Article abstract

Intellectual correlates of electroencephalographic epileptiform activity were examined by administering the Wechsler Adult Intelligence Scale to epileptic patients divided into groups on the basis of presence or absence, average rate, and topographic distribution of discharges. The results showed that lower intelligence levels were associated with the presence of discharges, especially when they were generalized rather than focal and when they occurred at an average rate of more than one per minute. An examination of patients having discharges ipsilateral and contralateral to their handedness showed few findings, as did an analysis based on an assessment of strengths and weaknesses within individuals. The results suggest that electroencephalographic epileptiform activity is significantly related to the intellectual functioning of epileptics.

Relationships between intelligence and electroencephalographic epileptiform activity in adult epileptics

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That electroencephalographic epileptiform activity may be associated with deficits in performance on cognitive-motor tasks has been demonstrated on a number of occasions.[1-4] However, the interaction of this electroencephalographic abnormality with various measures of intelligence has not been fully explored, and complicating factors have obscured the results of previous research. A general source of ambiguity is that a number of investigations were not designed to clearly distinguish the role played by epileptiform discharges in relationship to intelligence. For example, electroencephalographic abnormalities consisting of epileptiform as well as nonepileptiform patterns have often been considered together,[5-7] and electroencephalographic findings in epileptic patients have not always been studied independently of those of individuals with other neurologic disorders.[8,9]

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More specifically, few researchers have evaluated the significance of the average rate of occurrence of epileptiform activity and its relationship to intellectual abilities. However, one study[10] showed that individuals with frequent epileptiform discharges did more poorly on the performance measures of the Wechsler Adult Intelligence Scale (WAIS) than persons having only a small amount of such activity. Neither group performed as well as patients having no epileptiform discharges. Thus, the relative abundance of epileptiform discharges appears to be relevant to intelligence, but this has not been completely explored.

Another factor is the possible association between topographic distribution of epileptiform activity and intelligence. There is some evidence that generalized discharges may have a more substantial impact than focal discharges on intellectual abilities,[10,11] but this has not been demonstrated consistently.[12,13] Kløve[8] has reported that electric abnormalities involving the left cerebral hemisphere are typically associated with lowered verbal abilities on the Wechsler-Bellevue Scale, while similar findings involving the right hemisphere are associated with lowered performance abilities. Other investigators[10,14,15] have raised the possibility that the Similarities and Picture Arrangement subtests may be

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related to the functioning of the dominant and nondominant hemispheres, respectively, but none have specifically evaluated epileptiform activity in this regard.

Finally, some discordant results in this area can perhaps be related to differences in the tests used to evaluate intelligence. For example, two groups of investigators[13,16] used the Wechsler-Bellevue Scale and found that individuals with focal electroencephalographic epileptiform discharges performed more poorly on tests of verbal intelligence than on tests of performance intelligence. Two other groups,[10,12] however, used the WAIS and reached exactly the opposite conclusion, regardless of the presence or absence or topographic distribution of epileptiform activity. Thus, it is not clear even what basic profiles of intellectual decrement are related to these electroencephalographic parameters.

In view of the contradictory and incomplete results cited, the present investigation was designed to systematically assess the possible relationships between aspects of intelligence and the presence or absence, topographic distribution, and average rate of occurrence of electroencephalographic epileptiform discharges in adult epileptics.

Materials and methods. The 90 patients included in this investigation were uncontrolled epileptics being treated at the Seizure Clinic at the University of Washington Hospital. These 57 males and 33 females averaged 28.38 years of age (SD = 8.74) and 12.26 years of formal education (SD = 2.00). Information available on 88 of these patients revealed that they had been experiencing seizures since the mean age of 12.50 years (SD = 8.65) and that the average duration of their seizure disorders was 15.92 years (SD = 9.60). Table 1 shows a classification of these subjects on the basis of their electroencephalographic findings. Clinically, their primary seizure diagnoses were as follows: Six had generalized tonic-clonic seizures, 12 had generalized seizures other than tonic-clonic, 16 had elementary partial seizures, 55 had complex partial (psychomotor) seizures, and one had unclassified seizures. In addition, 47 of these patients had reported generalized tonic-clonic seizures on one or more occasions.

