Brain Aging and Metabolic Syndrome: a Study in Cenischia Valley (Piedmont)

M. Rinaldi[1], G. Graffi[2], S. Gallone[3], E. Rabino Massa[1]

[1] Laboratory of Anthropology, Department of Life Sciences And Systems Biology, Via Accademia Albertina 13, 10123 Torino. E-mail: marianna.rinaldi@unito.it
[2] ASL TO3, District of Susa, Piazza San Francesco 4, 10059, Susa (TO)
[3] Laboratory of Neurogenetics, Department of Neuroscience, Via Cherasco15, 10126 Torino

KEY WORDS: metabolic syndrome, cognitive decline, aging, MMSE.

Introduction

Metabolic Syndrome (MetS) is a cluster of conditions, each of which represents a risk factor for cardiovascular disease: central obesity hyperglycemia, dyslipidemia and hypertension. MetS can be diagnosed when three or more of these criteria are present (Grundy et al., 2004): waist circumference ≥102 cm (male) or ≥88 cm (female); triglycerides >150 mg/dl or lipid lowering drugs use; HDL cholesterol <40 mg/dl (male) or <50 mg/dl (female); blood pressure >130/85 mmHg or antihypertensive drugs use; fasting plasma glucose >100 mg/dl or hypoglycemic drugs use.

Any of these conditions and MetS itself have been associated to Alzheimer's Disease and Vascular Dementia (Duron and Hanon, 2008).

The purpose of our research is the study of brain aging and cognitive decline in a sample of elderly people (n=200) belonging to a rural alpine community, in relation to MetS. The study includes analysis of nutritional, behavioral and cultural factors and the assessment of their influence on maintaining health and functionality in aging. Here we report some of the preliminary results on a first sample of 80 people.

This research has been reviewed and received ethics approval by the Bioethics Committee of the University of Turin.

Materials and Methods

80 persons aged 65 and over were recruited in the community of Venaus (Cenischia Valley) through the local healthcare service (ASL TO3). They all are people whose families have been living in the valley for at least three generations. Blood samples were collected from every study participant in the morning to determine plasma total (TC), High Density Lipoprotein cholesterol (HDL-C), triglycerides and fasting plasma glucose level. Waist circumference, height and weight were measured. Moreover, each volunteer was interviewed about his medical history and about some behavioral and cultural

aspects (eating habits, physical activity, social relations, use of new technologies, reading books and/or newspapers, watching television, taking care of people and/or animals). Finally, it was administered the Mini Mental State Examination, MMSE (Folstein et al., 1975) which is the most highly used screening test for cognitive impairment. MMSE allows the quantification of cognitive abilities and their changes over time and it has a good reliability (sensitivity = 87%; specificity = 82%). The MMSE total combines scores from five cognitive domains (orientation, language and comprehension, memory, attention/calculation and praxis), where each domain contributes approximately equal weight to the overall score. The total score was corrected by age and educational level using the score-adjustment coefficients proposed by Magni et al. (1996).

All data were entered into Excel® spreadsheets (Microsoft 2007) and analyzed with SPSS Statistics 17.0. Indipendent groups were statistically compared using the Mann-Whitney U test.

Results

The total sample (n=80) was composed of 33 men (mean ± SD age: 75,7 ± 6,2) and 47 women (mean ± SD age: 77,2 ± 8,7). The sample was divided into three age classes: 65-74 years (n=37), 75-84 years (n=30) and ≥85 years (n=13). *Body composition and medical history:* 46% of the total sample was overweight (BMI between 25 and 29,9) and 13% obese (BMI ≥30,0); 90% suffered from hypertension (blood pressure >135/85 mmHg or antihypertensive medication use); 14% presented an altered fasting glucose (fasting blood glucose between 110 and 125 mg/dl) and 22% suffered from diabetes mellitus (fasting blood glucose ≥126 mg/dl or hypoglycemic drugs use); 39% had total cholesterol level (TC) <200 mg/dl (50% of these people were under treatment with cholesterol lowering drugs); 29% had TC between 200 and 239 mg/dl and 32% had TC ≥240 mg/dl. For what concerns the prevalence of cardiovascular diseases (myocardial infarction, brain stroke, atrial fibrillation, cardiomyopathy or peripheral artherial disease), they affected 35% of the total sample. *Mini Mental State Examination (MMSE):* 77% of the sample presented normal MMSE scores (26-30), 5% borderline scores (25-25,9), 16% mild cognitive impairment scores (18-24,9) and 2% moderate/severe cognitive impairment

