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Evaluation and treatment of epilepsy in multiply handicapped individuals

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Abstract

The evaluation and treatment of patients with seizures and multiple handicaps are challenging. An orderly approach to these patients, however, can be especially rewarding. As in other patient populations, evaluation rests on the clinical cornerstones of history, examination, imaging, and electroencephalography. Several disease entities are overrepresented in the multiply handicapped population. Here, we review the principles of evaluation and some of the most common etiologies of recurrent seizures afflicting handicapped individuals. Practical issues that arise in institutional settings are highlighted, and basic treatment principles are discussed.

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1. Introduction

Medical problems in multiply handicapped individuals are generally complex and multifactorial, and often incompletely understood. Specific diagnoses are often inadequate and sometimes impossible. Communication with the patient is often difficult, and extensive testing may be limited or impractical. From the physician's perspective, most historical information comes from caregivers. Patients often cannot express their own concerns, and those with significant handicaps may be unable to express complaints or desires. In institutional settings, including developmental centers and group homes, caregivers typically work in teams, and information can be enhanced or degraded as it is passed on. Ultimately, the entire team carries the burden of advocacy. Nonetheless, the goals of neurological evaluation and treatment of seizure disorders are identical to those in other patient populations: that is, to identify treatable causes for seizures; to define the need for specific treatment; to choose the optimal treatment; balancing efficacy against toxicity; and to facilitate lifestyle planning

to allow patients to reach their maximum individual potential.

Diagnosis in the multiply handicapped population relies on the same cornerstones as in other patient populations: history, examination, imaging, and electroencephalography.

2. History

History is often limited. Patients frequently cannot tell physicians the details of their illness, and as they get older, parents and other potentially informative sources may no longer be available. Medical records may be sketchy and incomplete. It is helpful to focus initially on the likely etiology of the patient's seizures and disability. In our experience, the following processes are grossly overrepresented in the multiply handicapped population with seizures: perinatal injury, remote central nervous system infection, trauma, and developmental and genetic brain disorders.

2.1. Perinatal injury

While the incidence of perinatal injury has declined because of improvements in obstetric care and

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technique, difficulties during delivery continue to be a major risk factor for later development of sometimes disabling seizures [1]. Broadly speaking, neurological injury during delivery may be related to prematurity, birth trauma (e.g., forceps delivery), or perinatal hypoxia. Significant prematurity renders infants vulnerable to occurrence of periventricular hemorrhage and periventricular leukomalacia. These lesions, which may result in the classic pattern of spastic diplegia, are also associated with seizures in approximately 25–50% of affected individuals. While the major burden of neuropathological injury is in the white matter, injury to adjacent cortex and disruption of normal neuronal migration are both likely to contribute to the later evolution of seizures [2].

Birth trauma may result in brain injury. Forceps delivery may increase risk of intracranial hemorrhage. In one series, the incidence of seizures was approximately doubled in patients delivered by forceps as compared with those delivered without instruments [3]. Nelson and Ellenberg [4] have emphasized, however, that underlying nervous system injury or developmental abnormality may be the cause of both seizures and the need for assisted delivery.

Perinatal asphyxia may result in seizures in 30–40% of affected full-term infants [5]. Asphyxia may result from obstetric catastrophes such as umbilical cord prolapse and placental abruption, from severe meconium aspiration, or from a mechanical interference with the umbilical blood flow, such as a nuchal cord. Acute total asphyxia principally affects deep gray matter structures, including diencephalon and basal ganglia, while prolonged partial asphyxia is more likely to affect cortex and subcortical white matter. The latter condition is most likely to result in epileptogenic lesions.

2.2. Remote central nervous system infection

A history of remote central nervous system infection is commonly found in institutionalized patients with

epilepsy and central nervous system dysfunction. Neonatal or childhood meningitis, often complicated by venous infarction, may cause extensive gray matter injury with associated neurological deficits and chronic seizures. Viral encephalitis, often due to herpes simplex infection, is also overrepresented in this population.

2.3. Trauma

Significant traumatic brain injury may result in severe seizure disorders and neurocognitive dysfunction. Hemorrhage and depressed skull fracture are important risk factors for posttraumatic seizures, whereas diffuse axonal injury may contribute to cognitive and behavioral disturbance. The mechanism of posttraumatic seizures is unknown, but the iron deposition that may result from bleeding is highly epileptogenic. Many patients with posttraumatic seizures have multifocal epilepsies, but some types of trauma, e.g., low-energy injuries, may result in a single focus of epileptic activity. Early treatment of trauma patients with anticonvulsants has no demonstrated prophylactic value with respect to the risk of developing later epilepsy [6].

2.4. Developmental and genetic brain disorders

Recent advances in neuroimaging, especially the development of magnetic resonance imaging (MRI), have allowed the identification of a wide variety of developmental brain abnormalities, and advances in genetics are leading to identification of an increasing number of specific genetic abnormalities responsible for developmental disturbances. Structural disturbances of brain development can occur throughout the period of brain formation and maturation [7,8] (Table 1). Specific genetic defects have been associated with several disorders of cerebral development (Table 2).

