34th Annual International Conference of the IEEE EMBS
San Diego, California USA, 28 August - 1 September, 2012

Negative Effects of Obesity Analyzed through Bioimpedance, Indirect Calorimetry, the Sympathovagal Index and the Orthoclinostatic Test*

Miguel Cadena, Joaquín Azpiroz, Fabiola Martínez, Gisella Borja, Norma Ramos, Consuelo Velázquez, Magdalena Rodríguez and Rafael Díaz

Abstract— **Early analysis of the negative effects of obesity is important to prevent the development of chronic diseases related to this condition. There is a need to monitor these effects through simple instrumentation that measures fat-free mass (FFM) catabolism. Obesity leads to a decrease in the FFM energy expenditure and to an increase in the autonomic nervous system (ANS) activity. Thus, the measurement of FFM dynamic catabolism can provide information regarding the effects of obesity. The hypothesis is that this increased ANS activity produces an increase of energy expenditure of carbohydrates and fats when the subjects are under stress; in this case after an 8-hour fast and while they are undergoing an orthoclinostatic test. A pilot study was conducted on 29 volunteers, 16 women and 13 men. The results show significant statistical differences ($p<0.1$) in fat and carbohydrate utilization during the orthoclinostatic tests: A move from the clinostatic to the orthostatic positions produced the following: Fat metabolism varied from 97.2 to 105.9 gr/day of fat for women and 24.9 to 35.7 gr/day of fat for men; carbohydrate metabolism changed from 38 to 39 gr/day for women and 239 to 277 gr/day for men; FFM averages were 47 Kg for women and 57.6 Kg for men; changes in the sympathovagal index (SVI) averages were 0.4 to 1.8 for women and 0.8 to 2.7 for men. The conclusions show that the methodology's sensitivity is such that gender differences can be used as a model to prove FFM metabolic differences. We believe that further studies will lead to the development of a robust methodology for the early detection of the negative effects of obesity .**

I. INTRODUCTION

The public health, governmental and private institutions that are interested in curtailing the global obesity epidemic and its associated diseases (hypertension, cardiac disease, diabetes, etc.) must consider preventive methods that have the capability to quantify the early physiological negative effects of obesity. For instance, obesity produced by human genes and by the obesogenic environment of modern industrialized societies should be measured with simple non-invasive instruments, preferably using physiological maneuvers, which are fast and easy to implement [1].

One obstacle to develop a model for the negative effects of obesity is the fact that a specific etiology for obesity does not exist. There are several points of view that are currently being debated and can be summarized through two main questions: Is obesity more genetic than environmental in nature? Or is it caused by changes in our lifestyle, including our diet and physical activity, or both? Controversial studies are being published constantly in the scientific literature on the etiology of obesity, but solutions to prevent this global epidemic have rarely been proposed [2-3].

One problem is that instruments and techniques that address the issue of medical prevention do not yet exist. For instance, the importance of employing instruments that correlate body composition metabolism with the autonomous nervous system (ANS) activity have been underestimated. Most of the literature presents fat tissue models as sealed ring cells with a thin layer of cytoplasm surrounding a large fat droplet, while in fact this thin layer of cytoplasm is actually a highly complex endocrine, inflammatory, and metabolic tissue, which regulates the storage and breakdown of fat. This tissue plays an important role in the body composition and the inflammatory response and its effects should be monitored by instruments that are capable to measure the non-fat tissue metabolic energy expenditure [4].

We believe that that a comprehensive view of the negative effects of obesity can be obtained by a simple on-line instrument combining measurement of the energy expenditure, body composition and the ANS activity. The aim is to be able to classify different subtypes of obesity and excess weight more specifically, and to use this classification in order to develop different approaches to weight management and to the prevention of chronic diseases. For instance, sarcopenic obesity effects raise challenging issues related to the use of diet and exercise strategies [5]

Questions remain in the sense of: how is it possible to measure the benefit of such approaches at an affordable cost-benefit? It is important to avoid high price technology like the medical imaging techniques and to promote the widespread use of simple instrumentation not yet in the market.

Body composition analysis (BCA) is important to determine the negative effects of obesity once it is considered to be a physiological and pathological process on

*Research supported by Instituto de Ciencia y Tecnología del DDF (ICYT) México, under project number PICSA11-75.

