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Relationship between Education and Cognitive Performance among Healthy Malay Adults

(Hubungan antara Pendidikan dan Prestasi Kognitif dalam Kalangan Dewasa Melayu Sihat)

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ABSTRACT

*Higher level of education is associated with better cognitive performance and lower risk of developing dementia. However, the effect of education on cognitive performance varies across different cognitive domains and in different populations. The aim of this study was to determine the relationship between education and performance of different cognitive domains among healthy Malay adults. A total of 53 individuals aged 29 to 77 years participated in a battery of neurophysiological tests consisting of Mini-Mental State Examination, Montreal Cognitive Assessment, digit span, visual reproduction and digit symbol speed test (DSST). Blood test was performed for each participant to obtain their biochemical profile. Educational level was divided into level 1 (PMR), level 2 (SPM), level 3 (STPM), level 4 (Diploma) and level 5 (Degree). Simple linear regression indicated that years of education was positively associated with scores of delayed visual reproduction (*b=*1.348*, p=*0.002*) and DSST (*b=*3.257*, p=*0.012*). However, scores of all the tests were not significantly different among different levels of education after controlling for age, gender and blood test profile by ANCOVA. Multiple linear regression analysis showed that MMSE score was associated with red cell distribution width (*b=*-0.628*, p=*0.005*), age (*b=*-0.119*, p<*0.001*) and there was interaction between high density lipoprotein (HDL) with age (*b=*0.047*, p<*001*). MoCA score was associated with age (*b=*-0.121*, p<*0.001*), gender (male compared to female,* b=*1.870*, p=*0.020*) and HDL (*b=*1.681*, p=*0.047*). Age was associated with backward digit span (*b=*-0098*, p<*0.001*) and immediate visual reproduction (*b=*-0.348*, p<*0.001*), resp. Delayed visual reproduction was associated with age (*b=*-0.323*, p<*0.001*) and potassium level (*b=*-4.471*, p=*0.016*). DSST was associated with age (*b=*-0.911*, p<*0.001*) and alanine aminotransferase (*b=*-0.754*, p=*0.002*). The lack of association between educational level and cognitive performance after adjusting for confounders in this study maybe due to multiple factors influencing cognitive performance and further studies with a larger sample size are needed to further identify the factors involved.*

Keywords: Cognitive performance; education; healthy Malay adults

ABSTRAK

*Tahap pendidikan yang tinggi telah dikaitkan dengan prestasi kognitif yang lebih baik dan risiko perkembangan dementia yang lebih rendah. Namun, kesan pendidikan terhadap prestasi kognitif berbeza antara domain kognitif dan populasi yang berlainan. Kajian ini bertujuan untuk menentukan hubungan antara pendidikan dengan prestasi pada domain kognitif yang berlainan pada individu dewasa Melayu yang sihat. Seramai 53 individu yang berumur antara 29 hingga 77 tahun telah menyertai ujian neuropsikologi yang terdiri daripada Pemeriksaan Keadaan Mental Mini, Penilaian Kognitif Montreal, digit span, penghasilan semula visual dan ujian kelajuan simbol digit (DSST). Tahap pendidikan dibahagikan kepada tahap 1 (PMR), tahap 2 (SPM), tahap 3 (STPM), tahap 4 (Diploma) dan tahap 5 (Ijazah Sarjana Muda). Regresi linear mudah menunjukkan bahawa tahap pendidikan berhubung kait secara positif dengan penghasilan semula visual tertunda (*b=*1.348*, p=*0.002*) dan DSST (*b=*3.257*, p=*0.012*). Namun, semua skor ujian menjadi tidak berbeza antara tahap pendidikan yang berbeza selepas mengambil kira kesan konpengasas dengan menggunakan ANCOVA. Regresi linear berganda menunjukkan bahawa skor MMSE berhubung kait dengan lebar taburan sel merah (*b=*-0.628*, p=*0.005*), umur (*b=*-0.119*, p<*0.001*) dan interaksi antara lipoprotein ketumpatan tinggi (HDL) dan umur (*b=*0.047*, p<*001*). MoCA didapati berhubung kait dengan umur (*b=*-0.121*, p<*0.001*), jantina (lelaki berbanding perempuan,* b=*1.870*, p=*0.020*) dan HDL (*b=*1.681*, p=*0.047*). Umur juga berhubung kait dengan digit span ke belakang (*b=*-0098*, P<*0.001*) dan penghasilan semula visual segera (*b=*-0.348*, p<*0.001*). Penghasilan semula visual tertunda berhubung kait dengan umur (*b=*-0.323*, p<*0.001*) dan tahap kalium (*b=*-4.471*, p=*0.016*). DSST berhubung kait dengan umur (*b=*-0.911*, p<*0.001*) dan alanin aminotransferase (*b=*-0.754*, p=*0.002*). Hubungan antara tahap pendidikan dan prestasi kognitif tidak dikesan selepas mengambil kira kesan konpengasas yang mencadangkan bahawa prestasi kognitif mungkin dipengaruhi oleh pelbagai faktor dan kajian lanjut dengan bilangan sampel yang lebih besar diperlukan untuk mengenal pasti faktor ini.*

