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Homocysteine and cognitive function in the elderly

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ABSTRACT

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Dementia is prevalent among elderly people, and projections show that the number of affected might triple over the next 50 years, because of a large increase in the oldest segment of the population. The objective of this study was to investigate the relationship between cognitive function and serum homocysteine level. This study was a cross-sectional study carried out in Mampang district, South Jakarta. A total of 94 elderly people was recruited for this study consisting of 44 females and 50 males. In this study serum homocysteine level was assessed by fluorescent polarization immunoassay and cognitive function with the mini mental state examination (MMSE). In elderly women MMSE scores for plasma homocysteine concentrations of <11.7 μmol/L, 11.7-14.9 μmol/L and >14.9 μmol/L were 24.00 ± 3.68, 23.80 ± 6.51, and 20.80 ± 9.00 respectively, with p=0.000. In elderly men the MMSE scores for plasma homocysteine concentrations of <11.7 μmol/L, 11.7-14.9 μmol/L and >14.9 μmol/L were respectively 27.66 ± 2.06, 26.33 ± 3.79 and 24.03 ± 5.52 with p=0.008. Homocysteine concentrations of >14.9 μmol/L were more commonly found in males (66%) than in females (22.70%). The results of a regression analysis indicated that the factors influencing cognitive function were level of education (p=0.001) and age (p=0.035), whereas gender and homocysteine concentration did not affect cognitive function (p=0.554 and p=0.714, respectively). Plasma homocysteine concentration was inversely related to cognitive function. The most important factors affecting cognitive function were level of education and age.

Keywords : Plasma homocysteine, cognitive function, elderly

INTRODUCTION

No other organ system in the human body is as dependent on nutritional intake as the central nervous system, while conversely this system also affects nutritional intake. Several theories have been put forward regarding the functions of brain receptors for cholecystokinin, opioid-like endorphins and serotonin that play a role in determining human food habits.[1,2]

Studies on experimental animals indicate that with advancing age there is a decline in the functioning of the brain and in the number of brain receptors. In the elderly there is also a diminished sense of taste and a decline in olfactory nerve functions that affect appetite.[2,3]

The nervous system requires a constant intake of glucose for adequate functioning of the brain, which is particularly dependent on intake of essential nutrients. Deficiencies of vitamins and minerals, such as vitamin B12, folate, vitamin B6 and trace minerals, may result in disturbances of brain functions such as cognitive functions.[4,5]

Vitamin deficiencies commonly occur in the elderly, especially of the vitamin B group, caused by various factors, such as gastric atrophy with achlorhydria or hypochlorhydria, which in the elderly may account for up to 20-50% of cases. Studies have yielded evidence for an association in the elderly between decreased levels of vitamin B12, folate, and vitamin B6 on the one hand and impaired cognitive function on the other.[1,5]

One of the manifestations of impaired cognitive function is dementia, which is characterized by a progressive decline in cognitive function, resulting in a decreased ability for conducting activities of daily living. Dementia affects 8% of the elderly population over 65 years of age, and in Canada it gives rise to more than 60.000 new cases annually. Another disease, Alzheimer's, is the cause of 50% of all cases of dementia in Canada,[6] whereas other studies indicate that dementia due to Alzheimer's disease may account for up to 70% of all dementia cases.[7] It is estimated that in the following 50 years the number of dementia cases may undergo a threefold rise due to a increase in the elderly population.[8] The prevalence of this disorder is extremely high and as the disorder may lower the quality of life of the elderly, prevention and early detection are important.[6] Factors that have been associated with the risk of dementia are age and level of education, which are of the highest relevance for dementia. Recently high homocysteine levels have also been associated with an increased risk of dementia.[6,7,9]

Homocysteine is an amino acid resulting from the metabolism of methionine that is dependent on cobalamine, vitamin B_6, and folic acid.[8,10] Plasma homocysteine level is an indicator for vitamin B status, including that of folic acid, where a high homocysteine concentration implies an inadequate vitamin B status. Data from several laboratories have shown that high homocysteine level is extremely common in old age and does not depend on vitamin status.[11-13] High total plasma homocysteine level is a major vascular risk factor that is associated with an increased risk of atherosclerotic sequelae, including death due to cardiovascular disease, coronary heart disease, carotid atherosclerosis and stroke.[7,14,15]

