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

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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

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(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.