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Stroke Risk Predicts Verbal Fluency Decline in Healthy Older Men: Evidence From the Normative Aging Study

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Risk factors for stroke cause ischemic changes in the cerebral white matter that may affect frontal lobe functions more than other brain functions. Therefore, stroke risk could specifically affect performance on behavioral indexes traditionally associated with frontal lobe function such as verbal fluency. The authors examined this hypothesis in 235 healthy older men (mean age = 66.41 years) who received concurrent medical and neuropsychological examinations twice at a 3-year interval. Relations between stroke risk and decline in verbal fluency, memory, and visuospatial performance were analyzed through regression, controlling for age and education. Age was associated with decline in all cognitive functions; stroke risk was associated with decline only on verbal fluency. The relation between stroke risk and fluency decline was 80% as large as that between age and fluency decline. These results suggest that stroke risk rivals the effects of aging on verbal fluency performance.

RISK factors for stroke (e.g., age, hypertension, diabetes mellitus, cardiac disease) predispose even relatively healthy older adults to experience ischemic changes in the brain, predominantly in the periventricular white matter, basal ganglia, and pons prior to the development of frank cerebrovascular disease (CVD; e.g., McPherson & Cummings, 1997; Pantoni & Garcia, 1997; Raz, Gunning-Dixon, Head, Dupuis, & Acker, 1998). A large proportion of this white-matter pathology appears to occur in the ascending and descending pathways between the frontal cortex and the basal ganglia and brain stem, as well as in connections between frontal and other cortical regions (e.g., Chui & Willis, 1999; Goldberg & Bilder, 1987). Furthermore, it has been suggested that this white-matter pathology interrupts the integrity of frontal-subcortical circuits that are thought to be important to frontally mediated cognitive functions (Cummings, 1993; McPherson & Cummings, 1997). Therefore, stroke risk factors may have greater or specific deleterious effects on frontally mediated cognitive functions, compared with cognitive functions largely mediated by other brain regions (e.g., memory, visuospatial functions).

A commonly used behavioral index of frontally mediated cognitive function is verbal fluency. On verbal fluency tests, persons are asked to generate as many unique words as possible in a given time period (usually 1 min). For example, letter fluency requires the person to say words that begin with a particular letter (e.g., *F*), whereas category fluency requires the person to say words from a particular semantic category (e.g., animals). Evidence that verbal fluency indexes frontal lobe function comes from neuropsychological studies showing that persons with frontal lobe lesions exhibit deficits on this test to a relatively greater extent than do persons with lesions to other brain regions (e.g., Miceli, Caltagirone, Gainotti, Masullo, & Silveri, 1981; Perret, 1974; Ramier & Hécaen, 1970; see however, Joanette & Goulet, 1986; Martin, Loring, Meador, & Lee, 1990). Additionally, neuroimaging studies of healthy individuals (e.g., Frith, Friston, Liddle, & Frackowiak, 1991; Mummery, Patterson, Hodges, & Wise, 1996) have consistently demonstrated physiological activation of the frontal lobes during performance of these tests; however, several studies have also noted activation occurring in other brain regions (e.g., Frith et al., 1991; Mummery et al., 1996). Although some researchers have suggested that letter fluency is more sensitive to frontal dysfunction than is category fluency (e.g., Moscovitch, 1994), direct evidence of this has been equivocal (e.g., Baldo & Shimamura, 1998; Gourovitch et al., 2000; Mummery et al., 1996). Regardless, there is a preponderance of converging neuropsychological and neuroimaging evidence showing that performance on both letter and category fluency tests is dependent on frontal lobe function to a greater degree than on other brain functions.

