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Executive Functioning and the Metabolic Syndrome: A Project FRONTIER Study

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Abstract

Decrements in cognitive functioning have been linked to the metabolic syndrome (MetS), a risk factor for cardiovascular disease defined by the presence of three of the following: elevated blood pressure, increased waist circumference, elevated blood glucose, elevated triglycerides, and low high-density lipoprotein cholesterol. We examined the relationship between four measures of executive functioning (EF) and MetS as diagnosed by National Heart, Lung, and Blood Institute-American Heart Association criteria. MetS was examined in a rural population of 395 persons with a mean age of 61.3 years, 71.4% women, 37.0% Hispanic, 53.7% White non-Hispanic. There was a 61.0% prevalence of MetS. We derived a factor score from the four executive function measures which was used to compare those with and without the syndrome, as well as any additive effects of components of the syndrome. Those with MetS exhibited significantly poorer performance than those without the syndrome. However, there was no additive effect, having more components of the syndrome was not related to lower performance. The presence of MetS was associated with poorer EF in this rural cohort of community dwelling volunteers.

Keywords: Executive functioning; Metabolic syndrome; Cardiovascular risk factors

Introduction

The term "metabolic syndrome" (MetS) that first appeared in 1998 (Grundy et al., 2005) was defined formally in 2001(National Cholesterol Education Program, National Heart, Lung, and Blood Institute, National Institutes of Health, 2002, Adult Treatment Panel III) and revised in 2005 by the National Heart, Lung, and Blood Institute/American Heart Association (Grundy et al., 2005). The syndrome is thought to identify individuals at increased risk of developing cardiovascular disease due to certain metabolic abnormalities that often co-occur below the diagnostic threshold of a clinical disorder, such as hypertension, dyslipidemia, or elevated blood glucose concentration. The current National Heart, Lung, and Blood Institute/American Heart Association definition includes abdominal obesity (waist circumference >102 cm for men and ≥ 88 cm for women), triglyceride levels ≥ 150 mg/dL, high-density lipoprotein (HDL) levels <40 mg/dL for men and <50 mg/dL for women, systolic blood pressure ≥ 130 or diastolic pressure ≥ 85, and elevated fasting plasma glucose levels ≥ 100 mg/dL (Grundy et al., 2005). The presence of any three components is sufficient for the diagnosis; medication for the treatment of hypertension, triglyceridemia, and low HDL are also counted as meeting the respective requirement.

MetS increases risk of developing cardiovascular disease (Lindblad, Langer, Windgard, Thomas, & Barret-Connor, 2001) and this risk increases with age (McNeill, Katz, & Girman, 2006). The prevalence of MetS is higher among those of lower socioeconomic status (Gallo, de los Monteros, Ferent, Urbina, & Talevera, 2007; Langenberg, Kuh, Wadsworth, Brunner, & Hardy, 2006), which may put minorities and residents of rural communities at heightened risk.

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There have been numerous investigations of the relationship between cognition and MetS (Gatto, Hendersen, St John, McCleary, Hodis, & Mack, 2008; Yaffe, Weston, Blackwell, & Kreuder, 2009; Yaffe et al, 2004), and the individual components of MetS appear to increase the risk of developing cognitive deficits (Abbatecola et al., 2004; Watari et al., 2008). Among investigations examining the relationship of cardiovascular risk factors to cognition, executive functioning (EF) has received increased attention (Bokura, Nagai, Oguro, Kobayashi, & Yamaguchi, 2010; Schuur et al., 2010). EF includes focusing attention on task-relevant information, inhibiting task-irrelevant information, switching attention between subcomponents of a task, planning how to string subcomponents together to complete a task, monitoring information held in working memory, updating behavioral strategies, and encoding information (Royall et al., 2002). Compared with other cognitive domains, EF may be impacted more by metabolic abnormalities as EF relies on extensive networks of cortical brain regions that may have a higher susceptibility to damage caused by MetS components (Schuur et al., 2010). Performance on tasks of EF has been found impaired in patients with insulin resistance (Abbatecola et al., 2004), type two diabetes (Watari et al., 2008), morbid obesity (Boeka and Lokken, 2008), and hypertension (Schillerstrom et al., 2005), which are related to the specific cardiovascular risk factors composing MetS.

