JNS JOURNAL OF NUTRITIONAL SCIENCE



RESEARCH ARTICLE

Association between adiposity levels and cognitive impairment in the Chilean older adult population

Y. Concha-Cisternas^{1,2}†, F. Lanuza³†, H. Waddell⁴† , Anne Sillars⁴, A. M. Leiva⁵, C. Troncoso⁶, M. A. Martinez⁷, M. Villagrán⁸, L. Mardones⁸, M. Martorell⁹, G. Nazar¹⁰, N. Ulloa¹¹, A. M. Labraña⁹, X. Diaz-Martinez¹², K. Sadarangani^{13,14}, C. Alvarez¹⁵, R. Ramirez-Campillo¹⁵, Alex Garrido-Mendez¹⁶, Cristian Luarte¹⁷, Frederick Ho¹⁸, Stuart R. Gray⁴, F. Petermann-Rocha¹⁸, C. Celis-Morales^{4,18,19}* and on behalf of the ELHOC Research Group

(Received 4 April 2019 - Final revision received 28 June 2019 - Accepted 1 July 2019)

Journal of Nutritional Science (2019), vol. 8, e33, page 1 of 8

doi:10.1017/jns.2019.24

Abstract

Although both obesity and ageing are risk factors for cognitive impairment, there is no evidence in Chile on how obesity levels are associated with cognitive function. Therefore, the aim of the present study was to investigate the association between adiposity levels and cognitive impairment in older Chilean

Abbreviations: CNHS, Chilean National Health Survey; MMSE, Mini-Mental State Examination; WC, waist circumference.

† Contributed equally to this paper; therefore, they are considered joint first authors.

© The Author(s) 2019. This is an Open Access article, distributed under the terms of the Creative Commons Attribution licence (http://creative-commons.org/licenses/by/4.0/), which permits unrestricted re-use, distribution, and reproduction in any medium, provided the original work is properly cited.

¹Escuela de Kinesiología, Facultad de Salud, Universidad Santo Tomás, Talca, Chile

²Universidad Autónoma de Chile, Talca, Chile

³Departamento de Pediatría y Cirugía Infantil, Universidad de la Frontera, Temuco, Chile

⁴Institute of Cardiovascular and Medical Science, University of Glasgow, Glasgow, UK

⁵Instituto de Anatomía, Histología y Patología, Facultad de Medicina, Universidad Austral de Chile, Valdivia, Chile

⁶CIEDE-UCSC, Facultad de Medicina, Universidad Católica de la Santísima Concepción, Concepción, Chile

⁷Instituto de Farmacia, Facultad de Ciencias, Universidad Austral de Chile, Valdivia, Chile

⁸Departamento de Ciencias Básicas, Universidad Católica de la Santísima Concepción, Concepción, Chile

⁹Departamento de Nutrición y Dietética, Facultad de Farmacia, Universidad de Concepción, Concepción, Chile

¹⁰Departamento de Psicología y Centro de Vida Saludable, Universidad de Concepción, Concepción, Chile

¹¹Departamento de Bioquímica Clínica e Inmunología, Facultad de Farmacia y Centro de Vida Saludable de la Universidad de Concepción,

¹²Grupo de Investigación Calidad de Vida, Departamento Ciencias de la Educación, Universidad del Biobío, Chillán, Chile

¹³Escuela de Kinesiología, Facultad de Ciencias de la Salud, Universidad San Sebastián, Santiago, Chile

¹⁴Escuela de Kinesiología, Facultad de Salud y Odontología, Universidad Diego Portales, Santiago, Chile

¹⁵Grupo de Investigación en Área Prioritaria Bienestar Humano y Calidad de Vida, Departamento de Ciencias de la Actividad Física, Actividad Física y Deporte, Universidad de los Lagos, Osorno, Chile

¹⁶Departamento de Ciencias del Deporte y Acondicionamiento Físico, Universidad Católica de la Santísima Concepción, Concepción, Chile

¹⁷Escuela de Educación Física, Universidad San Sebastián, Concepción, Chile

¹⁸Institute of Health and Wellbeing, University of Glasgow, Glasgow, UK

¹⁹Centro de Investigación en Fisiología del Ejercicio (CIFE), Universidad Mayor, Santiago, Chile

^{*} Corresponding author: Carlos Celis-Morales, email Carlos.Celis@glasgow.ac.uk



adults. This cross-sectional study includes 1384 participants, over 60 years of age, from the Chilean National Health Survey 2009–2010. Cognitive impairment was evaluated using the Mini-Mental State Examination. BMI and waist circumference (WC) were used as measures of adiposity. Compared with people with a normal BMI, the odds of cognitive impairment were higher in participants who were underweight (OR 4·44; 95 % CI 2·43, 6·45; P < 0.0001), overweight (OR 1·86; 95 % CI 1·06, 2·66; P = 0.031) and obese (OR 2·26; 95 % CI 1·31, 3·21; P = 0.003). The associations were robust after adjustment for confounding variables. Similar results were observed for WC. Low and high levels of adiposity are associated with an increased likelihood of cognitive impairment in older adults in Chile.

