

# A Simple Non-Invasive Screening to Prevent Obesity through Body Composition Analysis (Bia-Acc)

Flora Ippoliti<sup>1\*</sup> and Dario Boschiero<sup>2</sup>

<sup>1</sup>Associate Professor, Psycho-Neuroimmunology, Sapienza University Rome, Italy

<sup>2</sup>Director of Research and Development, BioTekna, Venice, Italy

We would like to describe the new criteria for the prevention of obesity and related disease highlighting the common link between stress, cytokines, adipokines and myokines.

An exciting current research field, NeuroImmunoModulation, studies whether environmental or psychosocial stress affects the onset of disease [1]. In an innovative study, Ader and Cohen first coined the term PsychoNeuroimmunology (PNI) to indicate the relationships between stress, immune system (IS) and health outcomes [2]. There is ample evidence underlying the major role played by chronic stress in accumulating visceral fat, secondary to uncorrect/abnormal eating behavior [3,4]. Obesity is now growing at an alarming rate reaching epidemic proportions worldwide thus increasing morbidity and mortality rates for chronic disease. Several studies have reported that obesity, generally defined as a BMI>30, increases the disease and all-cause mortality risks severely impacting life expectancy [5,6]. The cytokines/adipokines, inflammatory mediators, produced and secreted within the expanded activated adipocyte pool and local macrophages, induce a low-grade chronic inflammatory state in obese patients. All this involves an energy dysregulation that produces altered body composition leading to the onset of Medically Unexplained Symptoms (MUS); the latter result the very reason why the patient to seek medical advice [1].

Increased abdominal obesity is a major risk factor for insulin resistance, for type 2 diabetes, for cardiovascular diseases (CVD) and many other chronic diseases. The etiology is multifactorial, with genetic influences, environmental, socio-economic, and behavioral and/or psychological causes, playing a significant role and a relative increase in both morbidity and mortality.

Obesity is the ultimate consequence of a chronic positive energy balance, regulated by a complex signalling network that links the endocrine and central nervous system in search of "comfort food" (high fat and sugar content). In fact in overweight and obese subjects there is increasing evidence that in the hedonic urges involve the same brain reward circuits activated in perpetuating drug abuse. In animals and in humans dopamine increases the motivation for food intake [7].

The role of adipose tissue as an endocrine organ capable of secreting a number of adipose tissue-specific or enriched hormones (adipokines) could have a pathogenic role in CVD; an imbalance between increased inflammatory stimuli and decreased anti-inflammatory mechanisms may depend by a state of chronic stress. Thus, it was not surprising to find a positive correlation between stress, obesity and CVD. In fact the chronic inflammatory state accompanying both insulin resistance and endothelial dysfunction is highly deleterious for vascular function [8].

Psychological stress should be conceptualized as a "social pollutant" which can be "breathed" into the body and disrupt a number of physiological pathways similar to how air pollutants and other physical toxicants may lead to increased risk for atopy [9], but in our opinion, more frequently of diseases. Psychological stress can cause the outbreak of behavioral changes and lifestyle alterations reflected in the values of the anthropometric indices (weight/height: BMI, waist/hip ratio W/H). Continuous psychological stress in relation to specific events

is considered an important antecedent of eating disorders because it can alter the normal regulation of appetite, cause significant altered perception of body image and affect the ability to cope successfully with weight gain and dismorphia [1,4,7,8].

Cultural factors are still important in the development of psychological inadequacy. It has been noted, in fact, that variations from normal weight are usually associated with internalized behavior problems and discomfort, but not with externalizing attitudes [10].

Thus, high BMI values are associated with introversion that can induce, in the most vulnerable persons, depression and anxiety. Inflammatory status seems to be an important mediator of emotional distress in obese individuals [3,4].

