62° CONGRESSO NAZIONALE SIGG NAPOLI2017 29 novembre - 2 dicembre INVECCHIAMENTO: SCENARIO 2.0

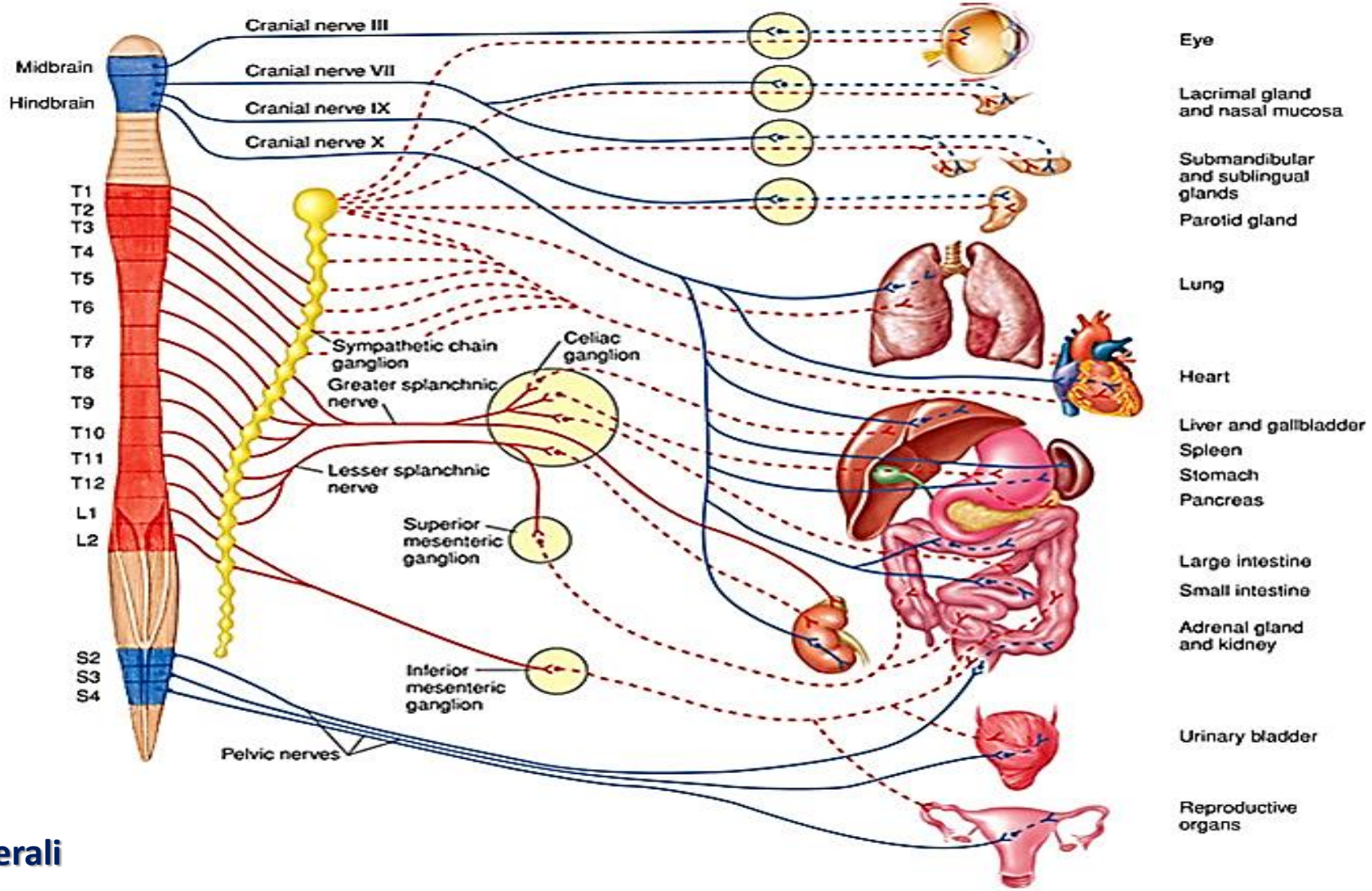
SOCIETÀ ITALIANA DI GERONTOLOGIA E GERIATRIA

Disregolazione Autonomica ed Invecchiamento

Martina Rafanelli, MD

Syncope Unit, Geriatria e UTIG,
Università degli Studi di Firenze,
AOU Careggi, Firenze

Come funziona il SNA?



Neuroni viscerali

Afferenti

Efferenti

Strutture di integrazione encefaliche

Regolazione muscolatura liscia, muscolo cardiaco, attività ghiandolare

Manifestazioni cliniche

- Cardiovascolari – Ipotensione Ortostatica
- Termoregolatorie – Anidrosi, intolleranza al caldo
- Gastroenteriche – Xerostomia, disfagia, stipsi, diarrea
- Urinarie – Nicturia, frequenza, urgenza, incontinenza, ritenzione

Mathias CJ. *N Engl J Med* 1997

Manifestazioni cliniche

- Sistema riproduttivo – Disfunzione erettile ed eiaculatoria
- Respiratorie – Stridore, gasping inspiratorio involontario, apnee
- Oculari – xeroftalmia, aniscoria, S. di Horner
- Altri deficit neurologici – segni parkinsoniani, cerebellari e piramidali

Mathias CJ. *N Engl J Med* 1997

Invecchiamento e controllo cardiovascolare

Aging of the autonomic nervous system and possible improvements in autonomic activity using somatic afferent stimulation

Harumi Hotta and Sae Uchida

In elderly people, autonomic functions are relatively well maintained at rest, but patients' ability to adapt to environmental or visceral changes are often seriously impaired.

Geriatr Gerontol Int 2010

Aging of the autonomic nervous system and possible improvements in autonomic activity using somatic afferent stimulation

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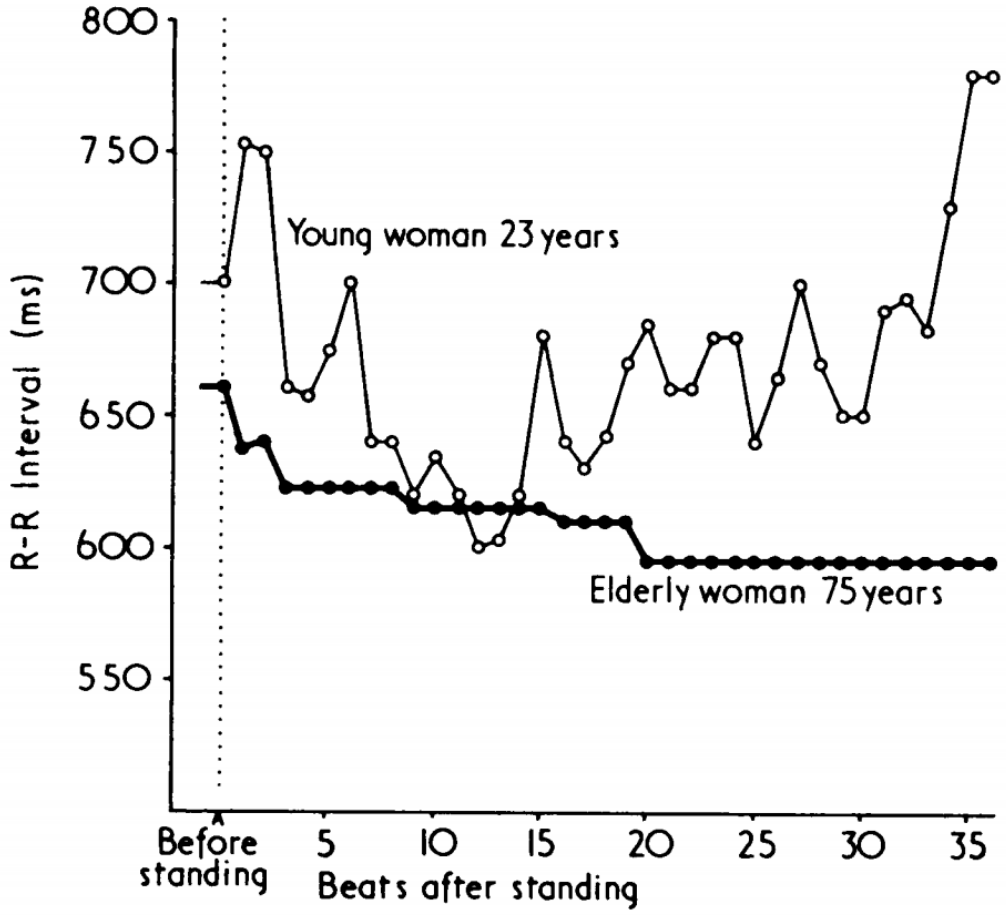
The age-related changes in autonomic nervous system activity and regulatory functions are involved in both sustained hypertension and transient hypotension in the elderly.

Geriatr Gerontol Int 2010

Heart-rate response to standing as a test for autonomic neuropathy



Heart rate response to standing in an elderly subject and a healthy young control.

Age Ageing. 1980 Feb;9(1):17-24.

Functional changes in autonomic nervous responses with ageing.

Collins KJ, Exton-Smith AN, James MH, Oliver DJ.

