

Clinical Research

Nonepileptic Seizure Outcome Varies by Type of Spell and Duration of Illness

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Summary: *Purpose:* To determine whether differences in clinical manifestations of psychogenic nonepileptic events are associated with differences in outcome and whether the length of illness before diagnosis correlates with outcome.

Methods: We reviewed ictal videotapes and EEGs in 85 patients diagnosed with exclusively nonepileptic psychogenic seizures during inpatient CCTV-EEG monitoring at the University of Michigan between June 1994 and December 1996. They were classified into groups of similar ictal behaviors. Fifty-seven of these patients were available to respond to a follow-up telephone survey about their condition 2–4 years after discharge. We examined demographics, baseline EEG abnormalities, and outcome of treatment interventions. We also evaluated whether interventions were more likely to succeed if patients were diagnosed early in the course of the illness.

Results: We found that the largest groups consisted of pa-

tients with motionless unresponsiveness (“catatonic,” $n = 19$) and asynchronous motor movements with impaired responsiveness (“thrashing,” $n = 19$). Infrequent signs included tremor, automatisms, subjective events with amnesia, and intermittent behaviors. There was a higher incidence of baseline EEG abnormalities in the thrashing group (31%) than in the catatonic group (0%). There was a higher incidence of complete remission of spells in the catatonic group (53%) than in the thrashing group (21%). Patients who had a more recent onset of seizures (most often within 1 year) were much more likely to have remission of spells after diagnosis.

Conclusions: Classification of nonepileptic seizures is useful in predicting outcome and may be valuable in further investigation of this complex set of disorders. **Key Words:** Nonepileptic events—Outcome—Personality testing—Pseudo-seizures.

Carefully refined classification systems for both seizures and epilepsy syndromes have substantially improved the diagnosis and management of patients with epilepsy (1,2). These tools provide a level of detail that suggests separate etiologies and possibly even separate mechanisms of pathogenesis. A new set of revisions in these systems incorporating new knowledge is being developed (3). Observing patients with psychogenic nonepileptic spells, distinct patterns also seem to emerge. These spells are as disabling as epilepsy and tend to be even more refractory to several modes of treatment. The largest outcome study to date (4) documented a 60% refractory rate. On the basis of our observations that patients with minor motor manifestations seemed to fare better than others, we undertook this study to begin to identify potentially separate syndromes with distinguishable etiologies and natural histories.

For several years, clinicians studying psychogenic nonepileptic events have discerned differences in predispositions and MMPI profiles that they believed warranted division of their groups into “convulsive” or “non-convulsive” patterns (5), or major versus minor motor episodes. Most patients have relatively stereotyped episodes, although up to 12% in some series have mixed patterns (6). Clinical observations also indicate that there are psychological differences between patients with long episodes of motionless unresponsiveness and patients with brief thrashing episodes. We have attempted to describe behavioral differences and provide long-term outcome data on 57 of these patients whose only active spells were documented on CCTV-EEG to be psychogenic. Our hypothesis was that it might be possible to predict a relative prognosis for these two broad categories of patients (which we have referred to as the catatonic and thrashing groups). Our hope is that by categorizing patients with different semiologies (behavioral manifestations), we will eventually improve our understanding of the pathogenesis and natural history of this common disorder.

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METHODS

All patients admitted to the inpatient CCTV-EEG monitoring unit at the University of Michigan from June 1994 to January 1997 were reviewed, and 85 patients whose only active spell type was documented to be psychogenic were included for further study. Videotapes, EEG recordings, and medical records were retrospectively reviewed and classified blinded to outcome data obtained later.

The video recordings of ictal behaviors were classified into six basic types: catatonic, characterized by long periods of motionless unresponsiveness, often accompanied by waxy flexibility; thrashing, relatively brief, four-extremity asynchronous, often violent movements, with or without ictal cries; automatisms, small-amplitude, near-purposeful movements of the face or upper extremities with amnesia for ictal events; tremor, rhythmic synchronous bilateral low-amplitude movements; intermittent, long spells that included unusual behaviors such as rocking, screaming, and sometimes thrashing with interspersed sudden motionless unresponsiveness; and subjective, reports of sensory or emotional experiences, generally with retained consciousness and behavior but amnesia for the events.

All patients except the 10 classified as subjective were behaviorally unresponsive during at least half of their events, and the patients with subjective spells were all amnesic for items presented during at least one of their events. In six cases, two different semiologies occurred, and these patients were classified according to the type responsible for at least 80% of their episodes. None of these patients had a combination of thrashing and catatonic spells, and most were a mixture of tremor, intermittent, and thrashing spells.

