Clinical Nutrition xxx (2016) 1–8

Contents lists available at ScienceDirect

Clinical Nutrition

journal homepage: http://www.elsevier.com/locate/clnu

Original article

Abdominal fat sub-depots and energy expenditure: Magnetic resonance imaging study

Dana Serfaty [a, 1], Michal Rein [a, 1], Dan Schwarzfuchs [b, 1], Ilan Shelef [c], Yftach Gepner [a], Nitzan Bril [a], Noa Cohen [a], Elad Shemesh [c], Benjamin Sarusi [b], Julia Kovsan [a], Shira Kenigsbuch [a], Yoash Chassidim [c], Rachel Golan [a], Shula Witkow [a], Yaakov Henkin [c], Meir J. Stampfer [d], Assaf Rudich [a], Iris Shai [a, *]

[a] *Faculty of Health Sciences, Ben-Gurion University of the Negev, P.O.B. 653, Beer-Sheva, 8410501, Israel*
[b] *Nuclear Research Center Negev, P.O.B 9001, Dimona, 84190, Israel*
[c] *Soroka University Medical Center, P.O.B 151, Beer-Sheva, 84101, Israel*
[d] *Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard School of Public Health, 677 Huntington Avenue Boston, MA, 02115, USA*

A R T I C L E I N F O

Article history:
Received 1 September 2015
Accepted 11 May 2016

Keywords:
Resting energy expenditure
Visceral-adipose-tissue
Deep-subcutaneous-adipose-tissue
Superficial-subcutaneous-adipose-tissue
Non-exercise activity thermogenesis

S U M M A R Y

Background & aims: We aimed to assess the association between the distinct abdominal sub-depots and resting energy expenditure (REE).
Methods: We performed magnetic resonance imaging (MRI) to quantify abdominal visceral-adipose-tissue (VAT), deep-subcutaneous-adipose-tissue (deep-SAT), and superficial-subcutaneous-adipose-tissue (superficial-SAT). We measured REE by indirect-calorimetry. Non-exercise activity thermogenesis (NEAT) [1−3 metabolic equivalents (METs)] and exercise thermogenesis (activities of 4+$METs_S$) were estimated based on 6-days of accelerometry to assess total physical activity energy expenditure (PAEE).
Results: We studied 282 participants: 249 men [mean age = 47.4 years, body-mass-index (BMI) = 31 kg/m^2, mean VAT proportion from total abdominal fat = 34.5%, mean superficial-SAT proportion from total abdominal fat = 24.3%] and 33 women (mean age = 51.2 years, BMI = 30.1 kg/m^2, mean VAT proportion from total abdominal fat = 22.8%, mean superficial-SAT proportion from total abdominal fat = 37.8%). As expected, women had lower REE [by 32.4% (1488 ± 234 kcal/day vs. 1971 ± 257 kcal/day; $p < 0.01$)] and lower REE/kg [by 8% (19.6 ± 3 kcal/kg vs. 21.2 ± 2 kcal/kg; $p < 0.01$)] than men. Exercise and total PAEE were positively associated with REE/kg ($p < 0.01$ for both) and a positive correlation between NEAT and REE/kg was borderline ($p = 0.056$). Participants, in whom abdominal VAT was the dominant proportional depot, had higher REE (1964 ± 297 kcal/day vs. 1654 ± 352 kcal/day; $p < 0.01$) and higher REE\kg (22.2 ± 2.3 kcal/kg/day vs. 19.6 ± 2.5 kcal/kg/day; $p < 0.01$) than participants in whom superficial-SAT was the largest proportional depot. In multivariate models, adjusted for age, gender and residual BMI, increased VAT proportion was independently associated with higher REE ($\beta = 0.181$; $p = 0.05$). Likewise, increased VAT proportion ($\beta = 0.482$; $p < 0.01$) remained independently associated with higher REE/kg. In this model younger age ($\beta = -0.329$; $p < 0.01$) was associated with higher REE/kg.

