Cross-sectional association between homocysteine and motor function in the elderly

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Abstract—*Objective:* To determine if there is a cross-sectional association between homocysteine (tHcy) level and measures of gait and balance in elderly subjects. *Methods:* We studied 3,609 noninstitutionalized subjects aged 65 to 85 years from the Dijon (France) center of the Three-City Study. tHcy concentration was measured from fasting blood samples. Motor function was assessed by measuring walking speed and by using a modified version of the Tinetti scale. *Results:* After adjustment for confounders, mean maximum walking speed (MWS) decreased with increasing tHcy levels ($p = 0.001$). The odds ratio (OR) (95% CI) for having a MWS below the 40th percentile was 1.9 (1.4 to 2.5) in subjects with tHcy levels in the upper quintile compared with those in the lowest quintile. Compared with subjects in the lowest tHcy quintile, the OR for having a modified Tinetti score below 16 ranged from 1.0 (0.8 to 1.4) in the second quintile to 1.9 (1.3 to 2.6) in the upper quintile ($p < 0.0001$). *Conclusions:* Elevated homocysteine concentrations are associated with worse motor performances in the elderly. These findings support the hypothesis of a vascular contribution to motor function.

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Elevated plasma total homocysteine (tHcy) concentrations increase the risk of cardiovascular disease,[1] cognitive decline,[2] and white matter hyperintensities (WMHs) seen on brain MRI.[3,4]

A vascular contribution to motor dysfunction in elderly individuals has been suggested,[5] and WMHs may play a role in this relation.[6] Although elevated tHcy concentrations are a cardio- and cerebrovascular risk factor, to our knowledge, only one study has examined the role of this amino acid in gait and balance impairment. In this study of 499 highly functioning subjects aged 70 to 79 years, there was a significant association between increased tHcy level and the risk of being in the worst quartile of decline in physical function.[7]

We conducted a cross-sectional study of the relation between tHcy concentration and measures of gait and balance, as part of the baseline phase of the Three-City (3C) Study in Dijon (France).[8]

Additional material related to this article can be found on the *Neurology* Web site. Go to www.neurology.org and scroll down the Table of Contents for the September 26 issue to find the title link for this article.

Methods. The 3C Study is a multicenter cohort study, conducted in three French cities (Bordeaux, Dijon, and Montpellier) and designed to estimate the risk of dementia and cognitive impairment attributable to vascular factors. Between March 1999 and March 2001, noninstitutionalized individuals aged 65 or over were selected from electoral rolls. The detailed description of the study protocol has been published elsewhere.[8] In addition to the main objective of the study, a specific substudy on the role of vascular risk factors in motor function was conducted in Dijon. The study protocol was approved by the Ethical Committee of the University Hospital of Kremlin–Bicêtre. Each participant signed an informed consent.

tHcy and other biologic markers. Fasting plasma (tHcy) or serum (folate, B_{12}) samples were obtained at study baseline, immediately centrifuged, and stored at −80 °C. tHcy, vitamin B_{12}, and folate concentrations were determined using an automated chemiluminescence immunoassay (ADVIA Centaur; Bayer).

Gait and balance assessment. Subjects aged 85 or younger visited the study center where we conducted two tests to assess gait and balance. First, to measure walking speed, two photoelectric cells connected to a chronometer were placed in a corridor 6 m apart, and subjects were timed as they walked this distance at their usual and maximum speed. Walking speed was the ratio between distance and time; because our analyses of the relation between tHcy and usual walking speed or maximum walking speed (MWS) yielded similar results, we will present only those based on MWS. Second, a simplified version of the Performance-Oriented Assessment of Mobility Instrument (Tinetti scale) was used. The Tinetti scale is an index of gait and balance function that grades features such as stride, step continuity, symmetry, path deviation, and balance on standing.[9,10] Whereas the original

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scale has 20 items, our version included 13 items (maximum score = 18). As part of this study, the complete version of the Tinetti scale was assessed in a sample of 100 randomly selected subjects (50 men and 50 women). The correlation between the complete and the shortened versions of the scale was high (Spearman correlation coefficient = 0.95, $p < 0.0001$).

