B B M R I • N L

Biobanking and Biomolecular Resources Research Infrastructure

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

Melanie Neijts, Gonneke Willemsen, Eline Bangert, Dorret I Boomsma, Eco JC de Geus

Department of Biological Psychology,
Neuroscience Campus Amsterdam, EMGO+ institute, VU University Amsterdam

Background

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, IL-6 and IL-6R. 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. excluded subjects taking medication affecting immune functioning.

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 fasting blood sample was collected in the morning and values of 5 immune parameters were determined: CRP, fibrinogen, TNF-α, IL-6 and IL-6R. In our HRV analyses we excluded subjects taking medication affecting the autonomic nervous system. In the analyses of the immune parameters we additionally excluded subjects taking medication affecting immune functioning.

Results

Associations between the different pro-inflammatory markers were most apparent between the two acute phase reactants, CRP and fibrinogen (r = .472, P < .01). Of the cytokines, IL-6 appeared to be moderately associated with all other inflammatory markers (with *r* ranging from .22 to .39) while the association of TNF-α was only restricted to its cytokine counterpart.

	CRP	*Fibrinogen*	*TNF-α*	*IL-6*
CRP	-			
Fibrinogen	*.47***	-		
TNF-α	*.04*	*.03*	-	
IL-6	*.31***	*.39***	*.24***	-
IL-6R	*.06*	*.18***	*.07*	*.22***

** *Correlation significant at the .01 level (2-tailed)*
* *Correlation significant at the .05 level (2-tailed)*

The three different HRV measures were highly correlated, which indicates the same construct is measured. In addition, body posture and/or activity did not impact the strength of this association (.70 < r_{lying} .89; .75 < $r_{sitting}$ < .89; .71 < r_{active} < .80).

	Lying		*Sitting*		*Active*	
	RMSSD	*SDNN*	*RMSSD*	*SDNN*	*RMSSD*	*SDNN*
SDNN	***.89*****		.89**		.80**	
RSA	***.85*****	.70**	.85**	.75**	.76**	.71**

Moderate but consistent associations between HRV and the pro-inflammatory state over time were seen between HRV and the plasma levels of the acute phase reactants (CRP and fibrinogen) and IL-6.

	CRP	**Fibrinogen**	**TNF-α**	**IL-6**	**IL-6R**
	RMSSD				
Lying	-.13*	-.16**	-.02	-.10*	.06
Sitting	-.13*	-.14**	-.03	-.13*	-.10
Activity	-.09	-.17**	-.05	-.13*	-.06
	SDNN				
Lying	-.17**	-.17**	-.03	-.12*	-.01
Sitting	-.14**	-.16**	-.01	-.13*	-.07
Activity	-.16**	-.20**	-.05	-.16**	-.10
	RSA				
Lying	-.11*	-.10*	-.04	-.13*	-.02
Sitting	-.13*	-.13**	-.01	-.16**	-.11
Activity	-.098	-.16**	-.02	-.19**	-.06

Conclusion

Low HRV, reflecting decreases in parasympathetic cardiac activity, predicts a higher pro-inflammatory state over a 5 year follow-up period. This is in keeping with the recent hypothesis that parasympathetic activity can inhibit cytokine production (Tracey, 2009).

References:

Stacey, K . J. (2009). Reflex control of immunity. *Nature Reviews Immunology, 9,* 418-428.

Acknowledgments: BBMRI-NL (*CP8*); ZonMW (Middelgroot 911-09-032); VU-AMS fund (*PhD support*)