Previous research has linked the components of MetS to decreases in EF, yet whether the syndrome in its aggregate form leads to greater deficits has been less clear. A relationship between the syndrome and EF processes would have important implications, as EF deficits may undermine the effectiveness of intervention strategies that rely on cognitive input to produce behavior change. Conversely, a relationship may provide an avenue to mitigate cognitive decline by treating the individual components. This study aims to clarify the relationship between EF, MetS, and its components by examining four EF tasks across individuals in a multiethnic rural population. We hypothesized that individuals with MetS (three or more components) would exhibit decreased EF performance when compared with those without the syndrome (two or fewer components) and that EF performance would be inversely related to the number of MetS components present.

Methods

Participants

Participants were 395 community-dwelling individuals from an ongoing rural health study, Project FRONTIER (Facing Rural Obstacles to Healthcare Now Through Intervention, Education & Research; O'Bryant et al., 2011). This epidemiologic study was established in part to determine the prevalence of cardiovascular disease and the associated risk factors, evaluate the prevalence of cognitive impairment and dementia syndromes, and examine the link between the two.

Individuals enrolled in Project FRONTIER were ≥40 years of age and residents of either Cochran or Parmer County; both are on the Texas/New Mexico Border. All participants signed written informed consent prior to participation in the study. Participants underwent a medical examination in their county of residence, a neuropsychological battery, an in-depth interview, and provided contact information for the completion of a structured informant telephone interview approved by the Texas Tech University of Health Sciences Center Institutional Review Board. A detailed description of the cohort and community-based participatory research procedures has been published elsewhere (O'Bryant et al., 2009). We have also previously demonstrated the comparability of our recruited cohort to that of the entire community (O'Bryant et al., 2011).

Neuropsychological measures

Participants underwent a clinical interview and a neuropsychological battery, although only neuropsychological measures thought to assess EF were included in this study. The selected tests and the raw score variables used for analysis were time to completion from Trail Making Test B (TMT-B; Reitan & Wolfson, 1993), clock drawing task score (CLOX1; Royall, Cordes, & Polk, 1998), total score from the Executive Interview (EXIT25; Royall et al., 1992), and total words generated during the Controlled Oral Word Association Test (COWAT; Strauss, Sherman, & Spreen, 2006). The COWAT was included in this study as it was found to be sensitive to EF deficits in persons with neurological insult (Kavé et al., 2011).

Metabolic measures

All participants underwent a medical examination with fasting blood work. Blood was drawn for a lipid panel, comprehensive metabolic panel, complete blood count, blood glucose, HbA1c, B12, thyroid levels, and gamma-glutamyl transferase. Blood pressure was taken at three times during the evaluation and average diastolic and systolic pressure was computed for analysis.

Abdominal girth was measured at the umbilicus with the participants standing. National Heart, Lung, and Blood Institute/American Heart Association criteria were used to determine if an individual met diagnostic criteria for each MetS component.

Prior to analysis, data on triglycerides, HDL, fasting glucose, waist circumference, and blood pressure were examined for the accuracy of data entry and missing values. CLOX1, EXIT25, COWAT, and TMT-B were examined for the accuracy of data entry, missing values, and fit between their distributions and the assumptions of multivariate analysis. Missing values were excluded list-wise from analysis for all variables.

The significance of kurtosis and skewness was examined for each variable. The distributions for CLOX1 and TMT-B reached significance for skewness and kurtosis, whereas the EXIT25 distribution was significantly skewed. Raw score transformations which resulted in the greatest reduction in kurtosis and/or skewness were selected, varying as a function of the distribution of raw scores. TMT-B and the inverse of CLOX1 were logarithmically transformed, reducing kurtosis and skewness for both distributions. The EXIT25 was transformed by taking the square root of each score.

