

Scientific evidences of the association between work stress and job strain with autonomic nervous system Prof. Marco M. Ferrario **Research Center in Epidemiology and Preventive Medicine**

Dept. of Medicine and Surgery; University of Insubria, Varese (Italy)

http://epimed.uninsubria.eu

May 3rd 2017

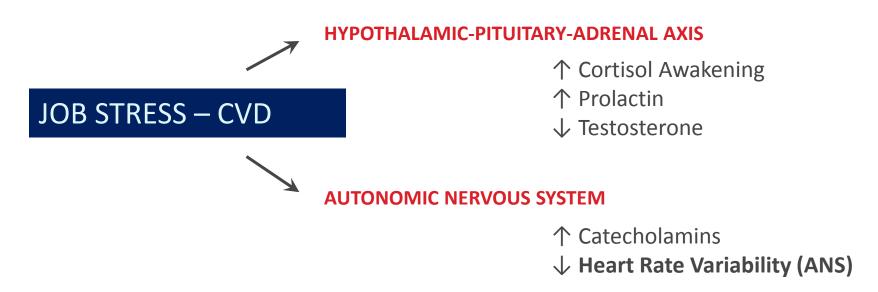
MMFerrario¹, R Borchini²

Financial disclosure: No relevant financial relationship exists

 Research Centre in Epidemiology and Preventive Medicine, Department of Medicine and Surgery, University of Insubria, Varese, Italy.
Occupational Medicine Unit, Varese Hospital and University of Insubria, Varese, Italy

JOB STRESS and CVD

JOB STRESS can be defined as the harmful physical and emotional responses that occur when the requests of the job do not match the capabilities, resources, or needs of the worker. Job stress can lead to poor health, increase the risk of mental and CVD diseases and injuries. *NIOSH 1999*



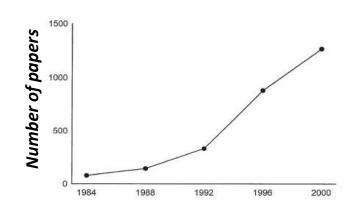
Heart Rate Variability – HRV

HRV is the variability of the heart rate (HR) during beat-to-beat time interval.

HRV analysis represents a measurement of the fluctuation of time intervals between two consecutive heartbeats.

It portrays cyclic HR modifications during a 24h time period as a result of Autonomic Nervous System (ANS) control on sinus node.

Akselrod, 1981 → HRV provides information about sympatho- vagal cardiac control in a non invasive way



Years

HRV - MEASUREMENTS

TIME DOMAIN analysis

(%)

Measurement of the heart cycle and its beat-to-beat variation. Quantitative estimation of heart cycle variation.

MEASURES

SDNN: standard deviation of all normal RR intervals(ms)

SDNN index: mean of all the 5-minute standard deviations of NN (normal RR) intervals during the 24-hour period (ms)

r-MSSD: square root of the mean of the squared differences between successive NN intervals over 24 hours (ms)

pNN50: percentage of differences between successive NN intervals over 24 hours that are greater than 50 ms

FREQUENCY DOMAIN analysis

Measurement of the fluctuation rate of the heart cycle. Qualitative and quantitative estimation of fluctuation rate.

MEASURES

HF (High Frequency) bandwidth between 0.15 and 0.45 Hz.

These frequencies are an expression of <u>vagal activation</u> and they are linked to respiratory activity.

LF (Low Frequency) bandwidth between 0.04 and 0.15 Hz.

These frequencies are an expression of <u>sympathetic</u> <u>activation</u> but they also reflect vagal modulation.

There are two main validated models of work stress.

