Epileptic Disord 2003; 5: 145-8

EEG characteristics in juvenile Huntington's disease: a case report and review of the literature

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Received May 26, 2003; Accepted June 27, 2003

ABSTRACT – The clinical features of Juvenile Huntington's Disease (J-HD) differ from those of the more common adult-onset form, and include cognitive decline, parkinsonism, myoclonus and seizures. A paucity of literature is available describing the electroencephalographic (EEG) findings. We describe the clinical and EEG characteristics of a patient with genetically confirmed J-HD. A review of previously published cases yielded EEG descriptions in only 23 patients whose disease onset was prior to the age of 32, and only 14 of these were prior to the age of 20. Epileptiform abnormalities were noted in 17 (74%), which was considerably more common than in the adult form. Generalized discharges were noted in nine, with six having polyspike and wave. The remainder had focal or multifocal epileptiform discharges. With genetic testing now available, refinement of the EEG data will be possible.

KEY WORDS: epilepsy, Huntington's disease, electroencephalography, myoclonus

Juvenile Huntington's disease (J-HD) is usually defined as the onset of symptoms prior to 20 years of age [1]. There are distinct clinical and genetic abnormalities that differentiate it from the more common adult-onset form. The clinical manifestations seen in J-HD are usually those of the parkinsonian, Westphal variant of Huntington's disease (HD), and include akinesia, rigidity, seizures and a rapidly progressive dementing process [2]. In the juvenile form, more 60 triplicate repeats of the coding molecules cytosine, adenosine, and guanine (CAG) are invariably observed. An unstable trinucleotide expansion is noted during spermatogenesis, which can explain why the father is the affected parent in 90% of J-HD cases [3]. There have been few reports in the literature regarding the electroencephalographic (EEG) findings in this subset of patients. We report one such case and review the literature.

Case history

The patient is as recently found in a family with a 27-year-old woman with genetically confirmed J-HD. Onset

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was noted at the age of 14 when she began to display cognitive decline, personality changes, decreasing coordination, and dysarthria. When first evaluated at the age of 16, she had an IQ of 74, and signs of parkinsonism which included rigidity, bradykinesia and a low amplitude, irregular action tremor. Her estranged father had a diagnosis of HD with symptoms presenting at age 26. Her diagnosis of J-HD was genetically confirmed, revealing 71 CAG repeats.

In her late teens, she began to display mild multifocal myoclonus, with gait and eye motility abnormalities. At age 20 she had a generalized seizure. Over the ensuing four years she was treated with valproic acid (VPA) and had only one seizure. VPA was discontinued secondary to gastrointestinal side effects and carbamazepine was initiated. Seizures recurred within a month at a frequency of 2-3 per week. Upon reinitiating VPA one and a half years later, there was a dramatic decline in seizure frequency to 1-2 per year with a similar reduction in her myoclonus. More recently, the effect began to wane despite continued treatment with VPA.

Currently, she is nonambulatory, profoundly rigid and akinetic, with a Unified Huntington Disease Rating Scale, Motor Assessment score of 81/124. She is demented but can communicate and follow simple commands. A pericutaneous gastrostomy tube has been placed for feeding.

EEG at age 20 was normal. EEG at age 24 showed brief unstained alpha activity, with all rhythms less than 15 μV amplitude. No epileptiform activity. At the age of 26 an EEG showed numerous generalized polyspike and slow-wave complexes (PSW) and spike and slow-wave complexes (SW). See *figure 1*. Intermittent photic stimulation did not induce activation. The background rhythm consisted of 5-6 Hz, 10-20 μV activity.

Discussion

A vigilant review of the literature yielded EEG findings in 23 HD patients whose symptom onset ranged from three to 32 years [4-12]. Only one patient had genetic confirmation of the diagnosis; a nine-year-old child with 115 CAG repeats who developed progressive myoclonic epilepsy at the age of six [4]. The EEG showed generalized SW discharges. Without genetic testing available in the previously reported cases, there is a possibility that other inherited diseases accounted for some. