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Neuropsychological Evaluation in Epilepsy

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Epilepsy is a symptom of brain dysfunction. At the time of an epileptic seizure, it is unquestionably true that the brain is not functioning normally. However, it is also known that the electrical abnormalities characteristic of epilepsy tend to persist even between seizures. It is for this reason that interictal electroencephalographic (EEG) tracings may be of great benefit in establishing a diagnosis of seizure disorder. When these facts are considered together with the knowledge that the brain is the seat of mental abilities, it is natural to expect that losses in performance would be evident between as well as during seizures. Furthermore, the extent of social and behavioral problems with individuals having seizures is well known and correlates with losses in abilities often seen in epilepsy (3). It is reasonable to conclude, therefore, that epilepsy, with its inherent disruption of brain functions, provides a theater of brain-related problems where information about brain functioning can be gathered through an evaluation of the behavioral correlates of their disruption.

Neuropsychology provides for the evaluation of ability and behavioral correlates of brain lesions and other pathological conditions affecting the nervous system. This discipline arises from both neurology and psychology. From neurology, information about the central nervous system (CNS) and disease processes is obtained. From psychology, techniques of precision in measurement and assessment are borrowed. Neuropsychology rests on the assumptions that the brain is lawfully and systematically organized, that the behavior of the organism is related to the condition of the brain, and that an index of the condition of the brain can be inferred by carefully evaluating the behavior and abilities of the organism. Through a systematic and rather extended evaluation of each person with seizures, it is possible to determine to what extent (if any) there is evidence for brain damage or impaired brain processes and also to determine to what degree any such impairment may impact ability to function in daily life.

In this chapter, a comprehensive approach of neuropsychological evaluation is described. This has been developed specifically for individuals having seizure problems and has been standardized on epileptic patients. Disrupted performances on the tests are systematically related to the EEG abnormalities that epilepsy provides for study. Furthermore, the tests are sensitive to alterations in anticonvulsant regimens, and samples of both EEG and anticonvulsant studies are presented. In general, we have attempted to take advantage of these conditions and circumstances in order to learn more about how the brain functions.

PROCEDURES OF NEUROPSYCHOLOGICAL EVALUATION

The quality of neuropsychological evaluations by psychologists varies widely. One of the basic reasons for this pertains to the general approach that is taken. The brain is extremely complicated in its functions, and, in the viewpoint of this writer, it is therefore not possible to provide a reasonably adequate assessment of such functions unless the techniques used are sophisticated and far reaching. To hope to evaluate the brain by a simple test requiring the drawing of a few figures is grossly inadequate both conceptually and practically. To be sure, if there is sufficient organic involvement, decreased performances on even a simple test may be seen. However, more subtle forms of impairment will certainly be missed; patterns of impairment cannot be sought out, and very little can be said about the impact of such a neurological condition on performance in daily life. It is for these reasons that a series of tests must be administered which cover a broad range of brain functions. Furthermore, each of these tests must be shown to have sensitivity to impaired brain conditions. This entire approach, developed by Halstead and Reitan (see ref. 7), underlies the development of the Halstead-Reitan neuropsychological battery, which has achieved international recognition.

Although the general approach used by Halstead and Reitan is enthusiastically endorsed by the present author, a direct application of their tests to individuals with seizures may not provide optimal results. It is noted, for example, that the Halstead-Reitan battery was not designed to be sensitive to EEG epileptiform discharges characteristic of epilepsy, nor did it include measures in advance known to be sensitive to the effects of anticonvulsant medications. Furthermore, no standardization of these tests has been available with individuals having seizure disorders, and several other such limitations are evident. Therefore, the Neuropsychological Battery For Epilepsy (2) was developed following a series of investigations on the correlates of certain variables with performance, including seizures, EEG variables, and anticonvulsant effects. A battery of tests resulted, which typically requires approximately 7 hr for individual administration by a highly trained technician. The battery consists of two types of tests: general and discriminative measures.

General Measures

The first category includes indicators of general intelligence, emotional status, and preference in handedness. For adults, intelligence is evaluated by the Wechsler Adult Intelligence Scale, whereas with children, assessment is made by means of the Wechsler Intelligence Scale for Children—Revised. Emotional adjustment is assessed in adults by means of the Minnesota Multiphasic Personality Inventory (MMPI), while early adolescents complete the Eysenck Personality Inventory. Emotional assessment is typically not formally done with young children. Preference in handedness is evaluated by means of the Lateral Dominance Examination developed by Reitan and Davison (7).

