Preventive Medicine Reports 4 (2016) 128–133

Contents lists available at ScienceDirect

Preventive Medicine Reports

journal homepage: http://ees.elsevier.com/pmedr

Abdominal obesity is a risk factor for dysexecutive function in chronic kidney disease

Andrea R. Zammit [a,b,*], Mindy J. Katz [a,b], Carol Derby [a,b], Markus Bitzer [d], Richard B. Lipton [a,c]

[a] Saul B. Korey Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, United States
[b] Einstein Aging Study, Albert Einstein College of Medicine, Bronx, NY, United States
[c] Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, United States
[d] Department of Internal Medicine, University of Michigan, MI, United States

ARTICLE INFO

Article history:
Received 28 December 2015
Received in revised form 1 June 2016
Accepted 5 June 2016
Available online 07 June 2016

Keywords:
Dysexecutive function
Chronic kidney disease
Metabolic syndrome
Abdominal obesity

ABSTRACT

The aim of this study was to assess the influence of the metabolic syndrome and its components on dysexecutive function (DF) in individuals with and without CKD. Among 588 participants aged over 70 from the Einstein Aging Study (EAS), we defined DF as performance of 2SDs below the mean on any one test or 1.5SDs below the mean on any two of the following: Block Design, Digit Symbol Coding and the Trail-making Tests A and B. We defined CKD as an eGFR below 60 mL/min/m^2. MetS was defined according to recent guidelines from the National Cholesterol Education Program. 149 participants had CKD at cross-section, 16.1% of which also showed DF. Of the 439 participants without CKD, 12.3% displayed DF. Abdominal obesity as measured by waist circumference, was an independent risk factor for dysexecutive function in CKD (OR = 14.3, 95%CI = 2.21–91.93, $p = 0.005$) but not in non-CKD. None of the other MetS components were associated with DF. Results suggested that abdominal obesity, recognized as an integral part of the MetS, is a strong risk factor for DF in individuals with CKD.

1. Introduction

The metabolic syndrome (MetS), which is a combination of vascular and metabolic risk factors, has been associated with numerous chronic conditions, including diabetes, atherosclerosis, cerebrovascular disease (CVD) and chronic kidney disease (CKD)(Beddhu et al., 2005); it has also been linked to brain aging and dysexecutive function (Segura et al., 2009; Viscogliosi et al., 2012).

In our previous research we found an association between the MetS and CKD (Zammit et al., 2015a) and an association between CKD and executive function (Zammit et al., 2015b) and dysexecutive function (Zammit et al., 2015c), which disrupts executive tasks including attention, task-switching and mental speed. Previous research has shown that executive function is affected by vascular conditions, in particular associations have been found between dysexecutive function and cardiovascular disease, kidney disease and insulin resistance (Kurella Tamura et al., 2011), all of which are byproducts of the MetS. There is speculation that the presence of CKD aggravates the impact of other existing conditions, such as worsening hypertension or elevating glucose levels, which will in turn affect cognition (Anand et al., 2014; Seliger et al., 2005). However no studies to our knowledge have examined this.

Herein we assessed the individual components of the MetS in the presence and absence of CKD; our main aim was to determine if individual components of the metabolic syndrome are associated with dysexecutive function in persons with and without CKD. Based on previous research, we hypothesized that associations between MetS components and dysexecutive function will be present in both the healthy and the CKD groups, with the CKD group showing higher odds of risk. We also hypothesized that the associations will be more pronounced in the CKD group due to the presence of a chronic condition.

2. Methods

A cross-sectional analysis was conducted in a subset of the Einstein Aging Study (EAS) cohort (Katz et al., 2012). EAS enrolls community-dwelling, English-speaking residents of Bronx county in New York who are 70 years or older. Participants were systematically recruited from the Health Care Financing Administration/Centers for Medicaid and Medicare Services rosters for Medicare-eligible persons and from New York City Board of Elections. Individuals are first mailed introductory letters about the study and are then followed up by research assistants phoning to obtain oral consent and administer a brief screening interview. Participants were excluded if they had visual and/or auditory impairments that interfere with neuropsychological testing, psychiatric symptomatology that interferes with test completion, or a nonambulatory status. The EAS cohort has a mean baseline age of 78.4; 39.3% are males, and 70% are white (Katz et al., 2012). These demographics are generalizable to the whole population

* Corresponding author at: Einstein Aging Study, 1300 Morris Park Avenue, Van Etten Building, Room 3C9A, Bronx, NY 10461, United States.
E-mail address: andrea.zammit@einstein.yu.edu (A.R. Zammit).

http://dx.doi.org/10.1016/j.pmedr.2016.06.007

(Ortman et al., 2014). The analysis sample includes participants who completed an EAS clinic visit from 2004. The subset of EAS participants included in this study were active and agreed to blood collection between July 2003 and December 2013. Within this subset, participants' mean age was 78.4 years; 37% were male, and 70% white, which characteristics are similar to the overall EAS cohort. The study protocol was approved by the local institutional review board (Katz et al., 2012). Written informed consent is obtained on the first clinical visit. Individuals with dementia and diabetes were excluded from these analyses.

