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Pathological Association and Dissociation of Functional Systems in Multiple Sclerosis and Huntington's Disease*

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ABSTRACT

This study examined pathological associations and dissociations of functional cognitive systems in patients with multiple sclerosis and Huntington's disease. Using the subtests of the WAIS-R, two motor tests, and the word fluency test, the intertest correlations showed distinct patterns. In comparison to normals, the two clinical groups exhibited a greater degree of association among the tests. Subsequently, word fluency performance was predicted from these tests. For the normals, the overall predictive power was quite low (7%). For the MS group, the predictive power rose to 28%. For the HD group, the predictive power was 50%. These results suggest that pathological association of functional systems may be a marker of brain dysfunction and that the affected systems may be delineated by these methods.

Pathological association and dissociation of brain functions are well-accepted tenets of behavioural neurology and neuropsychology. Strub and Geschwind (1983) may have best formalized these tenets in their definition of a neurological syndrome. As a concrete example, they suggest that to a trained clinician, the presence of language disturbance and right-sided motor impairment should suggest left hemisphere pathology. In this example, language and right-sided motor functions are pathologically associated, whereas right- and left-sided motor functions are pathologically dissociated. This type of formulation or theoretical model can be easily translated into testable statistical hypotheses. However, unlike in many clinical studies of neuropsychological abnormalities, the statistic of interest should be a test of association (i.e., a correlation coefficient) not a test of group differences in performance (i.e., a *t* test or more generally, an analysis of variance). The question of interest thus becomes whether intertest correlations change with brain disease or insult (Fogel, 1962).

Given the paucity of studies examining this theoretical model from a statistical standpoint, it would be premature at this stage to make precise statistical hypotheses regarding the changes in test relationships in different clinical populations. Rather, broader statistical hypotheses are required to determine: (1) which functional systems come into play while performing a specific task, and (2) whether these systems are the same or different in clinical populations.

Examination of these intertest correlations in clinical samples is of import for two reasons. First, the correlations may provide insight into why a clinical sample does poorly on a particular test. Specifically, if one accepts that most tests require a degree of integration of different brain functions in order to frame a response, the actual impaired functions may vary among clinical samples. Stated simply, there may be more than one explanation for poor performance on a

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given test. Therefore, from both a clinical and theoretical standpoint, the reason for poor performance is of interest. The second reason is in a sense the converse of the first. In some circumstances, a clinical sample's performance may not differ from normal but the functional systems engaged in successful completion of the task may differ from those employed by a normal sample.

For example, the figures on the Benton Visual Retention Test may be encoded either verbally (i.e., a small square and a larger circle, then an equal-sized triangle to the right) or visually. Clearly a verbal strategy will break down on more complex stimuli but it may be sufficient to obtain a normal score. Such hypothesis can be explored by examining variations in intertest correlations between clinical and normal samples.

Although these points are recognized in conceptual models of brain function, systematic empirical studies are rare in the literature (for review see Ryan, Clark, Klonoff, & Paty, 1993). Therefore, the purpose of the current study was to examine the relationship between performance on the WAIS-R subtests, tests of motor functions, and the word fluency test in samples of normal subjects (n = 92), and patients with multiple sclerosis (n = 196) or with Huntington's disease (n = 70). Multiple sclerosis and Huntington's disease were chosen because the underlying neuropathology (i.e., demyelination and atrophy of the caudate nuclei) is well accepted. The word fluency test was chosen as the neuropsychological measure for a number of reasons. First, given the ease of administration and sensitivity to brain dysfunction, the test is often used in research studies and clinical assessments (Borkowski, Benton, & Spreen, 1967; Lezak, 1976). Second, although simple in terms of task demands, poor performance can occur for many reasons. For example, Martin, Wiggs, Lalonde, and Mack, (1994) suggest that the fluency test requires lexical search, retrieval, speech, response initiation, and maintenance as well as switching of set. Third, based on Luria's work, a tacit or common assumption is that the test is a measure of left anterior frontal lobe function (Luria, 1966). Although this assumption is correct for some cases, it is clearly not correct for many others. For these reasons, the question of interest was which functional systems predict word fluency performance in normal subjects and the two neurological samples.

In the current study, because speech production is essential for the verbal form of the word fluency test, the subjects were given two tests of motor function, finger tapping and the Klove pegboard. Similarly, the subjects were given the verbal subtests of the WAIS-R as a measure of language facility and resources. Finally, the performance subtests of the WAIS-R were given as measures of nonverbal cognitive functions. The Digit Symbol subtest was excluded because of the relatively large motor component in this test.