There were 395 participants with information on all five MetS variables and the four EF tasks. Of these, 25 (6.3%) had no MetS component, 47 (11.9%) had one, 82 (20.8%) had two, 86 (21.8%) had three, 81 (20.5%) had four, and 74 (18.7%) had all five components. Demographic data are presented by group membership in Table 1. Significant differences were observed between the groups with regard to age and education. Specifically, those with no components were significantly younger than those with four and five components at $p < .05$, and those with two components were significantly younger than those with one, three, four, and five components, all at $p < .05$. With respect to education, those with no component had completed significantly more years of education than the group with two components ($p < .05$).

Among the 395 participants, 263 (66.6%) individuals met criteria for the blood pressure component, the most prevalent component. There were 256 (64.8%) individuals who met criteria for waist circumference, 229 (58.0%) for elevated triglycerides, 230 (58.2%) for reduced HDL, and 185 (46.8%) for elevated blood glucose. Overall, 241 (61.0%) individuals met the clinical diagnostic criteria for MetS.

Using SPSS version 20 FACTOR procedure, we conducted a maximum likelihood factor analysis on the four EF tasks. This was conducted to determine the factor structure of the variables and to compute an Executive Factor score that was used in the following analyses. The factor structure was determined by examining the scree plot and Eigen values. The regression approach available through SPSS was used to derive a composite factor score for the EF tasks. This Executive Factor score was then entered into subsequent analyses as the dependent variable. We conducted two main analyses to examine the Executive Factor score; a comparison of those with and without MetS and a comparison with the participants divided by the number of MetS factors. Both used analysis of covariance (ANCOVA) through SPSS 20 to examine the relationship between the Executive Factor score and MetS with age, education, ethnicity, and gender entered as covariates. The first analysis had two levels, those with two or fewer components of MetS and those with three or more components. For the second analysis, the independent variable had six levels, those with no components, and those with one, two, three, four, or all five MetS components. The levels were independent of each other, with no overlap in membership between component groups.

Table 1. Number of MetS components by education, age, gender, ethnicity, and measures of EF

Number of components	0 ($n = 25$)	1 ($n = 47$)	2 ($n = 82$)	3 ($n = 86$)	4 ($n = 81$)	5 ($n = 74$)	Total ($N = 395$)
Education in years ($M \pm SD$)	13.6 ± 3.2	11.7 ± 3.5	11.1 ± 3.9	11.9 ± 3.8	11.2 ± 3.8	11.4 ± 3.9	11.55 ± 3.8
Age ($M \pm SD$)	55.3 ± 10.5	63.6 ± 14.7	56.5 ± 11.0	62.5 ± 13.6	63.3 ± 12.0	63.7 ± 10.8	61.3 ± 12.5
Ethnicity (*n* [%])							
White non-Hispanic	22 (88.0)	26 (55.3)	28 (34.1)	47 (54.7)	45 (55.5)	44 (59.5)	212 (53.7)
Hispanic	3 (12.0)	18 (38.3)	40 (48.8)	27 (31.4)	30 (37.0)	28 (37.8)	146 (37.0)
African American	0	2 (4.2)	6 (7.3)	7 (8.1)	5 (6.2)	2 (2.7)	22 (5.6)
Native American		1 (2.1)	8 (9.8)	5 (5.8)	1 (1.2)	0	15 (3.8)
Gender (*n* [%])							
Women	23 (92.0)	37 (78.7)	58 (70.7)	59 (68.6)	55 (67.9)	50 (67.6)	282 (71.4)
CLOX1 ($M \pm SD$)	13.4 ± 1.4	12.1 ± 2.6	12.5 ± 2.0	12.5 ± 1.8	12 ± 2.2	12 ± 2.1	12.3 ± 2.1
EXIT25 ($M \pm SD$)	4.3 ± 2.7	6.8 ± 4.6	5.9 ± 3.9	7.6 ± 5.1	8.1 ± 4.5	6.6 ± 3.8	6.8 ± 4.4
COWAT ($M \pm SD$)	34.4 ± 15.9	28.3 ± 11.5	30.4 ± 11.6	29.1 ± 10.5	27.8 ± 12.0	28.7 ± 11.0	29.3 ± 11.7
TMT-B ($M \pm SD$)	82.8 ± 41.2	134.6 ± 84.2	118.5 ± 70.2	131.1 ± 71.7	134.1 ± 89.0	132 ± 73.4	126.6 ± 76.3
EF factor score ($M \pm SD$)	−0.69 ± .86	0.06 ± .95	−0.16 ± .86	0.08 ± .92	0.18 ± .90	0.08 ± .75	