M. Cadena, J. Azpiroz and F. Martínez are with Universidad Autónoma Metropolitana-Iztapalapa at the Research Center on Instrumentation and Medical Imaging, EE Department, México City, 09340, Phone: +52-55-8502-4569, (e-mail: mcm@xanum.uam.mx).

G. Borja is with the Bioingenieering Center, Universidad Autónoma del Caribe, Barranquilla, Colombia.

N. Ramos, C. Velázquez, M. Rodríguez and Rafael Díaz are with Universidad Autónoma Metropolitana-Xochimilco D.C.B.S./D.A.S at the Research Unit on Energy Expenditure and Body Composition, México City.

body morphology and structure of tissues and organs [6]. Similarly, indirect calorimetry is essential not only to estimate the energy balance and substrate utilization at rest (REE) but also as a means to dynamically compute the energy requirements of the main organs (heart, lung, liver, kidney and brain) and muscles when the human body is under the consequences of obesity.

The dynamic energy expenditure changes of the fat-free mass should consider that 70% of the REE is consumed by the main organs, which only represent 7% of the actual body weight (ABW), while fat, muscle and other body parts represent 21%, 32%, and 40% of the ABW, respectively [6].

The human body can be modeled by two compartments: fat-free mass (FFM) and fat mass (FM), where the former has different energy expenditure behavior and neural control which is dependent on an increase or decrease of the fat mass [7].

Another technique to study the negative effects of obesity is through the ANS activity, using the heart rate variability (HRV) which is a technique that has already proved its power as it associates an increased sympathetic activity to a reduction of the vagal tone in subjects with obesity [ref]. Therefore, subjects with higher FM increase carbohydrate utilization, sympathetic activity and energy expenditure, even when they have fasted for 8 hours and are undergoing an orthoclinostatic maneuver [10].

The hypothesis is that body composition analysis combined with the energy expenditure and heart rate variability measurements can reveal the decrease of the FFM metabolism when there is an increase of the fat mass due to obesity or simple excess weight. The idea is to measure the FFM metabolism's changes, which are more evident in subjects stimulated with the orthoclinostatic test.

This paper presents a preliminary study where this methodology was applied to a population of volunteer subjects. The BCA plus the REE and the HRV measurements were carried out in order to estimate gender differences in metabolism as a means to prove that the methodology is sensitive enough to be able to detect FFM metabolic differences.

II. Methodology

A. The Model

The negative effects of obesity were summarized in three parts as a manner to create a 3D-cube geometrical figure (see Fig. 3). The three magnitudes on the sides of the triangle are difference between women and men's metabolic parameters. The first side corresponds to the FFM difference. The second side corresponds to the difference between the EE minus the REE. The third side of the cube corresponds to the differences in the SVI. Two cubes with different volumes "A" and "B" represent differences between populations since catabolic activity is different for both populations.

B. Experimental Design

REE, EE , bioimpedance and HRV measurements were carried out in a student volunteer population of 32 subjects (14 women and 16 men) with ages between 20 and 40 years. The subjects were selected using BMI greater than 18 and less than 40 (Kg/m^2), without chronic diseases or metabolic disorders, and with a sedentary life style. Subjects were in an 8-hour fasting condition when this experiment was conducted during morning hours at 2400 meters above sea level (Mexico City) with an ambient temperature between 20 and 23 ºC.

The experiment started with a glucose measurement to assure absence of possible diabetes. The subjects were placed in supine (clinostatic) position with a half mask with 22 mm of tubing connected to the input of an indirect calorimeter for the measurement of expired gases in order to estimate the REE. Subjects were asked to stay quiet for 5 minutes before gas collections started. This phase lasted for about 15 minutes to assure steady state conditions for measurements. Then subjects went to the orthostatic position while holding 3 Kg hand weights in each hand. This measurement phase was performed for 15 minutes, three minutes after the subjects were placed in the orthostatic position.

