

# CIRC and the “new” Translational and Epigenetic Medicine

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# DISCLOSURE

- ⦿ **Consultant to Medi**
- ⦿ **No Medi interference on the material presented here**

# CIRC

## Center of Interdisciplinary Research on Compression

An independent research institute for compression therapy, among other companies supported by Medi, in order to develop new therapy concepts, to design clinical trials and studies, as well as to research on compression on an international cooperation basis

# CIRC is moving...

- CIRC 2020 in Moscow
- Website implementation:  
<https://www.circ-research.com/circ/>
- Calendar of phlebology, lymphology, ....  
(compression-including) events
- Newsletter
- Multi-center CIRC-endorsed research projects
- Youtube channel («Living veins and lymphatics»?)
- YOUR INPUTS MOST WELCOME !!!

# What we can address

- \* Pathophysiology of disorders that may be improved by compression
- \* Main mechanisms of action of compression
- \* Possible innovations in Compression Therapy

The main intention of CIRCC is to bring together experts who are able and willing to contribute to this scientific pathway

- **Science is provisional and we are by no means anywhere near the point of knowing all**
- **Science is a constantly changing base of knowledge**
- **We know about 4% of our reality and of science about health and diseases**

- **Lee Know «Mitochondria: the future of Medicine: The Key to Understanding Disease, Chronic Illness, Aging, and Life Itself “, 2018**

# **Translational medicine**

**“an interdisciplinary branch of the biomedical field supported by three main pillars: benchside, bedside and community”.**

**The goal of TM is to combine disciplines, resources, expertise, and techniques within these pillars to promote enhancements in prevention, diagnosis, and therapies. It is a highly interdisciplinary field which wants to join different biomedical cultures to improve the global healthcare system significantly**

# Epigenetics

“The science of phenotype changes that do not involve alterations in the DNA sequence”. It implies features that are "on top of" or "in addition to" the traditional genetic basis for living organisms.

Epigenetics most often involves changes that affect gene activity and expression, but the term can also be used to describe any heritable phenotypic change.

Such effects on cellular and physiological phenotypic traits result from **external or environmental factors**.

Main mechanisms: DNA methylation, histone modification, microRNA production. Transcription factors are essential to these modifications to silence or activate genes.



# Evaluation of Therapeutic Compression Stockings in the Treatment of Chronic Venous Insufficiency

G.D. MOTYKIE, MD, J.A. CAPRINI, MD, J.I. ARCELUS, MD, PhD,\* J.J. REYNA, MD,\* E. OVEROM, AND D. MOKHTEE

**Table 2.** The Mean Value of Symptom Severity Scores Reported by Patients Initially, and after 1 and 16 Months of Treatment with Compression Stockings

	<i>Initial</i>	<i>One Month*</i>	<i>16 Months**</i>
Swelling	2.45 (1.25)	1.47 (0.83)	1.13 (0.51)
Pain	2.94 (1.29)	1.77 (1.09)	1.38 (0.69)
Discoloration	2.76 (1.29)	2.23 (1.22)	1.81 (0.99)
Cosmetic problems	3.03 (1.41)	2.50 (1.41)	1.98 (0.99)
Activity tolerance	2.33 (1.35)	1.71 (1.19)	1.38 (0.73)
Depression	1.72 (1.12)	1.42 (0.87)	1.29 (0.81)
Sleep problems	2.00 (1.25)	1.46 (0.99)	1.24 (0.63)

\*p < 0.001 for comparison between initial and 1 month severity scores across all categories.

\*\*p < 0.001 for comparison between 1 and 16 month severity scores across all categories.

Statistical analysis via the Wilcoxon Signed Rank Test.

Numbers in parentheses are SD.

Mediven  
stocking kl II as  
a treatment  
also for PNEI  
and well-  
being....

Epigenetics  
arriving within  
Translational  
medicine...

# **The nature of care in the management of lymphoedema; not without laughter!**

T.Ryan, J of Lymphoedema . Jun2019, Vol. 14(1) 62-63

- ....the application of care to the leg also requires humanity,... sympathy and compassion....
- Contemporary studies of the limbic system of the brain indicate that cheer that includes laughter is probably more desirable than compassion
- In the management of the swollen leg, the nature of care deserves a rethink of how best practice can relieve pain and anxiety by the release of endorphins, or by switching the autonomic nervous system towards the vagal from the sympathetic

# Psychoneuroendocrineimmunology (PNEI) and longevity

Cavezzi Attilio\*, Ambrosini Lorenzo, Quinzi Valentina, Colucci Roberto, Colucci Enza