Three primary questions were addressed statistically. First, did the three groups differ significantly in terms of levels of performance on each test? Second, did the patterns of intertest relationships differ among the three groups? Third, did the three groups differ in terms of task importance or weighting in predicting performance on the word fluency test? In addition, because gender, age, and level of education may be related to performance on cognitive tasks, the relationship between these variables and test performance in the three groups was also examined (Parsons & Prigatano, 1978). Because age corrections are applied to the three IQ estimates for the WAIS-R, these correlations were not examined.

METHODS

Subjects

The data for this study originated from two independent studies. The patients with multiple sclerosis (MS) (n = 196) and the normal controls (n = 92) were initially examined to determine the effect of early stage or mild MS on cognitive functions. The selection criteria for the patients with MS were as follows: (1) age less than 50 years; (2) a diagnosis of clinically definite MS with a relapsing/remitting course (Poser et al., 1983); (3) in remission at the time of assessment; (4) diagnosis made before the age of 40; (5) functionally independent as assessed by the Kurtzke Clinical Rating Scales and the Expanded Disability Status Scale (Kurtzke, 1961, 1983); (6) no medication or excessive nonprescri-

bed drug usage; (7) no other complicating medical condition; and (8) no history of psychiatric illness predating the diagnosis of MS.

Where possible, the subjects with MS were asked to find a same-gender unrelated control with similar background and interest. Once potential normal subjects were identified, they were interviewed by phone to ensure that they met the same criteria in terms of age, medical complications, psychiatric history, and drug usage. These procedures ensured that the two groups were well matched in terms of gender (72.9% female in the MS group, 70.7% in the normal group), mean age (34.4 and 35.5 years, respectively) and mean education level (13.5 and 13.9, years, respectively). For the MS group it should be noted that the mean Kurtzke mentation score was 0.06, whereas the mean Extended Disability Status score was 1.95; thus suggesting minimal neurological disability.

The patients with Huntington's disease (HD) (n = 70) were volunteers for a drug study who had been neuropsychologically assessed prior to drug administration. Entry criteria included: (1) a positive family history for HD; (2) a disease duration of less than 5 years; (3) manifestation of early symptoms (Paulson, 1979); (4) no caudate atrophy on structural imaging scans and (5) no other complicating medical condition. The diagnosis of HD was made by two independent neurologists. The sample was 57% female with a mean age of 44.3 years and mean education level of 12.3 years. Because the average life-span post-onset is 12–17 years and the mean duration of symptoms was 3.4 years, this sample may be considered as in the early stages of HD (Hayden, 1981).

Although the MS and normal samples are well matched in terms of demographic variables, there are obvious differences between these two samples and the HD sample. First, the male to female gender ratio is higher in the HD sample than the other samples. Because HD occurs almost equally in men and women (Hayden, 1981) whereas MS is more frequent in women than men (Peyser & Poser, 1986), such a difference is a function of the disease and is to be expected. Similarly, because on average MS symptoms manifest earlier than HD symptoms, the HD group is about 9 years older than the MS and normal groups. In addition, the MS group and the normal group attended school for approximately 1 year longer than the HD group. This difference cannot be accounted for by the disease process because for both clinical groups, disease onset clearly post-dates the normal educational period. Both age and education have been cited as variables that may affect neuropsychological test performance. For this reason, the relationships between these variables and test performance were examined within each group. Gender was also similarly analyzed because the groups differed on gender distribution.

Assessment Materials

The Wechsler Adult Intelligence Scale-Revised was administered to each subject in the standard manner (Wechsler, 1981). Finger tapping speed (FTT; Halstead, 1947) was measured three times for a span of 10s for the dominant and nondominant hands. The three trials were then averaged for each hand. The Klove Grooved Pegboard Test (Klove, 1963) was administered using each hand and an average time per peg calculated for the dominant hand and nondominant hands. The verbal Word Fluency Test (subtest of the Primary Mental Abilities tests; Thurstone & Thurstone, 1962) was given using the letters *f*, *a*, and *s* with a 1-min response period for each letter. The sum of the number of acceptable responses was calculated. The abbreviations used for each test in the tables are given in Table 1.

Analysis

The data were considered from four perspectives. First, the correlations between the test scores and the demographic variables (i.e., age, gender, and education) were calculated for groups to determine if the same relationship existed within each group or whether the disease process disrupted the normal relationship. Second, an analysis of variance was done on each variable with group membership as the independent variable. Tukey post hoc technique for paired comparisons was used to determine on which variables the groups differed ($p <$ .05). Third, intertest correlations were calculated to determine if they were different for the two clinical groups in comparison to the normal subjects. Given the number of correlations, significance was defined as $p < .01$. This procedure reduces the Type I error rate and hence increases the reproductibility of the findings. Finally, a step-wise regression was used to predict word fluency performance from the other tests and the demographic variables for each group. In these analyses, two questions were of interest: (1) did the three groups differ in terms of the magnitude of prediction, and (2) did the predictive variables differ among the three groups?