Other measurements. Sociodemographics and medical data were collected at home during an interview by trained psychologists. Participants were asked to report a history of hypercholesterolemia, Parkinson disease (PD), hip fracture (in the previous 2 years), fall (in the previous year), myocardial infarction, stroke, angina, bypass cardiac surgery, angioplasty, peripheral vascular disease, diabetes mellitus, and osteoporosis. Ischemic heart disease (IHD) was defined by a history of myocardial infarction, bypass cardiac surgery, or angioplasty. Systolic (SBP) and diastolic (DBP) blood pressures were measured, and subjects were classified as hypertensive if using antihypertensive medication or if SBP $\geq$ 160 mm Hg or DBP $\geq$ 95 mm Hg. Subjects were classified as never, former, and current smokers. Frequency of weekly alcohol consumption was assessed. Anthropometric measures (weight, height, waist ratio) were taken. Information on use of psychotropic drugs (antidepressant, anxiolytics, benzodiazepines, hypnotics), nonsteroidal anti-inflammatory drugs (NSAIDs) for joint pain, and drugs containing folate or vitamin B_{12} were also collected.

Depressive symptoms were appraised using the Center for Epidemiologic Studies Depression Scale (CES-D). Participants underwent cognitive testing using a battery of tests (including the Mini-Mental State Examination [MMSE]; total score, 0 to 30) and were screened for dementia.[8] A standardized clinical protocol was used to diagnose prevalent cases of dementia in subjects who screened positive. The diagnosis and classification of dementia cases were made by the 3C Study local investigators according to Diagnostic and Statistical Manual for Mental Disorders (4th ed.) criteria. Dementia cases were validated by a panel of expert neurologists independently of the 3C Study investigators.[8]

Statistical analysis. We excluded from our analyses subjects with conditions that strongly affected motor function (PD, dementia, hip fracture in the previous 2 years, disabling stroke, IHD, peripheral vascular disease). Analysis of covariance and logistic regression were used to study the relation between tHcy and MWS or the modified Tinetti scale. Because tHcy and MWS were not normally distributed, logarithmic transformations of these variables were used in analysis of covariance. Inverse transformations were performed to compute geometric means and their 95% CI.

In logistic models, MWS and the modified Tinetti scale were considered as the dependent variables. Because the choice of the cut-off used to categorize MWS was arbitrary, we first used multinomial regression with canonical link function to analyze the association between tHcy and MWS. MWS was considered as the dependent variable categorized in quintiles (the reference being the highest quintile, i.e., subjects with the highest walking speed) and tHcy was the independent variable. Each response category (probability of having a MWS in the first, second, third, or fourth quintile of MWS) was contrasted against the reference category. We observed that the ORs associated with tHcy were similar (and significantly different from 1.0) in the two lowest MWS quintiles, whereas subjects in the third and fourth quintiles had ORs not significantly different from 1.0 (data not shown). We therefore categorized MWS at the 40th percentile and compared subjects in the lowest two quintiles with subjects in the three highest quintiles of MWS. The modified Tinetti scale was categorized at the 25th percentile. In each model, tHcy was the independent variable and was introduced as a continuous variable or as an ordinal variable defined by the quintiles of its distribution. Because the main variables of interest (tHcy, MWS, modified Tinetti scale) were strongly associated with age, sex, and education level, all analyses were adjusted for these confounders.

Analysis of covariance and logistic regression were also used to study the relation between other potential covariates and tHcy, walking speed, or the modified Tinetti scale. We finally performed multivariate analyses using analysis of covariance or logistic regression. The variables included in the model were those that were associated with either tHcy level or MWS (or the modified Tinetti score) with a p value of 0.05 or less in univariate analyses or those that had biologic plausibility according to current knowledge.

All analyses were performed using SAS (SAS version 9.0 for Windows; SAS Institute, Cary, NC).

Results. Of 4,399 participants aged 85 or younger, 4,063 had complete data on tHcy and on at least one of the two motor tests. Subjects who had no data for tHcy or both motor tests were older, were more often depressed, and had a lower triglycerides level than those who had complete data; there were no differences for other variables (data not shown). We excluded from the analyses 454 subjects with one or more conditions that strongly affected motor function (PD, n = 47; peripheral vascular disease, n = 132; disabling stroke, n = 36; hip fracture, n = 11; dementia, n = 33; IHD, n = 246). The remaining 3,609 persons constituted the baseline study sample (3,285 measures were available for MWS and 3,283 for the modified Tinetti scale).

