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Modifiable Risk Factors as Predictors of Global Cognition in Adults: A Pilot Study of Two Rural Communities in Anambra State, Nigeria

Valentine A. Ucheagwu[1], Rita N. Ugokwe-Joseph[1], Cyriacus C. Ajaelu[1]

[1]Department of Psychology, Nnamdi Azikiwe University, Awka, Nigeria

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ABSTRACT

Modifiable risk factors are behaviours and exposures that can raise or lower a person's risk of developing diseases. These risk factors by themselves are modifiable and have been shown to drive midlife chronic diseases. This study investigated the roles of modifiable risk factors (i.e., hypertension, diabetes, stroke, measures of adiposity, and physical activity among others) on global cognition in rural community dwellers from southeast Nigeria. One hundred and fifty participants (95 females and 55 males; age = 58.6; SD age = 4.8) were recruited for the study through a door-to-door approach. Montreal Cognitive Assessment was used to capture global cognition. Self-report measures and standardized instruments were used respectively, to gather information on modifiable risk factors and measures of adiposity. Because this was a pilot study, two rural communities were selected based on proximity and convenience for the research team. Linear analysis of variance and multiple regression statistics were used for data analysis. Result showed significant differences at $p< 0.05$ level on global cognition between diabetic and non-diabetic groups as well as stroke and non-stroke groups. Physical activity was shown as significant predictor of global cognition while sleep and social relations were not. Equally, arm (Beta = 0.31) and waist (Beta= 0.12) circumferences significantly predicted global cognition and underweight participants performed significantly worse $F(3,148) = 2.6$ on global cognition.

Key words: *Cognition, MoCA, Modifiable risk factors, BMI*

INTRODUCTION

Global cognitive tests, such as Mini Mental Status Examination (MMSE) and Montreal Cognitive Assessment (MoCA), serve as brief screening measures, including various domain functions, language, attention, memory, visuo-constructive and abstract functioning or executive ability: This is in contrast to specific domain function tests such as memory, attention and executive functions. Multiple aspects of cognitive functions decline with age and existing studies suggest that modifiable risk factors and overall poor health behaviours interact with age to accelerate cognitive decline. For example, measures of central adiposity are associated with higher risks for cognitive impairments and dementia (Beydoun et al. 2008; Kerwin et al. 2011). In women waist circumference was correlated significantly with lower language and/or semantic categorization performance, executive functioning, and overall cognition after controlling for other cognitive confounders (Abbatecola et al. 2010; West et al. 2016). In a related study, Kerwin et al. (2011) showed a significant interaction between body mass index (BMI) and waist-hip ratio (WHR) and incident cognitive impairment. They reported that women with a WHR of 0.80 or greater with a BMI of 20.0 to 24.9 kg/m^2 had a greater risk of cognitive impairment and probable dementia than more obese women or women with a WHR less than 0.80. In a meta-analysis on Alzheimer's disease (AD) risk with

Correspondence: Valentine A. Ucheagwu, PhD; Department of Psychology, Nnamdi Azikiwe University, P.M.B 5025, Awka, Nigeria. E-mail: va.ucheagwu@unizik.edu.ng; Phone: +23480 66640319; ORCID: 0000-0002-7968-864X

obesity, diabetes and related disorders, Profenno et al. (2010) showed that obesity measured by BMI had pooled effect size of 1.59 for AD, while diabetes had pooled effect size of 1.54. Since these disorders are highly comorbid, Profenno et al. (2010) combined all studies of obesity, diabetes, and abnormal glucose or insulin levels, which yielded a highly significant pooled effect size for AD of 1.63. Their findings showed that obesity and diabetes significantly and independently increase the risk for AD.

Lu et al. (2009) carried out a systematic review and meta-analysis of diabetes and the risk of multi-system aging phenotypes: Fifteen studies examined the association of diabetes mellitus (DM) with cognitive dysfunction. DM was associated with a faster decline in cognitive function among older adults. The pooled adjusted risk ratio (RR) for all dementia when persons with DM were compared to those without DM was 1.47 (95% CI, 1.25 to 1.73). Four of 5 studies found a significant association of DM with faster mobility decline and incident disability. Biessels et al. (2006) reviewed the risk of dementia in DM patients and identified 14 eligible longitudinal population-based studies of variable methodological qualities. Their findings showed that the incidence of dementia was higher in individuals with diabetes in seven of ten studies reporting aggregate outcome. This high risk included both AD and vascular dementia (eight of 13 studies and six of nine studies, respectively). The limitations of the study were the absence of detailed data on modulating and mediating effects of glycaemic control, microvascular complications and comorbidity (e.g., hypertension and stroke). Their findings suggest that vascular disease and alterations in glucose, insulin, and amyloid metabolism underlie the pathophysiology. Aside from DM, other modifiable vascular factors are associated with cognitive impairments (Barnes and Yaffe 2011; Snyder et al. 2014; Baumgart et al. 2005). In Nigeria, hypertension (Ogunniyi et al. 2011) and diabetes (Yarube and Mukhtar 2018; Yarube and Gwarzo 2019) are shown to be associated with an increased risk of dementia and its appropriate treatment may lower the risk.