Table 1. Test Abbreviations Used in Subsequent Tables.

Abbreviation	Test Name
WAIS-R	Wechsler Adult Intelligence Scale-Revised
VIQ	Verbal Intelligence Quotient
PIQ	Performance Intelligence Quotient
FSIQ	Full Scale Intelligence Quotient
Inf	Information Subtest
DSp	Digit Span
Voc	Vocabulary
Ari	Arithmetic
Com	Comprehension
Sim	Similarities
PC	Picture Completion
PAr	Picture Arrangement
BD	Block Design
OA	Object Assembly
FTD	Finger Tapping Dominant
FTND	Finger Tapping Nondominant
GPD	Klove Grooved Pegboard Dominant
GPND	Klove Grooved Pegboard Nondominant
WFT	Word Fluency Test

RESULTS

Correlations of Demographic Variables with Test Scores

The correlations for each group between the test scores (i.e., standard scaled scores for the WAIS-R) and the demographic variables age and level of education, are presented in Table 2. For age, one significant correlation was found in each group. For the normal subjects, performance on the Grooved Pegboard Test with the nondominant hand was significantly correlated with age, whereas for the clinical subjects, age was significantly correlated with the Vocabulary subtest for the MS group and with the Information subtest for the HD group. Given that the number of significant correlations approximate chance expectancy (i.e., 3 of 45) and no consistent pattern was found, these data suggest that age is not a potentially confounding variable.

For education, a different pattern emerges. For the normals, as expected, education was significantly correlated with four of the WAIS-R verbal subtests (Information, Vocabulary, Comprehension, and Similarities). The number of significant correlations increased to eight for the MS group: All of the WAIS-R subtests except Digit Span and Object Assembly were significantly correlated. In contrast for the HD group, the number of significant correlations fell to two; the Information and Vocabulary subtests were significantly correlated. The differences in these correlation patterns cannot be attributed to differences in statistical power due to sample size, because the numerical coefficients are typically larger in the MS group. Although it is beyond the scope of this paper to rationalize why the number of significant correlations increases in the MS group and decreases in the HD group, these results would preclude conventional analysis of covariance for examining between-group differences, because the within-group regression coefficients differ.

Finally, for gender, significant correlations were found for the finger tapping test (for both the dominant and nondominant hands) in all three groups with males posting higher scores. Because the effect sizes were approximately equivalent (r was approximately .35), and confined to finger tapping, this variable was not included in subsequent analyses.

Table 2. Demographic and Test Correlations by Group.

	Age			Education		
	Norm	MS	HD	Norm	MS	HD
Inf	.12	.17	.27*	.46*	.50*	.38*
DSp	−.02	−.04	.06	.21	.13	−.11
Voc	.09	.21*	.12	.43*	.44*	.41*
Ari	.12	−.02	−.03	.14	.25*	.13
Com	.11	.15	.19	.36*	.38*	.07
Sim	.03	.09	.17	.35*	.29*	.13
PC	−.06	.01	−.03	.15	.26*	−.12
PAr	−.08	−.04	−.08	.10	.24*	.02
BD	−.25	−.09	−.14	.16	.27*	.04
OA	−.14	.01	−.05	−.08	.12	.12
FTD	−.06	−.13	.04	.03	.08	−.05
FTND	−.16	−.05	.04	.05	.09	−.03
GPD	.17	−.08	−.20	−.14	−.15	.00
GPND	.28*	−.05	−.10	−.07	−.14	.01
WFT	.15	.10	−.04	.14	.14	.10
Mean	35.5	34.4	44.3	13.9	13.5	12.3
SD	7.3	7.8	10.5	2.2	2.2	2.4

Group Differences

The group means, standard deviations, resulting *F*-values and the results of the Tukey post hoc comparisons are given in Table 3 for each test. Each of the 18 omnibus *F*-tests was significant ($p < .01$). With respect to the post hoc comparison, the MS group performed significantly lower than the control group on 9 of the 18 tests. These tests were Performance Intelligence Quotient, Full Scale Intelligence Quotient, Picture Completion, Block Design, Object Assembly, Klove Grooved Pegboard Nondominant hand, Finger Tapping Dominant hand, Finger Tapping Nondominant hand, and Word Fluency Test. The HD group performance was significantly lower than either the control group or the MS group on all 18 variables. However, although significant performance differences were present, it is of interest to note that based on group averages, the FSIQ of the MS group would be classified as normal and the standard deviations do not suggest excessive variability around the mean. Specifically, the observed variability is equivalent to the control group (i.e., *SD* = 10.7 and 11.9) and less than that reported for the standardization sample (*SD* = 15). The mean FSIQ of the HD group fell in the high end of the low average range with a similar standard deviation (*SD* = 10.2). Therefore, these results suggest impairment or reduction of cognitive function but intellectual functions on average remain within normal limits (Wechsler, 1981).