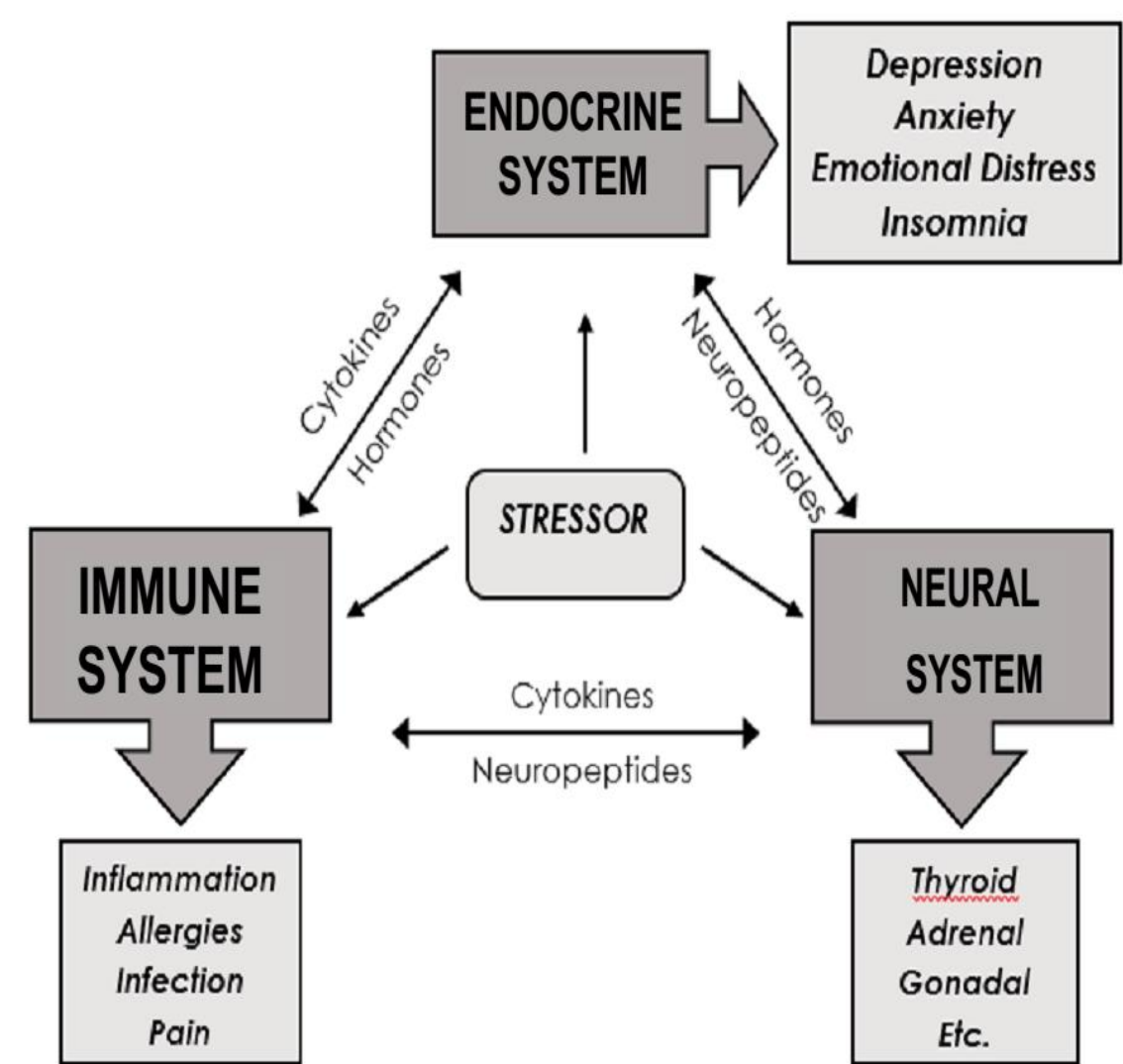
Psychoneuroendocrineimmunology (PNEI) is the science which studies the interactions between psychological, neural, endocrine and immunological processes.

The concept of the PNEI system was developed in the seventies and eighties through the discoveries of the interaction between immune system and molecules with neuroendocrine activity targeting multiple organs; the interdependence between immunological, psychological and neuroendocrine mechanisms has been elucidated through several studies subsequently.

PNEI system is a self-regulation network which is involved in the homeostasis of the organisms, in the maintenance of chemical-physical-neuropsychological balance in response to stimuli of various nature.

The present review provides an overview of the fundamental scientific literature on PNEI and its interaction with chronic low grade cellular inflammation processes and consequently with longevity. Similarly literature data on the strict link between hormetic processes and PNEI system are discussed, with reference to resilience as a key-factor in the natural/pathologic evolution of aging.

**Keywords:** PNEI, Psychoneuroendocrineimmunology, Psychoneuroimmunology, Longevity, Hormesis, Inflammation, Polyphenols



**Figure 1.** PNEI: Interconnections and signaling among psychological, neural, endocrine and immune systems.

**Psychoneuroendocrineimmunology (PNEI)** is the scientific discipline which studies the interactions between mind and body, between psychological, neural, endocrine and immunological processes.



## STRESS

- EARLY LIFE ADVERSITIES
- TRAUMA, ABUSE
- MAJOR LIFE EVENTS

## EPIGENETIC CHANGES IN NEURAL CIRCUITRY AND BRAIN FUNCTION

### STRESS SYSTEM

#### SNS

NORADRENALINE

BRAIN IMMUNE  
CELLS

NFkB

#### HPA

ADRENAL  
GLAND

CORTISOL

### MOOD AND OTHER PSYCHIATRIC DISORDERS

### NEUROPLASTIC CHANGES

- AMYGDALA
- PFC
- OFC
- HIPPOCAMPUS

### BEHAVIOR CHANGES

- DIET
- SMOKING
- SEDENTARY LIFESTYLE
- SOCIAL AVOIDANCE
- DRINKING
- ADDICTION

## BIOLOGICAL SYSTEMS

CIRCULATORY, METABOLIC,  
ENDOCRINE, IMMUNE,  
PERIPHERAL NERVOUS

## ORGANS

HEART, LIVER, GUT,  
GONADS, LUNG.

