

Cognitive, Olfactory, and Affective Determinants of Body Weight in Aging Individuals

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Abstract

Objective: A complex interplay of factors including cognitive, sensory and affective aspects has been associated in a controversial way with anthropometric measures related to body weight.

Methods: Here we propose two studies to investigate whether and how cognitive, olfactory and affective variables resulted associated with body weight during healthy aging. In Study 1, we investigated the cognitive status, the odor identification skills, and the BMI of 209 individuals (50–96 yo). In Study 2 an extensive evaluation of cognitive functions (in particular executive functions and memory), odor threshold, discrimination and identification and affective skills (i.e., depression and anxiety) was performed in a group of 35 healthy, free-living aging individuals (58–85 yo).

Results: In Study 1, greater BMI was not associated with performance on the odor identification task but was significantly associated with better cognitive skills. In Study 2, we observed that executive functions seemed to favor a successful managing of body weight, and individuals with greater BMI and waist circumference showed significantly better odor discrimination skills. Finally, lower waist circumference (but not BMI) was found significantly associated with greater levels of anxiety.

Conclusions: These results confirm that cognitive, olfactory and affective factors may influence body weight during healthy aging.

Keywords: Anxiety; Body weight; Cognitive functions; Depression; Olfaction

Introduction

Understanding factors associated with healthy aging is vitally important to explain how our rapidly aging population may unfold. In particular, body weight and nutritional health represent key issues in evaluating the well-being and quality of life of older adults. By and large, in healthy adults, body weight and body fat increase through approximately age 55–65 years in both men and women and typically decrease after approximately age 65–75 years, leading to a condition described as “anorexia of aging”, which is characterized by reduced appetite and food intake (Barone et al., 2006; Peter, Fromm, Klenk, Concini, & Nagel, 2014). However, obesity prevalence has dramatically increased in the last years in all age groups, including those of 65 years old and older (Fakhouri, Ogden, Carroll, Kit, & Flegal, 2012), thus making the aging individuals a heterogeneous group with respect to BMI. Importantly, according to the *obesity paradox*, being obese before turning 65 years has a positive association with cardiovascular disease and dementia, while such association is negative in those aged 65 and over (Chapman, 2010; Hainer & Aldhoon-Hainerová, 2013). It became thus mandatory for the clinicians to understand factors associated with body weight

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changes during aging. Overall, these mechanisms are complex and include both metabolic and non-metabolic factors (for a review see De Boer, Ter Horst & Lorist, 2013). Metabolic factors consider – among others – alterations in energy intake and expenditure as well as changes in neuroendocrine mechanisms (i.e., Michalakis et al., 2013; Visvanathan, 2015), whereas non-metabolic factors refer to sensory, cognitive and affective aspects. Recently, the interest for the impact of non-metabolic factors on body weight dynamics has greatly increased, producing a wealth of research in this area (Doets & Kremer, 2016).

As one gets older, sensory disturbances are frequently experienced, particularly within the chemical senses, the sensory modalities that affect more directly food choices and consumption (e.g., Doets & Kremer, 2016). Indeed, decreased olfactory function is commonly reported, with percentages varying from 13.9% to 50% in older people between 65 and 80 (Doty et al., 1984; Schubert et al., 2011, 2017) and from 62.5% to 80% in those aged more than 80 years old (Murphy et al., 2002; Lafreniere et al. 2009). In particular, the aging individuals perceive odors as less intense and have poorer odor threshold, discrimination and identification (for reviews see Doty, Kamath, 2014 and Hummel, Heilmann, & Murphy, 2002). It is generally accepted that this decline in the ability to perceive odors in the aging individuals may be responsible for their diminished appetite, reduced food liking and in turn, poor nutritional status. However, strong evidence in this sense is scarce and the relationship with BMI is controversial (Doets & Kremer, 2016). While some studies have found a positive correlation between BMI and sensory performance (Aschenbrenner et al., 2008; Boesveldt, Lindau, McClintock, Hummel & Lundström, 2011; Kim, Hur, Cho, & Lee, 2003; Simchen, Koebnick, Hoyer, Issanchou, & Zunft, 2006), others have found no association at all (Duffy, Backstrand, & Ferris, 1995; De Jong, Mulder, de Graaf, & van Staveren, 1999). Recently, Toussaint, de Roon, van Campen, Kremer, and Boesveldt (2015) assessed the relationship between olfactory performance and nutritional status in two samples: a group of 445 healthy aging individuals and a group of 138 geriatric older adults with cognitive decline. A significant correlation between olfaction and BMI was observed only in the second group. However, the correlation lost its significance after controlling for confounding factors such as age, cognitive status and depression, suggesting that a complex interplay between sensory and cognitive factors may underline BMI.

