THE BODY FAT-COGNITION RELATIONSHIP IN HEALTHY OLDER INDIVIDUALS: DOES GYNOID VS ANDROID DISTRIBUTION MATTER?

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> Abstract: Objective: To examine the relationship between regional and whole body fat accumulation and core cognitive executive functions. Design: Cross-sectional study. Settings and participants: 78 healthy men and women aged between 65 and 75 years recruited through consumer's database. Measurements: DXA measured percentage total body fat, android, gynoid distribution and android/gynoid ratio; inhibition and working memory updating through Random Number Generation test and cognitive flexibility by Trail Making test. First-order partial correlations between regional body fat and cognitive executive function were computed partialling out the effects of whole body fat. Moderation analysis was performed to verify the effect of gender on the body fatcognition relationship. Results: Results showed a differentiated pattern of fat-cognition relationship depending on fat localization and type of cognitive function. Statistically significant relationships were observed between working memory updating and: android fat (r = -0.232; p = 0.042), gynoid fat (r = 0.333; p = 0.003) and android/ gynoid ratio (r = -0.272; p = 0.017). Separating genders, the only significant relationship was observed in females between working memory updating and gynoid fat (r = 0.280; p = 0.045). In spite of gender differences in both working memory updating and gynoid body fat levels, moderation analysis did not show an effect of gender on the relationship between gynoid fat and working memory updating. Conclusions: Results suggest a protective effect of gynoid body fat and a deleterious effect of android body fat. Although excessive body fat increases the risk of developing CDV, metabolic and cognitive problems, maintaining a certain proportion of gynoid fat may help prevent cognitive decline, particularly in older women. Guidelines for optimal body composition maintenance for the elderly should not target indiscriminate weight loss, but weight maintenance through body fat/lean mass control based on non-pharmacological tools such as physical exercise, known to have protective effects against CVD risk factors and age-related cognitive deterioration.

Key words: Regional body fat, cognition, executive functions, gender, aging.

Introduction

It has long been known that obesity is associated with numerous health risks including metabolic and cardiovascular (CV) diseases. In particular, fat accumulation in the abdomen is a key factor associated with the development of such conditions even in normal weight individuals, particularly in women (1-4). This seems to be due to the greater metabolic activity of visceral fat relative to subcutaneous fat. Such metabolic activity is linked with the production of adipocytokines and the development of systemic inflammation linked with cardiometabolic diseases (5, 6).

Research has also consistently associated obesity with poor general cognition across the lifespan (5, 7, 8) and increased risk of developing dementia and Alzheimer's disease at older ages (6). This negative association also specifically applies to higher-level cognition, the executive functions (9-11) which are responsible for flexibility and adaptability in daily living and therefore crucial in aging (12). The accumulation of visceral fat seems a key determinant in cognitive deterioration at all ages, possibly mediated by "negative" metabolic and CV conditions (5, 13, 14). However, for older age groups, results are not so clear-cut. Some authors report the attenuation of the negative relationship between body fat and cognition with advancing age (15), and some studies have observed an association between cognitive decline and low levels of body fatness (BMI and small waist size) (5, 14, 16) particularly in women (17, 18), with weight loss unequivocally preceding the onset of dementia in both men and women (19, 20). Over the age of 70 years, women's executive functions seem to benefit from being overweight, while for men a positive fat-cognition relationship seems to be true only within a middle range of body fatness (20).

Such contradictory results may be explained by the fact that the association between body fat and cognitive dysfunction is complex, and is moderated by gender and age and their effect on body composition. With respect to gender, body fat has been shown to protect women against cognitive decline, CV and metabolic diseases (at least at a younger old age; 17). It is well known that body fat accumulates differently in the two genders due to the influence of sex hormones. In normal conditions, estrogens lead to higher gynoid fat accumulation at the hip in women, and testosterone to android fat accumulation at the abdomen in men (22). With aging, however, fat is redistributed from the lower body to the abdomen, thus reducing sex differences in android fat accumulation (23). Adipose tissue is known to contribute to the maintenance of estrogen levels, possibly through endogenous conversion (24). Estrogens, in turn, are reported to have a stimulating effect on areas of the brain such as the hippocampus and the frontal cortex (25). On the other hand, higher testosterone levels have been suggested to interfere with cognitive task performances, particularly in women (26). Given the above, it is unclear if, in older individuals, the body fat-cognition relationship is linked more to whole or regional (android/gynoid) body fat accumulation, or to the joint influence of gender and gender-specific fat localization.

The matter is further complicated by the methodological differences across the studies in both anthropometric and cognitive measurement, which make generalization of results difficult. Regarding body fat assessment, BMI, waist circumference and waist to hip ratio are the most commonly used proxy measures. However, due to the typical loss of muscle mass with aging (27), these measures are likely to underestimate true body fat content, with the result that lower BMI may not reflect reduced body fat, but rather reduced lean mass (28, 29). Similarly, different cognitive domains have been assessed across the studies including general intellectual abilities or memory and attention (16-18, 30). Among the different domains of cognitive function, executive functions appear to be of special significance in the body fat-cognition relationship (7, 9, 11, 31) both for their role in regulating behaviour (i.e., eating, physical activity; 32, 33) and for their likely susceptibility to the deleterious effect of fat produced adipocytes (31). Consequently, our understanding of the role of whole and regional body fat accumulation on executive functions in healthy older individuals is currently incomplete (7).