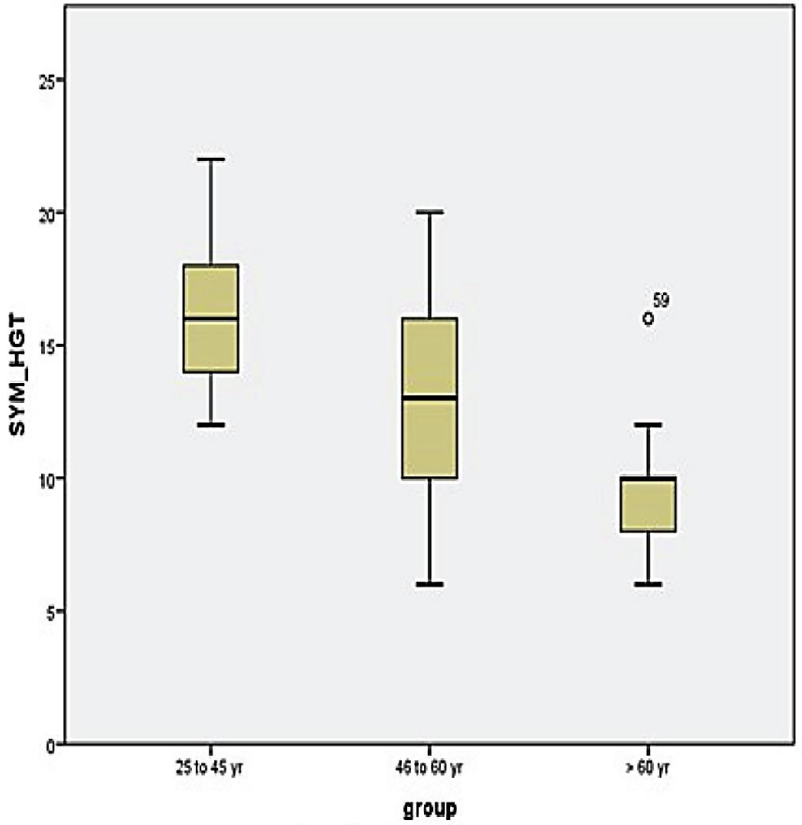
Abstract

The effects of ageing on autonomic nervous responses have been investigated in 29 young adults, 64 healthy elderly in the age range 66 to

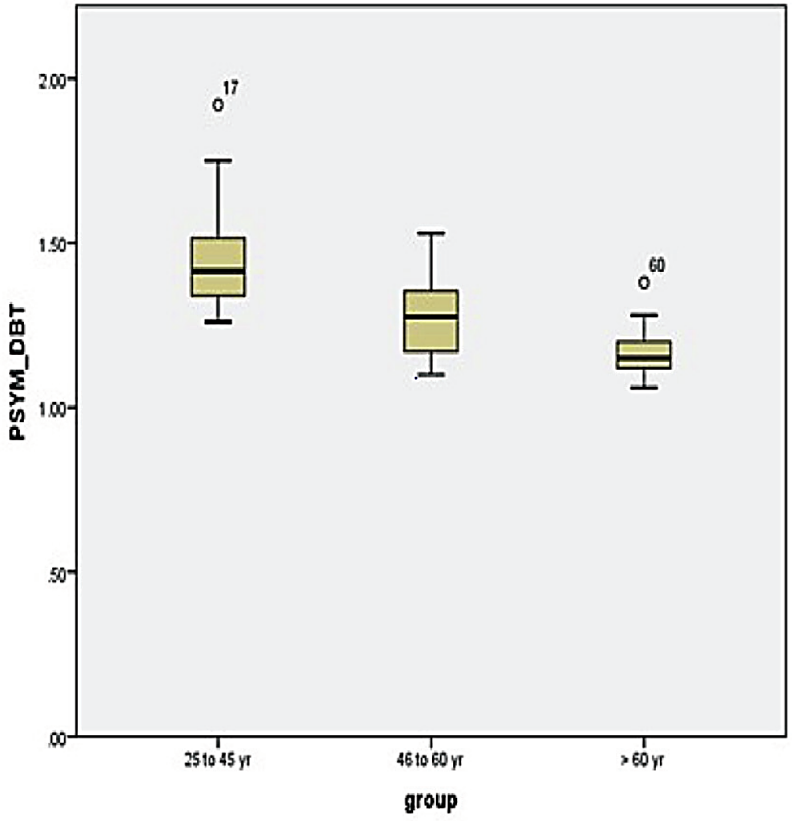
In the healthy elderly group, the beat-to-beat variation in response to postural change was significantly diminished, the vasoconstrictor response to cooling reduced and baroreflex sensitivity during lower-body negative pressure was decreased compared with young adults.

autonomic disturbances suggests that physiological impairment may occur in autonomic neural pathways with ageing.

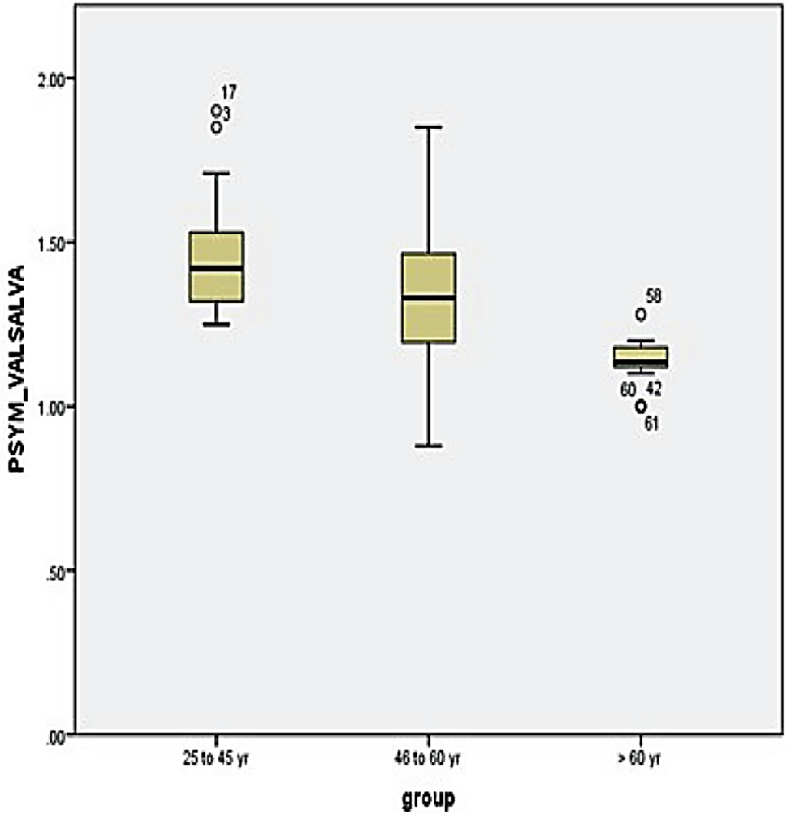
Age Related Changes in Autonomic Functions



a-sympathetic handgrip test



c- parasympathetic deep breathing test



d-parasympathetic Valsalva maneuvre

Parashar R. et al. Journal of Clinical and Diagnostic Research. 2016

Aging of the autonomic nervous system and possible improvements in autonomic activity using somatic afferent stimulation

Harumi Hotta and Sae Uchida

Age-related changes in sympathetic nerve activity

Sympathetic nerve activity at rest (sympathetic tone; measured by a variety of indirect methods) is widely found to increase during aging in many parts of the body. There is an increase with age in plasma noradrenaline concentration[3] and an increase in the burst discharge rate on muscle sympathetic nerve fibers measured by microneurography.

Geriatr Gerontol Int 2010

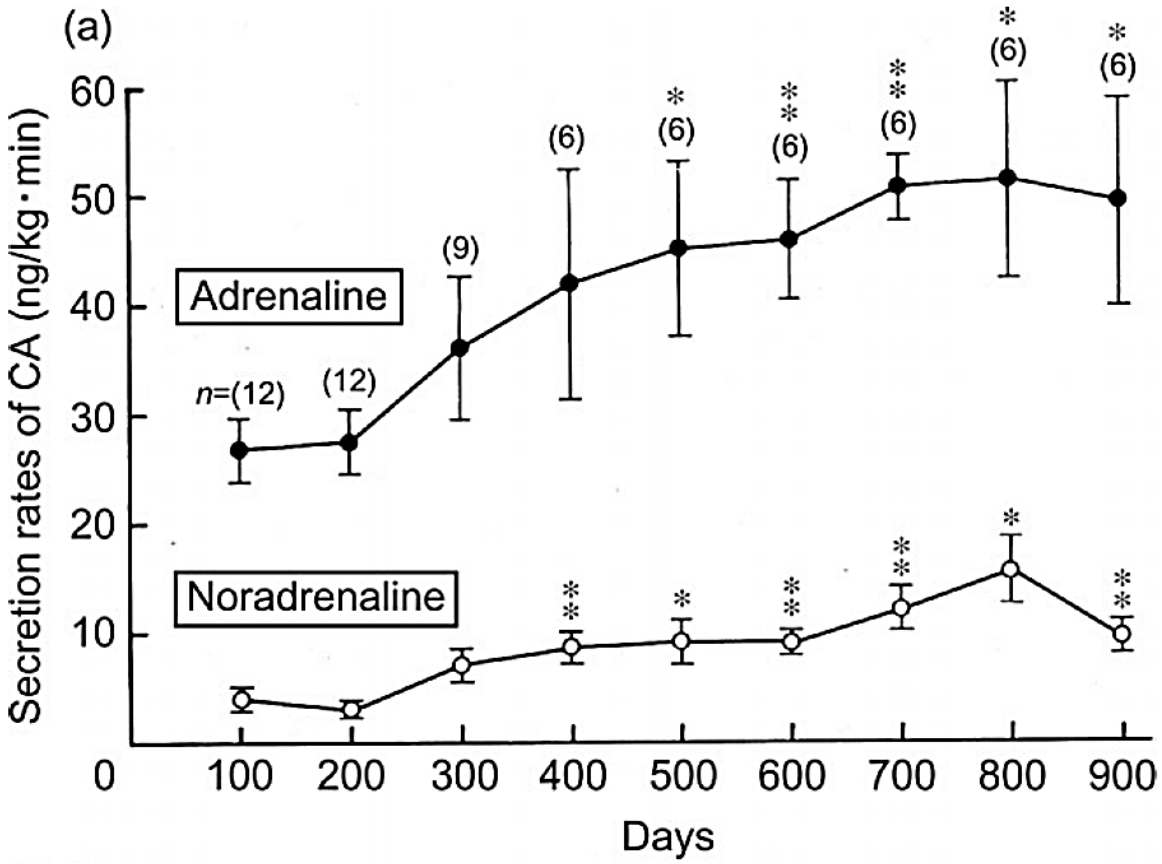
ELSEVIER

Neuroscience Letters

Volume 69, Issue 3, 12 September 1986, Pages 263-268

Increases in adrenal catecholamine secretion and adrenal sympathetic nerve unitary activities with aging in rats

Kenichi Ito, Akio Sato, Yuko Sato, Harue Suzuki



Aging of the autonomic nervous system and possible improvements in autonomic activity using somatic afferent stimulation

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Age-related changes in sympathetic nerve activity

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Geriatr Gerontol Int 2010

Human ageing and the sympathoadrenal system

Douglas R. Seals*† and Murray D. Esler‡

- MSNA increases with age even in healthy, normotensive adults.
- MSNA essentially doubles between the ages of 25 and 65 in these healthy adults.