Kata kunci: Dewasa Melayu sihat; pendidikan; prestasi kognitif

Introduction

Education is an act or process of giving or acquiring knowledge, developing the skills of reasoning and judgement and generally preparing oneself or others intellectually for mature life. There are three types of education that were applicable among the community which are formal, informal and non-formal education. Informal study is more on acquiring attitude, values, skills and knowledge from experience on a daily basis influenced by the environment whereas formal education is based on hierarchically structured education system running from primary to university level providing a platform for full-time technical and professional training; non-formal education is focussed on educational activity outside of formal education system (Combs & Prosser 1973). Measuring duration or time frame of informal and non-formal education of an individual may pose a problem as the method of acquiring knowledge are not planned or predictable and are sometimes short and spontaneous (Jonassen 2004). As such, it is reasonable to use formal education as a measure of level of education because it is structured and guided with a clear time frame.

There are several divisions of formal education systems prescribed by the Ministry of Education, Malaysia which are primary, lower secondary, upper secondary, senior secondary and higher education where each stage is assessed by UPSR (Primary School Evaluation Test), PMR (Lower Secondary Assessment), SPM (Malaysian Certificate of Education), STPM (Malaysian Higher School Certificate) or matriculation/diploma and degree examination, respectively. Generally, the duration of schooling is fixed among primary (six years), lower secondary (three years), upper secondary (two years) and senior secondary (two to four years) (WENR 2014). The Malaysian Examination Syndicate (LPM) is responsible for ensuring the reliability of each assessment under the purview of the Ministry of Education Malaysia (Awang 2009).

Higher level of education is associated with better cognitive performance on domains such as memory, executive and visuospatial function, language and attention (dos Santos et al. 2011; Ganguli et al. 2010). Higher level of education was also reported to be associated with a lower risk to mild cognitive impairment (Tervo et al. 2004) and dementia (Qiu et al. 2001). Nevertheless, the interpretation of the relationship between education and cognitive performance remained controversial and more importantly is influenced by both genetics and the environment (Sharp & Gatz 2011). Education factors may interact with age (Alley et al. 2007), health status and disability (Christensen et al. 1997) and chronic diseases (Dodd 2015; Hung et al. 2009). The positive association between education and cognitive performance has been attributed to higher cognitive reserve, higher brain reserve and brain battering hypothesis. Higher cognitive reserve provided a higher threshold to protect the brain from neural damage or compensate damage by providing alternative ways (Stern 2002). Brain reserve hypothesis proposed that educational attainment slowed dementia progression by increasing neocortical synaptic density (Katzman 1993). Brain battering hypothesis suggested that individuals with higher educational level are generally associated with higher socioeconomic status and healthier life styles which spare the brain from neurotoxicity exposure (Del Ser et al. 1999).

While the biological basis of the effect of education on cognitive performance remains to be elucidated, the effect of education on cognitive performance varies across populations or regions (Sharp & Gatz 2011). Besides, the effect of education may vary in the different cognitive domains as measured by different instruments. Education level has been reported as a stronger predictor for crystallised intelligence, but a weak predictor for fluid intelligence or processing speed (Anstey & Christensen 2000). Since chronic diseases may mask the association of education and cognitive performance, it is more valuable to assess the presence of any association in healthy populations. Besides, multiple assessments representing a variety of cognitive functions may better evaluate the association of education level with cognitive function. In tandem with the varied neurophysiological tests used, we reported here preliminary findings on the relationship between level of education on cognitive performances with the different cognitive domains tested among healthy individuals after controlling for age, gender and blood test profile.