In a masked fashion, telephone interviews were conducted on the 57 available patients by one of the authors (L.M.S.) to assess the perceived usefulness of their stay and diagnostic information, recurrence of spells (outcome), use of psychiatric services, and continued reliance on antiepileptic drugs (AEDs). Medical records were retrospectively reviewed to ascertain age, sex, duration of these episodes, presence or absence of EEG abnormalities (including focal or diffuse slowing and interictal epileptiform activity), number of AEDs, and employment status.

Statistical analysis of the data was performed to assess for any baseline demographic differences (chi-square with one degree of freedom)—specifically, we checked for differences in age, percentage of women, spell onset, and EEG abnormalities. We also evaluated a proposed difference in outcome in the two largest groups (catatonic vs. thrashing, chi square) and examined the correlation of outcome type with the duration of the illness (Mann-Whitney test, two-tailed).

RESULTS

Between June 1994 and January 1997, 359 patients were admitted for CCTV-EEG monitoring at the University of Michigan. Two hundred thirty of these patients were admitted for diagnosis of the nature of their spells, and 129 were patients with refractory epilepsy admitted as part of an evaluation for epilepsy surgery. Monitoring reports for all diagnostic admissions were screened to identify 85 patients with only nonepileptic, apparently psychogenic events, without concomitant recorded epileptic seizures and with no unrecorded active spell or seizure types. Of the 57 patients who could be contacted for follow-up telephone interviews, most fell into the thrashing ($n = 19$) or catatonic ($n = 19$) categories. Subjective spells were next most common ($n = 10$); tremors ($n = 4$), automatisms ($n = 3$), and intermittent behaviors ($n = 2$) were relatively rare. We also examined clinical data and semiology on the 28 patients who were lost to follow-up and could not be reached by phone: this group contained nine with thrashing spells, seven with catatonic spells, six with subjective episodes, three with tremor, two with intermittent behavior, and one with automatisms. This distribution did not significantly differ from the 57 patients who were contacted and from whom outcome information was obtained.

In the group where outcomes were available, we examined semiology versus various demographic factors (sex, duration of spell syndrome before diagnosis, and number of EEG abnormalities, Table 1). Distribution of gender in the groups was not significantly different, but groups with minor motor manifestations tended to include more women. There was a significant difference in the number of patients with baseline EEG abnormalities in the two largest semiologic categories: there were none in the catatonic group and 32% (6/19) in the thrash group ($p < 0.02$). The abnormalities identified in the thrashing group included generalized slowing ($n = 3$), focal slowing ($n = 2$), interictal sharp waves ($n = 2$), and fragmentary sharp and slow wave discharges ($n = 1$). Four of these six patients with abnormal EEGs had never had any other spell type than those recorded at this time, but two of these patients had had rare nocturnal seizures with a somewhat different semiology 4 to 6 years or more before their monitoring that had not recurred after monitoring. Both of these patients with an unrecorded past seizure type had new spell types within 1 year of monitoring. One of these patients had bilateral independent temporal spikes and the other had rare fragmentary sharp and slow discharges. Patients in the subjective group also had a high incidence of EEG abnormalities, all consisting of focal temporal or hemispheric slowing. None of these patients had a previous or different semiology than recorded.

TABLE 1. Demographics

	Catatonic	Thrash	Subjective	Tremor	Automatisms	Intermittent
Number of patients	19	19	10	4	3	2
Age (y)	40.0 (± 9.5)	38.8 (± 16.9)	43.5 (± 13.1)	34.3 (± 4.3)	37.7 (± 16.9)	42.0 (± 14)
% female	79%	58%	100%	50%	70%	50%
Spell onset (y)	9.8 (± 13.6)	11.6 (± 11.3)	7.6 (± 12.8)	11.8 (± 13.3)	17 (± 25.5)	5.5 (± 5.0)
EEG abnormalities	0	32%	40%	25%	0	0

At the time of discharge, AEDs were discontinued in patients as much as possible. The only exceptions in the largest groups are the two thrashing patients mentioned above with a distant past history of another type of spell, two patients in the catatonic group who refused to stop medications, and one in the thrashing group who left against medical advice. Four patients were maintained on AEDs used only for pain or mood stabilization (two thrashing, two catatonic).