## TREATMENT

- MIND-BODY THERAPIES
- PSYCHOTHERAPY
- PSYCHOPHARMACOLOGY

### EPIGENETIC REVERSION

HPA

CORTISOL

MOOD  
BALANCE

SNS

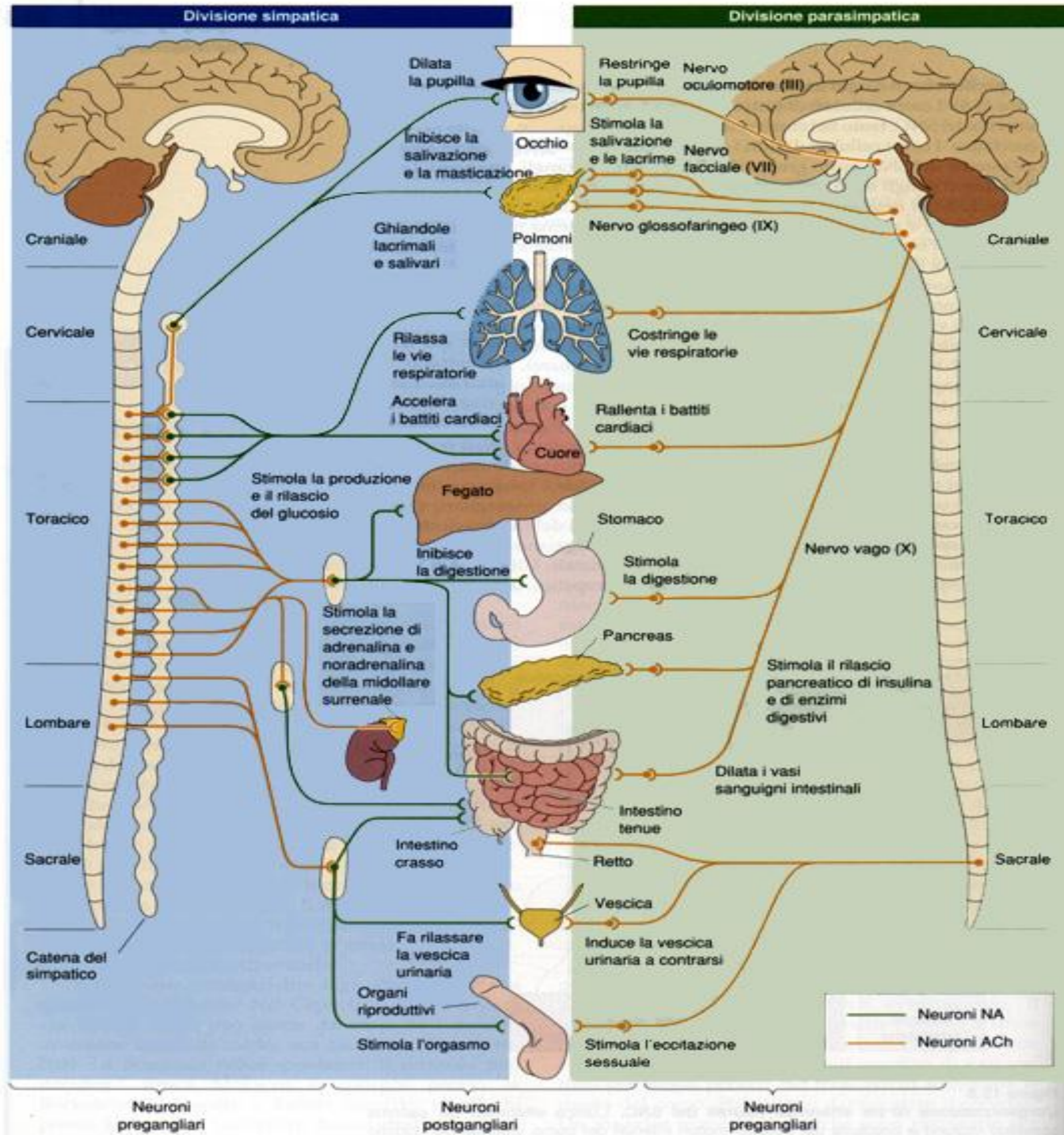
NFkB

IMMUNE  
BALANCE

## RESILIENCE

Bottaccioli AG, Bottaccioli F. & Minelli A. (2018)  
*Annals New York Academy of Sciences*  
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# BASICS FROM SCIENTIFIC RESEARCH ON SKIN STIMULATION

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- **Interoception** (emotional component) is stimulated with **light and slow massage, typical of compression garments** (in absence of pain) on free nerve components of the skin, subcutaneous layers and deeper layers
- **Proprioception** is stimulated with **deeper massages**
- **Tissue inflammation** activates the consequent deposition of the neoconnective, which increases in a vicious circle inflammation, edema and tissue **fibrosis** (reduce hydration of the connective bands). The so called **GENTLE TOUCH (compression treatment a well?)** reduces this pathological process

# BASICS FROM SCIENTIFIC RESEARCH ON SKIN STIMULATION (by means of Compression as well ?)

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## •PATHWAYS OF THE PAIN/COMFORT STIMULATION

- 1) **Local/Mechanical RECEPTOR** component stimulation, due to hyper-activity and release of **inflammatory mediators**; mechanical stimulation desensitizes the receptors which ultimately release fewer mediators and in a lower dose.
- 2) Mechanical stimulation works on **medullary neural information** which travels to the **spine** neural component inducing a feeling of pleasure and helps to reduce the release of inflammatory mediators. (**reflex arch**)
- 3) **From the spine** neural component the impulse ascends **to the central neural system** with greater activation of the parasympathetic system, decreasing the orthosympathetic activity (**GENTLE TOUCH**). This **stimulation of the parasympathetic system** has a notorious anti-inflammatory effect