Materials and Methods

Subjects

This cross-sectional study is part of the Toward Useful Aging (TUA) study funded by Long-term Research Grant Scheme (LRGS) in Universiti Kebangsaan Malaysia (UKM). This study was approved by the Ethics Committee of the Medical Research Secretariat UKM. After obtaining written informed consent, a total 1768 volunteers were screened at 25 locations around the Klang Valley and Selangor. The screening process involved taking medical history, physical examination and biochemical tests. From the screening process, a total of 53 healthy subjects aged between 29 and 77 years old were recruited. They were divided into five groups based on their levels of formal education; from lower secondary schools to tertiary education. Group 1 (PMR; 9 years of formal education), Group 2 (SPM; 11 years), Group 3 (STPM/Matriculation; 13 years), Group 4 (Diploma; 14 years) and Group 5 (Degree; 15 years). The inclusion criteria for this study were individuals who have no known physical or mental illness (self-report), Malay and not more than 15 years of formal education. The exclusion criteria were individuals who smoked, have less than 15 years of formal education, individuals who were diagnosed with psychiatric disorder or with chronic diseases such as cancer, diabetes, kidney failure or coronary

heart disease, and individuals with a history of neurological diseases affecting cognitive functions such as stroke and dementia (self-report). Blood (35 mL) was taken from the selected subjects and sent to local diagnostic laboratory (Quantum Diagnostics, Petaling Jaya) for biochemical tests which included total blood count, fasting blood glucose, lipid profile, liver and renal profile. Information sheets and verbal explanation were given before written consent is taken.

Neuropsychological Measures

MMSE test is widely used as an early screening tool to detect dementia. It involves 11 types of questions which consisted of orientation, registration, attention, calculation, recall, naming, repetition and 3 stage command, reacting, writing and copying. The test takes approximately 15 min to complete with a total score of 30. MMSE scores of 26 or below indicate possible mild cognitive impairment. A score of 21 or less is suggestive of dementia when corrected for gender and education (Razali et al. 2014).

Montreal Cognitive Assessment (MoCA) is a relatively simple tool which takes approximately 10 min to complete and assess eight cognitive domains which are visuospatial/executive function, naming, memory, attention, language, abstraction and orientation. For this study, the Bahasa Malaysia version of MoCA (MoCA BM) was used as described previously (Razali et al. 2014). The maximum score is 30 points and one point will be added to the MoCA score for individuals with 12 years or less of formal education.

Digit Span, Visual Reproduction and Digit Symbol Speed Test (DSST) test are part of the Wechsler Adult Intelligence Scale-Revised (WAIS-R) test (Wechsler 1981). The Digit Span test was designed to measure working memory, attention as a function of working memory and also can be used to evaluate a variety of impairments (Colom et al. 2007). This test can be divided into forward recall test (forward digit span, FDS) and backward recall test (backward digit span, BDS). In the FDS, the subjects were presented with a series of strings on increasing length, from three to nine digits and asked to repeat each string immediately after it was presented. The test involves subjects having to process information by memorizing digits, recalling and sequencing the digits and then the reply is verbalised in the correct order. While in the BDS, the subject was also presented with a series of string of numbers and asked to repeat the number in a reverse order immediately after it was presented.

Visual reproduction test consists of two tests which are immediate visual recall (VR-I) and delayed visual recall (VR-II). VR-I is used to assess memory for nonverbal visual stimuli. In this test, a series of four geometrical pictures were shown to the participants, one at a time for 10 s each. After each picture was presented, the participant was asked to draw the design of the geometrical pictures based on the participant's memory. Each of the geometrical pictures has different complexity. Subsequently, VR-II involves assessing long-term visual-spatial memory with free recall and recognition tasks. Firstly, the subject was asked by the examiner to draw geometrical pictures immediately in any order. Secondly, the subject was asked to choose which of the four geometrical pictures match the original design shown previously.

DSST is used to assess processing speed. It is the most widely used instrument for describing the performance of younger and older adults in cognitive aging studies. The different cognitive components tested comprise of scanning, matching, switching and writing operations that are reflective of several higher cognitive functions such as perception, encoding and retrieval processes, transformation of information stored in active memory and decision making (Salthouse 1996). In this study, the subject was given a lookup table showing pairs of digits and hieroglyphic-like symbols and rows of boxes with a digit in the top section and an empty space in the bottom section of each box. The subject has to put the correct symbol in the empty box that represents the number within 90 s. The total score of DSST is 117. DSST has been shown to exhibit strong correlation to perceptual speed and processing speed with age.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) software version 22 (IBM, Armonk, NY, USA) was used to analyse data obtained in the study. A value of $p<0.05$ was considered significantly different for all analyses. One-way analysis of variance (ANOVA) was used to compare different among groups with Bonferroni (homogeneity of variance assumed) or Tamhane (homogeneity of variance not assumed) post-hoc tests. Analysis of covariance (ANCOVA) was performed using univariate general linear model controlling for age, gender and blood test profile. For multiple linear regression (MLR), stepwise, forward and backward selection methods were used to select the most stable model. Linear model fitness and assumption were tested.