score (<18).The two individuals that suffered from severe cognitive impairment aged 85 or over (see Tab. 1).
Metabolic Syndrome (MetS): In our sample MetS has a great prevalence: 60% of the people recruited presents three or more diagnostic criteria for MetS, more frequently among women (63,8%) than men (54,5%).The syndrome is evenly distributed in all age classes in which the sample was divided (65-74 years; 75-84 years; ≥85 years).
People with MetS present a significantly lower MMSE score than people without MetS (26,0 vs 27,8; U=481,5; DF=32,48; P=0,005).A similar result is obtained analyzing women (27,9 vs 26,1; U=167,5; DF=17,30; P=0,050) and men (27,7 vs 25,8; U=73,5; DF=15,18; P=0,026) separately. This trend is also present in every age class even if it doesn't reach the statistical significance.
Moreover, in each age class the group affected by MetS presents a higher prevalence of cases of cognitive impairment (Tab.1).

and pre-diabetes increase risk of dementia and accelerated cognitive decline (Lithell et al., 2003; Kanaya et al., 2004; Van den Berg, 2008).Also dyslipidemia and obesity are increasingly being recognized as possible modifiable risk factors for dementia (Reitz et al., 2004; Elias et al., 2003). High levels of high-density lipoprotein (HDL), conversely, appear to be associated with a reduced risk for Alzheimer's disease in older adults (Reitz et al., 2010).The metabolic syndrome may be a risk factor for cognitive decline because it summarizes the joint effects of the individual risk factors.Another possibility is that elders with the metabolic syndrome often have elevated levels of inflammation and that this in turn could increase cognitive impairment since several studies have implicated inflammation in the pathogenesis of dementia (Yaffe et al., 2004; McGeer and McGeer, 1999).

Age classes	MMSE score	No MetS (n)	MetS (n)
65-74 years	≥26 (normal)	12	17
	25-25,9 (borderline)	1	2
	18-24,9 (mild cognitive impairment)	0	5
	≤17,9 (moderate-severe cognitive impairment)	0	0
75-84 years	≥26 (normal)	12	12
	25-25,9 (borderline)	1	0
	18-24,9 (mild cognitive impairment)	1	4
	≤17,9 (moderate-severe cognitive impairment)	0	0
≥85 years	≥26 (normal)	3	5
	25-25,9 (borderline)	0	0
	18-24,9 (mild cognitive impairment)	2	1
	≤17,9 (moderate-severe cognitive impairment)	0	2

Tab. 1. *Total sample (n=80): distribution of MMSE score for individuals with (MetS) or without (No Mets) metabolic syndrome in each age class. In each age class the group affected by MetS presents a higher prevalence of cases of cognitive impairment.*

Life style: we investigated some lifestyle components that are generally mentioned as important factors in the modulation of brain aging (eating habits, physical activity, social relations, use of new technologies, reading books and/or newspapers, watching television, taking care of people and/or animals) but no one of these factors were associated to better or worse cognitive abilities in our sample.

Discussion

Several studies indicate an association between cardiovascular risk factors (especially that in midlife) and risk of developing dementia or mild cognitive impairment (MCI) in late life (Milionis et al., 2008; Whitmer et al., 2005).There are evidences that hypertension, diabetes

Conclusions

The results of the MMSE administration indicate mild cognitive impairment in 16% and moderate-severe cognitive impairment in 2% of the sample.
There were no significant associations between MMSE score and the lifestyle factors we investigated.
People with MetS present a significantly lower MMSE score than people without MetS (26,0 vs 27,8; U=1054,5; DF=32,48; P=0,004).This result is presentin both sexes and all age groups in which the sample was divided (65-74 years, 75-84 years, ≥ 85 years).
Moreover, in each age class the group affected by MetS presents a higher prevalence of cases of cognitive impairment.
These results, however, should be confirmedwith further investigations using a larger sample size.