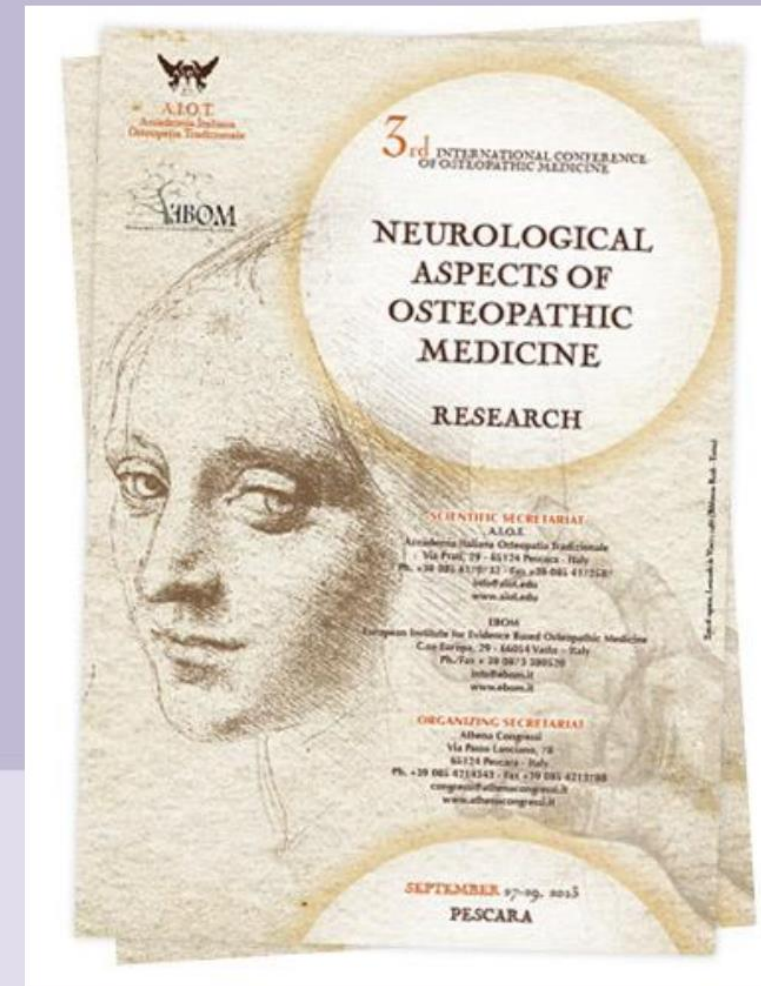
# Touch as an epigenetic stimulus for the central nervous system

Dr Jorge Esteves, PhD, MA, BSc, DO  
British School of Osteopathy

**Can compression therapy exert «the gentle touch»?**



THE BRITISH SCHOOL  
OF OSTEOPATHY







# Heart rate variability: a noninvasive electrocardiographic method to measure the autonomic nervous system

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*Juan Sztajzel*

Cardiology Center and Medical Policlinics, University Hospital, Geneva, Switzerland

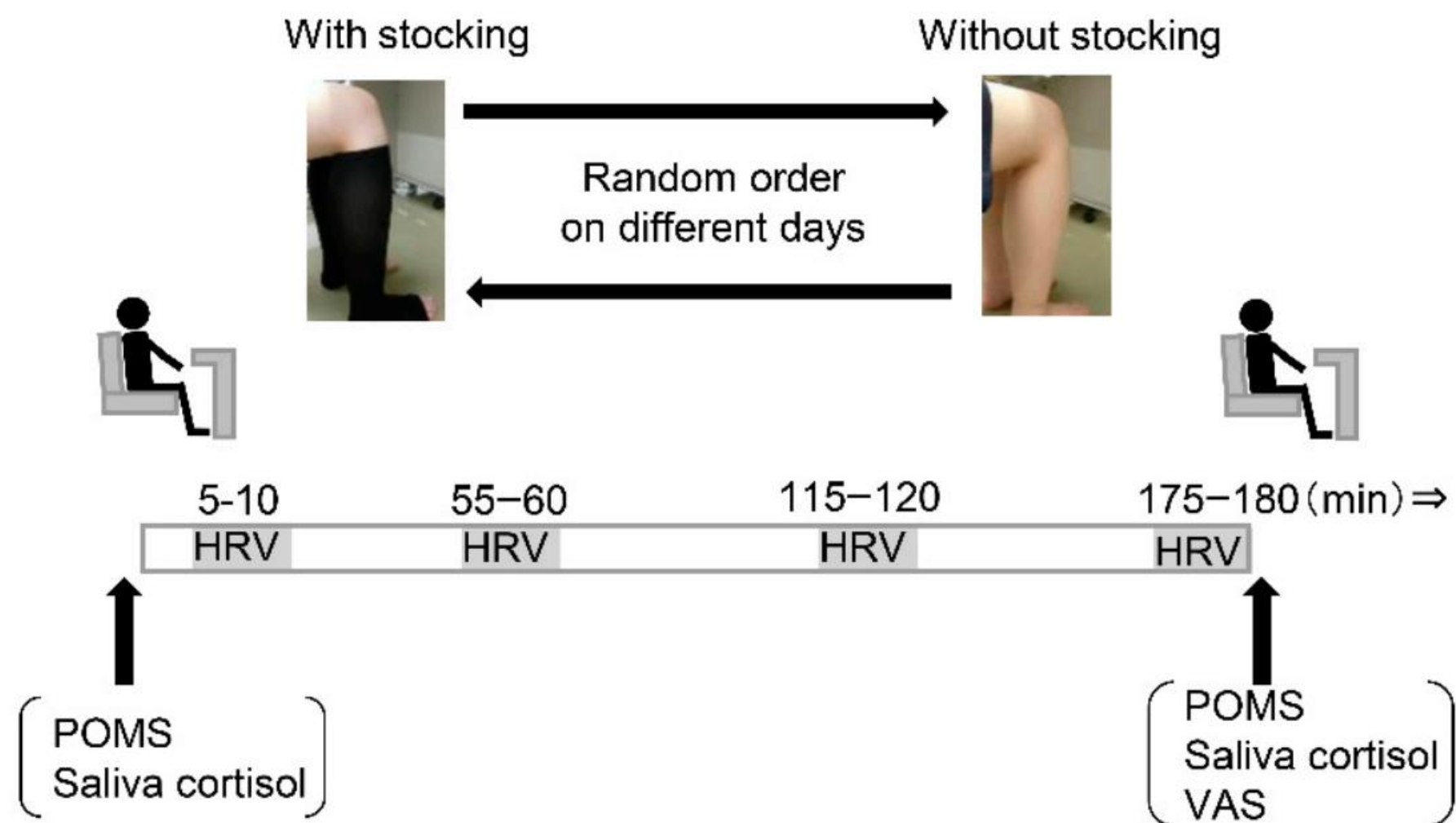
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- The higher the HRV, the better :
- a) the health, the RESILIENCE
- b) the balance between sympathetic and parasympathetic (vagal) system,
- c) the aging,
- d) the cardiovascular and metabolic state
- e) the PNEI

