

# Modifications of Activity of Autonomic Nervous System, and Resting Energy Expenditure in Women Using Hormone-Replacement Therapy

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## Abstract

Menopause is a significant period characterized by physiological change. Hormonal changes are largely related to estrogen depletion and subsequent cessation of ovarian function. This study analyzed vegetative modulation, expressed as heart rate variability (HRV) power spectral analysis, resting energy expenditure, and body composition in women in post-menopause with and without hormone-replacement therapy (HRT). 87 Sedentary women were enrolled, 41 (age: 53-54) women with BMI of  $21.6 \pm 2.6$  kg/m<sup>2</sup> were on HRT and 46 (age: 52-63) with BMI of  $22.4 \pm 1.8$  kg/m<sup>2</sup> were not. This experiment marks aspects regarding the relationship between the autonomic nervous system and body weight in HRT and menopause.

**Keywords:** Autonomic nervous system; Resting energy expenditure; Menopause

## Introduction

Menopause is a significant period characterized by important physiological changes. Hormonal changes are largely related to estrogen depletion and subsequent cessation of ovarian function [1-4].

Many women that enter menopause are worried about weight gain and for this reason assume hormone-replacement therapy (HRT) to be a causal factor. Evidence from cross-sectional studies suggests that declines in resting metabolic rate and physical activity may be accelerated in the postmenopausal years [5-8]. An acceleration in the loss of fat-free mass and increased central adiposity may indicate a worsening cardiovascular risk profile [9-12].

Many women are worried about weight gain and the use of HRT is often assumed to be a causal factor. With longer term use (1 year), Reubinoff et al. [13] found a similar increase in body weight and fat mass among women taking HRT and those who declined its use [14-17]. They observed that there was a significant shift from gynoid to android fat distribution in women not taking HRT but not in those women taking the treatment.

Resting energy expenditure (REE) accounts for 60-75% of total daily energy expenditure and decreases with age and physical inactivity. It is well known that fat-free mass (FFM) accounts for the majority of inter-individual variability in REE [18-21], but other physiological factors

also have a role, such as sympathetic nervous system (SNS) activity and endocrine status [22-25].

The SNS is an important control mechanisms for the body [26-29]. The SNS shows physiological fluctuations with age which are related also to differences in the REE [1,30-33].

The aim of this study was to determine whether healthy, not obese, menopausal women submitted to a long-term HRT treatment (>2 year) had changed of the REE and autonomic asset respect at not obese menopausal women.

## Methods

87 Sedentary women were enrolled at the Clinical Dietetic Service of the Second University of Naples, Italy; 41 (age: 53-54) women with BMI of  $21.6 \pm 2.6$  kg/m<sup>2</sup> were on HRT and 46 (age: 52-63) with BMI of  $22.4 \pm 1.8$  kg/m<sup>2</sup> were not taking HRT.

Informed consent was provided by all participants, they had to be healthy and meet the following inclusion criteria: no serious physical incapacity; not smoker; moderate drinker; stable weight during the preceding 6 months;  $20 < \text{BMI} < 24.9$  kg/m<sup>2</sup>; no medications, or nutritional supplements that could influence metabolism or autonomic functions, with the exception of HRT, vitamins, and minerals; absence of menses for the preceding 12 months at least. At the time of the study, women were on HRT since at least 2 years (group 1) or were not on HRT. HRT treatment consisted of estrogen 0.625 mg/day plus progesterone 2.5 mg/day).

Autonomic nervous system was measured by the HRV-power spectrum that was evaluated on a 5-min long ECG recording. The R-R-intervals sequence was re-sampled to obtain a constant-time based signal (10 samples/sec). The Fast Fourier Transform was applied to this signal and visualized in the form of power spectrum. The absolute values of this spectrum were summed in the low frequency (0.04-0.15 Hz; LF), and high frequency (0.15-0.40; HF) range. LF, HF were the values used to estimate the sympathetic and parasympathetic activity [34].

REE was measured by breath-by-breath respiratory gas exchange with an indirect calorimetric device (V Max 29, Sensor Medics, USA).

