The association of metabolic syndrome and aging with cognition in Asian men

Short Title: Metabolic syndrome, memory and perception capacities and aging in men

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ABSTRACT

Background: The present cross-sectional study examined the associations of individual metabolic factors and age with the short-term memory and perceptual capacity in 472 healthy Asian men. **Methods:** The symbol digit and digit span tests from the Swedish Performance Evaluation System were used to assess the perceptual capacity and memory cognitive domains. Linear regression with the stepwise method, and multivariate analyses of the General Linear Model with the Bonferroni correction for multiple comparisons were carried out with the SPSS 21.0 package. **Results:** High blood pressure and HDL were not significantly associated with either short-term memory or perceptual capacity. Age and glucose level were negatively associated but regular physical exercise was positively associated with perceptual capacity. On the other hand, high triglyceride level (TG) was positively associated but high waist/height ratio was negatively associated with short-term memory. When men without any component of the metabolic syndrome (MetS), were compared with men with one, two or three or more components of MetS, no significant differences in cognitive performance were noted. **Conclusion:** Not all the metabolic factors were significantly associated with short-term memory or the perceptual capacity domains. Those that were did not show a sufficiently consistent pattern of association to support a role for MetS as a whole in cognitive decline with aging. It may not be meaningful to evaluate the association of MetS as a whole with cognition. (226 words)

INTRODUCTION

Age is associated with a decline in cognition and as the population ages every society is faced with the challenge of addressing the increasing number of elderly with cognitive impairment and/or dementia [1]. Different domains of human cognition are thought to be variably affected by behavioral, psychological, lifestyle, environmental and other factors including metabolic syndrome (MetS) risk factors [2-15].

Metabolic syndrome (MetS) is not a disease but comprises a group of risk factors including high blood pressure, impaired levels of blood cholesterol, altered glucose metabolism or insulin resistance, and obesity. These risk factors together increase the likelihood of heart disease, stroke, peripheral vascular disease, and type 2 diabetes. Proposed definitions of MetS include those by the World Health Organization [16], the European Group for the Study of Insulin Resistance (EGIR) [17], the US National Cholesterol Education Program (ATPIII) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [18] and one introduced in 2005 by the International Diabetes Federation (IDF) [19].

In Australia, based on the ATPIII definition of MetS, the overall prevalence is 22.1% with the prevalence in men higher than in women (24.4% versus 19.9%, respectively) [20]. Numerous studies have shown that MetS can adversely affect cognition and increase the risk for dementia [11-15]. When coupled with obesity, MetS is associated with a greater decline in cognitive performance [21]. However, the association of MetS with cognitive decline is equivocal. Differences were observed when different cognitive domains were assessed and when different cognitive function tests with varying sensitivity were employed. MetS was significantly associated with memory and visuospatial but not with the executive cognitive domains [22]. Gender, age, educational

levels, and race have also been shown to have a bearing on cognitive performance. It has been shown that MetS was associated with an increased risk of cognitive decline in adults aged between 65 and 74 year, but in the oldest of old (those $\geq 80y$), the association disappeared [22-25]. Other studies have variably noted that MetS had a gender-dependent association with cognition, affecting cognition more in men [26, 27], more in women [12], while in others, no gender difference was noted [11]. Most of the earlier studies evaluated subjects with MetS, those with at least 3 out of the 5 risk factors and compared the cognitive performance of those without MetS. However, the control group may not be a true control group in that subjects may have none or up to 2 MetS risk factors. Relatively few studies evaluated the association of the individual components of the metabolic syndrome with cognition [13]. It is not valid to assume that every risk factor of the MetS is associated with cognition, in the same manner and to the same degree. In this cross-sectional study we sought to clarify the association of the individual risk factors of MetS, other metabolic factors and MetS as a whole, with cognition.

SUBJECTS, MATERIALS AND METHODS

Subjects

This study involved analyses of data collected from a group of 472 men. Details of recruitment of the subjects have been reported in several earlier publications [28, 29]. Subjects were healthy men, aged between 29y to 72y living in the community.

Methodologies

Each subject answered a self-administered and investigator-guided questionnaire. Questions asked include their medical, dietary, social, sex, and family histories and other histories regarding consumption of hormones, supplements and medication and the types and frequency of beverages consumed.