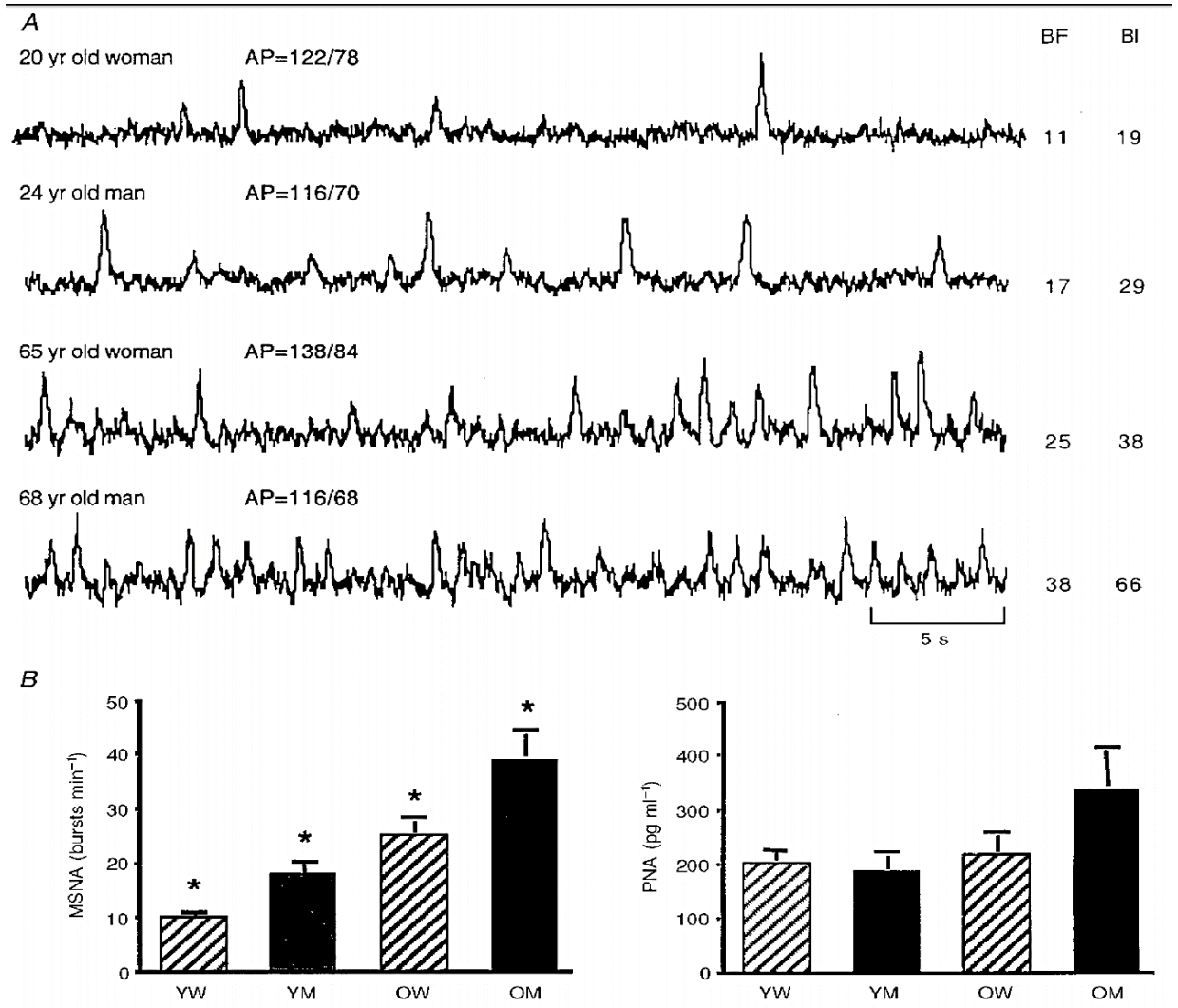


Figure 1. Age-associated increases in muscle sympathetic nerve activity

- this increase in MSNA is observed in both men and women.
- these age associated elevations in MSNA are not always discernable based on venous antecubital PNA concentrations-

Journal of Physiology (2000)

Aging of the autonomic nervous system and possible improvements in autonomic activity using somatic afferent stimulation

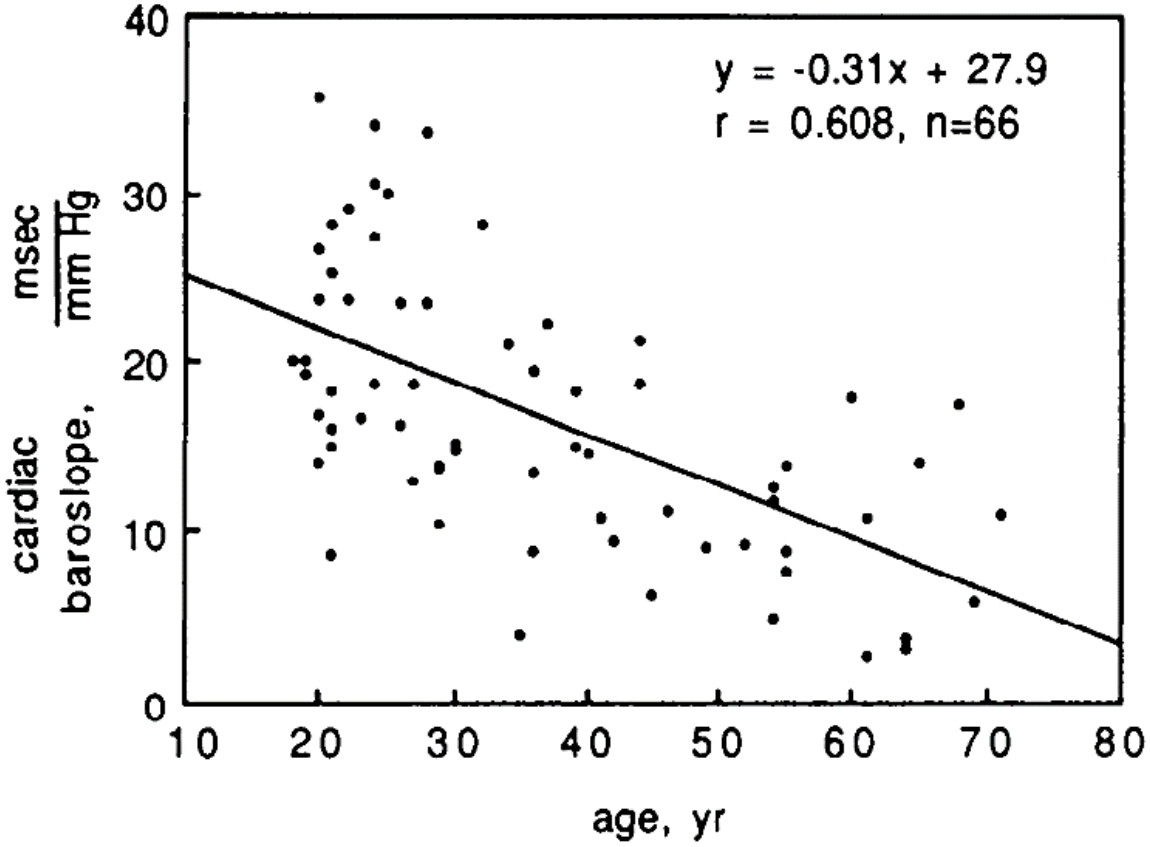
Harumi Hotta and Sae Uchida

It is hypothesized that any age-related increase in resting sympathetic nerve activity is a result of a reduction of the sensitivity of the arterial baroreceptor reflex, which tonically inhibits sympathetic outflow.[5]

Geriatr Gerontol Int 2010

Effects of aging on baroreflex regulation of sympathetic activity in humans

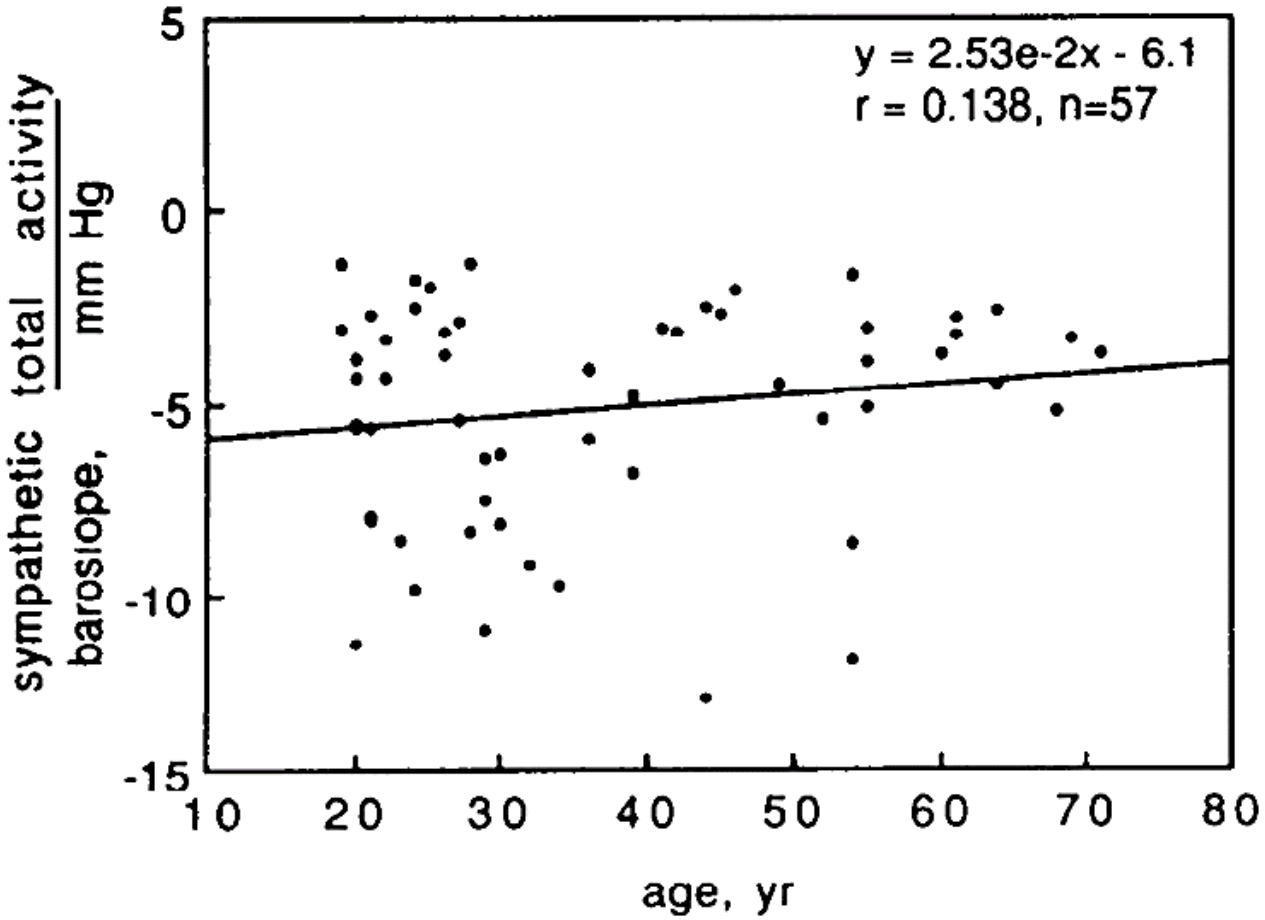
Individual cardiac baroreflex sensitivities plotted vs. age. Regression analysis revealed a significant ($P < 0.05$) inverse relationship between these 2 variables.