Results

Although a total of 1768 individuals were screened, only 53 participants fulfil all inclusion criteria including normal biochemical profiles and completed all the neuropsychological tests. Participants ranged in age from 29 to 77 years and 72% were female (Table 1). The highest number of participants were in Education level 2 followed by levels 5, 4, 3 and 1. Mean age was significantly different among different education levels, but not according to gender. Education levels 4 and 5 had younger participants than levels 1 and 2. Blood test profile showed that all the parameters measured were not significantly different among the different education levels except mean corpuscular haemoglobin concentration (MCHC), red cell distribution width (RDW-CV), estimated

TABLE 1. Demographic data of participants (n=53) by education levels

Level of education	1	2	3	4	5	p value
Years of education	9	11	13	14	15	-
N (%)	3 (6%)	22 (42%)	6 (11%)	10 (19%)	12 (23%)	-
Age, year (SD)	56.7 (4.0)[b,c]	53.7 (10.2)[b,c]	45.2 (15.9)	38.0 (6.2)	37.2 (8.2)	<0.001[a]
Gender						0.480[d]
Male	1	6	0	3	5	-
Female	2	16	6	7	7	-

a One-way ANOVA
b Tamhane post-hoc test was used (homogeneity of variance not assumed); Compared to educational level 4.
c Tamhane post-hoc test was used (homogeneity of variance not assumed); Compared to educational level 5.
d Pearson Chi-square test (Monte Carlo method)