The WAIS was used to assess intelligence. This scale contains six subtests of verbal intelligence (Information, Comprehension, Arithmetic, Similarities, Digit Span, Vocabulary) and five subtests of performance intelligence (Digit Symbol, Picture Completion, Block Design, Picture Arrangement, Object Assembly). The test was given and scored according to standard instructions.[17]

Electroencephalograms (EEGs) were done during wakefulness on 16-channel electroencephalographs (Beckman Accutrace) using the international 10-20 system of electrode placement.[18] Tracings were obtained during wakefulness for a minimum of 40 minutes, which included 5 minutes of hyperventilation and stroboscopic stimulation. If the patients became drowsy, they were alerted by noises or conversation. All EEGs were interpreted by the same electroencephalographer who was not aware of the patients' clinical course. In each instance, the WAIS and the EEG were performed as closely together as possible; the median number of days between these two procedures was 1.24. No patients were studied while they were obviously postictal.

Criteria for identifying epileptiform patterns were those delineated by Zivin and Ajmone Marsan,[19] with some modifications.[20] Spikes and sharp waves with or without slow wave components were individually counted for the first 20 minutes of each tracing with the patient at rest, and their average rate of occurrence on a per minute basis was calculated. Groups of spike-and-slow wave, sharp wave and multiple spike-and-slow wave bursts were counted as single epileptiform discharges unless they exceeded 3 to 4 seconds in duration. In the last instance, they were arbitrarily classified as electric seizures.

Four series of analyses of the data were conducted. In the first, the intellectual correlates of the average rate of electroencephalographic epileptiform discharges were assessed with patients grouped as follows: (1) those with no discharges (discharges absent, N = 32), (2) those with discharges occurring at an average rate of less than one per minute (discharges low, N = 27), and (3) those with such activity occurring at an average rate of more than one per minute (discharges high, N = 31). This last group included five subjects who would have been classified in the second group except for the presence of electric seizures. In order to make this study more directly comparable with preceding investigations,[10,13] the variable "Verbal IQ minus Performance IQ" was included in this and in several succeeding analyses. The technique of one-way analysis of variance was applied for each psychologic variable, and where significant F statistics appeared, the Neuman-Keuls procedure for unequal Ns was employed to assess differences between groups.[21]

In order to assess the relationships of topographic distribution of electroencephalographic epileptiform activity with intelligence, the patients were divided in two

Table 1. Topographic distribution of electroencephalographic epileptiform patterns in patients undergoing neuropsychologic tests

Findings	Patients (N)
Generalized	19
Right temporal	14
Right frontal	1
Other right focal or unilateral widespread	2
Left temporal	5
Left frontal	2
Other left focal or unilateral widespread	4
Bitemporal independent	5
Bifrontal independent	2
Small widespread spikes	4
None	32
Total	90

ways. First, patients were grouped according to whether they had (1) no discharges (discharges absent, N = 32), (2) discharges that were focal or unilateral (focal, N = 35), or (3) generalized epileptiform discharges (generalized, N = 19). The one-way analysis of variance technique was applied to these data in the same fashion as indicated previously. In this and the following analyses, four subjects showing only small widespread spikes ("small sharp spikes"[22]) were excluded, since these patterns are believed to be of no localizing or lateralizing significance.[23] The correlates of topographic distribution were secondly assessed by comparing individuals having epileptic discharges that were (1) ipsilateral (N = 19) or (2) contralateral (N = 9) to handedness as determined by the lateral dominance examination.[24] The *t* statistic for independent means was then applied to these data.