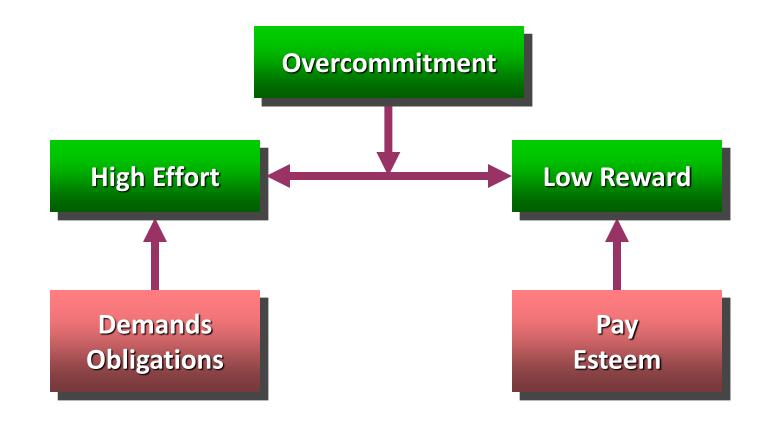
The demands-control-support model (Karasek and Theorell, 1990) measures three factors: psychological job demands, decision latitude (or job control) and social support at work.

The theoretical approach of the effort–reward imbalance (ERI) model is focused on the notion of social reciprocity where efforts are equalized by respective rewards (Siegrist, 1998).

Demand-Control Model



Effort-Reward Imbalance Model



The analysis of HRV has been shown to be a reliable, **noninvasive measure of the neural control of the heart** *(Thayer et al., 2012)*

It has been consistently shown that measures of vagalmediated HRV have independent associations with mortality and morbidity.

In cardiopathic patients the HRV reduction is a negative prognostic factor. (*Porges, 2007; Thayeret al., 2010*).

Some studies have shown on a transitory HRV reduction after acute mental stress.

Limited number of studies focused on the association between **HRV and prolonged work stress and strain**. In the review that we present we attempt to summarize the evidence of **the association between psychosocial work environment and autonomic nervous system**

function in apparently healthy employees.

Self-Reported Sleep Quality, Job Stress, and Daytime Autonomic Activities Assessed in Terms of Short-Term Heart Rate Variability among Male White-Collar Workers

Kageyama et al . – 1998

N. 223 whites collars *Japanese* men employed in different industries

Study design: cross sectional

Job Stress assessed with a non validated questionnaire

5 min - ECG in working day

Major findings: <u>No association</u> <u>between JS and HF or LF</u>

Table 7. GLM analysis of HRV parameters

Dependent variable (Posture)	In(HF) (supine rest)	C-CV _{HF} (supine rest)	ln(HF) (standing rest)	C-CV _{HF} (standing rest)	ln(LF) (supine rest)	C-CV _{HI} /C-CV _{HI} (supine rest)	ln(LF) (standing rest)	C-CV _{HF} /C-CV _{HF} (standing rest)
F-value	4.9***	4.5**	2.2*	2.0*	0.7	1.9*	1.6	2.5++
Independent variable								
Age	F=19.5***	F=22.2***	F=2.6	F=3.4	F=0.8	F=4.0*	F=5.3*	F=0.1
BMI	F=5.7***	F=4.7**	F=1.6	F=1.2	F=1.0	F=2.0	F=1.7	F=1.1
Current smoking status	F=1.1	F=0.0	F=1.3	F=2.4	F=0.1	F=0.7	F=1.2	F=0.3
Current alcohol consumption	F=1.4	F=1.0	F=0.1	F=0.2	F=0.6	F=0.8	F=1.6	F=2.1
Commuting time	F=2.7	F=3.2*	F=1.6	F=1.4	F=1.4	F=3.3*	F=0.0	F=2.7*
Amounts of overtime	F=1.4	F=1.4	F=3.6*	F=2.4	F=0.3	F=0.1	F=0.8	F=6.0**
Self-reported sleep quality	F=0.0	F=0.0	F=9.3**	F=6.6*	F=0.1	F=1.1	F=1.2	F=7.7**

N=223. HF and LF, power densities of HF and LF (msec²); C-CV_{HF} and C-CV_{LF}, component coefficients of HF and LF (%). BMI (body mass index, kg/m²), smoking status, and alcohol consumption were categorically analyzed, while age was analyzed as a covariate (see ref. 26). F-test for model; ⁺p<0.05, ⁺⁺p<0.01, ⁺⁺⁺p<0.001. F-test for independent variables; ^{*}p<0.05, ^{*+}p<0.01, ^{*++}p<0.001.

