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The Relation Between Morbidity and Cognitive Performance in a Normal Aging Population

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Background. Factors related to physical health have been implicated in both normal and pathological aging of cognitive abilities. To substantiate this notion, we studied existing morbidity, as diagnosed by the general practitioner according to well-defined criteria, as a potential predictor of cognitive test performance.

Methods. A sample of 1360 individuals, aged 24–81 years and living in the community, was stratified for age, sex, and general ability. Active and total morbidity in this group were classified according to the International Classification of Primary Care. Neurocognitive tests were used to assess the domains of verbal memory, sensorimotor speed, and cognitive flexibility.

Results. Multiple regression analyses with adjustment for age, sex, and educational level showed both insulin-dependent and noninsulin-dependent diabetes to be negatively associated with all cognitive measures. More specific negative associations were found for chronic bronchitis (performance speed) and presbyacusia (memory). Single or aggregated cardiovascular morbidity (including hypertension) was unrelated to test performance.

Conclusions. Existing morbidity as a whole contributes only modestly (up to 3.5%) to total variance in cognitive function. However, some specific, relatively common diseases of the elderly, such as diabetes and chronic bronchitis, may aggravate the age-related decline in cognitive ability.

ON a population level, most cognitive abilities such as memory function, information processing speed, and attentional capacity tend to decline with advancing age (1,2). It is clear that the preservation of cognitive abilities is of primary importance to older people, as cognitive decline in the aged can result in a loss of independence and autonomy (3). Interindividual differences, however, exist in the rate of decline of specific cognitive functions that can, at least in part, be mediated by individual differences in physical health (4,5). Several studies have suggested that health-related factors, such as closed head injuries, general anesthesia, and chronic psychotropic medication use (6,7), may be involved in the enhanced cognitive decline seen with increasing age. In addition, several disease entities have been associated with a reduced cognitive capacity in epidemiological surveys and clinical case-control studies (8). For example, disorders such as thyroid disease, renal or hepatic failure, cardiac insufficiency, or chronic obstructive pulmonary disease may be accompanied by relatively nonspecific neuropsychological deficits (9) and may aggravate a dementia syndrome in geriatric populations (10).

Mild cognitive impairment with no frank dementia (CIND) has recently been recognized as a relevant clinical entity that must be identified in an early stage of its development (11). The family physician may play a crucial role in recognizing patients who are at risk of cognitive deterioration that is mediated by physical disease or disability, as he or she is pre-eminently confronted with early stages of disease. It is unclear, however, if the findings on cognition-related morbidity in clinical populations can be readily transposed to general practice. Clinical studies most often refer to advanced stages of disease and are thus biased to overestimate the potential effect of specific morbidity on cognitive function in earlier stages. A cross-sectional design was used to ascertain the potential relevance of well-described morbidity categories as mediators of cognitive function in a large sample of community living adult individuals, using established classification criteria for existing morbidity in general practice.

Methods

Sample Frame

This study was part of a larger research program on determinants of normal cognitive aging, the Maastricht Aging Study (MAAS; ref. 12). Participants were recruited from the Registration Network Family Practices (RNH; ref. 13). The Registration Network was established primarily as a sampling frame for research purposes. It consists of the background characteristics and health problems of patients in 15 general practices that are updated on a continuous basis via a computerized system. Health problems are classified according to the International Classification of Primary Care (ICPC; ref. 14), together with the dates of becoming active and, for some problems, of becoming inactive. A health problem is acknowledged as such when it

affects the functional status of the individual at present or in the future. Therefore, as a rule, only permanent, chronic, or recurrent problems are included (13).

The a priori knowledge on the medical status of Registration Network patients enabled exclusion of individuals with evidence of stroke, chronic neurological pathology (e.g., dementia, epilepsy, parkinsonism, and malignancies related to the nervous system), mental retardation, or chronic psychotropic drug use: 4.0% of the patients in the register who were eligible with respect to age criteria were thus omitted from the sampling procedure. Participants were stratified for age (12 age classes, ranging from 25 ± 1 year, 30 ± 1 year, to 80 ± 1 year), sex, and level of general ability (two levels, based on the achievement in professional life; ref. 15), to control these background variables that in itself may affect cognitive performance (12). The study populations of the first three MAAS panel studies, executed between April 1993 and December 1995, were combined in this study. Of the 8340 patients who were drawn from the register to accommodate these panel studies (including a large postal survey into memory and memory-related function in the first panel study, which is not discussed here) and who were invited directly by their general practitioner, 3741 patients basically agreed to participate (44.9%). From this group, a sample of 1905 patients was actually contacted by the researchers by telephone. They were screened for the current use of psychotropic medication and extremely poor visual or auditory function incompatible with cognitive testing. This resulted in exclusion of 11.7% of the patients. In addition, 16.3% withdrew before or after more in-depth information about the test program had been given. Of the resulting 1373 patients who actually took part in the test program, 13 were not included in the present analysis due to one or more missing values in the cognitive data set. Participating and nonparticipating groups did not differ with respect to the number of medical problems or the presence of chronic diseases, as recorded by their general practitioners. Noncomplying subjects in the first step of recruitment were found more often in the youngest or oldest age classes, were less well educated, and were more often female (12).