2.1. Risk factors

CKD was defined as eGFR below 60 mL/min/1.73 m^2. We estimated eGFR in mL/min/1.73 m^2 using the Modification of Diet in Renal Disease (MDRD) (Levey et al., 2009) formula:

$$\text{eGFR} = 186 \times \text{Serum Creatinine}^{-1.154} \times \text{Age}^{-0.203} \times [1.210 \text{ if Black}] \times [0.742 \text{ if Female}]$$

The MDRD formula has been recommended for use in older people (Cirillo et al., 2005).

Metabolic syndrome components were based on criteria from the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP), 2001). Waist circumference was measured in our lab using a standardized protocol that required the participant to stand upright with the abdomen relaxed, arms at sides and feet together, while the tester places the end of measuring tape at the level of the natural waist and positioning it in a horizontal position. Measurements are recorded to the nearest 0.1 cm. Central obesity was defined as a waist circumference of ≥102 cm in men, and ≥88 cm in women. Universal precautions were employed during blood collection. Fasting blood samples were used for elevated blood triglycerides (≥150 mg/dL), elevated glucose levels (≥100 mg/dL), and hypertension (systolic ≥130 and diastolic ≥85 mm Hg or the use of antihypertensive medications). For hypertension, we included both treated (73%) and untreated participants (27%). Low HDL cholesterol was defined as <40 mg/dL in men and <50 mg/dL in women.

Metabolic syndrome was defined as the presence of three or more components from those listed above (Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP), 2001; Grundy, 1999).

2.2. Cognitive status

In previous work (Zammit et al., 2015b) we defined executive function by employing a principal components analysis on four psychometric tests: Block Design and Digit Symbol Coding from the Wechsler Adults Intelligence Scales (Wechsler, 1997), and the Trail-making Tests A and B (Battery, 1944) were the tests that composed this domain. Dysexecutive function was considered to be present if a participant scored either 2SDs below the mean on any one test or 1.5SDs below the mean on any 2 tests. This classification is also based on our previous work (Zammit et al., 2015c).

2.3. Covariates

Age, gender, race, years of education, current smoking status and alcohol intake in the past month were used as covariates in our models. These were collected from the clinical interview. Smoking and alcohol were included due to their known association with CKD.

In addition, we included inflammation and insulin resistance as covariates in our models because of their associations with the metabolic syndrome (Beddhu et al., 2005).

High sensitivity C-reactive protein (hsCRP, mg/L) was used to assess inflammation. The distribution of HsCRP was examined and rescored into tertiles termed high, moderate and low inflammation. The highest inflammation tertile was considered the reference group.

Insulin resistance (IR) was defined using the homeostasis model assessment insulin resistance (HOMA-IR) equation (Matthews et al., 1985) [fasting plasma insulin (mU/mL) × fasting plasma glucose (mmol/L)/22.5]. Quintiles were formed, with the highest IR quintile serving as the reference group.

2.4. Statistical analysis

Stratification was performed on all analyses in this study by presence or absence of CKD. For descriptive demographic and clinical analyses, participants were further divided into those with and without dysexecutive function. Participants were also stratified by gender to describe the MetS's components sample characteristics.

Binary logistic regressions were used to explore the associations between individual components of the metabolic syndrome and dysexecutive function in CKD and non-CKD participants. We adjusted for demographics initially, and for demographics and hs-CRP, and demographics and HOMA-IR in subsequent models. In the final model, we adjusted for all covariates. All components of the MetS were entered in the models at all times.

Table 1
Demographic and clinical characteristics of the study participants with and without dysexecutive function, and stratified according to with and without CKD.

CKD	Dysexecutive function		
No (n = 439, 74.7%)	No (n = 385, 87.7%)	Yes (54, 12.3%)	p
Demographics			
Age, y	78.4 (4.9)	81.8 (5.9)	0.000
Males (%)	145 (37.7)	16 (29.6)	0.251
Whites (%)	268 (69.6)	21 (38.9)	0.000
Blacks (%)	97 (25.2)	30 (55.6)	0.000
Education, y	14.6 (3.1)	12.1 (4.1)	0.000
Current smokers (%)	16 (4.2)	1 (1.9)	0.428
Alcohol consumption in past month (%)	56 (14.5)	6 (11.3)	0.528
Clinical characteristics			
eGFR (1.73/min/m^2)	78.9 (14.1)	79.7 (12.7)	0.698
Executive function (z score)	0.4 (0.6)	−1.1 (0.6)	0.000
CRP (mg/L)	3.3 (5.3)	4.0 (4.6)	0.453
HOMA-IR	5.0 (6.5)	3.8 (2.5)	0.212

