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Independent Effects of Alzheimer's Disease on Neuropsychological Functioning

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A new analytical procedure, single common factor analysis, was carried out on the data from a relatively large sample of normals (n = 101) and patients with Alzheimer's disease (AD; n = 180) to examine the extent to which there were independent effects of disease status on different neuropsychological variables. This technique uses structural equation methods to determine what all of the variables have in common, and then controls this common factor when examining the relationship between diagnostic group and each individual test variable. To the extent that AD represents the sum of independent breakdowns of different information processing domains, then there should be sets of variables that have weak or nonexistent links to the other variables. However, the results revealed that a large proportion of the AD-related effects on test scores was shared and was not independent of the AD-related effects on other variables.

Alzheimer's disease (AD) is an insidious progressive dementia syndrome whose hallmark is the occurrence of profound memory loss early in its clinical course (American Psychiatric Association, 1994; McKhann et al., 1984). As the disease progresses, a wider range of cognitive functions becomes clinically impaired, including most prominently language (particularly semantic–lexical referents and retrieval of such information), visuospatial, and executive functions. A variety of neuropsychiatric syndromes may develop as a consequence of the deteriorating function of the CNS, including the development of delusions, hallucinations, and other signs of impaired information processing.

Although AD had been considered a generalized dementia syndrome, more recent evidence has established that at least early in the course of the dementia patients can present with relatively restricted cognitive impairments. Thus, for example, some patients meeting the diagnostic criteria for dementia of the Alzheimer type (using either the National Institute of Neurological and Communications Disorders and Stroke and Alzheimer's Disease and Related Disorders Association [NINCDS—ADRDA; McKhann et al., 1984] or American Psychiatric Association [1994] criteria) may present with impaired language or impaired visuospatial function out of proportion to other aspects of their performance (Martin et al., 1986; Martin, Cox, Brouwers, & Fedio, 1985). Indeed, these subgroups (Jorm, 1985) of AD patients have different patterns of regional cortical glucose metabolism than patients with less focal patterns of impairment (Martin et al., 1986). That is, those patients with pronounced language dysfunction had lower glucose metabolism over the temporal cortex than did patients with profound visuospatial defects. By contrast, the patients with visuospatial deficits had lower metabolism over the parietal cortex than did the language-impaired patients (i.e., a double dissociation of function). Subsequent studies have demonstrated other dissociations (Baddeley, Bressi, Della Sala, Logie, & Spinnler, 1991; Baddeley, Della Salla, & Spinnler, 1991; Becker, 1988; Becker, Bajulaiye, & Smith, 1992; Becker, Huff, Nebes, Holland, & Boller, 1988; Becker, Lopez, & Wess, 1992), have confirmed and extended these data, and have at least suggested that there may be biological differences between patients in these various subgroups (Butters, Lopez, & Becker, 1996).

Although such subgroups of patients exist, by and large the impairments in cognitive function seen in any individual patient tend to be roughly equivalent across cognitive domains. The primary exception to this is the memory loss that seems most profound early in the disease relative to other cognitive functions (although see Berrios & Freeman, 1991, p. 27, for a discussion of the history of the use of memory loss as a diagnostic criterion). Given the data on the heterogeneity of presentation of AD, and the apparent sensitivity of memory tests to the presence of the dementia, it is reasonable to ask whether the cognitive syndrome of AD represents the results of the additive effects of several independent focal impairments (either neuroanatomical or functional) or has at its core a single broad influence that can account for a significant amount of the variability in the patterns of cognitive impairment.

Although traditional univariate data analytic techniques do not lend themselves well to addressing this sort of question, newer multivariate procedures based on factor

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analysis and structural equation models may be more helpful. The purpose of this report is to describe our efforts to understand the degree to which there are independent and distinct effects associated with the presence of AD on measures of cognitive functioning. That is, although the performance of AD patients is significantly impaired relative to that of healthy control participants on a variety of measures of cognitive function, the extent to which the effects of AD on different variables are independent of one another is not yet known.

In the present article, we describe the results of an analysis of a large corpus of neuropsychological data using a new analytical technique designed to answer this question, single common factor analysis (SCFA). The basic analysis consists of using structural equation methods to evaluate a model such as that portrayed in Figure 1. In the current context, *group* refers to diagnostic status, where normal individuals are coded as 0, and individuals with AD are coded as 1. The technique is analogous to determining what all of the variables have in common and then controlling for an estimate of that common factor when examining the relationship between the diagnostic grouping variable and each performance variable. A major question of interest in this analytical procedure concerns the strength of the direct relations from the group variable to the individual variables, which are represented as dashed lines in Figure 1. However, because the purpose of the procedure is to determine which variables have distinct effects related to group status, independent of the effects on what all the variables have in common, the fit of the model to the entire data is only of secondary interest in this application of structural equation modeling. That is, there is no attempt to consider relations among the variables except to the extent that they are related to the group status variable, and, thus, indices of how accurately the model fits the covariance pattern for all variables are not directly relevant to the issue of determining which variables have unique covariance with the group variable.