Measurements

All participants filled in a questionnaire pertaining to socioeconomic background and medical history. Educational level was measured on an 8-point scale, ranging from primary school to higher vocational training and university degree (12).

Cognitive Assessment

Standard neuropsychological tests were used to assess the cognitive domains of memory, sensorimotor speed and information processing speed/cognitive flexibility (16).

The *Word Learning Task* (WLT) evaluates the ability to acquire and retain new verbal information (17). A set of 15 frequently used monosyllabic words is presented in fixed order at a rate of one every 2 sec in each of five trials. After every trial the participant is to reproduce the memorized words (immediate recall). Twenty minutes after the last trial the participant is asked again to reproduce the set of words (delayed recall). Recorded are the total of correctly reproduced words on five trials, the maximum score in five trials, and the number of correctly reproduced words after 20 min.

The *Concept Shifting Task* (CST) evaluates behavioral planning and evaluation (18). It measures one's ability to alternate two psychological concepts during task performance, i.e., number, letter, and number/letter cancellation in correct order. Outcome is the time required to complete each task.

Selective attention and susceptibility to perceptual interference was measured in the *Stroop Color Word Test* (SCWT; ref. 19). It consists of three subtasks; color word naming (I), color naming (II), and naming of color words printed in a different color (interference task III).

The *Letter Digit Substitution Test* (LDST) is a paper-and-pencil task, measuring basic information processing speed.

Word Fluency was scored as the total number of unique animal names correctly reproduced in 60 sec (category fluency) (20). This test reflects the organizational level among clusters of meaningfully related words.

Morbidity Status

The active and total morbidity status at the time of cognitive testing was retrieved from the Registration Network database for each individual. ICPC morbidity classes with a sample prevalence of 13 (=1%) or more were determined to be used in the analyses, including those with potential direct or indirect impact on brain functioning: cardiovascular diseases, obstructive pulmonary disease, atherosclerotic disease, hypertension, endocrine disorders (such as diabetes and thyroid disease), malignancies, hepatic or renal disease, neurological disturbances, and hearing loss (8,9). The same procedure was followed for total (active + inactive) morbidity in order to test the potential effect of relevant health events that are only temporarily coded as active, e.g., acute myocardial infarction or brain concussion. The list of all codes that were retained is presented in Table 1.

Data Reduction

To limit the number of dependent variables and to improve the robustness of the underlying cognitive construct, most of the raw test scores were clustered in three compound performance indices, labeled *memory, cognitive flexibility,* and *sensorimotor speed.* For all participants the raw scores were transformed to standardized *Z*-scores ($z = [x - \bar{x}] / SD$). *Z*-scores from tests that were included in each compound performance index were averaged. Thus, the memory score was derived from the total, maximal, and delayed recall scores of the WLT; the cognitive flexibility score included the C-version of the CST and subtask III of the SCWT; and sensorimotor speed was calculated from the 0, A, and B versions of the CST, and subtask I of the SCWT. Signs of the speed and flexibility scores were inverted to make them reflect above average performance when positive and below average performance when negative. LDST and fluency test outcomes were not included in compound scores, as the performance on these tests is far less dependent on the integrity of one specific cognitive domain.

Several single morbidity codes were uniquely combined in more broad morbidity clusters, including chronic diseases

Table 1. Number of Single *Active* (and *Total*) Health Problems by Levels of Age and Sex (Total n = 1360)