Cognitive and emotional factors may indeed play an important role in influencing body weight during aging. On the one hand, studies on neurological populations have highlighted a possible link between body weight, food intake alterations and cognitive functions, especially executive functions and memory (Aiello, Eleopra, & Rumiati, 2015, 2016). *Executive functions* is an umbrella term grouping distinct processes involved in the control of goal directed behavior, which include mental flexibility/set shifting, working memory and inhibitory control (Funahashi, 2001). It has been shown that a reduced performance on executive tasks allows distinguishing obese from non-obese individuals, with worse executive functions associated with increased food intake and risk of weight gain (Vainik et al., 2013). In addition, low BMI has also found to be associated with better working memory (as well as nonverbal memory) skills. Executive functions and memory typically decline with aging (Marschner et al., 2005), but little is known as to whether and how a decline of these functions may influence body weight regulation in healthy aging individuals (Smith, Hay, Campbell & Trollor, 2011, but see Aiello et al., 2018).

On the other hand, body weight and food intake are closely linked to affective disturbances such as depression and anxiety (Zhao et al., 2009). Depression, which is commonly reported among older adults (Valiengo, Stella, & Forlenza, 2016), is often accompanied by a decrease in appetite and body weight loss in individuals above 55 years of age and has been found to be a predictor of malnutrition among the aging individuals (De Boer et al. 2013). Instead, trait anxiety is positively associated with food intake in stressful situations (Pollard, Steptoe, Canaan, Davies, & Wardle, 1995), as well as increments in food intake in obese but not in lean individuals (Schneider, Appelhans, Whited, Oleski, & Pagoto, 2010).

Our exploratory studies aim to investigate whether and how cognitive, olfactory and affective variables influence body weight during healthy aging. In Study 1, we enrolled a large sample of individuals ($N = 209$) aged between 50 and 96 years old and collected data on cognitive status, olfactory skills and BMI. In Study 2, we enrolled a smaller sample of 35 individuals aged between 58 and 85 years old and assessed their cognitive functions (in particular executive functions and memory), olfactory performance (threshold, discrimination, and identification measures) and also affective status (anxiety and depression). Since aging is often characterized by a progressive decrease in muscle mass accompanied by an increase in fat mass (Kalyani, Tra, Egan, Ferrucci, & Brancati, 2014), and BMI does not capture this aspect, in this second study, we also measured waist circumference.

Methods

Study 1

Participants. Recruitment was carried out through flyers (distributed, for example, at the university campus, bakeries, pharmacies, and fitness studios), advertisement in local newspapers and word of mouth. All participants gave their informed consent to take part in the study. This cooperative project was approved by the Ethics Committee of the Technische Universität

Measures

Data Analysis

Results

Study 2

Table 1. Description of the sample included in Study 1

$N = 209$	Levels	Overall	Range/max
Sex	M	70 (33.5%)	
	F	139 (66.5%)	
Country	Germany	153 (73.2%)	
	Italy	56 (26.8%)	
BMI		26.15 (4.15)	18–39
Age (years)		70.45 (11.42)	50–96
MMSE		29.40 (1.00)	26–30/30
Odor ID		11.00 (3.35)	2–16/16

Note: Categorical variables are reported as *N* (%) whereas continuous variables are reported as mean (*SD*).

Table 2. Heterogeneous correlation matrix for Study 1

	Sex	Country	BMI	Age	MMSE	Odor ID
Sex		−0.312	−0.048*	−0.008**	0.023***	0.251
Country	<i>NA</i>		−0.186	0.174***	−0.003***	−0.177*
BMI	<i>0.023</i>	<i>0.139</i>		−0.116*	0.033***	0.127
Age	<i>0.003</i>	<i>3.40E−05</i>	<i>0.005</i>		−0.046***	−0.599
MMSE	<i>1.45E−42</i>	<i>1.43E−42</i>	<i>9.13E−38</i>	<i>1.47E−39</i>		−0.015***
Odor ID	<i>0.302</i>	<i>0.025</i>	<i>0.293</i>	<i>0.589</i>	<i>1.68E−38</i>	