CKD	Dysexecutive function		
Yes (n = 149, 25.3%)	No (n = 125, 83.9%)	Yes (n = 24, 16.1%)	p
Demographics			
Age, y	80.0 (5.8)	83.5 (6.6)	0.009
Males (%)	47 (37.6)	8 (33.3)	0.692
Whites (%)	109 (87.2)	14 (58.3)	0.001
Blacks (%)	13 (10.4)	7 (29.2)	
Education, y	14.5 (3.3)	11.5 (2.4)	0.014
Current smokers (%)	4 (3.2)	0 (0)	0.374
Alcohol consumption in past month (%)	21 (16.8)	4 (16.7)	0.987
Clinical characteristics			
eGFR (1.73/min/m^2)	49.1 (7.6)	43.1 (11.7)	0.002
Executive function (z score)	0.4 (0.6)	−1.1 (0.5)	0.000
CRP (mg/L)	3.8 (5.6)	4.9 (4.5)	0.390
HOMA-IR	6.3 (7.9)	8.6 (14.1)	0.250
Total n = 588			

Note. CKD = chronic kidney disease. eGFR = estimated glomerular filtration rate. CRP = C-Reactive Protein. HOMA-IR = Homeostasis model assessment insulin resistance.

3. Results

Table 1 shows the demographic and clinical characteristics of the sample in participants with and without dysexecutive function stratified by presence or absence of CKD. Of 588 participants in the sample, 149 (25.3%) had CKD, 24 (16.1%) of those also had dysexecutive function. Of the 439 (74.7%) participants of the sample without CKD, 54 (12.3%) had dysexecutive function. Individuals with dysexecutive function were significantly older and had fewer years of formal education in both CKD and no CKD groups. There were a total of 98 participants who had CKD but no MetS and 41 participants who had both. The most prevalent MetS component in the total sample was elevated blood pressure (ranges from 75.9% in the no CKD dysexecutive function group to 87.5% in the CKD dysexecutive function group), followed by elevated waist circumference (ranges from 37% in the No CKD dysexecutive function group to 62.5% in the CKD dysexecutive function group). Table 2 shows mean values of individual components of the MetS in association with dysexecutive function stratified by CKD and gender. There were no significant differences in any of the components. Table 3 shows the proportions of individuals with individual components of the MetS. In separate analyses we distinguished among no HTN, treated HTN, and untreated HTN; we found that risk for dysexecutive function in treated and untreated HTN did not significantly differ compared to the no HTN participants in both CKD (OR = 0.49, 95%CI = 0.22–1.23 and OR = 0.49, 95%CI = 0.18–1.30) and non CKD groups (OR = 0.41, 95% CI = 0.70–2.48 and OR = 0.45, 95%CI = 0.05–4.14), thus we combined the treated and untreated groups together and analyzed them as presented in Table 4. Table 4 shows the odd ratios for dysexecutive function when the MetS composite score, and its components, are present with and without CKD. In individuals without CKD, absence of Mets was significantly associated with lower odds of presence of dysexecutive function (OR = 0.35, 95%CI = 0.13–0.95, $p = 0.039$). In individuals with CKD, elevated waist circumference was the only component of MetS significantly associated with higher odds of dysexecutive function. In individuals with CKD, elevated waist circumference was the only MetS component that was significantly associated with higher odds of presence of dysexecutive function independent of covariates (Model 4; OR = 14.25, 95%CI = 2.21–91.93, $p = 0.005$). No other components were significant. In Fig. 1 we illustrate the prevalence of individuals with CKD and abdominal obesity stratified by dysexecutive function.

Table 2
Characteristics of the individual components of the metabolic syndrome in the total sample stratified by CKD and no CKD and by gender.