	Age Class (years)						Sex		
	25–30	35–40	45–50	55–60	65–70	75–80	M	F	All
Total n per cell	236	240	239	238	241	166	688	672	1360
Single Codes									
D85 Duodenal ulcer	0	1	2	3	3	1	9	1	10
	(0)	(1)	(5)	(8)	(15)	(9)	(33)	(5)	(38)
D86 Other peptic ulcer	0	0	0	5	1	2	7	1	8
	(0)	(0)	(2)	(10)	(4)	(7)	(14)	(9)	(23)
D93 Irritable bowel syndrome*	3	0	3	4	5	1	2	14	16
	(4)	(0)	(5)	(6)	(9)	(4)	(7)	(21)	(28)
D98 Cholecystitis/cholelithiasis*	1	1	1	2	5	4	2	12	14
	(1)	(6)	(6)	(16)	(20)	(23)	(15)	(57)	(72)
H84 Presbyacusia*	0	0	1	1	14	15	22	9	31
	(0)	(0)	(1)	(1)	(14)	(15)	(22)	(9)	(31)
H85 Acoustic trauma/noise-related deafness*	0	2	0	6	4	1	12	1	13
	(0)	(2)	(0)	(6)	(4)	(1)	(12)	(1)	(13)
H86 Deafness or hearing loss n.c.e.**	2	2	11	7	12	9	23	20	43
	(2)	(3)	(11)	(7)	(13)	(10)	(26)	(20)	(46)
K00 Family history of vascular disease*	4	4	4	10	4	2	16	12	28
	(4)	(4)	(4)	(10)	(4)	(2)	(16)	(12)	(28)
K74 Angina pectoris*	0	0	4	7	11	17	26	13	39
	(0)	(0)	(5)	(7)	(16)	(20)	(33)	(15)	(48)
K75 Acute myocardial infarction*	0	0	1	3	4	8	14	2	16
	(0)	(0)	(3)	(6)	(16)	(24)	(42)	(7)	(49)
K76 Ischemic heart disease, other and chronic*	0	0	2	2	12	12	23	5	28
	(0)	(0)	(2)	(3)	(14)	(18)	(29)	(8)	(37)
K77 Heart failure	0	0	0	1	3	8	7	5	12
	(0)	(0)	(0)	(2)	(5)	(10)	(10)	(7)	(17)
K78 Atrial fibrillation/-flutter*	0	0	0	3	5	9	12	5	17
	(0)	(0)	(0)	(3)	(7)	(15)	(15)	(10)	(25)
K80 Ectopic heart rhythm, all types	0	1	1	4	2	2	5	5	10
	(0)	(1)	(2)	(5)	(4)	(2)	(7)	(7)	(14)
K84 Other heart disease	0	0	1	7	2	2	8	4	12
	(0)	(0)	(2)	(7)	(3)	(3)	(9)	(6)	(15)
K85 Increased blood pressure/no hypertension*	0	1	2	7	5	2	11	6	17
	(0)	(2)	(3)	(8)	(6)	(2)	(14)	(7)	(21)
K86 Hypertension/no organ damage*	5	2	19	29	51	30	58	78	136
	(5)	(2)	(20)	(30)	(53)	(34)	(59)	(85)	(144)
K87 Hypertension/organ damage*	0	0	1	1	4	7	7	6	13
	(0)	(0)	(1)	(1)	(4)	(7)	(7)	(6)	(13)
K91 Atherosclerosis, not in heart/brain*	0	0	1	6	6	3	13	3	16
	(0)	(0)	(1)	(6)	(7)	(6)	(16)	(4)	(20)
K92 Other peripheral arterial diseases*	0	1	1	7	7	6	19	3	22
	(0)	(1)	(1)	(7)	(9)	(11)	(24)	(5)	(29)
L01 Cervical symptoms/complaints [not N01]	1	2	0	4	1	1	2	7	9
	(3)	(4)	(0)	(4)	(1)	(2)	(4)	(10)	(14)
L02 Back symptoms/complaints*	1	8	6	10	3	4	20	12	32
	(3)	(13)	(7)	(12)	(4)	(5)	(23)	(21)	(44)
L03 Low back pain/no radiation [not L86]*	4	20	12	17	3	3	32	27	59
	(6)	(22)	(16)	(20)	(6)	(3)	(37)	(36)	(73)
L83 Cervical syndromes; other*	1	2	6	11	16	10	21	25	46
	(1)	(4)	(8)	(15)	(19)	(14)	(29)	(32)	(61)
L84 Spinal arthrosis*	1	2	1	14	11	19	26	22	48
	(1)	(2)	(2)	(14)	(13)	(19)	(27)	(24)	(51)
L86 Degenerated intervertebral disk + radiation*	4	2	15	13	19	8	31	30	61
	(7)	(6)	(24)	(22)	(37)	(17)	(61)	(52)	(113)
L88 Rheumatoid arthritis/ankylosing spondylitis*	3	0	2	4	4	2	9	6	15
	(4)	(0)	(3)	(7)	(7)	(5)	(15)	(11)	(26)
N01 Headache [not R09/N89/N02/N03]	2	2	0	1	1	2	4	4	8
	(4)	(3)	(2)	(2)	(4)	(2)	(9)	(8)	(17)

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Table 1. Number of Single *Active* (and *Total*) Health Problems by Levels of Age and Sex (Total $n = 1360$) *(Continued)*