Key words: Cognitive impairment: Adiposity: Obesity: Ageing: Elderly

In recent decades there has been a demographic shift characterised by an increase in the proportion of the population over 60 years of age⁽¹⁾. Indeed, it has been estimated that between 2015 and 2050 this population will rise to more than two billion people⁽²⁾. This shift has been observed in the Chilean population, where the prevalence of older adults is expected to increase from 19·9 % in 2017 to 21·6 % in 2050, reaching an average age of 80·5 years⁽³⁾. This will make it the nation with the highest life expectancy in Latin America⁽³⁾ and thus susceptible to the concurrent problems associated with an ageing population. Indeed ageing is, unfortunately, accompanied by a marked increase in chronic non-communicable diseases such as diabetes mellitus type 2, arterial hypertension and some types of cancer⁽⁴⁾.

On top of this, in Chile, an increase in the prevalence of underweight and obesity has been reported, affecting 7.8 and 65.4% of people aged over 65 years, respectively⁽⁵⁾. Older adults are likely to experience important body composition changes inherent with ageing⁽⁶⁾; however, in many cases, this undernutrition or obesity may be related to the adoption of unhealthy lifestyles, including poor diet and low levels of physical activity^(7,8). Previous studies have shown that underweight and obesity cause functional limitation⁽⁹⁾ and disability⁽¹⁰⁾ in the older adult. It has also been associated with some geriatric syndromes, such as urinary incontinence, falls and cognitive impairment^(11–14). Furthermore, cognitive impairment has been ranked as the sixth leading cause of death, and is responsible for 4% of premature deaths in adults aged >60 years, in Chile⁽¹⁵⁾.

As a result, nutritional status must be assessed as a health indicator in older adults, where BMI and waist circumference (WC), considered validated measurements of adiposity and metabolic risk, may be associated with the development of neurodegenerative diseases (16,17). Several studies have suggested that having high adiposity and, therefore, a high BMI and WC during adulthood, increases the probability of developing cognitive impairment and dementia in old age (12,18,19). In contrast with this, some studies indicate that older adults with low, but not high, BMI are at increased risk of dementia, going so far as to suggest that high adiposity could be protective (20–22). Such associations have yet to be investigated in Chile. Therefore, the aim of the present study was to investigate the association between adiposity and cognitive impairment in the older adult population in Chile.

Materials and methods

Study design

This cross-sectional study included a total of 1384 adults aged over 60 years (based on the WHO definition of older/elderly

persons) from the 2009 to 2010 Chilean National Health Survey (CNHS)⁽²³⁾. The CNHS is a cross-sectional study conducted in homes from a national, probabilistic, stratified and multistage sample and includes people with an age range of 15–98 years with national, regional and urban/rural representativeness. The present study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Ethics Committee of the School of Medicine at the Pontifical Catholic University of Chile (approval no. 09–113). Written informed consent was obtained from all participants⁽²³⁾.

Abbreviated Mini-Mental State Examination

The abbreviated version of the Mini-Mental State Examination (MMSE) was used to measure cognitive impairment (23). This instrument has been widely used due to its proven high reliability and has been validated previously in the Chilean population (24,25). It evaluates executive function, visuo-constructive capacity, memory, ability to understand instructions and temporo-spatial orientation (26). The abbreviated version consists of six questions, with a maximum score of nineteen points. A score below 13 on the MMSE indicates the presence of cognitive impairment (23). This abbreviated version has showed a higher sensitivity and specificity than the original long-format version (27).

Determination of adiposity levels

Body weight, height and WC were measured by trained nurses using standardised protocols. BMI was derived from body weight divided by height squared and nutritional status was derived using the following cut-off points: underweight: $\leq 18.5 \text{ kg/m}^2$; normal weight: $18.5-24.9 \text{ kg/m}^2$; overweight: $25.0-29.9 \text{ kg/m}^2$ and obesity: $\geq 30.0 \text{ kg/m}^{2(28)}$. Central obesity was defined as a WC ≥ 88 cm for women and ≥ 102 cm for men⁽²³⁾. In order to assess the association between cognitive impairment and WC, sex-specific quartiles were derived for men (quartile 1: ≤ 89 cm; quartile 2: 89-97 cm; quartile 3: 98-104 cm; quartile 4: ≤ 104 cm) and women (quartile 1: ≤ 86 cm; quartile 2: 86-93 cm; quartile 3: 94-102 cm; quartile 4: ≤ 102 cm).

Sociodemographic and lifestyle variables

Sociodemographic variables such as age, sex, education level (elementary <8 years, secondary: 8–12 years, higher education >12 years), income (low <250 000; medium: 250 000 to 650 000; high >650 000 Chilean pesos) and lifestyle factors such as



Table 1. Population characteristics according to the Mini-Mental State Examination (Numbers of subjects; percentages and 95 % confidence intervals; mean values and 95 % confidence intervals)