Occupational determinants of heart rate variability

Van Amellsvoort et al. – 2000

135 Dutch healthy men and women

Employed in manufacturing and office works.

Study design: cross sectional

JS assessment: JCQ

24 h-monitoring ECG in working day

	Heart rate (beats/min)	SDNNi (ms)	%LF	Log(LF) [log(s ²)]	Log(HF) [log(s ²)]
Job strain categories Low demands, high control ^a Low demands, low control High demands, high control High demands, low control	82.6 (1.4) 83.3 (1.6) 83.1 (1.8) 88.1 (1.9)*	72.7 (3.1) 71.7 (3.6) 68.9 (3.8) 72.5 (4.2)	73.2 (1.3) 77.9 (1.5)** 77.7 (1.6)* 77.7 (1.7)*	-2.657 (0.032) -2.635 (0.037) -2.658 (0.038) -2.562 (0.043)	-3.143 (0.043) -3.224 (0.050) -3.224 (0.053) -3.134 (0.059)

Reference classification for r values of category variables

 $\Gamma > 0.05, \ \ \Gamma > 0.01$

Hypertension 2000;35;880-886

Effects of Work Stress on Ambulatory Blood Pressure, Heart Rate, and Heart Rate Variability

Tanja G.M. Vrijkotte, Lorenz J.P. van Doornen, Eco J.C. de Geus

Vrijkotte et al.– 2000

109 Dutch white-collar healthy men (No CVD or hypertension. No therapy.)

Study design: cross sectional

JS assessment: ERI

24 h-monitoring ECG for three days:2 working days and 1 rest day

Major findings: <u>↓ rMSSD only in</u> working days in high-imbalance

r-MSSD: square root of the mean of the squared differences between successive NN intervals over 24 hours (ms)

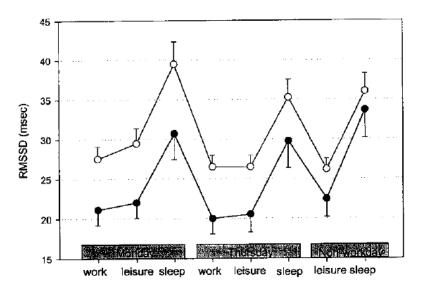


Figure 2. SBP, HR, and RMSSD (mean±SD) during work, leisure, and sleep (only HR and RMSSD) on 2 workdays and 1 nonworkday for the high- (●) and low-imbalance (○) groups.

Yonsei Medical Journal Vol. 45, No. 5, pp. 838-846, 2004

Association between Job Stress on Heart Rate Variability and Metabolic Syndrome in Shipyard Male Workers

Myung Guen Kang¹, Sang Baek Koh², Bong Suk Cha², Jong Ku Park², Jong Min Woo³, and Sei Jin Chang²

169 men, healthy (No alcohol – Non smokers, normal ECG)

Setting: Shipyard Industry, South Korea

Study design: cross sectional

JS assessment: JCO

Kang – 2004

5 min - ECG in two days: Working day and Rest day

Table 5. Relationships between Job Strain, Metabolic Syndrome, and Heart Rate Variability Mean (S.D.)

Variables	Lower strain* + Normal <u>(N</u> =99)	Lower strain + metabolic syndrome (N=15)	High strain + Normal (N=32)	High strain + metabolic syndrome (N=10)	<i>p</i> -value
SDNN [†]	39.6 (11.3)	35.9 (10.2)	35.1 (9.8)	31.1 (8.4)	0.04
log (Tp [†])	7.0 (6.1)	6.8 (0.4)	6.7 (0.6)	6.6 (0.5)	0.09
log (Vlf [†])	6.4 (0.6)	6.1 (0.5)	6.1 (0.6)	5.9 (0.7)	0.04
log (Lf [§])	5.6 (0.7)	5.5 (0.6)	5.5 (0.7)	5.5 (0.4)	0.87
log (Hf ^I)	4.9 (0.8)	4.9 (0.9)	4.8 (0.8)	4.4 (0.4)	0.45
LF/HF ratio [¶]	2.4 (3.1)	2.8 (1.6)	2.9 (2.9)	2.9 (0.7)	0.21

*Lower strain group; low strain + passive group + active group. [†]SDNN, standard deviation of all NN interval; [‡]TP, total power; [§]VLF, very low frequency; [†]LF, Low frequency; [†]HF, high frequency; **LF/HF, index of cardiac sympathetic activity; log, log transformationLower strain group.