Note: The cells above the diagonal represent the polychoric (ordinal/continuous variables) or Pearson's (continuous/continuous variables) correlation coefficients depending on the pair of variables associated. The cells below the diagonal (italic) represent the *p*-values for the tests of bivariate normality. * = *p* < .05; ** = *p* < .01; *** = *p* < .001.

olfactory abilities. In addition, we also evaluated affective dimensions such as depression and anxiety, which were neglected in Study 1, through self-report measures. Moreover, we measured waist circumference, which is considered a more reliable body weight index than BMI during aging. In this study, we aimed to identify clusters of variables that segregate into various domains, capturing patterns of associations between anthropometric, cognitive, affective, and sensory variables (Table 3).

Participants

Recruitment and selection of participants were the same as Study 1. The project was approved by the SISSA ethic committee and complied with the Declaration of Helsinki.

Measures

Neuropsychological Test Battery. The neuropsychological test battery included the following measures: the Mini Mental State Examination (MMSE; Folstein et al., 1975) and the Montreal Cognitive Assessment (MOCA; Nasreddine et al., 2005), two tests assessing general cognitive functions; forward digit span, Corsi span and the Serial Position Curve Test (Spinnler & Tognoni, 1987) which assess short and long-term memory; phonemic and semantic fluency tasks which evaluate response generation and maintenance of task instructions in memory (Novelli et al., 1986); the Stroop Color/Word Interference Test (Caffarra et al., 2002), the Trail Making Test, Parts A (TMT-A) and B (TMT-B) (Giovanoli et al., 1996) which measure processing speed/attention with a component of executive functions and finally, the Frontal Assessment Battery (FAB) for frontal functioning (Appollonio et al., 2005). This last battery is composed by six subtests: conceptualization (similarities task), mental flexibility (phonological fluency task), motor programming (Luria's motor series), sensitivity to interference (conflicting instructions task), inhibitory control (go/no-go task) and environmental autonomy (prehensile behavior).

Standardized olfactory testing. Olfactory testing was performed using the Sniffin' Sticks test kit (Hummel, Kobal, Gudziol, & Mackay-Sim, 2007) which includes tests for *odor threshold*, *odor discrimination*, and *odor identification*. *Odor threshold* is assessed by a single-staircase, 3-alternative forced choice procedure. Three pens are presented to the participant. Two of them contain odorless solvent and the other an odorant in a certain dilution. The participant has to indicate the pen with the odorant. Concentration is increased if one of the blanks is chosen and decreased if the correct pen is identified twice in a row. The mean of the last four reversal points is used as detection threshold (ranging from 1 to 16). Sixteen odor concentrations are tested starting from a 4% stock solution. In the *discrimination task*, 16 triplets of pens are presented to the participants, each including two identical odors and a different one. The participant has to indicate the pen, which have a different odor. The score is the sum of correct responses ranging from 0 to 16. The *odor identification* was the same as in Study 1. The sum of the scores from the three subtests gives a TDI-score (Threshold, Discrimination, Identification) with a maximum of 48 points. A score of 30.5 or more indicates normosmia, a score between 16.5 and 30 indicates reduced olfactory function in terms of hyposmia, and a score of less than 16.5 indicates functional anosmia (Hummel et al., 2007).

Affective evaluation

We used the Beck Depression scale (BDI-II; Beck et al., 1961) to assess the presence of depression and measure severity of depressive symptoms. Scores at this questionnaire range from 0 to 63. In addition, participants filled the Hospital Anxiety and Depression Scale (HADS, Zigmond et al., 1983) and the State-Trait Anxiety Inventory (STAI, Spielberger et al., 2017).