	Age Class (years)						Sex		
	25–30	35–40	45–50	55–60	65–70	75–80	M	F	All
Single Codes *(Continued)*									
N02 Tension headache*	5	6	4	5	2	1	12	11	23
	(5)	(8)	(7)	(5)	(3)	(2)	(15)	(15)	(30)
N79 Brain concussion	0	0	0	0	0	0	0	0	0
	(5)	(4)	(2)	(3)	(4)	(1)	(9)	(10)	(19)
N89 Migraine*	5	8	6	3	4	4	11	19	30
	(5)	(10)	(6)	(3)	(6)	(4)	(11)	(23)	(34)
P01 Anxious feelings/nervousness*	1	9	4	8	9	3	16	18	34
	(5)	(10)	(9)	(10)	(11)	(4)	(23)	(26)	(49)
P03 Depressive feelings	1	1	1	2	3	2	0	10	10
	(1)	(5)	(2)	(4)	(5)	(3)	(5)	(15)	(20)
P15 Chronic alcohol abuse	0	3	1	1	0	1	6	0	6
	(0)	(3)	(5)	(4)	(0)	(4)	(10)	(6)	(16)
P76 Depressive neurosis*	1	4	2	4	1	1	4	9	13
	(3)	(8)	(9)	(12)	(6)	(4)	(19)	(23)	(42)
R70 Pulmonary tuberculosis	0	0	0	1	1	1	3	0	3
	(0)	(0)	(1)	(8)	(7)	(8)	(20)	(4)	(24)
R91 Chronic bronchitis/bronchiectasis*	4	3	1	7	8	12	25	10	35
	(5)	(7)	(2)	(7)	(8)	(12)	(27)	(14)	(41)
R95 Emphysema*	0	1	2	2	6	13	18	6	24
	(0)	(1)	(2)	(2)	(6)	(13)	(18)	(6)	(24)
R96 Asthma*	11	9	6	10	8	4	33	15	48
	(12)	(10)	(8)	(10)	(10)	(4)	(38)	(16)	(54)
T83 Obesity*	6	3	5	9	9	8	18	22	40
	(7)	(3)	(6)	(9)	(9)	(8)	(20)	(22)	(42)
T85 Hyperthyroidism	1	1	1	2	1	0	1	5	6
	(1)	(2)	(2)	(5)	(3)	(2)	(2)	(13)	(15)
T90 Diabetes mellitus*	1	2	3	11	12	21	27	23	50
	(1)	(4)	(6)	(12)	(12)	(23)	(27)	(31)	(58)
T93 Disorder of lipid metabolism*	0	2	12	22	12	8	28	28	56
	(0)	(2)	(12)	(24)	(12)	(9)	(28)	(31)	(59)
Aggregated Codes									
Anaemia [B78/B80/B81/B82]	2	2	0	2	1	3	5	5	10
	(3)	(2)	(1)	(3)	(3)	(5)	(5)	(12)	(17)
Peptic ulcers [D85/D86]	0	1	2	8	4	3	16	2	18
	(0)	(1)	(7)	(16)	(19)	(16)	(45)	(14)	(59)
Hearing loss [H83/H84/H85/H86]	2	4	14	15	30	26	57	34	91
	(2)	(5)	(14)	(15)	(32)	(27)	(60)	(35)	(95)
Cardiac insufficiency [K77/K82]	0	0	0	1	3	8	7	5	12
	(0)	(0)	(0)	(2)	(5)	(10)	(10)	(7)	(17)
Cardiac rhythm disturbances [K78/K79/K80]	0	1	1	8	9	12	18	13	31
	(0)	(2)	(2)	(10)	(12)	(19)	(22)	(23)	(45)
Cervical syndromes [L01/L83/L84]	3	6	7	28	27	29	47	53	100
	(5)	(10)	(10)	(32)	(32)	(32)	(56)	(65)	(121)
Lumbar syndromes/lumbar hernia [L02/L03/L86]	8	30	32	38	25	15	83	65	148
	(14)	(39)	(45)	(51)	(46)	(24)	(117)	(102)	(219)
Chronic disease[b]	52	59	80	117	142	133	310	273	583
	(66)	(77)	(99)	(133)	(157)	(143)	(351)	(324)	(675)
Malignant disease[b]	0	5	2	5	12	27	30	21	51
	(0)	(6)	(3)	(8)	(18)	(33)	(40)	(28)	(68)
Cardiovascular disease[c]	5	5	25	55	86	78	145	109	254
	(5)	(6)	(31)	(58)	(95)	(88)	(159)	(124)	(283)
COPD[d] [R91/R95/R96]	14	13	8	19	21	26	70	31	101
	(16)	(18)	(12)	(19)	(26)	(28)	(81)	(38)	(119)

Notes: Only those *total* morbidity categories are shown that were present in at least 1% of this population: these codes were used in the regression analyses. Categories of *active* morbidity that were used in the regression analyses (with an associated $n \geq 13$) are marked with an asterisk (*). Aggregated morbidity categories are displayed in the second half of the table. Letter/digit codes refer to the respective category in the ICPC coding system.

[a]n.c.e. = not coded elsewhere.

[b]For full description, see ref. 21.

[c]Aggregated codes K28, K71, K74 to K80, K82 to K84, K86 to K89, and K91.

[d]COPD = chronic obstructive pulmonary disease.

and malignancies (according to ref. 21), hearing loss, cardiovascular diseases, cardiac rhythm disturbances, and obstructive pulmonary disease (aggregated codes in Table 1).

Statistical Analysis

Separate linear regression models were fitted for cognitive parameters, adjusting for age, sex, and educational level, by using active or total ICPC morbidity codes that occurred at least in 1% of all participants (backward elimination procedure). This procedure was repeated for both the active and total aggregated morbidity clusters. All analyses were performed using the SPSS statistical program series (Statistical Package for the Social Sciences, Chicago, IL). Values of $p = .01$ or less were considered to be statistically significant unless indicated otherwise.