Because both MS and HD affect motor functions, the motor test results are consistent with expectancy, with the MS group exhibiting impairment on three of the four variables as compared to the control group and the performance of the HD group being worse than the MS and normal group on all four variables. The greater level of motor involvement in the patients with HD as compared to the patients with MS is consistent also with clinical presentation in the two disorders. For the word fluency test, the performance of the MS group, although significantly lower than that of the normal controls, was still within the normal range based on available normative data (Lezak, 1976). In contrast, for the HD group the mean word fluency score fell al-

Table 3. Test Results for Each Subject Group: Means with Standard Deviations in Parentheses.

		Controls		MS		HD		F[1]	Comparisons[2]
WAIS-R	VIQ	106.8	(11.7)	104.6	(11.4)	91.5	(10.4)	43.0	C MS HD
	PIQ	107.9	(10.4)	100.2	(12.9)	85.8	(11.7)	67.2	C MS HD
	FSIQ	107.8	(10.7)	102.8	(11.9)	88.1	(10.2)	64.7	C MS HD
Subtests	Inf	10.3	(2.6)	10.4	(2.5)	8.9	(2.7)	9.7	C MS HD
	DSp	11.1	(2.3)	10.7	(2.9)	7.3	(2.3)	54.5	C MS HD
	Voc	12.0	(2.6)	11.4	(2.3)	9.5	(2.5)	23.4	C MS HD
	Ari	11.1	(2.7)	10.7	(2.7)	7.6	(2.3)	42.4	C MS HD
	Com	11.3	(2.3)	10.6	(2.3)	8.7	(2.3)	27.0	C MS HD
	Sim	10.9	(2.3)	10.4	(2.2)	7.6	(2.0)	54.9	C MS HD
	PC	10.1	(2.2)	9.4	(2.3)	6.6	(2.6)	40.6	C MS HD
	PAr	10.9	(2.6)	10.3	(2.9)	6.5	(2.8)	59.6	C MS HD
	BD	11.1	(2.3)	9.7	(2.6)	7.3	(2.4)	46.4	C MS HD
	OA	10.0	(2.7)	8.4	(2.7)	6.6	(2.9)	27.5	C MS HD
Motor	GPD	2.5	(0.3)	3.2	(1.1)	5.1	(1.8)	65.0	C MS HD
	GPND	2.6	(0.3)	3.5	(1.4)	5.0	(1.9)	64.2	C MS HD
	FTD	48.1	(6.9)	42.0	(6.5)	35.3	(10.6)	55.7	C MS HD
	FTND	42.7	(6.2)	37.5	(6.7)	30.3	(10.6)	53.2	C MS HD
	WFT	41.4	(10.3)	37.1	(11.6)	22.3	(8.9)	68.0	C MS HD

[1] $p < .001$ for all F values; [2] Underlined groups are not significantly different.

most two standard deviations below the score for the normal group or below the fifth centile.

Intertest Correlations for the Three Groups

The intertest correlations for the normal group are reported in Table 4. Of the 105 unique correlations, 29 were significant ($p < .01$). This number of significant correlations clearly exceeds chance expectancy. The pattern of correlations for the WAIS-R subtests is consistent with those reported in the WAIS-R manual although the overall magnitude is lower (Wechsler, 1981). Specifically, the verbal subtests were significantly correlated (i.e., 13 of 15 possible correlations were significant). Similarly, the performance subtests were significantly correlated but to a lesser degree (3 of 6 possible correlations were significant). In addition, the verbal subtests are significantly correlated with some of the performance subtests (11 of 24 possible correlations were significant). Ten of these correlations are accounted for by the Picture Completion and Picture Arrangement subtests. Both of these subtests probably require verbal mediation. The word fluency test was significantly correlated with the Arithmetic subtest, whereas the motor tests were not correlated with any other tests; only the dominant/nondominant measures were significantly correlated.