C. Rejection criteria

Rejection criteria were flu, fever, academic stress (exams), or women during their menstrual period. Subjects with consumption of any type of medical prescription, alcohol, coffee or tea during the last 12 hours before the experiment commences were also rejected as were subjects showing glucose measurements above 115 mg/dL or symptoms of intolerance to the orthoclinostatic test like dizziness or temporary fainting or those unable to support the 3 Kg hand weights during the test. Finally, subjects with variation coefficients (VC) greater than 10% of the V_{O_2} and V_{CO_2} for REE calculation were rejected since a lack of physiological steady-state was assumed.

D. Instrumentation

The following equipment was employed:

- Research Indirect Calorimeter (Utah Medical Products Inc, model MGM-2) with mixing chamber.
- Bioimpedance measurement system (Inbody 720, Biospace Inc.) with weight scale included.
- HRV measurement system (Megaoyi Inc.).
- Commercial glucometer (Medisense Inc).

E. Data Analysis

The experimental group of 53 subjects was divided into two: one for male and another for female subjects for statistical analysis. The groups were further refined by their variation coefficients: Subjects with VC>10% in the clinostatic and VC>20% in the orthostatic positions were rejected. This criterion assured different levels of physiological stationariety so that differences in the HRV

and the REE vs EE could be tested using the t-student test with statistical significance at $p<0.1$

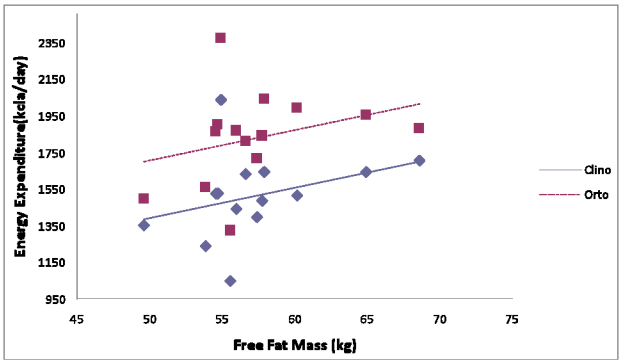
III. RESULTS

Table I shows the demographic data for the groups of subjects.

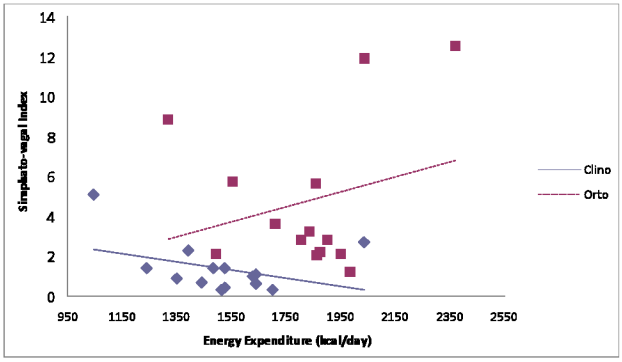
TABLE I
demographic data

	8 hours of fasting		
	Males n =13	Females n = 16	p
Age (Years)	25.8 ± 3.20	22.1 ± 1.89	$p < 0.1$
ABW (Kg)	74.3 ± 5.98	59.9 ± 8.02	$p < 0.1$
Size (meters)	1.8 ± 0.06	1.6 ± 0.08	$p < 0.1$
BMI (Kg/m^2)	24.0 ± 2.01	23.1 ± 1.48	0.35
Glucose (mg/dl)	97 ± 13.64	96.5 ± 5.78	0.93
Fasting time (min)	748.0 ± 135.17	747.6 ± 118.80	1.00

ABW: Actual Body Weight, BMI: Body Mass Index



(a)

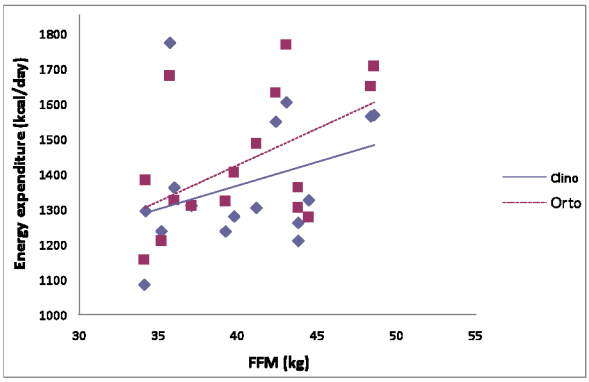


(b)