There is evidence (e.g., Lafosse et al., 1997; Starkstein et al., 1996; Wolfe, Linn, Babikian, & Albert, 1990) that verbal fluency performance is disproportionately impaired relative to tests of other cognitive functions (e.g., memory) in persons with stroke-related cognitive dysfunction (e.g., vascular dementia); however, little is known about whether there is an insidious decline in verbal fluency performance prior to the onset of frank CVD as a function of increasing stroke risk. This is important to consider because such a finding would suggest that "preclinical" cognitive impairment may begin prior to the onset of CVD and, further, may suggest that a specific pattern of cognitive decline is occur-

ring. Evidence also suggests that individual stroke risk factors such as age (e.g., Boone, Miller, Lesser, Hill, & D'Elia, 1990; Whelihan, 1985; see however, Parkin & Walter, 1991) and diabetes mellitus (e.g., Knopman et al., 2001; Strachan, Ewing, Deary, & Frier, 1997) are associated with reduced verbal fluency performance. No study, however, has used multiple stroke risk factors to address the association between increasing risk and fluency performance from a multivariate perspective (see, however, Desmond, Tatemichi, Paik, & Stern, 1993, for a multivariate analysis of relations between individual stroke risk factors and other cognitive abilities).

There are, however, several studies (M. F. Elias, Elias, D'Agostino, Silbershatz, & Wolf, 1998; M. F. Elias, Elias, Robbins, Wolf, & D'Agostino, 2001; P. K. Elias, Elias, D'Agostino, & Cupples, 1997) that have examined relations between verbal fluency performance and cardiovascular risk from a multivariate perspective. Although there are some differences between the risk-factor profiles for cardiovascular disease (Wilson et al., 1998) and stroke (Wolf, D'Agostino, Belanger, & Kannel, 1991), such as the inclusion of cholesterol in the former but not the latter, the studies by Elias and colleagues used similar risk factors to those for stroke (e.g., age, hypertension, diabetes mellitus, cigarette smoking). Two of these studies (M. F. Elias et al., 2001; P. K. Elias et al., 1997) examined the association of multiple risk factors with fluency concurrently, whereas M. F. Elias and colleages (1998) used cumulative risk factors (i.e., the number of risk factors) to assess the relation between the severity of cardiovascular risk and fluency performance. Regarding this latter study, Elias and colleagues found that increasing cardiovascular risk (i.e., a greater number of risk factors) was associated with decreased verbal fluency performance, as well as decreased performance on several memory tests. Therefore, this evidence of a relation between cardiovascular risk and verbal fluency performance partially supports the possibility of a similar relation between stroke risk and verbal fluency.

These studies provide valuable information about potential relations among individual stroke risk factors and verbal fluency and suggest that increasing stroke risk may be associated with greater deficits in fluency performance. Accordingly, these results are also consistent with the suggestion, stated above, that risk factors for stroke may have greater or specific deleterious effects on frontally mediated cognitive functions compared with cognitive functions largely mediated by other brain regions.

A logical question that arises from these findings is whether people who are at greater risk for stroke exhibit a greater longitudinal decline in fluency performance relative to other cognitive functions, compared with those at lower risk; however, no longitudinal study has addressed this possibility. Therefore, the present investigation sought to examine the relation between stroke risk and decline in fluency performance by analyzing longitudinal neuropsychological and medical variables in a sample of older men participating in an ongoing study of aging. Rather than use an arbitrarily designed index of stroke risk (e.g., number of stroke risk factors), we used a risk profile from the Framingham Heart Study (Wolf et al., 1991). We were interested in whether stroke risk affected only verbal fluency performance or performance in other cognitive domains as well. We hypothesized that (a) stroke risk would be associated with decline in verbal fluency performance and (b) stroke risk would exhibit a greater relation with fluency decline than with decline in other cognitive abilities such as memory.

Methods

Sample

The Normative Aging Study (NAS) at the Department of Veterans Affairs Medical Center in Boston is an ongoing longitudinal study begun in 1963 that has collected extensive medical, psychological, and lifestyle information on a cohort of 2,280 initially healthy men. Details on the recruitment of participants into the study have been described elsewhere (Bossé, Ekerdt, & Silbert, 1984). It is important to note that all participants initially recruited into the study were optimally healthy, meaning that no participant had cardiac disease, hypertension, cataracts, loss of hearing, or abnormal laboratory tests (e.g., liver function) on entering the study.