Ebert T.J et al. American Journal of Physiology - Heart and Circulatory Physiology 1992

Effects of aging on baroreflex regulation of sympathetic activity in humans

Individual sympathetic baroreflex sensitivities plotted vs. age.
Regression analysis revealed no relationship (P > 0.10) between the 2 variables.

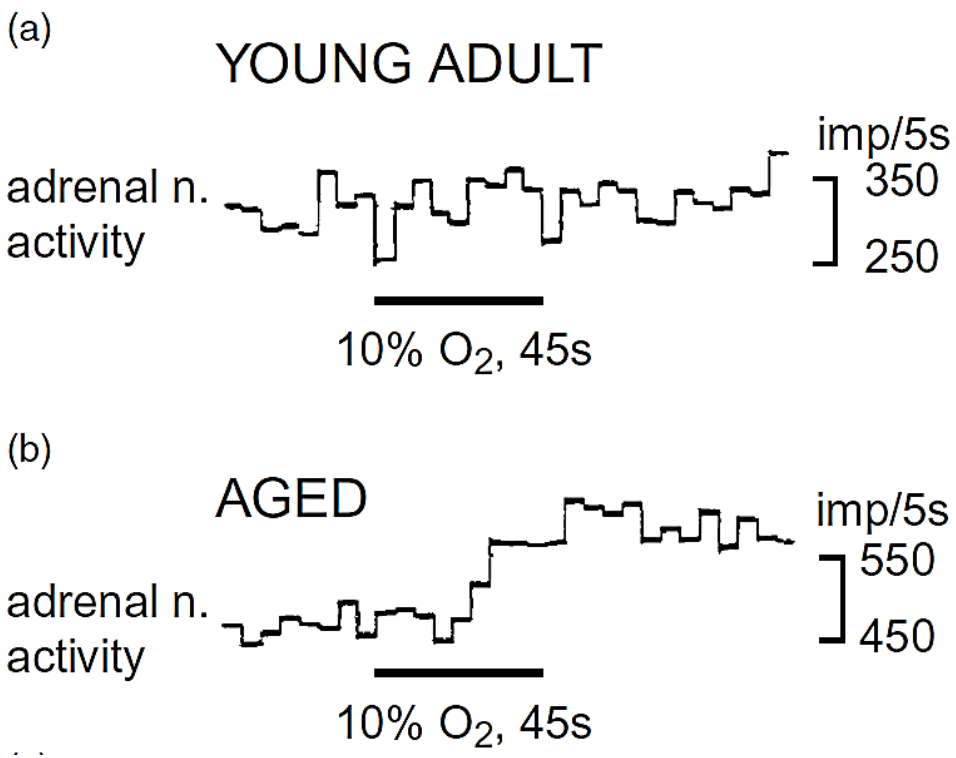


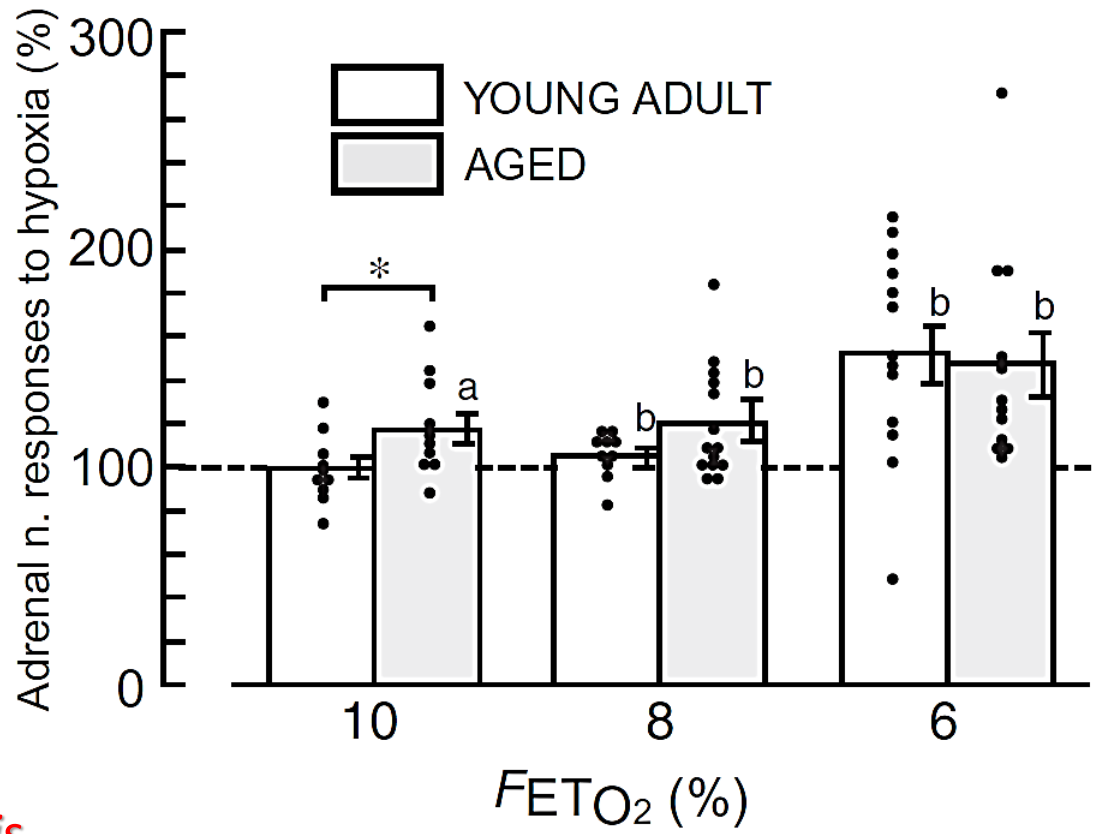
Ebert T.J et al. American Journal of Physiology - Heart and Circulatory Physiology 1992

J Auton Nerv Syst. 1991 Jan;32(1):63-8.

Reflex responses in adrenal sympathetic nerves to stimulation of glucoreceptors and chemoreceptors in aging rats.

Sato A[1], Sato Y, Suzuki H, Trzebski A.





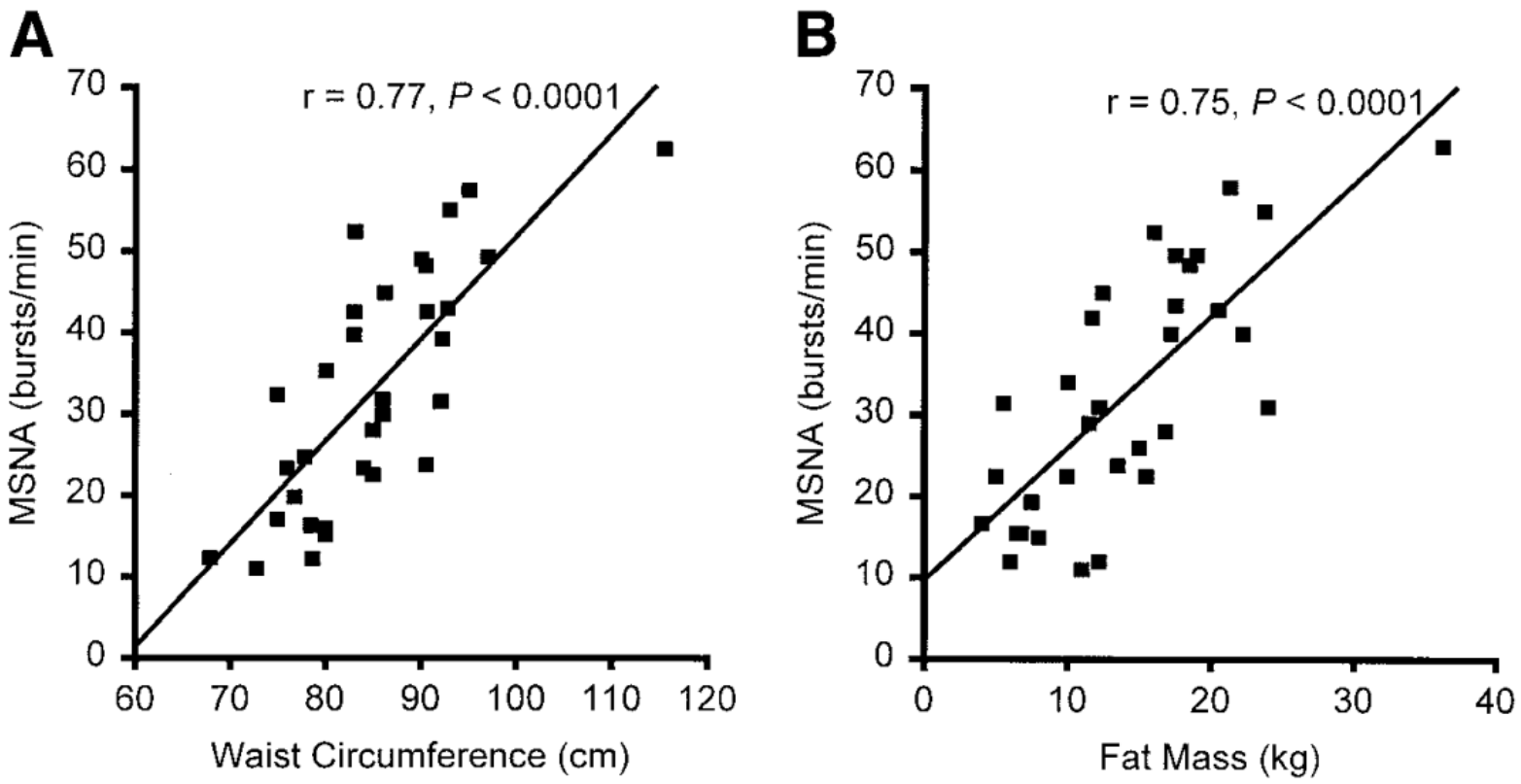
oxygen exchange in the lung declines with age and this would favor a decreased partial pressure of arterial oxygen

Chronic Sympathetic Activation

Consequence and Cause of Age-Associated Obesity?

