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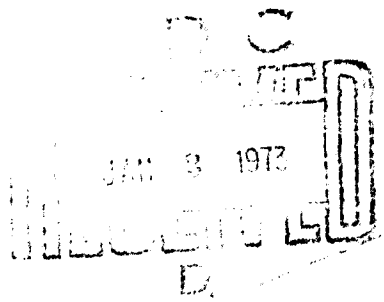

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13. ABSTRACT

Seventy-seven navy enlisted men with a mean age of 23.2 years (range 17 to 48) were admitted to the hospital after their first seizure and given a provisional diagnosis of convulsive disorder. The subjects were followed-up for three years to see if reliable predictors of subsequent seizures and diagnosis could be obtained at the first examination. If not readmitted because of a second seizure, each patient was recalled at the end of his first and third year in the study for follow-up examinations.

Following a second seizure and readmission to the hospital, 39% were diagnosed as having a convulsive disorder, 18% a psychiatric disorder, and 5% a neurological illness. Thirty-six percent never had a second seizure. Of those experiencing a second seizure, 77% were readmitted during the first year. Three variables were found to be useful predictors of second seizures and final diagnoses: type of seizure (major motor); electroencephalographic classification (spikes with or without slow waves); and presence of post-ictal confusion and disorientation.

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Diagnostic Factors in Adult Males Following Initial Seizures

A Three-Year Follow-Up

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Seventy-seven navy enlisted men with a mean age of 23.2 years (range, 17 of 48) were admitted to the hospital after their first seizure and given a provisional diagnosis of convulsive disorder. The subjects were followed-up for three years to see if reliable predictors of subsequent seizures and diagnosis could be obtained at the first examination. If not readmitted because of a second seizure, each patient was recalled at the end of his first and third year in the study for follow-up examinations.

Following a second seizure and readmission to the hospital, 93% were diagnosed as having a convulsive disorder, 18% a psychiatric disorder, and 5% a neurological illness. Thirty-six percent never had a second seizure. Of those experiencing a second seizure 77% were readmitted during the first year. Three variables were used as predictors of second seizures and final diagnoses: type of seizure (major motor); electroencephalographic classification (spikes with or without slow waves); and presence of postictal confusion and disorientation.
(27:193-197, 1972)

The studies reported to date of late onset seizures have been in patients with multiple seizures and with a positive diagnosis of convulsive disorders.[1-4] To our knowledge, there is no definitive study on how many patients experiencing their first seizure at this age do not experience subsequent seizures.

The purposes of this study were (1) to determine how many patients experiencing their first seizure in young adulthood or later would have a second seizure, and (2) to determine if reliable predictors of subsequent seizures and the final diagnosis could be made from data obtained at the first examination.

Method and Material

The series consisted of enlisted Navy patients admitted to the San Diego Naval Hospital with a complaint of a single convulsion, seizure, or unexplained loss of consciousness,

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The opinions and assertions contained herein are the private ones of the writers and are not to be construed official or as reflecting the views of the Navy Department.

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who were given a provisional admitting diagnosis of epilepsy, who had at least one year of active service remaining, and who were beyond recruit training. No patients in these categories were excluded unless they were found to have (1) seizures existing prior to entry into service; (2) demonstrable organic causes for their complaints, or other medical findings that would prevent their return to duty; (3) administrative reasons that would prevent return to duty; or (4) chronic alcoholism. No patient admitted to a history of recent drug use.

We were interested in only those patients for whom there could be found no organic causes for their presenting symptoms at first evaluation. Patients who had fainted while in parade formation, while blood was being drawn, or during an inoculation were not included. Patients whose seizures appeared to have been precipitated by sleep loss and fatigue were included.