Adipose tissue is now seen as an endocrine organ with high metabolic activity where adipocytes produce and secrete many proteins acting as veritable hormones responsible for regulating energy uptake and expenditure: tumor necrosis factor (TNF- $\alpha$ ), leptin, interleukin-6 (IL-6), interleukin-8 (IL-8), the agouti protein, angiotensinogen and plasminogen activator inhibitor-1, TGF- $\beta$ . Notably, visceral fat (VF) is associated with a low-grade inflammation due to the increased secretion of numerous pro-inflammatory cytokines from adipocytes and their associated macrophages [11]. In the presence of free fatty acids (FFA) TNF- $\alpha$  induces ectopic adipose tissue formation by blocking the physiological adipogenesis [12]. Under these conditions the subsequent release of IL-6 induces inflammation in the ectopic tissue and increase in triglycerides. Also FFA send endocrine signals impacting insulin sensitivity, causing type 2 diabetes [13].

The most recent literature focuses on cytokines/adipokines that aggravate both inflammatory organ diseases (particularly cardiovascular), and severely impact patient behaviour inducing mood alterations and depression. The negative emotions and stressful life experiences directly promote the release of the same cytokines that contribute to the chronicity of a pathological event. TNF- $\alpha$  is the main promoter of the severe inflammatory response syndrome due to macrophage activation during stress [14,15].

Straub et al. [16] reported that neuroendocrine pathways are involved in energy regulation (energy appeal reaction): inflammation induces an increase in cortisol serum levels, by stimulating HPA axis and sympathetic nervous system (SNS), inducing a marked decrease in the muscle, brain and gut activities [16,17].

**\*Corresponding author:** Flora Ippoliti MD PhD, Associate Professor, Psycho-Neuroimmunology, Sapienza University Rome Italy, Tel: 06-3701159; E-mail: [flora.ippoliti@uniroma1.it](mailto:flora.ippoliti@uniroma1.it)

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During prolonged stress the mobilization of energy storage, mainly as glycogen in liver and triglycerides in adipose tissue in favour of activated IS, is served by the temporary inhibition of insulin action (insulin resistance) in target tissues by proinflammatory cytokines and stress hormones. Tsatsoulis et al. [18] supports the hypothesis that insulin resistance evolved as a physiological adaptive mechanism in human survival and that the same mechanism is inappropriately activated on a chronic basis in the current environment, leading to the manifestations of the metabolic syndrome [18].

Fat gain depends, inter alia, on a lack of physical activity which determines muscle loss and increased leptin levels leading to cachectic obesity [16]. Prolonged exposure to proinflammatory cytokines/adipokines impairs also synaptic plasticity, contributing to cognitive and mood disorders [19].

The recent identification of skeletal muscle as an endocrine organ that produces and releases myokines during contraction expands our knowledge on how the nervous, endocrine, and immune systems contribute to homeostasis maintenance, especially when energy demands are increased [20]. Visceral and subcutaneous adipose tissues have been regarded as the major sources of adipokines; however, accumulating data suggest that contracting skeletal muscles release myokines exerting specific endocrine impact on visceral fat or mediating direct anti-inflammatory effects [21].

Stress is a serious problem seeing a surge in medical spending especially for CVD, as well as a reduced work-time and higher absenteeism rates in the business world [22,23]. The brain-reward system of eating in response to prolonged unresolved stress can promote obesity and related diseases particularly when are available highly palatable foods containing hidden fats and sugars (obesogenic environment) [24].

Interventions should focus on top-down strategies intended to influence brain function in ways that will improve allostasis and minimize allostatic load [25]. Lack of physical activity, especially among children, is a major cause for overweight/obesity and the early onset of many cardiovascular or metabolic conditions that could negatively impact adult life [26]. These diseases constitute a network of related diseases, also called “the diseasome of physical inactivity” [20].

Exercise not only should be highly recommended for keeping and enhancing physical health, but also to improve academic and mental performance. This effect may, in part, result in endogenous stress reduction and protection potential, and a related neurobiological involvement of brain limbic portions of the brain as well as the underlying molecular pathways, already discussed [19-23].

For all these reasons explained above according to and in response to the Editorial of Selthofer-Relatic published in this journal [26], it is very important that the medical community would be aware of the scientific basis of PNI and new diagnostic strategies about the body composition [27].