Douglas R. Seals and Christopher Bell

Among healthy young and older men, MSNA is strongly and positively related to both percent body fat and waist circumference



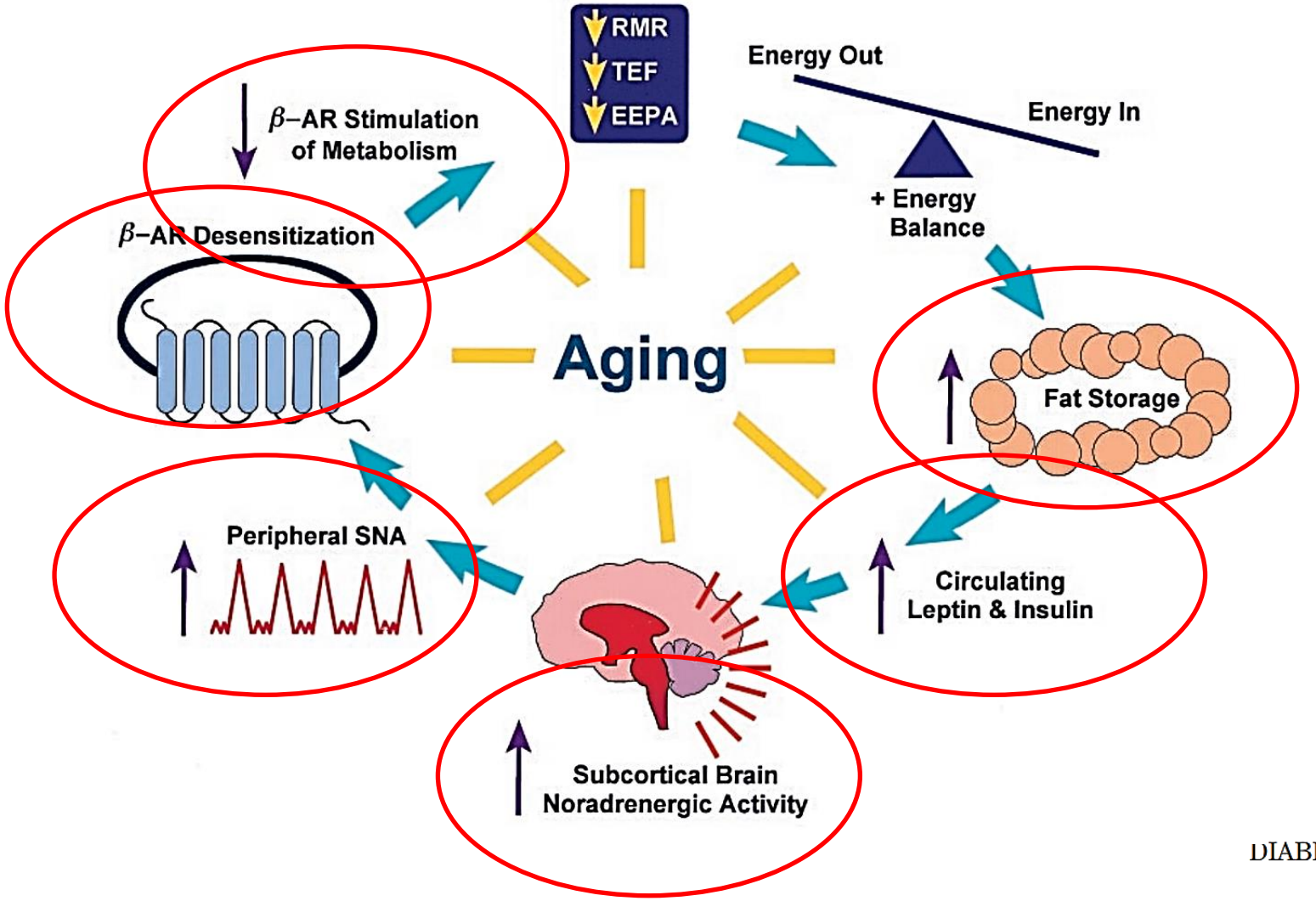
DIABETES, VOL. 53, FEBRUARY 2004

Chronic Sympathetic Activation

Consequence and Cause of Age-Associated Obesity?

Douglas R. Seals and Christopher Bell

resting metabolic rate (RMR), thermic effect of food (TEF), physical activity–related energy expenditure (EEPA)



DIABETES, VOL. 53, FEBRUARY 2004

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Geriatr Gerontol Int 2010

Disregolazione autonomica e Fragilità ?

Research Agenda for Frailty in Older Adults: Toward a Better Understanding of Physiology and Etiology: Summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults

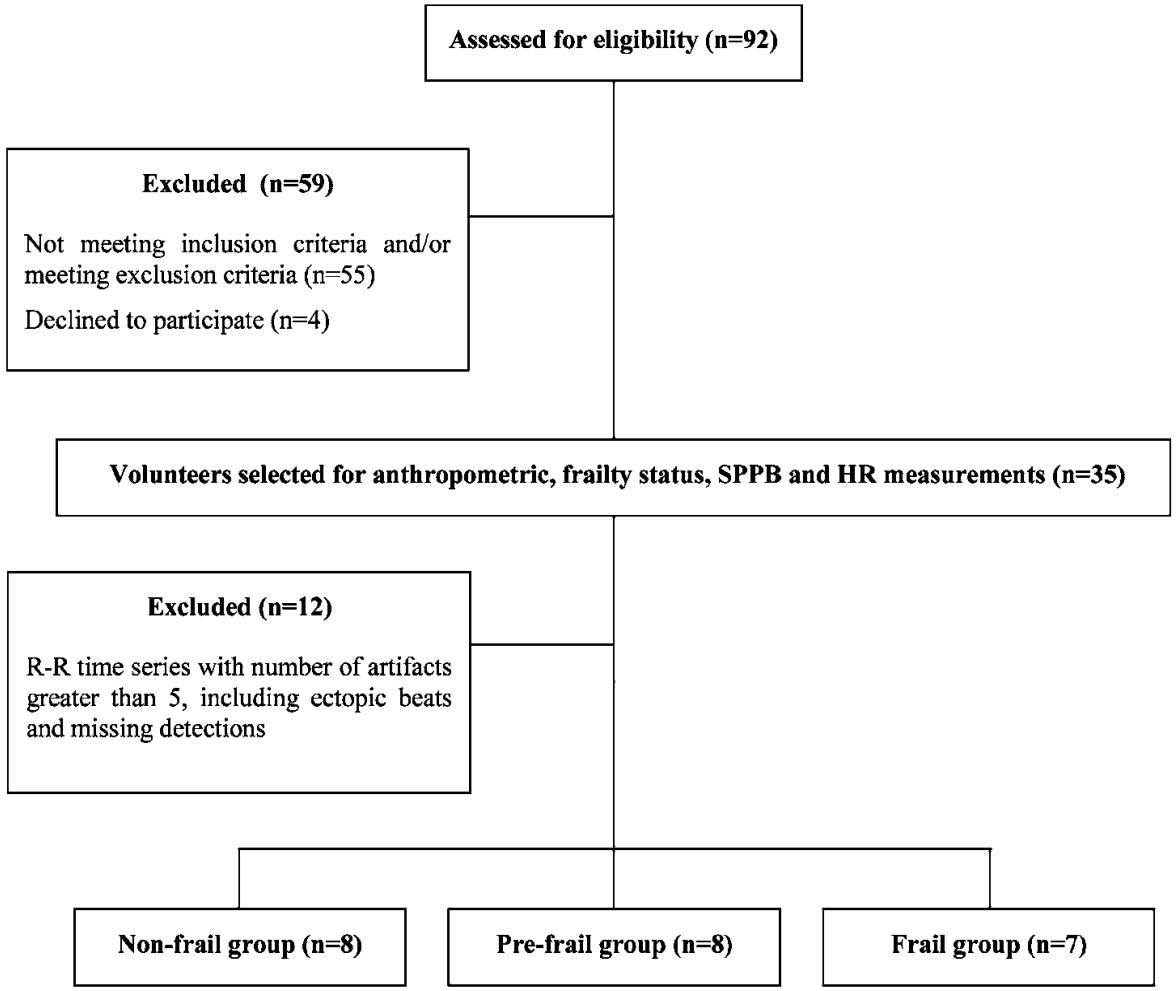
Jeremy Walston, MD,[*] Evan C. Hadley, MD,[†] Luigi Ferrucci, MD, PhD,[†] Jack M. Guralnik, MD, PhD,[†] Anne B. Newman, MD, MPH,[‡] Stephanie A. Studenski, MD, MPH,[§‖] William B. Ershler, MD,[¶] Tamara Harris, MD,[†] and Linda P. Fried, MD, MPH[*]

- Frailty is a geriatric syndrome characterized by reduced functional reserve and high vulnerability to health adverse outcomes.
- An increased vulnerability to stressors indicates an imbalance in multiple physiological systems, leading to a loss of homeostasis and ability to respond to internal and external stressors.

J Am Geriatr Soc 54:991– 1001, 2006.