Seventy-seven patients were accepted in the study. All were given (1) a detailed history and physical examination (with stress on neurological and possible precipitating causes for their complaints); (2) repeated electroencephalograms using various activation procedures, including sleep, sleep deprivation, photic stimulation, and hyperventilation; (3) a family-history questionnaire, which was mailed to a parent or closest relative; (4) laboratory studies of blood, urine, chemistry, and cerebrospinal fluid (CSF) to rule out systemic causes; (5) a lumbar puncture; (6) an x-ray film series of the skull; (7) psychological tests including measures of intelligence (Wechsler Adult Intelligence Scale [WAIS]) visual-motor functioning (Bender-Gestalt, Memory for Designs), personality (Minnesota Multiphasic Personality Inventory), and a somatic complaints questionnaire, Cornell Medical Index (CMI); and (8) a psychiatric examination.

In addition, contrast procedures were used when indicated.

After this evaluation, the patients were sent back to unlimited duty with no anticonvulsant medication. The only diagnosis made at this time was "observation medical," which is a discharge diagnosis used by the Navy after a period of hospitalization to indicate that a diagnosis of a specific illness or disease was not made. Instructions were placed in each patient's medical records stating that he was a member of a special seizure study, that no seizure medication was to be given, and that the patient was to be returned to the San Diego Naval Hospital if he had subsequent complaints similar to those on first examination. These instructions were also given to each patient. Except for one patient who was sensitive to photic stimulation and whose duty was on the flight deck of a carrier, no restrictions were placed on a patient's assignment. It was recommended this patient not be assigned to the flight deck.

Those patients who did not have a subsequent spell or seizure during their first year in the study were called back at their anniversary date for reevaluation and then were again returned to duty. After two more years, they were again called back for study, if not admitted because of a second seizure during this period.

Results

The total sample mean age was 23.2 ± 5.93 years, with a range from 17 to 48 years. The average intellectual level was WAIS IQ 104.7 ± 9.60 with a range from 88 to 130.

Of the total sample of 77, 49 (63.6%) were invalided from the service during their three-year follow-up period.

Thirty (38.9%) were diagnosed by the neurology staff and discharged from the service as having seizure disorders. The discharge diagnoses for the seizure patients were major motor seizures, 27 patients; psychomotor seizures, two patients; and focal motor epilepsy, one patient. The grand mal convulsions in two patients were precipitated by reading, but no other reflex-type seizures were present, although one patient with grand mal seizures was sensitive to flickering light on examination.

Fourteen patients (18.1%) were given a psychiatric diagnosis of personality-trait disorder after their second admission.

Four patients (5.2%) were given a neurological diagnosis after their second seizure. These diagnoses included the following: one chronic alcoholism with seizures; one vascular malformation with cortical atrophy; one posttraumatic encephalopathy; and one encephalopathy secondary to arteriosclerosis. Except for these four patients, no significant neurological signs were found in any patient on initial or follow-up examinations. No neoplasms or space-occupying lesions were found.

One patient was given a discharge diagnosis of syncope associated with Wolff-Parkinson-White syndrome, without evidence of cardiac disease or disability.

Twenty-eight patients (36.4%) were never given a diagnosis. Nine of these completed their tour of duty during the second or third year of the study and were released from the service asymptomatic. Nineteen returned for their three-year follow-up study and were free of seizures.

None of the patients injured himself or was reported to have endangered others as a result of his initial or subsequent seizures.

Interval Between First and Second Evaluations.—Seventy-seven percent of the 49 patients with a second seizure returned within one year of their initial evaluation; 26 (53%) returned within six months; and an additional 12 (24%) returned during the second six-month period. Six seizure patients returned during the second year and one returned during the third year. There was no significant difference in time interval between first and second seizure for the seizure disorder, psychiatric, and neurological groups. (Three patients have reported a major motor seizure since the termination of the three-year study. Two occurred five years after and one six years after the first seizure.)

Diagnostic Factors.—This analysis used the findings from the first examination to obtain criteria that would identify those patients who would have a second seizure and to determine if these predictors differed with respect to the final diagnosis. (A detailed analysis of the findings from the first examination and of the statistical analysis used in obtaining the diagnostic criteria can be obtained from the first author.) Because of the small number, the one syncope patient and the four neurological patients were not included. Through use of discriminating-function analysis, weights were computed for each variable reflecting their contributions to the final diagnosis. Because of the large number of possible predictors (472), randomly chosen analysis and cross-validation samples were used for this analysis.[5] In each sample, there were 15 seizure disorders, seven psychiatric disorders, and 14 undiagnosed patients.