The SCFA procedure has been used in several recent studies concerned with effects of aging on cognitive functioning (e.g., Lindenberger, Mayr, & Kliegl, 1993; Salthouse, 1994, 1996; Salthouse, Hancock, Meinz, & Hambrick, 1996). In each of those studies, it was found that a large proportion of the age-related variance in many different cognitive variables was shared and was not distinct. In terms of the model portrayed in Figure 1, the group variable was replaced by the variable of age, and the independent age-related influences, corresponding to the dotted lines, were few in number and small in magnitude. That is, once the relationship between age and what all the variables had in common was taken into account, only a few variables were found to have independent relations with age. These findings were interpreted as consistent with the idea that increasing age in adulthood affects a small number of cognitive processes, or neuroanatomical structures, that in turn have an impact on a wide variety of cognitive variables (e.g., Salthouse, Fristoe, & Rhee, 1996). The issue here is whether, in contrasting normal elderly and AD patients, a similar pattern would be found in which most of the effects of group membership on individual variables are shared with other variables.

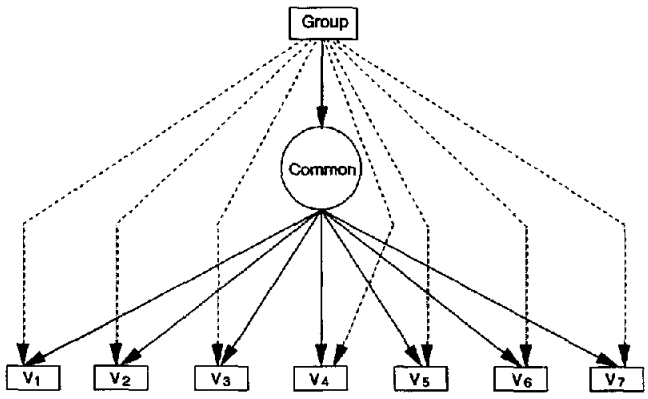

Figure 1. Hypothesized structural model in which diagnostic group is related to a factor representing what all variables have in common and possibly also to the individual variables. V = variable.

Relations among variables with significant independent group effects can also be examined in the SCFA procedure. For example, two specific factors could be postulated in addition to the common factor (see Figure 2). One specific factor might consist of variables in which the independent group effects are in the same direction as the group-common relation, and the other factor might consist of variables in which independent group effects are in the opposite direction as the group-common relation. Not all variables need be associated with one of these specific factors, however, and thus some variables with independent effects associated with diagnostic status may be found to be unrelated to the other variables with independent effects.

In this study, we use SCFA procedures to describe the relationship between a large set of neuropsychological test score variables and the group variable corresponding to AD classification (i.e., AD vs. normal). To the extent that the syndrome of AD represents the sum of independent breakdowns of different domains of information processing, then there should be sets of variables that have weak or nonexistent links to the other variables. However, to the extent that there is a single factor that links the performance of the patients on all of the variables, then the different neuropsychological test scores should all have moderate-to-high loadings on the common factor, and independent relations between the group status variable and the neuropsychological variables should be weak and limited to a few variables.

Method

Participants

The data for the analyses to be reported are based on participants in the Pittsburgh Alzheimer's Research Program, a National Institute on Aging (NIA) funded study of the natural history of AD and related dementias (F. Boller, Program Director; Becker, Boller, Lopez, Saxton, & McGonigle, 1994; Becker et al., 1988; Huff et al., 1987). There are three major advantages of these data for the current purposes. First, the samples are relatively large, with 101

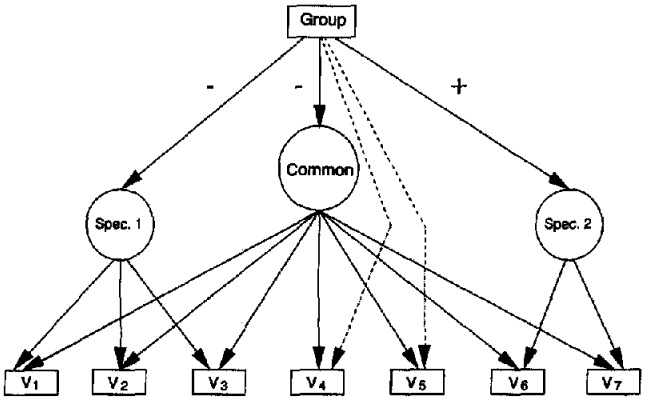

Figure 2. Structural model in which variables sharing the same direction of independent group effects form specific (Spec.) factors in addition to the common factor. V = variable.

normal adults and 180 individuals classified as probable or definite AD. Second, the diagnoses were based on extensive medical and psychiatric examinations and have been confirmed with autopsy results in a large percentage of the cases where autopsies were available (e.g., Becker et al., 1994). Third, many variables were obtained from each participant, and these variables represented a wide range of cognitive abilities, including memory, speed, spatial, reasoning, and language derived from psychometric and neuropsychological tests. The participants enrolled in the Alzheimer's Research Program (Becker et al., 1988, 1994; Huff et al., 1987) were carefully screened to exclude those with confounding conditions that might in and of themselves account for the dementia syndrome, that is, possible AD (McKhann et al., 1984). This was important because the stated purpose of the project was to identify those factors that would increase the reliability and validity of the diagnosis of AD, an especially critical undertaking in 1983, the year that the project began. In the present context, therefore, the sample can be considered to represent a relatively pure cohort of AD patients, and thus the findings described here cannot be attributed to comorbid conditions. Although this might have the effect of reducing between-subject variability (because the sample is homogeneous with regard to diagnosis), it increases the certainty that our conclusions are valid with regard to AD. Demographic characteristics of the sample and means and standard deviations for the 49 relevant variables are summarized in Table 1.

