Sex Hormone Binding Globulin and Verbal Memory in Older Men

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Objective: *Cognitive function in older adults may be affected by multiple factors, such as sex hormone levels, metabolic disturbances, and neuropsychiatric illness. However, relatively few studies have tested the associations between these factors and cognitive function in a single sample. A cross-sectional analysis was conducted to examine the association between sex hormones, metabolic parameters, and psychiatric diagnoses with verbal memory in nondemented older men.* **Methods:** *Participants were 112 men (mean age: 61.3 years) from the Baltimore Epidemiologic Catchment Area Follow-Up Study who completed measures of blood sex hormone levels, metabolic parameters (e.g., lipid profiles), and verbal memory.* **Results:** *Higher levels of serum sex hormone binding globulin (SHBG) were associated with lower delayed verbal memory scores (standardized coefficients [beta] = −0.19, t = −2.07, df = 1, 105, p = 0.04), and higher body mass index (BMI) was associated with better immediate (beta = 0.21, t = 2.41, df = 1,105, p = 0.02) and delayed (beta = 0.22, t = 2.46, df = 1,105, p = 0.02) verbal memory performance after adjustment for age, education, and psychiatric disorders. There was an inverse correlation between SHBG levels and BMI (Pearson's r = −0.37, N = 112, p <0.001). Estimated free testosterone levels revealed curvilinear associations with verbal memory performance.* **Conclusion:** *Our data suggest that higher SHBG levels are associated with worse verbal memory, whereas a higher BMI is associated with better verbal memory in older men. Higher SHBG levels due to lower adiposity may be a risk factor for cognitive dysfunction. The mechanisms linking SHBG to cognitive function have yet to be elucidated.* (Am J Geriatr Psychiatry 2013; ■:■−■)

Key Words: Sex hormone binding globulin, sex hormones, cognitive function, obesity

INTRODUCTION

Human cognitive performance is affected by factors such as age and educational attainment. In addition, studies suggest that physical conditions (e.g., sex hormone imbalances,[1,2] metabolic disturbances,[3] and psychiatric disorders[4–7]) may have a substantial impact on cognitive performance.

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Evidence derived from animal models suggests that testosterone may have a neuroprotective effect and prevent cognitive decline.[8,9] Hence, age-related declines in testosterone levels[2] may be linked to cognitive decline in men. However, research evaluating the association between the bioavailability of endogenous testosterone and levels of free testosterone (FT) with cognitive function in men provides mixed results.[2] Sex hormone binding globulin (SHBG) is a testosterone transport protein that affects circulating levels of FT. Few studies have tested the relationship between serum SHBG levels and cognitive function; however, a study identified a negative correlation between SHBG levels and cognition in elderly men.[10] Similarly, a separate study demonstrated that older men and women with higher levels of SHBG had an elevated risk for developing Alzheimer disease.[11]

Metabolic syndrome has been defined as a clustering of clinical and biochemical risk factors, including central obesity, dyslipidemia, hypertension, and insulin resistance, that increase the risk for developing Type 2 diabetes and cardiovascular disease.[12] The relationship between metabolic syndrome and cognition has been extensively studied. Moreover, obesity,[13] hypertension,[14] and Type 2 diabetes[15] have been linked to cognitive impairment. To date, relatively few studies have assessed the association between cognitive function with both sex hormones and metabolic parameters in older men; even fewer studies have used structured psychiatric interviews to measure the extent of psychopathology. However, use of appropriate assessment measures evaluating psychopathology is paramount in this line of research because psychiatric illness may confound the association between hormones and/or metabolic parameters with cognitive outcomes. Our study evaluated the association of testosterone, SHBG, and metabolic parameters with memory performance in older men from the Baltimore Epidemiologic Catchment Area (ECA) study.

METHODS

Sample

The Baltimore ECA Follow-Up Study is an ongoing, longitudinal, population-based cohort of adults originally interviewed in 1981 (N = 3,481) and followed-up in 1982 (N = 2,768), 1993 (N = 1,920), and 2004 (N = 1,071). The ECA study was designed to collect data on the prevalence and incidence of psychiatric illness in an adult community sample according to the *Diagnostic and Statistical Manual of Mental Disorders, Third Edition Revised* (DSM-III-R) criteria as well as the use of, and need for, psychiatric services by individuals with psychiatric illness. Methods for the Baltimore ECA Follow-Up Study have been described in detail elsewhere.[16] We used data from Wave 4 (2003−2004), in which a sample of blood was requested from each of the 1,071 respondents. The characteristics of the 683 who agreed to donate a blood sample are reported by Mezuk et al.[17]

Although the ECA study Wave 4 consists of 1,071 participants, we selected individuals who met following criteria: (1) male gender (397 of 1,071, 37%), (2) 50 years and older (282 of 397, 71%), (3) completed verbal memory assessment described below (244 of 282, 87%), (4) completed Mini-Mental State Exam[18] (MMSE) and scored at least 27 (205 of 244, 84%), (5) had body mass index (BMI) assessed (183 of 205, 89%), and (6) donated blood at the interview (112 of 183, 61%), resulting a final sample size of 112. Compared with the 959 participants excluded from our analysis, the 112 participants included were older (61.3 years old versus 58.6 years old; $t = 2.08$, $df = 1,069$, $p = 0.04$), more likely to be white (78% versus 60%; $\chi^2 = 13.3$, $df = 1$, $p < 0.01$), had more education (13.1 years versus 12.4 years; $t = 2.58$, $df = 1069$, $p = 0.01$), and had a similar BMI (29.2 versus 30.0; $t = -0.98$, $df = 940$, $p = 0.3$). We used a relatively high MMSE cut point in an attempt to exclude subjects with mild cognitive impairment or dementia; the conventional cut point ($\geq$24) would likely permit the inclusion of more participants with clinical levels of cognitive impairment, especially among the highly educated.[19]

The study was approved by the Johns Hopkins Bloomberg School of Public Health Institutional Review Board. All participants provided written informed consent.

Assessment of Cognitive Function

Verbal memory was assessed by a modified version of the Rey Verbal Learning Test.[20] Detailed procedures of verbal memory assessment have been