Biochemical measurements

An overnight 12h fasting blood sample was collected, and serum levels of cholesterol (TC) and triglycerides (TG) were measured using an automated procedure. High density lipoprotein-cholesterol (HDL) was determined after precipitation of apolipoprotein B-containing lipoproteins with sodium phosphotungstate and magnesium chloride [30]. Low density lipoprotein cholesterol (LDL) was computed according to the following formula: LDL = TC − (HDL + [TG x 0.45]). The ratio of TC to HDL (TC/HDL) was used as the atherogenic index [31]. Fasting glucose level was measured using the hexokinase method on an Abbott Architect automated platform (Abbott Laboratories, Abbott Park, Illinois, U.S.A).

Whole body DEXA scan

Every man had a whole body scan using the DEXA Hologic, Bedford, MA, USA [28]. The total body fat (%BF) based on the Siri formula used by the DEXA machine was used in the present study.

Anthropometric measurements

Bodyweight (Wt) in kilogram was measured without shoes using an electronic measuring scale. Height (Ht) was taken to the nearest centimeter. The body mass index (BMI) was calculated as bodyweight in kilogram divided by height in meter squared. Waist circumference (W) in centimeter was measured midway between the lower costal margin and iliac crest during the end-expiratory phase, while hip circumference (H) was measured in centimeters. In addition, the waist/hip (W/H) and waist/height (W/Ht) ratio were computed as indices of body fat.

Blood Pressures

Brachial systolic (Sys) and diastolic (Dia) blood pressures were measured by trained clinical researchers using a standardized manual sphygmomanometric method after subjects had five minutes of rest in the supine position. Both blood pressures were recorded as millimeter of mercury (mmHg).

Cognitive function tests

Two tests from the Swedish Performance Evaluation System (SPES), the Symbol Digit for perceptual capacity and Digit Span for short-term memory, were used in the study [32].

<u>*Symbol Digit*</u> – The Symbol Digit is a test of perceptual capacity which includes matching, memory and the speed of processing. In one row, a key to this coding task is given by the pairing of symbols with randomly arranged digits, 1 to 9. The task is to key in as fast as possible the digits corresponding to the symbols presented in random order in a second row. Each set consists of nine pairs of randomly arranged symbols and digits, and a total of 10 sets are presented. Performance is evaluated as the mean reaction time (msec) (RT) and the number of errors (Err) for the last 54 pairs of the test. Symbol digit

tests the individual's ability to interpret and correctly match what he sees as well as the speed of his mental perception. It also involves hand-eye coordination. The two components of this test are reaction time (RT) and the number of errors (Err) [32].

Digit Span – The Digit Span is a test of short-term memory capacity. In this test, a series of digits is presented on the screen. The digits are presented one at a time with a 1-second presentation time, and the task is to reproduce the series on the keyboard. Depending on the answer, the length of the following series is either increased or decreased. The test starts with a series of three digits and it is terminated after six incorrect answers. Performance is evaluated as the maximum string of numbers (DSpan) that the subject could remember successfully. A longer DSpan indicates a better short term visual memory [32].

The digit symbol and digit span are computer-based tests. All participants underwent a familiarization trial test before the actual scorings were recorded.

Exercise scores and groupings

The type, duration and frequency/week of exercise for each participant were collated from data from the self-administered and investigator-guided questionnaire. The intensity of the physical exercise was scored using the Metabolic Equivalent of Task (MET) for each exercise type. The scoring took into account the duration of each exercise episode and the frequency of the exercise per week to derive an exercise score. In accordance with the guidelines for Americans [33], the MET cut-off values were as follow: light intensity (<3 MET), moderate intensity (3−6 MET) and high intensity (>6 MET). The total exercise score per week was expressed as metabolic equivalent-min (MET-min). A total exercise score for each individual was derived from data from the self-administered questionnaire. Each exercise type was given a value for

MET. For example, jogging and walking were assigned a MET of 8.5 and 3.0, respectively. An individual who jogs four times a week and each time for 45 min will have a total score/week (ExSc) of 1530 (8.5 x 45 x 4) MET-min. A person who walks for 60 min and six times per week will have an ExSc of 1080 (3 x 60 x 6) MET-min. Those who did not exercise routinely were given an arbitrary score of zero MET-min. By this scoring formula, all exercise type can be given a score which is used to indicate how intensely an individual was exercising as a lifestyle habit. Only when the exercise regime was carried out for at least 6 months was it considered a lifestyle habit. By using this index of intensity of exercise, association studies with various exercise regimes as lifestyle habits could be evaluated.