Circulation 2005;111;3071-3077 Does Autonomic Function Link Social Position to Coronary Risk?

The Whitehall II Study

Whitehall II Study – 2005

Harry Hemingway, FRCP; Martin Shipley, MSc; Eric Brunner, PhD; Annie Britton, PhD; Marek Malik; Michael Marmot, FRCP

N 2344 out of N. 10308 English civil servants

Study design: cross sectional

JS assessment: JCQ

ECG 5 min in work day only

Major findings: $\sqrt{\text{SDNN}} \sqrt{\text{HF}} \sqrt{\text{LF in low job control}}$

	Participants, n	Heart Rate, bpm	SDNN, ms	LF Power, ms	² HF Power, ms
Psychosocial factors					
Depression					
No	1424	68.6 (68.1–69.3)	34.5 (33.8–35.3)	335 (319–351)	119 (112–125)
Yes	701	69.2 (68.4-70.1)	33.6 (32.6-34.7)	313 (292–335)	112 (103–122)
Р		0.3	0.18	0.12	0.27
Low social networks					
No	1482	68.5 (67.9-69.1)	34.5 (33.7–35.2)	332 (317–348)	120 (113–127)
Yes	584	69.5 (68.6-70.4)	33.4 (32.3–34.6)	307 (284–331)	107 (98–117)
Р		0.07	0.15	0.09	0.03
Low job control*	\mathbf{i}				
No	1190	68.1 (67.5-68.7)	36.3 (35.5–37.2)	379 (360–399)	133 (125–141)
Yes	271	70.8 (69.6–721)	33.7 (32.0-35.4)	319 (286–355)	114 (101–130)
P /		<0.001	0.006	0.004	0.03

*Job control was estimated only in those 1461 participants still working.

Job Strain and Autonomic Indices of Cardiovascular Disease Risk

Collins and Karasek – 2005 of Cardina Sean M. Collins

Sean M. Collins, PT, ScD, CCS, ¹* Robert A. Karasek, PhD,² and Kevin Costas, MPH²

36 men (35 – 59 y/o) No CVD, No therapy

Setting: healthcare employees in the US

Study design cross sectional

JS assessment: JCQ

48 h-Holter ECG in two consecutive days (Working day and Rest day)

Major findings <u>V SDNN and HF in</u> WD in low job control

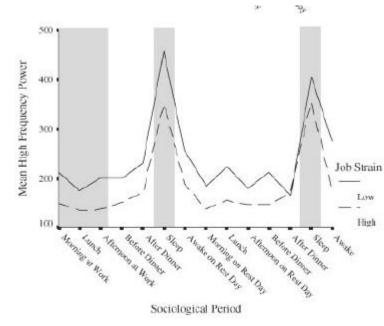


FIGURE 1. Heart rate variability and high frequency power during sociological periods.

Int Arch Occup Environ Health (2011) 84:185-191 The perception of work stressors is related to reduced

parasympathetic activity

Els Clays · Dirk De Bacquer · Vincent Crasset · France Kittel · Patrick de Smet · Marcel Kornitzer · Robert Karasek · Guy De Backer

653 Belgian healthy men from different job titles and industrial sectors (25% blue collars – 75% white collars)

Study design: cross sectional

JS assessment: JCQ

Clays – 2011

24 h-monitoring ECG in working day

Mean HRV values	(SD) in work stressor groups; results from <i>t</i> -test and analysis of covariance ($N = 653$)
	Work stressor index groups