Lifestyle factors, such as physical activity, sleep and social activity, are shown to be protective against cognitive impairments. In a study on modifiable lifestyle factors, Kimura et al. (2019) showed that the number of walking steps, conversation time, and heart rate were protective factors for cognitive function, whereas total sleep time was a risk factor. Research on modifiable risk factors in Nigeria population is sparse. The Indianapolis-Ibadan dementia project was the first large survey in Nigeria that included modifiable risk factors for dementia and mild cognitive impairments. However, the Indianapolis-Ibadan dementia project was done within a given geographical area with a particular ethnic group. There is a need to improve the Indianapolis-Ibadan dementia project through increased research on modifiable risk factors for dementia in other ethnic groups and other parts of the country. The present pilot study was an effort to address the lacunae by examining the roles of modifiable risk factors in global cognition among rural community dwellers in Anambra State, Nigeria. For the study, we investigated the roles of hypertension, diabetes and stroke on global cognition. We also investigated the contributions of physical activities, social relations and sleep on global cognition. Our study hypotheses that hypertension, diabetes and stroke would respectively play significant roles on global cognition as measured by MoCA, and that exercise, social relations and sleep will also be significant contributors to cognition in the participants.

MATERIALS AND METHODS

Instruments: Dependent Variable

The dependent variable in the study was global cognition. This was captured with the Montreal Cognitive Assessment (MoCA) test, which is a quick (10 minutes administration) screening tool to measure cognitive impairment in medical settings. The total possible score is 30 points, with a score of 26 or above considered within normal limits. MoCA test assesses several cognitive domains such as orientation to time and place, language functions (e.g., verbal fluency task, brief confrontation naming, and sentence repetition), attention (e.g., repeating numbers, serial subtraction, and tapping), and visuospatial functions (e.g., clock and Necker cube reproduction).

Instruments: Independent Variables

For independent variables, we evaluated participants' levels of physical activity, social relations and sleep behaviour using subjective rating scales. For a six-month level of physical activity, participants rated themselves using "rarely (rated 2), monthly (rated 4) weekly (rated (6) daily (rated 8)," as a rating guide on a continuous scale. For a six-month sleep behaviour, participants rated themselves using "all the time (rated 10), most of the time (rated 8), sometimes (rated 6), few times (rated 4), rarely (rated 2)". For a six-month social relation based on the nature of the communities studied, participants rated themselves dichotomously (yes/no) based on: 1) church activities, 2) village meetings, 3) age group meetings and other union meetings in the village. Participants' measures of metabolic and cardiovascular status were assessed through self-report; including if clinically diagnosed with high blood pressure (HBP), diabetes, stroke or high cholesterol, and if on medications for HBP, diabetes and sleep-related problems or cholesterol.

Waist and arm circumferences in centimetres were measured using a tape. For the waist circumference, the tape was placed at the navel level and the waist perimeter measured at the end of exhalation, while the arm circumferences (left and right) were measured at the biceps muscles level and the average calculated. Body weight was measured using a balance, while the height gauge was used for the height, with the participant standing in an upright position barefoot on the floor. The body mass index (BMI) was calculated using the body weight and height measurements. Participants were classified into 4 categories according to BMI WHO standard: underweight, normal weight, overweight and obese.

Participants

One hundred and fifty rural community dwellers (95 females and 55 males) within the age range of 50 – 69 years (Mean age: 58.6; SD age: 4.7) were recruited for the study. The participants were recruited from Azia and Mbosi towns in Ihiala Local Government Area, Anambra State. Ethical approval from the Health Department of Ihiala LGA was obtained, and the participants gave informed consents.