The main characteristics of the study participants are shown in table E-1 on the *Neurology* Web site (www.neurology.org). The relations between tHcy and the subjects' characteristics are shown in table 1; the corresponding regression coefficients are presented in table E-2. Male gender, increasing age, decreasing education level, lower vitamin B_{12} and folate levels, current smoking, alcohol drinking, increasing creatinine and glycemia levels, increasing waist ratio, hypertension, and hypercholesterolemia were associated with increased mean tHcy levels. Neither MMSE score nor depressive symptoms, diabetes mellitus, osteoporosis, triglycerides, NSAIDs, nor psychotropic use was associated with tHcy. Among these covariates, female gender, increasing age, lower education level, increasing folate, creatinine, glycemia, and triglyceride concentrations, alcohol drinking, increasing waist ratio, decreasing MMSE score, depressive symptoms, hypertension, diabetes mellitus, and NSAID or psychotropic use were associated with a lower mean MWS. No statistical association was found between cigarette smoking, hypercholesterolemia, osteoporosis, cholesterol or vitamin B_{12} levels, and MWS. Similar results were found for the modified Tinetti scale (data not shown), except that hypercholesterolemia and higher creatinine level reduced the risk of having a lower modified Tinetti score.

In linear regression analysis adjusted for age, sex, and education level, mean MWS decreased with increasing tHcy concentration ($p = 0.0002$; table 2). Logistic regression analysis showed that the OR for having a MWS lower than the 40th percentile of its distribution increased with tHcy quintiles (table 3; $p < 0.0001$); the OR for an increase of 1 SD in tHcy was of 1.2 (95% CI = 1.1 to 1.3; $p < 0.0001$). Similar results were found when MWS was dichotomized according to the first quintile of its distribution (data not shown).

We then performed multivariate analyses with adjustment for variables found to be associated with tHcy or MWS (table 1) and found similar results both in linear ($p = 0.001$; table 2) and logistic (table 3; OR for an increase of 1 SD in tHcy = 1.2; 95% CI = 1.1 to 1.4; $p < 0.0001$) regression models.

Table 3 shows that there was an association between tHcy quintiles and lower scores for the modified Tinetti scale ($p < 0.0001$). Additional adjustment for variables found to be associated with tHcy or modified Tinetti score did not alter the results (table 3; $p < 0.0001$). When tHcy was considered as a continuous variable, each SD increase

Table 1 *Relation between selected characteristics and homocysteine or maximum walking speed*