A subsample with a narrower range of age and education was also created to replicate the analyses when there were smaller group differences in those two variables. Only individuals between 60 and 80 years of age and with at least 12 years of education were retained in this subsample. Demographic characteristics of the 62 normals and 96 AD individuals in this subsample, and means and standard deviations for the relevant variables, are summarized in Table 2. Comparison of Tables 1 and 2 reveals that the group differences in age and education in this subsample were reduced by about 50% relative to the original sample.

Data Analysis

A two-step procedure was followed for each analysis, and in all cases the analyses were based on the raw data for individuals with no missing values for the variables included in the analysis. The first step consisted of estimating the common-variable and group-common relations using maximum likelihood techniques with the EQS structural equation package (Bentler, 1996). In the second step, the parameters from the first step were fixed to the estimated values, and then the EQS program was used to estimate the group-variable relations for each variable. Relations between group and the individual variable were retained in the final model when the coefficients differed from 0 by at least 2 *SE*s.

Four additional analyses were conducted on the data from the complete sample. First, the analysis was repeated without the Mini-Mental Status Examination variable, because this variable was one of those considered in making the initial diagnosis and, hence, indirectly used in the assignment of individuals to the two groups. Two analyses were each performed with only 50% of the variables. One analysis was based on the variables with odd ranks in terms of the group-variable correlations (see the last column of Table 3), and the other analysis was based on variables with even ranks in terms of the group-variable correlations. The fourth analysis was conducted contrasting normal adults with individuals classified as having mild AD, as defined on the basis of Mini-Mental Status Examination scores of 18 or greater. A total of 95 AD individuals met this criterion and were compared with the same 101 normals included in the primary analyses.

Results

Results from the major analyses are summarized in Tables 3 and 4. The signs of the variables in which higher scores correspond to poorer performance (e.g., measures of time or errors) were reversed so that all group-variable correlations were negative and all common-variable loadings were positive.

The additional analyses on the data from the complete sample yielded results very similar to those in Table 3. To illustrate, the group-common relations were −.840 in the analysis without the Mini-Mental Status variable, −.850 for the analysis based on the odd-ranked variables, and −.834 for the analysis based on the even-ranked variables compared to the value of −.851 in the overall analysis. The correlations of the common-variable loadings from these analyses and those from the analyses with the complete data were greater than .99 in all cases. Furthermore, the patterns of variables with significant independent group effects were nearly identical, with a few fluctuations depending on whether a particular variable exceeded the 2 *SE* criterion in a given analysis.[1]

Four points should be noted about the results summarized

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[1] Two additional analyses were carried out to examine the effects of age on these variables. One analysis was identical to that summarized in Table 3 except that age was added as another variable, along with group, having relations to the common factor. The pattern of results in this analysis was similar to that in the other analyses, and the standardized coefficient for the age-common path in that model was −.07 (*ns*). It can, therefore, be inferred that the results of the primary analyses are not attributable to variations in age across the samples.

A second analysis was conducted on the data from the normal adults, with age replacing the AD group variable. Only variables having absolute correlations of age greater than .1 were included in this analysis. A total of nine variables were found to be related to age in this sample, and all had a significant loading on the common factor. The standardized coefficient for the age-common path in this analysis was −.46, which is slightly smaller than that found in analyses with a wider age range (e.g., Salthouse et al., 1996).