Results

Table 1 shows the single and aggregated morbidity categories with an associated prevalence of .01 or higher. It is clear from these data that discrepancies between active and total morbidity status depend in large part on the impact of the disease or complaint on current health and physical functioning. For example, prevalence of active and total presbyacusia (H84) is exactly the same, presumably as the impact of age-associated hearing loss for daily functioning is permanent, but consequences of a disease such as angina pectoris (K74) may disappear after initiation of proper treatment.

All single codes in Table 1 ($n = 43$) were entered in the analyses for total morbidity, and the codes marked with an asterisk ($n = 31$) were used in the analysis of active morbidity. Table 2 displays the results of regression analysis of age, sex, educational level, and specific ICPC morbidity codes on cognitive outcome variables. The regression coefficients in the first column demonstrate that age and education are highly associated with all cognitive parameters, and that women out-perform men on memory, cognitive flexibility, and letter-digit copying. Together, the variance in performance explained by age, sex, and educational level ranged between 17% for fluency and 48% for sensorimotor speed.

Final regression models including morbidity codes are displayed in Table 2 for active (column 2) and total morbidity (column 3). All morbidity codes that remained in the models were negatively associated with the performance scores. Most consistently diabetes (T90) was associated with lower performance scores on all cognitive parameters, ranging from –.36 *SD* in memory to –.52 *SD* in cognitive flexibility (Table 2, column 2: active morbidity), adjusted for the other factors in the model. Other associations between morbidity codes and cognitive parameters were more sporadic, but consistent in the analyses for both active and total morbidity. Chronic bronchitis (R91) remained in the models for sensorimotor speed and cognitive flexibility. Presbyacusia (H84) was present in the model fitted for memory, whereas cholecystitis (D98) accounted for variance in the cognitive flexibility score only when coded as *total* (column 3). Two other morbidity categories coded as *total* were present in the model fitted for verbal fluency only: hyperthyroidism (T85) and disturbances in atrial rhythm (K78).

Similar analyses were repeated with the aggregated morbidity codes, as displayed in Table 1, for active and total morbidity separately. No single significant relation was found between these new variables and cognitive performance levels.

Given the strong association between diabetes and cognitive test performance we did post hoc tests with diabetes as independent variable (coded *active*), first to evaluate a potential age by diabetes interaction, and second, to differentiate between associations with cognitive function for insulin- and noninsulin-dependent diabetes mellitus (IDDM and NIDDM, respectively). When diabetes and the age by diabetes interaction were entered during the regression procedure, no significant interaction was present on any cognitive parameter on a $p \leq .05$ level. This indicates that the association between diabetes and cognitive function is not age dependent. We then repeated the analysis after splitting the diabetes group in insulin users and noninsulin users [$n = 15$ and $n = 35$, mean ages 59.6 (*SD* 14.9) and 69.9 (*SD* 10.1), respectively, $p < .05$], based on reported information about medication use by the participant (Table 3). Except for verbal fluency in the NIDDM group, all remaining cognitive outcome measures were negatively associated with both types of diabetes. Regression coefficients for both types of diabetes were quite comparable in size in all models.

Discussion

Associations between active and total ICPC morbidity and objective neurocognitive test performance were investigated in a healthy adult population sample. Significant negative associations were found between diabetes and all studied cognitive domains, and, more sporadically, between presbyacusia and memory performance and between chronic bronchitis and performance speed (psychomotor speed and cognitive flexibility). Other single associations were only related to total morbidity codes for cholecystitis, hyperthyroidism, and atrial rhythm disturbances. However, related morbidity codes that were aggregated in newly formed clusters did not add to the proportion of explained variance in cognitive measures. Several issues need to be discussed before conclusions can be drawn from these data.

Study participants were stratified for age, sex, and general ability, which are recognized confounding variables in cognitive research. Although demographically this group is not a representative sample of the general population, possible sampling bias due to the stratification procedure was adjusted for by controlling these variables in the regression analyses.

Several specific classes of disease that are theoretically important with respect to brain function (e.g., hepatic cirrhosis) could not be included in the present analyses because their prevalence did not reach the 1% level criterion. Potential significant relations between relatively rare diseases and measures of mental efficiency are unlikely to be identified in a study such as this, because the standard error, and thus the significance, of the regression coefficients describing such a relation strongly depends on the number of cases that are present in the study population. This problem was partly avoided because categories of related morbidity were combined in larger clusters, but only

Table 2. Results of Regression Analysis of Demographic Variables (After Step 1) and Active or Total Morbidity (Final Models) on Cognitive Performance Measures