To address the above issues, the present study examined the relationship between accurately measured (using DXA) whole and regional body fat accumulation and core executive functions (inhibition, working memory and cognitive flexibility) fundamental for effective day to day living (12). To the best of our knowledge, no studies have assessed the relationship between regional (android/gynoid) body fat and the different facets of core executive functions in healthy older individuals. Two studies examined this issue in relation to android fat only and reported inconsistent findings of a negative (30) or no relationship (21).

Crucially, given the known negative relationship between whole body or abdominal (android) fat accumulation and executive function, and the presence of gender differences in age-related changes in fat deposition, it seems plausible to hypothesize a differential body fat-cognition relationship depending on fat localization. It was therefore hypothesized that in older individuals, higher body fat accumulation in the abdomen and at the hip would be associated with poorer and better executive functions respectively, and that this association might be moderated by gender.

Methods

Participants

Participants were 78 healthy men and women aged between 65 and 75 years (mean 69.7 \pm 3.2) recruited through a consumer list database. The exclusion from our sample of older individuals, who may be "selected survivors", made the sample a better representation of the majority of the still sufficiently healthy older population who can benefit from interventions targeted at prevention and compression of morbidity. To further this aim, they were also medically screened through blood pressure measurement and administration of a functional ability questionnaire (34) and a medical history questionnaire (35) to meet the criteria of "medically stable". In brief, they had to be free from cardiovascular and respiratory illness, severe obesity (BMI > 35) or lower limb arthritis, musculoskeletal or neurological diseases, uncontrolled metabolic disease (i.e., diabetes, metabolic syndrome) or other pathological conditions potentially influencing study outcomes, with blood pressure within 199/99 mmHg, and not on medication such as betablockers. Moreover, they had to be sedentary (not practicing any structured physical activity or exercise more than once a week), non-smokers and fully functional for daily living.

Following approval by our institutional ethics board and participant consent, tests for anthropometry, body composition and cognitive functions were carried out.

Measurements

Anthropometry and Body composition

Stature and body mass were measured following standard procedures with a stadiometer and a balance scale, respectively. Total, android and gynoid body fat were measured via dual energy x-ray absorptiometry (DXA, GE Healthcare Diagnostic Imaging, UK) to obtain percentage of body fat (%). As an additional measure, the ratio between android and gynoid body fat was calculated dividing android by gynoid fat percentage. At the start of each measurement day, the system was calibrated using a phantom spine following the manufacturer guidelines. For the measurement, participants were asked to wear loose, comfortable clothes and to remove all metal objects. To ensure the correct position, the participant laid inside the marked space on the measuring table with their spine aligned with the centre line. The head was about 10 cm from the top line, the feet relaxed but not flexed or extended; legs were positioned slightly apart with feet a few cm distant from the centre line on either side. Participants were asked to lie still for the duration of the procedure; a strap was placed around the ankles so that the participant could relax their feet against it. Analysis of total body fat and proportions of android and gynoid fat were performed using Lunar IDXA Prodigy enCORE software (version 12.30.00 GE medical systems, GE Healthcare, UK). Briefly, the programme automatically delimits the areas just below the rib cage and above the pelvis, completely within

the trunk region, as android, and that of the hips and upper thighs, overlappping the leg and trunk regions, as gynoid. For determining the android fat region of interest, the upper boundary was above the pelvis cut by 20% of the distance between the pelvis and the femoral neck cuts. For the gynoid fat region of interest the upper boundary was below the pelvis line by 1.5 times the height of the android region of interest. The total height of the gynoid region was twice the height of the android region.

Executive Functions

Cognitive flexibility was assessed using the Trail Making test, which tests attention, speed and mental flexibility (36). For this test the participant is required to make a trail with a pencil joining 25 circles distributed over a sheet of paper.

The test is composed of two parts (A and B). In part A the circles are numbered 1 to 25; in part B the circles include numbers (1 to 12) and letters (A to L). For both parts participants are asked to draw lines as quickly as possible, to connect the circles in an ascending order, using numbers only for part A and alternating between numbers and letters in part B (i.e., 1-A-2-B-3-C etc.). Time taken in seconds was recorded.

As correction of errors forms part of the completion time for the task, any errors were pointed out immediately to participants by reminding them of the correct sequence (i.e. number, or letter). They were then asked to revert to the last correct number/letter reached and continue from there. A composite score (Δ trail) was calculated by subtracting time taken to complete part B from time for part A, and used for analysis.

Inhibition and working memory updating were assessed through the Random Number Generation (RNG) test (37, 38). During this test, participants vocally produced a sequence of 100 numbers, chosen between 1 and 9 in random order, speaking at a frequency paced by a metronome set at 40 bpm. Participants were seated in a quiet room, and once instructions were given they performed two trials: one familiarization and one test. The produced numbers were manually and electronically recorded by the examiner. If more than three mistakes were made (i.e. no production of number at one or more beats, the production of numbers smaller than 1 or greater than 9) the trial was repeated (39).