Discriminative Measures

The second group of tests consists of a series of 16 test indicators that have been developed and standardized specifically with epileptic patients (2). The 11 tests from which the 16 indicators arise are briefly described here.

Stroop Test

A single color plate is used in which color names (such as "red" and "green") are presented in incongruous colors (such as "blue" and "orange"). The time required to simply read the words ignoring the colors is one indicator. In the second part, the person must read the color of print while ignoring what the word says. When the time required to complete the first part is subtracted from that required for the second part, an indicator of attention to the task is obtained. This appears to be a good index of distractability.

Wechsler Memory Scale (Form I)

This test is well known, but only two portions were ultimately adopted. These parts are Logical Memory and Visual Reproduction, which are indicators of verbal and nonverbal memory, respectively.

Reitan-Kløve Perceptual Examination

This and the other tests developed by Halstead and Reitan are described elsewhere in detail (7). It includes an assessment of tactual, auditory, and visual perception under a variety of conditions, with a large number of trials pertaining to both sides of the body. The tests evaluate accuracy of perception under conditions of unilateral and bilateral simultaneous stimulation, as well as the extent of agraphagnosia, finger agnosia, and astereognosis. As with many of the tests, a comparison of the performances associated with both sides of the body is possible, as is an indication of general level of performance.

Name Writing Procedure

This consists of the calculation of the average number of letters per second executed by the preferred and nonpreferred hand as the full name is written.

Interestingly, this simple measure of motor speed is sensitive to phenytoin toxicity.

Halstead Category Test

Using an apparatus by which feedback is given concerning adequacy of performance, this test evaluates a person's ability to form concepts, to solve problems in a novel situation, and to effectively utilize information given about performance. It appears to be an index of a person's ability to cope with problems of life.

Halstead Tactual Performance Test

The subject is blindfolded and required to put blocks of various sizes and shapes in a board placed on a table. The Time Component consists of the total time required to position the blocks with the preferred hand, the nonpreferred hand, and both hands together. After the board is taken away, a picture of the board is drawn. The number of blocks out of 10 remembered is the Memory Component, and the number placed in the proper place in the drawing is the Localization Component. Thus three of the discriminative measures come from this test.

Seashore Rhythm Test

This is one of the tests from the Seashore Measures of Musical Talents. By using a tape recorder, 30 pairs of rhythmic beats are presented. The patient must determine if the rhythms are the same or different in each pair.

Seashore Tonal Memory Test

In a manner similar to the rhythm test, 30 series of notes are played twice over the tape recorder. In each second playing, one note is different. The person must determine which one has been changed. Both the Rhythm Test and the Tonal Memory Test appear to require auditory discrimination and sustained attention to the task.

Halstead Finger Tapping Test

In this test of motor speed, a small key is propelled as rapidly as possible by the index finger of each hand independently. The total performance of both hands is added together to obtain a final index of performance.

Trial Making Test

Twenty-five circles are printed on one page for part A and on another page for part B. In part A, the circles are numbered, and the patient must draw a line connecting them as quickly as possible. In part B, numbers and letters must be connected, in order, in an alternating fashion. The time required to do so is the discriminative measure.

The Halstead-Wepman Aphasia Screening Test

This is a test of various aspects of language functions. It is scored according to a manual designed by the present author for various problems in naming, reading, spelling, pronunciation, and so on. The total number of errors made is obtained for each subject. Along with this test, a number of visuospatial reproductions are done which serve as a basis for judging the extent to which there is constructional dyspraxia or distortion in visuospatial relationships.

As can be seen from the brief description of the tests given above, a broad range of abilities is assessed. Furthermore, the range of normal performance has been identified for each test measure. Ranges of overall impairment also have been identified and are based on the total number of tests falling outside normal limits. In addition, performances on the tests are evaluated with respect to the relative efficiencies of the right and left sides of the body, and also with respect to the appearance of specific neurological deficits. A considerable amount of information is now known about the neurological correlates of performances on these tests, as well as their implications for adjustment to the demands of everyday life. We now turn to research findings relative to performance on the tests.