The intertest correlations for the MS group are presented in Table 5. Of the 105 unique correlations, 66 were significant ($p < .01$). For the WAIS-R subtests only 2 of the 45 possible correlations were not significant. In comparison to normal subjects where the word fluency test was virtually independent of the other tests (i.e., one significant correlation), this test was significantly correlated with all of the WAIS-R subtests. The motor tests were also significantly intercorrelated (5 of 6 possible correlations were significant) and sporadic significant correlations were present between the motor tests and the performance subtests. The increase in the number of significant correlations cannot be ascribed to the larger sample size in the MS group, because the magnitude of the correlations was also larger (Cohen, 1977). Clearly, a comparison of the two correlation matrices suggests greater

Table 4. Intertest Correlations for Normal Subjects.

	Inf	DSp	Voc	Ari	Com	Sim	PC	PAr	BD	OA	WFT	FTD	FTND	GPD	GPND
Inf	1.00	.23	.69*	.44*	.37*	.48*	.24*	.37*	.22	.20	.20	.11	.03	−.14	.00
DSp		1.00	.45*	.34*	.25	.25*	.27*	.27*	.21	−.11	.16	.04	.02	.00	−.02
Voc			1.00	.49*	.68*	.62*	.23	.39*	.25	.08	.21	.07	.02	−.15	−.04
Ari				1.00	.32*	.42*	.32*	.36*	.39*	.06	.28*	.11	.08	−.06	−.01
Com					1.00	.57*	.30*	.09	.19	.00	−.04	−.06	−.09	−.04	−.05
Sim						1.00	.31*	.28*	.22	.06	.18	−.03	−.01	−.09	−.10
PC							1.00	.13	.39*	.18	.19	−.06	.04	−.14	−.06
PA								1.00	.26*	.15	.13	.10	.07	−.00	−.01
BD									1.00	.53*	.00	.04	.07	−.21	−.09
OA										1.00	−.09	.06	−.04	−.24	−.02
WFT											1.00	.08	.03	−.07	−.04
FTD												1.00	.80*	−.04	−.08
FTND													1.00	.07	.00
GPD														1.00	.46*
GPND															1.00

* $p < .01$, two-tailed.

Table 5. Intertest Correlations for Subjects With Multiple Sclerosis.

	Inf	DSp	Voc	Ari	Com	Sim	PC	PAr	BD	OA	WFT	FTD	FTND	GPD	GPND
Inf	1.00	.26*	.66*	.46*	.57*	.43*	.32*	.31*	.39*	.27*	.39*	.12	.10	−.17	−.15
DSp		1.00	.30*	.44*	.25*	.26*	.28*	.16	.27*	.11	.36*	.08	.04	−.07	.04
Voc			1.00	.43*	.60*	.50*	.38*	.29*	.32*	.28*	.36*	.04	−.03	−.14	−.13
Ari				1.00	.36*	.33*	.31*	.24*	.43*	.35*	.31*	.18	.13	−.13	−.07
Com					1.00	.49*	.30*	.38*	.35*	.22*	.36*	.10	.13	−.15	−.15
Sim						1.00	.40*	.30*	.37*	.28*	.39*	.14	.12	−.16	−.13
PC							1.00	.35*	.38*	.25*	.25*	.10	.28*	−.14	−.18
PAr								1.00	.38*	.33*	.26*	.11	.17	−.31*	.26*
BD									1.00	.58*	.32*	.25*	.23*	−.28*	−.21
OA										1.00	.27*	.13	.16	−.33*	−.26*
WFT											1.00	.13	.17	−.19	−.17
FTD												1.00	.71*	−.39*	−.18
FTND													1.00	−.36*	−.38*
GPD														1.00	.61*
GPND															1.00

* $p < .01$, two-tailed.

dependency both within and between functional systems for the patients with MS.

The intertest correlation matrix for the HD group is reported in Table 6. Of the 105 unique correlations, 68 were significant ($p < .01$). The overall pattern of correlations is very similar to that of the MS group, with a high number of significant correlations among the WAIS-R subtests (35 of the 45 possible correlations were significant), a high number of significant correlations among the motor tests (4 of 6 possible correlations were significant), and a dependence between the motor and cognitive tests (18 of 44 correlations were significant). The word fluency test was also significantly correlated with all of the cognitive tests but in addition, it was significantly correlated with 3 of the 4 motor tests.

From these tables, it is apparent that in comparison to the normal group, the intertest dependency is much greater for the HD and MS groups. Two statistical reasons could account for these differences. First, as discussed earlier, the difference in sample size might increase statistical power in the MS group. However, because the magnitude of correlation coefficients was higher in the MS group and similar results were found for the HD group, which had the smallest sample size, such an explanation is unlikely. Second, if the variance in the clinical groups was much larger than in the normal group then the correlation coefficients in the normal sample might be smaller due to attenuation. However, for the WAIS-R subtests, the observed standard deviations were more or less equal among the three groups. For the word fluency test, the standard deviation was larger in the MS group than in the normals whereas it was smaller for the HD group. For the Grooved Pegboard Test, the standard deviations were higher in the clinical groups than in the normals whereas for finger tapping, the standard deviations were more or less equivalent in the normal and MS groups, but larger in the HD group. Given the lack of a pattern consistent with systematic variance attenuation, it is unlikely that the observed patterns of intertest correlation are a function of statistical artifact.