The intensities of exercise were categorized into three groups: ExGp1 (no exercise, MET-min = 0), ExGp2 (moderate intensity, MET-min = 53 - 1230), ExGp3 (high intensity, MET-min = 1260 - 4320) The 75 percentile of all men with an exercise score >0 MET-min was 1250. Therefore ExGp3 represented those men who have had exercise intensity above the 75 percentile.

Age groups (AgeGp)

Men were categorised into 4 age groups as follows: AgeGp1 (29-40y), AgeGp2 (41-50y), AgeGp3 (51-60y) and AgeGp4 (61-72y). The decade interval in age groupings was commonly used in many of our earlier studies [28, 29, 34, 35]

Metabolic Syndrome Groupings

The most commonly used NCEP ATPIII definition of MetS [18] was used for the purpose of this study. It is a simple scoring system with no single dominant component, and is used by several studies evaluating the association of MetS with human cognition [13, 26, 36]. In the present study, we evaluated the association of MetS as a whole as

well as the individual risk components with the different parameters of cognition. Povel et al [37] had suggested that using the NCEP ATPIII definition to compose one entity from MetS risk factors, MetS could predict Type 2 Diabetes and cardiovascular disease. However, it may not necessarily be applicable to cognition assessment. An earlier study in fact found that MetS as an entity did not show a significant association with cognition, while some of the individual risk components of MetS did [13].

According to the recommendations of the NCEP ATP III [18], the 5 risk factors of MetS were defined as follows:

High density lipoprotein cholesterol (HDL) <1.03mmol/l

Fasting glucose level (GLU) $\geq$5.6mmol/l

Systolic blood pressure/diastolic blood pressure - B/P $\geq$130/$\geq$85 mmHg

Triglyceride level (TG) $\geq$ 1.7mmol/l

Waist circumference (W) $\geq$92.5cm (W of $\geq$92.5cm was the index for central obesity found to be appropriate for the local population) [38].

Each risk factor of the MetS and other metabolic parameters was divided into two categories, one above and the other below the recommended cut-off points. Other indices of obesity: body mass index (BMI), the percent body fat (%BF) as derived from the whole body DEXA scan using the Siri formula, waist/hip ratio (WH), and waist/height ratio (WHt) were included in the analyses. We also evaluated other lipids and lipoproteins in the analyses including total cholesterol (TC), low density lipoprotein cholesterol (LDL) and the TC/HDL ratio. Therefore the groups used in the multivariate analyses for this study were:

TG groups (TGGp):	TGGp1 <1.7 mmol/l	TGGp2 ≥1.7mmol/l
HDL groups (HDLGp):	HDLGp1 ≥1.03 mmol/l	HDLGp2<1.03mol/l
TC groups (TCGp):	TCGp1 <6.2 mmol/l	TCGp2 ≥6.2 mmol/l
LDL groups (LDLGp):	LDLGp1 <4.14 mmol/l	LDLGp2 ≥ 4.14 mmol/l
TC/HDL groups (TC/HDLGp):	TC/HDLGp1 <5.0	TC/HDLGp2 ≥5.0
GLU groups (GLUGp):	GLUGp1 <5.6mmpl/l	GLUGp2 ≥5.6mmol/l
%BF groups (%BFGp):	%BFGp1 <25%	%BFGp2 ≥25%
BMI Groups (BMIGp):	BMIGp1 <27kg/m^2	BMIGp2 ≥27kg/m^2
W groups (WGp):	WGp1 <92.5cm	WGp2 ≥92.5
W/H ratio groups (WHGp):	WHGp1 <0.94	WHGp2 ≥0.94
W/Ht ratio groups (WHtGp):	WHtGp1 <0.55	WHtGp2 ≥0.55

The indices for obesity were established earlier for this same sample of men [38]. The World Health Organization recommended a BMI of 30kg/m^2 as the cut-off value for obesity [39]. However, we have shown that a BMI of 30kg/m^2 correlated very poorly with a measure of obesity based on DEXA-derived percent total body fat of 25% in the sample of Singaporean men [38]. In this study, the DEXA-derived percent body fat as a measure of obesity and the more appropriate BMI of 27kg/m2 were used in the analyses. The cut-off values for W, W/H and W/Ht of 92.5cm, 0.94 and 0.55 appropriate for the Singaporean men [38] differed from those in the Caucasian population.