Cardiac autonomic modulation in non-frail, pre-frail and frail elderly women: a pilot study

Pedro Lourenço Katayama · Daniel Penteado Martins Dias · Luiz Eduardo Virgilio Silva · Jair Sindra Virtuoso-Junior · Moacir Marocolo



	Non-frail group (n=8)	Pre-frail group (n=8)	Frail group (n=7)
Age (years)	70.0 ± 2.2	67.0 ± 2.1	73.0 ± 3.5

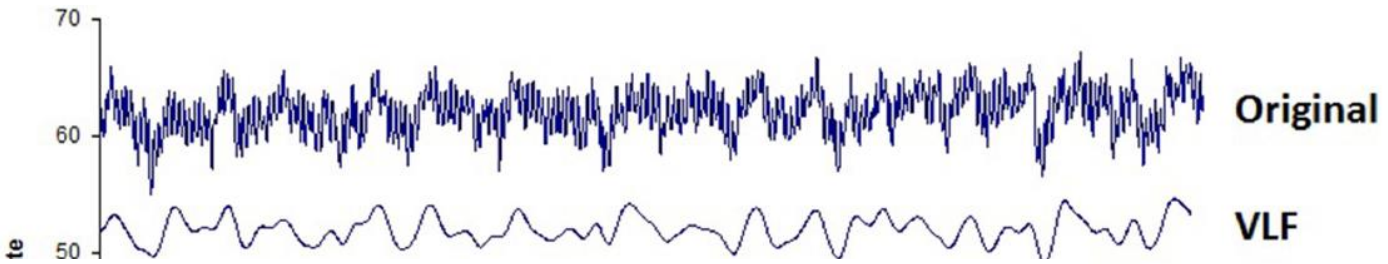
Aging Clin Exp Res (2015) 27:621–629

frontiers in
PSYCHOLOGY

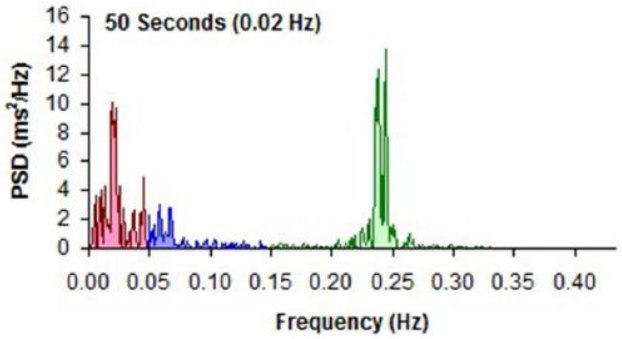
REVIEW ARTICLE
published: 30 September 2014
doi: 10.3389/fpsyg.2014.01040

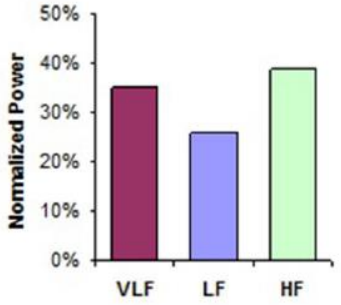
A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability

Fred Shaffer[1], Rollin McCraty[2] and Christopher L. Zerr[1]*



For example, we now know that the normal resting sinus rhythm of the heart is highly irregular during steady-state conditions rather than being monotonously regular, which was the widespread notion for many years. *A healthy heart is not a metronome.*





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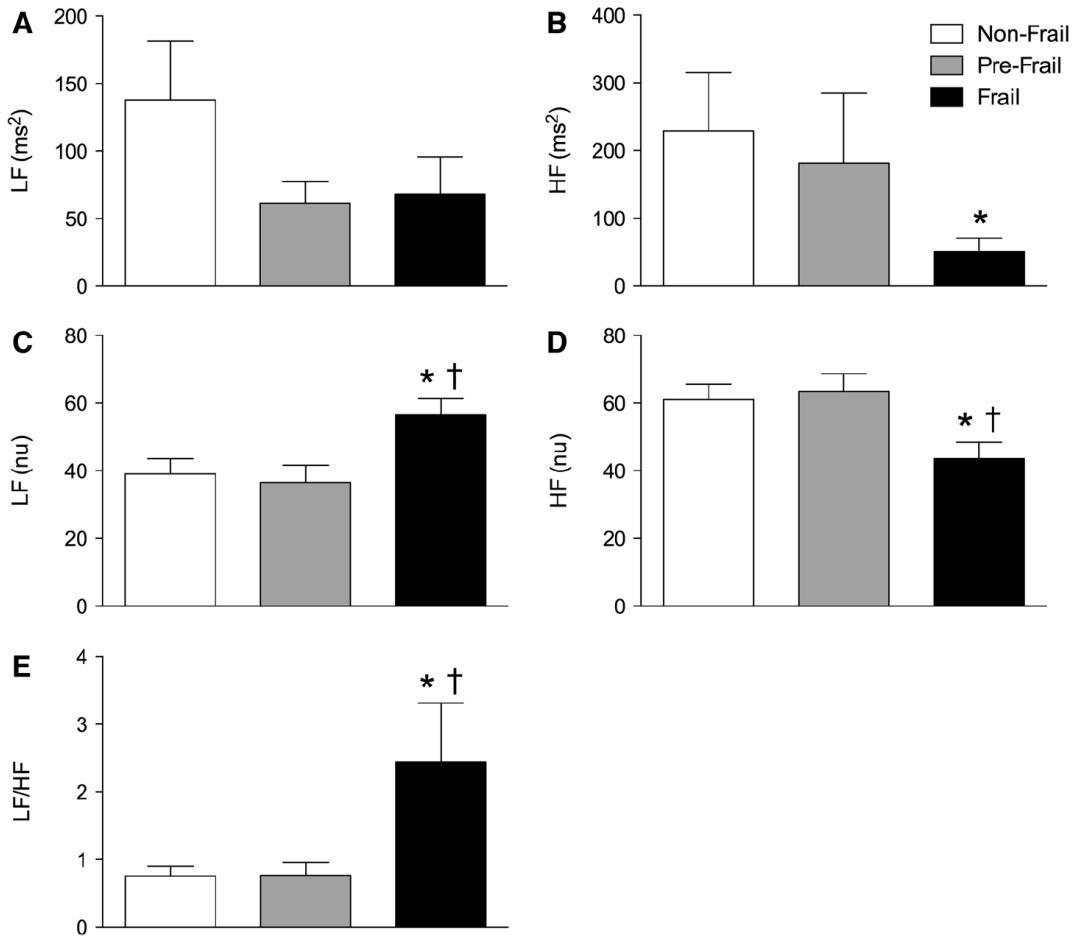


The main findings were that frail group showed decreased power in HF band (absolute values) in comparison to non-frail group.

Frail group presented increased power of the LF band (normalized units) of the cardiac interval spectrum and increased LF/HF ratio as compared to non-frail and pre-frail groups.

Frail elderly women showed a higher sympathetic and lower parasympathetic cardiac modulation in comparison with pre-frail and non-frail elderly women.

Aging Clin Exp Res (2015) 27:621–629

Regulation of Cardiac Autonomic Nervous System Control across Frailty Status: A Systematic Review

Gerontology. 2015

Mean values of heart rate and heart rate variability parameters for different frailty categories. Summary of findings are presented for studies that do not provide quantitative values.

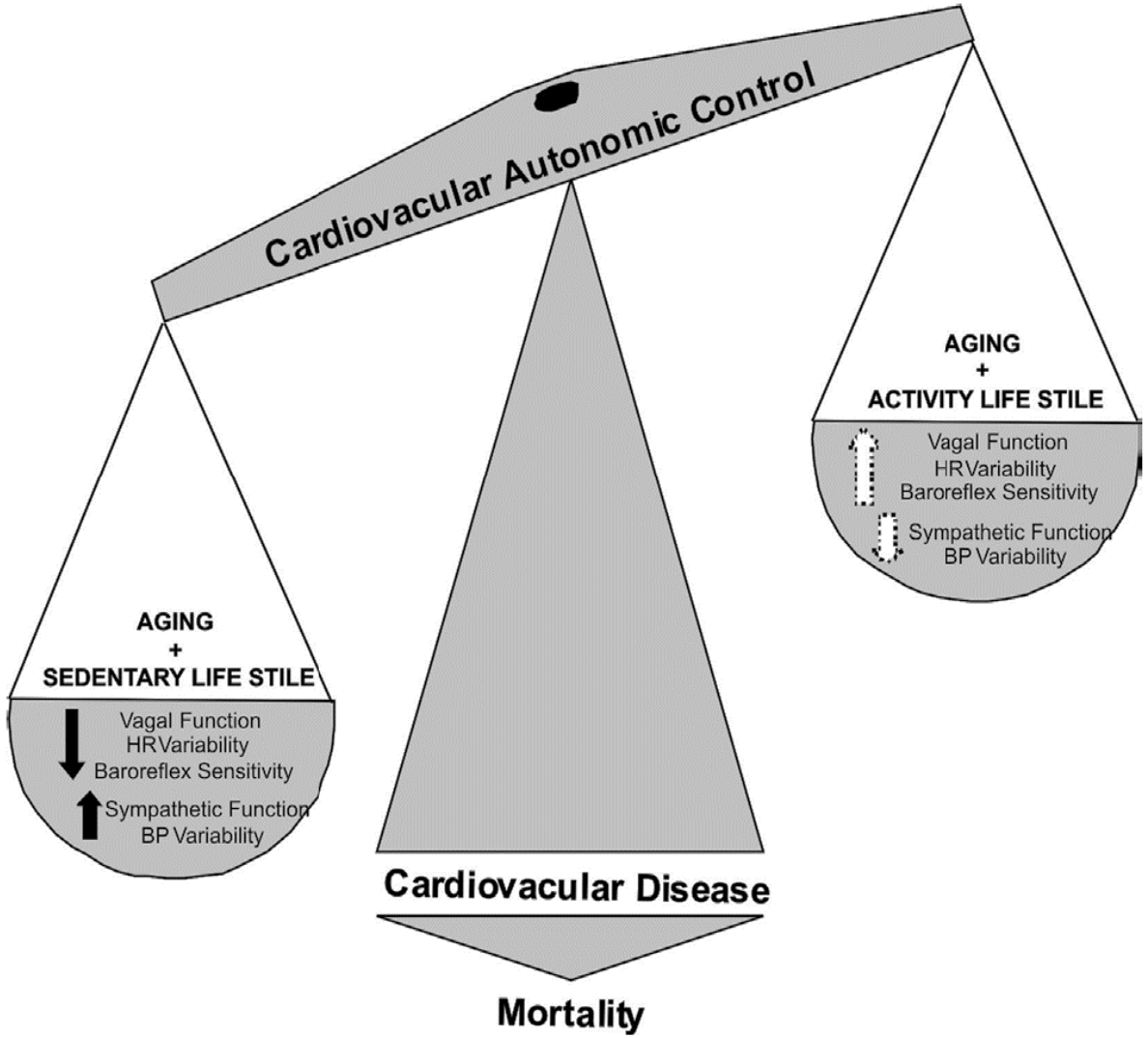
Reference	Parameters and Results
Chaves et al. 2008	- Median $ApEn_{HR}$ was lower in frail compared to non-frail (P-value=0.03). - Analysis of HRV revealed that a lower SDNN, SDANN, TP, pVLF, pLF and LF/HF were associated with a higher probability of frailty (P-value<0.05). However, no significant association was observed for RMSSD and pHF.
Varadhan et al. 2009	- Second principal component (PC2) used for aggregation of recorded traditional HRV measures was the best predictor of Frailty (P-value<10^{-5}). - PC2 can capture the long-range correlation in heartbeat fluctuations across frequency bands (VLF to HF). - pVLF, pLF, SDNN, LF/HF and PC2 had a significant and negative association with frailty (P-value<0.05).