Table 1
Descriptive Characteristics of the Complete Sample

Variable	Normals			Probable or definite AD			
	n	*M*	*SD*	*n*	*M*	*SD*	*t*
Age	101	63.29	8.34	180	70.97	8.30	−7.43
Sex (% females)	101	44	0.50	180	32.80	0.47	1.80
Education	101	14.34	2.92	180	12.10	2.99	6.07
Mini-Mental State Examination	98	29.05	1.06	180	18.33	4.84	21.62
Verbal Paired Associates							
Easy (trials to criterion)	101	9.36	0.93	179	16.34	7.36	−9.48
Hard (trials to criterion)	101	14.28	5.35	179	30.30	4.91	−25.38
Easy Delayed Recall	101	2.77	0.51	180	1.02	1.02	16.23
Hard Delayed Recall	101	2	1.09	180	0.14	0.49	19.64
Face–Name Associates							
Trials to criterion	101	12.41	1.08	180	27.93	9.51	−16.34
Delayed Recall	101	3.83	0.45	180	1.25	1.38	18.23
Story Recall							
Immediate	100	7.43	2.60	179	1.65	1.80	21.84
Delayed	100	6.46	2.80	179	0.41	1.10	25.56
Modified Rey Figure							
Figure Copy	101	23.52	0.94	177	16.92	7.25	9.11
Immediate Recall	101	19.95	3.31	176	5.73	4.96	25.69
Delayed Recall	101	19.61	3.34	176	3.92	5.23	27.16
Recognition Memory							
Words False Alarms	101	0.23	0.49	180	3.16	3.73	−7.86
Words Misses	101	0.25	0.57	180	1.82	1.57	−9.72
Faces False Alarms	101	0.44	0.81	180	3.97	4.12	−8.52
Faces Misses	101	0.27	0.53	180	1.67	1.66	−8.27
President's Test							
Verbal Naming	101	5.93	0.52	180	3.67	2.08	10.75
Verbal Sequence	101	0.98	0.05	179	0.46	0.41	12.78
Photo Naming	101	5.95	0.50	180	2.85	2.23	13.78
Photo Sequence	101	0.98	0.05	180	0.49	0.38	12.92
Picture Memory							
Naming	101	2.84	0.46	180	0.43	0.84	26.61
Gestures	101	3	0.00	180	2.53	0.79	6.03
Orientation							
Time	101	0.12	0.45	179	37.30	39.94	−9.35
Personal	101	7.94	0.44	180	5.67	2.32	9.73
Place	101	4	0.00	180	2.47	1.36	11.36
Cancellation Time	101	66.50	16.86	179	122.76	53.36	−10.30
Trail Making Test—Part A	101	39.19	13.94	177	121.32	70.77	−11.53
Trail Making Test—Part B	101	90.51	39.13	176	223.69	36.42	−28.51
Simple reaction time	101	0.33	0.10	180	0.68	0.57	−6.19
Go/no go reaction time	101	0.43	0.09	180	0.85	0.56	−7.50
Match/mismatch reaction time	101	0.42	0.09	180	0.88	0.56	−8.14
Similarities	101	11.29	1.15	178	4.92	3.57	17.40
Weigl	64	11.95	1.81	150	5.81	3.51	13.25
Ravens	64	32.52	4.50	149	16.74	7.68	15.35
Simple Drawings	101	16.27	1.30	178	11.86	3.19	13.30
Block Design	101	43.17	1.78	178	29.88	15.09	8.81
Form Discrimination	100	29.81	2.21	178	20.71	8.75	10.21
Facial Recognition	101	47.27	4.78	177	37.47	12.13	7.78
Verbal Fluency							
Letter	101	18.63	4.34	180	7.60	4.34	20.47
Category	101	14.23	4.74	178	5.82	4.22	15.29
Object Naming	101	38.62	2.77	180	23.07	9.33	16.34
Auditory Comprehension	101	59.79	0.84	179	57.75	3.27	6.16
Token Test (Part VI)	101	12.09	1.18	179	7.40	3.22	14.08
Reading	101	39.45	2.04	178	29.24	10.55	9.62
Writing	101	21.88	0.37	180	19.16	4.01	6.79
OLSIST (Zachman, Huisingh, Jorgensen, & Barnett, 1977) Sentence Repetition	101	139.69	1.03	180	133.01	14.31	4.69
Responsive Naming	101	29.88	0.59	180	28.20	4.37	3.84
Semantic Correction Task							
Correct	101	9.78	0.46	180	8.49	1.82	7.04
Plausible Reconstruction	101	6.16	0.83	180	4.05	1.94	10.39

Note. AD = Alzheimer's disease. OLSIST = Oral Language Sentence Imitation Screening Test.

Table 2
Descriptive Characteristics of the Sample Between 60 and 80 Years of Age With at Least 12 Years of Education