Characteristics		Homocysteine, μmol/L			Maximum walking speed, m/s		
		n	Mean (95% CI)	p*	n	Mean (95% CI)	p*
Sex	Male	1,278	14.9 (14.7–15.2)		1,169	1.67 (1.65–1.69)	
	Female	2,331	13.6 (13.4–13.7)	$<10^{-4}$	2,116	1.42 (1.41–1.43)	$<10^{-4}$
Age, y‡	<73	1,685	13.4 (13.2–13.6)		1,573	1.58 (1.57–1.60)	
	≥73	1,924	14.6 (14.4–14.8)	$<10^{-4}$	1,712	1.43 (1.42–1.44)	$<10^{-4}$
Education level	Low	734	14.5 (14.2–14.8)		658	1.44 (1.41–1.46)	
	Medium low	1,587	14.1 (13.9–14.3)		1,445	1.46 (1.44–1.48)	
	Medium high	690	14.0 (13.6–14.3)		633	1.55 (1.53–1.57)	
	High	596	13.4 (13.1–13.8)	$<10^{-4}$	547	1.65 (1.63–1.68)	$<10^{-4}$
Alcohol consumption,	0	760	13.6 (13.3–13.9)		689	1.43 (1.41–1.45)	
drinks/wk	<13	1,766	13.9 (13.7–14.1)		1,605	1.48 (1.46–1.49)	
	≥13	904	14.8 (14.5–15.1)	0.02	823	1.60 (1.58–1.62)	0.02
Cigarette smoking	Never	2,308	13.6 (13.5–13.8)	—	2,103	1.46 (1.44–1.47)	—
	Ex	1,119	14.7 (14.4–15.0)	0.01	1,016	1.60 (1.58–1.61)	0.98
	Current	182	15.1 (14.4–15.8)	0.0009	166	1.56 (1.56–1.61)	0.74
CES-D score	<threshold†	3,122	14.0 (13.9–14.2)		2,845	1.52 (1.51–1.53)	
	≥threshold	454	14.1 (13.7–14.6)	0.66	410	1.41 (1.38–1.44)	$<10^{-4}$
MMSE score‡	<28	1,508	14.2 (14.0–14.5)		1,354	1.45 (1.44–1.47)	
	≥28	2,097	13.9 (13.7–14.1)	0.15	1,927	1.54 (1.53–1.55)	$<10^{-4}$
Hypertension	No	1,352	13.3 (13.1–13.5)		1,252	1.55 (1.53–1.57)	
	Yes	2,257	14.5 (14.3–14.7)	$<10^{-4}$	2,033	1.47 (1.46–1.49)	$<10^{-4}$
Hypercholesterolemia	No	1,501	13.5 (13.3–13.7)		1,356	1.54 (1.52–1.55)	
	Yes	2,106	14.4 (14.2–14.6)	$<10^{-4}$	1,927	1.48 (1.47–1.49)	0.48
Diabetes mellitus	No	3,334	14.0 (13.8–14.1)		3,044	1.51 (1.49–1.52)	
	Yes	250	14.5 (13.9–15.1)	0.35	221	1.46 (1.42–1.50)	0.001
Osteoporosis	No	2,702	14.1 (14.0–14.3)		2,447	1.53 (1.52–1.54)	
	Yes	738	13.5 (13.2–13.8)	0.56	684	1.43 (1.41–1.45)	0.44
Regular NSAID use	No	3,016	14.0 (13.9–14.2)		2,758	1.52 (1.51–1.54)	
	Yes	553	14.1 (13.8–14.5)	0.28	490	1.39 (1.36–1.41)	$<10^{-4}$
Psychotropic drugs use	No	2,696	14.0 (13.8–14.1)		2,454	1.54 (1.53–1.55)	
	Yes	913	14.2 (13.9–14.5)	0.10	831	1.40 (1.38–1.42)	$<10^{-4}$
Vitamin B_{12}, pg/mL‡§	<367	1,792	14.8 (14.5–15.0)		1,633	1.51 (1.49–1.52)	
	≥367	1,808	13.3 (13.1–13.5)	$<10^{-4}$	1,645	1.50 (1.49–1.51)	0.76
Folate, ng/mL‡§	<7.6	1,626	15.4 (15.2–15.6)		1,472	1.49 (1.48–1.51)	
	≥7.6	1,697	12.9 (12.7–13.0)	$<10^{-4}$	1,544	1.51 (1.49–1.52)	0.0008
Creatinine, μmol/L‡	<80	1,742	12.9 (12.7–13.0)		1,579	1.44 (1.42–1.45)	
	≥80	1,863	15.2 (15.0–15.5)	$<10^{-4}$	1,702	1.57 (1.55–1.58)	0.02
Total cholesterol, mmol/L‡‖	<5.80	1,800	14.4 (14.1–14.6)		1,643	1.52 (1.50–1.53)	
	≥5.80	1,806	13.7 (13.5–13.9)	0.30	1,639	1.49 (1.47–1.50)	0.84
Triglycerides, mmol/L‡‖	<1.07	1,778	13.9 (13.7–14.2)		1,648	1.52 (1.51–1.54)	
	≥1.07	1,825	14.1 (13.9–14.3)	0.70	1,632	1.48 (1.47–1.50)	$<10^{-4}$
Glycemia, mmol/L‡¶	<4.93	1,771	13.7 (13.5–13.9)		1,624	1.50 (1.49–1.52)	
	≥4.93	1,829	14.4 (14.1–14.6)	0.22	1,652	1.51 (1.49–1.52)	0.0006
Waist ratio, cm‡	<87.0	1,733	13.3 (13.1–13.5)		1,605	1.51 (1.49–1.52)	
	≥87.0	1,800	14.7 (14.5–14.9)	$<10^{-4}$	1,617	1.50 (1.49–1.52)	$<10^{-4}$

* Adjustment for age, sex, and education level.
† CES-D sex-specific threshold equals 17 in men and 23 in women.
‡ Continuous variables were categorized using the median of their distribution as a cut-off for an easier presentation of the results. The corresponding p values are computed by introducing the continuous variables in the regression models; standardized regression coefficients are presented in table E-2.
§ Adjustment for use of vitamin B supplements.
‖ Adjustment for use of lipid-lowering drugs.
¶ Adjustment for use of antidiabetic drugs.