The obtained lists of numbers were subsequently processed using RGCalc software (40). Six indices of specific subgroups of executive control functions were obtained, three for inhibition (adjacency, turning point index, runs) and three for working memory-updating function (redundancy, mean repetition gap and coupon). In brief, Adjacency reflects the ability to inhibit counting; this score may range between 0%, for absence of contiguous pairs, and 100%, for complete sequence of such pairs. The Turning Point Index indicates the use of "arithmetic chains" to produce responses rather than randomness, as assessed by the change between ascending and descending sequences. It is a percentage score reflecting the proportion between observed and expected values. Values higher than 100% indicate the presence of too many turning points than expected and vice-versa for values less than 100%. The Runs, a further measure of randomness, describes the variability in the phase lengths (distance between turning point indices). From the produced sequence, the ascending phase length is determined and then the variance of these sequences lengths is calculated. The lower the value the better is the performance. The Redundancy score reflects the ability to avoid repetition of numbers. It is the ratio of ideal and observed frequencies expressed as a percentage where 0% indicates no redundancy, and 100% complete redundancy. The Coupon measures the mean number of responses given before all the response alternatives are used. Using the complete set of alternatives constantly will produce low coupon scores, therefore the lower the value the better the performance. The Mean Repetition Gap is the mean number of responses given until each digit reoccurs in the sequence; therefore the higher the score, the better the performance.

From these individual scores, two separate composite indices were calculated for the separate inhibition and memory updating functions to be used for statistical analysis. First, raw data of all six indices were z standardised ((score-x, -) / sd). Then, measures for which a smaller number meant a better performance (redundancy, coupon, adjacency and runs) were reverse-scored by multiplying them by -1. The average of the three indices of each function was next calculated to obtain a combined score for updating (mean updating) and for inhibition (mean inhibition).

Statistical Analysis

Data were analyzed using IBM SPSS version 20. The level of statistical significance was set at p<0.05 for all computations. Preliminary analyses included the calculation of descriptive statistics and unpaired Student's t-tests for differences between genders on all the measured variables with additional Levene's test for unequal variances.

To explore the relationship between core executive functions (inhibition, working memory updating, cognitive flexibility) and regional body fat distribution (android, gynoid, and android/gynoid ratio), first-order partial correlations were computed partialling out the effects of whole body fat on the whole sample. Given the well-known differences between men and women in body fat distribution, data were also analyzed separately for the two genders.

Given the sex differences in regional body fat accumulation, sex might also influence the prediction of executive functions accrued by regional body fat. Therefore, moderation analysis was performed to explore whether gender enhanced, buffered or antagonized such prediction and whether one gender was more susceptible than the other to such effects. To test for moderation, interaction variables (i.e. body fat measures x gender) were therefore created to be included in a model of multiple regression for all cognitive outcome indices (inhibition, working memory updating, cognitive flexibility).

Results

Characteristics of the participants and results of unpaired Student's t-tests are reported in Tables 1 and 2. For the whole sample average height and weight were 1.65 m \pm 0.08 and 71.56 kg \pm 11.12, respectively. Average percentage (%) of total, android and gynoid body fat were 33.21 ± 7.50 ; 41.91 \pm 10.62 and 40.25 \pm 10.25, respectively. Average scores of working memory, inhibition and cognitive flexibility were $0.02 \text{ (std)} \pm 0.85, -0.51 \text{ (std)} \pm 0.65 \text{ and } 44.89 \text{ (s)} \pm 32.20.$ More detailed data divided by gender are reported in Tables 1 and 2. Compared with men, women had significantly higher total body fat (p < 0.001), due to higher android (p = 0.029) and particularly gynoid fat (p < 0.001) and therefore lower android/gynoid ratio (p < 0.001) (Table 1). Also, women had significantly higher working memory updating performance (p = 0.017) (Table 2). Levene's test did not show significant between-groups differences in the variances of all variables, except for inhibition (p = 0.003), that might affect the following main outcomes of correlational analyses.

Table 1

Descriptive statistics for anthropometric and body fat characteristics of participants. Significant differences between genders are reported

	Women (n = 54)	Men (n = 24)
Age (years)	69.45 ± 3.27	70.00 ± 3.26
Weight (kg)	67.28 ± 8.90	81.18 ± 9.59***
Height (m)	1.62 ± 0.06	$1.73 \pm 0.05^{***}$
BF (%)	38.13 ± 6.48***	28.65 ± 5.17
Android fat (%)	$43.65 \pm 11.11*$	37.99 ± 8.37
Gynoid fat (%)	$45.69 \pm 6.02^{***}$	28.00 ± 6.51
Android/Gynoid Ratio	0.94 ± 0.20	$1.38 \pm 0.26^{***}$

Statistically significant difference between males and females at * p < 0.05, ** p < 0.01, *** p < 0.001

Results of partial correlation between executive functions and regional body fat distribution controlled for total body fat (Table 3) showed statistically significant relationship between working memory updating and: android fat (p = 0.042), gynoid fat (p = 0.003) and android/gynoid ratio (p = 0.017). The correlation with the other executive functions (inhibition and cognitive flexibility) was non-significant and therefore these were excluded from further analyses.