	Low (N = 261)	$\begin{array}{l} \text{Medium} \\ (N = 288) \end{array}$	High (<i>N</i> = 74)	Р	P ^a
HR	80.4 (8.7)	81.3 (8.9)	83.2 (8.1) ^b	<0.05	0.08
pNN50 (ln)	1.33 (1.1)	1.15 (1.2)	0.99 (1.2) ^b	< 0.05	< 0.05
SDNN	140.6 (37.0)	134.9 (36.9)	135.0 (36.9)	0.16	0.21
LF (ln)	6.71 (0.6)	6.66 (0.6)	6.70 (0.6)	0.57	0.39
HF (ln)	5.08 (0.8)	4.99 (0.8)	4.88 (0.9)	0.14	0.10
LF/HF (ln)	1.64 (0.5)	1.66 (0.5)	1.82 (0.5) ^{b,c}	< 0.05	< 0.05

^a Adjusted for age, language, occupation, smoking, BMI, total cholesterol, systolic blood pressure and leisure time physical activity

^b p < 0.05—results LSD post hoc test: significance of difference from first category

^c p < 0.05—results LSD post hoc test: significance of difference from second category

Job Strain and Heart Rate Variability in Resident Physicians Within a General Hospital

Hernandez – 2013

N. 54 healthy men and women - resident physicians from *Mexico City*

Study design: cross-sectional

JS assessment: JCQ

24 h-Holter ECG in Working Day

Major findings: \downarrow SDNN, \downarrow HF, \downarrow LF in «passive» \downarrow LF, \downarrow LF/HF in high JS

		SDNN ^{a,b}		High-frequency power ^a			
Variable	%	95% CI ^c	Pvalue	%	95% CI ^c	P value	
Job strain categori Low strain ^d	ies						
Passive	-9.089	-17.97,0.74	0.069	-25.75	-45.00, 0.22	0.052	
Active	0.180	-8.57, 9.77	0.968	- 10.42	- 31.51, 17.12	0.421	
Highstrain	-0.240	- 10.21, 11.94	0.965	-7.70	-21.52,49.60	0.626	
	ı	.ow-frequencypower ^a		Low-fre	quency/high-frequency	ratio ^a	
Variable	%	95% CI ^b	P value	%	95% Cl ^b	P value	
Job strain categorie Low strain ^c	IS						
Passive	-26.95	-39.00, -12.53	0.001	- 1.95	-18.67, 18.18	0.836	
Active	-5.29	- 19.42, 11.29	0.509	5.68	-10.55,24.89	0.516	
High strain	- 17.85	-32.34, -0.25	0.047	-24.29	-38.08, -7.42	0.007	

Scand J Work Environ Health 2004;30(6):477-485

Job strain in relation to ambulatory blood pressure, heart rate, and heart rate variability among female nurses

Riese et al. – 2004 by Harriëtte Riese, PhD,¹ Lorenz JP Van Doornen, PhD,² Irene LD Houtman, PhD,³ Eco JC De Geus, PhD¹

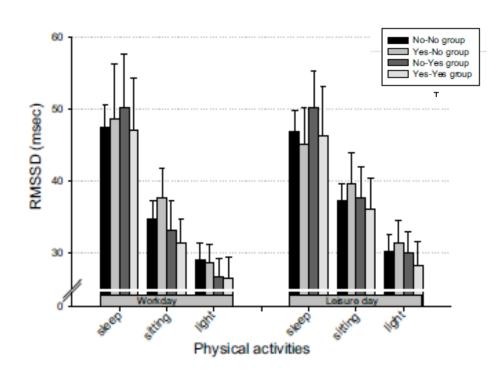
159 female healthy Dutch nurses (No CVD – No therapy)

Study design: Longitudinal

JS assessment: JCQ (submitted on two separate occasions, one year apart)

24-h monitoring ECG in two days: Working day and Rest day

Major findings: <u>No association</u> <u>between JS and any HRV parameters.</u>



International Journal of Occupational Medicine and Environmental Health 2015;28(1):42 – 51 PROLONGED JOB STRAIN REDUCES TIME-DOMAIN HEART RATE VARIABILITY ON BOTH WORKING AND RESTING DAYS AMONG Borchini Ferrario - 2015 CARDIOVASCULAR SUSCEPTIBLE NURSES

N. 36 healthy male and female Nurses *Italy*

Study design: Longitudinal

JS assessment: JCQ and ERI (submitted on two separate occasions, one year apart)