No of MetS symptom groups (Msym)

Subjects were categorised into four Msym groups based on the number of metabolic risk factors they had as follows:

Msym0   0 risk factor

Msym1	1 risk factor out of 5 listed for MetS
Msym2	2 risk factors out of 5 listed for MetS
Msym3	≥3 risk factors out of 5 listed for MetS

Statistical analysis

Statistical analyses were performed using SPSS for windows version 21.0. Basic descriptive statistics and the Multivariate analyses of the General Linear Model coupled with the Bonferroni correction for multiple comparisons were used on continuous measurements. All the individual risk factors of MetS, other metabolic factors together with age, and exercise score (MET-min) were subjected to multiple linear regression analyses. To evaluate the parameters which were independently correlated to the cognitive parameters, the "stepwise" method of linear regression analyses was adopted. Significant correlation was set at a p-value of <0.05.

Initial analyses showed that age, MET-min, TG, GLU and WHt were independently associated with cognitive functions. Hence, in the final analyses, all multivariate analyses were carried out with age, MET-min, TG, GLU and WHt as covariates.

RESULTS

Table 1 shows the metabolic parameters included in the linear regression analyses using the stepwise method, age, exercise score (MET-min), triglyceride level (TG), fasting glucose level (GLU) and the anthropometric parameter of WHt that were independently and significantly correlated with one or two of the three measures of cognition studied. Age was associated with longer RT in the perceptual capacity domain, while high GLU was associated with poorer perceptual capacity, with higher Err and longer RT (Table 1). Higher MET-min was associated with shorter RT (Table 1). High TG, on the other hand, was associated with better short–term memory, with longer DSpan (Table 1). WHt, an index of central obesity, was negatively associated with DSpan (Table 1). No significant correlation with the cognitive parameters was noted for other components of the metabolic syndrome: blood pressure, waist circumference, HDL and other indices of obesity BMI, W, WH, and %BF and LDL, TC and TC/HDL.

It was shown with the multivariate analyses that older aged men had longer RT than younger men. Men above the age of 60y had significantly longer RT, by up to 12.9% when compared to men 40 y old or younger (Table 2). Men who had a regular physical exercise regime as a lifestyle habit (ExGp2), on the other hand, had shorter RT, by up to 6.8%, when compared to men without a regular physical exercise regime (ExGp1, Table 2). Table 2 also shows that age is significantly associated with some of the metabolic factors. Higher systolic and diastolic blood pressure, WH and WHt and fasting glucose levels were associated with age, while the number of risk factors for MetS was higher in older men (Table 2).

Of the five components of MetS, only two had significant association with cognitive functions when using the multivariate analyses. High fasting glucose, >5.6mmol/l

(GLUGp2) was associated with higher Err, but not with RT in the perceptual capacity test as compared to men with GLU below 5.6mmol/l (GLUGp1), and was not associated with short-term memory (Table 3). High TG, $\geq$1.7mmol/l (TGGp2), on the other hand, had a positive association with short-term memory; DSpan being about 3.9% longer but not significantly associated with perceptual capacity (Table 3). Of all the other metabolic factors evaluated, only high total body fat, $\geq$ 25% (%BFGp2) was associated with poorer short-term memory, DSpan being shorter by 8.8% in obese men when compared with non-obese men (%BFGp1) (Table 3). No other metabolic factors were significantly associated with any of the 3 measures of the short-term memory and perceptual domains of cognition (Table 3).

Regular physical exercise as a lifestyle habit was significantly associated with only the RT component of the perceptual capacity. A moderate to high intensity of exercise (ExGp2 & ExHGp3) was associated with lower RT when compared to men who did not have regular exercises (ExGp1) (Table 3). It is interesting to note that in the men studied, men aged above 60y old were exercising more intensely than all the younger men (Table 2).

Out of 472 subjects who had all the essential parameters for evaluation of the metabolic syndrome, 41.5% had no MetS symptom, 32.7% had 1 symptom, many of these men had high TG >1.7mmol/l. About 20.3% had 2 symptoms, and 5.5% had 3 to 4 symptoms. When compared to men without any MetS risk factor (Msym0), men with 1 (Msym1), 2 (Msym2) and 3 or more symptoms (Msym3) showed no significant differences in any of the three components (Err, RT and DSpan) of cognition (Table 3).