References

Duron E., Hanon O. 2008.Vascular risk factors, cognitive decline, and dementia. *Vasc. Health Risk Manag.,*4(2): 363-381.

Elias M.F., Elias P.K., Sullivan L.M.,Wolf P.A., D'Agostino R.B. 2003. Lower cognitive function in the presence of obesity and hypertension: the Framingham heart study. *Int. J. Obes. Relat. Metab. Disord.,* 27: 260-268.

Folstein M.F., Folstein S.E., McHugh P.R. 1975.'Mini-Mental State'.A practical method for grading the cognitive state of patients for the clinician. *J. Psychiatr. Res.* 12(3): 189-198.

Grundy S.M., Brewer H.B. Jr, Cleeman J.I., Smith S.C. Jr, Lenfant C. 2004.American Heart Association; National Heart, Lung, and Blood Institute. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. *Circulation,* Jan 27,109(3):433-438.

Kanaya A.M., Barrett-Connor E., Gildengorin G.,Yaffe K. 2004. Change in cognitive function by glucose tolerance status in older adults: a 4-year prospective study of the Rancho Bernardo study cohort. *Arch. Intern. Med.,*164: 1327-1333.

Lithell H., Hansson L., Skoog I., Elmfeldt D., Hofman A., Olofsson B., Trenkwalder P., Zanchetti A., SCOPE Study Group 2003.The Study on Cognition and Prognosis in the Elderly (SCOPE): principal results of a randomized double-blind intervention trial. *J. Hypertens.,* 21: 875-886.

Magni E., Binetti G., Bianchetti A., Rozzini R.,Trabucchi M. 1996. Mini-mental State Examination: a normative study in Italian elderly population. *Eur. J. Neurol.,* 3:1-5.

McGeer E.G., McGeer P.L. 1999. Brain inflammation in Alzheimer disease and the therapeutic implications. *Curr. Pharm. Des.,* 5(10): 821-836.

Milionis H.J., Florentin M., Giannopoulos S. 2008. Metabolic syndrome and Alzheimer's disease: a link to a vascular hypothesis? *CNS Spectr.* Jul,13(7): 606-613.

Reitz C.,Tang M.X., Luchsinger J., Mayeux R. 2004. Relation of plasma lipids to Alzheimer disease and vascular dementia. *Arch. Neurol.,* 61: 705-714.

Reitz C.,Tang M.X., Schupf N., Manly J.J., Mayeux R., Luchsinger J. 2010.Association of Higher Levels of High-Density Lipoprotein Cholesterol in Elderly Individuals and Lower Risk of Late-Onset Alzheimer Disease. *Arch. Neurol.,* 67(12): 1491-1497.

Van den Berg E., Dekker J.M., Nijpels G., Kessels R.P., Kappelle L.J., De Haan E.H., Heine R.J., Stehouwer C.D., Biessels G.J. 2008. Cognitive functioning in elderly persons with type 2 diabetes and metabolic syndrome: the Hoorn study. *Dement. Geriatr. Cogn. Disord.,* 26(3):261-269. Epub. 2008, Oct 8.

Whitmer R.A., Sidney S., Selby J., Johnston S.C.,Yaffe K. 2005. Midlife cardiovascular risk factors and risk of dementia in late life. *Neurology,* 64: 277-281.

Yaffe K., Kanaya A., Lindquist K., Simonsick E.M., Harris T., Shorr R.I., Tylavsky F.A., Newman A.B. 2004. The metabolic syndrome, inflammation, and risk ofcognitivedecline. *JAMA,* Nov 10, 292(18): 2237-2242.