The third analysis was designed to assess the average rate and topographic distribution (focal, generalized) of electroencephalographic epileptiform discharges in combination. The patients were divided as was done previously, according to the average rate (low versus high) and topographic distribution (focal versus generalized) of discharges. This resulted in four groups of subjects: (1) low focal (N = 13), (2) high focal (N = 22), (3) low generalized (N = 10), and (4) high generalized (N = 9). The two-way analysis of variance procedure was then applied to each intellectual variable, and estimates of the joint impacts of electroencephalographic variables on intelligence were thereby provided.

In recognition of the unique constellation of abilities of each patient, the final analysis involved the examination of the subtest scores for each person to determine if relationships could be detected between the pattern of intellectual abilities and the electroencephalographic variables considered in this study. For each individual, the score on each subtest was subtracted from the average subtest score for the entire test. These results were averaged to provide a profile for the groups defined on the basis of electroencephalographic criteria. These derived scores were independent of general level of group performance, since they were determined from variations around the common subtest mean for each person and were designed to indicate that person's strengths and weaknesses. Individuals were grouped again as in the third analysis but with the addition of the discharges absent group (N = 32). The one-way analysis of variance technique was then applied across the groups for each subtest.

No statistically significant differences were detected among the groups for each analysis with respect to age, education, or total number of attacks in the month preceding the evaluations. Furthermore, the 12 patients with abnormal findings on neurologic examination were spread across all the groups studied. However, the mean age at onset of the seizure disorder did significantly differ ($F = 3.29$, $p < 0.05$) for the initial analysis involving the average rate of epileptiform discharge, the means for the discharges high, low, and absent groups being 9.30, 14.00, and 14.29 years, respectively. With individuals grouped in exactly the same fashion, there was also a statistically significant difference ($F = 3.79$, $p < 0.05$) with respect to duration of seizure disorder for the discharges high, low, and absent groups (means of 19.57, 13.07, and 14.87 years, respectively). No significant differences were detected between any of the groups studied with respect to serum diphenylhydantoin levels, although it is to be noted that all patients were on this anticonvulsant medication alone and that the overall mean serum level of this drug was 30.05 μgm per milliliter (SD = 15.59).

Results. Table 2 presents the data on the relationships of the average rate of electroencephalographic epileptiform activity (regardless of topographic distribution) to the various intellectual measures. On each of the subtests and summary scores, the group having no discharges did best, the group having these patterns at an average rate of less than one per minute scored on an intermediate level, and the group with discharges at a rate greater than one per minute did the poorest. Several statistically significant differences overall appeared and were most frequently found between the discharges absent and the discharges high groups. When significant differences involving the discharges low group did appear, they tended to occur within comparisons between this group and the discharges absent group.

Table 3 presents the results of the first of two analyses in relationship to topographic distribution of epileptiform patterns. In this analysis, the presence or absence and topographic distribution of discharges were studied. Once again, an orderly decrease in intelligence scores was observed as groups without discharges were compared with those with focal and then generalized discharges. An even larger number of statistically significant differences was present than in the previous analysis, but again the Verbal IQ minus Performance IQ variable was not statistically significant. Statistically significant differences occurred routinely when the group without discharges was compared with the one with generalized epileptiform activity, but few differences involved the group with focal discharges in relationship to either of the others.

The second analysis of topographic distribution considered patients having discharges ipsilateral or contralateral to their handedness, and the results are shown in table 4. The one clearly significant difference was with respect to the Picture Arrangement subtest, in which discharges over the nondominant hemisphere were associated with poorer scores. Differences of marginal statistical significance ($0.05 > p < 0.10$) appeared on the Picture Completion subtest and the Verbal IQ minus Performance IQ variable.