Another class of developmental disorders, those belonging to the autism-pervasive developmental disturbance spectrum, have no clear anatomic basis. These

Table 1
Disorders of brain development

Classification	Example	Associated sign	Notes
Disorders of ventral induction	Holoprosencephaly	Midline facial defects	Prolonged survival is rare
Disorders of proliferation	Micrencephaly Megalencephaly Tuberous sclerosis (TS) Dysembryoplastic neuroepithelial tumors (DNETS)	Cutaneous signs common in TS	Wide spectrum of severity of neurological dysfunction seen in TS and DNET
Disorders of migration	Agyria-pachygyria Bilateral central macrogyria Focal heterotopia Cortical dysplasia	Lissencephalopathy Band heterotopia Periventricular Nodular heterotopia	Conditions may be bilateral, unilateral, focal, or multifocal

Table 2
Genetic basis of malformations of cortical development

Syndrome ^a	Locus	Gene	Protein
ILS ^{DCX}	Xq22.3-q23	<i>DCX = XLIS</i>	DCX or doublecortin
SBH ^{DCX}	Xq22.3-q23	<i>DCX = XLIS</i>	DCX or doublecortin
MDS	17p13.3	Several contiguous	PAFAH1B1 and others
ILS ^{LIS1}	17p13.3	<i>LIS1</i>	PAFAH1B1
SBH ^{LIS1}	17p13.3	<i>LIS1</i>	PAFAH1B1
LCH ^{RELN}	7q22	<i>RELN</i>	Reelin
FCMD ^{FCMD}	9q31	<i>FCMD</i>	FCMD or fukutin
MEB	1p32	Unknown	Unknown
BPNH	Xq28	<i>FLM1</i>	Filamin-1
TSC1	9q32	<i>TSC1</i>	Hamartin
TSC2	16p13.3	<i>TSC2</i>	Tuberlin

Source. Adapted, with permission, from Barkovich et al. [7].

^a ILS, isolated lissencephaly sequence; SBH, subcortical band heterotopia; MDS, Miller–Dieker syndrome; LCH, lissencephaly with cerebellar hypoplasia; FCMD, Fukuyama congenital muscular dystrophy; MEB, muscle-eye-brain disease; BPNH, bilateral periventricular nodular heterotopia; TSC, tuberous sclerosis complex.

disorders, which are defined clinically, classically manifest with: (1) disturbances of reciprocal social interaction, (2) disturbances of communication, and (3) disturbances in the normal variation in behavior [8]. Some component of each element of this diagnostic triad should be present for the diagnosis to be made. The prevalence of autism is estimated at about 1 per 1000, and males with autism outnumber females by about 3 to 1. Although numerous specific disorders, including fragile X syndrome and other chromosomal abnormalities, neurofibromatosis, Rett syndrome, and congenital CNS infection, have been associated with autism, close to 50% of cases appear idiopathic. The onset of autistic features typically occurs before age 3. Several neurological abnormalities are overrepresented in patients with autism and related disorders. Epilepsy occurs in up to 40% of this population [9]. Perhaps half of these patients experience the onset of seizures during early childhood, often with infantile spasms, whereas the rest experience onset in adolescence, when partial seizures are most common. Mental retardation occurs in up to 80% of patients with autism, hearing loss in 20%, and visual dysfunction in a smaller percentage. Because of the profound behavioral disturbance many of these patients manifest, it is especially important to choose anticonvulsant treatments that have minimal behavioral consequences.

2.5. Seizure history

Particular historical attention should be focused on characterizing the events in question to determine whether they are seizures and, if so, how best to classify them. Frequently, direct-care staff are not available to provide detailed descriptions of the patient's events; however, vigorous efforts to interview witnesses should be undertaken. Review of seizure charts, maintained at some institutions, should be undertaken with care.

A representative chart is shown in Fig. 1. Classification of behaviors by direct-care staff may be inaccurate. For example, the notation of tonic–clonic activity lasting 3 s should raise suspicion. Similarly, dramatic changes in seizure frequency noted on such records may indicate a change in the vigor of observation rather than a change in the activity of the patient's illness.

A major problem leading to over- or inappropriate treatment is the misclassification of nonepileptic events. Frequent nonepileptic paroxysmal events that are confused with seizures include behavioral outbursts, movement disorders, painful conditions such as migraine headaches and abdominal pain, and syncope [10] (Table 3). Pseudoseizures are well documented in the mentally handicapped population; thus, the common wisdom that pseudoseizures cannot occur in individuals with IQs below 50 should be questioned. In patients with frequent events, electroencephalographic (EEG) monitoring may be especially helpful (see EEG discussion below). The major goal in classification is to determine whether events are focal, multifocal, or generalized in origin.