24 h-monitoring ECG in Working Day and Rest Day (time-domain only)

Major findings: ↓SDNN and ↓SDNN Index in WD (and borderline stat sign in RD) among prolonged high JS only. Table 3. Age- and smoking-adjusted geometric means (M) of time-domain HRV parameters according to the job strain categ

HRV time domain				
parameter	SLS (N = 19)	RHS (N = 7)	PHS (N = 10)	p*
SDNN (ms)				
WD	169.1 ± 9.3	145.3 ± 13.2	128.3±9.7	0.0185
RD	171.1±7.9	158.9 ± 12.0	142.4±9.0	0.0786
SDNN_Index (ms)				
WD	70.4 ± 4.0	59.5 ± 5.6	54.8±4.3	0.0370
RD	71.9 ± 4.2	69.2±6.7	56.5±4.6	0.0654
SDANN (ms)				
WD	148.1±8.9	131.8 ± 13.1	116.5 ± 9.7	0.0760
RD	144.0 ± 6.9	133.1±10.5	125.2±8.2	0.2298
RMSSD (ms)				
WD	48.8±6.2	46.8±9.8	37.0 ± 6.5	0.4418
RD	52.2±6.5	66.1±13.6	40.6 ± 7.0	0.2010
PNN50 (%)				
WD	9.7±2.4	4.9 ± 2.0	4.6±1.6	0.1544
RD	11.1±2.7	8.5±3.4	4.9 ± 1.6	0.1570
HR (bpm)				
WD	76.3±1.3	82.4±2.4	78.3±1.9	0.0879
RD	73.5±1.3	75.1±2.1	77.1±1.8	0.2811

Abstract on the 7° ICOH International Conference on Work Environment and Cardiovascular Diseases – May 2017

Heart Rate Variability Frequency Domain alterations among healthy nurses exposed to prolonged job-strain

Borchini Ferrario - 2015

N. 36 healthy male and female Nurses *Italy*

Study design: Longitudinal

JS assessment: JCQ and ERI (submitted on two separate occasions, one year apart)

24 h-monitoring ECG in Working Day and Rest Day (time-domain only) Major findings: ↓HF in WD and ↓LF in WD and RD Age and smoke adjusted geometric mean of Frequency Domain HRV

	SLS	RHS	PHS	beta	P-value
WD	139.1±23.9	79.1±22.4	76.3±18.2	-0.32	0.0347
RD	217.1±49.0	177.3±65.9	115.6±36.0	-0.31	0.1096
WD	753.3±119.0	494.7±128.8	380.2±82.8	-0.35	0.0124
RD	820.2±154.6	660.9±205.2	377.1±98.0	-0.38	0.0219
WD	5.4±0.8	6.3±1.4	5.0±1.0	-0.03	0.8009
RD	3.8±0.6	3.7±1.0	3.3±0.7	-0.07	0.621
	RD WD RD WD	WD 139.1±23.9 RD 217.1±49.0 WD 753.3±119.0 RD 820.2±154.6 WD 5.4±0.8	WD 139.1±23.9 79.1±22.4 RD 217.1±49.0 177.3±65.9 WD 753.3±119.0 494.7±128.8 RD 820.2±154.6 660.9±205.2 WD 5.4±0.8 6.3±1.4	WD 139.1±23.9 79.1±22.4 76.3±18.2 RD 217.1±49.0 177.3±65.9 115.6±36.0 WD 753.3±119.0 494.7±128.8 380.2±82.8 RD 820.2±154.6 660.9±205.2 377.1±98.0 WD 5.4±0.8 6.3±1.4 5.0±1.0	WD 139.1±23.9 79.1±22.4 76.3±18.2 -0.32 RD 217.1±49.0 177.3±65.9 115.6±36.0 -0.31 WD 753.3±119.0 494.7±128.8 380.2±82.8 -0.35 RD 820.2±154.6 660.9±205.2 377.1±98.0 -0.38 WD 5.4±0.8 6.3±1.4 5.0±1.0 -0.03