Article

# Impact of Wearing Graduated Compression Stockings on Psychological and Physiological Responses during Prolonged Sitting

Masahiro Horiuchi <sup>1,\*</sup> , Chieko Takiguchi <sup>1</sup>, Yoko Kirihara <sup>1</sup> and Yukari Horiuchi <sup>2</sup>



**Figure 1.** Illustration of experimental procedure. HRV, heart rate variability; POMS, Profile of Mood States; VAS, visual analogue scale.

# RESULTS



- \* Wearing stockings suppressed a subjective uncomfortable sensation (e.g., pain; fatigue; swelling) in the lower limbs,
  - \* Increase in heart rate at 1 h and 3 h was significantly greater without than with stockings.
  - \* An indicator of **parasympathetic nerve activity** showed **higher values with** than without **stockings** throughout the 3 h sitting period
  - \* Changes in saliva **cortisol** were positively associated with higher uncomfortable sensations of **VAS** in the lower limbs
- These findings suggest that **patients wearing graduated compression stockings may benefit from subjective comfort, increased parasympathetic nerve activity and HRV as overall**

# Effects of Skin Pressure from Compression Legwear on Resting Salivary Cortisol and Urinary Catecholamines Excretion in Women

RONG LIU, PhD,\* YI LIN KWOK, PhD,\* AND TERENCE TZU HSI LAO, MBBS, MD<sup>†</sup>

## RESULTS

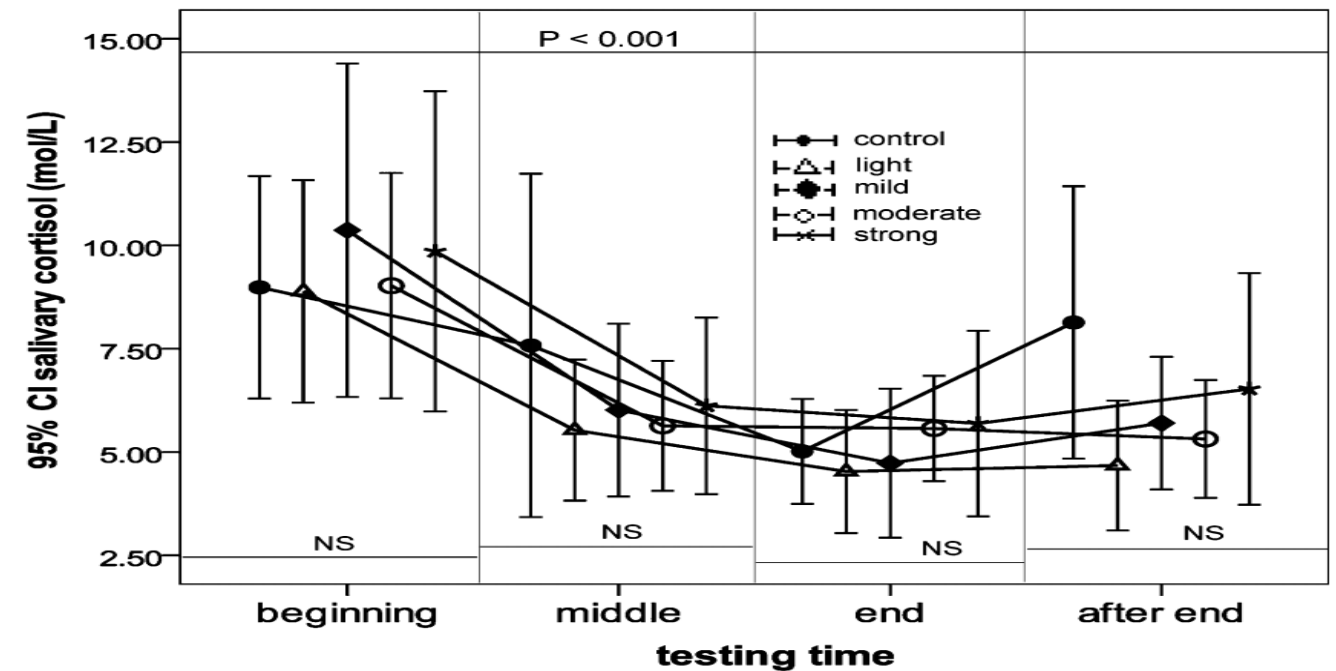
- the secretion of **salivary cortisol** (SSC) showed a **significant decrease** during the 180 minutes of the testing period that was maintained up to 10 minutes after the compression was removed
- **Urinary excretion of adrenaline and noradrenaline decreased with increasing pressure** levels and was lower in response to higher clothing pressure when tested in the afternoon.