The first community had 5 villages and the second community had 6 villages. The reasons for choosing the two communities were (1) they belong to area that can be classified as rural community taking into consideration the level of basic amenities and nature of activities characterizing urban area in Nigeria and (2) their proximity to our university given the research team easy access to the field at a reduced cost. Because this was a pilot study to determine the feasibility of door to door knocking for dementia research for our main project, we randomly selected two villages respectively from each town. Participants were recruited through house door to door knocking. The major criteria for participation were the participants' willingness to join the study and participants being within the age range required (55-70), while the exclusion criteria were participants with severe psychiatric disturbances and obvious dementia that may limit significantly their inability to participate in the study. Each house was visited twice: The first was to identify participants who met the inclusion criteria for study and their written consents. The second visit was for data collections with prior notice. All the questionnaires and tests were administered within 9am-12noon.

Design and Statistics

Sample size was calculated using the formula for one sample size for continuous outcome and a sample size of 110 was accepted. The reason for the method was to determine the sample size needed to ensure that the margin of error is sufficiently small to be informative (Sullivan, 2004).

A community survey design was used for the study. Multiple analysis of covariate (MANCOVA) and multiple regression statistics were used for data analysis. Because many variables were involved in the study, multiple independent statistical analyses were conducted. At first data was checked for normality assumption and skewness using the histogram normal curve. Our continuous data showed relative normal bell curve (Fig. 1). Based on the normality of the data, we were able to perform ANOVA statistics for between group differences. The statistical analysis was divided into 4: Analysis 1 was on the roles of hypertension, diabetes and stroke on cognition. This was analysed using the 3-way MANCOVA controlling for age and education simultaneously. The reason controlling for age and education was that the two variables are known to affect cognition. Analysis 2 was on the predictive strength of physical activity, social relations and sleep on cognition. The data was analysed using multiple linear regression. Analysis 3 was on the roles of years of illness and medication use on cognition using 2 Way ANOVA. The last analysis was on roles of anthropometry on cognition using again multiple linear regression. All analyses were done at $p<0.05$ level of testing.

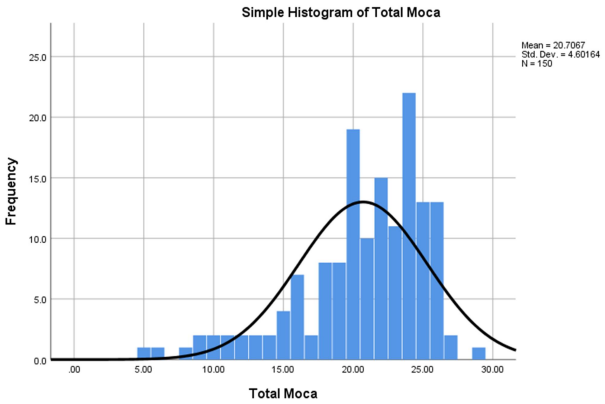

Fig. 1: Normality assumptions for MOCA data
MoCA = Montreal Cognitive Assessment

$n = (\frac{Z\sigma}{E})^2$: where z= value from the standard normal distribution reflecting the confidence interval (95%= 1.96), σ = standard deviation of outcome variable, E= desired margin error

RESULTS

Ninety-three participants (62%) reported having 12 years and above of formal education and 103 (68.6%) were civil servants. Sixty-four (42.7%) of the participants reported being on anti-cholesterol prescription as prescribed by a physician, 28 (18.7%) reported taking sleeping pills and 70 (46.7%) reported short sleep duration. All participants that reported being diagnosed with type 2 diabetes

mellitus (DM) were on metformin, with 40 DM participants reported having glibenclamide as supportive medication to metformin. All participants that reported being diagnosed with high blood pressure (HBP) were on one form of anti-hypertensive or a combination of two different forms. Table 1 shows the descriptive statistics for the modifiable risk factors in the sample. Sixty-five of the participants reported having high blood pressure, 66 reported being diabetic while 17 reported having stroke.

Table 1: Descriptive Statistics of Modifiable Risk Factors in the Study

	BP	Diabetes	Stroke	BP drugs	Diabetic drugs	Years on HBP	Years on diabetes	Years on stroke	Stroke side	BMI diagnosis
Normal	61	43	Nil:101	65	76	1-5 years:25	1-5 years:23	1-5 years:09	R: 13	N:45
High	65	76	Yes:17			6-10 years:22	6-10 years :22	6-10 years:04	L: 04	U:08
UR	24	31	UR:32			Above 10 years:19	Above 10 years:27 UR: 4	Above 10 years:04		OV:25 OB:71

BP: Blood pressure; HBP: High blood pressure; UR: Unreported; R: Right; L: Left; BMI: Body mass index; N:Normal BMI; U: Underweight; OV: Overweight; OB: Obese.