TABLE 2. Blood test profile of participants by education levels

Level of education	1	2	3	4	5	p value[a]
Haemoglobin, g/L	136.0 (12.8)	127.2 (11.6)	127.7 (12.6)	128.2 (15.9)	134.8 (14.3)	0.496
RBC, 10^{12}/L	4.6 (0.6)	4.6 (0.5)	5.0 (0.3)	4.9 (0.7)	4.8 (0.7)	0.474
HCT, L/L	0.41 (0.05)	0.40 (0.03)	0.42 (0.04)	0.41 (0.04)	0.43 (0.05)	0.469
MCV, fL	79.3 (14.2)	87.3 (5.6)	83.7 (7.0)	85.0 (8.4)	89.0 (4.9)	0.166
MCH, pg	29.3 (1.2)	27.5 (2.3)	25.2 (2.6)	26.6 (3.4)	28.1 (1.7)	0.078
MCHC, g/L	334.7 (18.2)[b,c,d]	315.9 (12.8)	304.0 (6.1)	311.9 (12.4)	314.3 (7.0)	0.008
RDW-CV, %	12.5 (0.8)	13.7 (1.3)[e]	13.4 (0.5)	13.0 (0.7)	12.6 (0.7)	0.026
WBC, 10^9/L	7.9 (2.3)	7.0 (2.1)	7.0 (1.2)	7.8 (2.2)	6.6 (1.6)	0.623
Neutrophils, 10^9/L	4.5 (2.0)	4.0 (1.6)	3.8 (1.0)	4.4 (1.8)	3.5 (1.1)	0.607
Lymphocytes, 10^9/L	2.5 (0.1)	2.4 (0.6)	2.5 (0.6)	2.6 (0.7)	2.3 (0.5)	0.795
Monocytes, 10^9/L	0.62 (0.26)	0.45 (0.12)	0.42 (0.07)	0.47 (0.21)	0.47 (0.16)	0.422
Eosinophils, 10^9/L	0.19 (0.08)	0.17 (0.12)	0.24 (0.14)	0.23 (0.20)	0.28 (0.13)	0.315
Basophils, 10^9/L	0.09 (0.086)	0.08 (0.036)	0.12 (0.024)	0.09 (0.043)	0.11 (0.052)	0.337
Platelet count, 10^9/L	245.0 (57.5)	298.2 (66.6)	302.5 (66.4)	248.5 (34.9)	265.3 (67.9)	0.159
Sodium, mmol/L	140.0 (1.0)	142.0 (2.2)	142.0 (2.9)	141.3 (0.9)	140.8 (2.0)	0.276
Potassium, mmol/L	4.2 (0.4)	4.3 (0.5)	4.0 (0.3)	3.9 (0.5)	4.2 (0.6)	0.330
Chloride, mmol/L	99.3 (1.2)	102.2 (2.6)	101.5 (1.9)	103.0 (2.9)	102.1 (3.4)	0.368
Urea, mmol/L	3.4 (1.2)	3.8 (1.0)	4.2 (0.7)	3.2 (1.2)	3.5 (0.6)	0.205
Uric acid, mmol/L	241.3 (55.3)	279.9 (88.9)	289.2 (45.3)	327.8 (83.8)	291.3 (48.6)	0.395
Creatinine, mmol/L	53.0 (7.0)	74.3 (20.1)	59.2 (5.8)	68.3 (19.7)	71.4 (16.0)	0.188
eGFR, mL/min/1.73m^2	116.0 (18.4)[b]	81.5 (19.9)	98.3 (13.7)	97.5 (22.9)	89.3 (14.7)	0.019
Calcium, mmol/L	2.3 (0.08)	2.3 (0.06)	2.4 (0.12)	2.3 (0.07)	2.4 (0.11)	0.163
Corrected Calcium, mmol/L	2.3 (0.09)	2.4 (0.06)	2.4 (0.09)	2.3 (0.08)	2.4 (0.09)	0.288
Phosphate, mmol/L	1.0 (0.09)	1.2 (0.15)	1.4 (0.30)[d]	1.0 (0.17)	1.2 (0.24)	0.047
Total protein, g/L	72.7 (1.2)	75.7 (4.4)	77.0 (1.1)	76.8 (3.7)	77.5 (4.1)	0.339
Albumin, g/L	43.3 (1.5)	44.8 (2.9)	46.3 (3.4)	47.3 (2.8)	46.4 (2.5)	0.088
Globulin, g/L	29.3 (2.5)	30.9 (3.6)	30.7 (3.9)	29.4 (2.6)	31.3 (2.8)	0.645
Bilirubin (Total), μmol/L	6.2 (4.3)	10.6 (3.3)	7.5 (2.0)	8.8 (2.8)	9.0 (2.1)	0.042
Alkaline phosphatase, U/L	73.7 (18.9)	72.8 (19.1)	64.7 (12.2)	68.4 (22.0)	67.6 (19.7)	0.859
GGT, U/L	39.3 (27.6)	24.0 (14.5)	22.7 (8.7)	23.3 (7.1)	22.8 (14.6)	0.435
Aspartate transferase, U/L	19.0 (1.0)	20.6 (7.2)	21.8 (5.2)	20.1 (5.7)	21.8 (6.9)	0.935
Alanine transaminase, U/L	23.0 (5.6)	16.5 (5.6)	25.3 (12.6)	19.9 (10.5)	17.2 (7.1)	0.140
Total cholesterol, mmol/L	5.7 (1.3)	5.5 (0.8)	5.7 (1.0)	5.6 (0.5)	5.1 (0.5)	0.393
Triglycerides, mmol/L	1.6 (1.2)	1.0 (0.4)	1.4 (0.6)	1.5 (0.7)	1.1 (0.8)	0.166
HDL cholesterol, mmol/L	1.6 (0.5)	1.7 (0.4)	1.4 (0.5)	1.4 (0.4)	1.6 (0.4)	0.551
LDL cholesterol, mmol/L	3.7 (0.8)	3.4 (0.7)	3.6 (1.0)	3.5 (0.5)	3.0 (0.6)	0.272
Total cholesterol/HDL, mmol/L	3.7 (0.9)	3.5 (1.1)	4.2 (1.3)	4.2 (1.1)	3.5 (1.6)	0.446
Glucose, mmol/L	5.7 (0.6)[d,f]	4.8 (0.6)	4.8 (0.6)	4.4 (0.8)	4.4 (0.3)	0.012

a One-way ANOVA
b Bonferroni post-hoc test; Compared to educational level 2.
c Bonferroni post-hoc test; Compared to educational level 3.
d Bonferroni post-hoc test; Compared to educational level 4.
e Tamhane post-hoc test (homogeneity of variance not assumed); Compared to educational level 5.
f Bonferroni post-hoc test; Compared to educational level 5.
Numbers in parentheses indicate SD.
Abbreviation: estimated glomerular filtration rate, eGFR; gamma-glutamyl transferase, GGT; haematocrit, HCT; high density lipoprotein, HDL; low density lipoprotein, LDL; mean corpuscular haemoglobin, MCH; mean corpuscular haemoglobin concentration, MCHC; men corpuscular volume, MCV; red blood cell, RBC; red cell distribution width, RDW-CV; white blood cell, WBC

glomerular filtration rate (eGFR), phosphate and glucose levels (Table 2). Education level 1 had higher MCHC value than levels 2, 3 and 4. Education level 2 had higher RDW-CV value than level 5. Education level 1 had higher eGFR value than level 2. Education level 3 had higher phosphate value than level 4. Education level 1 had higher glucose value than levels 4 and 5.