Given these results, and because men and women differed significantly in android and gynoid fat composition, partial correlation computations were recalculated on working memory updating separately for males and females. Results (Table 3) showed in males non-significant relationships with android (p =

0.837), gynoid (p = 0.276) and android/gynoid ratio (p = 0.709). In women the relationship was positive and significant with gynoid (p = 0.045) and almost significant with android/gynoid ratio (p = 0.075). That with android fat was non significant (p = 0.313).

 Table 2

 Descriptive statistics for executive functions (composites scores) of participants

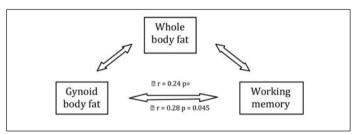
	Women (n = 54)	Men (n = 24)
Working Memory Updating (std)	$0.17\pm0.68*$	-0.32 ± 1.07
Inhibition (std)	-0.46 ± 0.75	-0.07 ± 0.83
Cognitive flexibility (s)	39.05 ± 29.46	52.90 ± 34.66

* Statistically significant difference between males and females at p<0.05

Regarding the analysis of moderation by gender on the prediction of executive functions by body fat, no regression models showed any interactive prediction of cognitive performances by gender with body fat composition, therefore results are not reported here.

Figure 1

Graphic representation of partial correlation between percentage of gynoid body fat and working memory updating controlled for percentage of whole body fat. R values and significance for the two genders are reported



Discussion

The present study investigated the relationship between executive functions and regional body fat accumulation in healthy older individuals. Results support the notion of an association between executive functions and body fat accumulation, and contribute to filling a gap in previous literature by relating the efficiency of core executive functions needed for independent living with body fat accumulation in specific body regions.

The importance of body fat in many human functions, including the cognitive, is becoming more apparent. In general, overall obesity is linked to cognitive difficulties and has a negative effect on decision-making, planning and problemsolving in individuals aged 18 and over (7) as well as on several cognitive domains such as inhibition and attention, learning

THE BODY FAT-COGNITION RELATIONSHIP IN HEALTHY OLDER INDIVIDUALS

Table 3

Partial Pearson's correlation coefficients (r) between body composition and core executive functions (composite scores of working memory updating, inhibition and cognitive flexibility) for the whole sample (n=78) and separately for men (n=24) and women (n=54). Levels of significance are reported.

Controlled for % body fat	Working memory updating	Inhibition	Cognitive flexibility
% Android fat			
total sample	-0.279*	0.121	0.052
males	0.045	-0.014	-0.108
females	-0.141	0.158	-0.101
% Gynoid fat			
total sample	0.368**	-0.037	-0.103
males	0.237	0.232	-0.190
females	0.280*	0.009	0.175
Android/Gynoid ratio			
total sample	-0.303*	0.065	0.139
males	-0.082	-0.023	0.174
females	-0.247	0.061	-0.166

and memory across the life-span (6, 13, 41). The literature also suggests an attenuation of such negative relationship after the age of 70 years (15, 42) preceded by an inverted U-shaped relationship between 55 and 65 years, as both underweight and overweight individuals demonstrate cognitive impairment with respect to normal weight people (20).

In particular the complex relationship between cognitive executive functions and body fat is being revealed by extensive research. In the literature, positive, negative or non-significant results can be found, due partly to differences in body fat and cognition measurement protocols, but also to the many factors known to determine or influence the relationship. Cognitive aging and age-related body fat changes, as well as their relationships, may be interactively influenced by a number of factors that range from the organic domain, such as cardiovascular, metabolic (5), hormonal factors (43) including vitamin D deficiency (44, 45), to the lifestyle domain, including education, diet, exercise, social engagement (46, 47) and daily living abilities (20). Also, gender seems to affect the direction and shape of the relationship between body fat and executive function: women with higher body fat show better executive function than those with lower, while this seems to hold for men only up to a certain point (21).

The present study furthers our understanding of the body fat-cognition relationship, suggesting a possible differential link depending on fat localization (gynoid) and type of cognitive function (working memory). This represents a novel result which has not been previously reported. In fact, research has either combined measures of whole body fat with specific cognitive functions including the executive 11, 16, 31), or of regional (mainly central) body fat, with general cognitive measures (15, 17, 18, 48), while only rarely have studies employed both specific executive functions and regional body fat assessments (21, 30, 47), thus overlooking potential associations with gynoid body fat.

There is evidence that being overweight has positive effects on cognition and specifically on executive function (21). In contrast, greater adiposity, specifically localized in the abdomen, seems to be associated with cognitive impairment in older adults (14, 15, 47). It should not be forgotten that localized body fat of android type is a known risk factor for cardiovascular, metabolic and cognitive impairment even in the absence of high overall body fat (15). Our findings support this negative association of cognition with android fat, highlighting a selective link to one core executive function, working memory updating (Table 3). Given that factors such as insulin resistance, hypercholesterolaemia, triglyceridaemia are associated with android body fat (49), they might represent biomedical mechanisms underlying the negative association between android fat and working memory updating observed in the present study.