After several analyses, only three variables were found to be reliable predictors of the eventual diagnosis and were selected for use on the cross-validation sample. The results on the cross-validation sample for these three variables were also significant, $P < .02$. These variables were the following: (1) average of the ratings, on a five-point scale from "definitely yes" to "definitely no," by the three medical officers (two neurologists and one psychiatrist) as to the presence of a true seizure, ie, a seizure with loss of consciousness and with motor involvement; (2) electroencephalographic classification as to degree of abnormality; and (3) presence of postictal confusion or disorientation, or both. While all the intercorrelations among these three variables were positive, only the correlation between rating of true seizure and electroencephalographic classification was significant, $r = .27$, $P < .05$.

The EEGs were classified as mildly, moderately, or markedly abnormal. Electroencephalographic records with spike-wave complexes or bursts of delta waves of more than 60μv were classified as showing marked abnormality, grade 3. Records with either generalized or focal theta bursts, sharp waves or paroxysms of more than 30μv were called moderately abnormal, grade 2. Records with rhythmic or arrhythmic activity, either generalized or focal and of less than 30μv, were called minimally abnormal. Only the records with spikes or spike and slow-wave discharges significantly differentiated the groups. Spike or spike and slow-wave discharges were found in 43% of the patients with seizure disorder and in 11% of the undiagnosed patients, but no psychiatric patient's record contained spike-wave discharges. One neurological patient's EEG contained spikes during a clinical seizure, but all of his interictal records were normal. One neurological patient had a slow-wave focus, and two patients' records were all normal on first admission. The syncope patient's record was normal.

Ten (33%) of the 30 patients with a seizure disorder had all three signs, ie, a rating of a true seizure, an EEG with spike and wave complexes, and postictal confusion, on their first admission. The presence of two signs occurred in 16 (53%), and three of the patients (10%) had one of the three signs. One patient with a seizure disorder (0.03%) had none of the three predictor variables on his first admission.

Only one of the 28 undiagnosed patients

Seizure Index Scores				
	Sample			
	Analysis		Cross-Validation	
Final Diagnosis	Mean	SD	Mean	SD
Seizure disorder	8.82	2.47	8.70	1.66
Undiagnosed	6.46	2.21	6.58	1.94
Psychiatric	3.98	1.74	4.18	1.92

(4%) had all three signs at first admission; nine (32.0%) had two signs; 13 (46%) had one of the signs, and 5 (18%) did not have any of the diagnostic variables.

None of the patients diagnosed as having a psychiatric disorder on their second admission had all three abnormal signs on their first admission. One of the 14 (7%) had two signs, one (7%) had one sign, but 12 (86%) did not have any of the diagnostic variables.

The presence of only one of the three diagnostic variables did not significantly predict a second seizure of epileptic origin, but if all three were present in the same patient, the odds were extremely high (96%) that he would return and be given a diagnosis of seizure disorder. Sixty-seven percent of the seizure patients, however, did not have all three predictors on their first evaluation. If a physician refused to make a seizure diagnosis unless all three signs were present, he would make a false-positive diagnosis only 4% of the time, but his false-negative rate would be 67%. Even though two or more signs occurred in 86% of the seizure patients, a clinician requiring two signs would make a false-positive diagnosis of seizure disorder in 43% of his patients, since 36% of the undiagnosed patients and 7% of the psychiatric patients had at least two signs.

The two signs that occurred together were (1) a positive rating as to the presence of a major motor seizure and (2) either an EEG with spike-wave activity or confusion or disorientation, or both. The latter two occurred with a positive rating as to true seizure in about equal proportion, but spike-wave electroencephalographic activity and confusion and disorientation never occurred with a low rating (one, two, or three on a five-point scale) as to the presence of a major motor seizure.