Beginning in 1993, a battery of neuropsychological tests (see Payton, Riggs, Spiro, Weiss, & Hu, 1998; and Riggs, Spiro, Tucker, & Rush, 1996, for a description of this battery) was administered to continuing participants at each examination to assess the effects of aging and disease on cognition. The administration of several tests was subsequently discontinued to reduce respondent burden. From April 1993 through December 1997, 1,033 (87%) of 1,184 men who reported for exams were tested; of these, 321 were tested twice at a 3-year interval. We omitted 6 men who had had a previous cerebrovascular event and selected participants with complete data on the cognitive measures described below who also had received concurrent medical examinations. This yielded a sample of 235 stroke- and dementia-free men.

Procedure

Measures.—During each visit, NAS participants were given a standardized clinical exam by a board-certified internist that included a medical history, review of systems, electrocardiogram, physical and neurological exams, and chest X-ray. The presence of dementia was determined either through the clinical judgment of the internist, the person administering the neuropsychological battery, or the report of the participant's family. Laboratory tests for fasting and postchallenge (100 g) glucose levels were conducted on blood samples drawn after an overnight fast. Blood pressure was measured with the participant seated using a standard mercury sphygmomanometer with a 14-cm cuff. Systolic (SBP) and fifth-phase diastolic blood pressure (DBP) were measured to the nearest 2-mm Hg. The average of measures taken in both arms was used.

On the basis of data gathered in the first medical exam during or after 1993, stroke risk was calculated for each participant using the Framingham stroke risk profile (FSRP; Wolf et al., 1991). Wolf and colleagues developed the FSRP on a sample of 5,734 initially stroke-free individuals from

Table 1. Point Values for Each Stroke Risk Factor

Risk factor	0	1	2	3	4	5	6	7	8	9	10
Age (years)	54–56	57–59	60–62	63–65	66–68	69–71	72–74	75–77	78–80	81–83	84–86
SBP (mm Hg)	95–105	106–116	117–126	127–137	138–148	149–159	160–170	171–181	182–191	192–202	203–213
Hyp Rx	No		Yes								
DM	No		Yes								
Cigs	No			Yes							
CHD	No			Yes							
AF	No				Yes						
LVH	No						Yes				

Notes: This table is adapted from Wolf, D'Agostino, Belanger, and Kannel (1991), with the permission of the author. SBP = systolic blood pressure; Hyp Rx = under hypertensive therapy; DM = history of diabetes mellitus; Cigs = smokes cigarettes; CHD = history of myocardial infarction, angina pectoris, or coronary insufficiency; AF = history of atrial fibrillation; LVH = left ventricular hypertrophy on electrocardiogram.

the Framingham Heart Study. This sample was followed for a decade to determine stroke incidence. On the basis of this information, Wolf and colleagues developed the FSRP, a 40-point index that quantified 10-year stroke probability based on the independent contribution of stroke risk factors that were identified from 36 years of longitudinal data collected by the Framingham study. The FSRP is used to calculate a gender-specific risk score (see Table 1 for the index for men) that is the sum of points that are assigned to a person on the basis of the following risk factors: age, SBP, antihypertensive therapy, diabetes mellitus, current cigarette smoking, cardiovascular disease, atrial fibrillation, and left ventricular hypertrophy (LVH). The more severe the risk factor (e.g., LVH), the greater the number of points associated with that risk factor. Because age is a risk factor for both stroke and cognitive decline, and, furthermore, because we were interested in evaluating the independent effects of age and medical stroke risk on cognition, we decided to consider it as a separate variable in the regression equations to better assess age effects in general. Therefore, we recalculated the FSRP omitting age (referred to below as the "modified FSRP"; mFSRP), to provide an assessment of the effects of medical stroke risk factors on cognitive decline.

We used the mFSRP, rather than individual stroke risk factors (e.g., SBP of 160 mm Hg) or the number of stroke risk factors for each person (e.g., two for a person with age greater than 56 who had diabetes) to assess stroke risk for several reasons. First, using an epidemiologically validated stroke risk index based on 36 years of longitudinal data from the Framingham Heart Study was technically preferable to constructing our own arbitrary index. Second, the stroke-risk index allows our results to be comparable with the larger medical literature on stroke risk. Third, using a composite measure to assess stroke risk allowed us to maximize the sample size-to-independent-variable ratio in our regression analyses as suggested by Cohen and Cohen (1983).