Variable	Normals			Probable or definite AD			
	n	*M*	*SD*	*n*	*M*	*SD*	*t*
Age	62	67.32	5.24	96	70.23	5.99	−3.12
Sex (% females)	62	47	0.50	96	31	0.47	1.95
Education	62	14.40	2.38	96	13.45	2.15	2.62
Mini-Mental State Examination	60	28.93	1.15	96	19.31	4.91	14.92
Verbal Paired Associates							
Easy (trials to criterion)	62	9.40	1.11	96	15.79	7.53	−6.63
Hard (trials to criterion)	62	14.47	5.52	96	29.77	5.16	−17.71
Easy Delayed Recall	62	2.77	0.53	96	1.04	1.03	12.30
Hard Delayed Recall	62	2	1.07	96	0.18	0.58	13.84
Face–Name Associates							
Trials to criterion	62	12.45	0.99	96	26.99	9.16	−12.44
Delayed Recall	62	3.86	0.44	96	1.35	1.35	14.07
Story Recall							
Immediate	62	7.39	2.38	95	1.75	1.51	18.18
Delayed	62	6.28	2.73	95	0.38	0.99	19.27
Modified Rey Figure							
Figure Copy	62	23.53	0.84	94	17.69	7.04	6.49
Immediate Recall	62	19.77	3.63	94	6.23	4.99	18.38
Delayed Recall	62	19.35	3.62	94	4.35	5.57	18.75
Recognition Memory							
Words False Alarms	62	0.27	0.55	96	3.08	3.85	−5.70
Words Misses	62	0.21	0.55	96	1.62	1.49	−7.16
Faces False Alarms	62	0.47	0.86	96	3.80	4.11	−6.29
Faces Misses	62	0.21	0.48	96	1.32	1.42	−5.94
President's Test							
Verbal Naming	62	6	0.00	96	3.95	2.19	7.36
Verbal Sequence	62	0.99	0.03	95	0.53	0.39	9.47
Photo Naming	62	6	0.00	96	3.27	2.19	9.80
Photo Sequence	62	0.98	0.04	96	0.55	0.37	9.40
Picture Memory							
Naming	62	2.80	0.51	96	0.36	0.74	22.78
Gestures	62	3	0.00	96	2.59	0.75	4.32
Orientation							
Time	62	0.15	0.54	96	33.39	39.93	−6.55
Personal	62	7.90	0.57	96	5.87	2.24	7.03
Place	62	4	0.00	96	2.54	1.35	8.53
Cancellation Time	62	70.21	16.89	95	113.80	48.28	−6.84
Trail Making Test—Part A	62	42.48	14.71	94	116.44	73.43	−7.82
Trail Making Test—Part B	62	96.18	40.23	94	214.25	43.47	−17.10
Simple reaction time	62	0.34	0.11	96	0.66	0.56	−4.42
Go/no go reaction time	62	0.45	0.09	96	0.83	0.56	−5.22
Match/mismatch reaction time	62	0.43	0.08	96	0.84	0.56	−5.69
Similarities	62	11.36	0.91	95	5.55	3.62	12.36
Weigl	37	12.08	1.83	76	6.38	3.76	8.72
Ravens	37	32.63	2.49	76	18.20	7.20	11.83
Simple Drawings	62	16.35	1.19	95	12.32	3.25	9.36
Block Design	62	43.26	1.39	95	31.73	14.78	6.12
Form Discrimination	62	29.55	2.32	95	22.20	8	7.04
Facial Recognition	62	46.87	5.21	95	38.22	11.86	5.41
Verbal Fluency							
Letter	62	18.23	4.37	96	8.59	4.78	12.80
Category	62	14.69	4.89	95	6.52	4.79	10.37
Object Naming	62	38.52	2.84	96	24.50	9.70	11.06
Auditory Comprehension	62	59.77	0.93	96	58.28	2.71	4.17
Token Test (Part VI)	62	12.24	0.95	96	8.22	3.17	9.72
Reading	62	39.36	2.20	95	30.28	10.74	6.58
Writing	62	21.86	0.42	96	19.61	3.61	4.90
OLSIST (Zachman, Huisingh, Jorgensen, & Barnett, 1977) Sentence Repetition	62	139.60	1.23	96	134.93	10.66	3.43
Responsive Naming	62	29.95	0.39	96	27.99	4.89	3.15
Semantic Correction Task							
Correct	62	9.84	0.41	96	8.72	1.60	5.39
Plausible Reconstruction	62	6.31	0.72	96	4.28	1.96	7.80

Note. AD = Alzheimer's disease. OLSIST = Oral Language Sentence Imitation Screening Test.

Table 3
Analysis Performed for All Participants With Complete Data on All Variables Except Ravens and Weigl (n = 264)

Variable	Common factor parameters		Correlation group variable
	Common-variable	Group-variable	
Mini-Mental State Examination	.934	—	−.791
Verbal Paired Associates			
Easy (trials to criterion)	.783	.095	−.493
Hard (trials to criterion)	.778	−.143	−.847
Easy Delayed Recall	.788	—	−.697
Hard Delayed Recall	.676	−.154	−.765
Face–Name Associates			
Trials to criterion	.841	—	−.705
Delayed Recall	.756	−.093	−.740
Story Recall			
Immediate	.754	−.141	−.819
Delayed	.711	−.177	−.841
Modified Rey Figure			
Figure Copy	.691	—	−.479
Immediate Recall	.824	−.114	−.839
Delayed Recall	.773	−.147	−.852
Recognition Memory			
Words False Alarms	.609	—	−.431
Words Misses	.573	—	−.497
Faces False Alarms	.604	—	−.463
Faces Misses	.516	—	−.435
President's Test			
Verbal Naming	.724	—	−.534
Verbal Sequence	.743	—	−.602
Picture Naming	.808	—	−.631
Picture Sequence	.720	—	−.608
Picture Memory			
Naming	.733	−.166	−.846
Gestures	.504	—	−.338
Orientation			
Time	.772	.090	−.492
Personal	.733	—	−.509
Place	.729	—	−.559
Cancellation Time	.725	—	−.523
Trail Making Test—Part A	.777	—	−.567
Trail Making Test—Part B	.762	−.159	−.862
Simple reaction time	.537	—	−.343
Go/no go reaction time	.627	—	−.407
Match/mismatch reaction time	.640	—	−.436
Similarities	.819	—	−.721
Simple Drawings	.823	—	−.620
Block Design	.689	—	−.460
Form Discrimination	.704	—	−.518
Facial Recognition	.585	—	−.425
Verbal Fluency			
Letter	.783	−.097	−.772
Category	.725	—	−.666
Object Naming	.855	—	−.696
Auditory Comprehension	.512	—	−.367
Token Test (Part VI)	.797	—	−.643
Reading	.705	—	−.497
Writing	.599	—	−.382
OLSIST (Zachman, Huisingh, Jorgensen, & Barnett, 1977) Sentence Repetition	.456	—	−.337
Responsive Naming	.398	—	−.215
Semantic Correction Task			
Correct	.493	—	−.397
Plausible reconstruction	.671	—	−.524

Note. Group: normal individuals are coded as 0, and probable or definite Alzheimer's disease individuals are coded as 1. Coefficient between group and common factor = −.851. OLSIST = Oral Language Sentence Imitation Screening Test.