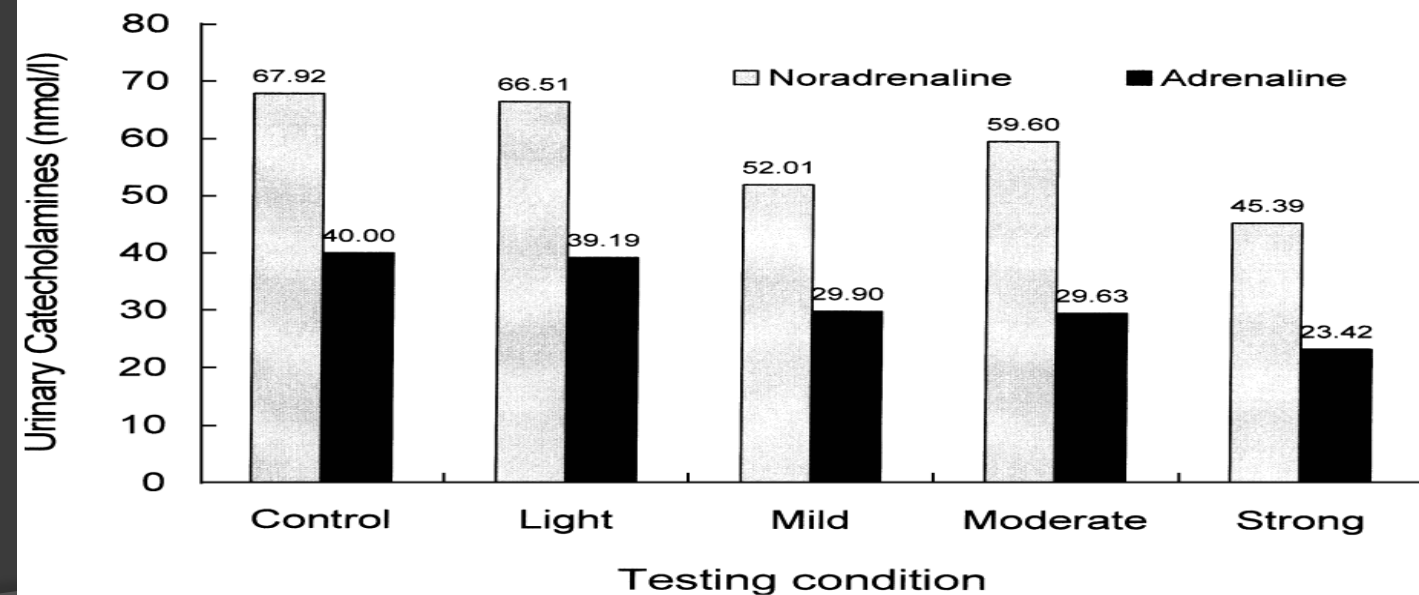
# Effects of Skin Pressure from Compression Legwear on Resting Salivary Cortisol and Urinary Catecholamines Excretion in Women

RONG LIU, PhD,\* YI LIN KWOK, PhD,\* AND TERENCE TZU HSI LAO, MBBS, MD<sup>†</sup>

The higher  
the pressure,  
the higher  
the effect



**Figure 3.** Variation in secretion of salivary cortisol under different pressures with time.



**Figure 4.** Variation in urinary catecholamines (adrenaline and noradrenaline) between different testing conditions.

# Compression and stretch fit garments

12

*A. Yu, K.L. Yick*

The Hong Kong Polytechnic University, Hung Hom, Hong Kong

The dynamic **interactions among the garments, the human body**, and the environment can trigger different sensation receptors, which lead to ... overall **psychophysiological responses** (Guo et al., 2008; Corbera´n et al., 2010; Tanaka et al., 2006; Okura et al., 2000; Lee et al., 2000).

**A whole-body compression sportswear** can help lower the 24-h concentration of creatine kinases and lactate dehydrogenase in the bloodstream, thereby a sign of **enhanced repair** throughout the body **musculature** (Kraemer et al., 2010).

**Pressure on the skin exerted by compression wear can affect physiological parameters in humans, such as heart rate, blood pressure, and levels of urinary catecholamines and cortisol** (Mori et al., 2002; Liu et al., 2012).

## The Impact of Technical Textiles on Health and Wellbeing Current Developments and Future Possibilities

Diane E\*

Faculty of Sports Science, Leisure and Nutrition, Liverpool John Moores University, UK

- The impacts of technical textiles upon society have been influential and as populations continue to age, patient expectations for implant performance will continue to rise
- **Technical textiles have the potential to perform better, last longer and increase comfort in the body**
- This paper examines key areas in which innovation in textile technology is promoting **health and wellbeing.**