	CKD	MetS components	Dysexecutive function		
			No (mean, SD)	Yes (mean, SD)	*p*
Male	No	N	145 (24.7)	16 (2.7)	
		Waist circumference (cm)	98.2 (9.8)	97.3 (9.1)	0.738
		Triglycerides (mg/dL)	99.5 (48.1)	95.4 (39.2)	0.743
		HDL cholesterol (mg/dL)	51.6 (11.9)	48.9 (11.9)	0.402
		Systolic BP (mm Hg)	135.1 (17.5)	133.1 (17.8)	0.681
		Diastolic BP (mm Hg)	77.2 (8.3)	78.5 (11.5)	0.576
		Fasting glucose (mg/dL)	92.0 (12.1)	90.1 (4.8)	0.226
	Yes	N	47 (8.0)	8 (1.4)	
		Waist circumference (cm)	98.2 (7.4)	105.4 (16.0)	0.250
		Triglycerides (mg/dL)	113.0 (54.7)	109.5 (35.1)	0.862
		HDL cholesterol (mg/dL)	49.5 (11.1)	51.4 (11.9)	0.666
		Systolic BP (mm Hg)	132.7 (19.8)	134.3 (6.8)	0.688
		Diastolic BP (mm Hg)	74.3 (11.4)	77.3 (6.9)	0.484
		Fasting glucose (mg/dL)	95.1 (12.6)	97.4 (14.1)	0.632
Female	No	N	240 (40.8)	38 (6.5)	
		MetS components			
		Waist circumference (cm)	89.1 (11.7)	87.5 (13.8)	0.449
		Triglycerides (mg/dL)	115.0 (68.3)	101.0 (60.0)	0.240
		HDL cholesterol (mg/dL)	64.1 (16.2)	65.7 (16.9)	0.587
		Systolic BP (mm Hg)	137.1 (16.4)	142.4 (22.0)	0.155
		Diastolic BP (mm Hg)	78.6 (8.6)	77.8 (10.5)	0.616
		Fasting glucose (mg/dL)	90.1 (10.9)	88.4 (11.1)	0.398
	Yes		78 (13.3)	16 (2.7)	
		Waist circumference (cm)	91.2 (11.3)	93.2 (12.1)	0.538
		Triglycerides (mg/dL)	114.7 (52.6)	134.1 (55.2)	0.186
		HDL cholesterol (mg/dL)	61.5 (16.1)	56.0 (12.3)	0.202
		Systolic BP (mm Hg)	136.3 (17.6)	142.5 (19.2)	0.225
		Diastolic BP (mm Hg)	75.5 (11.6)	75.9 (8.7)	0.890
		Fasting glucose (mg/dL)	93.1 (9.9)	94.7 (10.1)	
Total N					588 (100)

Table 3
Proportions of total sample with MetS components stratified by CKD and dysexecutive function.

CKD		Dysexecutive function			
		Yes	No	Sum	χ^2
Yes (%)		24 (4.1)	125 (21.3)	149 (25.3)	
	Waist obesity (%)	15 (10.4)	59 (41.0)	74 (51.4)	0.148
	Elevated triglycerides (%)	6 (4.0)	26 (17.4)	32 (21.5)	0.646
	Low HDL cholesterol (%)	7 (4.7)	24 (16.1)	31 (20.8)	0.469
	Hypertensive (%)	21 (15.1)	105 (75.5)	126 (90.6)	0.906
	Elevated glucose (%)	6 (4.0)	30 (20.1)	36 (24.2)	0.095
No (%)		54 (9.2)	385 (64.5)	439 (74.7)	
	Waist obesity (%)	20 (4.8)	168 (40.4)	188 (45.2)	0.297
	Elevated triglycerides (%)	7 (1.6)	65 (14.8)	72 (16.4)	0.498
	Low HDL cholesterol (%)	6 (1.4)	58 (13.2)	64 (14.6)	0.271
	Hypertensive (%)	41 (10.0)	308 (74.9)	349 (84.9)	0.100
	Elevated glucose (%)	71 (16.2)	5 (1.1)	76 (17.3)	0.917
Total N		78 (13.3)	510 (86.7)	588 (100)	

4. Discussion

Results from this study revealed that abdominal obesity, which is recognized as an integral part of the metabolic syndrome, is a stronger risk factor associated with dysexecutive function than the MetS as a composite entity in individuals with CKD. In otherwise healthy individuals, none of the other individual metabolic syndrome components or the composite Mets scores itself were associated with dysexecutive function.

In the new definition of the metabolic syndrome by the International Diabetes Federation (Federation, 2016), central obesity is the main prerequisite, along with any other two risk factors, for a diagnosis to be made. This illustrates the elevated risks that central obesity as an individual component has. Previous research also suggests that obesity represents a significant problem in individuals with CKD (Satirapoj et al., 2013; Chen et al., 2013). A well-known associate of obesity is hypertension, which is also a well-recognized contributor of decline in kidney function. Obesity may also lead to kidney injury, even in non-diabetic adults due to its contributions to decline in metabolic and vascular conditions, which adversely influences kidney function (Hall et al., 2003). Because this study is cross-sectional, we cannot make strong directional causal inferences. Our results support previous studies that show an association between obesity and cognitive impairment (Elias et al., 2003), in this case dysexecutive function. Our results further show that this association is only present in individuals with CKD. Indirectly the results of this study also imply an association between CKD and obesity (Satirapoj et al., 2013; Hall et al., 2003) and an association between CKD and dysexecutive function (Zammit et al., 2015b; Kurella et al., 2005). However, we did not study these associations directly.