To determine whether stroke risk was specifically related to verbal fluency performance rather than to cognitive performance in general, it was important to sample performance on tests of cognitive abilities besides verbal fluency. Therefore, we selected neuropsychological tests of multiple cognitive domains from the NAS battery for which longitudinal data were available; thus, tests of verbal fluency, memory, and visuospatial functions were selected. Category fluency (animal) was the verbal fluency measure. In this test, persons were given 60 s to verbally generate a list of animal names. The dependent variable was the number of unique items generated in 60 s. Digit span backward from the Wechsler Adult Intelligence Scale–Revised (WAIS-R; Wechsler, 1981) and a 10-item word-list learning test with both immediate and delayed recall trials were used to measure memory function. For the digit span test, persons were given a series of single-digit numbers (e.g., 4, 2) and were asked to repeat the series in reverse order (e.g., 2, 4). The series starts at two digits and progresses to a maximum of eight. Two trials are given at each series level, and if a person correctly remembers at least one of the two trials, the next level is given. If a person missed two trials of the same series, the test was discontinued. The dependent variable was the total number of trials correctly remembered. In the word-list learning test, persons were auditorally presented with a list of 10 words for immediate recall. Three recall trials of the same word list were given, and the number of items recalled for each trial was recorded. Recall was again tested at a delay of 20 min. We used the number of items recalled from the third trial for an immediate recall measure and the delayed recall measure as dependent variables. Visuospatial function was assessed using a speeded-pattern comparison test presented by computer (Letz, 1991). Participants were visually presented with two patterns side-by-side and had to make a speeded response as to whether they were identical. Their response was recorded by a manual keypress. We used the mean response latency (measured in seconds) of correct trials as the dependent variable.

Data analyses.—We examined relations between stroke risk and cognitive change by conducting a hierarchical regression analysis for each neuropsychological test. Thus, for each analysis, the dependent variable was Visit 2 test performance and the independent variables were Visit 1 test performance, age, education, and the mFSRP (entered in that order; see Appendix, Note 1). We entered the independent variables in this order because of our a priori causal assumptions regarding the effects of these variables on cognitive decline. We believed that, after controlling for baseline cognitive performance, age and education effects should be

accounted for before assessing the effects of medical stroke risk because the influence of the former on cognitive performance occurred prior to the onset of stroke risk.

Results

First, given that our longitudinal sample comprised a subset of the total NAS sample, we compared the 235 men for whom we had longitudinal cognitive data with the remaining men for whom longitudinal data were not available (n = 712) to assess any potential sample selection biases. The former group was slightly younger in mean age, 66.41 (SD = 6.73) versus 68.63 (SD = 7.49), $t(1031) = 3.92$, $p < .001$, had a marginally lower mean level of education, 14.03 (SD = 2.62), versus 14.33 (SD = 2.67), $t(1027) = 1.95$, $p < .06$, and had lower mean stroke risk on the mFSRP, 5.06 (SD = 2.57) versus 5.62 (SD = 2.91), $t(1027) = 2.62$, $p < .01$. Using age and education as a covariate, we used regression to compare scores on the cognitive tests at baseline between the two groups. Differences in adjusted means were observed between three of the five tests, indicating better performance in the longitudinal group. There were no differences in verbal fluency or in digit span, but men in the longitudinal group performed better than men who were not retested on both immediate (Ms = 7.86 and 7.55, respectively) and delayed (Ms = 6.59 and 6.29, respectively) recall, and for response latency on the pattern-comparison task (Ms = 5.44 and 5.73, respectively). All differences were significant at $p < .05$ or less. Therefore, the sample of 235 men in this study were younger, marginally less educated, healthier, and exhibited slightly better performance on some tasks (e.g., measures of memory and speed) than the rest of the NAS sample.