The current systematic review provides evidence of cardiac autonomic nervous impairments in frail compared to non-frail older adults. This impairment is characterized by a reduction in complexity of heart rate dynamics, reduction in heart rate variability, or impaired heart rate response to daily physical activities.

	CI (stand)	0.67±0.08	0.69±0.12	0.73±0.08	>0.05, n.s
	$ApEn_{HR}$ (supine)	3.90±0.48	3.86±0.46	4.07±0.33	<0.05 *, ↑ in frail
	$ApEn_{HR}$ (stand)	3.55±0.58	3.58±0.67	3.93±0.46	<0.05, ↑ in frail
Katayama et al. 2015	- Non-significant higher mean RR (lower mean HR) observed in non-frail compared to pre-frail and frail in supine position. - A non-significant trend to lower HRV captured by SDNN and RMSSD in frail group compared to pre-frail and frail. Reduction in SDNN and RMSSD in frail group can be an indicator of reduced global HRV and decrease in parasympathetic activity, respectively. - Frail group showed a significant decrease in pHF compared to non-frail group (P-value<0.05) which is an indicator of reduction in activity of parasympathetic nervous system. - Frail group presented significant increase in pLF and LF/HF as compared to the other groups (P-value<0.05). - Regarding non-linear methods, symbolic analysis revealed that frail group had a significant lower incidence of patterns in 2LV family compared to non-frail group (P-value<0.05). This suggests that parasympathetic activity is decreased in frail as compared to non-frail. - A non-significant trend towards a lower SE in pre-frail and frail groups compared to non-frail group was observed. It suggests that frailty is linked to lower physiological complexity.				

…quale intervento?

A BRIEF REVIEW OF CHRONIC EXERCISE INTERVENTION TO PREVENT AUTONOMIC NERVOUS SYSTEM CHANGES DURING THE AGING PROCESS



Aging combined with a sedentary lifestyle is associated with changes in the autonomic nervous system's control of the cardiovascular system.

Autonomic changes involve decreases in vagal function, HR variability and baroreflex sensitivity, as well as increased sympathetic function and BP variability. These changes are associated with high rates of cardiovascular disease and mortality.

Chronic exercise prevents these autonomic changes and reduces the rates of cardiovascular disease and mortality as they relate to aging.

Wichi RB et al. Clinics 2009

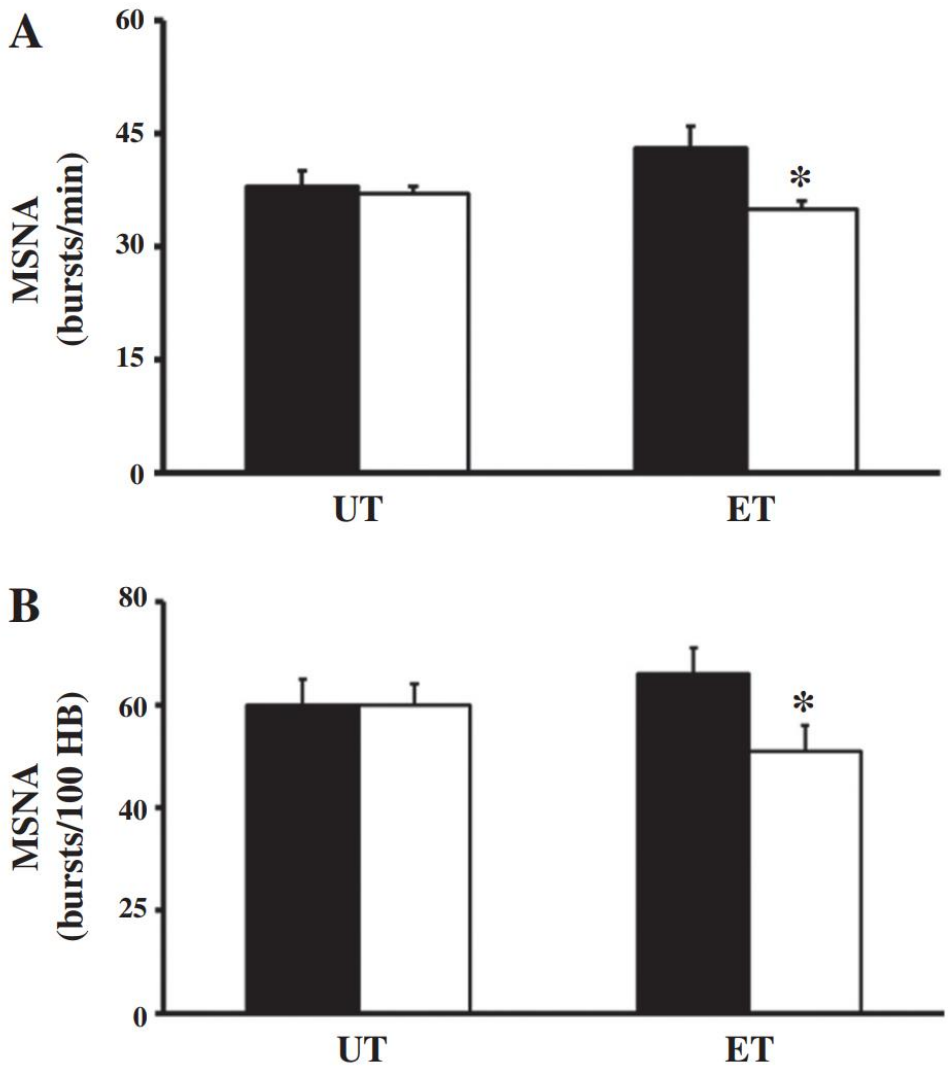
Exercise training-induced modification in autonomic nervous system: An update for cardiac patients

Besnier F. et al. Annals of Physical and Rehabilitation Medicine 2017

References	No. of patients	Training protocol	MSNA basal values	MSNA post-training values
CHF patients				
Antunes-Correa, 2012	52	4 months 3 × 60 min/week Stretching Cycling Strengthening Intensity: anaerobic threshold up to 10% below the respiratory compensation point	43–50 bursts/min according to the group with no difference between them	In trained groups: 27–29 bursts/min ($p < 0.001$) Unchanged in untrained groups No age effect ($p = 0.69$)
Antunes-Correa, 2010	40		43–50 bursts/min according to the group with no difference between them	In trained groups: 30 bursts/min ($p < 0.001$) Unchanged in untrained groups No gender effect
			40–50 bursts/min	In reply to: trained groups ~30 bursts/min ($p < 0.001$) Unchanged in untrained groups HF trained group did not differ from trained healthy control group after training
Fraga, 2007	27		45 bursts/min	In trained group: 35 bursts/min ($p = 0.001$) Unchanged in untrained groups
Mello Franco, 2006	29		43–45 bursts/min	In trained group: 35 bursts/min ($p = 0.007$) Unchanged in untrained groups
Post-ACS patients				
Martinez, 2011	28	6 months/3 × 60 min/week Stretching/cycling/strengthening/anaerobic threshold	42–45 bursts/min	In trained group: ~20 bursts/min ($p < 0.001$) (similar to healthy control group) Unchanged in untrained groups

regular ET can normalize the basal overactivation of the sympathetic nerve

Exercise training prevents the deterioration in the arterial baroreflex control of sympathetic nerve activity in chronic heart failure patients

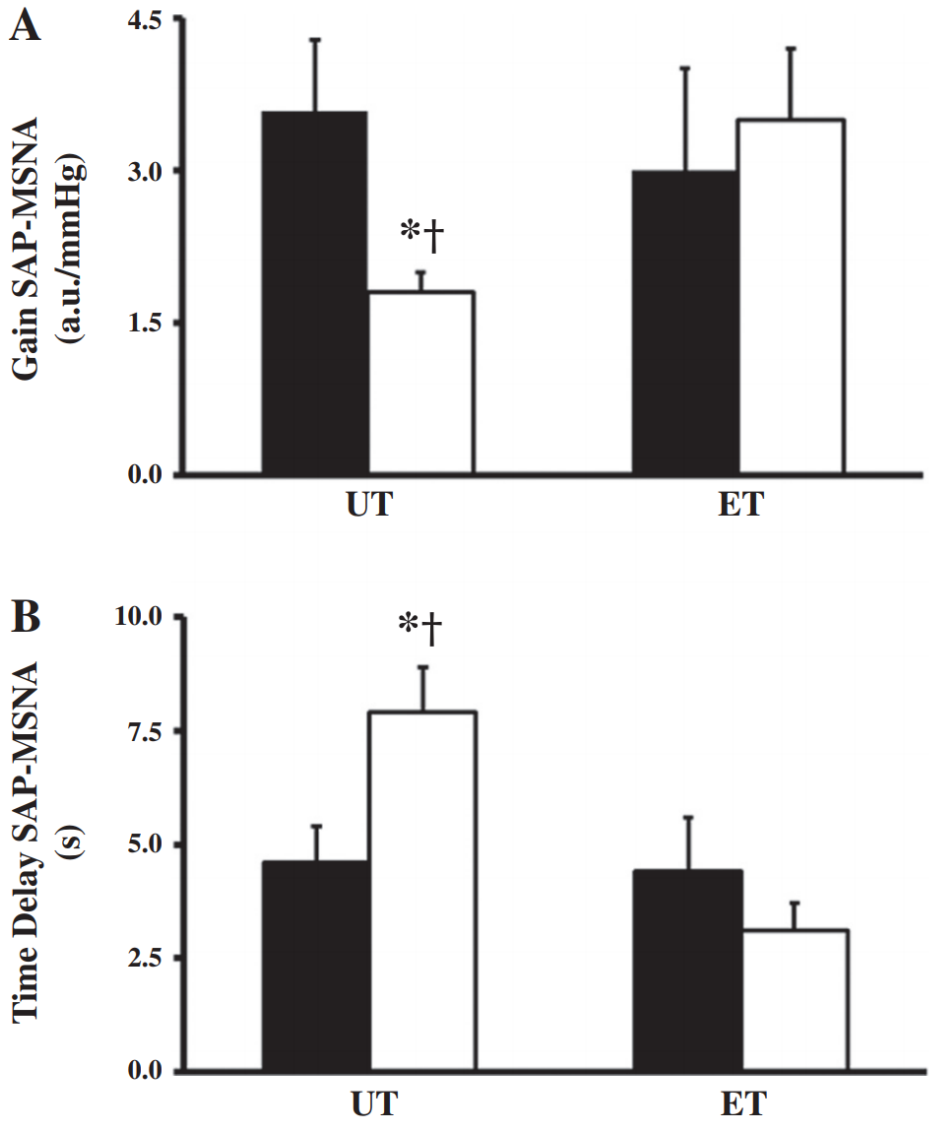


Resting muscle sympathetic nerve activity (MSNA) frequency (A) and incidence (B) before and after 4 mo follow-up in untrained (UT) and exercise trained (ET) chronic heart failure patients