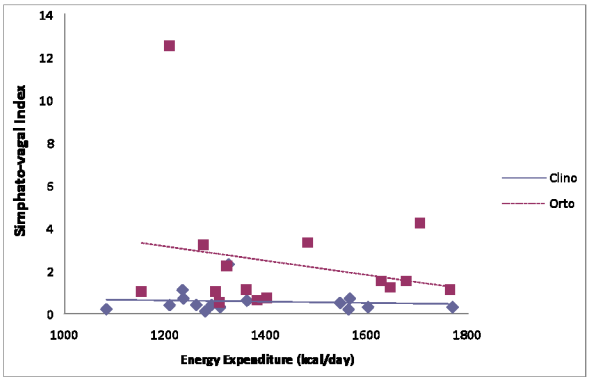
Figure 1. Pearson correlation Parameter curves for the male population. (a) The correlation coefficients between FFM vs EE in clinostatic and orthostatic positions were 0.30 and 0.33, respectively. (b) The correlation coefficients between EE vs SVI in both positions are -0.37 and 0.25, respectively.

Out of the original volunteer population only 29 subjects were considered for data analysis because the rest fell into the rejection criteria. Statistical significance differences were proved using the t-student test between the groups. Glucose and fasting time did not show statistical significance ($p>>0.1$). BMI did not show statistical significance ($p=0.35$) either.

Figure 1 shows the correlation curve fitting parameters for the male group when the orthoclinostatic test was applied. In figure 1 (a), the average REE and EE changed from 1531 to 1779 Kcal/day, while the FFM average was 57.6 Kg. In figure 1 (b) the SVI average changed from 0.8 to 2.7 for the male population but with the correlation coefficients in an inverted slope.



(a)



(b)

Figure 2. Pearson correlation Parameter curves only in women population are shown. (a) The correlation coefficients between FFM vs EE in clinostatic and orthostatic positions were 0.34 and 0.51, respectively). (b) The correlation coefficients for EE vs SVI in both positions were -0.11 and 0.22 respectively.

Figure 2 shows the Pearson correlation coefficients for the female group during the orthoclinostatic test. In Figure 2(a) the average REE and EE changed from 1427 to 1494 Kcal/day, while in figure 2(b) the SVI changed from 0.4 to 1.8 with the same positive slope in the correlation coefficients

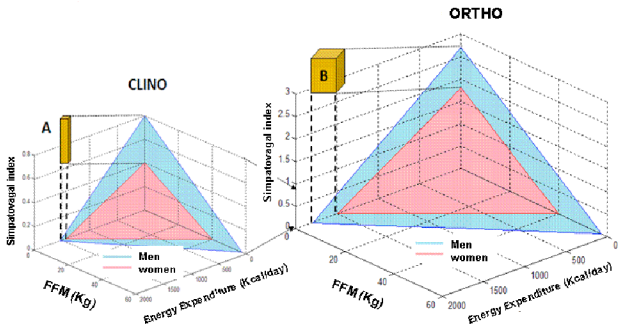


Figure 3. The 3D-cube shape negative effects of obesity are shown. Cube "A" is generated for the clinostatic position, while cube "B" is created from the orthostatic position. The pink zone corresponds to the female metabolic dynamics and the blue zone represents the male population.

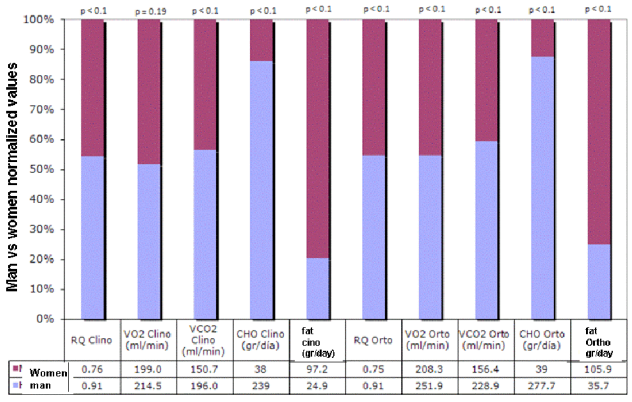


Figure 4. Normalized values for female vs male populations are shown. The main differences between both populations are noticeable in the carbohydrate and fat substrate utilization during the orthoclinostatic test. Despite this, bar differential heights show similar behavior between females and males. The actual change in fat goes from 97.2 to 105.9 and 24.9 to 35.7 gr/day, respectively. A similar situation is shown for carbohydrate (CHO) utilization that goes from 38 to 39 and from 239 to 277.7 gr/day, respectively.