NEUROPSYCHOLOGICAL CORRELATES OF EEG ABNORMALITIES

For many years, attempts have been made to relate the EEG to psychological test performance. This has most frequently been done by gross inspection of the EEG tracings and by use of intelligence tests alone. In a series of studies (5,8), the relationships between certain EEG variables of interest in epilepsy and performance on the neuropsychological tests were explored. These papers differ from others in the literature in that only individuals with epilepsy were studied, the range of functions assessed was not restricted to intelligence, and a detailed and painstaking analysis of the EEG tracings was made.

Neuropsychological Correlates of Epileptiform Discharges

The first project pertained to types of electrical abnormalities of special interest to epilepsy and represents an opportunity by which one can gather information concerning brain function. Single standard waking EEGs were obtained on adult epileptic individuals within 30 days of neuropsychological testing and were evaluated under resting conditions for the presence or absence, rate, and topographic distribution of epileptiform patterns. Of the 90 persons involved in the study, 32 had no discharges on single tracings, 27 had discharges of one type or another at an average rate of less than one per minute, and 31 had discharges at a rate greater than one per minute. Criteria for the identification of epileptiform patterns were those delineated by Zivin and Ajmone-Marsan (9). Groups of spike-and-slow wave, sharp wave, and multiple spike-and-slow wave bursts were counted as single discharges unless they exceeded 3 sec in duration, in which case they were automatically classified as having epileptiform discharges at a rate greater than one per minute.

Rate of Epileptiform Discharge

When individuals were categorized according to rate of epileptiform discharges, three groups of patients emerged, as identified above. The performances across the three groups were compared by analysis of variance. Statistically significant differences appeared on approximately half of the neuropsychological variables and pointed to an orderly decrease in performance with increasing discharge rates. Several types of functions were affected, including nonverbal memory, psychomotor problem solving, and both verbal and visuospatial intelligence. It was also observed that the two groups most similar to one another were those having discharges. Therefore, the sharpest loss in abilities was noted when discharges were present.

Type of Epileptiform Discharge

The patients were then classified according to the type of discharge. Of the 58 patients who demonstrated discharges in a single EEG record, it was observed that 35 had only focal discharges and 19 had generalized epileptiform patterns (three had "small sharp spikes" and were excluded from the analysis). When individuals were thus classified and their performances contrasted with persons having no discharges, statistically significant differences appeared on approximately three-fourths of the neuropsychological variables. These differences were also of greater magnitude than those found with respect to rate of epileptiform discharges. Furthermore, the group with generalized discharges consistently did worst, the group with focal discharges performed in an intermediate fashion, and the group without discharges did the best. The extent of differences between the focal and generalized groups was more than that seen between the no-discharge and focal-discharge groups. Nearly every type of psychological function tested showed such effects except, oddly enough, those tasks requiring the greatest attention and sustained concentration.

Rate and Type of Epileptiform Discharge

Finally, individuals were grouped according to both type and rate of discharge. Among those patients with discharges, the best performance was obtained from individuals with focal discharges at a rate less than one per minute. The worst performance was obtained from persons with generalized discharges at a rate greater than one per minute. Furthermore, a rather marked dispersion in test scores was observed, which was greater than that seen when either topographic distribution or rate of discharge was considered alone.

In our studies of neuropsychological correlates of epileptiform discharges, we were consistently impressed with the systematic and orderly alterations in test scores when patients were divided according to presence or absence, topographic distribution, and average rate of epileptiform patterns. When more of the brain was involved and the involvement was more frequent, greater losses in abilities were observed. It should be noted that this was true despite the fact that the EEG tracings and the neuropsychological testing were never done simultaneously.

The present series of analyses indicates that even though it may be technically difficult to demonstrate losses in ability simultaneously with focal discharges, it is not difficult to demonstrate that epileptic subjects evincing frequent focal discharges (in a single EEG record) are also likely to show losses in functions more generally, whether or not they show focal discharges at the time of testing. The condition of the brain is believed to underly both the appearance of the abnormal electrical patterns and the decreased performance. Such an explanation does not rule out the possibility that epileptiform discharges of even a focal nature may have specific correlates with abilities, but rather emphasizes the fact that the brain is dysfunctional in these patients and that in most cases we may merely have two aspects of the same dysfunction in evidence either simultaneously or at different times.