CES-D = Center for Epidemiologic Studies Depression Scale; MMSE = Mini-Mental State Examination; NSAID = nonsteroidal anti-inflammatory drug.

in tHcy level was associated with a higher odds of having a modified Tinetti score below 16 in multivariate analysis (OR = 1.2, 95% CI = 1.1 to 1.2; $p = 0.007$).

In sensitivity analyses, we excluded 1,132 subjects who reported a history of osteoporosis or declared to regularly take NSAIDs for joint pain, and we found similar results. For MWS, the standardized regression coefficient (SE) for tHcy in the multivariate regression model was −0.058 (0.021) ($p = 0.007$). For the modified Tinetti score, each SD increase in tHcy level remained associated with a higher

Table 2 *Relation between total homocysteine (tHcy) level and maximum walking speed (MWS) (analysis of covariance)*

tHcy, μmol/L *	n	Mean MWS (95% CI), m/s	β (SE)†	*p*†	β (SE)‡	*p*‡
<11.0	648	1.53 (1.51–1.56)	Ref.	—	Ref.	—
11.0–12.9	657	1.50 (1.47–1.52)	−0.009 (0.004)	0.04	−0.011 (0.004)	0.005
13.0–14.7	658	1.51 (1.48–1.53)	−0.009 (0.004)	0.03	−0.010 (0.004)	0.02
14.8–17.8	665	1.51 (1.48–1.53)	−0.015 (0.004)	0.0006	−0.015 (0.004)	0.0003
≥17.9	657	1.47 (1.45–1.50)	−0.016 (0.004)	0.0005	−0.016 (0.005)	0.0009
			p for trend	0.0002	*p* for trend	0.001
Continuous tHcy§			−0.055 (0.015)	0.0003	−0.056 (0.018)	0.001

* Quintiles.

† Regression coefficients and SEs adjusted for age, sex, and education level.

‡ Regression coefficients and SEs adjusted for age, sex, education level, waist ratio, Mini-Mental State Examination score, Center for Epidemiologic Studies Depression Scale score, hypertension, osteoporosis, creatinine level, total cholesterol level, triglyceride level, glycemia, vitamin B_{12} level, folate level, alcohol and tobacco consumption, use of vitamin B supplements or nonsteroidal anti-inflammatory drugs, and use of psychotropic, lipid lowering or antidiabetic drugs.

§ For tHcy as a continuous variable, we present standardized regression coefficients.

odds of being in the lowest quartile (OR = 1.1, 95% CI = 1.0 to 1.3; $p = 0.03$).

Discussion. In subjects aged 65 to 85 years, we found a relation between increasing tHcy levels and poorer performances on two tests of gait and balance. This relation was independent of age, sex, education level, and other covariates, including waist ratio, hypertension, osteoporosis, alcohol and tobacco consumption, cognitive function, depressive symptoms, regular NSAIDs use for joint pain, vitamin B supplements or psychotropic drug use, and biologic variables such as vitamin B_{12}, folate, creatinine, and triglycerides. These findings are consistent with those from the MacArthur Study of Successful Aging; among 499 individuals ages 70 to 79 years at baseline, those with tHcy levels in the higher quartile of the distribution (13.38 to 40.00 μmol/L) had a 4.1-fold higher risk of being in the worst quartile of decline in physical function (assessed using several physical performance tests, including walking speed over a distance of 3 m) compared with those with tHcy in the first quartile (3.93 to 8.86 μmol/L).[7]

The strengths of our study include its large size, an automated measure of walking speed that is considered to be a good predictor of functional dependence in the elderly,[11,12] the use of performance-based tests that are more reliable than self-reports, the centralized measurement of tHcy and vitamins B_{12} and folate, and the assessment of numerous potential confounders, including cognitive function and depression. Several studies, including ours, have shown that poorer cognitive function and depression are associated with poorer motor function.[13,14] There is also evidence that poorer cognitive function and depression are associated with higher tHcy levels.[15,16] However, in our study, after the exclusion of subjects with conditions that strongly affected motor function, cognitive function and depressive symptoms were not strongly related to tHcy, and adjustment for MMSE and CES-D scores did not affect the relation between tHcy and tests of motor function.