IV. Discussion

The results in Figures 1 and 2 show important statistical differences between REE and the EE during the orthoclinostatic test in females as well as males. Similar differences are observed with regard to the SVI vs EE that correspond to differences in FFM from 40 to 57.6 Kg in females and males respectively. These findings lead us to think that the hypothesis is correct in the sense that the 3D-cube shape in Fig. 3 correctly reflects the fat-free mass' dynamic catabolism. Particularly, it can assumed that higher SVI values correspond to hyperactivity of the ANS, mainly in the sympathetic pathway, which produces an energy expenditure increase using carbohydrate substrates and reduces fat utilization. This substrate utilization is reflected by the respiratory quotient (RQ) of 0.91 for men and 0.76 for women

V. Conclusion

In summary, the findings show:

1. The hypothesis can be accepted because the FFM dynamic catabolism is shown clearly in Fig. 3 when the 3D "A" cube is small compared with the "B" cube, both reflecting the orthoclinostatic test results.
2. The fat-free mass' gender differences can be used as a model to explore other types of population since this method is sensitive to monitoring at least from 20 to 30 % of fat differences which is typical between males and females.
3. The gender SVI differences, that are correlated, with differences in EE and substrate utilization agree with other publications. The contribution of this work is to use these indices as an instrument that is capable to monitor small FFM metabolic changes. More research is needed to test this method with different types of populations. Further studies will lead to the development of a robust methodology for the early detection of the .

Acknowledgment

This work was supported by a grant from the ICYT, project PICSA11-75, and by DCBI-Iztapalapa. The authors acknowledge the help of the staff of Unidad Metabólica y de Composición Corporal from UAM-Xochimilco. We also thank Erika Stanford, Rafael Hernández and Héctor Sandoval for their invaluable help.

References

[1] Siervo, M. and S. Jeeb. "Body Composition Assesment: Theory and Practice". IEEE Engineering in Medicine and Biology Magzine, P-P 48-57, January/February, 2010.

[2] McClave S and Snider "Use of indirect calorimetry in clinical nutrition": invited review, *NCP* **7** 256-267, 1992.

[3] McClave S and Snider "Dissecting the Energy Needs of the Body": Nutr. Metab Care 4: 143-147, 2001.

[4] Marra M et al, "Are the General equations to Predict BMR Applicable to Patienets with Anorexia Nervosa", Eat Weight Disord. Mar; 7(1):53-9, 2002.

[5] Stenholm, S et al, "Sarcopenic obesity, definition-ethiology and consequences", Curr Opin Clin Nutr Metab Care, 11 (6), 693-700, 2008.

[6] Ferrannini E, "The theoretical bases of indirect calorimetry" *Metabolism* **37** 287-30, 1988.

[7] Treton C, Turner W "Actual or Ideal Body Weigth: Which should be Used to predict Energy Expenditure?", J. Am Diet. Assoc. Vol. 91 (1), 193-195, 1991.

[8] Holdy K, "Monitoring Energy Metabolism with Indirect Calorimetry: Instruments, Interpretation, and Clinical Application", Nutrition in Clinical Practice 19: 447-454, 2004.

[9] McClave S et al, "Achievement of steady state optimizes results when performing indirect calorimetry", *JPEN* **27** 16-20, 2003.

[10] Heymsfield S, et al, "Body Composition Modeling: Application to Exploration of the Resting Energy Expenditure Fat-Free Mass Relationship" Ann N.Y. Acad Sci, 904: 290-297, 2000.

[11] Cadena M et al. "Understanding Gas Exchange Variability in Indirect Calorimetry", (in progress) submitted for publishing to The IFMBE, Medical an Biological Engineering & Computing, April, 2012.