Table 3. Description of the sample included in Study 2

<i>N</i> = 35	Overall	Range/max
Demographics		
Sex		
M	14 (40.0%)	
F	21 (60.0%)	
Age (years)	73.7 (6.1)	58–85
Education (years)	12 (3.7)	8–18
Weight		
BMI	26.6 (3.5)	20–34
Waist circumference (cm)	83.5 (18.6)	46–117
Cognition		
MMSE	29.5 (0.8)	26–30
MOCA	24.9 (2.7)	20–30
Digit Span	6.1 (0.9)	4–8
Corsi Span	4.9 (1.0)	3–7
SPC Primacy	5.2 (2.3)	1–10
SPC Recency	13.8 (4.0)	4–19
Phonemic Fluency	45.5 (12.8)	24–85
Semantic Fluency	47.1 (9.4)	32–71
TMT (A) (s)	40.9 (13.6)	16–77
TMT (B) (s)	110.3 (46.0)	50–219
TMT (B-A) (s)	69.4 (38.7)	21–165
FAB	15.9 (1.7)	11–18
Emotion		
HADS – Anxiety	5.7 (3.6)	0–15
HADS – Depression	4.0 (3.2)	0–14
BDI	7.4 (6.2)	0–26
STAI Trait	35.1 (9.1)	21–53
Perception		
Odor Threshold	7.1 (4.0)	0–16
Odor Discrimination	10.7 (3.1)	4–14
Odor Identification	10.5 (2.7)	5–15
Odor TDI	28.2 (6.8)	10–40

Note: Categorical variables are reported as *N* (%) whereas continuous variables are reported as mean (*SD*). Neuropsychological data are reported as raw data. BMI = body-mass index; MMSE = Mini mental State Examination; MOCA = Montreal Cognitive Assessment; SPC = Serial Position Curve Test; TMT = Trial Making Test; FAB = Frontal Assessment Battery; HADS = Hamilton Anxiety and Depression Scale; BDI = Beck Depression Inventory; STAI = State and Trait Anxiety Inventory.

The HADS, is a 14-item self-report scale for symptoms of both depression and anxiety (HADS-D and HADS-A). The score may range between 0 and 21 per subscale. The STAI consists of a state anxiety scale and a trait anxiety scale; both have 20 items. The sum score has a range from 20 to 80.

Anthropometry

We measured weight, height and waist circumference. Weight was measured using an electronic balance with participants wearing clothing without shoes. Height was measured using a meter in cm. Waist circumference was taken from the natural waist using a standardized measuring tape. Body mass index (BMI, kg/m²) was computed using weight (kg) divided by height squared (m²).

Analyses

Most measures are standardized following the criterion higher number indicates lower impairment (e.g., MMSE). However, some are not (i.e., in TMT, higher RT, higher impairment). As a first step, we have put all variables in the same space by changing the sign to some measures (i.e., the TMT RT was reversed). Subsequently, a principal component analysis (PCA) was implemented using FactoMineR (Factor analysis and data Mining with R) package (Husson, Josse, Lê & Mazet, 2009) via the function *PCA*. Such function uses the singular value decomposition method considered the one that achieves the best numerical accuracy and scales the variables. The approach used by the FactoMineR package is based on the

maximization of the variance of the projected points and does not use rotational algorithms. Each dimension (or principal component) of a multivariate analysis can be described by the variables (quantitative and/or qualitative; active or supplementary) and by the individuals (active or supplementary). An active variable or individual is included in the initial analysis; supplementary variables and individuals are used to test whether the structure of the data is reliable. For each quantitative variable, dimension by dimension, the correlation coefficient between the variable and the coordinates of the active individuals on the axis is calculated. To facilitate the discussion, we only considered variables with coefficient correlations ≥ 0.5 . To sort the variables from the most to the least correlated, the significance of each correlation is evaluated. For each qualitative variable, one-way ANOVAs with the coordinates of the individuals on the axis explained by the qualitative variable are performed. In all cases, the significance level was set at 0.05.

Results

Figure 1 represents the screeplot of the eigenvalues of each dimension (or principal component). The first dimension shows the highest eigenvalue and it explains the most variance, whereas the subsequent dimensions show decreasing eigenvalues and contribute progressively less to the explanation of additional variance. According to the Kaiser–Harris criterion, we first selected eight components with eigenvalues greater than 1, which overall explain 81% of the variance.

Based on the significant correlations of the variables describing each dimension, we reduced the number of relevant dimensions to 5 (Table 4). Considering the contribution of each variable, we can interpret the five dimensions as representing: (1) high executive functions and low affective disturbance; (2) high cognitive status and olfaction; (3) high body weight, high odor discrimination and low cognitive flexibility; (4) high anxiety and low waist circumference; and (5) high cognitive performance.