Abbreviations: REE, Resting energy expenditure; TEE, Total energy expenditure; PAEE, Physical activity energy expenditure; NEAT, Non-exercise activity thermogenesis; VAT, Visceral-adipose-tissue; SAT, Subcutaneous-adipose-tissue; MRI, Magnetic resonance imaging; WC, Waist circumference; TG, Triglycerides; HDL-c, High-density-lipoprotein-cholesterol; FLASH, Fast-low-angle shot; METs, Metabolic equivalents; BP, Blood pressure; LDL-c, Low-density-lipoprotein-cholesterol; BMI, Body-mass-index; FFM, Fat-free mass; FFA, Fatty acids.

* Corresponding author. Department of Public Health, Faculty of Health Sciences, Ben-Gurion University of the Negev, P.O. Box 653, Beer-Sheva, 84105, Israel. Tel.: +972 8 647 7449/3; fax: +972 8 647 7637/8.

E-mail addresses: Serfaty.dana@gmail.com (D. Serfaty), lerner.michali@gmail.com (M. Rein), dan.nurit@gmail.com (D. Schwarzfuchs), shelef@bgu.ac.il (I. Shelef), gepner@bgu.ac.il (Y. Gepner), nitzanbril@gmail.com (N. Bril), noale86@gmail.com (N. Cohen), elad234@gmail.com (E. Shemesh), benny@rotemi.co.il (B. Sarusi), julayk@gmail.com (J. Kovsan), shiraken5@gmail.com (S. Kenigsbuch), yoash.chassidim@gmail.com (Y. Chassidim), golanra@bgu.ac.il (R. Golan), witkow@galon.org.il (S. Witkow), yaakovh@bgu.ac.il (Y. Henkin), STAMPFER@hsph.harvard.edu (M.J. Stampfer), rudich@bgu.ac.il (A. Rudich), irish@bgu.ac.il (I. Shai).

[1] Equal contribution.

http://dx.doi.org/10.1016/j.clnu.2016.05.009

Conclusions: Abdominal fat distribution patterns are associated with varying levels of resting energy expenditure, potentially reflecting different metabolic rates of adipose sub-depots and providing an anatomic/anthropometric link to physiological obese sub-phenotypes.

1. Introduction

In humans, resting energy expenditure (REE) accounts for the majority (60–75%) of total energy expenditure (TEE) [1]. Decreased REE has been associated with elevated risk of chronic energy surplus and thereby, to obesity. REE decreases with age by an average of 1–2% per decade from the second to the seventh decade of life [2].

Physical activity energy expenditure (PAEE) accounts for 10–30% of TEE [3]. PAEE consists of two subcomponents: non-exercise activity thermogenesis (NEAT), i.e. all energy expended due to spontaneous physical activity (walking, climbing stairs), and exercise thermogenesis, i.e. the calories spent on planned physical activity [3]. It is still unclear how PAEE components affect REE, beyond PAEE's short-term capacity to elevate REE [4].

Obesity is associated with elevated total REE [5], but with decreased REE per kg body weight [5], likely reflecting body composition, as fat tissue expends less energy than the equivalent lean mass/muscle. Nevertheless, the association between metabolic rate and the specific abdominal fat tissues compartments is unknown.

The diversity of adipose tissue depots and their differential contribution to pathophysiology adds a further level of complexity [6,7]. Intra-abdominal visceral-adipose-tissue (VAT) is strongly associated with cardio-metabolic risk [6], and its association with REE is controversial [8]. Abdominal subcutaneous-adipose-tissue (SAT) is composed of two sub-depots [9]- superficial-subcutaneous-adipose-tissue (superficial-SAT) and deep-subcutaneous-adipose-tissue (deep-SAT) – that are differentially associated with risk biomarkers: While superficial-SAT is neutral or beneficially associated with cardio-metabolic parameters [10], as we and others recently suggested, deep-SAT may be associated with increased cardio-metabolic risk, especially in diabetics [11,12].

Here, we aimed to examine the association between REE, as measured by indirect-calorimeter, and abdominal fat sub-depots, as imaged by magnetic resonance imaging (MRI). With increasing need to sub-phenotype obese people to enhance personalized interventions, we hypothesized that abdominal fat sub-depots distribution may manifest by different REE and/or REE/kg body weight, thereby differentially affecting the proposed association between REE and obesity risk.