Lifespan research shows that obesity, measured by waist circumference, waist-to-hip circumference, and body mass index (BMI), is inversely associated with memory and executive function (Cournot et al., 2006; Sabia et al., 2009). Studies are few and less consistent in the elderly. Elias et al. (2003) have shown in the Framingham Heart Study that higher BMI is associated with lower cognitive performance;

Table 4
Odds ratios for dysexecutive function in the CKD and no CKD groups according to the MetS composite and to individual components of the metabolic syndrome with adjustments as described below.

		Odds ratio (95% confidence interval)			
		Model 1	Model 2	Model 3	Model 4
CKD	Independent variable	Adjusted for demographics	Adjusted for demographics + CRP	Adjusted for demographics + IR	Adjusted for demographics + CRP + IR
Yes	MetS	1.76 (0.60–5.15), 0.304	1.71 (0.54–5.38), 0.359	1.01 (0.30–3.39), 0.985	0.97 (0.27–3.48), 0.969
No		0.35 (0.13–0.95), 0.039*	0.41 (0.14–1.22), 0.109	0.49 (0.17–1.43), 0.189	0.67 (0.20–2.09), 0.458
Yes	Reduced HDL cholesterol	2.95 (0.59–14.73)	2.45 (0.41–14.52)	3.24 (0.42–25.19)	3.16 (0.31–32.64)
	Elevated fasting glucose	0.69 (0.18–2.67)	0.39 (0.08–1.85)	0.44 (0.08–2.35)	0.17 (0.20–1.41)
	Elevated waist circumference	4.56* (1.27–16.36)	7.29** (1.72–30.94)	5.46* (1.35–22.12)	14.25** (2.21–91.93)
	Elevated Triglycerides	0.47 (0.09–2.58)	0.33 (0.05–2.28)	0.19 (0.02–1.65)	0.10 (0.01–1.42)
	Elevated blood pressure	0.56 (0.07–4.33)	0.87 (0.05–15.05)	0.39 (0.04–3.95)	0.94 (0.04–25.27)
No	Reduced HDL cholesterol	1.21 (0.44–3.35)	1.30 (0.40–4.20)	1.32 (0.43–4.06)	1.70 (0.50–5.76)
	Elevated fasting glucose	0.37 (0.12–1.16)	0.45 (0.13–1.49)	0.45 (0.13–1.51)	0.56 (0.15–2.06)
	Elevated waist circumference	0.61 (0.29–1.29)	0.65 (0.27–1.53)	0.67 (0.30–1.52)	0.84 (0.34–2.08)
	Elevated Triglycerides	0.37 (0.12–1.16)	1.05 (0.35–3.18)	0.56 (0.15–2.04)	0.70 (0.17–2.89)
	Elevated blood pressure	0.47 (0.20–1.10)	0.43 (0.15–1.24)	0.58 (0.22–1.49)	0.48 (0.50–5.76)

Note. CKD = chronic kidney disease. Demographics = age, gender, race, education, smoking and alcohol intake. CRP = C-reactive protein. IR = insulin resistance. HDL = high-density lipoprotein. All individual components were included in each model.
* $p < 0.05$.
** $p < 0.01$.

Cattin et al. (1997) also showed similar results in a smaller cohort. However, Kuo et al. (2006) found that obese elderly outperformed their fellow normal-weight individuals on visuospatial speed of processing andDahl Aslan et al. (2015) found no association between BMI and cognitive function in old age. Although the neurocognitive tests varied from study to study, some factors may be contributing to this discrepancy. First, body composition in old age changes – muscle mass declines and body fat increases (also known as sarcopenia); this may make the definition of obesity in older adults more difficult (Miller and Spencer, 2014). Second, in old age a lower body weight has been associated with mortality (Thinggaard et al., 2010) and being slightly overweight has been associated with better health (Dahl Aslan et al., 2015; Thinggaard et al., 2010). Finally, weight loss may be associated with the onset of Alzheimer's disease.

In the present study, results showed that participants with abdominal obesity but without CKD were not at increased risk of experiencing dysexecutive function; however, participants with elevated waist circumference and CKD were at increased risk of dysexecutive function, even if they were otherwise healthy. This is in line with previous suggestions that CKD may aggravate the impact of existing conditions (Anand et al., 2014; Seliger et al., 2005). The waist obesity-dysexecutive function association was present only in individuals with CKD. Participants with abdominal obesity may already have a low eGFR; both obesity and low eGFR may be proxies for prediabetes (Chen et al., 2013; Hall et al., 2003).