Cognitive function may be assessed through various instruments, such as the mini mental state examination (MMSE). This test comprises five categories of criteria, viz. criteria on orientation with a maximum score of 10, registration criteria with maximum score of 3, attention and calculation with maximum score of 5, recall criteria with maximum score of 3, and language criteria with maximum score of 9. In addition to these five criteria the subjects are also asked to write a sentence and copy a drawing.[8]

Research results on the influence of homocysteine on cognitive function in the elderly are still subject to controversy. A number of studies have demonstrated a significant assciation,[7,15-17] whereas other studies have shown contradictory results.[8,18-19] An Italian study by Ravaglia et al.[9] on dementia-free

elderly found an increased risk of low MMSE scores with increasing plasma homocysteine levels, although homocysteine was not directly associated with cognitive disorders.

The objectives of the present study were to find an association between plasma homocysteine concentration and cognitive function in the elderly and to determine the factors that might play a role in the occurrence of dementia.

METHODS

Subjects

The study subjects were randomly selected residents aged 60 years and over from the catchment area of the Mampang Prapatan District Health Center in South Jakarta. The inclusion criteria were as follows: age 60 years and over, mobile, not having terminal diseases or being comatous, and not suffering from severe psychotic disorders. The study subjects had also expressed their willingness to participate in the present study by signing a letter of informed consent. Exclusion criteria were acute infection, intake of vitamins, cod liver oil or other supplements within the previous month, and abnormal renal function.

Assessment of renal function and cognitive function

As renal function affects the metabolism of homocysteine,[15] subjects with a creatinine concentration above reference level were considered to have abnormal renal function. The reference level for females is 0.5-1.3 mg/dL and for males 0.5-1.4 mg/dL.[14] Cognitive function was assessed by the MMSE. An MMSE score of 26-30 is considered questionably significant/no cognitive impairment, a score of 21-25 implies mild cognitive impairment, a score of 10-20 suggests moderate cognitive impairment and 0-9 indicates severe cognitive impairment.[13]

Data collection

The study participants were interviewed by field workers using a questionnaire that had been tested in a preliminary trial. The filling in of questionnaires was performed daily from Monday to Friday, and the weekly number of elderly who completed their interviews was around 25. These later were invited for a visit to the Mampang Prapatan District Health Center on the following Saturday. For the purpose of collection of a blood sample for laboratory examination, the elderly were asked to conduct a 10 – 12 hour fast prior to their visit to the health center. The following Saturday morning the participants underwent measurement of blood pressure, pulse rate, weight, height, waist circumference, and hip circumference. The measurements were taken by two nurses previously trained in the appropriate techniques. Data collection was performed four times within the period of one month between November 2006 and December 2006.

Assessments

Height (cm), waist circumference (cm) and hip circumference (cm) of the subjects were measured using a standard tape measure accurate to 1 mm. Weight (kg) was measured on a calibrated scale accurate to 0.5 kg with normal indoor clothing. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters). Blood pressure measurements were performed with the subject sitting, using a standard sphygmomanometer accurate to 5 mmHg. Hypertension was defined as a systolic blood pressure of $\geq$140 mmHg and/or a diastolic blood pressure of $\geq$90 mmHg.

Laboratory examinations

From each study subject 5 mL of venous blood was collected using a vacutainer without anticoagulant. The blood sample was centrifuged at 300 RPM for 10 minutes in order to obtain

serum for assessment of renal function and homocysteine level. Determination of homocysteine level was performed only on the serum of subjects with a renal function consistent with reference values. Creatinine concentration was determined by the Jaffe method on a TRX, whereas homocysteine was assessed by fluorescent polarization immunoassay on an Abbott IMX. The coefficient of variation (CV) of creatinine was 2.1% for normal concentrations and 1.6% for high concentrations, whilst the corresponding CV values for homocysteine were 3.4% and 2.3%, respectively.

Data analysis

For data analysis the Statistical Program for Social Sciences (SPSS) was used. Normality of data distribution was determined by the Kolmogorov – Smirnov (KS) test. For normally distributed data the mean and standard deviation was calculated and for non-normally distributed data the median and standard deviation. To determine the presence of a statistically significant difference between groups for normally distributed data the analysis of variance (anova) was used, whilst for non-normally distributed data the Kruskal – Wallis test was applied. For determining correlation between homocysteine level and cognitive function, for normally distributed data the Pearson's product moment correlation was used and for non-normally distributed data the Spearman rho test. A multiple linear regression was done to examine the cross-sectional association between homosysteine blood levels and mean MMSE scores adjusted for sociodemographic factors. Statistical significance was defined for all analyses as $P < 0.05$.