	Step 1: Demographic Variables				Final Model: Active Morbidity				Final Model: Total Morbidity			
	B	*(SE)*	*p*	R^2	*B*	*(SE)*	*p*	R^2	*B*	*(SE)*	*p*	R^2
Memory												
Age[a]	−.024	(.001)	.00		−.022	(.001)	.00		−.022	(.001)	.00	
Sex[b]	.481	(.043)	.00		.472	(.042)	.00		.477	(.042)	.00	
Education	.102	(.012)	.00		.101	(.012)	.00		.101	(.012)	.00	
T90, diabetes[c]					−.462	(.113)	.00		−.439	(.105)	.00	
H84, presbyacusia					−.374	(.143)	.01		−.377	(.144)	.01	
				.327				.339				.339
Sensorimotor speed												
Age	−.027	(.001)	.00		−.025	(.001)	.00		−.026	(.009)	.00	
Sex	.054	(.032)	.09		.045	(.032)	.16		.051	(.032)	.11	
Education	.120	(.009)	.00		.118	(.009)	.00		.118	(.009)	.00	
T90, diabetes					−.369	(.085)	.00		−.301	(.080)	.00	
R91, chronic bronchitis					−.338	(.100)	.00		−.281	(.093)	.00	
				.476				.487				.485
Cognitive flexibility												
Age	−.029	(.001)	.00		−.027	(.001)	.00		−.027	(.001)	.00	
Sex	.103	(.036)	.00		.092	(.036)	.01		.114	(.036)	.00	
Education	.139	(.010)	.00		.137	(.010)	.00		.136	(.010)	.00	
T90, diabetes					−.523	(.096)	.00		−.410	(.090)	.00	
R91, chronic bronchitis					−.369	(.113)	.00		−.328	(.105)	.00	
D98, cholecystitis									−.235	(.082)	.00	
				.458				.474				.474
LDST												
Age	−.033	(.001)	.00		−.033	(.001)	.00		−.033	(.001)	.00	
Sex	.135	(.039)	.00		.134	(.039)	.00		.137	(.039)	.00	
Education	.141	(.011)	.00		.142	(.011)	.00		.142	(.011)	.00	
T90, diabetes					−.364	(.104)	.00		−.283	(.097)	.00	
				.491				.495				.493
Fluency												
Age	−.013	(.002)	.00		−.012	(.014)	.00		−.011	(.002)	.00	
Sex	.042	(.050)	.39		.041	(.050)	.41		.052	(.050)	.29	
Education	.150	(.014)	.00		.150	(.014)	.00		.149	(.014)	.00	
T90, diabetes					−.414	(.133)	.00		−.321	(.124)	.01	
T85, hyperthyroidism									−.618	(.236)	.01	
K78, atrial fibrillation/-flutter									−.491	(.186)	.01	
				.168				.174				.181

Notes: Shown are the regression coefficients *B* and its standard error, the associated *p*-value and the total proportion of variance explained (R^2), after step 1 and in the final models. LDST = Letter Digit Substitution Test.

[a]Age is chronological age.

[b]Sex: 0 = men, 1 = women.

[c]Morbidity codes: 0 = absent, 1 = present.

at the cost of a larger disease heterogeneity and lower specificity within the newly defined predictor variables.

Two factors that, at least theoretically, can modulate the relation between morbidity and cognitive processes were not included in our models because they could not be reliably assessed: *disease duration* and *intervention* (success). First, although it seems reasonable to expect that the impact of disease on cognitive processes is mediated by the duration of exposure to the disease, we consider in most cases the available "date of diagnosis" by the general physician as an inexact indicator of disease duration. In general practice, date of diagnosis is for a large part dependent on patient and physician-related characteristics that are not associated with the actual onset of a disease process: unless identified as a health problem by one or both parties, a disease can remain undetected. Second, adequacy or success of therapeutic intervention is disease-specific and may not be defined in a straightforward sense for purposes such as in this study.

It has been suggested that problems with information processing in patients with a chronic disease are related to restrictions in functional health (3). However, not all participants with a chronic disease in this study experience functional limitations in daily life. An explanation for the absence of a relationship in our data between chronic diseases and cognitive function could be found in the selective

Table 3. Regression of Active Insulin- and Noninsulin Dependent Diabetes (IDDM and NIDDM; $n = 15$ and $n = 35$, respectively) on Cognitive Outcome Measures

	Entered on Step 1							Entered on Step 2				
	Age[a]		Sex[b]		Education			IDDM		NIDDM		
	B	*(SE)*	*B*	*(SE)*	*B*	*(SE)*	R^2	*B*	*(SE)*	*B*	*(SE)*	R^2
Memory	−.023	(.001)***	.479	(.042)***	.102	(.012)***	.327	−.505	(.202)*	−.449	(.135)***	.336
Sensorimotor speed	−.026	(.001)***	.052	(.032)	.119	(.009)***	.476	−.304	(.152)*	−.396	(.102)***	.483
Cognitive flexibility	−.027	(.001)***	.101	(.036)**	.139	(.010)***	.458	−.576	(.171)***	−.498	(.114)***	.470
LDST	−.033	(.001)***	.134	(.039)***	.142	(.011)***	.491	−.442	(.184)*	−.330	(.123)**	.495
Fluency	−.012	(.002)***	.043	(.050)	.151	(.014)***	.168	−.771	(.236)**	−.258	(.158)	.176

Notes: Displayed are regression coefficients (*B*, and *SE* of *B*) and proportion of explained variance (R^2) after each step. LDST = Letter Digit Substitution Test.

[a]Age is chronological age.

[b]Sex: 0 = men, 1 = women.