3. Examination

As in other patient populations, examination may provide important clues. Focal neurological signs point to underlying structural brain lesions, which are frequently responsible for seizures. General examination may reveal evidence of tuberous sclerosis, endocrinopathy, or dysmorphic syndromes. Examination also may offer evidence of medication toxicity. For example, choreiform movements may be the result of long-term anticonvulsant treatment and may respond to a change in medication. Drooling or sedation may point to cognitive toxicity that may further compromise an already limited functional status.

CLIENT		BEFORE SEIZURE ACTIVITY					SEIZURE ACTIVITY										AFTER SEIZURE ACTIVITY				STAFF		
First and Last name		DATE	TIME A.M. OR P.M.	DURATION	FOCAL	GENERALIZED	OTHER (SPECIFY)	CHECK ONLY ONE OF THESE FIRST FIVE					Blinking or Staring (SPECIFY)	Chewing or Lip-Smacking (Specify)	Bizarre Behavior (Specify)	With Injury (A/R)	Other (Specify)	RAPID RECOVERY (LESS THAN 1 MINUTE)	SLEEP (HOW LONG?)	CHANGES BEHAVIOR (SPECIFY)	OTHER (SPECIFY)	First initial last name.	
					ONE SIDE OF BODY	immediate loss of consciousness		BOTH SIDES OF BODY	TONIC: CLONIC	TONIC	CLONIC	BRIEF SUDDEN JERK											LOSS OF MUSCLE TONE

OTHER IN THIS SECTION IS USED TO RECORD:

- If you did not witness the beginning of the seizure write NOT SEEN.
- If you are not sure if what you saw was focal or generalized, write a brief description.
- If you know what triggered the seizure, such as: Emotional upset, flashing lights, loud noise, fatigue, hunger, menstrual cycle, etc.

OTHER IN THIS SECTION IS USED TO RECORD:

- STATUS SEIZURES: which are seizures that last 5 minutes or longer. Write Status: and that you notified the nurse when the seizure reached 3 minutes.
- SERIAL SEIZURES: which are a series of repeated seizures a few seconds or minutes apart from each other.
- Use this column to indicate if a person voids or defecates during a seizure.
- If what you saw does not fit in the other columns in this section, write a description across the SEIZURE RECORD

OTHER IN THIS SECTION IS USED TO RECORD:

- If anything unusual occurs after the seizure is over.
- If recovery period takes longer than usual for this person.

Fig. 1. Representative seizure chart from a developmental center.

Table 3
Distinguishing between seizures and behavioral events

Features of seizures	Features of behavioral events
Abrupt unpredictable onset	Gradual onset
Stereotyped activity and evolution	Variable activity and evolution
Reduced responsiveness	Identifiable provocative features
Abrupt ending	Gradual ending
Postictal confusion, fatigue, headache	Normal postictal state

4. Imaging

Especially in patients with evidence of focal seizures or focal signs, neuroimaging may clarify the responsible process. In the absence of progressive signs of neurological dysfunction, however, in most cases it is difficult to argue that imaging will change outcome, although it does contribute to an improved understanding of the individual's disease. In addition, imaging frequently requires sedation or even anesthesia, forcing physicians to make a careful determination about the relative risks and benefits.

5. Electroencephalography

EEG examination is critical in this population. Slow spike and wave suggests a secondary generalized epilepsy, whereas focal or multifocal spikes suggest underlying structural lesions. Focal slowing may represent structural pathology, whereas generalized slowing may reflect diffuse cerebral dysfunction. Generalized slowing or excessive fast activity should raise the question of medication toxicity. As indicated above, because historical information is often limited, event recording may be extremely helpful. Newer ambulatory techniques permit recording of events of interest in the patient's home or institutional setting, avoiding the disruption of hospital admission. These studies, which are typically performed under the observation of direct care staff, also permit the neurologist to form an opinion about events of uncertain nature. Frequently, events reported as seizures turn out to be behavioral outbursts related to discomfort, frustration, or impaired coping strategies.

6. Conclusion

Treatment of patients with multiple handicaps and seizures should be aimed at controlling the seizures with minimal toxicity. Many such patients are still being treated with sedating doses of barbiturates, resulting in further compromise of their level of function. The introduction of valproate in 1978 was a major advance for this population, and the recent introductions of felbamate, lamotrigine, and topiramate have opened a new window of opportunity. All reasonable efforts should be taken to choose nonsedating agents, to minimize polypharmacy, and to select the most appropriate drug for the specific seizure type. Particular attention should be focused on the cognitive and behavioral effects of potential anticonvulsant agents. In this patient population, the repertoire of available responses is typically limited, which may magnify the behavioral response to specific agents in a sometimes dramatic fashion. Only a team approach involving physicians, nurses, and direct-care staff can effectively monitor therapeutic programs and respond appropriately to adverse effects.

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