RESULTS

A total of 94 elderly consisting of 44 (47%) females and 50 (53%) males meeting the inclusion and exclusion criteria participated in this study. The age of the subjects ranged from 60 - 80 years, with mean age of 64.5±8.4 years for females and 66.3±5.2 years for males. The characteristics of the study subjects are presented in Table 1.

There was no appreciable difference in age between female and male subjects, whereas the body mass index (BMI) was higher in the male group compared with the female group, which was consistent with the greater weight and stature of

Table 1. Mean values of main characteristics of female and male subjects

Variable	Female (n = 44) Mean ± SD	Male (n = 50) Mean ± SD	Nilai p
Age (years)	64.5 ± 8.4	66.3 ± 5.1	0.223
Body Mass Index (BMI) (Kg / m^2)	21.7 ± 4.3	22.1 ± 3,5	0.504
Education (years)	4.8 ± 0.5	5.2 ± 0,3	0.630
Weight (kg)	49.4 ± 10.7	57.4 ± 9,9	0.000*
Height (cm)	150.7 ± 3.9	160.9 ± 4,4	0.000*
Waist circumference (cm)	78.2 ± 11.9	81.7 ± 10,7	0.127
Hip circumference (cm)	89.4 ± 9.9	89.3 ± 6,9	0.622
Systolic BP (mm Hg)	148 ± 21	141 ± 23	0.003*
Diastolic BP (mm Hg)	87 ± 12	85 ± 12	0.530
Creatinine (mg/dL)	0.68 ± 0.21	1.01 ± 0.17	0.000*
Homocysteine (μmol/L)	13.50 ± 3.69	18.96 ± 7.56	0.000*
MMSE	23.18±6.4	25.11±5.03	0.096

Table 2. Plasma homocysteine levels of study subjects

Homocysteine level (μmol/L)	Females	Mean	Males	Mean
< 11.7	14 (31.8 %)	9.9 ± 1.4	6 (12 %)	10.3 ± 1.3
11.7 – 14.6	20 (45.5%)	13.2 ± 0.8	12 (24 %)	13.5 ± 1.1
> 14.6 μmol/L	10 (22.7%)	19.2 ± 2.4	32 (66 %)	22.1 ± 7.3
Total	44 (100%)		50 (100%)	

males. The educational level of male subjects was higher than that of females. Waist circumference of males was greater than that of females, but in both groups it did not exceed the recommended waist circumference values according to Asia-Pacific criteria, i.e. 80 cm for females and 90 cm for males. Hip circumference was similar in males and females.

Both systolic and diastolic blood pressures were higher in females than in males, with p=0.03 for systolic BP and p= 0.30 for diastolic BP, whilst mean systolic BP was > 140 mmHg in both groups. Creatinine and homocysteine levels were both higher in males than in females, with p=0.000, indicating a significant difference between both genders. MMSE scores tended to be higher in males compared with females, but did not show a significant difference.

In Table 2 homocysteine levels were divided into three categories, i.e. <11.7 μmol/L, 11.7 - 14.6 μmol/L and >14.6 μmol/L, both for females and males. Among the study subjects with homocysteine levels above 14.6 μmol/L, there were 10 females (22.70%) with mean homocysteine level of 19.2 ± 2.4 μmol/L and 32 males (66%) with mean homocysteine level of 22.1 ± 7.3 μmol/L. Homocysteine levels above 14.6 μmol/L were more frequent in males compared with females.

Table 3 presents MMSE scores in females and males by category of homocysteine level, showing a significant difference between categories in females with p=0.000 and in males with p=0.008. From the table it may be concluded that higher plasma homocysteine levels are associated with lower MMSE scores. In Table 4 are shown homocysteine levels and MMSE scores by age and level of education. Homocysteine levels in males for the categories of no education, primary school, junior high school and senior high school were greater than 14.6 μmol/L, whereas in females for primary school, senior high school and university education homocysteine levels were <14.6 μmol/L. There was no significant difference in homocysteine concentrations of females and males at various levels of education. MMSE scores were proportional to level of education, with higher MMSE scores being found at higher levels of education (p=0.000).