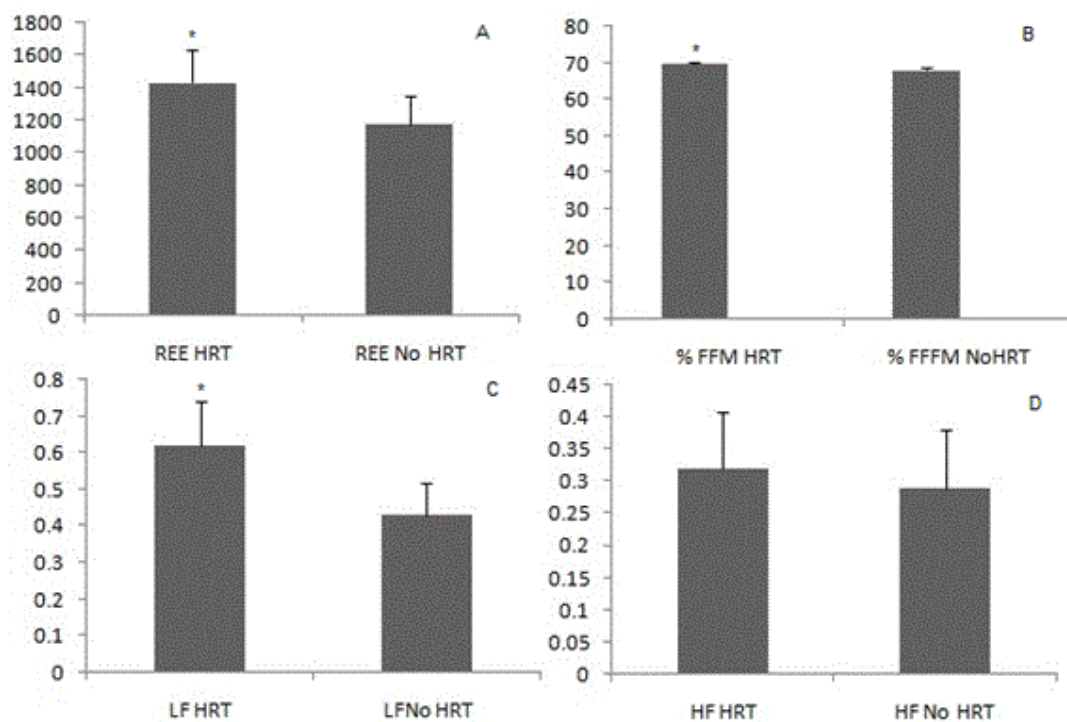
Body composition was calculated by bioelectric impedance (Akern BIA-101, Italy).

The R Project for Statistical Computing software (version 3.1.0) was used for statistical analyses. Means and SD were calculated for each of

the analyzed variables and statistical significance was set at  $p < 0.05$ . The Shapiro-Wilk test was used to verify the normal distribution of variables.

## Results

Figure 1a shows that the REE of HRT-treated women was higher than that of non HRT-treated women ( $p < 0.01$ ). Figure 1b shows that FFM of HRT-treated women were higher than that of non HRT-treated women. Menopause induced a decrease in percentage of the FFM in subjects not HRT ( $p < 0.01$ ). Figure 1c reports the values of LF in HRT and HRT not women. LF values of menopause women are lower than values of HRT women. The menopause induced a same decrease in LF values in HRT not but not in subjects HRT ( $p < 0.01$ ). Figure 1d reports the values of HF in HRT and HRT not women. HF values of menopause women are similar than values of HRT women ( $p = 0.16$ ).



**Figure 1:** Means  $\pm$  Standard Error of hormone-replacement therapy (HRT) women and not HRT women: a. Resting energy expenditure (Kcal/day); b. Free fat mass (%); c. Low Frequency ( $\text{sec}^2/\text{Hz}$ ) of HRV-power spectrum; d. High Frequency of HRV-power spectrum (\* $p < 0.01$ ).

## Discussion

The present experiment demonstrated a modification of vegetative modulation in HRT-treated women with an increase of the sympathetic component [35-38], which is an important factor in maintaining the highest REE in women in HRT compared to women in menopause [39-41].

In this experiment, the autonomic activity of menopausal women was lower than that of HRT subject [42-44].

The age-related decline in the vegetative control can be an important factor in the reduction of resting energy expenditure in both

groups. Indeed, it has been shown that the lack of sex hormones due to menopause reduces resting energy expenditure in young healthy women, through a reduction of the autonomic nervous activity [24,40,45].

The originality of this experiment is to emphasize the changes in sympathetic activity induced by HRT and on the relationship between the sympathetic nervous system and REE [46,47].

Other literature data have demonstrated a significant influence of the sympathetic activity on eating behavior also through an increase in thermogenesis [12,35,48].

The results of this experiment are consistent with the hypothesis that a reduction in the autonomic activity could play a determinant role producing an excess in food intake relative to the energy expenditure and resulting in weight gain in menopausal women [49-52]. It emphasizes aspects about the complex relationship between the autonomic nervous system and body weight in HRT and menopause. These results could be useful in the explanation of the pathologic mechanisms of feminine obesity.

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