Notes: CLOX1 = clock drawing task score; EXIT25 = total score from the Executive Interview; COWAT = Controlled Oral Word Association Test; TMT-B = Trail Making Test B; EF = executive functioning.

Results

Factor analysis

The dimensionality of EF measures was analyzed with maximum likelihood factor analysis. The number of factors was based on two criteria: the scree plot and the interpretability of the factor solution. The four EF tasks loaded onto a single factor that explained 57.04% of the variance. The scree plot indicated a one-dimensional factor structure. Based on the scree plot one factor was extracted from the four variables and, therefore, not rotated. The factor loadings were 0.791 for TMT-B, 0.757 for EXIT25, −0.637 for COWAT, and 0.425 for CLOX1. Each variable loaded onto the factor so that higher positive scores indicated lower performance. This factor score was used as the dependant variable in the subsequent analyses.

One way ANCOVA by the presence of MetS

After controlling for age, education, gender, and ethnicity the relationship between the presence of MetS and the Executive Factor Score was significant—$F(5, 389) = 4.2$, $p = .041$—with a small effect size, ($\eta^2 = 0.011$), as those without the MetS ($M = -0.18$, $SD = 0.91$), had a lower factor score which indicates higher EF performance than those with MetS ($M = 0.15$, $SD = 0.98$).

One-way ANCOVA by MetS components

The sample population was categorized into the six groups described above and compared on the Executive Factor score, with age, education, ethnicity, and gender entered as covariates. The relationship between the number of components of MetS and the Executive Factor score was not significant, $F(9, 385) = 1.52$, $p = .182$. Means and standard deviations for each group are presented in Table 1.

Discussion

We found the expected association between the presence of MetS and performance on EF tasks in this multiethnic sample of rural subjects, although the effect size indicated that only an ∼1% of variance was shared between the Executive Factor score and the presence of MetS after accounting for several demographic variables. Contrary to our hypothesis, the effect of MetS components on EF was not additive. The presence of MetS itself was significantly related to the Executive Factor score but having more components of the syndrome was not associated with lower EF. Our findings are consistent with other investigations that have found decreased performance in EF tasks to be associated with MetS (Bokura et al., 2010; Schuur et al., 2010; Segura et al., 2009).

Although the relationship was significant, the shared variance between EF and MetS was minimal after accounting for relevant demographic variables. Previous research has been mixed with regard to the magnitude of the association between EF and MetS, with some investigations reporting results similar to the current study (Schuur et al., 2010) and others reporting slightly larger effect sizes (Segura et al., 2009). Although the reason for these differences is not clear, the findings indicate the relationship between MetS and cognition, particularly EF, varies as a function of the population studied (Bokura et al., 2010). Demographic factors, such as age, may contribute to disparate findings. For example, the relationship may be stronger among older populations, as older individuals with MetS may be more likely to meet criteria for the syndrome over a longer period of time or be more susceptible to adverse effects related to MetS, resulting in greater discrepancies in cognition between those with and without the syndrome (Yaffe et al., 2009). However, some studies have reported that better cognitive performance was associated with the presence of MetS in individuals over the age of 80 (Laudisio et al., 2008; van den Berg, Biessels, de Craen, & Westendorp, 2007), indicating complex, age-related changes in the relationship between MetS and cognition. Methodological differences between studies may be another contributing factor. Cross-sectional studies are unable to account for the duration of MetS, grouping individuals who recently developed MetS with those meeting the criteria over an extended period of time, which may diminish observable effects (Akbaraly et al., 2010).