*$p \leq .05$; **$p \leq .01$; ***$p \leq .001$.

participation of relatively fit and healthy participants in this study. This possibility cannot be ruled out entirely, but earlier analyses have shown that participants in MAAS did not differ with the original Registration Network sample with respect to the number of active or total morbidity codes (12), thus making a strong health selection bias due to the inclusion procedure less likely. An intriguing question remains, however, if different aspects of functional health could have accounted for the relation that we found between specific morbidity classes and cognitive function. A post hoc analysis was therefore performed in which available measures of subjective health, IADL (instrumental activities of daily living) and depressive mood, were entered in the regression model together with the significant (active) morbidity variables, but no evidence was found that these functional measures could substitute for morbidity or attenuate the relationship between morbidity and cognitive outcome in any of the final models.

The observed associations between ICPC morbidity and cognitive function in part corroborate earlier findings. Diabetic patients have been found to perform worse on tasks of memory and learning, psychomotor speed, and problem solving when compared to healthy controls, possibly due to cerebral changes in blood supply and metabolism, but the affected cognitive domains and the extent of performance deficit vary widely across studies (22). Elderly NIDDM patients have repeatedly performed worse than controls on verbal and complex cognitive tasks (23–25). In this study the domains of verbal memory and information processing speed were also negatively related to diabetes, irrespective of age and insulin dependency. Moreover, comparison of the regression coefficients for IDDM and NIDDM in Table 3 suggests that the strength of association is not substantially different in both types of diabetes. Initially this observation may seem remarkable when disease duration is taken into account. As mentioned earlier, reliable information on disease duration was not available in this group, but generally IDDM is of the early onset type, which would suggest more structural damage and, as a result, more cognitive impairment in IDDM than in NIDDM. One possibility is that progression of cognitive functional loss is limited in the early phase of IDDM in young adulthood to middle age, when the brain has more reserve capacity to compensate for the loss of functional integrity than the brain in older patients with NIDDM (26), but this explanation remains largely speculative.

Lowered auditory thresholds have been implicated in reduced performance on verbal memory when stimuli are presented acoustically (27). In this study target words were presented visually to reduce the negative effect of hearing disorders. Still, if older individuals experienced more difficulty in understanding the verbal instruction to the task, the observed negative association between presbyacusia and memory performance may reflect a procedural artifact that needs further consideration.

Interestingly, we did not find relations between single or aggregated cardiovascular morbidity codes and cognitive performance, apart from an isolated single association between word fluency and atrial rhythm disturbances. Other studies have suggested that cardiovascular disease and its risk factors, such as hypertension, are particularly implicated in cognitive decline and dementia (28, 29). However, cross-sectional studies with a wide age range such as ours may be biased toward underestimating such associations, as vascular disease is the most important cause of death in middle-aged groups, thereby yielding older groups with attenuated vascular risk profiles.

As this study was performed in participants with no overt signs of a cognitive disorder such as dementia, it may be difficult to interpret the clinical relevance of the found associations between several health problems and performance. One way to describe the predictive value of a significant morbidity category for cognitive performance, in the absence of age by morbidity interactions, is to express it in terms of another predictor in the statistical model, in this case the chronological age. For example, one can calculate the average number of years that specific groups of patients are *cognitively older*, by taking the ratio between the regression coefficients associated with the morbidity code and with age –in years. Thus, active diabetes in our model adds –.462/–.022 = 21 years to the *cognitive age* on memory function, or –.523/–.027 = 19 years on cognitive flexibility. Even though we cannot make direct infererences on causality, this may seem a rather dramatic notion.

On a more general level, it seems that prevalent morbidity does not explain a large proportion of individual differences in cognitive abilities. For example, additional variance explained after entry of all active morbidity codes ranged from 1.5% (not significant) to 3.5% ($p < .001$), for digit copying and word fluency, respectively. This observation may cast some doubt on the contention that physical health is an important mediator of cognitive aging (4,6,10,18,30). The prevalence of many health problems correlates strongly with chronological age (Table 1), albeit age itself still remains the most powerful predictor of cognitive abilities. Other as yet covert individual characteristics related to age need to be identified to account for this age-associated pool of variance.

In conclusion, the strong negative association between both IDDM and NIDDM and a broad spectrum of cognitive abilities may warrant careful follow-up of these functions by the physician in attendance from the time of diagnosis onward, and should be considered as a possible mediating factor when cognitive dysfunction is found.