Autors	Year	Subj	Sex	Work	JS	ECG	WD RD	HRV	JS - HRV
Kageyama	1998	223	М	WC	Quest	5 m.	WD	FD	None
Van Amellsvoort	2000	135	M F	WC	JCQ	24 h	WD	TD - FD	↑ LF
Vrijkotte	2000	109	М	WC	ERI	24 h	WD RD	TD	\downarrow rMSSD WD
Riese	2004	159	F	Nurse	JCQ	24 h	WD RD	TD	None
Kang	2004	169	М	BC	JCQ	5 m.	WD RD	TD	\downarrow SDNN WD
Hemingway	2005	2344	М	WC	JCQ	5 m.	WD	TD - FD	\downarrow SDNN HF LF WD
Collins Karasek	2005	36	М	WC	JCQ	48 h	WD RD	TD - FD	\downarrow SDNN HF WD
Clays	2011	653	Μ	WBC	JCQ	24 h	WD	TD FD	↓pNN50 ↑LF/HF <mark>WD</mark>
Hernandez	2013	54	M F	Doctor	JCQ	24 h	WD	TD - FD	\downarrow SDNN \downarrow HF \downarrow LF/HF WD
Borchini Ferrario	2015	36	M F	Nurse	ERI + JCQ	24 h	WD RD	TD	\downarrow SDNN \downarrow SDNN Index WD
Borchini Ferrario	2017	36	M F	Nurse	ERI + JCQ	24 h	WD RD	TD	\downarrow HF WD \downarrow LF WD RD

JS – HRV ASSOCIATION IN REVIEWED STUDIES

No Association Job Strain - HRV

- Kageyama 1998
- Riese 2004

Association Job Strain - HRV

- Van Amellsvoort 2000
- Vrijkotte 2000
- □ Kang 2004
- Collins e Karasek 2005
- Whitehall II study 2010
- Clays 2011
- Hernandez 2013
- Borchini Ferrario 2015
- Borchini Ferrario 2017

CONCLUSIONS

Most of the studies that have shown an association between JS and HRV, with the following findings in the high JS group:

- reduction of HRV measurements in the Time Domain.
- reduction of spectral HF component
- increase or reduction of spectral LF

This findings support the hypothesis of an altered sympatho-vagal balance during work stress, with a prevailing sympathetic component.



The studies reviewed indicate:

HRV analysis \rightarrow useful tool for identifying **alterations of the cardiac sympatho-vagal balance**

HRV analysis can be used for **early detection of JS effects on the** cardiovascular system

CONSIDERATIONS FOR FUTURE STUDIES ON JS- HRV

- Accurate sample selection: healthy subjects with no history of diseases or conditions and treatments that could interfere with the autonomic nervous system (ANS).
- Adoption of validated possibly multiple measures of JS
- Longitudinal studies are needed, to assess the effect of prolonged JS exposures

CONSIDERATIONS FOR FUTURE STUDIES ON JS- HRV

- ECG monitoring for HRV analysis
- If monitoring is performed for short periods of time, respiratory rate and posture need to be standardised as they have a known effect on the HF component.
- 24h or 48h monitoring should be preferred, although they have may be possible only for small size samples
 → they provide a more comprehensive HRV analysis.
- ECG-monitoring in working and rest days allows to compare these two different settings.

CONSIDERATIONS FOR FUTURE STUDIES ON JS- HRV

 Finally: collaborative multisite well-standardised studies are need to allow to increase the statistical

REVIEW PAPERS

International Journal of Occupational Medicine and Environmental Health 2010;23(3):293–312 DOI 10.2478/v10001-010-0035-2

DESCRIPTION OF A LARGE-SCALE STUDY DESIGN TO ASSESS WORK-STRESS-DISEASE ASSOCIATIONS FOR CARDIOVASCULAR DISEASE

ROBERT KARASEK12, SEAN COLLINS3, ELS CLAYS4, ALICJA BORTKIEWICZ5, and MARCO FERRARIO6

Thanks for paying attention.

It's not what you look at that matters, it's what you see. Henry David Thoreau - 1817–1862, American poet, philosopher, abolitionist, naturalist, tax resister, development critic, surveyor, and historian.