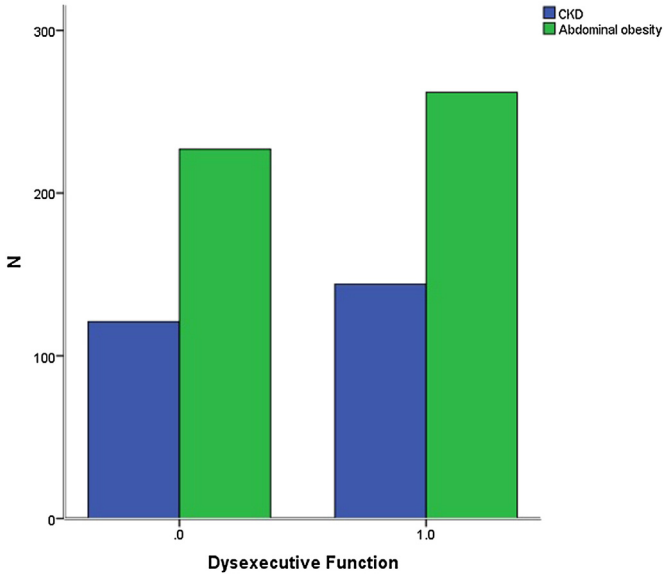

Fig. 1. Prevalence of individuals with CKD and abdominal obesity stratified by dysexecutive function.

Elevated waist circumference is an indicator of obesity. It has been known to contribute to both the development and progression of CKD in the general population (Evans et al., 2012; Ferris et al., 2007; Tozawa et al., 2002; Stengel et al., 2003). However, the mechanisms by which abdominal obesity may lead to dysexecutive function is debatable especially because waist circumference has been overlooked as a direct determinant of cognitive performance when compared to other MetS components, such as elevated blood pressure/hypertension (Levin et al., 2014; Dearborn et al., 2014) or elevated glucose/diabetes (Seetharaman et al., 2015; Hassing et al., 2004). Levin et al. (2014) have shown that elevated blood pressure was the strongest predictor of cognitive performance in four major cognitive domains (language, memory, executive function, and visual/motor skills) and that obesity (a factor composed of elevated waist circumference and high BMI) and elevated glucose independently predicted visual/motor declines in 1290 40+ year-old participants form the Northern Manhattan Study. Similarly,Seetharaman et al. (2015) found that elevated glucose was associated with reduced perceptual speed in 838 50 and older adults from the Swedish Adoption/Twin Study of Aging. Meanwhile Dearborn et al. (2014) found that all individual components of the MetS predicted a decline in the Digit Symbol Substitution Test and the Word Fluency Test in mid-life (45–65 years) in Atherosclerosis Risk in Communities study. However, abdominal obesity is known to worsen other MetS components including glucose levels, insulin resistance and blood pressure (Hall et al., 2003; Poirier et al., 2006) and may contribute to dysexecutive function through both vascular damage and neurodegeneration. Since abdominal obesity was associated with dysexecutive function in CKD participants but not in healthy ones, it is suggestive that the MetS or specific components of the MetS, such as abdominal obesity, operate via other mechanisms (e.g. CKD) that in turn affect cognitive function (e.g. executive function). Alternatively, this could also suggest Anand et al.'s (2014) conception that CKD acts through associated conditions which aids it in progressing cognitive impairment. Lastly, this observation could also be explained by the shared-environmental risk factor hypothesis whereby underlying metabolic and hemodynamic mechanisms may be affecting the kidney and executive function. Ultimately, our results suggested that

abdominal obesity per se is not a risk factor for dysexecutive function, but when it occurs with CKD, it becomes a significant risk.

In the wider context, the results of this study suggest that individual risk factors (e.g. the individual metabolic components) may be more useful both clinically and theoretically rather than as the single definition; and that cognitive impairment may be more the result of a variety of risk factors and/or chronic conditions rather than the direct result of a single condition in an otherwise healthy individual. This begs for clinicians and researchers to always look at the bigger picture, and avoid misinterpretation of risks and consequences when other factors may be mediating associations. These results should also be interpreted with caution in Asian populations, where studies have reported marked differences in waist circumference between Westerners and Asians (Patel et al., 2006), with the latter having smaller waists, and yet still reporting high levels of disease (Deurenberg et al., 2002). Thus different criteria from different sources (e.g. the NCEP definition, the World Health Organization definition, the IDF definition) have different cut-off points which are sometimes not as meaningful when evaluated in different ethnic populations, and may need more than just adding prevalent number of risk factors to target more accurately individuals at risk.

Our study's strengths include a multiethnic population representative of the Bronx County based on the U.S. Census, and a relatively large sample size. Despite this, because of stratification in our analyses, there were small number of individuals in certain groups which may have resulted in spurious associations. Another limitation was that since this was a cross-sectional study, we categorized individuals as "CKD" depending on their eGFR status at the time of the study. A CKD diagnosis requires a minimum of a three-month period with an eGFR below 60 mL/min/m^2. Previous cross-sectional studies have also categorized individuals in CKD groups at cross-section (Satirapoj et al., 2013; Kurella Tamura et al., 2008). Although a diagnosis cannot be made without information about any proteinuria or from just one time-point, these limitations they are a known feature of cross-sectional studies as is this one. In this study we only compared individuals with CKD to those without. The non-CKD individuals were included in the 'healthy' group but may be a misnomer. These individuals may have had other chronic conditions, such as CVD, that we did not consider in this study. We also speculate that the individuals with CKD had other comorbid conditions and that a possibly similar group of participants would have met the criteria for CVD. We plan to examine these conditions in future work.