By use of the discriminant weights obtained from the analysis sample for each of the three predictor variables, a Seizure Index Score was obtained for each patient.

The mean Seizure Index Scores and standard deviations for the analysis and cross-validation samples are presented in the Table. The differences between the three group means were significant at the .02 level or better for both the analysis and cross-validation samples. The mean score for the four neurological patients was 5.75 ± 2.27. (The discriminant weights, computing examples, and cutting scores for the Seizure Index Scale can be obtained from the first author.)

Comment

Our finding that only 39% of our patients were diagnosed as having seizure disorders is consistent with the view of many that a single convulsion may not be the first manifestation of recurring epileptic seizures. Our results also show that it is very difficult to make a valid prediction of second seizures and final diagnosis from the first examination of adult patients. Personal-history questionnaires, psychiatric interviews, and neurological examinations revealed that the psychiatric patient usually showed positive psychiatric and psychological data and noncontributory neurological and electroencephalographic findings. The difficult diagnostic problem was that of separating those patients who had a second seizure that was considered to be epileptic in origin from those who had no second seizure. Only the type of initial seizure, the electroencephalographic classification, and postictal confusion and disorientation were found to be useful predictors.

While all three predictor variables were positively correlated, only the correlation between clinical rating as to the presence of a true seizure and the electroencephalographic classification was significant; but, in this instance, the common variance was only 7.3%. Each variable thus contributed uniquely to the diagnostic prediction. These three measures may be likened to subtests on an intelligence scale. They correlate positively with each other, each contributes significantly to the final prediction, but no single variable is sufficient for reliable prediction.

By excluding the few patients with known organic cerebral lesions, we obviously removed a population of patients who could reasonably be expected to have second seizures. These patients generally do not pose a diagnostic problem, and it was not feasible to include patients with diagnosed cerebral lesions in this study, as our patients were to receive no treatment after their first examination. Our goal, thus, was not to study all patients with initial seizures, but only those patients where no cause for their seizures could be determined and, therefore, pose a difficult diagnostic and treatment problem.

While the clinician is always concerned over the possibility that a single seizure in adults is the first evidence of progressive brain damage by tumors, vascular disease, or degenerative disease, several studies have shown that these convulsions are not necessarily associated with cerebral lesions.[1-4] Four of our 77 patients were given a neurological diagnosis following their second seizure. No neoplasms were found. Raynor et al[3] found that the statistical probability of tumor was considerably increased by (1) the presence of abnormal neurological signs; (2) focal electroencephalographic abnormalities; (3) focal character of clinical seizures; and (4) initial onset of seizures after the age of 50.[6] Except for two patients who showed focal temporal lobe spikes and one with focal motor seizures, our patients had none of these signs or characteristics. It is entirely possible, though, that some of our patients may yet be found to have structural problems, but each year that passes without a second seizure or other symptoms decreases the probability that the initial seizure was due to such an undiagnosed organic problem. In a questionnaire study of the time interval between first seizures and other clinical signs of brain neoplasms, Douglas[7] found physicians reporting neoplasms as long as 20 years following a first seizure, but 50% of the neoplasms were found within three years of the first seizure. Thirty percent were found in the first year. There were no data as to the number of seizures in each patient before the diagnosis of a neoplasm was made.

The fact that two of our patients had seizures five years after and one patient six years after their first one indicates that other patients who were never given a medical diagnosis may yet have a second seizure. (One of the patients had two diagnostic signs and two had no predictors on first admission.) We do not believe that many of the remaining patients have had a second seizure for we would have been contacted. For patients no longer in the military service, our records will assist them in applying for Veterans Administration disability ratings. Our records are available to patients still in the service. Of the three patients with known seizures after the three-year follow-up study, one was a civilian and two were still in the service. In all instances, our findings were requested with the patient's consent. The question asked by the physician of one of the patients in the service is perhaps pertinent. Should a patient who has a second seizure after five years, induced by the same precipitating event (sleep loss), with a normal EEG be given a diagnosis of seizure disorder and given anticonvulsant medication?

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