Regarding the health of the 235 men, descriptive statistics for the biomedical indexes at Visit 1 were: SBP, mean (mmHg) = 137.17, standard deviation = 17.22; DBP, mean (mmHg) = 82.41, standard deviation = 9.18; fasting glucose, mean (mg/dL) = 105.20, standard deviation = 23.03; and total cholesterol, mean (mg/dL) = 231.83, standard deviation = 36.81. The percentage of the sample having the following health conditions was as follows: antihypertensive therapy, 36%; diabetes mellitus, 10%; cigarette smoking, 5%; cardiovascular disease, 14%; atrial fibrillation, 3%; and left ventricular hypertrophy, 3%. Thus, the most prevalent medical stroke risk factor was hypertension treatment, which had a similar prevalence rate to the national rate of 35% in older men (National Center for Health Statistics, 1998). Furthermore, this group had low rates of both cardiovascular disease and current cigarette smoking. For comparison, the sample in Wolf and colleagues (1991) had rates of 22% and 34%, respectively. Again, this is evidence of the relatively good health of our sample.

The mean FSRP (based on the model of Wolf et al., 1991, including age) at Visit 1 was 9.03 (range 1–21), which represented a 10-year probability of stroke of 8% (based on probability tables in Wolf et al.); the average stroke risk over a similar age range from Wolf and colleagues was 10%. The mean value in the NAS sample for mFSRP, which omitted age, was 5.06 (range 0–13). Given that the mean age of the sample was 66 years, and that an age of 66 receives 4 points in the FSRP (see Table 1), this accounts for the 4-point difference between means of the original and modified FSRP scores.

Table 2. Means and Standard Deviations of the Neuropsychological Measures by Visit

	Visit 1		Visit 2		
Measure	*M*	*SD*	*M*	*SD*	*t*(233)
Verbal fluency (no. of items generated)	19.0	4.8	18.3	4.9	−2.29*
Digit span backward (total score)	5.1	2.2	5.1	2.3	0.28
Word list IR (no. recalled)	7.9	1.5	7.6	1.5	−3.85***
Word list DR (no. recalled)	6.7	1.9	6.1	2.2	−6.02***
Pattern comparison(s)[a]	5.3	1.3	6.0	1.5	−8.75***

Note: IR = immediate recall; DR = delayed recall.

[a]Latency in seconds to make a correct response. An increase in response latency between Visit 1 and Visit 2 indicates a decline in performance.

*$p < .05$; ***$p < .001$.

Table 2 presents descriptive statistics for the neuropsychological tests for each visit. Significant 3-year decline was exhibited on all tests except for digit span backward. Looking at the digit span backward test score distributions, we found no evidence of a ceiling effect to account for the lack of decline over time. Digit span may have remained stable because the test was not sensitive to the memory decline that was detected by the immediate and delayed word-list recall measures. We calculated an effect-size measure for 3-year performance decline by subtracting Visit 2 from Visit 1 performance, and then divided this difference by the pooled standard deviation to express change as a percentage of the standard deviation. The values were as follows: verbal fluency, .14; immediate word-list recall, .20; delayed word-list recall, .29; and pattern comparison, −.50. The effect size for pattern comparison was negative because, given that response latency was the dependent measure, a decrease in performance over time resulted in a slower, or larger, value at Visit 2 relative to Visit 1. For the other measures, a decline in performance resulted in lower scores at Visit 2, and the resulting effect-size measure, although also representing decline in performance, was positive.

Table 3 presents zero-order correlations among the variables. Age at Visit 1 exhibited significant correlations with all Visit 1 and 2 test scores, with older age being associated with worse performance. Education was correlated only with Visit 1 and 2 verbal fluency and digit span scores, with greater education being associated with better performance. Looking across the correlations between Visit 1 and 2 test scores, each Visit 1 test score exhibited its largest correlation with its respective Visit 2 score, except for immediate word-list recall, which exhibited identical correlations with Visit 2 immediate and delayed word-list recall. As expected, the mFSRP at Visit 1 was correlated only with Visit 2 verbal fluency, suggesting a relation between medical stroke risk and verbal fluency decline that we examined further in the multiple regression analyses.