	No cogn	itive impairment	Cognitive impairment		
	%	95 % CI	%	95 % CI	
Sociodemographic					
Subjects (n)		1215		169	
Prevalence	88.4	84.8, 91.2	11.6	8.8, 15.2	
Sex					
Men	44.4	39.1, 49.8	52⋅6	38.6, 66.2	
Women	55.6	50.2, 60.9	47.3	33.8, 61.4	
Age (years)					
Mean	_	68.5	_	76.3	
95 % CI	6	7.8, 69.2	73	3.8, 78.8	
Area of residency					
Rural	14.4	11.8, 17.5	29.5	16.4, 47.1	
Urban	85.6	82.4, 88.2	70.5	52.8, 83.5	
Education level	47.0	44.0.50.0	04.4	70 5 04 0	
Elementary	47.0	41.8, 52.0	84.4	73.5, 91.3	
Secondary	38.0	32.8, 43.4	14.4	7.8, 25.2	
Technical university	15⋅0	10.9, 20.3	1.2	0.2, 4.7	
Income level					
Low	56.5	51.1, 61.7	83.5	71.2, 91.1	
Middle	32.6	27.7, 37.9	16⋅5	8.8, 28.7	
High	10.9	7·5, 15·6	0		
Anthropometrics					
Height (m)					
Mean		1.58		1.54	
95 % CI	1	·57, 1·59	1.	53, 1·57	
Body weight (kg)					
Mean		71.6		65⋅2	
95 % CI	7	0.2, 72.9	6	1.9, 68.6	
BMI (kg/m²)					
Mean		28.7		27.2	
95 % CI	2	8.1, 29.3	25	5.9, 28.6	
Nutritional status					
Underweight (<18.5 kg/m²)	1.1	0.4, 2.4	2⋅1	0.5, 7.3	
Normal (18·5–24·9 kg/m²)	24.0	19.2, 29.3	34.5	22.2, 49.1	
Overweight (25·0–29·9 kg/m²)	41.7	36.6, 46.9	34.3	21.2, 47.3	
Obesity (≥30·0 kg/m²)	33.3	28.6, 38.4	29.2	19.6, 41.1	
Waist circumference (cm)	95.7	94.6, 96.9	93.5	90.2, 96.9	
Central obesity					
Normal	47.3	42·1, 52·5	44.0	30.8, 58.1	
Obese	52.7	47.4, 57.9	56.0	41.9, 69.2	
Waist circumference quartiles					
Lowest	26.8	22.4, 31.8	35.0	23.1, 49.0	
Middle-low	24.2	19.8, 29.3	21.9	13.1, 34.3	
Middle-high	25.2	20.8, 30.2	17.4	10.3, 27.7	
Highest	23.5	19.4, 28.2	25.6	16.8, 37.0	
Lifestyle		,		,	
Total physical activity (MET/h per week)					
Mean		90.3		47.1	
95 % CI	76	5·7, 103·8	22	2.2, 71.9	
Prevalence of physical inactivity	,	,		,	
Active	69.9	65.1, 74.3	36-6	24.7, 50.4	
Inactive	30.1	25.7, 34.9	63.4	49.6, 75.3	
Sitting time (h/d)	00 1	207, 010	55 .	10 0, 70 0	
Mean		3.67		5.46	
95 % CI	3	·30, 4·04	3.	84, 7.07	
Fruit and vegetables intake (g/d)	O	00, 404	0	04, 7.07	
Mean		243.0		196-3	
95 % CI	၁၁	6·6, 259·4	161	5·7, 227·0	
Alcohol intake (g/d)	22	0 0, 200 -	10.	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
Mean		39.5		42.5	
95 % CI	0	9·4, 49·6	0.	42·5 1·6, 60·5	
	۷	ن.ب. بع.ن	۷	T-0, 00·0	
Hours of sleep	49.4	44.1 54.6	20.0	00 0 40 4	
<7 h 7–9 h		44.1, 54.6	32·0	20.3, 46.4	
7–9 n >9 h	34·5	29.6, 39.8	24.8	16.2, 36.1	
	16.1	12.9, 19.8	43.1	29.2, 58.2	
Healthy lifestyle score					

Y

Table 1. Continued

	No cogni	tive impairment	Cognitive impairment		
	%	95 % CI	%	95 % CI	
Unhealthy	30-3	35.1, 36.1	15.3	8.2, 26.5	
Slightly healthy	26.6	21.7, 32.2	23.9	14.6, 36.6	
Healthy	22.8	18.4, 27.8	28.9	15.5, 47.3	
Very healthy	20.3	16.6, 24.5	31.8	15.8, 53.7	
Smoking					
Never	45.4	40.2, 50.5	54.0	39.1, 68.2	
Ex-smoker	34.9	29.8, 40.2	33.4	24.2, 54.9	
Smoker	19.8	15.8, 24.3	7.6	3.5, 15.5	
Self-reported health and well-being					
Poor	2.8	1.5, 5.0	9.9	5.4, 17.5	
Average	34.2	29.4, 39.2	57.1	43.2, 70.0	
Good	63.0	57.9, 67.8	32.9	21.7, 46.5	
Mini-mental score					
Mean		17.1	8.6		
95 % CI	16	5·9, 17·3	-	7.6, 9.5	

MET, metabolic equivalents.

smoking, drinking alcohol, and fruit and vegetable intake data were obtained by validated questionnaires, as described previously⁽²³⁾.