DISCUSSION

Aging is associated with a decline in cognitive performance [40, 41]. However, the onset and rate of decline vary according to which cognitive domain is evaluated. In the present study, a significantly longer RT for perceptual capacity was noted only in men aged 50 years and above; and the RT appeared to be higher in men above 60y. On the other hand, age was not associated with a decline in the short-term memory domain in men up to 72 years old.

A regular physical exercise regime as a lifestyle habit is beneficial to the RT component of the perceptual capacity. Both moderate (ExGp2) and intense (ExGp3) physical exercises were associated with shorter RT than in men who were not exercising regularly (ExGp1). These observations imply the importance of a physically active lifestyle in warding off or attenuating the age-associated decline in cognitive performance [8, 9]. We therefore advocate the promotion of a lifestyle habit of physical exercises as an important, non-invasive modality to help maintain cognitive health in aging men.

Association of metabolic syndrome and with cognition has been equivocal, with studies showing negative, positive or neutral associations [10-13, 21, 23]. Gender and age may complicate the associations of MetS and cognition [11, 12, 22-27]. Hence, the observations noted in the present study are applicable only to men between the ages of 29 to 72 y and specific to the perceptual and short-term memory cognitive domains. We have shown that individually, not all the risk factors of the MetS had significant association with the two cognitive domains evaluated. Those that did showed associations with different cognitive domains and in opposite directions. High fasting glucose was negatively associated with the perceptual capacity, both in terms of the number of errors as well as the retention time, an observation that is similar to those of an

earlier paper [13]. High TG levels, on the other hand, were positively associated with short-term memory. High WHt ratio was negatively associated with the short-term memory. Contrary to the earlier study [13], no significant and independent correlations were noted for the other two components of the MetS, namely systolic and diastolic blood pressure, and HDL-C. No significant and independent correlations were noted for the other metabolic factors evaluated except for percent total body fat. Obesity in men was associated with poorer short-term memory when compared to non-obese men.

Low density lipoprotein cholesterol (LDL) and HDL are major transport lipoproteins of cholesterol and together with TG are independently associated with cardiovascular disease [42] and possibly cognitive impairment [43]. Some studies have shown conflicting associations of LDL, HDL and TG with cognition. Other studies have shown an association of high LDL, HDL and TG with decline in cognitive performance [44-47]. Still other studies have shown no association of high LDL, HDL and TG with cognitive functions [48-51]. Opposite associations were also noted for high LDL and HDL [52-54]. The present study found that high levels of TG, in contrast to earlier studies [47, 55] were associated with better short-term memory. Another recent study has shown that higher levels of LDL were associated with better general cognitive performance and processing speed [56]. It is possible that the conflicting findings of the association of LDL, HDL and TG may be due, in part, to age, gender, cognition outcome measures, levels of lipoproteins and lipids and varying degrees of adjustments of other confounding factors such as adjusting for exercise intensity, and/or other metabolic factors. Further research is needed to clarify the roles of the individual metabolic factors with cognition.

We have shown that different components of the MetS may be associated with different cognitive domains and in different directions. Therefore, it is not unexpected that we

found that dichotomizing men into MetS or Non-MetS overall did not predict scores in the cognitive parameters studied. This is especially true when the analyses were adjusted for confounding factors including, age and exercise intensity, etc. This observation was similar to that of an earlier paper [13]. Since different components of the MetS have none or varying associations with cognition it is therefore not meaningful to study the relationship between MetS as a single construct and cognition. We need to clarify the role of each component of MetS in cognitive performance, in order to establish modalities to help enhance cognitive performance and/or reduce its decline with age.

A limitation of this study is that it is a cross-sectional study; hence no causal effect is attributable to the observed associations. The number of cases in some groupings was small and may have limited the validity of the findings. Only two cognitive domains, the perceptual and memory domains, were studied, hence cross comparisons with studies with other domains of cognition could not be made. On the other hand, a positive contribution of the present study is the involvement of a relatively wide age range (29 years to 72 years) of Asian men who were healthy with no known illnesses that might mar the actual association of the metabolic factors with cognition.

Singapore. Prof. William Hart was intimately involved in the interpretation of findings, drafting of the article and critical revision of the article for submission.