While information on the negative role of android fat accumulation is generally accepted, a potential protective effect on cognition can only be indirectly evinced from research on gynoid fat protection against CVD (50). Reflective of higher estrogen levels, gynoid fat has long been suggested as protective against harmful cardiovascular conditions in women (50, 51) particularly before the menopause, after which estrogen levels decrease, gynoid fat is reduced and abdominal fat accumulates (23). Estrogens have been reported to protect from cognitive decline (17) through a stimulating effect on specific areas of the brain such as the hippocampus and the frontal

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cortex, areas rich in receptors for estrogens and implicated in working memory (25). As a consequence, a positive effect of gynoid fat on cognitive performance at an older age may be inferred. The protective role of estrogens on the brain is further supported by research showing that postmenopausal women with higher remaining circulating oestradiol levels appear less likely to suffer from cognitive impairment independent of age at menopause (52) and by studies on menopausal women on hormone replacement therapy which suggest a diminished risk of dementia (53). The present study is suggestive of such a protective effect. However, the notion of a positive link between greater adiposity and executive function was limited to the gynoid fat accumulation and the core executive function of working memory updating (Table 3).

Moreover in the present sample, women showed higher values of both gynoid and android fat with respect to men, and lower values of android/gynoid ratio, due to the more pronounced amount of accumulated gynoid fat. When correlations between body fat and cognitive performance were calculated separately for gender, gynoid fat was significantly related to working memory in women only and the android/ gynoid ratio almost reached significance. The ratio, as a measure relating android to gynoid body fat deposits, reflects the potential "risk" linked to android fat accumulation independent of the "protection" linked to gynoid fat. In women accumulating android fat may be particularly detrimental, while accumulating gynoid fat may compensate for these negative effects. Both adolescent (10) and older females (30) have been reported to be particularly sensitive, compared with males, to the detrimental effects of central (e.g., android) adiposity on cognition, hippocampal volume and verbal memory.

Although mechanisms explaining this phenomenon are not yet fully understood, a possible role of excessive testosterone in women has been suggested (26). Conversely, adipose tissue contributes, through testosterone conversion, to the maintenance of estrogens levels, which may reduce the risk of cognitive decline in overweight individuals (24, 25). Particularly in women following the menopause, adipose tissue becomes the major source of estrogens (54). Possibly because of this role, significant weight loss in older women, in whom the menopause considerably reduces estrogen levels, is associated with a greater risk of developing cognitive dysfunction (48). Moreover, some authors suggested that gynoid fat is a source of a long-chain polyunsaturated fatty acid (as omega-3 DHA) which makes up about 20% of the dry matter of neurons and seems to positively affect cognition (55).

The importance of maintaining a balanced body composition and a "healthy" amount of body fat in aging is also supported by the observation of pathologies such as the lipodystrophies which are characterized by a localized deficit of adipose tissue (56). In these cases, paradoxically, the affected individuals show disorders similar to those of the metabolic syndrome (56) which may also lead to a greater risk of developing dementia or cognitive deterioration (57).

The present findings may be of practical relevance for objective body fat monitoring and the development of guidelines for optimal body composition maintenance for the elderly. As the more common body mass index (BMI) in older individuals does not reflect true body composition and may underestimate lean and fat composition, body fat localization as well as weight need to be kept under control. The possibility has to be considered that the body-fat /cognition relationship may be circular in nature. Therefore, proposing interventions aimed at improving body composition may preserve cognitive functions, or alternatively, proposing interventions aiming at improving cognitive functions may stimulate healthy lifestyle and positively affect obesity. Clearly, recommendations for healthy aging cannot include being overweight, given the well-known detrimental effects obesity has on general health. However, it seems reasonable to support the notion that maintaining a certain proportion of body fat may help prevent cognitive decline. Physical exercise is known to have positive effects on weight maintenance, body fat/lean mass control, CVD risk factors and maintenance of cognitive functions. Therefore, it seems reasonable to recommend exercise of a multi-component nature, including strengthening to keep lean mass, mild aerobic exercise to keep weight under control, as well as exercise to improve cognitive functions such as that proposed by Forte et al. (58).

Limitations of the study include the correlational nature of the analyses and the cross-sectional design of the study, so that causality could not be inferred, and the lack of measurements of hormonal levels, so that the relationships between estrogen, gynoid fat and cognition could only be presumed. Also, the relatively small number of participants, especially men, does not allow more robust conclusions. Larger and gender balanced samples of participants could have enhanced the generalizability of the measured associations allowing a better understanding of the effects of body fat on cognition. Limiting the age range to healthy well-functioning young old (65-75 years) enabled the exclusion of ill-health as an influence on the variables of interest (e.g. hypertension, diabetes, hypercholesterolaemia, hypertriglyceridaemia) but reduced the representativeness of the sample. Furthermore, information regarding health was mainly self-reported, hence liable to errors, and the possibility can not be excluded that such conditions accounted for some of the effects on cognition. Future studies should employ direct measurements of these factors. Applying a prospective cohort design with a larger sample might allow the estimation of risk of cognitive deterioration in relation to body fat accumulation or changes. Other variables known to affect health and cognition, such as education, social engagement and marital status were not verified and their potential influence on the present results can not be excluded. The authors are aware of the fact that DXA is an indirect technique which cannot distinguish between visceral and subcutaneous fat. However, the advantages of using DXA include measures of subcutaneous fat, bone and

THE BODY FAT-COGNITION RELATIONSHIP IN HEALTHY OLDER INDIVIDUALS

fat-free tissue in the whole body or in specific regions, e.g. android and gynoid, with less radiation exposure to patients compared with direct measures such as CT scanning, and is less expensive than MRI. Furthermore, DXA has been found to be as valid as direct measurements in the elderly (59), and highly correlated with abdominal visceral fat in older subjects (4). Future studies might also take advantage from rapid and noninvasive measurements of body fat by means of three-dimensional photonic scanning (60). Finally, as regards the analysis of whether gynoid fat and gender jointly predicted working memory updating, the absence of significant results cannot be interpreted univocally, as a type II error could not be excluded because of the relatively small sample size for such type of analysis.