There was no significant difference between hypertensive participants and non-hypertensives on MoCA (F (1,114) = 1.7). However, there were significant difference between participants who reported being diabetic and their non-diabetic counterparts on MoCA (F(1,114) = 3.6; Mean: DM = 21.0, non-DM = 19.0) with diabetic group performing better than non-diabetic group (Fig. 2). DM participants significantly differed from non-DMs on abstraction (Mean: DM= 1.9, non-DM = 1.8) and orientation (Mean: DM = 5.8, non- DM = 5.5) items on MoCA. Significant difference was found between stroke participants and non-stroke group on MoCA (F(1,114) = 4.3; Stroke= 17.7, non-stroke= 21.2) with non-stroke group performing better than the stroke group. List of letters (Stroke= 0.6, non-stroke= 0.9), delayed recall (Stroke= 0.8, non-stroke= 2.2), orientation (Stroke= 5.4, non-stroke= 5.7) items in MoCA differed significantly between the groups. No significant interaction effects were seen among hypertension, diabetes and stroke as independent variables. Age as a covariate had no significant effect on MoCA (F (1,114) = 0.27 while education showed significant difference (F (1,114) = 10.38.

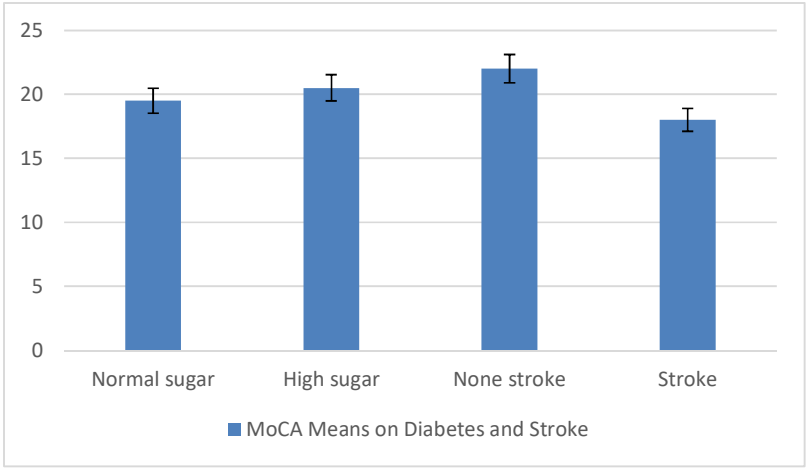

Fig. 2: Mean scores of diabetes and stroke on MoCA

Physical Activity, Social Relations and Sleep as Predictors of Performance on MoCA

Contributions of exercise, social relations and sleep on MoCA were analysed using a linear regression model. Table 2 shows physical activity as a better predictor of global cognition more than social relations and sleep, albeit the R2 value was low (0.06). The t-test showed significance at p< 0.05 level for physical activity, while the mean scores for two categories of physical activity (high and low in physical activities) were 19.94 and 21.38, respectively.

Impact of Years of Illness and Medication Use on MoCA Performance

Findings showed no significant effect of years of hypertension F (4,142) = 0.08; diabetes F (3,142) =0.08 and stroke F (3,142) = 5.99 on MoCA. There were no significant interaction effects on years of hypertension and diabetes F (9,142) = 0.70, hypertension and stroke F (5,142) = 0.31; and diabetes and stroke F (4,142) = 0.78 on MoCA. There was also no significant difference between participants on sleep medications and those without F(1,123) = 0.01, use of cholesterol medications F(1,123) = 1.57 and interaction effects of sleep and

cholesterol medications on MoCA F(1,123) = 1.63.

Roles of Anthropometry on MoCA Test

Table 3 shows individual contributions of weight, waist and arm circumferences on MoCA performance. Arm circumference showed the highest predictive strength in the sample, while the mean scores for the arm circumference categories (high and low arm circumferences) 22.0 and 19.7, respectively. The four groups of BMI (normal, underweight, overweight and obese) were significantly different on MoCA F (3,148) = 2.6; Mean: Normal=21.5; Underweight=17.5; Overweight=19.6; Obese = 21.0; effect size = 0.24). Pairwise comparison using the Scheffé's method showed a significant difference where the underweight group performed significantly low on MoCA followed by overweight group.