Figure 2 was created to spatially represent the relationships of the variables in the five dimensions. The biplot, which includes the projections plotted between the variables' loadings of dimension 1 and 2, uses the direction and length of a vector to show grouping patterns. Positively correlated variables are grouped together. Here, it is evident that the emotional variables (HADS_A, HADS_D, STAI_T, BDI) are grouped together, as are the TMT versions [TMT-A, TMT-B, TMT (B-A)], the olfactory variables (Odor THR, Odor DIS, Odor ID, Odor TDI) and the MMSE, and the remaining cognitive variables. Negatively correlated variables are positioned on opposite sides of the plot origin. The emotional variables are negatively correlated with the TMT variables, since they are grouped at different opposites of dimension 1. The distance between variables and the origin, as well as the color code, indicates the quality of the variables on the factor map. The variables that are positioned the farthest away from the origin are the reddest and are well represented on the factor map.

Plotting individuals on the identified dimensions allows us to characterize an individuals' contribution to each dimension as well as it provides the grounds to evaluate whether the influence of the supplementary individuals can be predicted. As evident from Fig. 3, the supplementary individuals are positioned within the factor map previously determined.

Discussion

With the present studies, we investigated the relative contribution of cognitive and affective factors and their interactions with olfactory performance in influencing body weight during healthy aging, thus clarifying the nature of the association between the anthropometric measures related to body weight. The first result of Study 1 is that the BMI of 209 individuals aged 50–96 years was positively associated with the cognitive status but not with odor identification ability. This result is in

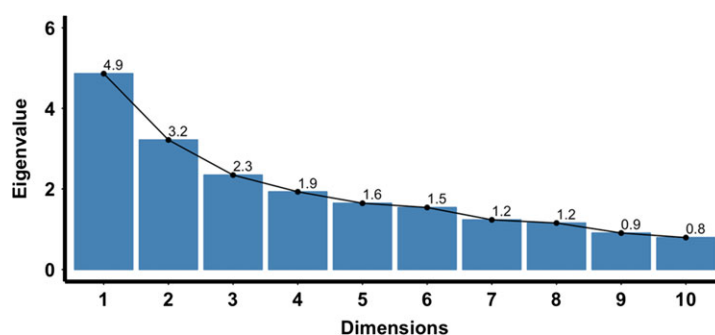


Fig. 1. Screeplot obtained by executing the PCA on all the variables included in Table 2 on 28/35 active individuals.

Table 4. Variables with significant correlations per dimension in the PCA.

Variables	Dimension 1		Dimension 2		Dimension 3		Dimension 4		Dimension 5	
	corr	p	corr	p	corr	p	corr	p	corr	p
TMT_B	0.7	0			−0.5	0.0056				
TMT_BA	0.6	1.00E−04			−0.6	6.00E−04				
TMT_A	0.6	1.00E−04								
Phonemic_Fluency	0.5	0.0019					0.4	0.014	−0.3	0.0473
Semantic_Fluency	0.5	0.0029					0.4	0.0083		
Education	0.5	0.0036								
MOCA	0.4	0.0111							0.6	3.00E−04
FAB	0.4	0.0256							0.5	0.0034
HADS_D	−0.6	2.00E−04								
BDI	−0.7	0					0.4	0.0189		
HADS_A	−0.7	0					0.5	0.0051	0.4	0.0242
STAI_T	−0.8	0								
Odor_TDI			0.9	0						
Odor_THR			0.7	0						
Odor_ID			0.7	0			0.4	0.0332		
MMSE			0.5	0.0073	0.4	0.0186			0.4	0.0104
CPS_Rececy			0.4	0.019						
Odor_DIS			0.4	0.0403	0.6	3.00E−04			0.4	0.0271
CPS_Primary			−0.3	0.0473						
Waist_Circumference			−0.4	0.0288	0.5	0.002	−0.5	0.0016		
BMI					0.6	4.00E−04				
Span_Corsi							0.4	0.0212	−0.4	0.0214
Eigenvalue	4.7		3.2		2.4		2		1.8	
Variance explained	20.60%		13.80%		10.30%		8.60%		7.80%	
Cumulative % of variance	20.6		34.4%		44.7		53.30%		61.10%	