Several possible mechanisms may underlie a relationship between MetS and EF. The brain circuitry involved in EF is highly susceptible to vascular compromise (Schuur et al., 2010), and components of the syndrome, such as elevations in blood pressure, may damage the vascular system of the brain at levels that do not meet the criteria for a clinical disorder. Another possible explanatory mechanism is altered cerebral hemodynamics. Changes in neurovascular coupling that can occur during mid-life may lead to a number of changes that place an individual at risk of poorer cognitive performance, such as small vessel disease, regional hypoperfusion, and neurodegeneration (Novak, 2012). Additionally, elevated glucose levels may also contribute to cognitive deficits as higher glucose levels, even in individuals without diabetes, increase the risk of dementia (Crane et al., 2013).

We found a 61% prevalence of the MetS in this sample of rural community dwelling individuals. This differs from prevalence rates from other studies, one of which found 44% of Latinos age 60 or older met criteria for MetS (Yaffe, Blackwell, Cherkasova, Whitmer, & West, 2007). The high prevalence of MetS in our study may be related to one or more of many factors associated with rural life, including diet and restricted access to healthcare. Although the mechanism underlying the elevated frequency of MetS in this sample is unknown, it suggests that individuals in similar communities may be disproportionately at risk for EF deficits related to MetS. This may be true for other populations that exhibit higher prevalence rates of MetS, including psychiatric and neurologic populations. The effects of EF deficits associated with MetS in such populations may be more profound than those in the current study. Taking EF deficits into consideration when treating components of MetS may be important, as interventions designed to treat the components involve complex, goal directed behavioral patterns (Hall, Fong, Epp, & Elias, 2008). Given the prevalence of MetS, even small decrements in EF performance could have significant net effects.

Although we do not know the directionality of the effect of impaired EF and MetS, our findings in conjunction with previous investigations suggest that educational measures that address cardiovascular disease risk factors may be more effective if they are augmented with support of executive function, such as a structured program. Current interventions aimed at reversing MetS rely on pharmacological treatment of the specific components or modifying behavior by improving diet and increasing exercise. Evidence exists for EF involvement in the successful implementation and adherence to a diet or exercise regimen, requiring the cognitive skills that enable goal-directed behavior (Hall et al., 2008).

There are several limitations to the generalizability of this study. The Executive Factor score accounted for ~57% of the variance across the EF tasks, which is low considering the measures were selected because they were conceptualized to assess EF. A separate selection of EF tasks may have resulted in a higher percentage of variance accounted for by the Executive Factor score. There were fewer individuals in the group with no MetS components and these participants were younger, had more years of education, and were more likely to be White, non-Hispanic, and women than the other groups. The effect of MetS on EF was minimal compared with the impact of these demographic variables, and only 1% of the observed variance in EF was shared with the presence of the MetS after controlling for several of these variables. Also, those with one component of the syndrome appeared to have poorer performance on several EF tasks than groups with more components, which may have negated an additive effect of MetS components on EF in this sample. Due to the cross-sectional design of this study, we cannot determine the duration of MetS and its components or whether this differentially impacted EF. Longitudinal studies have found that, at baseline, groups with or without MetS showed few differences on cognitive tasks, but those who had MetS show greater cognitive impairment at follow-up (Yaffe et al., 2009). Another investigation found that the duration of MetS accelerated decline in EF among women but not men (McEvoy et al., 2012).

Future research should examine the impact that the duration of MetS components has on EF and investigate the relationship between MetS and EF in different populations, as the effects may vary as a function of the population studied. Comparisons between EF and other domains of cognition are also needed to determine if EF is more susceptible to damage than other cognitive domains. Prospective studies could illustrate the patterns of deficits over time, as prolonged exposure to MetS may be related to cognitive decline. Investigating the effect that the treatment of MetS components has on improving EF deficits is also important. Such studies could help identify whether MetS leads to impaired EF or impaired EF leaves people susceptible to developing MetS. Understanding the relationship between MetS and EF could, potentially, have significant implications for public health.