In conclusion, the present results, by showing an association between gynoid fat and the executive function of working memory, suggests a possible protective role of gynoid fat particularly in older women. They contribute to the understanding of the body fat-cognition relationship by drawing attention to the importance of fat localization in relation to specific aspects of high-level cognition relevant in aging. Further studies should verify this role in larger cohort population samples and, due to the complexity of the relationship, through interdisciplinary research to better understand the mechanisms behind this relationship.

Ethical compliance: The experiments carried out in the study comply with the current laws of the country in which they were performed.

Conflict of interests: The authors have no conflict of interests to disclose

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References

- Fox CS, Massaro JM, Hoffmann U, Pou KM, Maurovich-Horvat P, Liu CY, Vasan RS, Murabito JM, Meigs JB, Cupples LA, D'Agostino RB Sr, O'Donnell CJ. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation 2007;116:39-48.
- Whitlock G, Lewington S, Sherliker P, Clarke R, Emberson J, Halsey J, Qizilbash N, Collins R, Peto R. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. Lancet 2009;28:1083-96. doi: 10.1016/S0140-6736(09)60318-4.
- Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, Lang CC, Rumboldt Z, Onen CL, Lisheng L, Tanomsup S, Wangai P Jr, Razak F, Sharma AM, Anand SS; INTERHEART Study Investigators. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. Lancet 2007;5:1640-9.
- Kang SM, Yoon JW, Ahn HY, Kim SY, Lee KH, Shin H, Choi SH, Park KS, Jang HC, Lim S. Android fat depot is more closely associated with metabolic syndrome than abdominal visceral fat in elderly people. PLoS One. 2011;6:e27694. doi: 10.1371/journal.pone.0027694.
- García-Ptacek S, Faxén-Irving G, Cermáková P, Eriksdotter M, Religa D. Body mass index in dementia Eur J Clin Nutr 2014;68:1204-9. doi: 10.1038/ejcn.2014.199.
- Whitmer RA, Gustafson DR, Barrett-Connor E, Haan MN, Gunderson EP, Yaffe K. Central obesity and increased risk of dementia more than three decades later. Neurology 2008;30:1057-64.doi: 10.1212/01.wnl.0000306313.89165.
- Fitzpatrick S, Gilbert S, Serpell L. Systematic review: are overweight and obese individuals impaired on behavioural tasks of executive functioning? Neuropsychol Rev 2013;23:138-56. doi: 10.1007/s11065-013-9224-7.
- Gunstad J, Lhotsky A, Wendell CR, Ferrucci L, Zonderman AB. Longitudinal examination of obesity and cognitive function: results from the Baltimore longitudinal study of aging. Neuroepidemiology 2010;34:222-9. doi: 10.1159/000297742.