One-way ANOVA indicated that scores of VRI and DSST were significantly different among different education levels, but not for MMSE, MoCA, FDS, BDS and VRII (Table 3). However, Bonferroni post-hoc test did not show any differences in VRI scores among education levels as ANOVA analysis showed only marginal significance (p=0.49). DSST scores of education levels 2 and 3 were lower than level 5. Simple linear regression (SLR) demonstrated that scores VRI and DSST were positively associated with years of education (Table 4).

Since the mean age and several blood tests are significantly different with the different levels of education levels, ANCOVA was performed to compare the neuropsychological scores with the different education levels while controlling for confounders such as age, gender and blood tests. ANCOVA results showed that each of the neuropsychological test scores was not significantly different with the different education levels (Table 5). Interestingly, some of the confounders were found to be significantly associated with the test scores. Therefore, MLR was performed to identify factors that were associated with the test scores (Table 6). Age was inversely associated with all the test scores, except FDS. RDW-CV was inversely associated, while interaction of high density lipoprotein (HDL) and age was positively associated with MMSE score. In MoCA score, males performed 1.87 times better than females and HDL is positively associated with the score. Potassium and alanine aminotransferase (ALT) were inversely associated with VRII and DSST scores, respectively.

Discussion

MMSE score has been passively associated with years of education (Brito-Marques & Cabral-Filho 2004; Matallana et al. 2010). However, not all domains in the MMSE are influenced by education. According to Matallana et al. (2010), the memory domain showed no correlation between MMSE scores and education. Similar findings were found by Laks et al. (2010) in which naming and registration memory were not related to years of education. An intervention study of health education for 12 months showed no significant association in cognitive performance (Johari et al. 2014). This suggests that although education plays an important role in determining MMSE scores, there is some deviation in the MMSE domain itself that maybe dependent on other factors or interaction of these factors with level of education. Our findings showed that MMSE score was not significantly associated with years of education. MMSE score varied across multi-ethnic and educationally diverse populations (Ng et al. 2007).

TABLE 3. Neuropsychological test scores of participants by education levels

Level of education	1	2	3	4	5	p value[a]
MMSE	28.0 (1.0)	27.1 (2.5)	26.8 (1.7)	27.4 (2.3)	28.5 (1.4)	0.355
MoCA	25.3 (1.5)	25.0 (4.1)	25.0 (3.0)	25.9 (2.5)	26.3 (2.0)	0.830
FDS	10.0 (1.0)	10.7 (2.5)	9.0 (3.0)	11.3 (2.7)	11.2 (2.7)	0.446
BDS	5.3 (0.6)	5.5 (2.3)	5.2 (3.0)	6.4 (3.2)	7.0 (2.5)	0.453
VRI	27.7 (2.5)	30.8 (6.6)	33.8 (4.9)	35.4 (5.3)	35.8 (5.2)	0.049
VRII	27.3 (1.2)	27.7 (9.1)	30.5 (5.0)	32.9 (8.1)	32.2 (7.7)	0.380
DSST	63.3 (5.1)	55.2 (16.8)[b]	48.3 (14.7)[b]	63.8 (18.2)	75.4 (15.3)	0.006

a One-way ANOVA
b Bonferroni post-hoc test; Compared to education level 5.
All tests were scored in points.
Numbers in parentheses indicate SD

TABLE 4. Simple linear regression analysis of years of education with neuropsychological test scores

Neuropsychological tests	R^2	b (95% CI)	p value[a]
MMSE	0.031	0.197 (-0.114, 0.508)	0.210
MoCA	0.022	0.245 (-0.220, 0.711)	0.294
FDS	0.009	0.132 (-0.249, 0.513)	0.491
BDS	0.052	0.309 (-0.062, 0.680)	0.101
VRI	0.174	1.348 (0.512, 2.174)	0.002
VRII	0.073	1.152 (-0.004, 2.309)	0.051
DSST	0.116	3.257 (0.733, 5.780)	0.012

a Years of education as independent variable, neuropsychological test scores as outcome.
b = crude regression coefficient