Table 4
Analysis Performed for Participants Between 60 and 80 Years of Age With at Least 12 Years of Education, With Complete Data on All Variables Except Ravens and Weigl (n = 151)

Variable	Common factor parameters		
	Common-variable	Group-variable	Correlation group variable
Mini-Mental State Examination	.928	—	−.766
Verbal Paired Associates			
Easy (trials to criterion)	.831	.115	−.464
Hard (trials to criterion)	.719	−.187	−.821
Easy Delayed Recall	.721	−.117	−.703
Hard Delayed Recall	.634	−.188	−.737
Face–Name Associates			
Trials to criterion	.856	—	−.705
Delayed Recall	.710	−.154	−.755
Story Recall			
Immediate	.702	−.197	−.821
Delayed	.656	−.237	−.845
Modified Rey Figure			
Figure Copy	.710	—	−.458
Immediate Recall	.780	−.160	−.831
Delayed Recall	.706	−.202	−.835
Recognition Memory			
Words False Alarms	.620	—	−.408
Words Misses	.579	—	−.493
Faces False Alarms	.638	—	−.445
Faces Misses	.484	—	−.440
President's Test			
Verbal Naming	.748	—	−.498
Verbal Sequence	.701	—	−.593
Picture Naming	.809	—	−.607
Picture Sequence	.725	—	−.589
Picture Memory			
Naming	.668	−.244	−.872
Gestures	.519	—	−.323
Orientation			
Time	.708	—	−.457
Personal	.742	—	−.486
Place	.767	—	−.559
Cancellation Time	.732	—	−.482
Trail Making Test—Part A	.795	—	−.528
Trail Making Test—Part B	.729	−.172	−.804
Simple reaction time	.532	—	−.324
Go/no go reaction time	.664	—	−.378
Match/mismatch reaction time	.699	—	−.415
Similarities	.852	—	−.701
Simple Drawings	.838	—	−.601
Block Design	.700	—	−.430
Form Discrimination	.684	—	−.478
Facial Recognition	.575	—	−.398
Verbal Fluency			
Letter	.758	−.105	−.718
Category	.708	—	−.627
Object Naming	.869	—	−.667
Auditory Comprehension	.519	—	−.288
Token Test (Part VI)	.818	—	−.604
Reading	.740	—	−.467
Writing	.650	—	−.367
OLSIST (Zachman, Huisingh, Jorgensen, & Barnett, 1977) Sentence Repetition	.453	—	−.261
Responsive Naming	.637	.217	−.235
Semantic Correction Task			
Correct	.504	—	−.409
Plausible reconstruction	.715	—	−.517

Note. Group: normal individuals are coded as 0, and probable or definite Alzheimer's disease individuals are coded as 1. Coefficient between group and common factor = −.811. OLSIST = Oral Language Sentence Imitation Screening Test.

in Tables 3 and 4. First, the pattern of results was quite robust across variations in the nature and size of the sample (compare Tables 3 and 4) and in the particular combination of variables included in the analyses (i.e., odd- vs. even-ranked variables, and with and without the Mini-Mental Status variable). This provides some assurance that the results are relatively stable and not critically dependent upon a specific configuration of individuals or variables.

Second, in all analyses there was a large negative relation between the group status variable and the common factor, indicating that the AD group was considerably lower than the normal controls on the factor representing the variance shared by all variables. This was not surprising because of the sizable group differences favoring the normal controls on all variables (see Tables 1 and 2) and the known relation between t values and correlations (i.e., $r^2 = \sqrt{[}\ (t^2) / (t^2 + df)\ ]$.

Third, all variables had moderate-to-high loadings on the common factor, with the absolute values ranging from .398 to .934. This indicates that all variables shared considerable individual differences variance with other variables and, hence, that they were not independent of one another.

And fourth, a very strong relation existed between the loadings on the common factor and the group-variable correlation contained in the last column of Tables 3 and 4 (e.g., the correlation for the variables in Table 3 was −.77). This finding indicates that the magnitude of the group differences on any given variable can be predicted quite accurately from the degree to which that variable shares variance with other variables. In fact, if there were no independent group-related effects on the variables, then all of the variation in the magnitude of the differences between AD patients and normals on the variables could be attributable to the variation in the loadings of the variables on the common factor and the relations of the group status to the common factor.