Follow-up ranged from 19 months to 4 years. Patients were asked to rate the quantitative improvement in frequency. The number of patients who were completely spell-free within 1 month of their monitoring was 23/57 (40%), and an additional 9 patients had a >90% reduction in episodes, for a total of 32/57 (56%) with substantial functional improvement since their diagnosis. Thirty-nine of the 57 patients (68%) were able to discontinue AEDs and remained medication-free at the time of follow-up. (All patients whose medications were restarted were followed up outside our program).

We asked patients whether they had ever seen a mental health professional, were taking any medications for anxiety, depression, or any emotional concerns, and whether they were receiving ongoing treatment from a mental health provider. Thirty-one patients (54%) had originally seen a psychiatrist, 22 (39%) were receiving ongoing treatment from a mental health professional, and 20 (35%) were taking medications for psychiatric disorders. Six of the patients taking medications for psychiatric concerns had never seen a psychiatrist and had their medications prescribed by a primary care physician or neurologist. Analysis of outcome in the group receiving ongoing treatment from a mental health professional indicated that 6/22 were spell-free (27%) and 5 more had a >90% reduction, for an overall rate of 11/22, or 50% substantial improvement in spells. This is not significantly different than our overall group.

The number of patients who were seizure-free varied by spell type. In the largest groups, there was a significant difference in the rate of remission between the catatonic (53%) and thrashing (21%) groups (Table 2, $p = 0.04$). (Exclusion of the six patients believed to have mixed elements would not have changed the significance.) The catatonic group also had the highest incidence of long-term discontinuation of AEDs: 84% versus 58% in the thrashing group. In the smaller groups, there

were variable rates of remission: 3/10 in the subjective group, 2/4 with tremor, 2/3 with automatisms, and 0/2 in the intermittent behavior group.

Finally, all patients were evaluated to determine whether the duration of illness before monitoring was a significant predictor of outcome. We found the length of their illness before diagnosis was much shorter in the spell-free outcome group than in those who showed no improvement ($p < 0.001$). For patients who no longer had events after diagnosis, 47% had onset within 1 year (mean duration 7 years, median 2 years); for patients with a >90% spell reduction after diagnosis, 54% had started within 1 year (mean duration 6 years, median 1 year). In those who did not improve after diagnosis, only 12% had had the events for <1 year, and they had an average duration of 15 years (median 14 years). Looking at the data from another perspective, in the group of patients whose spells started within 1 year, only 16% did not have at least a 90% reduction of spells after diagnostic monitoring.

DISCUSSION

The idea of dividing psychogenic nonepileptic events into subgroups is not entirely new. Many authors have recognized that there is significant diversity in semiologies. Some have segregated the spells into those mimicking complex partial seizures and in-phase or out-of-phase generalized movements (6). Early in the characterization of psychogenic patterns, Gulick et al. (7) divided the groups into bilateral motor, unilateral motor, multiple behavioral patterns, and impaired responsiveness without behaviors. More recently, Henry and Drury (8) chose to divide them into convulsive, hypokinetic, and hypotonic types. The incidence of what we describe as paroxysmal catatonic events varies from 20% in some of these earlier series to >50% in a group studied by Leis

TABLE 2. Outcome (1.5–4 y)

	Catatonic	Thrash	Significance
Spell-free	10/19 (53%)	4/19 (21%)	<0.05
>90% reduction in spells	13/19 (68%)	8/19 (42%)	NS
Off antiepileptic medications	16/19 (84%)	11/19 (58%)	NS

et al. (9). However, none of these studies have suggested there may be differences in the EEG findings or outcome among these groups. Our study was clearly limited by its small sample size, but even in this small population, significant differences in outcome and predispositions emerged that warrant further study.

Psychologists and psychiatrists have documented a variety of different personality profiles in patients with psychogenic paroxysmal events. Diverse psychological etiologies including conversion disorders, depression, post-traumatic stress disorder, anxiety, emotional trauma, dissociative disorders, psychosis, and impulse control problems have been implicated in its pathogenesis (10–13). Early authors simply clarified that there was a unique pattern of MMPI profiles and associated traumas that were not present in the equally disabled epileptic population (14,15). More sophisticated analyses of MMPI scores (6) divided patients into three groups: major motor, limited motor, and affectual-only types. Patients in the limited motor group had significantly elevated hysteria, hypochondriasis, and schizophrenia subscales compared with partial epilepsy patients. In the affectual-only group, the MMPI showed elevations in these three scales and also in the psychasthenia scale. Patients with major motor spells did not significantly differ from patients with generalized epilepsy in their MMPI profile (16).