DECLARATION OF INTEREST

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Table 1: Parameters with significant regression with the three cognitive parameters (number of errors (ERR), retention time (RT) and maximum length of string (DSpan) based on linear regression analyses using the "stepwise" method for all continuous variables including age, MET-min, %BF, systolic B/P, Diastolic B/P, BMI, waist circumference (W), waist/hip ratio (WH), waist/height ratio (WHt), total cholesterol (TC), high-density lipoprotein-C (HDL), low-density lipoprotein-C (LDL), TC/HDL ratio, fasting glucose concentration (GLU)

Cognitive functions		Standardized Coefficients (Beta)	p-value
Err	GLU	0.175	<0.001
RT (msec)	Age	0.285	<0.001
	MET-min	-0.116	0.015
	GLU	0.109	0.024
DSpan	TG	0.138	0.006
	WHt	-0.114	0.023

Table 2: The mean (+SE) of exercise score, metabolic and anthropometric parameters and 3 measures of cognitive function Err, RT and DSpan in the different age groups (MET-min, WHt, TG and GLU were covariates for analyses of Err, RT, and DSpan in different age groups).

	AgeGp1<40y (61)	AgeGp2 41-50(186)	AgeGp351-60(146)	AgeGp4 >60y (73)
Err	1.87 ± 0.299	1.59 ± 0.173	1.33 ± 0.187	1.68 ± 0.287
RT(msec)	2279 ± 50^a	2329 ± 30^b	2454 ± 31^c	2574 ± 48
DSpan	6.98 ± 0.162	7.05 ± 0.095^d	6.94 ± 0.103	6.55 ± 0.15
Met-min	436 ± 98^e	577 ± 58^e	575 ± 62^e	970 ± 92
Systolic (mmHg)	123 ± 1.9^f	124 ± 1.1^f	128 ± 1.1^f	137 ± 1.7
Diastolic (mmHg)	77.7 ± 1.2^g	78.2 ± 0.7^g	80.5 ± 0.7	82.7 ± 1.1
Ht (cm)	171.4 ± 0.76^h	169.5 ± 0.42^i	167.6 ± 0.45	166.3 ± 0.68
Wt (Kg)	70.2 ± 1.28	68.5 ± 0.71	67.8 ± 0.75	65.7 ± 1.14
BMI (kg/m^2)	23.9 ± 0.39	23.8 ± 0.21	24.1 ± 0.23	23.7 ± 0.35
W (cm)	83.9 ± 0.91	83.7 ± 0.51	85.3 ± 0.54	85.9 ± 0.82
H (cm)	97.0 ± 0.73^j	95.6 ± 0.40	95.6 ± 0.43	94.0 ± 0.65
W/H	0.87 ± 0.006^k	0.88 ± 0.003^l	0.89 ± 0.00^m	0.91 ± 0.005
W/Ht	0.49 ± 0.00^n	0.49 ± 0.003^o	0.51 ± 0.003	0.52 ± 0.005
TC (mmol/l)	5.77 ± 0.132	5.75 ± 0.073	5.72 ± 0.78	5.80 ± 0.118
TG (mmol/l)	1.31 ± 0.092	1.46 ± 0.051	1.56 ± 0.054	1.34 ± 0.082
HDL(mmol/l)	1.32 ± 0.039	1.33 ± 0.022	1.32 ± 0.023	1.42 ± 0.035
LDL (mmol/l)	3.87 ± 0.121	3.77 ± 0.067	3.71 ± 0.071	3.77 ± 0.108
TC/HDL	4.55 ± 0.144	4.50 ± 0.080	4.54 ± 0.085	4.23 ± 0.129
GLU (mmol/l)	4.91 ± 0.93	4.79 ± 0.051^p	4.99 ± 0.055	5.22 ± 0.083
No. Metsym	0.51 ± 0.12^q	0.71 ± 0.07^r	0.92 ± 0.07	1.07 ± 0.11

a= AgeGp1 is significantly lower than AgeGp3 & AgeGp4 (p = 0.003, <0.001)

b= AgeGp2 is significantly lower than AgeGp3 & AgeGp4 (p = 0.008, <0.001)

c= AgeGp3 is significantly lower than AgeGp4 (p = 0.036)

d= AgeGp2 is significantly higher than AgeGp4 (p = 0.036)

e= AgeGp1, AgeGp2 & AgeGp3 are significantly lower than AgeGp4 (p =<0.001, 0.002, 0.002)

f= AgeGp1, AgeGp2 & AgeGp3 are significantly lower than AgeGp4 (p = <0.001, <0.001, <0.001)

g= AgeGp1 & AgeGp2 are significantly lower than AgeGp4 (p = 0.018, 0.004)