Table 4 presents results from the hierarchical multiple regression analyses of the relations among age, education, medical stroke risk, and 3-year change on the test scores. The Visit 1 score was entered first into each respective equation, followed by age, education, and medical stroke

Table 3. Intercorrelations Between Visit 1 and Visit 2 Measures

	Variables from Visit 1								Variables from Visit 2				
	Age	EDUC	mFSRP	VF1	DSB1	WLIR1	WLDR1	PC1	VF2	DSB2	WLIR2	WLDR2	PC2
Age	—												
EDUC	−.04	—											
mFSRP	.19**	−0.12	—										
VF1	−.21**	.16*	−.11	—									
DSB1	−.16*	.16*	−.00	.10	—								
WLIR1	−.22**	.01	−.07	.09	.28***	—							
WLDR1	−.25***	.05	−.05	.22**	.21**	.72***	—						
PC1	.40***	−.07	.10	−.28***	−.22**	−.21**	−.21**	—					
VF2	−.28***	.22**	−.21**	.52***	.07	.19**	.18**	−.37***	—				
DSB2	−.20**	.20**	−.13	.26***	.56***	.21**	.18**	−.33***	.30***	—			
WLIR2	−.36***	.06	−.06	.27***	.31***	.49***	.58***	−.27***	.24***	.27***	—		
WLDR2	−.33***	.09	−.06	.30***	.22**	.49***	.71***	−.27**	.36***	.28***	.73***	—	
PC2	.44***	−.10	.07	−.33***	−.23***	−.26***	−.20**	.66***	−.40***	−.33***	−.32***	−.32***	—

Notes: EDUC = education; mFSRP = modified Framingham Stroke Risk Profile; VF = verbal fluency; DSB = digit span backward; WLIR = word list immediate recall; WLDR = word list delayed recall; PC = pattern comparison; 1 = Visit 1; 2 = Visit 2.

*$p < .05$; **$p < .01$; ***$p < .001$.

risk. In all analyses, Visit 1 test performance exhibited a high positive association with Visit 2 performance. Age exhibited a negative association with Visit 2 performance for all tests. Education was positively associated only with Visit 2 verbal fluency performance. Medical stroke risk was negatively associated only with Visit 2 verbal fluency. Furthermore, the magnitude of the relation between stroke risk and fluency decline (i.e., the standardized beta) was 80% as large as the relation between age and fluency decline (i.e., −.12/−.15 = .80). Although medical stroke risk explained only an additional 1% of the variance in verbal fluency decline, it is important to consider that these analyses examined 3-year decline in performance in a very healthy sample (i.e., a restricted range of performance).

Table 4. Hierarchical Regression Analyses Using Visit 1 (V1) Variables Predicting Visit 2 (V2) Test Score by Test ($N = 235$)

V2 score predicted, step, and V1 variable	*B*	*SEB*	β	ΔR^2
VF				
1. VF	.49	.06	.46***	.27***
2. Age	−.11	.04	−.15**	.03***
3. Education	.21	.10	.12**	.02**
4. mFSRP	−.24	.11	−.12*	.01*
DSB				
1. DSB	.55	.06	.53***	.32***
2. Age	−.03	.02	−.09*	.01*
3. Education	.08	.04	.10	.00
4. mFSRP	−.09	.05	−.10	.00
WLIR				
1. WLIR	.43	.06	.43***	.24***
2. Age	−.06	.01	−.27***	.07***
3. Education	.02	.03	.05	.00
4. mFSRP	−.01	.03	−.02	.00
WLDR				
1. WLDR	.74	.05	.67***	.50***
2. Age	−.05	.02	−.16***	.02***
3. Education	.04	.04	.05	.00
4. mFSRP	.00	.04	.00	.00
PC				
1. PC	.69	.06	.58***	.45***
2. Age[a]	.05	.01	.21***	.03***
3. Education	−.03	.03	−.05	.00
4. mFSRP	−.02	.03	−.03	.00

Notes: Significance level listed only for β, although the level applies to both β and *B*. VF = verbal fluency; mFSRP = modified Framingham Stroke Risk Profile; DSB = digit span backward; WLIR = word list immediate recall; WLDR = word list delayed recall; PC = pattern comparison.

[a]A positive β and *B* for age in the pattern comparison analysis indicated that increasing age was associated with increasing response latency, which was indicative of a decline in performance.

*$p < .05$; **$p < .01$; ***$p < .001$.