Table 5 presents comparisons of the combined effects of the average rate and topographic distribution (focal, generalized) of discharges on intelligence. The summary scores (Verbal IQ, Performance IQ, Full Scale IQ) revealed progressively poorer scores when the low focal, high focal, low generalized, and high generalized groups were successively considered. Scores for the subtests

Table 2. Means, standard deviations, and *F* statistics of WAIS variables on patients grouped according to absence and average rates of electroencephalographic epileptiform discharges (low = < 1/min, high = > 1/min)

Test variable	Groups						*F* statistic
	Discharges absent		Discharges low		Discharges high		
	Mean	SD	Mean	SD	Mean	SD	
Information	11.34[1]	2.36	9.89	3.53	9.10[1]	3.11	4.51[a]
Comprehension	11.16	3.31	10.44	3.56	9.35	2.69	2.54
Arithmetic	9.69	3.44	9.00	3.29	8.87	3.24	0.54
Similarities	12.00[1]	2.36	10.52	3.17	9.74[1]	3.25	4.82[a]
Digit Span	10.31	3.50	9.48	3.75	9.03	3.47	1.05
Vocabulary	11.03	2.90	10.22	3.34	9.03	3.37	3.09
Digit Symbol	8.88	2.77	7.89	2.06	7.48	2.90	2.33
Picture Completion	10.56[1]	2.18	9.63[2]	2.40	8.32[1,2]	2.04	8.18[c]
Block Design	9.72	2.28	8.52	2.21	8.29	3.02	2.85
Picture Arrangement	10.06[1,2]	2.71	8.15[1]	2.52	7.55[2]	2.01	9.14[c]
Object Assembly	9.34[1]	2.06	8.44	2.52	7.48[1]	2.93	4.28[a]
Verbal IQ	106.00[1]	13.52	99.70	16.08	95.77[1]	14.67	3.86[a]
Performance IQ	100.28[1,2]	10.57	91.56[1]	12.56	87.87[2]	13.23	8.67[c]
Full Scale IQ	103.81[1,2]	11.38	96.04[2]	14.52	92.00[1]	13.43	6.62[b]
Verbal IQ-Performance IQ	5.76	12.15	8.87	11.76	8.52	11.52	0.63

Note: Identical single superscript numbers within each test variable indicate significant differences of $p < 0.05$; if underlined, of $p < 0.01$. [a] $p < 0.05$ ($F \geq 3.11$), [b] $p < 0.01$ ($F \geq 4.86$), [c] $p < 0.001$ ($F \geq 7.56$).

Table 3. Means, standard deviations and *F* statistics of WAIS variables on patients grouped according to absence or presence of focal or generalized electroencephalographic epileptiform discharges

Test variable	Groups						*F* statistic
	Discharges absent		Focal		Generalized		
	Mean	SD	Mean	SD	Mean	SD	
Information	11.34[1]	2.36	9.83	3.48	8.53[1]	2.76	5.71[b]
Comprehension	11.16	3.31	10.03	2.71	9.58	4.10	1.66
Arithmetic	9.69[1]	3.44	9.86[2]	3.30	7.53[1,2]	2.78	3.57[a]
Similarities	12.00[1]	2.36	10.51	2.81	9.68[1]	3.82	4.25[a]
Digit Span	10.31	3.50	10.11	3.31	8.05	3.96	2.79
Vocabulary	11.03	2.90	9.74	3.23	9.11	3.63	2.48
Digit Symbol	8.88[1]	2.77	8.37[2]	2.02	6.63[1,2]	3.15	4.67[a]
Picture Completion	10.56[1,2]	2.18	9.17[2]	2.32	8.32[1]	2.29	6.50[b]
Block Design	9.72[1]	2.28	8.69	2.53	7.89[1]	2.96	3.27[a]
Picture Arrangement	10.06[1,2]	2.71	7.69[1]	2.21	7.79[2]	2.48	9.06[c]
Object Assembly	9.34	2.06	8.00	2.61	7.79	3.14	3.14[a]
Verbal IQ	106.00[1,2]	13.55	100.49[1]	14.08	93.11[2]	17.13	4.67[a]
Performance IQ	100.28[1]	10.57	91.69	12.04	85.74[1]	14.72	9.22[c]
Full Scale IQ	103.81[1]	11.38	96.57[2]	12.41	89.42[1,2]	16.21	7.55[b]
Verbal IQ-Performance IQ	5.76	12.15	9.34	12.21	7.42	10.29	0.79

Note: Identical single superscript numbers within each test variable indicate significant differences of $p < 0.05$; if underlined, of $p < 0.01$. [a] $p < 0.05$ ($F \geq 3.11$), [b] $p < 0.01$ ($F \geq 4.87$), [c] $p < 0.001$ ($F \geq 7.59$).