h= AgeGp1 is significantly higher than AgeGp3 & AgeGp4 (p = <0.001, <0.001)

i= AgeGp2 is significantly higher than AgeGp3 & AgeGp4 (p = 0.015, <0.001)

j= AgeGp1 is significantly higher than AgeGp4 (p = 0.018)

k= AgeGp1 is significantly lower than AgeGp3 & AgeGp4 (p = <0.001, <0.001)

l= AgeGp2 is significantly lower than AgeGp3 & AgeGp4 (p = 0.002, <0.001)

m= AgeGp3 is significantly lower than AgeGp4 (p = 0.004)

n= AgeGp1 is significantly lower than AgeGp3 & AgeGp4 (p = 0.003, <0.001)

p= AgeGp2 is significantly lower than AgeGp3 & AgeGp4 (p = 0.004, <0.001)

p= AgeGp2 is significantly lower than AgeGp3 & AgeGp4 (p = 0.036, <0.001)

q= AgeGp1 is significantly lower than AgeGp3 & AgeGp4 (p = 0.024, 0.004)

r= AgeGp2 is significantly lower than AgeGp4 (p = 0.031)

Table 3: The mean (+SE) of Err, RT and DSpan in the various metabolic factors (Analyses adjusted with the Table 3: Associations of exercise groups and various metabolic factors with the 3 measures of cognitive function using the multivariate analyses with the appropriate covariates including, MET-min, age, WHt, TG, and Glucose levels (GLU).

	ExGp1 (141)	ExGp2 (143)	ExGp3 (186)	
Err	1.95+0.196	1.39+0.194	1.45+0.171	
RT (msec)	2503+32[a]	2360+32	2365+28	
DSpan	6.88+0.107[c]	6.99+0.106	6.89+0.093	
	%BFGp1(411)	%BFGp2(19)		
Err	1.57+0.115	1.69+0.551		
RT (msec)	2416+19	2268+90		
DSpan	6.93+0.063[b]	6.28+0.298		
	WGp1 (421)	WGp2 (49)		
Err	1.58+0.119	1.53+0.372		
RT (msec)	2415+19	2359+61		
DSpan	6.92+0.065	6.77+0.204		
	WHGp1(423)	WHGp2 (47)		
Err	1.58+0.114	1.59+0.370		
RT (msec)	2402+19	2430+61		
DSpan	6.93+0.062	6.80+0.202		
	WHtGp1(399)	WHtGp2 (71)		
Err	1.56+0.116	1.72+0.279		
RT (msec)	2400+19	2431+46		
DSpan	6.95+0.064	6.75+0.153		
	BMIGp1 (436)	BM1Gp2 (15)		
Err	1.60+0.110	0.479+0.593		
RT (msec)	2401+18	2365+97		
DSpan	6.92+0.060	6.55+0.325		
	BPGp1(371)	BPGp2 (77)		
Err	1.55+0.121	1.65+0.268		
RT (msec)	2418+20	2329+44		
DSpan	6.91+0.065	6.79+0.146		
	HDLGp1(74)	HDLGP2 (396)		
Err	1.46+0.280	1.60+0.117		
RT (msec)	2396+46	2406+19		
DSpan	7.06+0.153	6.89+0.064		
	TGGp1 (328)	TGGp2 (142)		
Err	1.62+0.130	1.49+0.199		
RT (msec)	2416+21	2379+33		
DSpan	6.84+0.071[c]	7.11+0.110		
	GLUGp1 (427)	GLUGp2 (43)		
Err	1.49+0.113[d]	2.48+0.370		
RT (msec)	2397+18	2486+60		
DSpan	6.94+0.062	6.71+0.201		
No. METS symptoms	Msym0 (196)	Msym1 (154)	Msym2 (96)	Msym3 (26)
Err	1.50+0.18	1.46+0.19	1.75+0.29	2.14+0.51
RT (msec)	2429+29	2382+31	2385+48	2382+85
DSpan	6.91+0.10	6.83+0.102	6.97+0.16	6.95+0.28

a= ExGp1 is significantly higher than ExGp2 & ExGp3 (p = 0.005, 0.004)
b= %BFGp1 is significantly higher than %BFGp2 (p = 0.043)
c= TGGp1 is significantly lower than TGGp2 (p = 0.043)
d= GLUGp1 is significantly lower than GLUGp2 (p = 0.011)

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