Multiple Regression Analyses Predicting Word Fluency Performance

The results of the step-wise multiple regression analyses predicting word fluency performance from the other tests for each group are displayed in Table 7. For the normals, only one test was selected as a significant predictor, the Arithmetic subtest of the WAIS-R. Although this result is consistent with intertest correlations presented in Table 4, the finding is of interest for two reasons. First, the level of predictive power, although significant, is extremely low (7% of the total variability). Second, tests that one might suspect would make unique and significant contributions to the prediction equation (e.g., the verbal subtests) do not.

In the MS group, the predictive power increased substantially to 26% of the total variability. The predictors – Similarities, Digit Span, Information and Object Assembly – are

Table 7. Results of Step-Wise Regression Analysis.

Group	Step	R	R^2	$\hat{}R^2$	Adj R^2	Predictor
Normal	1	0.28*	0.08	–	0.07	Arithmetic
MS	1	0.39*	0.15	–	0.14	Similarities
	2	0.46*	0.21	0.06	0.21	Digit Span
	3	0.51*	0.25	0.04	0.25	Information
	4	0.52*	0.26	0.01	0.25	Object Assembly
HD	1	0.5*	0.30	–	0.30	Finger Tapping (ND)
	2	0.65*	0.43	0.13	0.41	Vocabulary
	3	0.72*	0.52	0.09	0.50	Digit Span

*$p < .01$.

Table 6. Intertest Correlations for Subjects With Huntington's Disease.

	Inf	DSp	Voc	Ari	Com	Sim	PC	PAr	BD	OA	WFT	FTD	FTND	GPD	GPND
Inf	1.00	.27	.74*	.50*	.63*	.70*	.34*	.19	.30*	.19	.37*	.07	.16	−.31*	−.17
DSp		1.00	.21	.46*	.40*	.37*	.48*	.35*	.34*	.43*	.50*	.27	.28	−.26	−.35*
Voc			1.00	.37*	.60*	.60*	.32*	.32*	.22	.18	.45*	.16	.16	−.24	−.17
Ari				1.00	.34*	.62*	.48*	.29	.37*	.31*	.43*	.12	.18	−.19	−.20
Com					1.00	.53*	.47*	.46*	.40*	.39*	.39*	.22	.25	−.20	−.38*
Sim						1.00	.55*	.16	.29	.29	.43*	.09	.13	−.31*	−.17
PC							1.00	.40*	.60*	.60*	.42*	.33*	.27	−.30*	−.41*
PAr								1.00	.57*	.58*	.36*	.38*	.36*	−.15	−.42*
BD									1.00	.73*	.42*	.31*	.31*	−.26	−.42*
OA										1.00	.44*	.45*	.41*	−.28	−.55*
WFT											1.00	.51*	.55*	−.25	−.44*
FTD												1.00	.91*	−.29	−.57*
FTND													1.00	−.26	−.57*
GPD														1.00	.81*
GPND															1.00

*$p < .01$, two-tailed.

all subtests of the WAIS-R. After the entry of Similarities into the equation, the remaining predictors made small (1% to 6%) but significant contributions to the equation. This pattern would suggest that the significant first-order correlations in Table 5 are reflecting a strong single dimension. For the HD group, the predictive power again increased substantially, to 50% of the total variability. However, unlike the MS group, over half of this predictive power (29%) arose from a motor test, that is, finger tapping with the nondominant hand. The remainder of the predictive power (21%) was accounted for by the Vocabulary and Digit Span subtests. Because the first-order correlations (Table 6) suggest that Vocabulary and Digit Span are relatively independent of nondominant finger tapping, these results suggest that both cognitive and motor function affect word fluency performance in HD and that these effects are relatively independent. Hence, dependent upon the nature of the neurological disease and its severity, different functional systems may account for poorer performance. Finally, it should be noted that education and age were included in these regression analyses but were never identified as significant predictors.