Nonepileptiform EEG Abnormalities

The other general classification of the EEG changes which we have evaluated in some detail pertains to generalized nonepileptiform abnormalities and in particular to slow wave abnormalities. These were evaluated in a short series of studies (5,6).

Dominant Posterior Rhythm Frequency

Initially, the same individuals evaluated in the studies of epileptiform discharges were classified according to dominant posterior rhythm frequency (DPRF, "alpha") in their EEGs. The rhythm was counted for 10 consecutive seconds in three different representative segments of each recording from either one or both sides of the head with the patient resting and the eyes closed. Random faster or slower potentials apparently mixed with but not obscuring this activity were disregarded. The value obtained in hertz was averaged and rounded to the first decimal point. The score that resulted was similar to that obtained by counting the same activity during a few seconds of maximal expression, as would be done for routine clinical interpretation. The reliability of this procedure was established.

The patients were arranged according to the DPRF from lowest (5.1 Hz) to highest (11.0 Hz). This distribution was divided into approximate thirds resulting in low (5.1 to 7.7 Hz), medium (7.8 to 8.7 Hz), and high (8.8 to 11.0 Hz) groups. Analyses of variance were conducted using as data the performances on the neuropsychological tests. The results manifested fewer statistically significant differences across neuropsychological tests than were seen with any of the analyses pertaining to epileptiform discharges. Furthermore, the two groups with faster rhythms performed approximately equally. It was only when the DPRF was definitely less than 8 Hz that decreased performance was observed. At that point, however, there was a rather noticeable drop in performance, which was perhaps seen the most on tests requiring visuospatial functions, but it was also noted on perceptual tasks and on one task requiring concentration. These findings confirm what has often been noted clinically; i.e., there appears to be little difference in abilities regardless of whether one's DPRF is 9.0, 10.0, or 11.0. It is apparent that equivalent differences in rhythm frequency at different ranges do not have the same significance in terms of brain functioning.

Generalized Nonepileptiform Abnormalities

A further attempt was made to evaluate the effects of nonepileptiform abnormalities, which were generalized by nature and not restricted to the parietal-occipital area. In this study (6), 111 adult epileptics were given standard waking EEGs and neuropsychological tests, as previously described. Criteria were established to classify generalized nonepileptiform abnormalities in representative, alert, but resting sections of the tracings recorded under eyes-closed conditions. Grading was according to a scheme of visual assessment of the relative preservation or distortion of physiological rhythms and the abundance of diffuse, slow wave patterns. Epileptiform discharges were disregarded, as were strictly regional slow waves. Individuals were classified as showing no or mild generalized abnormalities, moderate abnormalities, and marked abnormalities. Analyses of variance were then computed across these three groups for each of the neuropsychological test scores.

Results revealed statistically significant differences on almost every neuropsychological variable. Furthermore, the magnitude of the differences across the groups was striking, and an orderly dispersion of scores was observed. There was essentially no type of mental ability which did not demonstrate a correlation with the extent of nonepileptiform abnormalities.

The orderliness of the findings in the studies relating the EEG with performance was surprising. It is believed that the painstaking EEG analysis and the assessment of a broad range of abilities with brain-sensitive tests, instead of only measures of intelligence, contributed to the findings observed. It was also noteworthy that the type of EEG variable least frequently evaluated (generalized nonepileptiform abnormalities) rendered the most prominent and far-reaching statistically significant differences. It appears that the relationships seen might be further enhanced through the use of automated methods with simultaneously conducted EEG and neuropsychological studies.

NEUROPSYCHOLOGICAL CORRELATES OF ANTICONVULSANTS

While the assessment of the effects of anticonvulsants on performance has been of interest for many years, certain methodological difficulties exist, including the following: (a) When there is a change in anticonvulsants administered, there is often a change in seizure frequency, so that the effects of seizure frequency and medication on performance are confounded; (b) many studies examine only normal control individuals who may metabolize the drugs differently than epileptic patients; (c) the use of placebo in comparison with an active agent is not an effective technique for evaluating changes in performance, because the addition of any active agent to a preexisting drug regimen tends to decrease performance; (d) the majority of studies done in the area have used only a single test or at most a limited range of tests as indicators of performance; and (e) the majority of studies have evaluated patients on multiple drug regimens, so that the effects of single agents are difficult to address. It is because of considerations such as these that the single agent, double-blind, crossover design described in Chapter 13 has been repeatedly adopted by us in the evaluation of the correlates of anticonvulsant medication. Furthermore, it will become apparent that for each anticonvulsant evaluated, a pattern of changes in performance has appeared with respect to the various functions assessed, and the importance of using a full battery of neuropsychological tests is once again underscored. To illustrate the work that has been done, two of the studies are described.