As the BMI is no longer the only measure able to evaluate the loss of fat mass after appropriate low-calorie dietary regimen, modern technologies for analysis of body composition can have an important role to evaluation of the patient, especially in early stages of overweight, consenting the correction of both bad habits and altered body status for the prevention of cognitive disorders and CVD [1,19,28,29]. In fact, thanks to these non-invasive and low cost technologies it is possible to collect information on the above parameters and follow up the

alterations induced by the low level inflammatory status secondary to modifications in lifestyle, particularly when dietary restrictions and adequate physical activity are put in state [1,17-19].

In Italy, the BIA-ACC project (Bioelectric Impedance Analyzer - Analisi Composizione Corporea) was launched in 2004 to redefine the application of bio impedance measurement in the clinical setting. The body composition analysis based on the measurement of bio impedance is widely used, and has successfully been through several validation processes in nephrology, nutrition, sports and preventive medicine, yet much of the potential of this technique is still unknown because of early sectionalisation of clinical and technical research [30].

The BIA-ACC device allows a dual frequency bio impedance assessment. The classic “high frequency only” approach (50 kHz), is paired with a low frequency (1.5 kHz) measurement, proved to be critical to get a better evaluation of the extra cellular compartment. The BIA-ACC device, thanks to this feature, stands out for its reliability in detecting the parameters of body composition for patients suffering from chronic inflammatory processes or CIDs expansion of the extra-cellular water (ECW) compartment, increased catabolism of extra-cellular matrix (ECM) and from stress-related diseases.

This characteristic has made the BIA-ACC device particularly suited for use in contexts where the bioelectrical impedance technique was traditionally used only marginally, as is the case for general practice and primary care medicine, where the assessment of inflammatory disorders assumes a significant priority.

BIA-ACC consents assessment of chronic inflammation, MUS, stress neuro-immuno-regulatory situations allowed, also thanks to large clinical data sets collection, to highlight correlations that weren't observed previously, and to expand the tool's output through new analytical processing algorithms which are able to point out the strong relationships between bio impedance-derived parameters and other diagnostics indexes that are generally gathered by other measurement technologies, including invasive or expensive ones [30,31].

The BIA-ACC device has set the way for collaboration between technical and scientific research: technical improvements were made available to operators, allowing them to the use of the device in clinical practice and research and to collect so many more data and feedbacks that technologists could use in turn to better the device performance. The described synergy has been consolidated over time and has permitted the accumulation of different data sets (correlation/validation of bioelectrical parameters with other gold-standards diagnostic technologies even following reverse engineering processes) in particular large series of clinical data necessary to the development of innovative processing algorithms (analytical processing, molecular analysis of body composition, assessment of extra-cellular matrix, cardiovascular risk degree, body density, metabolism distribution, body fluids' turnover, etc.), which today by means of a rapid and non-invasive diagnostic test allows clinicians to dispose of a wide panel of diagnostic information, on several clinical settings.

The numerous parameters provided by BIA-ACC device, after appropriate low-calorie diet, permitted us to evaluate, also in the presence of a decrease in BMI, the real modifications in FM and FFM, in relation to all the other variables and the essential role of FFM preservation during weight loss (manuscript in preparation).

Thanks to the research briefly described the BIA-ACC device is now used in many fields of medicine and in interdisciplinary clinical research settings, such as MUS, stress and related diseases, chronic

inflammatory and autoimmune diseases, cardiovascular diseases, metabolic syndrome, clinical nutrition, anti-aging and preventive medicine.

Finally, the *Open Academy of Medicine* is an international specialization school of providing continuing medical education focusing on NeuroImmunoModulation, Metabolism, Clinical Nutrition and Physical Rehabilitation. The Academy founded in Venice (Italy) in 2013 aims to develop further studies on chronic diseases and disorders, using the latest scientific research results and the experience brought by Evidence Based Medicine.

The program offers courses on: Neuroscience, Immunology, Endocrinology, Clinical Nutrition and Diagnostic Technologies; for every area the Open Academy of Medicine provides the expertise of the most renown international experts, researchers in order to offer the best training experience available.

## Declaration

The authors declare that they have no conflict of interest.

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