Exercise training markedly decreased MSNA frequency and incidence, whereas clinical follow-up alone unchanged MSNA

Groehs R.V et al, Am J Physiol Heart Circ Physiol 2015

Exercise training prevents the deterioration in the arterial baroreflex control of sympathetic nerve activity in chronic heart failure patients



Arterial baroreflex control of muscle sympathetic nerve activity (ABRMSNA) in untrained (UT) and exercise-trained (ET) chronic heart failure patients

The gain (A) and time delay (response; B) of the arterial baroreflex control were unchanged in ET patients.

In the UT patients, the gain of the arterial baroreflex control was significantly reduced, whereas the time delay (response) of the arterial baroreflex control was significantly increased.

Groehs R.V et al, Am J Physiol Heart Circ Physiol 2015

Changes of plasma norepinephrine and serum N-terminal pro-brain natriuretic peptide after exercise training predict survival in patients with heart failure

Giuseppe Rengo [a,b,1], Gennaro Pagano [b,1], Valentina Parisi [b,1], Grazia Daniela Femminella [b,1], Claudio de Lucia [b,1], Daniela Liccardo [b,1], Alessandro Cannavo [b,c,1], Carmela Zincarelli [a,1], Klara Komici [b,1], Stefania Paolillo [d,1], Flavia Fusco [d,1], Walter J. Koch [c,1], Pasquale Perrone Filardi [d,1], Nicola Ferrara [a,b,1], Dario Leosco [b,*,1]

Changes in clinical, functional, and neurohormonal parameters after exercise training.

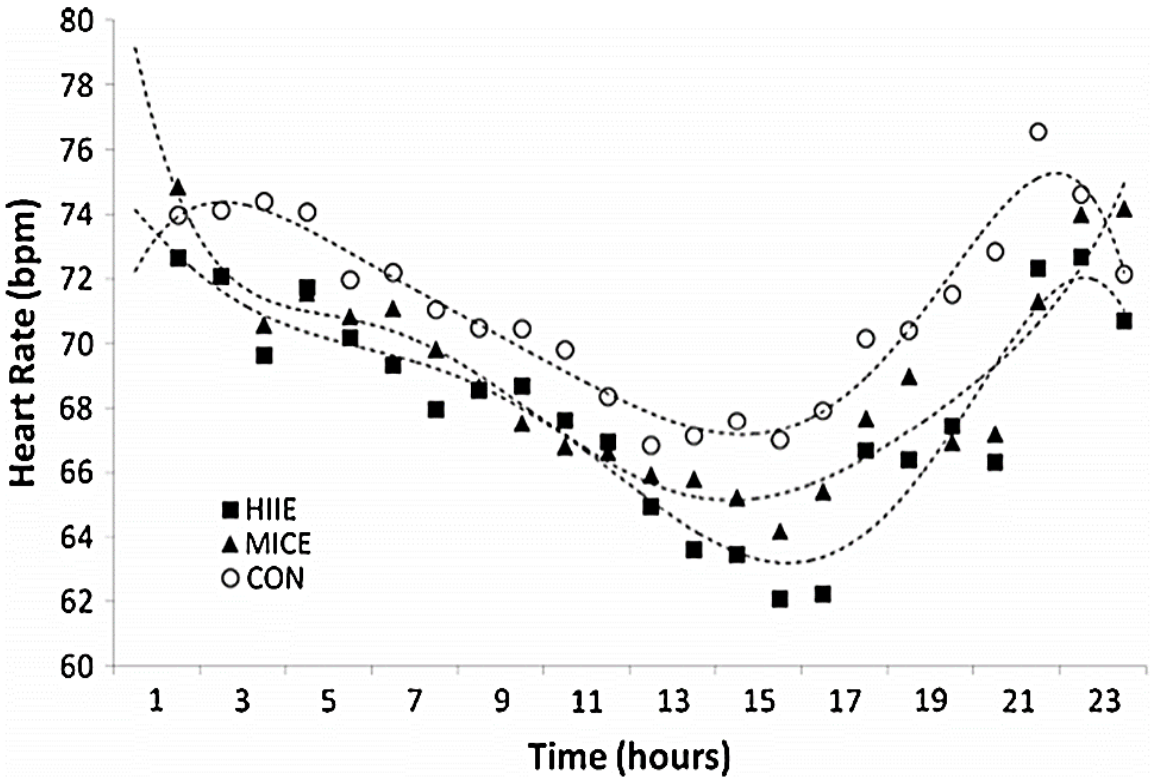
	Baseline	Post-training	p value
LVEF, %	32.5 ± 10.4	33.5 ± 10.5	<0.0001
Peak VO2, ml/min	12.36 ± 1.5	13.5 ± 1.94	<0.0001
HR, bpm	83.6 ± 24.5	69.2 ± 16.5	<0.0001
NT-proBNP, pg/ml	2111.4 ± 1145.6	1532 ± 851.5	<0.0001
Norepinephrine, pg/ml	641.8 ± 215.3	577.8 ± 266.6	<0.0001

Training significantly improved peak VO2 and LVEF, whereas NE, NT-proBNP, heart rate decreased after training

International Journal of Cardiology 171 (2014) 384–389

High-Intensity Interval Exercise Improves Vagal Tone and Decreases Arrhythmias in Chronic Heart Failure

THIBAUT GUIRAUD[1,2], MARC LABRUNEE[1,3,4], KEVIN GAUCHER-CAZALIS[1], FABIEN DESPAS[1,3,5], PHILIPPE MEYER[6], LAURENT BOSQUET[7], CELINE GALES[1], ANGELICA VACCARO[1], MARC BOUSQUET[2], MICHEL GALINIER[1,3], JEAN-MICHEL SÉNARD[1,3,5], and ATUL PATHAK[1,3,5]

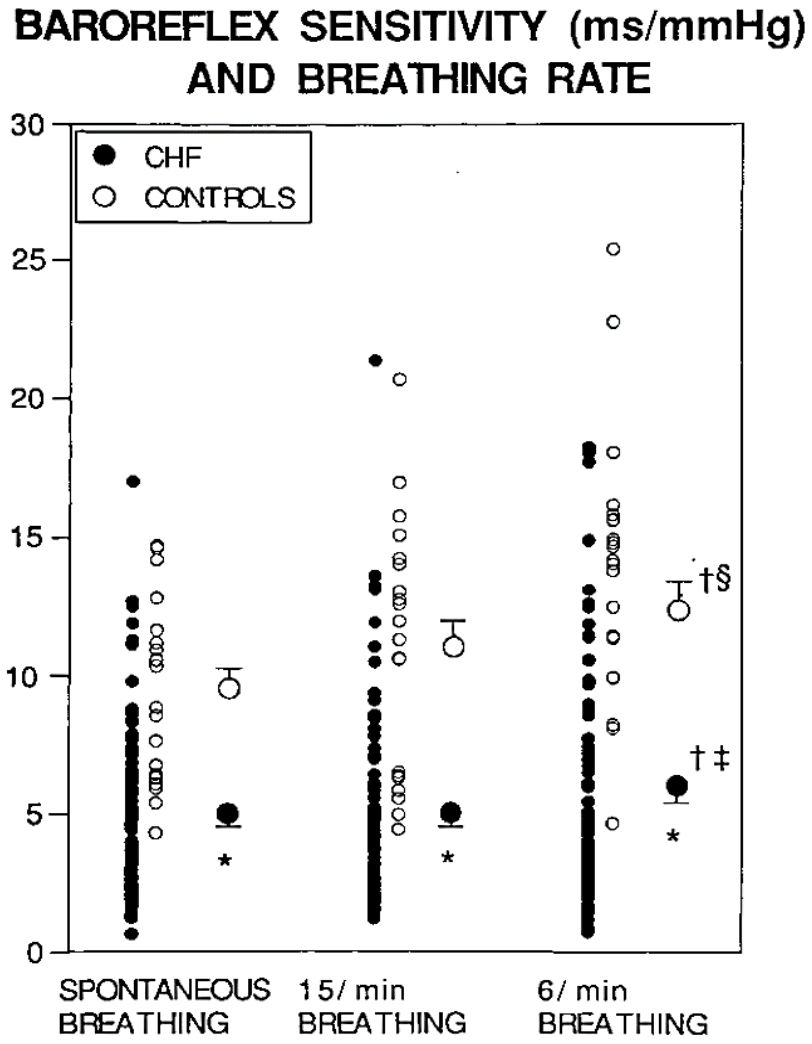


HIIE is safe and beneficial through an increase of the parasympathetic tone associated with a decrease in HR.

Med. Sci. Sports Exerc. 2013

Slow Breathing Increases Arterial Baroreflex Sensitivity in Patients With Chronic Heart Failure

Luciano Bernardi, MD; Cesare Porta, MD; Lucia Spicuzza, MD; Jerzy Bellwon, MD;
Giammario Spadacini, MD; Axel W. Frey, MD; Leata Y.C. Yeung, MD; John E. Sanderson, MD;
Roberto Pedretti, MD; Roberto Tramarin, MD



Breathing at 6 breaths/min, compared with spontaneous breathing, slightly increased overall spontaneous fluctuations in RR interval, reduced fluctuations in blood pressure, and significantly increased the baroreflex sensitivity in both CHF patients and controls.

Circulation. 2002

93 anni, meccanico di bici ancora in servizio

Grazie per l'attenzione