The total level of physical activity was determined using the Global Physical Activity Questionnaire (GPAQ v2)⁽²⁹⁾, which has previously been validated in the Latino population (30). Total physical activity is presented as the sum of the time reported in transport-related physical activity, moderate and vigorous intensity physical activity. This variable was expressed in metabolic equivalents (MET) for min/week. The cut-off for physical inactivity was an energy output of less than 600 MET-min/week^(29,31). The levels of sedentary behaviour were determined using the same questionnaire - GPAQ v2 - from the self-report of time devoted to activities that involve sitting or reclining in free time or at work (e.g. time seated in front of the computer or television, travelling by bus, train or car, amongst others). A person who spent more than 4 h per d sitting (equivalent to the population median) was considered to have a high level of sedentary behaviour⁽³²⁾.

In order to assess participant lifestyle, seven lifestyle factors were examined and scored to produce a healthy lifestyle score. The seven lifestyle factors were as follows: consuming five portions of fruit and vegetables per d, consuming <8 g of salt per d, an audit alcohol score of <8 (units), sleeping between 7 and 9 h per d, having never smoked, physical activity (>150 min a week of moderate-to-vigorous physical activity) and time spent sitting <4 h per d. Participants were assigned one point for each healthy behaviour and those who did not meet these recommendations were assigned a value of 0. The score was then categorised as unhealthy (≤1 healthy behaviours), slightly healthy (2–3 healthy behaviours), healthy (4–5 healthy behaviours) and very healthy (>5 healthy behaviours).

Statistical analyses

The general characteristics of the study population are presented as means and standard deviations for continuous variables, and as percentages for categorical variables. In order to investigate the association between adiposity levels (BMI and

WC) and cognitive impairment, logistic regression analysis was performed, and the results presented as the OR and 95 % CI. Participants with a normal BMI were defined as the reference group, whereas for WC the reference group were subjects in quartile 2 (86-93 cm for women and 89-97 cm for men). All analyses were adjusted for confounding variables using four statistical models: model 0 - unadjusted; model 1 - adjusted for age, sex, region and residency area (urban and rural); model 2 additionally adjusted for education level and income status; model 3 additionally adjusted for healthy lifestyle score; model 4 was adjusted form model 3 but it was also mutually adjusted for BMI and WC in order to identify whether the association of cognitive impairment with overall adiposity (BMI) was independent of central adiposity measured (WC) and vice versa. For all analyses the complex samples module in STATA SE v14 was used. The significance level was defined as P < 0.05.

Ethical standards disclosure

The CNHS 2009–2010 was funded by the Chilean Ministry of Health and led by the Department of Public Health, The Pontificia Universidad Católica de Chile. The CNHS 2009–2010 was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethics Research Committee of the Faculty of Medicine at the Pontificia Universidad Católica of Chile. Written informed consent was obtained from all subjects.

Results

The characteristics of the study population according to the results of the normal and altered MMSE are shown in Table 1. In the descriptive data for sociodemographic variables, it can be noted that participants with cognitive impairment were older, and had lower education level and income. With respect to anthropometric measurements, participants with cognitive impairment were more likely to be at the



extremes of BMI (underweight, overweight and obesity); however, WC was not different in normal individuals compared with those with cognitive impairment (99.8 v. 98.3 cm, respectively). In relation to lifestyle, an increased prevalence of physical inactivity, a greater number of time spent sitting during the day, and worse self-reported health and well-being was observed in participants with cognitive impairment.

The association between BMI and cognitive impairment is shown in Table 2. The statistically unadjusted model, model 0, identified an increase in the likelihood of cognitive impairment in those who were underweight (OR 4·44; 95 % CI $2\cdot43$, $6\cdot45$; $P<0\cdot0001$), overweight (OR $1\cdot86$; 95 % CI $1\cdot06$, $2\cdot66$; $P=0\cdot031$) and obese (OR $2\cdot26$; 95 % CI $1\cdot31$, $3\cdot21$; $P=0\cdot003$) when compared with those with a normal BMI. Models 2, 3 and 4 were adjusted for other confounding factors which reduced the magnitude of the resulting associations; however, the associations remained significant (Table 2 and Fig. 1(a)). When the association between BMI and cognitive impairment was adjusted for WC, the associations were attenuated but remained significant for underweight (OR $3\cdot00$; 95 % CI $1\cdot48$, $4\cdot52$; $P=0\cdot002$) and obese (OR $2\cdot13$; 95 % CI $1\cdot12$, $3\cdot14$; $P=0\cdot021$) individuals (Table 2).

The association between WC levels and cognitive impairment are presented in Table 3. Participants in the lowest WC quartile, quartile 1, had a greater likelihood of cognitive impairment (OR 2.20; 95 % CI 1.17, 4.16; P = 0.014) compared with participants in quartile 2. Additionally, similar results were observed in participants who were in the highest compared with the lowest WC quartile (OR 2.21; 95 % CI 1.16, 4.19; P = 0.015). However, participants in quartile 3 did not show a significant association with cognitive impairment. When these analyses were adjusted for confounding variables, the associations were weaker but remained statistically significant (Table 3 and Fig. 1(b)). When the association between WC and cognitive impairment was adjusted for BMI, the associations were only observed for the highest quartile, which somehow shows a stronger magnitude of association when BMI was included as a confounding factor in the model (Table 3).

