Neuroscience Campus Amsterdam

The association of heart rate variability at baseline and the pro-inflammatory state five years later

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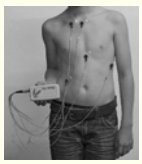
Introduction

Low-grade inflammation has recently been confirmed as a major risk factor for cardiovascular disease (CVD), it is characterized by increased levels of CRP, fibrinogen, TNF-α and IL-6. Reduced heart rate variability (HRV), which reflects lowered cardiac parasympathetic control, is another recently established risk factor for CVD. It has been hypothesized that there may be a direct and causal connection between these, at first sight rather different, risk factors for CVD.

Methods

462 participants registered by the Netherlands Twin Registry (NTR) were selected because they had taken part in both a 24-hour ambulatory study and a BioBank study, which took place approximately 5 years later. In the first study, a 24-hour electrocardiogram (ECG) signal was used to extract 3 HRV measures: SDNN, RMSSD and RSA. In the second study a blood sample was collected and values of 4 immune parameters were determined: CRP, fibrinogen, TNF-α and IL-6. In our HRV analyses we excluded subjects taking medication affecting the autonomic nervous system. In the analyses of the immune parameters we additionaly excluded subjects taking medication affecting immune functioning.



Results

- High correlations among the three different HRV measures (ranging from .695 to .896, P < .01) were found.
- Among the different immune markers, it was apparent that IL-6 correlated moderately with all other markers while TNF-α only correlated significantly with IL-6. The strongest correlation was found between the two acute phase proteins, CRP and fibrinogen (r = .444, P < .01).
- Most consistent associations between HRV and the pro-inflammatory state over time were seen between HRV and the acute phase proteins, CRP and fibrinogen, with the latter showing the most consistent pattern over different conditions

Table 1. Correlations among the four pro-inflammatory markers.

	CRP	Fibrinogen	TNF-α	IL-6
CRP	1 (402)			
Fibrinogen	.444** (396)	1 (414)		
TNF-α	-.022 (396)	.019 (409)	1 (416)	
IL-6	.314** (398)	.373** (408)	.228** (413)	1 (416)

** (N) Correlation significant at the 0.01 level (2-tailed)
* (N) Correlation significant at the 0.05 level (2-tailed)

Table 2. Correlations between HRV at baseline and the pro-inflammatory state five years later.

	CRP	Fibrinogen	TNF-α	IL-6
RMSSD *lying / sleeping*	-.127* (371)	-.161** (380)	-.023 (382)	-.101* (382)
RMSSD *sitting*	-.129* (384)	-.141** (394)	-.026 (396)	-.125* (396)
RMSSD *physical activity*	-.087 (385)	-.169** (395)	-.049 (397)	-.129* (397)
SDNN *lying / sleeping*	-.175** (369)	-.171** (378)	-.033 (380)	-.119* (380)
SDNN *sitting*	-.143** (384)	-.160** (394)	-.012 (396)	-.126* (396)
SDNN *physical activity*	-.162** (385)	-.196** (395)	-.051 (397)	-.164** (397)
RSA *lying / sleeping*	-.105* (371)	-.104* (380)	-.036 (382)	-.129* (382)
RSA *Sitting*	-.129* (386)	-.134** (396)	-.011 (398)	-.157** (398)
RSA *physical activity*	-.098 (386)	-.160** (396)	-.015 (398)	-.189** (398)

** (N) Correlation significant at the 0.01 level (2-tailed)
* (N) Correlation significant at the 0.05 level (2-tailed)

Conclusion

Low HRV, reflecting decreases in parasympathetic control, predicts a higher pro-inflammatory state over a 5 year follow-up period.

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