Discussion

This study addressed two hypotheses: (a) Greater stroke risk is associated with greater decline in verbal fluency performance and (b) stroke risk exhibits a greater relation with fluency decline than with decline in other cognitive abilities such as memory. The results supported both hypotheses. Even in this relatively healthy sample examined over a 3-year time span, and after controlling for the effects of age and education, higher medical stroke risk was associated with greater verbal fluency decline. Thus, the impact of medical stroke risk on verbal fluency and, more generally, other frontally mediated functions, could be substantially larger in samples with a wider range of health or a longer interval between examinations. Additionally, the magnitude of the association between medical stroke risk and verbal fluency decline was comparable to the association between age and verbal fluency decline. Furthermore, medical stroke risk was associated specifically with verbal fluency decline, but not with declines in memory and visuospatial function. Finally, we also showed that even after controlling for test performance at Time 1 and education, increasing age was associated with greater decline over 3 years in verbal fluency, memory, and visuospatial performance. Thus, the present longitudinal results suggest that, like the decline seen in memory and visuospatial performance, decline in verbal fluency performance is related to age. Unlike memory and visuospatial performance, however, decline in verbal fluency performance is also partly related to medical stroke risk. Therefore, persons with additional risk factors

for stroke beyond age may exhibit a pattern of cognitive decline that is dissociable from persons without such additional risk factors.

These results, along with those of previous studies (e.g., Boone et al., 1990; P. K. Elias et al., 1997; Knopman et al., 2001; Strachan et al., 1997; Whelihan, 1985) of stroke risk factors and verbal fluency, suggest that frontally mediated cognitive functions may be especially vulnerable to the pathophysiological processes resulting from stroke risk factors. Furthermore, as stroke risk worsens and leads to the onset of CVD, frontally mediated cognitive functions such as verbal fluency may become especially impaired relative to other cognitive abilities such as memory. In fact, there is a growing consensus suggesting that certain types of CVD-related cognitive impairment such as vascular dementia (VaD) exhibit such a pattern (e.g., Looi & Sachdev, 2000; McPherson & Cummings, 1997), and that such a pattern of cognitive dysfunction may aid in the early differential diagnosis of VaD and dementia of the Alzheimer's type. For example, Lafosse and colleagues (1997) showed that persons with VaD exhibited poorer verbal fluency, but better memory performance, than did persons with dementia of the Alzheimer's type who were closely matched in terms of age, dementia severity, education, gender, and premorbid verbal IQ.

These results are also consistent with findings in the cognitive aging literature documenting relations between increasing age and cognitive decline over a relatively short time period in nondemented older adults. Decline in performance over 18 months to 6 years has been demonstrated in older adults for verbal fluency (e.g., Sliwinski & Buschke, 1999; see however, Small, Basun, & Backman, 1998), list recall (e.g., Colsher & Wallace, 1991; see, however, Small et al., 1998), and visuospatial tasks (e.g., Small et al., 1998). Furthermore, our finding of no decline in digit-span-backward performance is consistent with Small and colleagues (1998), who also examined performance over a 3-year interval (see, however, Sliwinski & Buschke, 1999).

Given the present results, future studies of the effects of aging on verbal fluency and other frontally mediated cognitive functions should also document the degree of stroke risk in their samples. In fact, all studies of the effects of aging on cognition would benefit from the inclusion of multiple objective measures to assess the potential effects of health on age–cognition relationships. Because some stroke risk factors can be treated, cognitive decline related to stroke risk, and furthermore, to VaD, represents an opportunity in which dementia may, at least in theory (e.g., Gorelick, 1997), be prevented or its course modified through more aggressive treatment and improved compliance. Therefore, identifying a profile of cognitive deficits related to stroke risk prior to the onset of frank CVD would have profound implications for patient care, health care recommendations, and future research on cognitive aging.

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Appendix

Note

1. Please see Cohen and Cohen (1983) for a discussion of why this method for analyzing change in performance over time is preferable to other methods such as using difference, or change, scores (i.e., subtracting Visit 2 from Visit 1 performance). In short, the present method accounts for more test score variance and provides a more accurate estimate of change compared with using difference scores.