Discussion

The results of the present study confirm that both high and low levels of adiposity, quantified through BMI and WC, were associated with a higher probability of cognitive impairment in the older adult population. The findings were robust after adjusting for confounding variables, including sociode-mographic and lifestyle factors. In particular, older people who were underweight appeared to be more likely to have cognitive impairment than those who were overweight or obese. These results have the potential to inform the development of programmes or interventions for older adults in Chile and other nations in Latin America, including better lifestyle guidance for appropriate weight maintenance, and cognitive screening for both overweight and underweight older people. Considering the large numbers of older adults in Chile and the projection for this population to grow over the next three decades, the implications of these programmes could have a large social and economic impact.

The findings of the present study are largely consistent with the existing literature. For example, a prospective cohort study has found that BMI and WC were independent risk factors for dementia, where the presence of high BMI (>30.0 kg/m²) and higher WC were associated with a 3.6-fold risk, compared with those only with normal BMI and lower WC⁽¹⁸⁾. Additionally, longitudinal studies have revealed that a high BMI is a risk factor for cognitive impairment (33,34), and a recent meta-analysis indicated that obesity in middle age is a risk factor that increases the probability of developing dementia in old age⁽³⁵⁾. The association between obesity and cognitive impairment could be attributed to the vascular damage caused by excessive adipose tissue and hyperglycaemia, which may be capable of causing a neuronal injury and subsequently neurodegeneration (36,37). It has also been suggested that excessive adipose tissue triggers a low-grade chronic inflammatory process, causing the increased production of proinflammatory mediators, such as cytokines and macrophages, which can cross the blood-brain barrier and cause neuronal damage^(38,39). On the other hand, some studies indicate that underweight older adults are at higher risk for cognitive impairment than those who are overweight (22). Epidemiological studies have also reported that an annual reduction of 1 kg/m² in BMI increases the risk of developing cognitive impairment by 8 % (40). These findings suggest that weight loss and a low BMI could be partially related to brain pathology (22), consistent with the findings of the present study. Our findings also suggest that the association between BMI and cognitive

Table 2. Association between BMI levels and cognitive impairment (Odds ratios and 95 % confidence intervals)

Models	Underweight (<18·5 kg/m²)				lormal Overweight 24-9 kg/m²) (25-0–29-9 kg/m²)			²)	Obese (≥30·0 kg/m²)		
	OR	95 % CI	Р	OR	95 % CI	OR	95 % CI	P	OR	95 % CI	Р
Model 0	4.44	2.43, 8.12	<0.0001	1.00	Ref.*	1.86	1.06, 3.29	0.031	2.26	1.31, 3.90	0.003
Model 1	3.35	1.76, 6.39	<0.0001	1.00	Ref.	2.06	1.14, 3.72	0.016	2.46	1.38, 4.36	0.002
Model 2	3.24	1.69, 6.22	<0.0001	1.00	Ref.	2.01	1.11, 3.65	0.022	2.35	1.32, 4.21	0.004
Model 3	3.23	1.68, 6.20	<0.0001	1.00	Ref.	2.01	1.10, 3.64	0.022	2.35	1.31, 4.20	0.004
Model 4	3.00	1.48, 6.06	0.002	1.00	Ref.	1.95	0.87, 4.38	0.102	2.13	1.12, 4.07	0.021

Ref., reference; MMSE, Mini-Mental State Examination.

^{*} Ref.: the baseline group was comprised of people with normal BMI for older adults. A value greater than 1 indicates an increased risk of cognitive impairment (MMSE <13). The models were constructed as follows: model 0 – not adjusted; model 1 – adjusted for age, sex, region and geographical area; model 2 was adjusted for model 1, but also for education level and socio-economic level; model 3 was adjusted for model 2, but also for healthy lifestyle points; model 4 was adjusted for model 3 but also for waist circumference.



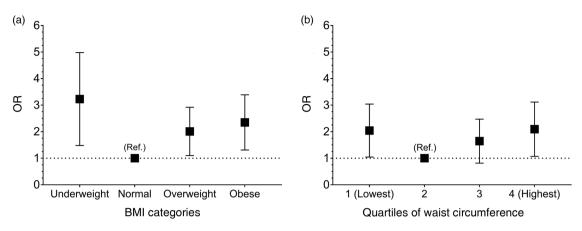


Fig. 1. Risk for cognitive impairment according to BMI (a) or waist circumference (b). Data are presented as odds ratios and their respective 95 % confidence intervals, represented by vertical bars. Ref.: the baseline group was comprised of people with normal BMI according to classification in older adults or waist circumference. A value greater than 1 indicates an increased probability of cognitive impairment (Mini-Mental State Examination <13). The analyses were adjusted for age, sex, region, geographical area, education level, socio-economic level and healthy lifestyle points. The cut-off for the waist circumference quartiles were sex-specific (men quartile 1: <89 cm; quartile 2: 89–97 cm; quartile 3: 98–104 cm; quartile 4: >104 cm; and women quartile 1: <86 cm; quartile 2: 86-93 cm; quartile 3: 94–102 cm; quartile 4: >102 cm). The cut-off points for BMI were: underweight <18-5 kg/m²; normal weight: 18-5–24-9 kg/m²; overweight: 25-0–29-9 kg/m² and obesity: ≥30-0 kg/m².

impairment was independent of central adiposity, measured by WC, but the association of WC with cognitive impairment was partially independent of BMI, as the association of cognitive impairment with the lowest quartile of WC disappeared but the magnitude of the association for the highest quartile increased. These results disagree with previous studies which have reported that central obesity is a stronger, and independent, risk factor for cognitive decline and dementia (18). This discrepancy may be explained as BMI is not only a marker of adiposity but also a marker of frailty (loss of muscle mass, especially in underweight individuals); therefore, adjusting for WC would only account for some of the variance of the association between BMI and cognitive impairment. However, accounting for BMI on the association of WC with cognitive impairment may capture most of the variance related to adiposity and its effect on cognitive function.