Other recent descriptions support the theory that minor motor spells are more likely to be dissociative, posttraumatic events and that those with major motor manifestations were generally without precipitants and tended to be “immature with global difficulties coping and relating” (17). One study found a higher rate of sexual abuse in the group with “swooning” or catatonic spell types (12). These observations may relate to differences in psychological profiles and may help explain the difference in remission rate we noted. Authors who did not classify their nonepileptic patients by semiologic type found much less striking personality differences between patients with epilepsy and those with nonepileptic seizures (17,18).

Nonepileptic seizure outcome data have never previously been found to differ by semiologic type. Overall, our outcome results are similar to those of other groups. We found an overall complete remission rate of 40%, which is similar to the 35% (19) and 44% (20) reported by other recent authors. In children and adolescents, substantially better outcomes are described, with one study documenting a remission rate of 78% in youngsters having an average duration of symptoms of 7 months (21). Another study suggested that younger children may be more likely to have episodes of motionless unresponsiveness (22). Meierkord et al. (4) also documented a 40% chance of complete remission in adults but did not agree so completely with our findings on other points. Their

study found no correlation between length of illness before diagnosis and outcome, but they did not perform a continuous analysis, and used 3 years as their cutoff for long versus short duration. Our data indicate a clear correlation between spell duration and outcome, as have other groups (19), and indicate that 1 year may be a more relevant discriminating point. Meierkord et al. also divided their patients into two groups (primarily limpness or collapse versus primarily motor activity) and found only nonsignificant differences in outcome (46% attack-free in the limp group, 36% in the motor group). We believe that semiologic classifications need to be more specific than this single division implies. For example, in our small groups with tremor, subjective spells, intermittent behavior, or automatisms, the remission rate was intermediate between the more purely distinguishable catatonic and thrashing spells. Had we attempted to include these patients into either category, our results would have been less clear. We believe that patients with prominent automatisms or subjective experiences with amnesia differ in many significant respects from those with motionless unresponsiveness. We believe our analysis was able to uncover differences among catatonic and thrashing patients because of a more rigorous classification system.

There are many reasons to attempt a very careful discrimination between these patients. Patients with primarily asynchronous thrashing movements are much more likely to be confused with those with frontal lobe epilepsy (23). Despite an awareness of the shorter duration of epileptic frontal seizures and of other features more specific to that diagnosis, including prominent versive movements and nocturnal occurrence, it is difficult to be certain in diagnosing nonepileptic seizures versus frontal lobe epilepsy in the absence of clear EEG or magnetic resonance imaging abnormalities. Kanner (24) suggested that filtering techniques, supplemental electrodes, and ictal single photon emission computed tomography may be helpful in these instances. These techniques need to be more routinely used in patients with stereotyped events that are nocturnal with prominent asynchronous movements or versive behaviors. Some patients currently classified as having nonepileptic seizures may be misdiagnosed. We found a significantly increased incidence of sometimes nonspecific EEG abnormalities in this group compared with the other semiologies. These abnormalities can be present with patients with pseudoseizures alone (25); nonetheless, subclassification of the nonepileptic behaviors highlights the need to consider the differential diagnosis in the thrashing group, particularly because their outcome when treated with conventional interventions seems poorer.

Current treatment strategies include supportive confrontation of the patient (26) and careful follow-up by neurologists or psychiatric personnel trained in an epi-

lepsy program (20). Another important facet of the treatment is avoiding the medical risks imposed by anticonvulsants and emergency treatment. The catatonic group, with its higher remission rate and its less physically threatening appearance, naturally fares better in avoiding potentially harmful medical interventions. By separating these patients into distinctive subsets, treatment might be better tailored to the needs of each type of patient. Further investigation with information about individual psychological profiles might indicate that certain behavior types were correlated with specific psychological predispositions and might respond to similar treatments. For instance, if the catatonic group proved to be more closely associated with conversion and grief reactions, supportive and insight-based psychotherapy could prove effective in this subset. Increased scrutiny could uncover some patients with frontal lobe epilepsy among the thrashing group, and one group might respond better than another to the idea of countermeasures (behavioral tools for maintaining consciousness).

Our results raise the possibility that early intervention could be valuable for patients with nonepileptic seizures. A prospective analysis of these patients divided into behavioral types, including detailed psychological profiles, might provide new insights about the pathophysiology in each group. We hope we have provided evidence that there is value in classifying these patients into subgroups with different natural histories and predispositions, with the ultimate goal of providing the best possible treatment for each patient.

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