From Table 4 it is also apparent that in females there was no significant difference in homocysteine levels between various age groups, whereas in males the homocysteine levels did show a significant difference between various age groups.

Table 3. MMSE scores by categories of homocysteine level

Homocysteine level (μmol/L)	MMSE Females	MMSE Males
< 11.7	24.0 ± 3.7	27.7 ± 2.1
11.7 – 14.6	23.8 ± 6.5	26.3 ± 3.8
> 14.6	20.8 ± 9.0	24.0 ± 5.5
p	0,000*	0.008*

Table 4. mean homocysteine concentration and MMSE score by age and level of education

Education	Females n (%)	Homocysteine (μmol/L)	MMSE	Males n (%)	Homocysteine (μmol/L)	MMSE
No education	16 (40%)	15.00 ± 2.43	17.50 ± 6.39	4 (8%)	20.80 ± 0.35	14.00 ± 4.62
Primary school	14 (35%)	13.21 ± 5.28	23.71 ± 5.14	25 (50%)	17.06 ± 5.51	26.85 ± 2.38
Junior high school	4 (10%)	18.50 ± 5.54	29.00 ± 0.00	11 (22%)	21.67 ± 10.00	25.33 ± 4.08
Senior high school	4 (10%)	12.20 ± 1.04	28.50 ± 0.57	10 (20%)	15.82 ± 4.02	27.60 ± 2.95
University	2 (5%)	11.90 ± 0.00	30.00 ± 0.00	0 (0%)		
p		0.118	0.000*		0.136	0.000*
Age (years)						
60-64	14 (31.8%)	17.97 ± 6.47	25.07 ± 3.77	18 (36%)	17.73 ± 7.12	24.80 ± 4.90
65-69	24 (54.5%)	17.81 ± 5.75	24.87 ± 5.70	21 (42%)	16.00 ± 3.37	24.91 ± 6.44
70-74	4 (9.1%)	19.95 ± 11.9	24.00 ± 9.40	5 (10%)	29.23 ± 11.10	27.33 ± 0.52
75-79	2 (4.5%)	25.30 ± 15.69	28.00 ± 1.40	6 (12%)	22.45 ± 7.30	24.75 ± 1.90
p		0.513	0.864		0.000*	0.734

According to the results of data analysis (Table 5), several factors were shown to play a role in cognitive function, i.e. age, level of education, and plasma homocysteine level. The results of the multiple linear regression analysis indicated that MMSE is affected by level of education and age, whilst homocysteine level did not influence MMSE score in males as well as in females.

Table 6 presents MMSE scores for the sub-items of temporal orientation, registration, attention and calculation, recall, and language, both in females and in males at several plasma homocysteine levels. Only female MMSE scores for attention and calculation and for language show a significant difference (p=0.041 and p=0.024).

DISCUSSION

In the present study homocysteine levels in females were lower compared with those in males, with means of 13.50 ± 3.69 μmol/L and 18.96 ± 7.56 μmol/L, respectively. Homocysteine levels showed a significant difference between females and males with p=0.000, therefore data analysis was done based on gender. The study conducted by Haan[4] showed comparable results, where mean homocysteine level in females (10.07 ± 4.13) was significantly different from that in males (11.80 ± 8.76), with the age of the subjects in the range of 60-80 years. In contrast, the study by Seshasdri[7] found no difference in homocysteine levels between females and males, the subjects being in the age range of 60 – 94 years.

Table 5. Factors affecting MMSE score

Factor	Females		Males	
	β	p	β	p
l of education	0.603	0.000*	0.388	0.006*
	-0.269	0.034*	0.314	0.030*
Homocysteine	0.070	0.525	-0.233	0.086

Table 6. MMSE scores category at several plasma homocysteine levels in females and males