Although our study reported that underweight and obesity are associated with cognitive impairment, this association may also be bidirectional, where cognitive decline could also lead to changes in adiposity levels. Recent evidence suggests that behavioural changes, such as physical activity, occur 10 years before neurodegenerative diseases are diagnosed⁽⁴¹⁾.

This implies that cognitive decline or impairment may lead to obesity or being underweight, as people with cognitive decline are more likely to have limited independence and therefore lower levels of physical activity (42,43). Moreover, other lifestyle behaviours such as poor-quality diet due to individuals with cognitive impairment incapable of performing essential daily living tasks (i.e. eating, shopping, cooking, etc.) may also lead to underweight or obesity (44). There are also other health-related illnesses that may mediate or moderate this association between obesity and cognitive impairment, such as CVD, as individuals with stroke, CHD or diabetes have a higher risk of cognitive impairment which could be explained by adiposity levels or differences in lifestyle behaviours (41,43-46). However, unfortunately due to the crosssectional nature of the present study we cannot elucidate the underlying roles of existing illness or the bidirectional association between cognitive impairment and adiposity.

Limitations of this study

It is also important to consider the use of the MMSE, which, although validated and widely used in the Chilean

Table 3. Association between waist circumference and cognitive impairment (Odds ratios and 95 % confidence intervals)

Models	Quartile 1 (lowest)			Quartile 2		Quartile 3			Quartile 4 (highest)		
	OR	95 % CI	Р	OR	95 % CI	OR	95 % CI	P	OR	95 % CI	Р
Model 0	2.20	1.17, 4.16	0.014	1.00	Ref.*	1.77	0.91, 3.45	0.092	2.21	1.16, 4.19	0.015
Model 1	1.83	0.94, 3.53	0.071	1.00	Ref.	1.46	0.73, 2.93	0.275	2.03	1.05, 3.95	0.035
Model 2	2.06	1.05, 4.01	0.033	1.00	Ref.	1.64	0.81, 2.31	0.163	2.12	1.08, 3.14	0.028
Model 3	2.04	1.05, 3.03	0.036	1.00	Ref.	1.64	0.81, 2.47	0.164	2.09	1.07, 3.11	0.031
Model 4	1.37	0.61, 3.04	0.436	1.00	Ref.	1.32	0.62, 2.78	0.465	3.06	1.47, 6.38	0.003

Ref., reference; MMSE, Mini-Mental State Examination.

^{*} Ref.: the baseline group was comprised of people with a waist circumference classified in quartile 2. A value greater than 1 indicates an increased risk of cognitive impairment (MMSE <13). The models were constructed as follows: model 0 – not adjusted; model 1 – adjusted for age, sex, region and geographical area; model 2 was adjusted for model 1, but also for education level and socio-economic level; model 3 was adjusted for model 2, but also for healthy lifestyle points; model 4 was adjusted for model 3 but also for BMI. The cut-offs for the waist circumference quartiles were sex-specific (men quartile 1: <89 cm; quartile 2: 89–97 cm; quartile 3: 98–104 cm; quartile 4: >104 cm; and women quartile 1: <86 cm; quartile 2: 86–93 cm; quartile 3: 94–102 cm; quartile 4: >102 cm;



population^(24,25), has demonstrated relatively low discriminative power for dementia and should not be considered a diagnostic test⁽⁴⁷⁾. Another limitation is that the variables associated with lifestyle, such as physical activity and time spent sitting, were self-reported and could therefore be subject to measurement errors, mainly related to the overestimation of healthy behaviours and, importantly, may be affected by the cognitive ability of the participants⁽⁴⁸⁾. Moreover, adiposity was measured using BMI and WC instead of more accurate measurements like dual-energy X-ray absorptiometry. Lastly, as with all cross-sectional and observational studies, causality cannot be confirmed due to the possibility of reverse causation and residual confounding.

Conclusion

The present study corroborates that both high and low adiposity levels are associated with an increased risk of cognitive impairment in older adults in Chile. These results are of great interest in terms of public health when it is considered that a third of cases of cognitive impairment in the elderly population are attributable to modifiable factors and are therefore potentially preventable if appropriate measures are taken⁽⁴⁹⁾.

Acknowledgements

We thank all participants for their co-operation, and the Chilean Health Ministry and Department of Public Health, and the Pontificia Universidad Católica de Chile for commissioning, designing and conducting the second National Health Survey 2009–2010.

There is no financial support to declare.