Table 2: Multiple Regression Analysis of Exercise, Social Relations and Sleep on MoCA

Independent Variables	Dependent Variables	Standardised Coefficient Beta	t	R Square	F
Physical activity	MoCA	0.21	2.29*	0.06	3.02*
Social relations	MoCA	0.14	1.63		
Sleep	MoCA	0.11	1.31		

Table 3: Multiple Regression Analysis of Body Weight, Waist and Arm Circumferences on MoCA

Independent Variables	Dependent Variables	Standardised Coefficient Beta	t	R Square	F
Body Weight	MoCA	0.14	1.60	0.12	6.40
Waist Circumference	MoCA	0.12	1.35		
Arm Circumference	MoCA	0.31	3.36*		

DISCUSSION

We evaluated the roles of hypertension, diabetes and stroke on cognition in adults of 55-70 years. Hypertensive group did not differ from non-hypertensive on measure of global cognition. However global cognition differences were found between diabetic and non diabetic group as well as the stroke and non-stroke groups respectively. Midlife hypertension is shown to be significant predictor of cognitive function at 8 years follow-up (Hestad et al. 2020) and at late life (Launer et al. 1995; Kilander et al. 1998). The problem with existing studies on contributions of hypertension to cognitive performance is that many of the researches failed to put into consideration the buffer effects of hypertensive control/treatment on cognition. The majority of previous studies implicating hypertension to cognition failed to factor in the contributions of hypertension treatment in moderating the hypertensive risks on cognition. May be the reason for our present finding was performance, because all hypertensive participants reported being on regular antihypertensive medications for more than 6 months from the study. The use of antihypertensive medications is more likely to moderate the effects of hypertension on cognitive performance. Baumgart et al. (2005) has shown strong and sufficient evidence from a population-based perspective that management of cardiovascular risk factors (diabetes, obesity, smoking and hypertension) reduce cognitive decline and may reduce the risk of dementia. Studies with African Americans showed that cognitive decline was lower in treated than untreated hypertensive patients (Tzourio et al. 1999; Murray et al. 2002). In a meta-analysis of antihypertensive drugs and cognitive decline involving observational and randomized clinical trial studies, Rouch et al. (2015) showed that antihypertensive drugs, particularly calcium channel and renin–angiotensin system blockers may be beneficial in preventing cognitive decline and dementia. Thus, results of our study, which show no significant difference on global cognition between hypertensive and non-hypertensive participants, are likely to be the result of the effects of antihypertensive medications taken by the hypertensive group.

Significant differences were found between diabetic and non-diabetic participants on the MoCA. Our result showed that diabetic group performed better than non-diabetic group. This result is strikingly different from previous findings. Past results predominantly from the West show significant differences between diabetic and non-diabetic groups on cognitive performance and possible dementia with the later performing better (Biessels et al. 2006; Kloppenborg et al. 2008; Profenno et al. 2010). However, recent studies showed significant positive contributions of metformin, a first line treatment medication for diabetes on cognitive performance (Campbell et al. 2018; Lin et al. 2018; Samaras et al. 2020). This is attributed to the capacity of metformin to penetrate the blood–brain barrier, protecting neurons via anti-inflammatory action and improvement of brain energy metabolism (Lin et al. 2018). Scherrer et al. (2019) demonstrated that metformin use is associated with a significantly lower risk of dementia in African American patients but not white patients with strongest magnitude of association observed among patients aged 50 to 64 years. Among those aged 65 to 74 years, metformin was significantly associated with lower risk of dementia in both races but was not associated with dementia in patients aged ≥75 years. As stated in the

participant section, all our participants that self-identified to be clinically diabetic were on metformin medication as prescribed by a physician. Our present finding may be attributed to the protective roles of metformin to the brain. To the best of our knowledge no other study in Nigeria has examined relationship between metformin and cognitive performance making it difficult to compare our finding with those of others in Nigeria. As expected, stroke patients performed poorly compared with healthy controls. The control group had better global cognition based on MoCA. Some factors including presence of high sensitivity C-reactive protein (hsCRP) in stroke patients (Buba and Yarube 2021), brain derived neurotrophic factors (BDNF) (Hassan and Yarube, 2018) and other diffuse cortical and axonal injuries may account for the differences in performance between stroke patients and the controls.