Table 4. WAIS performances of individuals having epileptiform discharges ipsilateral or contralateral to their handedness on the WAIS

Test variable	Ipsilateral group		Contralateral group		t
	Mean	SD	Mean	SD	
Information	9.89	3.45	8.78	3.60	0.79
Comprehension	10.26	2.92	9.67	3.20	0.49
Arithmetic	9.63	3.59	8.67	2.83	0.71
Similarities	10.58	3.17	11.00	3.12	−0.33
Digit Span	9.53	3.78	10.56	3.13	−0.71
Vocabulary	9.21	3.21	9.67	3.32	−0.35
Digit Symbol	8.53	2.06	8.11	2.09	0.50
Picture Completion	8.58	1.89	10.44	3.39	−1.88
Block Design	8.53	2.24	7.78	2.49	0.80
Picture Arrangement	6.79	2.25	9.11	2.03	−2.63[a]
Object Assembly	7.26	2.33	8.55	1.94	−1.44
Verbal IQ	99.58	14.72	98.89	15.45	0.12
Performance IQ	88.16	11.26	94.22	13.73	−1.24
Full Scale IQ	94.42	12.95	96.89	14.42	−0.45
Verbal IQ-Performance IQ	11.53	10.72	4.67	11.48	1.76

[a] $p < 0.05$, $t \geq 2.05$

Table 5. Means, standard deviations, and F statistics from two-way analysis of variance procedures on WAIS variables with patients grouped according to topographic distribution (focal, generalized) and average rate (low = < 1/min, high = > 1/min) of electroencephalographic epileptiform discharges

Test variable	Groups								F statistics		
	Focal low		Focal high		Generalized low		Generalized high		Main effects		Interaction effect
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Distribution	Rate	
Information	10.38	3.66	9.50	3.40	8.90	3.32	8.11	2.09	2.30	0.78	0.00
Comprehension	11.15	2.70	9.36	2.54	9.80	4.94	9.33	3.20	0.55	1.46	0.50
Arithmetic	10.38	3.23	9.54	3.38	7.80	3.26	7.22	2.28	7.20[b]	0.60	0.02
Similarities	11.31	2.02	10.04	3.14	10.30	4.11	9.00	3.57	1.36	1.55	0.01
Digit Span	11.31	3.66	9.41	2.94	8.00	3.56	8.11	4.60	5.09[a]	0.77	0.97
Vocabulary	10.38	3.02	9.36	3.36	9.90	3.78	8.22	3.46	0.66	1.99	0.10
Digit Symbol	9.15	1.77	7.91	2.04	6.80	1.75	6.44	4.33	7.06[a]	1.34	0.43
Picture Completion	9.92	2.87	8.73	1.86	9.20	2.04	7.33	2.24	2.76	5.36[a]	0.30
Block Design	9.23	2.20	8.36	2.70	7.70	2.00	8.11	3.89	1.19	0.12	0.73
Picture Arrangement	8.31	2.63	7.32	1.89	7.50	2.72	8.11	2.32	0.00	0.08	1.44
Object Assembly	8.62	1.90	7.64	2.94	8.40	3.24	7.11	3.06	0.18	2.05	0.03
Verbal IQ	105.23	13.33	97.68	14.02	94.90	18.75	91.11	16.01	3.74	1.64	0.18
Performance IQ	95.62	12.72	89.36	11.17	87.10	12.68	84.22	17.37	3.18	1.65	0.26
Full Scale IQ	101.23	12.57	93.82	11.73	91.10	16.33	87.56	16.85	4.24[a]	1.95	0.25
Verbal IQ-Performance IQ	9.62	11.79	9.18	12.73	7.90	12.28	6.89	8.25	0.04	0.34	0.00

[a] $p < 0.05$ ($F \geq 4.03$), [b] $p < 0.01$ ($F \geq 7.13$).