RESEARCH

Open Access

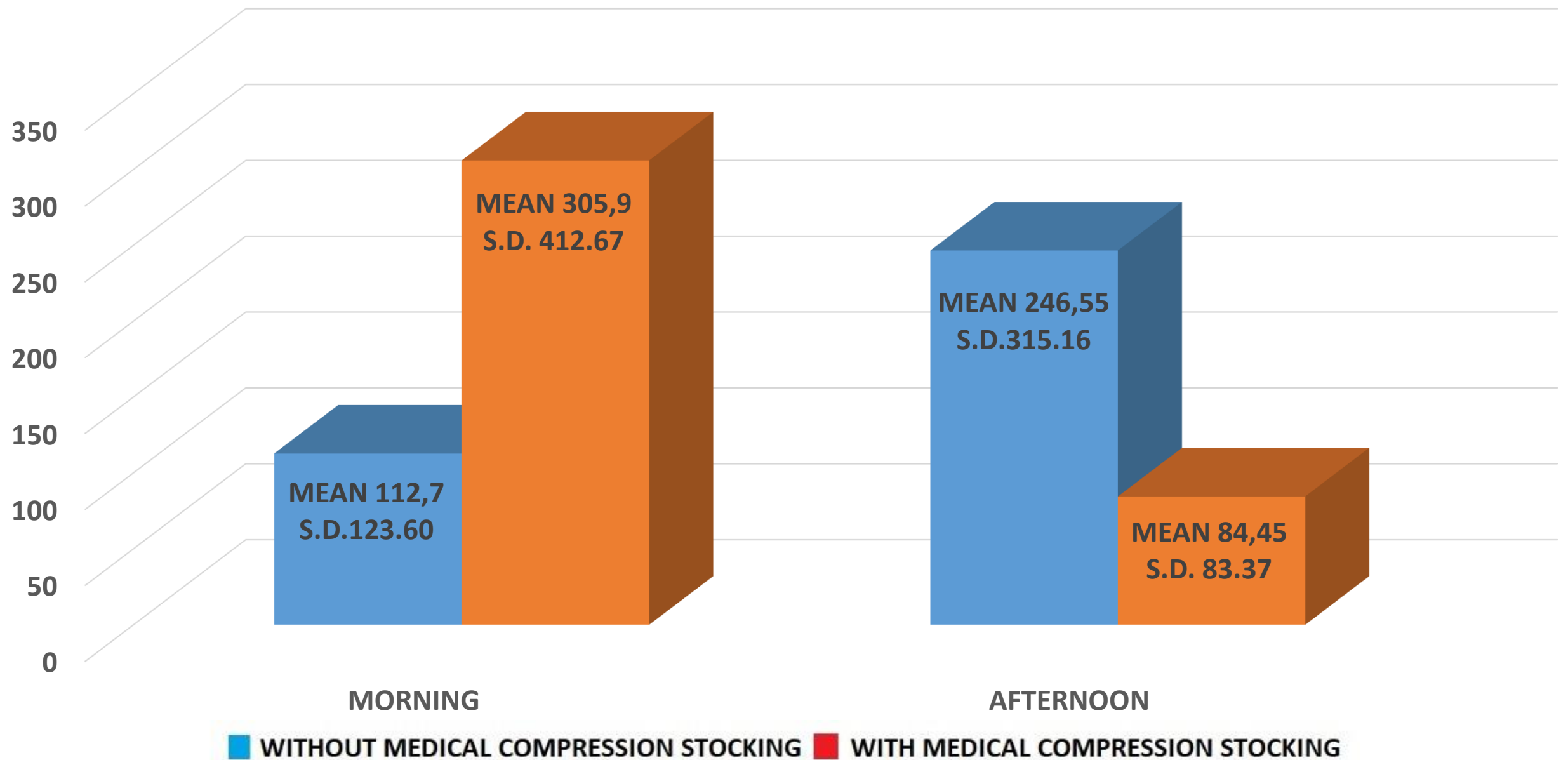


# The relationship between compression garments and electrocardiogram signals during exercise and recovery phase

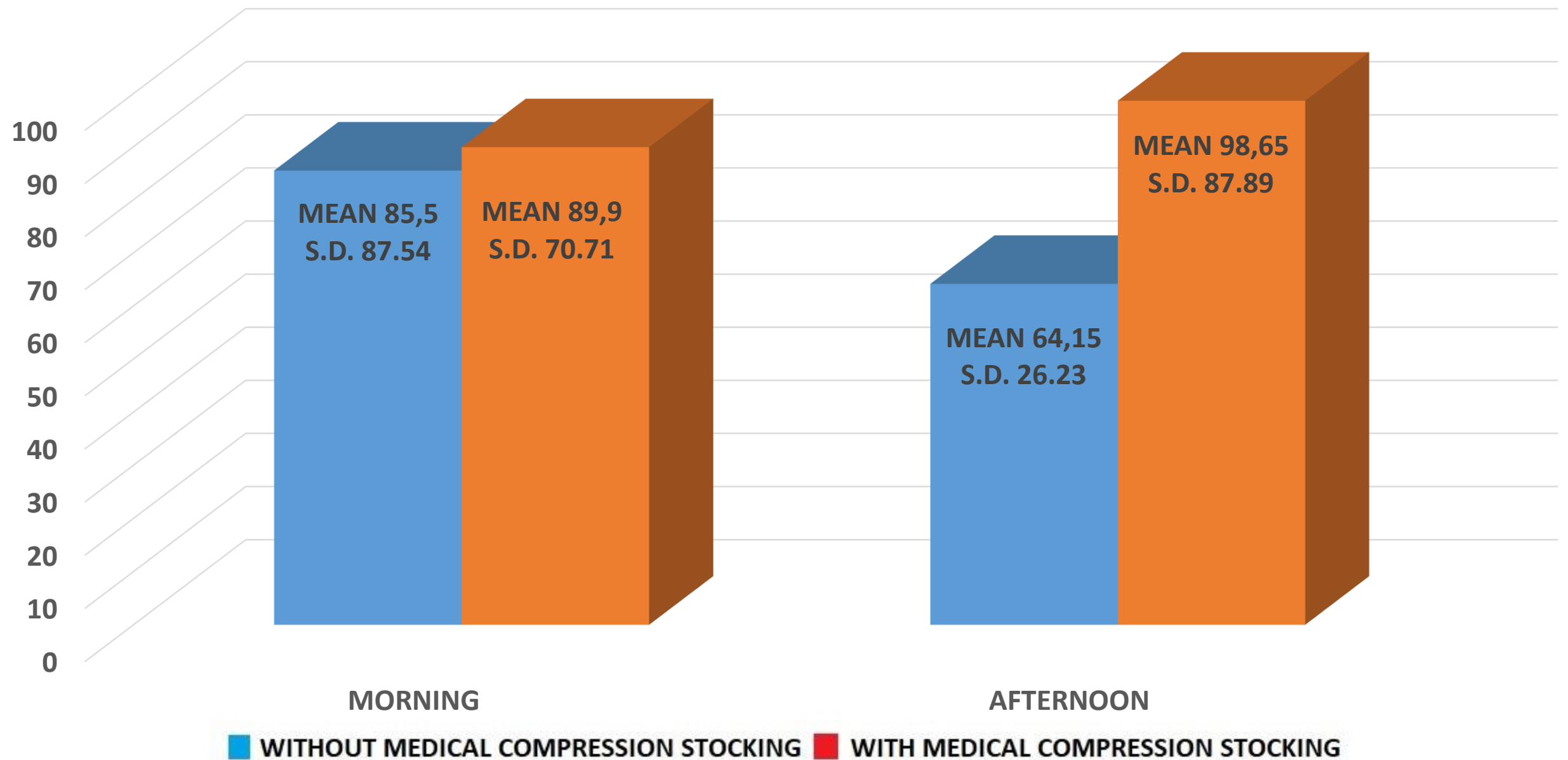
Lan Thi Nhu Nguyen<sup>1</sup> , David Eager<sup>2</sup> and Hung Nguyen<sup>3\*</sup>