The main limitation of our study is its cross-sectional nature that prevents us from assessing the temporal relation between tHcy increase and motor impairment; follow-up of the cohort will allow us to address this issue. In addition, subjects who partici-

Table 3 *Relation between total homocysteine (tHcy) level, maximum walking speed (MWS), and the modified Tinetti scale (logistic regression)*

	MWS < 40th percentile*			Tinetti score in lowest quartile*		
tHcy, μmol/L†	%	OR (95% CI)‡	OR (95% CI)§	%	OR (95% CI)‡	OR (95% CI)§
<11.0	16.7	1.0 (ref.)	1.0 (ref.)	15.4	1.0 (ref.)	1.0 (ref.)
11.0–12.9	20.8	1.4 (1.1–1.8)	1.5 (1.1–1.9)	17.0	1.0 (0.7–1.3)	1.0 (0.8–1.4)
13.0–14.7	19.4	1.3 (1.0–1.7)	1.3 (1.0–1.7)	20.0	1.2 (0.9–1.6)	1.3 (1.0–1.7)
14.8–17.8	19.7	1.6 (1.2–2.0)	1.6 (1.2–2.1)	21.2	1.4 (1.0–1.8)	1.5 (1.1–2.0)
≥17.9	23.4	1.8 (1.4–2.3)	1.9 (1.4–2.5)	26.4	1.6 (1.2–2.1)	1.9 (1.3–2.6)
p for trend		< 0.0001	0.0002		<0.0001	<0.0001

* The 40th percentile of the MWS distribution = 1.50 m/s; 25th percentile of the Tinetti score distribution = 16.

† Quintiles.

‡ Adjustment for age, sex, and education level.

§ Adjustment for age, sex, education level, waist ratio, Mini-Mental State Examination score, Center for Epidemiologic Studies Depression Scale score, hypertension, osteoporosis, creatinine level, total cholesterol level, triglyceride level, glycemia, vitamin B_{12} level, folate level, alcohol and tobacco consumption, use of vitamin B supplements or nonsteroidal anti-inflammatory drugs, and use of psychotropic, lipid-lowering, or antidiabetic drugs.

pated in the study were probably different from the French general population in terms of sociodemographic and medical characteristics. However, most of the associations described in the literature between tHcy or gait and balance measures and other characteristics were found in our study, thus suggesting that the selection of the study population did not lead to important bias. Another potential limitation is that our analyses are based on a single tHcy measurement, which may have underestimated the relation between tHcy and motor impairment; indeed, a study of the within-individual variations of tHcy in elderly subjects has shown that a single measure is likely to underestimate the strength of any risk association by 10 to 15% because of regression dilution.[17]

There are several possible hypotheses to explain the link between tHcy and tests of gait and balance. Some studies have suggested that high tHcy concentrations have a direct vascular effect on the brain, involving increased risk of arteriosclerosis.[18,19] This mechanism could explain why elevated tHcy levels have been associated with a higher frequency of WMHs in some studies.[3] In addition, previous studies have reported an association between WMHs and gait and balance dysfunction.[6,20-22] A direct neurotoxic effect of tHcy may contribute to explaining why tHcy is harmful to the brain: Increasing tHcy levels could elicit neuronal apoptosis[23] or activation of the *N*-methyl-D-aspartate receptor.[24] Alternative hypotheses can be formulated. For instance, tHcy levels could be associated with motor impairment through osteoporotic fractures; it has been suggested that higher tHcy levels are associated with an increased risk of osteoporotic fractures, and fractures are associated with a greater decline in physical performances.[25,26] We did not measure bone density in our study, but we excluded subjects who had a hip fracture in the previous 2 years and who were likely to be at higher risk of osteoporosis. Another mechanism could involve inflammatory markers, such as interleukin-6, that are related to tHcy[27] and to physical decline[28]; however, this hypothesis should be taken with caution, because the tHcy concentrations used in these experiments were higher than the physiologic ones. To better understand the mechanisms involved in the relation between tHcy and motor function, we plan to explore the association between motor tests, tHcy, and brain characteristics seen on MRI (WHMs, brain volumes). MRI scans were obtained for approximately 40% of the participants at baseline and are currently being analyzed using an automated method of image analysis.