In conclusion, results from this study revealed that elevated waist circumference is an integral part of the metabolic syndrome and a better risk factor for dysexecutive function than the composite MetS score in individuals with CKD. Results also showed that elevated waist circumference is not a risk factor for dysexecutive function in otherwise healthy non-diabetic older adults. Given the preventative and reversible nature of abdominal obesity, we strongly advocate the importance of simple intervention programs based on diet and exercise for at-risk individuals to avoid unnecessary disease and disability.

Support and financial disclosure

This research was supported by the Einstein Aging Study (PO1 AG03949) from the National Institutes on Aging program; the National Institutes of Health CTSA (1UL1TR001073) from the National Center for Advancing Translational Sciences (NCATS), the Sylvia and Leonard Marx Foundation, and the Czap Foundation. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NI.

Conflicts of interest

None.

Acknowledgments

We thank the EAS research participants. We thank Charlotte Magnotta, Diane Sparracio and April Russo for assistance in participant recruitment; Betty Forro, Alicia Gomez, Wendy Ramratan, and Mary Joan Sebastian for assistance in clinical and neuropsychological assessments; Michael Potenza for assistance in data management.

References

Anand, S., Johansen, K.L., Kurella Tamura, M., 2014. Aging and chronic kidney disease: the impact on physical function and cognition. J. Gerontol. Ser. A Biol. Med. Sci. 69A (3), 315–322.
Battery, A.I.T., 1944. Manual of Directions and Scoring. War Department, Adjutant General's Office, Washington DC.
Beddhu, S., et al., 2005. Associations of metabolic syndrome with inflammation in CKD: results from the third National Health and Nutrition Examination Survey (NHANES III). Am. J. Kidney Dis. 46 (4), 577–586.
Cattin, L., et al., 1997. Factors associated with cognitive impairment among older Italian inpatients. Gruppo Italiano di Farmacovigilanza nell'Anziano (G.I.F.A.). J. Am. Geriatr. Soc. 45 (11), 1324–1330.
Chen, S., et al., 2013. Central obesity, C-reactive protein and chronic kidney disease: a community-based cross-sectional study in southern China. Kidney Blood Press Res 37 (4–5), 392–401.
Cirillo, M., Anastasio, P., De Santo, N.G., 2005. Relationship of gender, age, and body mass index to errors in predicted kidney function. Nephrol. Dial. Transplant. 20 (9), 1791–1798.
Cournot, M., et al., 2006. Relation between body mass index and cognitive function in healthy middle-aged men and women. Neurology 67 (7), 1208–1214.
Dahl Aslan, A.K., et al., 2015. Cognitive consequences of overweight and obesity in the ninth decade of life? Age Ageing 44 (1), 59–65.
Dearborn, J.L., et al., 2014. The metabolic syndrome and cognitive decline in the Atherosclerosis Risk in Communities study (ARIC). Dement. Geriatr. Cogn. Disord. 38 (5–6), 337–346.
Deurenberg, P., Deurenberg-Yap, M., Guricci, S., 2002. Asians are different from Caucasians and from each other in their body mass index/body fat per cent relationship. Obes. Rev. 3 (3), 141–146.
Elias, M.F., et al., 2003. Lower cognitive function in the presence of obesity and hypertension: the Framingham heart study. Int. J. Obes. Relat. Metab. Disord. 27 (2), 260–268.
Evans, P.D., et al., 2012. Anthropomorphic measurements that include central fat distribution are more closely related with key risk factors than BMI in CKD stage 3. PLoS One 7 (4), e34699.
Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP), 2001e. Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). JAMA 285 (19), 2486–2497.
Federation, I.D., 2016. The IDF consensus worldwide definition of the metabolic syndrome. Available from: http://www.idf.org/webdata/docs/IDF_Meta_def_final.pdf.
Ferris, M., et al., 2007. Obesity, albuminuria, and urinalysis findings in US young adults from the Add Health Wave III study. Clin. J. Am. Soc. Nephrol. 2 (6), 1207–1214.
Grundy, S.M., 1999. Hypertriglyceridemia, insulin resistance, and the metabolic syndrome. Am. J. Cardiol. 83 (9, Supplement 2), 25–29.
Hall, J.E., et al., 2003. Obesity-associated hypertension and kidney disease. Curr. Opin. Nephrol. Hypertens. 12 (2), 195–200.
Hassing, L.B., et al., 2004. Type 2 diabetes mellitus contributes to cognitive decline in old age: a longitudinal population-based study. J. Int. Neuropsychol. Soc. 10 (4), 599–607.
Katz, M.J., et al., 2012. Age-specific and sex-specific prevalence and incidence of mild cognitive impairment, dementia, and Alzheimer dementia in blacks and whites: a report from the Einstein Aging Study. Alzheimer Dis. Assoc. Disord. 26 (4), 335–343.
Kuo, H.K., 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 (1), 97–103.
Kurella Tamura, M., et al., 2008. Kidney function and cognitive impairment in US adults: the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study. Am. J. Kidney Dis. 52 (2), 227–234.
Kurella Tamura, M., et al., 2011. Vascular risk factors and cognitive impairment in chronic kidney disease: the Chronic Renal Insufficiency Cohort (CRIC) study. Clin. J. Am. Soc. Nephrol. 6 (2), 248–256.
Kurella, M., Lo, J.C., Chertow, G.M., 2005. Metabolic syndrome and the risk for chronic kidney disease among nondiabetic adults. J. Am. Soc. Nephrol. 16 (7), 2134–2140.
Levey, A.S., et al., 2009. A new equation to estimate glomerular filtration rate. Ann. Intern. Med. 150 (9), 604–612.
Levin, B.E., et al., 2014. Modeling metabolic syndrome and its association with cognition: the northern Manhattan study. J. Int. Neuropsychol. Soc. 20 (10), 951–960.
Matthews, D.R., et al., 1985. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28 (7), 412–419.
Miller, A.A., Spencer, S.J., 2014. Obesity and neuroinflammation: a pathway to cognitive impairment. Brain Behav. Immun. 42, 10–21.
Ortman, J.M., Velkoff, V.A., Hogan, H., 2014. In: U.S.D.o. Commerce (Ed.), An Aging Nation: The Older Population in the United States. Census Bureau, U.S. (25-1140).
Patel, A., et al., 2006. Is a single definition of the metabolic syndrome appropriate?—a comparative study of the USA and Asia. Atherosclerosis 184 (1), 225–232.