An additional analysis was conducted with the complete data set by grouping together those variables in which the independent group relations were in the same direction as the group-common relation and then determining the extent to which this residual group-related variance was shared (significantly) with other variables. Only those variables whose loadings on the specific factor were significant (i.e., the coefficients differed from 0 by more than 2 *SE*s) were retained in the final model. A single specific factor emerged when the relations among the variables with significant independent effects of group status were examined in this analysis. The standardized path coefficient between the group variable and this specific factor was −.35, indicating that the group effects on these variables were underestimated by the influence through the common factor. All of the variables with significant loadings on this factor involved some type of episodic memory (i.e., trials to criterion and delayed recall with hard paired associates, immediate and delayed story recall, immediate and delayed figure recall, delayed face name recall, and picture memory naming). An apparent implication of this finding is that in addition to the effects associated with AD shared by all variables, there were independent AD-related deficits on variables reflecting various types of memory. Unique group effects were also significant on a few other variables, but they were apparently isolated because they were not related to the effects evident on other variables.

The final analysis involved a contrast between the normals and the mild AD individuals with Mini-Mental State scores of 18 or higher. The results from this analysis, summarized in Table 5, were very similar to those from the other analyses. For example, the group-common relation was −.885 compared to −.851 in the complete sample, and the correlation between the common-variable loadings in the two analyses was .89. However, there were two notable differences. The first was that the variables had weaker relations to one another in the sample of mild AD individuals. Thirty-five of the 47 variables had smaller common-variable loadings than they did in the total sample (compare Tables 3 and 5). The second major difference was that there was less evidence of independent group-related effects in the mild sample as only 3 variables had significant unique effects of AD compared to 12 variables in the total sample.

Discussion

In a model such as that shown in Figure 1, the total relation between the group classification and an individual variable is the sum of the product of the group-common and common-variable relations plus any group-variable relation that might exist. Individual variables can exhibit a number of interesting possibilities in this type of analysis. For example, one possibility is that a variable has a large common-variable loading and no direct (independent) group-variable relation (e.g., the variables in the President's Test). A pattern such as this indicates that the variable shares individual differences with other variables and that there is no unique influence of group status independent of the effects on other variables. In other words, this type of outcome implies that all of the effects associated with AD on the variable overlap with the effects of AD on other variables. A second possibility is that the variable has a large common-variable loading and also a direct group-variable relation (e.g., the two story recall variables). This type of pattern indicates that the variables shared individual differences with other variables but that there were also independent effects of group status. If the independent effects were in the same direction as the group-common relation (as in the case with the story recall variables), then the group effects on the variable would be underestimated by the common factor, perhaps because of an additional influence of group status above and beyond the general or shared effects. If the independent effects were in the opposite direction as the group-common relation, then the group effects would be overestimated by the common factor, possibly because of the involvement of qualitatively different influences that may offset, or compensate for, the influences through the common factor.

The major finding of these analyses is that a large proportion of the effects on cognitive variables associated with AD are interrelated. That is, only a small portion of the effects of AD on individual cognitive variables appears to be

Table 5
Analysis Performed for All Participants With Complete Data on All Variables Except Ravens and Weigl (n = 193)

Variable	Common factor parameters		Correlation group variable
	Common-variable	Group-variable	
Mini-Mental State Examination	.893	—	−.838
Verbal Paired Associates			
Easy (trials to criterion)	.725	.126	−.478
Hard (trials to criterion)	.856	—	−.799
Easy Delayed Recall	.746	—	−.673
Hard Delayed Recall	.731	—	−.706
Face–Name Associates			
Trials to criterion	.816	—	−.693
Delayed Recall	.827	—	−.720
Story Recall			
Immediate	.811	—	−.745
Delayed	.810	—	−.802
Modified Rey Figure			
Figure Copy	.575	—	−.454
Immediate Recall	.889	—	−.822
Delayed Recall	.885	—	−.832
Recognition Memory			
Words False Alarms	.590	—	−.410
Words Misses	.577	—	−.531
Faces False Alarms	.568	—	−.452
Faces Misses	.535	—	−.482
President's Test			
Verbal Naming	.610	—	−.482
Verbal Sequence	.739	—	−.616
Picture Naming	.767	−.089	−.597
Picture Sequence	.746	—	−.601
Picture Memory			
Naming	.769	—	−.820
Gestures	.447	—	−.287
Orientation			
Time	.664	.128	−.424
Personal	.611	—	−.435
Place	.649	—	−.504
Cancellation Time	.609	—	−.472
Trail Making Test—Part A	.708	—	−.558
Trail Making Test—Part B	.844	—	−.820
Simple reaction time	.475	—	−.347
Go/no go reaction time	.481	—	−.383
Match/mismatch reaction time	.529	—	−.413
Similarities	.775	—	−.719
Simple Drawings	.739	—	−.628
Block Design	.577	—	−.431
Form Discrimination	.630	—	−.526
Facial Recognition	.491	—	−.422
Verbal Fluency			
Letter	.769	—	−.742
Category	.631	—	−.624
Object Naming	.802	—	−.690
Auditory Comprehension	.462	—	−.329
Token Test (Part VI)	.698	—	−.638
Reading	.569	—	−.503
Writing	.439	—	−.343
OLSIST (Zachman, Huisingh, Jorgensen, & Barnett, 1977) Sentence Repetition	.340	—	−.217
Responsive Naming	.200	—	−.140
Semantic Correction Task			
Correct	.384	—	−.370
Plausible reconstruction	.494	—	−.490

