

Heritability of Ambulatory Heart Rate Variability

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Reduced heart rate variability (HRV) is associated with an increased risk for cardiac disease and overall mortality. In the laboratory, a significant genetic contribution to HRV has been established by twin and family studies. Heritability estimates (h^2) at rest range from 13-35% but during exposure to mental stressors h^2 increases to 50%.

The present study addresses the genetics of HRV during prolonged periods of ambulatory monitoring in a naturalistic setting.

Methods

• 229 MZ twins (84 men), 309 DZ twins (118 men) and 264 singleton siblings (101 men) from 341 families

• Using the VU-AMS (4.6) ambulatory monitor 24-hour recordings of ECG and ICG were made in naturalistic settings. Band pass filtered ICG yields a respiration signal. RSA was obtained in the time domain from the combined ECG and respiration signals (peak-to-trough method)

• ECG, respiration and motility data were combined with the diary information to divide recording into fragments that were stationary with regard to physical activity and posture. Means for RMSSD and RSA were computed for the morning, afternoon, evening and nighttime periods

• Age-adjusted twin correlations were computed twice: across all periods, and across periods where subjects were either sitting or lying

• Mx was used for genetic modeling

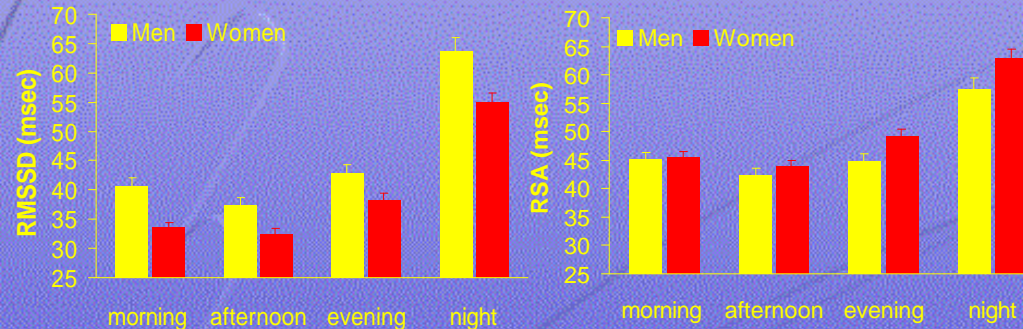


Figure 1. Means (SEM) of RMSSD and RSA over 24-hour period.

The difference in intrapair resemblance of MZ twins and DZ twins/full sibs gives an indication of the contribution of genes to the phenotype.

	RMSSD		RSA	
	rMZ	rDZ&sib	rMZ	rDZ&sib
Morning				
Men	.48 / .44	.37 / .24	.50 / .44	.36 / .30
Women	.51 / .43	.24 / .26	.63 / .48	.35 / .32
OS	-	.13 / .11	-	.02 / .03
Afternoon				
Men	.43 / .44	.29 / .24	.42 / .42	.32 / .26
Women	.48 / .58	.16 / .23	.65 / .63	.30 / .31
OS	-	.26 / .20	-	.10 / .04
Evening				
Men	.44 / .47	.25 / .21	.60 / .63	.27 / .26
Women	.48 / .54	.18 / .27	.53 / .61	.33 / .35
OS	-	.18 / .18	-	.11 / .09
Night				
Men	.57 / .55	.37 / .35	.64 / .63	.29 / .28
Women	.46 / .46	.17 / .16	.64 / .64	.32 / .32
OS	-	.20 / .17	-	.18 / .16

Table 1. Correlations indicate similarity of data including all postures (1st column) and data in sitting/lying posture only (2nd column). In addition, these correlations show that resemblance of MZ twins is almost twice as high as DZ twins/full sibs. OS = Opposite sex pairs. **Bold** indicates significance at 0.05 level

	RMSSD	RSA
Morning	33% (20-46%)	40% (26-52%)
Afternoon	42% (28-55%)	46% (32-59%)
Evening	40% (27-53%)	50% (36-62%)
Night	37% (22-50%)	54% (41-65%)

Table 2. Heritability estimates and their 95% CI's under the best fitting model (AE).

Genetic analysis showed that genetic (A) and unique environmental (E) factors suffice to explain all variance in RMSSD and RSA in all daily periods. No influence of shared environment (C) was found.

Conclusion

- Heritability of ambulatory RMSSD varies between 33 and 42%
- Heritability of RSA varies between 40 and 54%
- Strong confirmation that genes are important in the regulation of ambulatory HRV

Power to detect genes increases with heritability of the phenotype. Therefore, we consider ambulatory HRV a useful intermediate phenotype in the search for genetic variation influencing cardiovascular disease risk.