Phenytoin

Since phenytoin is the most widely used anticonvulsant agent, we have consistently elected to employ it as a basis for the evaluation of other compounds. Therefore, it was important for subsequent neuropsychological studies to identify the neuropsychological correlates of differing blood levels of phenytoin (1). We had available a series of 70 adult epileptic patients who had been tested while on phenytoin alone and for whom determinations of serum levels had been obtained near the time of testing.

Correlations were made between phenytoin serum level and neuropsychological performance. To do this, the patients were arranged from high to low serum level, and the distribution was cut in half with 34 patients having a level of 30 μg/ml or less (low group) and the remaining 36 patients having serum levels of 31 μg/ml or more (high group). The results by this grouping of patients demonstrated statistically significant findings at modest levels ($p \leq 0.05$ or ≤ 0.01) on a series of variables, all of which conspicuously involved motor performance. In fact, in no instance did a test render a statistically significant finding without motor performance being centrally involved. A second set of analyses was conducted with individuals classified according to extent of demonstrated clinical toxicity. Fewer statistically significant differences were evident in this analysis, but once again those tests showing differences relied heavily on motor functions.

Several comments about this study are in order. First, it was not possible to identify any differences between the groups on variables such as age, sex, education, seizure type, or seizure frequency. Second, the pattern of scores did not reveal a general decrease in performance across types of functions. Furthermore, the magnitude of differences was substantially less than that seen with most EEG variables. This was true even though the high group had extremely elevated serum levels (M = 43.14 μg/ml), which gave widespread and marked behavioral correlates every opportunity to appear.

Phenytoin versus Carbamazepine

With the beginning of the use of carbamazepine as an anticonvulsant in the United States, we undertook a single agent, double-blind study with a goal of comparing carbamazepine with phenytoin. The general format for the study is presented in Chapter 13; therefore, only the neuropsychological component of the study (4) is described here. There were 40 adult epileptic subjects whose neuropsychological status was examined under conditions of phenytoin administered alone and carbamazepine administered alone. The order of the drug trials was counterbalanced. Furthermore, because of the presumed psychotropic effects of carbamazepine, a few new neuropsychological tests were added to the battery.

Only a few differences in neuropsychological performance were demonstrated; however, all favored carbamazepine, and it was observed that they emphasized cognitive functions rather than motor or perceptual skills. In particular, the ability to maintain sustained attention to the task under distracting conditions was improved with carbamazepine, and the ability to work effectively and efficiently in solving a variety of problems was also better. Moreover, the MMPI profiles obtained during carbamazepine administration were also slightly better, and in general, the patient seemed to have fewer complaints and less tension and anxiety with this drug.

Our anticonvulsant studies have suggested that in addition to anticonvulsant effects, the impacts of these drugs are at least to some degree specific with respect to behavioral functions. It is possible that these agents affect only certain aspects of the nervous system or neuronal functioning. For example, it may be that phenytoin has a particular impact on the cerebellum, whereas carbamazepine may have certain impacts on the cerebrum which tend to be manifested in cognitive alterations. While the exact nature of the interactions here is certainly not known, these findings illustrate the ways in which neuropsychological studies can address questions about brain processes and can contribute to a better understanding of the nervous system.

CONCLUSIONS

In this chapter, an attempt is made to describe neuropsychological assessment in epilepsy and to show how it may enhance an understanding of the brain. The treatment of epilepsy (and epilepsy itself) has made this possible by providing alterations in brain conditions, the behavioral correlates of which could then be studied. The study of the brain through behavioral tests is unlike any of the other methods reported in this book. It complements the other approaches and has its own advantages, especially including the facts that it is noninvasive and provides indications of the ultimate function of the brain, namely, the ability to adjust to the demands of life.

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