Note. Group: normal individuals are coded as 0, and mild Alzheimer's disease individuals (defined on the basis of Mini-Mental Status Examination scores greater than 17) are coded as 1. Coefficient between group and common factor = −.885. OLSIST = Oral Language Sentence Imitation Screening Test.

independent of the effects on other variables. The primary evidence for this conclusion is that the independent group-related effects were few in number and small in magnitude. Only 12 of the 47 variables had significant independent effects of disease status in the major analysis on the complete sample, and the median absolute value of the coefficients was .142 compared to a median absolute total group relation of .829. These results indicate that if an adjustment is made for the general effects of AD, as estimated from the common factor, then there are no remaining effects of AD on nearly 75% of the variables and consistent independent effects only on variables assessing episodic memory.

Although we cannot yet specify the nature of the information-processing deficits responsible for the observed pattern of shared common and shared memory-specific effects, it is possible that this pattern reflects the operation of dysexecutive and amnesic syndromes. That is, the common factor may represent executive functions that are involved in many different types of cognitive tasks, and the specific memory factor may correspond to symptoms of amnesia disorders. This interpretation is consistent with earlier conclusions drawn by Morris and Kopelman (1986) that the memory loss in AD could be the result of the combination of the classic amnesic syndrome with the addition of another, independent information-processing deficit. The present interpretation is also compatible with recent evidence that there are patients with identifiable dysexecutive syndromes (Baddeley, Bressi, et al., 1991; Baddeley, Della Salla, et al., 1991; Becker, 1988, 1994; Becker et al., 1992) that are distinct from the more common amnesic syndrome seen early in AD.

As we and others (e.g., Becker, 1994; Jorm, 1985) have previously noted, there are subgroups of AD patients based on the pattern of neuropsychological deficits, and these subgroups may have different longitudinal courses (Butters et al., 1996). The data presented here do not invalidate these findings. As we have reported, this cohort includes small groups of patients with prominent visuospatial and lexical–semantic defects, as well as some groups with pronounced amnesic and dysexecutive syndromes. However, it must be emphasized that all of these subgroup patients met the diagnostic criteria for AD. The findings of the current analyses suggest that within the overall context of the disease there is a shared factor that accounts for a significant proportion of the variance in test scores. This common factor might be thought of as a characteristic that distinguishes a dementia syndrome from a focal amnesia or aphasia. In our view (see earlier discussion), this might best be viewed as a defect in a higher order cognitive process, perhaps related to a putative central executive system (Baddeley & Wilson, 1988; Baddeley, Bressi, et al., 1991; Baddeley, Della Salla, et al., 1991). Thus, although the subgroups of AD patients differ in the extent to which they express certain aspects of their syndrome, they share with all AD patients a common, global cognitive impairment.

The results of the analysis of the mild AD cases are provocative. There are statistical reasons why there were few (and small) group-related effects in this analysis because the sample size of AD patients (n = 92) was much smaller than in the total patients group (n = 181). The lack of stronger independent effects may also be the result of the necessarily smaller effects associated with group status, because the mild subgroup is less impaired relative to the controls than the AD group as a whole. However, it is tempting to speculate that these findings may represent a genuine phenomenon—that early in AD there are few specific effects of AD on particular cognitive variables. This would suggest a less specific loss of cognitive functions early in the disease than is currently assumed. Additional research using similar types of analytical procedures with samples of mildly impaired patients is clearly desirable to allow these speculations to be investigated.

Finally, an intriguing implication of the current results is that researchers focusing on different sets of variables may not necessarily be studying separate and distinct influences of AD. From the single common factor perspective, one can only be confident that there are unique or distinct influences on a variable if that variable has a significant relation from the group status variable independent of the relation through the common factor. In the analyses reported here, this was the case with many measures of memory and assorted measures of speed and spatial ability. Even with these variables, however, it should be noted that large proportions of the AD-related effects were shared with other variables because the direct (independent) AD effects were much smaller than the indirect ones mediated through the common factor. These results, therefore, imply that someone studying AD-related effects on a variable such as block design or trail making score is probably studying many of the same types of influences being studied by a researcher focusing on backward digit span or category fluency.

In conclusion, the SCFA procedure appears promising for identifying distinct influences associated with AD (or other diseases). Some cautions are needed, because the limitations of the procedure have not yet been fully explored; but the results of these analyses are intriguing. Assuming that similar patterns would be found in other data sets, including those with a wider range of variables and different proportions of patient subtypes, two issues appear to be of fundamental importance. First, researchers should attempt to discover why so many variables have shared group effects; that is, what is the nature of the common factor, and why is it related so strongly to the classification variable (i.e., AD)? Our hypothesis that this represents the dysexecutive component of the syndrome of AD is consistent with a variety of data and should be amenable to empirical investigation. It should also be possible to compare common factors across disease states (e.g., Huntington's disease). Second, efforts should be directed at determining what is responsible for the effects that are independent of the shared influences. Even if those effects are small relative to the common effects, they are important because they represent influences that have been established to be distinct from those operating through the common factor.

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