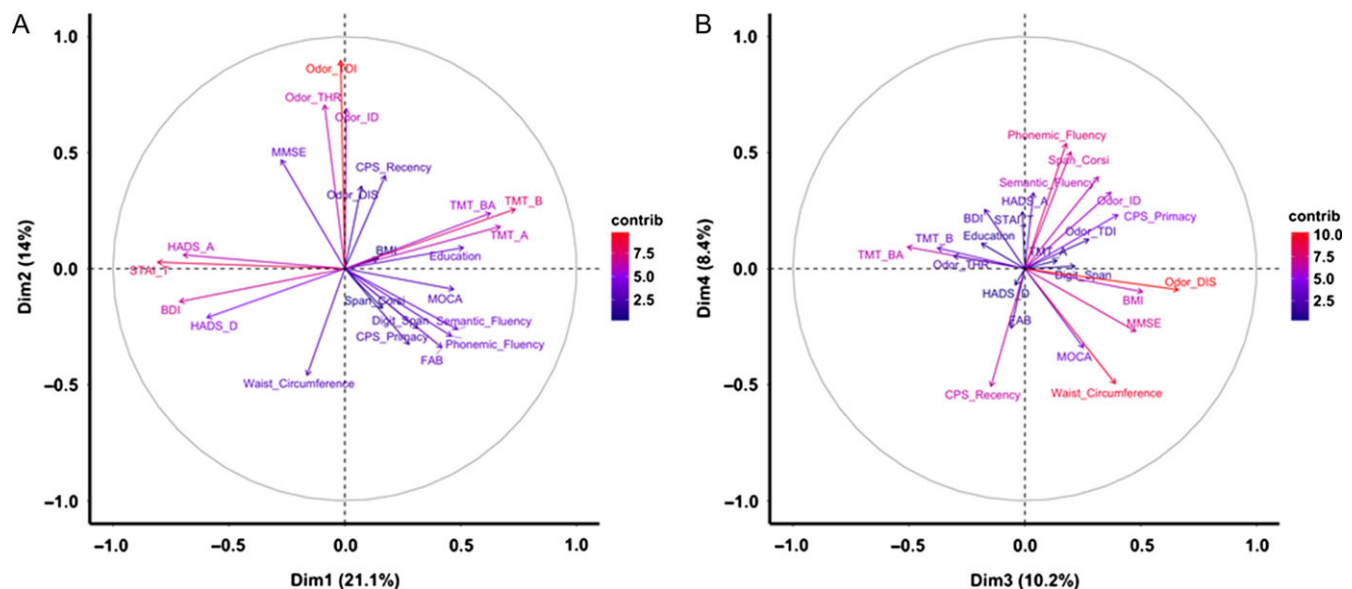


Fig. 2. Biplot to represent the factor map of the variables contributing to dimensions 1 and 2 (Panel A) and the variables contributing to dimensions 3 and 4 (Panel B). *Note.* The color code represents the contributions of variables in accounting for the variability in a given principal component are (in percentage): $(\text{variable.cos}^2 \times 100) / (\text{total cos}^2 \text{ of the component})$. Red values indicate the highest contributions, purple value the mid contributions and blue values the low contribution

accordance with different studies reporting that higher body weight in aging individuals is associated with better cognition and a reduced risk of cognitive decline. For instance, a recent large retrospective cohort study involving nearly 2 million individuals aged 40 years or older, has shown that being underweight in middle age and old age is associated with an increased