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REFERENCES

1. Salthouse TA. Age-related changes in basic cognitive processes. In: Storandt M, Vandenbos GR, eds. *The Adult Years: Continuity and Change.* Washington, DC: American Psychological Association; 1989:5–40.
2. Poon LW. Differences in human memory with aging: nature, causes, and clinical implications. In: Birren JE, Schaie KW, eds. *Handbook of the Psychology of Aging* (pp. 427–462). New York, NY: Van Nostrand Reinhold Co; 1985:
3. McSweeny AJ, Grant I, Heaton RK, Prigatano GP, Adams KM. Relationship of neuropsychological status to everyday functioning in healthy and chronically ill persons. *J Clin Exp Neuropsychol.* 1985;7:281–291.
4. Elias MF, Elias JW, Elias PK. Biological and health influences on behavior. In: Birren JE, Schaie KW, eds. *Handbook of the Psychology of Aging,* 3rd ed. San Diego, CA: Academic Press; 1990:79–102.
5. Salthouse TA. *Mechanisms of Age-Cognition Relations in Adulthood.* Hillsdale, NJ: Lawrence Erlbaum Associates; 1992.
6. Houx PJ, Jolles J. Vulnerability factors for age-related cognitive decline. In: Isaacson RL, Jensen KF, eds. *Toxins in Air and Water.* New York, NY: Plenum Press; 1994:25–41.
7. Houx PJ, Jolles J. Age-related decline of psychomotor speed: effects of age, brain health, sex, and education. *Percept Motor Skills.* 1993; 76:195–211.
8. Colsher PL, Wallace RB. Epidemiologic considerations in studies of cognitive function in the elderly: methodology and nondementing acquired dysfunction. *Epidemiol Rev.* 1991;13:1–27.
9. Tarter RE, van Thiel DH, Edwards KL. *Medical Neuropsychology: The Impact of Disease on Behavior.* New York, NY: Plenum Press; 1988.
10. Nolan KA, Blass JP. Preventing cognitive decline. *Clin Geriatr Med.* 1992;8:19–34.
11. Writing Committee Lancet Conference. The challenge of the dementias. *Lancet.* 1996;347:1303–1307.
12. Jolles J, Houx PJ, van Boxtel MPJ, Ponds RWHM, eds. *Maastricht Aging Study: Determinants of Cognitive Aging.* Maastricht, The Netherlands: Neuropsych Publishers; 1995.
13. Metsemakers JFM, Höppener P, Knottnerus JA, Kocken RJJ, Limonard CBG. Computerized health information in the Netherlands: a registration network of family practices. *Br J Gen Pract.* 1992;42:102–106.
14. Lamberts H, Wood M. *ICPC: International Classification of Primary Care.* Oxford, U.K.: Oxford University Press; 1987.
15. Van Berkel AB, Tax B. *Naar een standaardoperationalisatie van sociaal-economische status voor epidemiologisch en sociaal-medisch onderzoek* [Towards a standard operationalization of socio-economical status for epidemiological and socio-economical research]. Den Haag, The Netherlands: Ministerie van Welzijn, Volksgezondheid en Cultuur; 1990.
16. Lezak MD. *Neuropsychological Assessment.* 3rd ed. New York, NY: Oxford University Press; 1995.
17. Brand N, Jolles J. Learning and retrieval rate of words presented auditory and visually. *J Gen Psychol.* 1985;112:201–210.
18. Houx PJ, Vreeling FW, Jolles J. Age-associated cognitive decline is related to biological life events. In: Iqbal K, McLachlin DRC, Winblad B, Wisniewski HM, eds. *Alzheimer's Disease: Basic Mechanisms, Diagnosis, and Therapeutic Strategies.* Chichester, U.K.: Wiley; 1991:353–358.
19. Stroop JR. Studies of interference in serial verbal reactions. *J Exp Psychol.* 1935;18:643–662.
20. Luteijn F, van der Ploeg FAE. *Handleiding Groninger Intelligentietest (GIT)* [Manual Groningen Intelligence Test]. Lisse, The Netherlands: Swets & Zeitlinger; 1983.
21. Knottnerus JA, Metsemakers J, Höppener P, Limonard C. Chronic illness in the community and the concept of "social prevalence." *Fam Pract.* 1992;9:15–21.
22. Biessels GJ, Kappelle AC, Bravenboer B, Erkelens DW, Gispen WH. Cerebral function in diabetes mellitus. *Diabetologia.* 1994;37:643–650.
23. Reaven GM, Thompson LW, Nahum D, Haskins E. Relationship between hyperglycaemia and cognitive function in older NIDDM patients. *Diabetes Care.* 1990;13:16–21.
24. U'ren RC, Riddle MC, Lezak MD, Bennington-Davis M. The mental efficiency of the elderly person with Type II diabetes mellitus. *J Am Geriatr Soc.* 1990;38:505–510.
25. Worrall G, Moulton N, Briffett E. Effect of type II diabetes mellitus on cognitive function. *J Fam Pract.* 1993;36:639–643.
26. Satz P. Brain reserve capacity on symptom onset after brain injury: a formulation and review of evidence for threshold theory. *Neuropsychology.* 1993;7:273–295.
27. Rabbitt P. Mild hearing loss can cause apparent memory failures which increase with age and reduce with IQ. *Acta Otolaryngol Suppl Stockh.* 1991;476:167–176.
28. Waldstein SR. Hypertension and neuropsychological function: a lifetime perspective. *Exp Aging Res.* 1995;21:321–352.
29. Skoog I. Risk factors for vascular dementia: a review. *Dementia.* 1994;5:137–144.
30. Albert M. Neuropsychological and neurophysiological changes in healthy adult humans across the age range. *Neurobiol Aging.* 1993;14: 623–625.

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