2. Materials and methods

2.1. Study population

As part of the baseline measurements of the CENTRAL randomized controlled trial (ClinicalTrials.gov Identifier: NCT01530724) we performed a sub-study among 282 participants.

The inclusion criteria were abdominal obesity [waist circumference (WC) > 102 cm for men and >88 cm for women], or serum triglycerides (TG) > 150 mg/dl and high-density-lipoprotein-cholesterol (HDL-c) < 40 mg/dl for men and <50 mg/dl for women. Exclusion criteria included: pregnant or lactating women; serum creatinine ≥2 mg/dl or disturbed liver function (≥3 fold level above the upper normal values of Aspartate aminotransferase or Alanine aminotransferase enzymes), active cancer; or individuals who with more than 4 h/week of vigorous activity. The study protocol was approved by the Soroka University Medical Center Medical Ethics Board and Helsinki Committee. All participants provided written informed consent and received no financial compensation or gifts.

2.2. MRI acquisition and image analysis

MRI scans of the abdomen were performed using a 3-Tesla machine (Intera, Philips Medical Systems, Best, the Netherlands) using a body coil. The MRI scan lasted 45 min. Subjects were examined in the supine position with arms positioned parallel along the lateral sides of the body. MRI scans quantifying fat in the different compartments were assessed using a MATLAB-based program [10]. The scanner utilized a 3D mDIXON imaging technique, fast-low-angle shot (FLASH) sequence with a multi-echo two-excitation pulse sequence for phase-sensitive encoding of fat and water signals (TR,3.6 ms; TE1,1.19 ms; TE2,2.3 ms; FOV $520 \times 440 \times 80$ mm; $2 \times 1.4 \times 1$ mm voxel size). Fat tissue depots defined by specific anatomical landmarks were quantified [10]. The MRI scan allowed visualizing the fascia superficialis as a fine black line. To divide superficial-SAT and deep-SAT, we drew a continuous line over the fascia superficialis. After quantification, fat tissue depots were divided into color-coded groups: superficial-SAT = dark blue; deep-SAT = light blue; VAT = green; perimuscular fat (fat surrounding and within the latissimus dorsi and diaphragm) = purple; and nonclassified fat (fat surrounding the vertebrae and fat depots unrelated to any of the groups listed above) = red (Fig. 1). Quantification of the fat mass regions included the area of each fat type and the proportion (percentage) of the total area for all abdominal fat depots. In accordance with other studies [13–15], we calculated fat distribution using area of the slice in the L5-L4 inter-vertebral space. Perimuscular and the non-classified fat tissues, totaling a negligible fraction of total abdominal fat, were omitted from our analysis. A breath-hold technique and a preceding 2-h fast were used to avoid breath-artifacts and fat-disruption.

2.3. Resting energy expenditure (REE)

REE was measured in a metabolic unit, using an indirect-calorimeter device, Quark REE (Cosmed, Rome, Italy). Indirect-calorimetry is based on the measurement of gas exchange: carbon dioxide production (VCO_2) versus oxygen consumption (VO_2), which reflects energy metabolism according to Weir equation [16]. The measurements and required calibrations were performed according to the manufacturer's guidelines [17]. Turbine calibration was performed every day and gas calibration before each test, as per the manufacturer's instructions. During the measurement, the subjects were awake in a supine position, in a quiet room with stable temperature (22–24 °C), with their head covered with a ventilated canopy. A new filter was used for each patient. Participants were allowed to watch relaxing channels on TV in order to avoid falling asleep and extreme movements. Each measurement lasted for 20 min and gas calibration was done before each test. The first 4 min adaptation phase was excluded and the mean REE of the final 16 min was defined as baseline REE. Pretest conditions were at least 4 h of fasting and a minimum of 4 h refraining from alcohol, caffeine, smoking and physical activity [17]. Each subject received personal report of his REE test in the end of