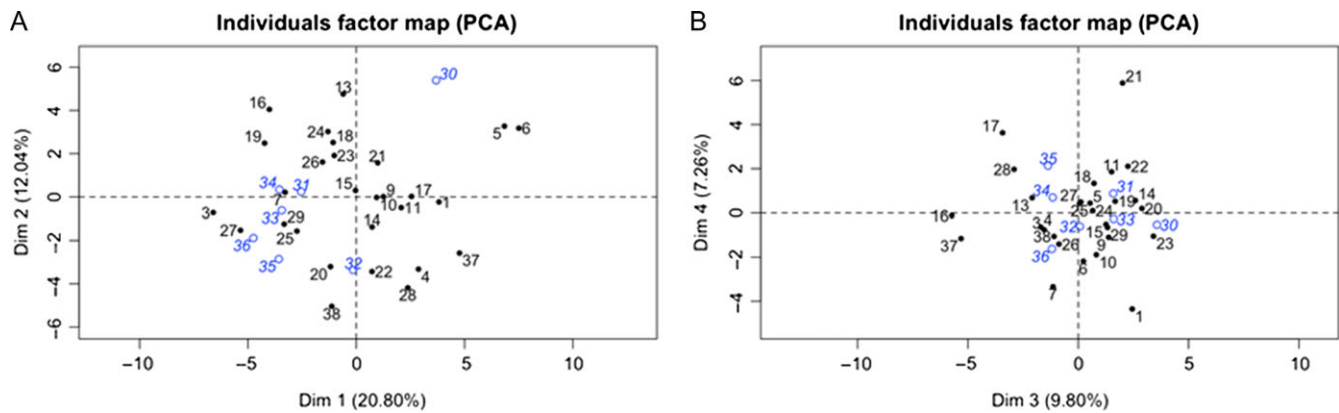


Fig. 3. Plot representing the factor map including the active individuals (in black) and the supplementary individuals (in blue) contributing to dimensions 1 and 2 (panel A) and to dimensions 3 and 4 (Panel B).

risk of dementia (Qizilbash et al., 2015). However, the association between BMI and cognitive status remains controversial, with some studies reporting even an inverse relationship, suggesting that other factors may mediate the association between BMI and cognition (see Albanese et al., 2017). The second finding of Study 1 is the absence of an association between BMI and olfactory identification skills. Studies that have addressed this issue have led so far to discordant results, with some showing a positive association (Duffy et al., 1995; De Jong et al. 1999) and others not being able to report such finding (Aschenbrenner et al., 2008; Boesveldt et al., 2011; Kim et al., 2003; Simchen et al., 2006). This inconsistency might be due to the differences across samples, and the measures that have been employed across studies. To account for a higher number of factors, in Study 2, we extended the evaluation of cognitive and olfactory abilities, and measured waist circumference. Moreover, we included an evaluation of affective measures such as the presence of symptoms of depression and anxiety. In this study, involving 35 healthy aging individuals aged 58–85 years, we performed a principal component analysis in order to identify clusters of variables that segregate into various domains capturing patterns of associations between anthropometric, cognitive, affective, and olfactory variables. We identified five dimensions accounting for 61.10% of the observed variance. A common variance was observed between high executive functions and low affective disturbance (*dimension 1*), high cognitive status and olfaction (*dimension 2*), high body weight, high odor discrimination and low cognitive flexibility (*dimension 3*), high anxiety and low waist circumference (*dimension 4*) and finally high cognitive performance (*dimension 5*).

Considering the aim of our study, three dimensions revealed interesting associations between body weight and non-metabolic variables (aka cognitive, olfactory and affective variables). *Dimension 3* showed that higher BMI and waist circumference were associated with worse executive functions, measured by the Trail Making Test-part B. The TMT is a widely used neuropsychological test, commonly administered to investigate cognitive decline in neurodegenerative diseases. In particular, the part B of this task measures set-shifting, attentional switching, simultaneous maintenance of two sequences and working memory. This result is line with the literature showing that overweight/obese individuals exhibit more difficulties with executive functions than normal weight individuals do and that BMI resulted inversely associated with prefrontal brain perfusion and performance in executive function tests (Vainik et al., 2013). At the same time, this result seems in contrast with what found in our Study 1 that BMI had an overall protective effect on cognition. As a matter of fact, obesity resulted associated with cognitive deficits, especially in executive functions, in children, adolescents and adults, but evidence is more controversial in older adults, with some studies showing that obesity is negatively associated with cognition and others reporting a positive association with cognitive performance (for reviews see, Smith et al., 2011 and Dahl & Hassing, 2012). Several aspects need, however, to be considered. First, the limitation of the BMI as a measure of adiposity in aging individuals; secondly, the type of cognitive measure used (Smith et al., 2011). Third, the fact that the relation between obesity and cognition may be mediated by comorbid metabolic and vascular disorders (see for instance, Gunathilake et al., 2016). This study suggests that, in order to understand the association between BMI and cognition, a deeper evaluation of cognitive functions is required.

In addition, BMI and waist circumference was associated also with better olfactory discrimination abilities, while no associations were found with odor identification (as we report in Study 1) and threshold scores. Even though this finding needs to be verified within a greater sample of participants, it points out a differential involvement of discrimination and identification olfactory abilities in influencing BMI. Olfactory discrimination requires participants to detect similarities and differences between odors and this operation requires working memory and decision-making processes. Therefore, performance in