- Reinert KR, Po'e EK, Barkin SL. The relationship between executive function and obesity in children and adolescents: a systematic literature review. J Obes 2013;2013:820956. doi: 10.1155/2013/820956.
- Schwartz DH, Leonard G, Perron M, Richer L, Syme C, Veillette S, Pausova Z, Paus T. Visceral fat is associated with lower executive functioning in adolescents. Int J Obes 2013;37:1336-43. doi: 10.1038/ijo.2013.104.
- Walther K, Birdsill AC, Glisky EL, Ryan L. Structural brain differences and cognitive functioning related to body mass index in older females. Hum Brain Mapp 2010;31:1052-64. doi: 10.1002/hbm.20916.
- Vaughan L, Giovanello K. Executive function in daily life: age-related influences of executive processes on instrumental activities of daily living. Psychol Aging 2010;25:343–355.
- Bove RM, Brick DJ, Healy BC, Mancuso SM, Gerweck AV, Bredella MA, Sherman JC, and Miller KK. Metabolic and Endocrine correlates of cognitive function in healthy young women. Obesity 2013;21:1343-49.
- West NA, Haan MN. Body adiposity in late life and risk of dementia or cognitive impairment in a longitudinal community-based study. J Gerontol A Biol Sci Med Sci 2009;64:103-9. doi: 10.1093/gerona/gln006.
- Yoon DH, Choi SH, Yu JH, Ha JH, Ryu SH, Park DH. The relationship between visceral adiposity and cognitive performance in older adults. Age Ageing 2012;41:456-61. doi: 10.1093/ageing/afs018.
- Kuo HK, Jones RN, Milberg WP, Tennstedt S, Talbot L, Morris JN, Lipsitz LA. Cognitive function in normal-weight, overweight, and obese older adults: an analysis of the Advanced Cognitive Training for Independent and Vital Elderly cohort. J Am Geriatr Soc 2006;54:97-103.
- Bagger YZ, Tankó LB, Alexandersen P, Qin G, Christiansen C. The implications of body fat mass and fat distribution for cognitive function in elderly women. Obes Res 2004;12:1519-26.
- Kanaya AM, Lindquist K, Harris TB, Launer L, Rosano C, Satterfield S, Yaffe K; Health ABC Study. Total and regional adiposity and cognitive change in older adults: The Health, Aging and Body Composition (ABC) study. Arch Neurol 2009;66:329-35. doi: 10.1001/archneurol.2008.570.
- Stewart R, Masaki K, Xue Q-L, et al. A 32-year prospective study of change in body weight and incident dementia. Arch Neurol 2005;62: 55–60. doi: 10.1001/ archneur.62.1.55
- Xiang X, An R. Body weight status and onset of cognitive impairment among U.S. middle-aged and older adults. Arch Gerontol Geriatr 2015;60:394-400. doi: 10.1016/j.archger.2015.02.008.
- Smith E, Bailey PE, Crawford J, Samaras K, Baune BT, Campbell L, Kochan N, Menant J, Sturnieks DL, Brodaty H, Sachdev P, Trollor JN. Adiposity estimated using dual energy X-ray absorptiometry and body mass index and its association with cognition in elderly adults. J Am Geriatr Soc 2014;62:2311-8. doi: 10.1111/ jgs.13157.
- Mayes JS, Watson GH. Direct effects of sex steroid hormones on adipose tissues and obesity. Obes Rev 2004;5:197-216.
- Mastaglia SR, Solis F, Bagur A, Mautalen C, Oliveri B. Kirschner MA, Samojlik E, Drejka M, Szmal E, Schneider G, Ertel N. Increase in android fat mass with age in healthy women with normal body mass index. J Clin Densitom 2012;15:159-64. doi: 10.1016/j.jocd.2011.12.006.
- Deslypere JP, Verdonck L, Vermeulen A. Fat tissue: a steroid reservoir and site of steroid metabolism. J Clin Endocrinol Metab 1985;61:564-70.
- McEwen BS, Alves SE, Bulloch K, Weiland NG. Ovarian steroids and the brain: implications for cognition and aging. Neurology 1997;48:S8-15.
- Schattman L, Sherwin B. Effects of pharmacologic manipulation of testosterone on cognitive functioning in women with polycystic ovary syndrome: a randomized placebo-controlled treatment study. Horm Behav 2007;51: 579–686.
- Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ, Lindeman RD. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol 147:755-63. Erratum in: Am J Epidemiol 1998;149:1161.
- Kyle UG, Genton L, Hans D, Karsegard L, Slosman DO, Pichard C. Age-related differences in fat-free mass, skeletal muscle, body cell mass and fat mass between 18 and 94 years. Eur J Clin Nutr 2001;55:663-72.
- Pasco JA, Holloway KL, Dobbins AG, Kotowicz MA, Williams LJ, Brennan SL. Body mass index and measures of body fat for defining obesity and underweight: a cross-sectional, population-based study. BMC Obes 2014;23:1:9. doi: 10.1186/2052-9538-1-9.
- Isaac V, Sim S, Zheng H, Zagorodnov V, Tai ES, Chee M. Adverse Associations between Visceral Adiposity, Brain Structure, and Cognitive Performance in Healthy Elderly. Front Aging Neurosci 2011;13:12. doi: 10.3389/fnagi.2011.00012.
- Boeka AG, Lokken KL. Neuropsychological performance of a clinical sample of extremely obese individuals. Arch Clin Neuropsychol 2008;23:467-74. doi: 10.1016/j.acn.2008.03.003.
- Calvo D, Galioto R, Gunstad J, Spitznagel MB. Uncontrolled eating is associated with reduced executive functioning. Clin Obes 2014;4:172-9. doi: 10.1111/ cob.12058.
- Annesi JJ, Porter KJ. Behavioural support of a proposed neurocognitive connection between physical activity and improved eating behaviour in obese women. Obes Res Clin Pract 2014;8:e325-30. doi: 10.1016/j.orcp.2013.08.001.