- The results demonstrated a significant difference between compression garments and non-compression garments at the end of the tests and from 90 min onwards during the recovery phase ( $p < 0.05$ ).
- Corrected QT (QTc), ST interval and heart rate (HR) indicated the significant difference between NCGs and CGs: **the CG group had a lower HR increase during exercise and a quicker recovery in HR, ST, and QTc after the exercise**

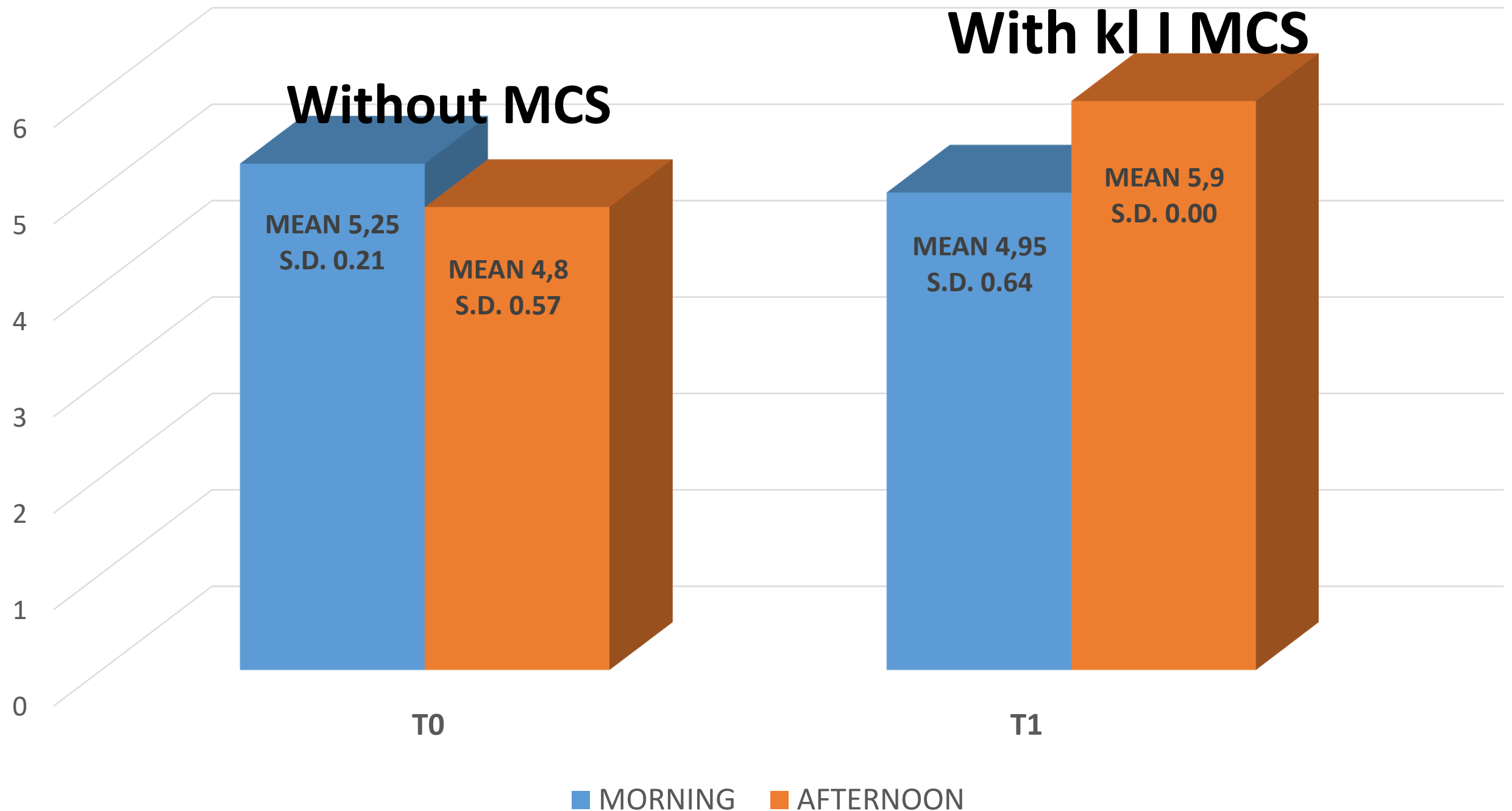
## NORMAL BREATHING 5 MINUTES – LF (barireflex activity, sympathetic mainly)



# NORMAL BREATHING 5 MINUTES – HF (parasympathetic, vagal activity)



## BIOIMPEDANCE - PHASE ANGLE RIGHT LEG



**Phase Angle (depending on reactance mainly, on cell membranes... ) is a reliable index of the overall subject's health**

# Conclusions

- Compression Garments exert a series of actions from the mechanical, biochemical, psychological point of view
- HRV and Bioimpedance Spectroscopy variations confirm the interaction between MCS in the lower limbs and edema/PNEI/well-being
- Further clinical studies may highlight this relationship better
- Possible new models of MCS, devices, or garments may target the overall PNEI/well-being condition

**Thank you**

**Grazie**

**Gracias**

**Merci**

**Obrigado**

**Dziękuję**

**Благодаря**

**谢谢**

**Bedankt**

**Hvala**

**Tak**

**Vd'aka**

**Teşekkürler**

**ありがとうございました**