Homocysteine level (μmol/L)	Temporal orientation	Registration	Attention and calculation	Recall	Language
Female					
<11.7	8.4 ± 1.4	3.0 ± 0.0	4.2 ± 0.7	3.0 ± 0.0	6.6 ± 1.3
11.7-14.6	8.3 ± 2.1	2.7 ± 0.7	3.1 ± 0.3	2.9 ± 0.3	6.1 ± 0.8
>14.6	7.7 ± 2.7	2.7 ± 0.8	2.5 ± 0.6	2.7 ± 0.8	4.0 ± 0.3
p	0.412	0.240	0.041*	0.102	0.024*
Males					
<11.7	9.8 ± 0.5	3.0 ± 0.0	4.5 ± 0.9	3.0 ± 0.0	8.0 ± 0.7
11.7-14.6	9.4 ± 0.8	3.0 ± 0.0	4.6 ± 0.8	3.0 ± 0.0	5.6 ± 0.8
>14.6	8.9 ± 1.7	2.8 ± 0.7	3.8 ± 0.9	2.8 ± 0.7	6.7 ± 0.4
P	0.125	0.344	0.181	0.344	0.426

Homocysteine is a sulfur-containing amino acid closely associated with the metabolism of methionine and cysteine. There is no DNA that codes for homocysteine synthesis. Homocysteine is not synthesized in nature but results from the metabolism of the amino acid methionine through a methylation cycle as a unique source of homocysteine. Methionine is obtained through intake of protein in the daily diet.[20,21]

Homocysteine occurs in several forms in plasma. The sulfhydryl or reduced form is designated homocysteine and the disulfide or oxidized form is designated homocystine. The disulfide form may occur together with cysteine and with proteins having reactive cysteine residues (protein-bound homocysteine), and this form is called mixed disulfide. The oxidized forms account for most of the homocysteine in plasma (98-99%), whilst the reduced forms make up only 1% of total homocysteine. Total homocysteine (tHcy) is the sum of all homocysteine forms present in plasma.[20,21]

Homocysteine is converted by the enzyme cystathionine β synthase (CBS) into cysteine with vitamin B6 as cofactor, in a process called demethylation. In the reverse process of remethylation, homocysteine is reconverted into methionine by the enzymes methylene tetrahydrofolate (MTHFR) and methionine synthase (MS), with folic acid, and vitamin B12 as substrates and cofactors. Thus a deficiency of one of these vitamins leads to hyperhomocysteinemia.[21-23]

Under normal conditions blood homocysteine levels are relatively low, ranging from 5-15 μmol/L. The homocysteine level in the extracellular compartment is determined by its intracellular synthesis, metabolism and excretion. If intracellular homocysteine synthesis exceeds the metabolic capacity, homocysteine is released into the extracellular compartment; in contrast, decreased synthesis leads to a fall in release of homocysteine from the cell. This mechanism maintains intracellular homocysteine at a low level. The homocysteine equilibrium may be upset by abnormal enzyme activity or as a result of a reduction in the number of cofactors that play a role in its metabolism.[22,24]

In Table 2 homocysteine levels were subdivided into several categories, i.e. <11.7 μmol/L, 11.7-14.6 μmol/L and >14.6 μmol/L. This was based on the results of a study conducted by Quadri[15] with the objective of finding a reference value for hyperhomocysteinemia, as currently there are no standard criteria for defining hyperhomocysteinemia. A number of investigators have used variable values for hyperhomo-

cysteinemia, e.g. Ravaglia[9] used a homocysteine level of >15 μmol/L, whilst Seshasdri[7] and Dufouil[2] used levels of >14 mol/L and >15 μmol/L, respectively.

In the present study, homocysteine levels over 14.6 μmol/L were found in a large proportion of males (32 subjects or 66%) with a mean level of 22.06 ± 7.25, but only in 10 females (22.70%). In comparison, in the study by Quadri[15] homocysteine levels of >14.6 μmol/L were found in 51.85% of subjects with vascular dementia and in 56.36% of control subjects. Mean homocysteine level was 14.6 ± 6.1 μmol/L in control subjects with mean age of 75.6 ± 8.5 years, whereas subjects with vascular dementia with mean age of 80.5 ± 5.7 years had a mean homocysteine level of 18.9 ± 7.9 μmol/L and those with Alzheimer's disease and mean age of 79.1 ± 7.7 years showed a homocysteine level of 16.8 ± 7.0 μmol/L. In contrast, the present study with a lower mean age showed a higher mean homocysteine level in males that was almost equal to the mean homocysteine level in patients with vascular dementia, although the study subjects had signs of mild cognitive impairment only.