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References

Abbatecola, A., Paolisso, G., Lamponi, M., Bandinelli, S., Lauretani, F., Launer, L., et al. (2004). Insulin resistance and executive dysfunction in older persons. *Journal of the American Geriatrics Society*, *52*, 1713–1718.

Akbaraly, T. B., Kivimaki, M., Shipley, M. J., Tabak, A. G., Jokela, M., Vitranen, M., et al. (2010). Metabolic syndrome over 10 years and cognitive functioning in late midlife: The Whitehall study. *Diabetes Care*, *33 (1)*, 84–89.

Boeka, A., & Lokken, K. (2008). Neuropsychological performance of a clinical sample of extremely obese individuals. *Archives of Clinical Neuropsychology*, *23*, 467–474.

Bokura, H., Nagai, A., Oguro, H., Kobayashi, S., & Yamaguchi, S. (2010). The association of metabolic syndrome with executive dysfunction independent of subclinical ischemic brain lesions in Japanese adults. *Dementia and Geriatric Cognitive Disorders*, *30*, 479–485.

Crane, P. K., Walker, R., Hubbard, R. A., Li, G., Nathan, D. M., Zheng, H., et al. (2013). Glucose levels and risk of dementia. *The New England Journal of Medicine*, *369*, 540–548.

Gallo, L. C., de los Monteros, K. E., Ferent, V., Urbina, J., & Talavera, G. (2007). Education, psychosocial resources, and metabolic syndrome variables in latinas. *Annals of Behavioral Medicine*, *34 (1)*, 14–25.

Gatto, N., Henderson, V., St John, J., McCleary, C., Hodis, H., & Mack, W. (2008). Metabolic syndrome and cognitive function in healthy middle-aged and older adults without diabetes. *Neuropsychology, Development, and Cognition. Section B, Aging, Neuropsychology, and Cognition*, *15*, 627–641. Retrieved August 19, 2009.

Grundy, S. M., Cleeman, J. I., Daniels, S. R., Donato, K. A., Eckel, R. H., Franklin, B. A., et al. (2005). Diagnosis and management of the metabolic syndrome: American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement (Executive Summary). *Circulation*, *112*, 2735–2752. doi:10.1161/CIRCULATIONAHA.105.169404.

Hall, P. A., Fong, G. T., Epp, L. J., & Elias, L. J. (2008). Executive functioning moderates the intention-behavior link for physical activity and dietary behavior. *Psychology and Health*, *23*, 309–326.

Kavé, G., Heled, E., Vakil, E., & Agranov, E. (2011). Which verbal fluency measure is most useful in demonstrating executive deficits after traumatic brain injury? *Journal of Clinical and Experimental Neuropsychology*, *33*, 358–365.

Langenberg, C., Kuh, D., Wadsworth, E. J., Brunner, E., & Hardy, R. (2006). Social circumstances and education: Life course origins of social inequalities in metabolic risk in a prospective national birth cohort. *American Journal of Public Health*, *96*, 2216–2221.

Laudisio, A., Marzetti, E., Pagano, F., Cocchi, A., Franceschi, C., Bernabei, R., et al. (2008). Association of metabolic syndrome with cognitive function: The role of sex and age. *Clinical Nutrition*, *27*, 747–754.

Lindblad, U., Langer, R. D., Wingard, D. L., Thomas, R. G., & Barret-Connor, E. L. (2001). Metabolic Syndrome and ischemic heart disease in elderly men and women. *American Journal of Epidemiology*, *153(5)*, 481–489. doi:10.1093/aje/153.5.481.

McEvoy, L. K., Laughlin, G. A., Barrett-Connor, E., Bergstrom, J., Kritz-Silverstrien, D., Der-Martirosian, C., et al. (2012). Metabolic syndrome and 16-year cognitive decline in community dwelling adults. *Annals of Epidemiology*, *22*, 310–317.

McNeill, A. M., Katz, R., Girman, C. J., Rosamond, W. D., Wagenknecht, L. E., Barzilay, J. I., et al. (2006). Metabolic syndrome and cardiovascular disease in older people: The cardiovascular health study. *Journal of the American Geriatric Society*, *54*, 1317–1324.