Y. C.-C., F. L., H. W. and C. M.-C. generated the research question; Y. C.-C., F. L., H. W. and C. M.-C. planned the analysis; Y. C.-C. and F. L. performed the literature search; C. M.-C. performed the analysis with support from Y. C.-C., F. L. and H. W.; Y. C.-C. and F. L. tabulated the data; Y. C.-C., F. L., H. W., A. S., S. R. G. and C. M.-C. interpreted the findings; Y. C.-C., F. L., H. W. and C. M.-C. wrote the first draft of the manuscript. All authors critically reviewed this and previous drafts. All authors approved the final draft for submission. C. M.-C. is the guarantor.

There are no conflicts of interests.

References

- World Health Organization (2011) Estadísticas Sanitarias Mundiales 2011 (World Health Statistics 2011). Talca, Chile: WHO.
- World Health Organization (2017) La Salud Mental de los Adultos Mayores (The Mental Health of Older Adults). Talca, Chile: WHO. https://www.who.int/es/news-room/fact-sheets/detail/la-salud-mental-y-los-adultos-mayores.
- INE (Instituto Nacional de Estadisticas Chile) (2017) Resultados Definitivos CENSO 2017 (Final Results CENSO 2017). Chile: INE.
- World Health Organization (2013) Global Action Plan for the Prevention and Control of NCDs 2013–2020. Geneva: WHO.
- MINSAL (2017) Encuesta Nacional de Salud 2016–2017 Ministerio de Salud (National Health Survey 2016–2017 – Ministry of Health). Santiago: MINSAL.

- Atlantis E, Martin SA, Haren MT, et al. (2008) Lifestyle factors associated with age-related differences in body composition: the Florey Adelaide Male Aging Study. Am J Clin Nutr 88, 95–104.
- Ganguli M, Fu B, Snitz BE, et al. (2013) Mild cognitive impairment incidence and vascular risk factors in a population-based cohort. Neurology 80, 2112–2120.
- Pedraza OL, Perilla HJ, Cruz A, et al. (2016) Deterioro cognitivo y factores de riesgo cardiovascular y metabólico en una muestra de adultos de Bogotá (Cardiovascular and metabolic risk factors, for cognitive impairment in adults from Bogotá). Acta Neurol Colomb 32, 91–99.
- Jensen GL & Friedmann JM (2002) Obesity is associated with functional decline in community-dwelling rural older persons. J Am Geriatr Soc 50, 918–923.
- Davis JW, Ross PD, Preston SD, et al. (1998) Strength, physical activity, and body mass index: relationship to performance-based measures and activities of daily living among older Japanese women in Hawaii. J Am Geriatr Soc 46, 274–279.
- Kuo HK, Jones RN, Milberg WP, et al. (2006) 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 54, 97–103.
- Kivipelto M, Ngandu T, Fratiglioni L, et al. (2005) Obesity and vascular risk factors at midlife and the risk of dementia and Alzheimer disease. Arch Neurol 62, 1556–1560.
- Kivimäki M, Luukkonen R, Batty GD, et al. (2018) Body mass index and risk of dementia: analysis of individual-level data from 1.3 million individuals. Alzbeimers Dement 14, 601–609.
- Saka B, Kaya O, Ozturk GB, et al. (2010) Malnutrition in the elderly and its relationship with other geriatric syndromes. Clin Nutr 29, 745–748.
- MINSAL (2017) Plan Nacional de Demencia (National Dementia Plan). Chile: MINSAL.
- Janssen I, Katzmarzyk PT & Ross R (2002) Body mass index, waist circumference, and health risk: evidence in support of current National Institutes of Health guidelines. Arch Intern Med 162, 2074–2079.
- Ortega FB, Sui X, Lavie CJ, et al. (2016) Body mass index, the most widely used but also widely criticized index: would a criterion standard measure of total body fat be a better predictor of cardiovascular disease mortality? Mayo Clin Proc 91, 443–455.
- Whitmer R, Gustafson D, Barrett-Connor E, et al. (2008) Central obesity and increased risk of dementia more than three decades later. Neurology 71, 1057–1064.
- Kerwin DR, Gaussoin SA, Chlebowski RT, et al. (2011) Interaction between body mass index and central adiposity and risk of incident cognitive impairment and dementia: results from the Women's Health Initiative Memory Study. J Am Geriatr Soc 59, 107–112.
- Driscoll I, Espeland MA, Wassertheil-Smoller S, et al. (2011) Weight change and cognitive function: findings from the Women's Health Initiative Study of Cognitive Aging. Obesity (Silver Spring) 19, 1595–1600.
- Anstey K, Cherbuin N, Budge M, et al. (2011) Body mass index in midlife and late-life as a risk factor for dementia: a meta-analysis of prospective studies. Obes Rev 12, e426–e437.
- Vidoni E, Townley R, Honea R, et al. (2011) Alzheimer disease biomarkers are associated with body mass index. Neurology 77, 1913–1920.
- MINSAL (2010) Encuesta Nacional de Salud 2009–2010 (National Health Survey 2009–2010. Chile: MINSAL.
- 24. Buiza C, Navarro A, Díaz-Orueta U, et al. (2011) Evaluación breve del estado cognitivo de la demencia en estadios avanzados: resultados preliminares de la validación española del Severe Mini-Mental State Examination (Brief evaluation of the cognitive state of dementia in advanced stages: preliminary results of the Spanish validation of the Severe Mini-Mental State Examination). Rev Esp Geriatr Gerontol 46, 131–138.
- Folstein MF, Folstein SE & McHugh PR (1975) 'Mini-mental state': a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 12, 189–198.
- McDowell I (2006) Measuring Health: A Guide to Rating Scales and Questionnaires. New York: Oxford University Press.



