL product: Sokolow-Lyon Product; C product: Cornell Product.

Supplementary Table S3. Pearson Twin Correlation coefficients for ECG variables (corrected for age and ECG machine) for MZ and DZ twin pairs separately.

	522 MZ twin pairs		839 DZ twin pairs	
	r	95% CI	r	95% CI
Heart rate	0.53	0.47-0.59	0.25	0.19-0.32
PR interval	0.55	0.49-0.61	0.28	0.21-0.34
QRS duration	0.52	0.46-0.58	0.29	0.23-0.35
QTc interval ^a	0.60	0.55-0.65	0.30	0.24-0.36
RV5+SV1 ^b	0.59	0.52-0.66	0.28	0.21-0.35
Sokolow-Lyon product ^c	0.58	0.49-0.67	0.25	0.18-0.32
Cornell product ^d	0.35	0.24-0.46	0.31	0.24-0.38
BMI ^e	0.75	0.70-0.79	0.45	0.40-0.50
Height	0.88	0.86-0.90	0.54	0.49-0.59

MZ: monozygotic; DZ: dizygotic; r: correlation coefficient; CI: confidence interval; BMI: body mass index. ^aQT interval additionally corrected for RR interval; ^bn_{MZ}=360, n_{DZ}=639; ^cn_{MZ}=242, n_{DZ}=658; ^dn_{MZ}=241, n_{DZ}=646; ^eBMI was log-transformed, n_{MZ}=431, n_{DZ}=802.

Supplementary Figure S1. Comparison of joint heritability estimates with single matrix estimates by GREML (using both MZ twins) for (A) the narrow-sense heritability and (B) the common SNP heritability. Dark grey bars show the joint heritability estimates from GREML and light grey bars show those using single matrices. In panel (B) also the heritability estimates are shown as determined using GREML-LDMS. For BMI and the Cornell product the GREML LDMS estimates could not be determined (indicated with n.a.). Error bars indicate the standard errors of the estimates. SL product: Sokolow-Lyon product; C product: Cornell product.