TABLE 5. Comparison of neuropsychological test scores among education levels by ANCOVA

Level of education	1	2	3	4	5	*p* value
MMSE	30.825 (24.033, 37.617)	27.894 (25.716, 30.073)	26.095 (22.596, 29.594)	26.095 (22.596, 29.594)	27.224 (25.055, 29.394)	0.213
MoCA	29.939 (19.017, 40.860)	28.101 (24.598, 31.604)	21.108 (15.481, 26.734)	24.876 (21.584, 28.168)	22.655 (19.167, 26.144)	0.302
FDS	10.683 (-2.927, 24.294)	12.226 (7.860, 16.591)	6.765 (-0.247, 13.777)	12.076 (7.974, 16.179)	9.985 (5.638, 14.333)	0.559
BDS	2.868 (-4.850, 10.586)	5.687 (3.212, 8.163)	2.671 (-1.305, 6.647)	7.124 (4.798, 9.450)	6.421 (3.956, 8.886)	0.214
VRI	24.067 (2.346, 45.788)	31.536 (24.569, 38.503)	36.835 (25.645, 48.026)	35.222 (28.675, 41.769)	30.732 (23.793, 37.670)	0.587
VRII	26.547 (-1.640, 54.734)	28.874 (19.834, 37.915)	34.816 (20.294, 49.338)	34.809 (26.313, 43.305)	24.176 (15.173, 33.180)	0.394
DSST	76.878 (4.008, 149.747)	49.243 (25.871, 72.615)	52.392 (14.850, 89.934)	52.402 (30.437, 74.366)	75.913 (52.637, 99.190)	0.371

Test scores are adjusted mean using ANCOVA controlling for age, gender and blood test profile.
Numbers in parentheses indicate 95% CI

TABLE 6. Factors associated with neuropsychological test score among the study population (*n*=53) by multiple linear regression analysis

Neuropsychological tests / Variables	R^2	*b* (95% CI)	*p* value
MMSE[a]	0.451		
Intercept		37.877 (32.153, 43.601)	<0.001
Red cell distribution width		-0.628 (-1.056, -0.199)	0.005
Age		-0.119 (-0.167, -0.071)	<0.001
HDL*Age		0.047 (0.025, 0.069)	<0.001
MoCA[b]	0.413		
Intercept		25.213 (20.634, 29.792)	<0.001
Age		-0.121 (-0.179, -0.064)	<0.001
Gender[c]		1.870 (0.308, 3.431)	0.020
HDL		1.681 (0.020, 3.341)	0.047
FDS[d]	-		
BDS[e]	0.218		
Intercept		10.470 (7.987, 12.952)	<0.001
Age		-0.098 (-0.150, -.0046)	<0.001
VRI[e]	0.488		
Intercept		49.049 (44.257, 53,842)	<0.001
Age		-0.348 (-0.449, -0.248)	<0.001
VRII[e]	0.368		
Intercept		63.469 (47.968, 78.971)	<0.001
Age		-.323 (-0.474, -0.172)	<0.001
Potassium		-4.471 (-8.071, -0.872)	0.016
DSST[e]	0.451		
Intercept		117.242 (99.188, 135.297)	<0.001
Age		-0.911 (-1.223, -0.599)	<0.001
Alanine aminotransferase		-0.754 (-1.216, -0.292)	0.002

a Model assumptions are met; The linear model fits reasonably well; There is an interaction between independent variables and no multicollinearity problem.
b Model assumptions are not met; The linear model fits reasonably well; There is no interaction between independent variables and no multicollinearity problem. However, there is present of an outlier and normality assumption is not met.
c Male compares to female.
d No model was derived by SPSS using stepwise and forward methods.
e Model assumptions are met; The linear model fits reasonably well; There is no interaction between independent variables and no multicollinearity problem

Education is postulated to affect cognitive performance through better functional health literacy. However, years of education may not necessary be equivalent or reflect the quality of the education which was beyond the scope of this study.