JNHA: CLINICAL NEUROSCIENCES

- Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living Gerontologist 1969;9:179-86.
- 35. Greig CA, Young A, Skelton DA, Pippet E, Butler FM, Mahmud SM. Exercise studies with elderly volunteers. Age Ageing 1994;23:185-9.
- Strauss E Sherman EM, Spreen O. Trail Making Test. In Strauss E, Sherman EMS, Spreen O (eds) A Compendium of Neuropsychological Tests. Administration, Norms, and Commentary 3rd edn. Oxford University Press, 2006;pp 655-677
- Baddeley A, Emslie H, Kolodny J, and Duncan J. Random Generation and the Executive Control of Working Memory. Q J Exp Psychol A 1998;51A: 819-852.
- Towse J and Cheshire A. Random number generation and working memory. European Journal of Cognitive Psychology 2007;19: 374-394.
- Albinet C, Tomporowski PD, Beasman K. Aging and concurrent task performance: cognitive demand and motor control. Educational Gerontology 2006;32:689–706.
- Towse J and Neil D. Analyzing human random generation behavior: A review of methods used and a computer program for describing performance. Behavior Research Methods, Instruments, & Computers 1998;30:583-591.
- 41. Kerwin DR, Zhang Y, Kotchen JM, Espeland MA, Van Horn L, McTigue KM, Robinson JG, Powell L, Kooperberg C, Coker LH, Hoffmann R. The cross-sectional relationship between body mass index, waist-hip ratio, and cognitive performance in postmenopausal women enrolled in the Women's Health Initiative. J Am Geriatr Soc 2010;58:1427-32. doi: 10.1111/j.1532-5415.2010.02969.x.
- Smith E, Hay P, Campbell L, Trollor JN. A review of the association between obesity and cognitive function across the lifespan: implications for novel approaches to prevention and treatment. Obes Rev 2011;12:740-55. doi: 10.1111/j.1467-789X.2011.00920.x.
- Zeki Al Hazzouri A, Haan MN, Whitmer RA, Yaffe K, Neuhaus J. Central obesity, leptin and cognitive decline: the Sacramento Area Latino Study on Aging. Dement Geriatr Cogn Disord 2013;33:400-9 doi: 10.1159/000339957.
- Pettersen JA. Vitamin D and executive functioning: Are higher levels better? Clin Exp Neuropsychol 2015;27:1-11.
- 45. Oliai Araghi S, van Dijk SC, Ham AC, Brouwer-Brolsma EM, Enneman AW, Sohl E, Swart KM, van der Zwaluw NL, et al. BMI and Body Fat Mass Is Inversely Associated with Vitamin D Levels in Older Individuals. J Nutr Health Aging 2015;19:980-5 doi: 10.1007/s12603-015-0507-y.
- Barnes DE, Cauley JA, Lui LY, Fink HA, McCulloch C, Stone KL, Yaffe K. Women who maintain optimal cognitive function into old age. J Am Geriatr Soc 2007;55:259-64.
- 47. Dore GA, Elias MF, Robbins MA, Budge MM, Elias PK. Relation between central

adiposity and cognitive function in the Maine-Syracuse Study: attenuation by physical activity. Ann Behav Med 2008;35:341-50. doi: 10.1007/s12160-008-9038-7.

- Lo AH, Pachana NA, Byrne GJ, Sachdev PS, Woodman RJ. Relationship between changes in body weight and cognitive function in middle-aged and older women. Int J Geriatr Psychiatry 2012;27:863-72. doi: 10.1002/gps.2797.
- Yates KF, Sweat V, Yau PL, Turchiano MM, Convit A. Impact of Metabolic Syndrome on Cognition and Brain: A Selected Review of the Literature. Arterioscler Thromb Vasc Biol 2012;32: 2060–2067. doi: 10.1161/ATVBAHA.112.252759
- 50. Vague J. A determinant factor of the forms of obesity. Obes Res 1996;4:201-203.
- Dixon JB, Strauss BJ, Laurie C, O'Brien PE. Smaller hip circumference is associated with dyslipidemia and the metabolic syndrome in obese women. Obes Surg 17:770– 777.
- Lebrun CE, van der Schouw YT, de Jong FH, Pols HA, Grobbee DE, Lamberts SW. Endogenous oestrogens are related to cognition in healthy elderly women. Clin Endocrinol 2005;63:50-5.
- 53. LeBlanc ES, Janowsky J, Chan BK, Nelson HD. Hormone replacement therapy and cognition: systematic review and meta-analysis. JAMA 2001;285:1489-99.
- Li J, Papadopoulos V, Vihma V. Steroid biosynthesis in adipose tissue. Steroids 2015;103:89-104. doi: 10.1016/j.steroids.2015.03.016.
- Bremser JA, Gallup GG Jr. Mental state attribution and body configuration in women. Front Evol Neurosci 2012;30;4:1. doi: 10.3389/fnevo.2012.00001.
- Hegele RA, Joy TR, Al-Attar SA, Rutt BK. Thematic review series: Adipocyte Biology. Lipodystrophies: windows on adipose biology and metabolism. J Lipid Res 2007;48:1433-44.
- Umegaki H. Type 2 diabetes as a risk factor for cognitive impairment: current insights. Clin Interv Aging 28:1011-9. doi: 10.2147/CIA.S48926.
- Forte R, Boreham CA, Leite JC, De Vito G, Brennan L, Gibney ER, Pesce C. Enhancing cognitive functioning in the elderly: multicomponent vs resistance training. Clin Interv Aging 2013;8:19-27. doi: 10.2147/CIA.S36514.
- Snijder MB, Visser M, Dekker JM, Seidell JC, Fuerst T, Tylavsky F, Cauley J, Lang T, Nevitt M, Harris TB. The prediction of visceral fat by dual-energy X-ray absorptiometry in the elderly: a comparison with computed tomography and anthropometry. Int J Obes Relat Metab Disord 2002;26:984-93.
- Shitara K, Kanehisa H, Fukunaga T, Yanai T, Kawakami Y. Validity of threedimensional photonic scanning technique for estimating percent body fat. J Frailty Aging 2013;2:192-197

THE BODY FAT-COGNITION RELATIONSHIP IN HEALTHY OLDER INDIVIDUALS