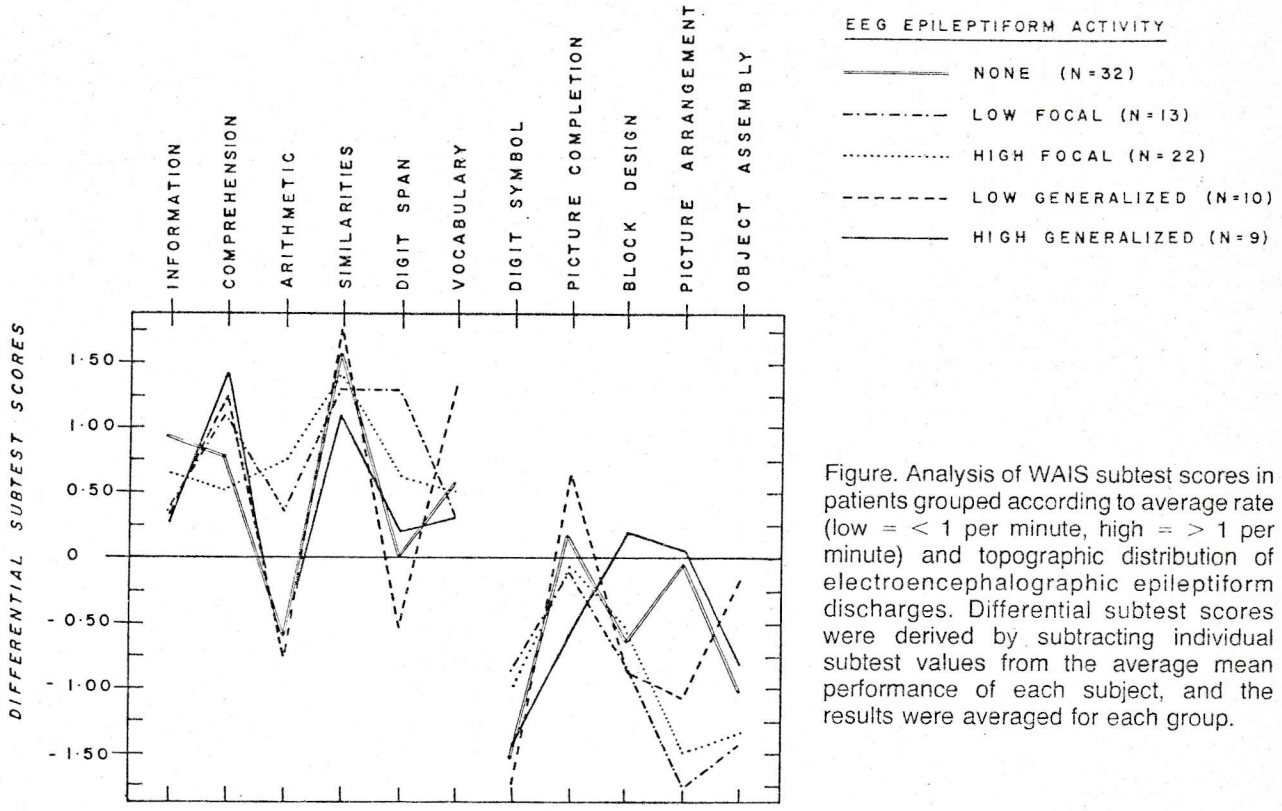

Figure. Analysis of WAIS subtest scores in patients grouped according to average rate (low = < 1 per minute, high = > 1 per minute) and topographic distribution of electroencephalographic epileptiform discharges. Differential subtest scores were derived by subtracting individual subtest values from the average mean performance of each subject, and the results were averaged for each group.

revealed a modest deviation from this pattern, but the low focal group always performed best. With the group without discharges excluded from this analysis, there were relatively few significant main effects for topographic distribution and only one for rate of discharges. No statistically significant interaction effects were present.