- Quiroga P, Albala C & Klaasen G (2004) Validación de un test de tamizaje para el diagnóstico de demencia asociada a edad, en Chile (Validation of a screening test for the diagnosis of age-related dementia, in Chile). Rev Méd Chil 132, 467–478.
- Organización Panamericana de la Salud (2003) Parte 1: Módulos de Valoración Clínica. Módulo 5: Valoración Nutricional del Adulto Mayor (Part 1: Clinical Evaluation Modules. Module 5: Nutritional Assessment of the Elderly). http://www.sld.cu/galerias/pdf/sitios/gericuba/modulo5.pdf (accessed August 2019).
- World Health Organization (2009) Global Physical Activity
 Questionnaire: GPAQ version 2.0. http://www.who.int/chp/steps/
 resources/GPAQ_Analysis_Guide.pdf (accessed August 2019).
- Hoos T, Espinoza N, Marshall S, et al. (2012) Validity of the Global Physical Activity Questionnaire (GPAQ) in adult Latinas. J Phys Act Health 9, 698–705.
- World Health Organization (2010) Global recommendations on physical activity for health. World Health Organization. http:// www.who.int/dietphysicalactivity/factsheet_recommendations/en/ (accessed August 2019).
- Celis-Morales C, Salas C, Alduhishy A, et al. (2016) Sociodemographic patterns of physical activity and sedentary behaviour in Chile: results from the National Health Survey 2009–2010. *J Public Health (Oxf)* 38, e98–e105.
- Gustafson D, Rothenberg E, Blennow K, et al. (2003) An 18-year follow-up of overweight and risk of Alzheimer disease. Arch Intern Med 163, 1524–1528.
- Whitmer RA, Gunderson EP, Barrett-Connor E, et al. (2005) Obesity in middle age and future risk of dementia: a 27 year longitudinal population based study. BMI 330, 1360.
- Shaw M, Sachdev P, Abhayaratna W, et al. (2018) Body mass index is associated with cortical thinning with different patterns in midand late-life. Int J Obes (Lond) 42, 455–461.
- Iadecola CJN (2013) The pathobiology of vascular dementia. Neuron 80, 844–866.
- Ahmadi S, Mainali R, Ravinder N, et al. (2017) Dietary polysaccharides in the amelioration of gut microbiome dysbiosis and metabolic diseases. Obes Control Ther 4, 00140.

- Nelson AR, Sweeney MD, Sagare AP, et al. (2016) Neurovascular dysfunction and neurodegeneration in dementia and Alzheimer's disease. Biochim Biophys Acta 1862, 887–900.
- Malandrino N, Capristo E, Taveira TH, et al. (2018) Cognitive function in individuals with normal weight obesity: results from the Third National Health and Nutrition Examination Survey (NHANES III). J Alzbeimers Dis 65, 125–135.
- Kitamura K, Watanabe Y, Nakamura K, et al. (2017) Weight loss from 20 years of age is associated with cognitive impairment in middle-aged and elderly individuals. PLOS ONE 12, e0185960.
- Kivimäki M, Singh-Manoux A, Pentti J, et al. (2019) Physical inactivity, cardiometabolic disease, and risk of dementia: an individual-participant meta-analysis. Br Med J 365, 11495.
- Varma VR & Watts A (2017) Daily physical activity patterns during the early stage of Alzheimer's disease. J Alzheimers Dis 55, 659–667.
- Livingston G, Sommerlad A, Orgeta V, et al. (2017) Dementia prevention, intervention, and care. Lancet 390, 2673–2734.
- Leritz EC, McGlinchey RE, Kellison I, et al. (2011) Cardiovascular disease risk factors and cognition in the elderly. Curr Cardiovasc Risk Rep 5, 407–412.
- World Health Organization (2019) Risk Reduction of Cognitive Decline and Dementia: WHO Guidelines. Geneva: WHO.
- Larsson SC, Traylor M, Malik R, et al. (2017) Modifiable pathways in Alzheimer's disease: Mendelian randomisation analysis. Br Med J 359, 15375
- Jimenez D, Lavados M, Rojas P, et al. (2017) Performance of an abbreviated mini mental examination to detect dementia in older people. Rev Med Chil 145, 862

 –868.
- Marsaux CF, Celis-Morales C, Hoonhout J, et al. (2016) Objectively measured physical activity in European adults: cross-sectional findings from the Food4Me Study. PLOS ONE 11, e0150902.
- Marín-Carmona JM (2015) Demencia de inicio en edades avanzadas: aspectos clínicos y fisiopatológicos diferenciales (Dementia of onset at advanced ages: differential clinical and pathophysiological aspects). Rev Esp Geriatr Gerontol 50, 261–263.