DISCUSSION AND CONCLUSIONS

Before discussing these findings and their implications, a number of potential methodological confounds should be considered. First, because the premise of this analysis strategy is to determine if differences in word fluency performance between normal subjects and the two clinical groups arise from impairment of the same or different functional systems, one must have confidence that the data are consistent with previous studies. For the normals, overall levels of performance are consistent with established values and do not suggest either superior or deficient abilities (Lezak, 1976; Wechsler, 1981). The variances around the WAIS-R IQ and subtest means are slightly less than expected and in all probability may reflect a sampling bias. Specifically, the sampling procedure for the normal subjects would exclude intellectually challenged individuals because the patients with MS had to be living independently and hence, for both groups institutionalized individuals would be excluded; thus causing an undersampling of the low end of the distribution of general intelligence. This sampling bias could account for the smaller than expected intertest correlations for the WAIS-R subtests. However, the overall pattern of correlations is consistent with those reported in the manual and with results of factor analytic studies (Leckliter, Matarazzo, & Silverstein, 1986; Waller & Waldman, 1990). Moreover, this bias would also exist in the MS sample where the variances are equivalent to the normal group but the intertest correlations are consistently larger. Although the overall IQ scores for the normals are in the normal range, and their pattern of intersubtest correlations are consistent with expectancy, the lower absolute values of these correlations may suggest that anomalies exist in the normal sample.

The second methodological issue is whether the performance of the MS and HD groups as compared to the normal group is compatible with previous research. For the MS group the presence of subtle cognitive anomalies in a proportion of patients with mild MS is now generally accepted (Beatty & Gange, 1977; Grant, McDonald, & Trimble, 1989; Peyser & Poser, 1986; Rao, 1986). Moreover, this cognitive impairment appears to be independent of other psychological phenomena such as depression or motor/sensory symptoms (Goldstein & Shelley, 1974; Good, Clark, Oger, Paty, & Klonoff, 1992; Rao et al., 1991). The comparisons with the normal group suggest that impairment of cognitive functions was present in this MS group in terms of scores on some WAIS-R performance subtests and the word fluency test. In addition, performance of the motor tests was also impaired as expected. The HD group performed significantly worse on all tests as compared to either the MS or normal groups. However, the mean FSIQ of the HD group fell at the high end of the low normal range, thus suggesting that these patients were at the early stages of the dementing process. As with the MS group, these results were expected based on previous research (Boll, Heaton, & Reitan, 1974; Fedio,

Cox, Neophytides, Canal-Fredrick, & Chase, 1979; Norton, 1975).

The third methodological concern is the influence of the demographic variables on the subsequent results. For age the number of significant correlations was consistent with chance and the overall magnitude of the correlation suggests a relatively small impact on overall performance (i.e., less than 8% of the total variability). For education, the normals had the expected significant correlations with the verbal subtests of the WAIS-R whereas for the MS group the performance subtest correlations with the exception of Object Assembly, were also significantly correlated with this variable. In contrast, for the HD group, only the Information and Vocabulary subtests were significantly correlated with education. These results when combined with the ANOVA results, suggest a subtle interaction between severity of disease-related impairment and level of education. Specifically, for the HD group, one can speculate that the disease process has almost removed the effect of education whereas for the patients with MS, education may provide a basis for adapting to the mild levels of impairment. However, for the purposes of this study, these results precluded using level of education as a covariate in the ANOVA procedures. Age and education were included for the within-group multiple regression analyses and found to be nonsignificant predictors.

The final methodological consideration is simply whether the observed disparities in intertest relationships can be accounted for by statistical explanations, namely, group differences in sample size and standard deviations (for review see Strauss & Brandt, 1985). These issues were discussed in the Results section; thus, the only statement to be made here is that the results were not consistent with such explanations.

From the discussion thus far, it is apparent that in terms of overall levels of performance and variation, the results are in the main consistent with expectation and the established literature. Therefore, the primary question of interest, namely, pathological association/dissociation and their implications to understanding disordered brain functioning, can be addressed. The first major finding of this study is that for both clinical groups, there was strong evidence to support pathological associations of brain functions. For the two clinical groups, 63.8% (or greater) of the unique intertest correlations were significant as compared to only 27.8% for the normal group. This finding by its nature precludes finding evidence for pathological dissociation in these data sets. For example, for the 29 significant correlations found for the normal group, only one was not significant in the MS group (Digit Span with Picture Arrangement), whereas in the HD group, 4 were not significant (Digit Span with Vocabulary and Information, Arithmetic and Similarities with Picture Arrangement). In addition to the higher number of significant correlations in the clinical groups, there was a trend for the magnitude of the correlations to be greater in these groups.

In a study of patients with MS, Beatty and Gange (1977) found increased intertest correlations in tests of memory and motor function both within and between these domains. Although not directly comparable to this study, increased intertest correlations are the common finding. In a study of patients with HD, Strauss and Brandt (1985) found less covariance and variance in the WAIS-subtest variance/covariance matrix of the HD group than in those of controls ($n = 43$) or subjects at risk for HD ($n = 38$).