The figure presents the results of the intra-individual subtest study, and it is apparent that the patterns are similar in each group. On only one of the 11 subtests (Picture Arrangement) was there a statistically significant difference ($F = 3.58$, $p < 0.01$), and here, both focal groups did poorest. Furthermore, while both groups with generalized epileptiform activity were highly similar to the group without discharges, both groups with focal discharges showed modest deviations from the other groups on several of the subtests.

Discussion. A number of findings from this study and their implications are worthy of particular note. The greatest incidence of statistically significant differences consistently occurred in comparisons of the group without epileptiform activity with those having such activity. Thus, the presence or absence of electroencephalographic discharges is one of the most important variables we studied with respect to intelligence. While it appeared that the performance scale of the WAIS was more intimately related than the verbal scale to the presence or absence of discharges, it was apparent that alteration of a wide range of abilities was associated with changes in this electroencephalographic variable.

The orderly arrangement of intelligence scores dependent on the average rate and topographic distribution (generalized, focal) cannot escape attention. It is clear that these electroencephalographic variables are significantly related to the average intellectual levels of the groups. Furthermore, when these variables were studied simultaneously (table 5), it was apparent that they were additive to some degree. At the same time, however, there were no statistically significant interactions associated with a joint examination of variables (i.e., there was no increase in the predictability of intelligence using electroencephalographic variables when the latter were considered simultaneously rather than sequentially). Both the average rate and topographic distribution of discharges are related to intelligence, although the latter may be more relevant than the former.

The present results also bear on the controversy that has existed concerning the relative levels of verbal versus performance intelligence among epileptics. In keeping with earlier observations,[11,16] the present study elicited better verbal than performance abilities within all groups, and this was especially true for individuals showing epileptiform discharges. As has been suggested, it is likely that characteristics of the WAIS are relevant to this finding and may contrast to some degree with characteristics of the Wechsler-Bellevue Scale. While our verbal minus performance differences were not nearly as substantial as those obtained by Gupta and associates,[12] who used a form of the WAIS adapted for India, those reported by Parsons and Kemp[10] were generally consistent with ours but just a little less in degree. We

should also note, however, that the epileptics evaluated by Parsons and Kemp[10] had a substantially later average age at onset and a shorter duration of illness than those in the present study.

The results of the analysis examining foci ipsilateral and contralateral to handedness resembled those of the intraindividual pattern analysis in that both resulted in a substantial number of statistically nonsignificant differences except on the Picture Arrangement subtest. While one might have hoped that the WAIS would differentiate between individuals having discharges in their dominant and nondominant hemispheres, it should be recalled that the early work in this area showing such differences was done with persons having verified brain damage, including many individuals with progressive lesions.[8] In our patients, the electric abnormalities were not routinely accompanied by clinically identifiable brain lesions. However, poorer scores on the Picture Arrangement subtest of the WAIS were associated with focal epileptiform discharges in the nondominant hemisphere. Since the majority of individuals we examined had discharges involving their temporal lobes, it appears that our conclusions are similar to those of others regarding the Picture Arrangement subtest.[10,14,15] However, we could not confirm the inferences made about the Similarities subtest by these same investigators.

This study demonstrates that the presence or absence of electroencephalographic epileptiform discharges is related to intelligence, as are the average rate and topographic distribution of such discharges. However, it does not provide evidence that such discharges are causally related to the poorer intellectual capabilities. Moreover, the question of whether or not particular deficits were temporally related to discharge bursts was not considered. While some investigators have suggested that a causal relationship may in fact exist between electroencephalographic discharges and impaired intellectual abilities,[3,25] it may simply be that the electroencephalographic abnormalities indicate the relative severity and distribution of cerebral pathologic or physiologic changes among the groups rather than represent the specific cause of the intellectual deficits. Further work is needed to distinguish between these possibilities and to identify possible interactions between them.

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