The mean MMSE score in male subjects in the present study was 25.11 ± 5.03, indicating that they had mild cognitive impairment, whereas in Quadri's study the mean MMSE score in vascular dementia was 18.6 ± 5.6, and in Alzheimer's disease 18.6 ± 5.1, signifying moderate cognitive impairment. The mean MMSE score in females was 23.18 ± 6.4, indicating mild cognitive impairment. According to several studies, the contribution of sex is controversial with regard to the risk of cognitive impairment. However, the results obtained by Huadong et al indicate that the incidence of cognitive impairment was 10.7% in men and 13.2% in women and that there was a significant association of sex and cognitive impairment.[30]

In the present study assessment of homocysteine levels was performed after the subjects had fasted for a minimum of 12 hours. Measurement of homocysteine on non-fasting subjects results in an increase in homocysteine levels of around 20% compared with those in fasting subjects. Comparison of MMSE scores in the three categories of plasma homocysteine levels (Table 3) indicated that MMSE scores in females were also lower than those in males for each category of plasma homocysteine level. Higher homocysteine levels were associated with lower MMSE scores in both female and males, with p=0.000 and p=0.008, respectively. This indicates that homocysteine level may presumably affect cognitive function.

Seshasdri's study[7] revealed a tendency for increased plasma homocysteine levels to precede the onset of dementia. Therefore it is probable that the increased homocysteine levels in the present study mark the early stages of a developing dementia, although the MMSE scores were categorized as mild cognitive impairment only.

In general, level of education can be said to affect cognitive function. According to the results of the present study cognitive function in elderly females and males was affected by level of education but not by plasma homocysteine levels. These results were similar with those of Huadong's study, where level of education was associated with cognitive function.[30]

Besides level of education, age may also affect MMSE scores and homocysteine levels. Tabel 4 shows that older subjects, both females and males, tended to have higher homocysteine levels, although these levels showed a significant difference in males only. MMSE scores showed no significant difference between age groups, both in females with p=0.864 as well as in males with p=0.734.

Multiple linear regression analysis revealed that the influencing factors on MMSE scores were level of education and age, whilst homocysteine levels were not significantly different in females and in males. This is consistent with the results of the study by Joosten[25] where no significant correlation was found between homocysteine levels and cognitive function. In the present study mean homocysteine level in males was >14.9 μmol/L but the decline in cognitive function was only slight. The study conducted by Bell[26] indicated that in normal subjects there was no significant correlation between plasma homocysteine level and MMSE score. A correlation was found only in subjects with depression. Borroni[27] and Miller[28] concluded from the results of their respective cross-sectional studies that raised plasma homocysteine concentration was not a causative factor in dementia and Alzheimer's disease, but was only a marker for concomitant vascular disease, independently of cognitive status. Their results are contrary to those of Seshasdri[7] where a correlation was found between increased plasma homocysteine levels and decreased MMSE scores, but the correlation was found only after 4 years of follow-up. Thus only long-term intervention trials can yield definitive evidence for a causal relation between hyperhomocysteinemia and cognitive impairment.

As already stated above, in the multiple linear regression analysis the factors affecting MMSE scores were found to be level of education and age. MMSE score was proportional to level of education, indicating better cognitive function in the better educated. Several investigators used subjects with a similar educational background to find a correlation between homocysteine levels and MMSE scores. The study by Ravaglia[9] indicates that in subjects with a similar educational background hyperhomocysteinemia was an independent predictor for the occurrence of dementia or Alzheimer disease. In the present study, arrangement of the homocysteine levels into the categories <11.7 μmol/L, 11.7-14.6 μmol/L and >14.6 μmol/L revealed a significant difference in MMSE scores. Thus although with the correlation regression analysis no significant correlation was to be found between homocysteine levels and MMSE scores, after categorization homocysteine levels appeared to also affect MMSE scores.

When the MMSE scores were categorized by component or sub-item, it became apparent that in female and male subjects the sub-items "attention and calculation" and "language" lead to the conclusion that homocysteine levels were inversely related to MMSE scores. The study by Levitt[29] showed similar results in that the significant MMSE scores were in the "attention and calculation" category. The associations between homocysteine and cognitive function in community-dwelling elderly are nonsignificant, whereas demographic variables, particularly age and education, were found to be much stronger determinants of cognitive function scores.

CONCLUSION

Although there is suggestive evidence that plasma homocysteine levels and MMSE are inversely associated, the most important factors affecting MMSE score are education and age. Therefore an interventional study is called for to provide definite data to ascertain the relationship between homocysteine levels and MMSE.

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