These findings are in direct contradiction to the results of the present study. Moreover, the two HD groups were virtually equivalent in terms of age, education, and gender distribution. The only clinical difference between the groups was duration of symptoms: the subjects in the current study had symptoms for less than 5 years, whereas the patients in the Strauss and Brandt study had been symptomatic for 5.1 years on average ($SD = 4.2$). Our only explanation for the difference may be the inherent difference between the WAIS and WAIS-R. For example, the WAIS typically yields an FSIQ estimate about 8 points higher than the WAIS-R (Wechsler, 1981). Hence, although the FSIQ estimates for the two studies appear comparable (88.1 vs. 88.6), the patients in the Strauss and Brandt study may actually have been performing at a lower level than the patients in the current study and hence the variance may be more atten-

uated. Although this explanation may explain the differences in part, it cannot account for difference in direction (i.e., greater vs. less covariance in HD) of the two findings. Hence, we suggest that this issue requires further examination.

On the surface, one might interpret these findings as a general deterioration factor. However, the multiple regression analyses predicting word fluency scores suggests otherwise. For the normals, the predictive power of the tests is surprisingly low. Only the Arithmetic subtest of the WAIS-R accounted for a significant portion of the variance on the word fluency test (7%). Because this test may measure aspects of attention and retrieval, this result supports the contention that these functional systems are involved in the task. However, 93% of the subject variation on this test could not be accounted for even though the test battery included tests often associated with verbal abilities.

For the patients with MS, the multiple regression analysis predicted 26% of the total variability on the word fluency test. Based on the first-order correlations and the small contribution of the second, third, and fourth tests, these predictors appear to represent a common domain with some functional specialization. For example, the Digit Span and Information subtests of the WAIS-R have been viewed as measuring attentional and memory retrieval systems whereas the Similarities and Object Assembly subtests may measure verbal and spatial abstraction or concept formation. In terms of a negative finding, the results of the intercorrelations and multiple regression analysis suggest that impaired motor functions do not account for the observed decrements on the word fluency test. Rather, this decrement results from impairment of cognitive systems, in particular,attention, retrieval, and perhaps concept formation.

For the patients with HD, the multiple regression analysis accounted for 50% of the observed variability on the word fluency test. This large increase arose primarily from the relationship between finger tapping and word fluency. This relationship would suggest that the motor process of producing the speech response is impaired in HD. This conclusion is clearly consistent with clinical observations of the swallowing difficulties in patients with HD and, at times, their accidental deaths by choking on food. Therefore, a percentage of the observed decrements on the word fluency task result from motor impairment associated with the disease, not cognitive impairment per se. However, the Vocabulary and Digit Span subtests did contribute a significant amount of variability to the prediction equation, thus suggesting cognitive impairment as well. The inclusion of the Digit Span subtest suggests impairment of the attentional/retrieval mechanism whereas the inclusion of the Vocabulary subtest may indicate disruptions more specific to language systems.

These results are of interest for theoretical and clinical reasons. Specifically, they suggest that pathological association of functional systems is common. Hence, poor performance on a particular test cannot be associated with a single cause. For example, even though MS is, by definition, a motor/sensory disease, the application of these techniques adds further support to the notion that independent cognitive impairment occurs. Moreover, the tests that were significant predictors of word fluency performance for the MS group, were actually not significantly lower than the normal scores in the univariate analysis of the group means except for the Object Assembly subtest. Equally important is the fact that these predictors were not significant predictors in the normal group. Although the HD group did differ from the control group on every test, the importance of the motor speech system for the subjects with HD in determining response output on the word fluency test is brought to the forefront by this analysis. Moreover, the contribution of cognitive systems is of a lesser magnitude than the motor systems. This cognitive component is of the same magnitude in both clinical groups and may in fact represent impairment of common (e.g., attention/retrieval) as well as unique systems (i.e., concept formation in the MS group vs. language in the HD group).

In conclusion, this study attempts to illustrate that by examining associations/dissociations of intertest correlations in normal and abnormal groups, we may better understand the inherent functional systems underlying specific beha-

viours and further understand which systems are impaired in neurological diseases. These data suggest that for these tests if functional systems are intact, the observed variability on a test may not be reliably predicted by other tests, as in the case of the normal group. However, when the system's functional capacity falls below a threshold, the impairment of this system may dramatically affect performance on the test of interest. By changing the focus of analysis strategies from the examination of group means to the examination of intertest relationships, our understanding of functional brain systems and disease will be greatly enhanced.

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