Several studies have reported that there was a positive association between educational level and MoCA performance (Malek-Ahmadi et al. 2015; Rossetti et al. 2011; Yeung et al. 2014; Yu et al. 2012; Zhou et al. 2014). In contrast, higher level of education was found to be associated with poorer MoCA performance among mild cognitive impairment and cognitively normal participants in Singapore (Ng et al. 2015). The negative association between educational level and MoCA score may be due to two reasons: Firstly, the negative association was due to a heterogeneous effect of education especially across different populations; and secondly, MoCA may not be sensitive enough for MCI detection, at least for Chinese or Asian populations (Ng et al. 2015). In agreement with the second hypothesis, Bahasa Malaysia version of MoCA was reported to be moderately concordant with MCI detection (Razali et al. 2014). Nevertheless, our data showed that educational level was not correlated with MoCA performance. The lack of association between educational level and MoCA score in either direction may be due to the small sample size in this preliminary report.

In addition, education is also a factor affecting performance in digit span test. The results of the study on the population of the elderly in Seoul found the digit span score also influenced by education in addition to age and gender (Choi et al. 2014). Murphy et al. (2016) also found a correlation between digit span scores and education although the strength of the correlation is weak. Our findings however, showed that years of education were not associated with FDS and BDS scores.

There were also studies showing the effect of education on individual performance in Visual Reproduction test whether immediate and delayed recalls. dos Santos et al. (2011) reported that respondents who have a low level of education showed a weak performance in Visual Reproduction test. Similar finding was reported by Ardila et al. (1989) where illiterate subjects obtained a lower score than the professionals. In addition, the impact of education on the visual reproduction test can be seen in the results obtained by Boone et al. (2007) where education and age can be a factor influencing the analysis. Although our results showed that VRI was positively associated with years of education in SLR, the relationship became insignificant after controlling for confounders. This finding indicated that VRI is a multifactorial domain and further analysis by MLR showed that increases in age was associated with poorer performance of VRI score.

The effects of education can also be seen on the individual performance of the DSST. Joy et al. (2004) showed that education affects significantly the subject scores although the effect is weaker. However, the large age difference of our subjects may masked the effect of education. There are also studies that showed the presence of contradictions between education and DSST (Park 2007). According to a meta-analysis conducted by Hoyer et al. (2004), education does not have a significant impact on the DSST score. Our results showed that the DSST score was directly associated with years of education in SLR. However, when other confounders were taken into account, years of education were not significantly associated with DSST score. In fact, both age and alanine aminotransferase were inversely associated with the test score.

Age is a well-known risk factor for cognitive performance (Deary et al. 2009). Our results showed that age was inversely associated with all the tests performed except FDS (no model was derived). Other factors have also been identified to affect the test scores. Unlike RDW-CV, the effect of interaction between HDL and age on MMSE score is difficult to interpret due to the interaction itself. RDW-CV is an inflammation marker and has been associated with Alzheimer disease (Öztürk et al. 2013). According to Lee et al. (2016), increased RDW-CV lead to higher prognosis for leukaoraiosis disease leading to cognitive decline. In addition, HDL concentrations showed positive correlation with cognitive function. Gillum and Obisesan (2011) showed that increasing the concentration of HDL significantly affects cognitive function of individuals. In addition, younger subjects showed encouraging results for MMSE performance than older subjects. In our data, MoCA score was passively associated with HDL level. Males was predicted to perform better than females on MoCA which is in agreement with previous study (Gao et al. 2015) but in contrast to other studies which showed no gender differences (Rossetti et al. 2011) or that females performed better than males (Mittal et al. 2012). However, this model has to be assessed with caution as the model assumption was not met. Increased ALT has been associated with lower DSST score in the US population (Seo et al. 2016). ALT is a biomarker for liver disease or damage (Kim et al. 2008), but its effect on cognitive performance remained unclear. Our results showed that potassium is inversely associated with VRII score but the effect of potassium level on VRII score is uncertain. Further studies are needed to establish the relationship of these factors with cognitive performance.

The measure of education level was based on formal education without taking personal life experiences into consideration. Knowledge maybe acquired throughout a person's working life or life time. While such influences are difficult to take into account for this study, the results should be considered carefully because the inadequately adjusted factors may affect the interpretation on cognitive performance. Nevertheless, the extent of influence by education on performance of different cognitive domains is worth determining among healthy adults in Malaysia. Further studies recruiting more participants will probably provide more information on the cognitive function of healthy adults and its correlation, if any, with the level of education.

Conclusion

This preliminary report showed that educational level was statistically significant associated with cognitive performance among healthy Malay adults after controlling for confounders such as age, gender and blood tests. Further studies with larger sample size are needed to ascertain the effect of education and these other factors on cognitive performance.

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