We evaluated the predictive strengths of physical activity, social relationship and sleep on global cognition. Physical activity significantly predicted global cognition. Surprisingly groups that reported less physical activity performed better than high physical activity group. Although there are mixed findings on the roles of exercise and physical activity on cognition, many studies are in support of positive effects of exercise on cognition particularly among older adults (van Gelder et al. 2004; Weuve et al. 2004;). Exercise can influence cognition through various mechanisms like improvement of cardiac health and production of neurotrophic factors (Kirk-Sanchez and McGough, 2014). In our study we asked participants to rate the extent of their physical activity. It is possible given the population we sampled which were rural men and women that engage in strenuous tasks including manualized farming and long-distance walks, that their rating of physical activity may be tilted in that direction. In this case the results may show inverse relation of physical activity to global cognition. Thus, our finding is in line that continuous strenuous activities could negatively affect an individual cognition. As such physical activity can be categorised into strenuous and non-strenuous: the latter is stressful while the former is enjoyable and can be referred as a form of aerobic exercise. Thus, taking a walk every evening to increase physical activity after a sedentary day work is different from doing a manual work for 10 h daily. We suggest that strenuous physical activities can be counterproductive in its own by producing proinflammatory cytokines and cortisol and lowering brain derived neurotrophic factors (BDNF) which are opposite of what exercise does. Our study shows that years of hypertension illness had no significant influence in cognition. Some longitudinal studies reported cognitive decline after 20 years following baseline hypertension (Taylor et al. 2013; Gottesman et al. 2014). Individuals on antihypertensive medications were reported to show better cognitive performance when compared with untreated individuals (Gottesman et al. 2014). Our result is plausible because our participants were on antihypertensive medication that may serve as buffer against further vascular brain damage due to their condition.

There are controversies surrounding the roles of adiposity on cognition among middle and old adults. We demonstrated that individuals with high arm circumference performed better than their counterparts with low arm circumference on global cognition. Although there are very few studies that examined the relationship between mid-upper arm circumference (MUAC) and cognition in old adults, MUAC has been shown to be good predictor of health status and mortality in the elderlies (Tsai et al. 2011). Lee et al. (2017) surveying older female Korean population showed that decreased upper arm circumference was associated with dementia and may represent a biological marker for this condition. Taylor et al. (2012) in a survey of seven low-income countries showed that dementia and its severity were both associated with smaller arm and waist circumferences with little evidence of confounding by socio-demographic and health status. However, associations between dementia/clinical dementia rating and arm circumference were homogeneous between countries whereas those with waist circumference were more heterogeneous. In Central African Republic, mild cognitive impairment (MCI) was associated with MUAC < 24 cm and dementia with BMI < 18.5 kg/m, arm muscular circumference (AMC) < 5th percentile and MUAC < 24 cm, while in the Republic of Congo (ROC), both MCI and dementia were associated with all markers of undernutrition, but only AMC < 5th percentile was significantly associated with MCI. This association may be explained by nutritional deficits or decreased physical activity.

Furthermore, there was a significant difference between underweight group and other groups (normal, overweight and obese) on MoCA score. Underweight is a measure of nutrition and may also account for poor global cognition as in the present study. In a large retrospective cohort Qizilbash et al. (2015) showed low risk for dementia among those who were overweight in midlife compared to underweight group. Compared with people of healthy weight, underweight people had a 34% (95% CI 29–38) excess risk of dementia and the incidence of dementia continued to fall for every increasing BMI category, with very obese people (BMI ≥40 kg/m2) having a 29% lower risk of dementia (95% CI 22–36) than those of a healthy weight (Qizilbash et al. 2015).

Due to the sample size used, results from our study should be interpreted with caution as we call for more investigations on roles of modifiable risk factors in cognition in sub-Sahara Africa. Secondly, some of our measures of modifiable risk factors were self-report and retrospective. For example, we did not measure blood pressure or sugar level but depended

on the diagnostic information as reported by the participants. Measures of activities and sleep were also self-reported and not objectively measured. These types of measures are known to be noisy and are likely to affect findings. Also, we failed to measure mood states of our participant as depression is shown to lower cognition.

Conclusion

We presented a pilot investigation on the roles of modifiable risk factors in global cognition in adults from two rural communities in Nigeria. The present study showed the protective effects of metformin and antihypertensive medications in global cognition. We demonstrated the effects of nutrition on cognition by showing the contributions of arm and waist circumferences and BMI in cognition. Overall, although our study was a pilot one, we were able to demonstrate that proper modification and management of metabolic syndrome can significantly improve and, or reduce the risk of decline in global cognition.

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Conflict of Interest
None declared.

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Authors Contribution
VAU - Conception, Statistical analysis, wrote the initial and final draft; RUJ - Contributed to writing the introduction and method sections and revised the initial draft; CCA - Read the final draft and contributed to data analysis.

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