National Cholesterol Education Program, National Heart, Lung, and Blood Institute, National Institutes of Health. (2002). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment on High Blood Cholesterol in Adults (NIH Publication No. 02-5215) Retrieved from http://www.nhlbi.nih.gov/guidelines/cholesterol/atp3full.pdf.

Novak, V. (2012). Cognition and hemodynamics. *Current Cardiovascular Risk Reports*, *6*, 380–396.

O'Bryant, S. E., Edwards, M., Menon, C. V., Gong, G., & Barber, R. (2011). Long-term low-level arsenic exposure is associated with poorer neuropsychological functioning: A project FRONTIER study. *International Journal of Environmental Research and Public Health*, *8*, 861–874.

O'Bryant, S. E., Zhang, Y., Owen, D., Cherry, B., Ramirez, V., Silva, M., et al. (2009). The cochran county aging study: Methodology and descriptive statistics. *Texas Public Health Journal*, *61*, 5–7.

Reitan, R. M., & Wolfson, D. (1993). *The Halstead-Reitan neuropsychological test battery: Theory and clinical interpretation* (2nd ed). Tucson, AZ: Neuropsychology Press.

Royall, D., Cordes, J., & Polk, M. (1998). CLOX: An executive clock drawing task. *Journal of Neurology, Neurosurgery & Psychiatry*, *64*, 588–594.

Royall, D., Lauterbach, E., Cummings, J., Reeve, A., Rummans, T., Kaufer, D., et al. (2002). Executive control function: A review of its promise and challenges for clinical research: A report from the committee on research of the American Neuropsychiatric Association. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *14*, 377–405.

Royall, D., Mahurin, R., & Gray, K. (1992). Bedside assessment of executive cognitive impairment: The executive interview. *Journal of the American Geriatrics Society*, *40*, 1221–1226. Retrieved from PsycINFO database.

Schuur, M., Henneman, P., van Sweiten, J. C., Zilikens, M. C., de Koning, I., Janssens, A. C., et al. (2010). Insulin-resistance and metabolic syndrome are related to executive function in women in a large family-based study. *European Journal of Epidemiology*, *25*, 561–568.

Schillerstrom, J., Horton, M., & Royall, D. (2005). The impact of medical illness on executive function. *Psychosomatics: Journal of Consultation Liaison Psychiatry*, *46 (6)*, 508–516.

Segura, B., Jurado, M. A., Freixenet, N., Albuin, C., Muniesa, J., & Junqué, C. (2009). Mental slowness and executive dysfunctions in patients with metabolic syndrome. *Neuroscience Letters*, *462 (1)*, 49–53.

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms, and commentary* (3rd ed.). New York: Oxford University Press.
van den Berg, E., Biessels, A. J., de Craen, A. J. M., Gussekloo, J., & Westendorp, R. G. J. (2007). The metabolic syndrome is associated with decelerated cognitive decline in the oldest old. *Neurology*, *69*, 979–985.
Watari, K., Elderkin-Thompson, V., Ajilore, O., Haroon, E., Darwin, C., Pham, D., et al. (2008). Neuroanatomical correlates of executive functioning in depressed adults with type 2 diabetes. *Journal of Clinical and Experimental Neuropsychology*, *30 (4)*, 389–397.
Yaffe, K., Haan, M., Blackwell, T., Cherkasova, E., Whitmer, R., & West, N. (2007). Metabolic syndrome and cognitive decline in elderly latinos: Findings from the Sacramento Area Latino Study of Aging Study. *Journal of the American Geriatrics Society*, *55 (5)*, 758–762.
Yaffe, K., Kanaya, A., Lindquist, K., Simonsick, E., Harris, T., Shorr, R., et al. (2004). The metabolic syndrome, inflammation, and risk of cognitive decline. *Journal of the American Medical Association*, *292 (18)*, 2237–2242.
Yaffe, K., Weston, A., Blackwell, T., & Krueger, K. (2009). The metabolic syndrome and development of cognitive impairment among older women. *Archives of Neurology*, *66 (3)*, 324–328.