Poirier, P., et al., 2006. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss: an update of the 1997 American Heart Association Scientific Statement on Obesity and Heart Disease from the Obesity Committee of the Council on Nutrition, Physical Activity, and Metabolism. Circulation 113 (6), 898–918.
Sabia, S., et al., 2009. Body mass index over the adult life course and cognition in late midlife: the Whitehall II Cohort Study. Am. J. Clin. Nutr. 89 (2), 601–607.
Satirapoj, B., et al., 2013. Obesity and its relation to chronic kidney disease: a population-based, cross-sectional study of a Thai army population and relatives. Nephrology (Carlton) 18 (3), 229–234.
Seetharaman, S., et al., 2015. Blood glucose, diet-based glycemic load and cognitive aging among dementia-free older adults. J. Gerontol. A Biol. Sci. Med. Sci. 70 (4), 471–479.
Segura, B., et al., 2009. Mental slowness and executive dysfunctions in patients with metabolic syndrome. Neurosci. Lett. 462 (1), 49–53.
Seliger, S.L., et al., 2005. Cystatin C and subclinical brain infarction. J. Am. Soc. Nephrol. 16 (12), 3721–3727.
Stengel, B., et al., 2003. Lifestyle factors, obesity and the risk of chronic kidney disease. Epidemiology 14 (4), 479–487.
Thinggaard, M., et al., 2010. Is the relationship between BMI and mortality increasingly U-shaped with advancing age? A 10-year follow-up of persons aged 70–95 years. J. Gerontol. A Biol. Sci. Med. Sci. 65 (5), 526–531.
Tozawa, M., et al., 2002. Influence of smoking and obesity on the development of proteinuria. Kidney Int. 62 (3), 956–962.
Viscogliosi, G., et al., 2012. Screening cognition in the elderly with metabolic syndrome. Metab. Syndr. Relat. Disord. 10 (5), 358–362.
Wechsler, D., 1997. Adult Intelligence Scale-III. third ed. Psychological Corporation, San Antonio, TX.
Zammit, A.R., et al., 2015a. Chronic kidney disease in non-diabetic older adults: associated roles of the metabolic syndrome, inflammation, and insulin resistance. PLoS One 10 (10), e0139369.
Zammit, A.R., et al., 2015b. Association between renal function and cognitive ability domains in the Einstein Aging Study: a cross-sectional analysis. J. Gerontol. A Biol. Sci. Med. Sci. 70 (6), 764–770.
Zammit, A.R., et al., 2015c. Low eGFR is associated with dysexecutive and amnestic mild cognitive impairment. Alzheimers Dement. (Amst) 1 (2), 152–159.