The potential severe consequences of motor dysfunction point out the importance of the identification of modifiable risk factors in epidemiologic studies. Our findings suggest that elevated tHcy levels are associated with poorer performances on tests of gait and balance. If confirmed by prospective studies and in other populations, they support the idea that cerebrovascular risk factors, such as tHcy, play a role in motor function in the elderly.

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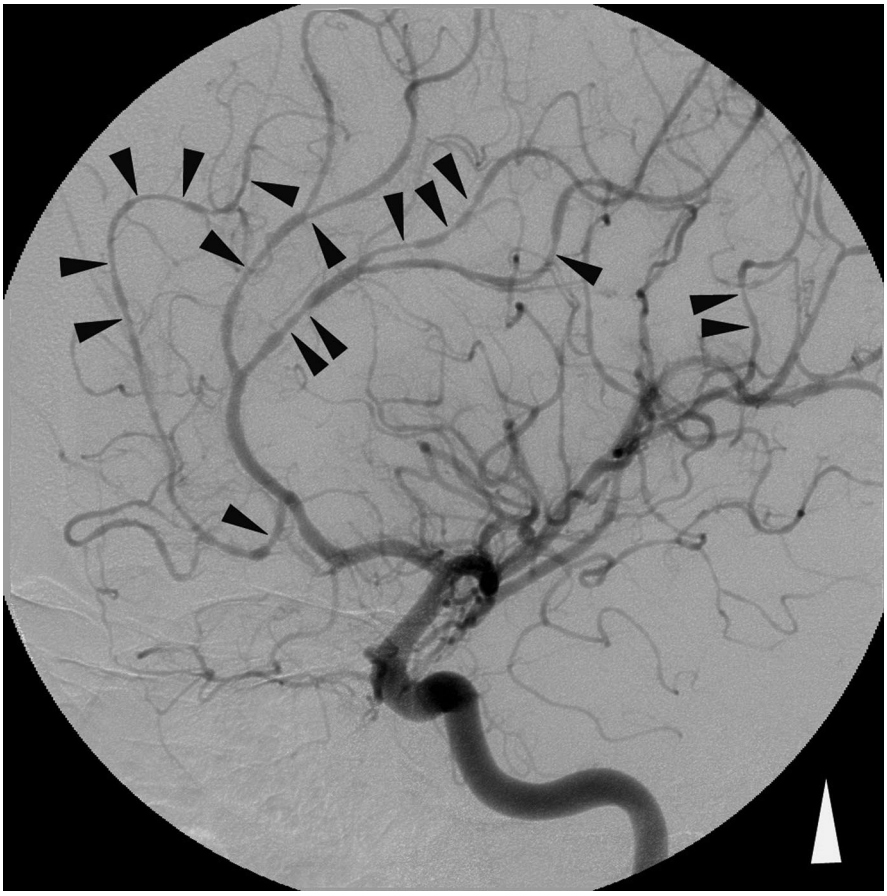

Figure. Conventional angiography demonstrating diffuse multifocal segmental vasoconstriction in anterior and middle cerebral artery.

Cerebral vasospasm in idiopathic thunderclap headache

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A 23-year-old man without medical history or substance abuse reported five attacks of diffuse throbbing severe headache within a 3-day period, each one lasting 20 minutes with acute onset during sexual intercourse.

Neurologic examination, CT, MRI, and CSF analysis revealed no abnormalities. In search of aneurysm, five days after onset of headache, angiography was performed which showed diffuse multifocal segmental cerebral vasoconstriction in second and third order branches of the circle of Willis (in anterior, middle, and posterior cerebral artery, but not in the circle of Willis itself) in absence of aneurysm (figure).

This angiographic pattern (with or without involving the circle of Willis) can be seen in idiopathic (i.e., in absence of subarachnoid hemorrhage) thunderclap headache.[1,2] This distribution of vasospasm is in contrast with that seen in isolated CNS vasculitis in which vasospasm are invariably restricted to distal arteries of less than 0.5 mm in diameter. Thunderclap headache with or without vasospasm is often precipitated by sexual activity, intensive exertion, Valsalva maneuver, acute hypertensive crisis, or ingestion of sympathomimetic drugs. This suggests the possibility of excessive sympathetic activity in thunderclap headache. The circle of Willis and proximal portions of cerebral branches are pain-sensitive structures, which may explain headache accompanying vasospasm involving these vessels.

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