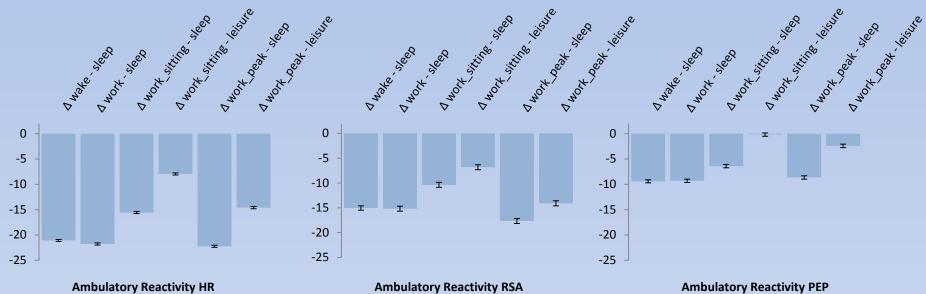
## Heritability and stability of ambulatory autonomic stress reactivity in unstructured 24-h recordings

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## **Background**

Measurement of ambulatory autonomic reactivity can help understand the long term health consequences of exposure to psychosocial stress in real-life settings. In this study, unstructured 24-h ambulatory recordings of cardiac parasympathetic and sympathetic control were obtained in 1288 twins and siblings, spanning both work time and leisure time. These data were used to define two ambulatory baseline (sleep, leisure) and four stress conditions (wake, work, work\_sitting, work\_peak) from which six ambulatory stress reactivity measures were derived. The use of twin families allowed estimation of heritability and testing for the occurrence of amplification or emergence of new genetic variance during stress compared to baseline conditions.



 $Reactivity,\ delta,\ scores\ with\ standard\ errors\ (error\ bars)\ for\ the\ different\ ambulatory\ HR\ (889 < N < 1242),\ RSA\ (889 < N < 1242),\ and\ PEP\ (881 < N < 1225)\ contrasts.$ 

## Results

Real-life reactivity has moderate to high temporal stability over a three-year period (0.43 < r < 0.83). Depending on the definition of ambulatory reactivity employed, significant heritability was found, ranging from 28 to 38% for heart rate, 30 to 39% for cardiac parasympathetic control (indexed as respiratory sinus arrhythmia, **RSA**), and 13 to 23% for cardiac sympathetic control (indexed as the pre-ejection period, **PEP**). Heritability of ambulatory reactivity was largely due to newly emerging genetic variance during stress compared to periods of rest.

	Heritability Baseline levels (99% CI)	Heritability Stress levels (99% CI)	Specific heritability due to genes emerging during stress (99% CI)	Heritability Ambulatory Reactivity (99% CI)
Heart rate				
wake - sleep	0.52 (0.41-0.62)	0.55 (0.44-0.64)	0.18 (0.11-0.25)	0.38 (0.24-0.51)
work - sleep	0.52 (0.41-0.62)	0.59 (0.47-0.69)	0.24 (0.13-0.34)	0.37 (0.21-0.52)
work_sitting - sleep	0.53 (0.41-0.63)	0.59 (0.47-0.69)	0.20 (0.11-0.30)	0.35 (0.19-0.50)
work_sitting - leisure	0.47 (0.35-0.58)	0.60 (0.49-0.70)	0.19 (0.09-0.29)	0.31 (0.13-0.47)
work_peak - sleep	0.53 (0.41-0.63)	0.56 (0.43-0.66)	0.21 (0.10-0.32)	0.33 (0.17-0.48)
work_peak - leisure	0.48 (0.36-0.58)	0.57 (0.45-0.68)	0.19 (0.07-0.30)	0.28 (0.11-0.44)
Respiratory Sinus				
Arrhythmia				
wake - sleep	0.46 (0.32-0.58)	0.55 (0.43-0.66)	0.27 (0.16-0.38)	0.34 (0.19-0.49)
work - sleep	0.46 (0.33-0.58)	0.51 (0.35-0.63)	0.34 (0.19-0.46)	0.39 (0.21-0.54)
work_sitting - sleep	0.46 (0.33-0.58)	0.48 (0.32-0.61)	0.31 (0.17-0.44)	0.39 (0.21-0.55)
work_sitting - leisure	0.37 (0.22-0.51)	0.49 (0.33-0.61)	ns	ns
work_peak - sleep	0.47 (0.33-0.59)	0.35 (0.18-0.50)	0.27 (0.11-0.41)	0.34 (017-0.50)
work_peak - leisure	0.40 (0.24-0.53)	0.35 (0.19-0.50)	0.21 (0.06-0.35)	0.30 (0.08-0.50)
Pre-ejection Period				
wake - sleep	0.38 (0.24-0.50)	0.41 (0.28-0.53)	0.11 (0.02-0.20)	0.18 (0.03-0.32)
work - sleep	0.39 (0.25-0.51)	0.47 (0.30-0.61)	0.16 (0.02-0.28)	0.22 (0.03-0.39)
work_sitting - sleep	0.39 (0.25-0.51)	0.45 (0.28-0.59)	0.16 (0.02-0.28)	0.23 (0.04-0.41)
work_sitting - leisure	0.24 (0.11-0.37)	0.41 (0.26-0.54)	ns	0.13 (0.02-0.31)
work_peak - sleep	0.38 (0.24-0.50)	0.39 (0.21-0.54)	ns	ns
work peak - leisure	0.22 (0.09-0.35)	0.35 (0.20-0.50)	ns	ns

Heritability. Heritability of the levels of heart rate, cardiac parasympathetic control (RSA), and cardiac sympathetic control (PEP) during the ambulatory baseline (sleep, leisure) and stress (wake, work, work\_sitting, work\_peak) levels, as well as the extent to which heritability of stress levels is due to genetic variation emerging specifically during stress. Last column depicts the heritability of ambulatory reactivity measures shown in the Figure.

## **Conclusion**

Ambulatory autonomic reactivity extracted from an unstructured real-life setting shows reliable, stable and heritable individual differences. Real-life mental and social engagement with the environment uncovers new and different genetic variation compared to that seen in resting baseline conditions, including sleep.







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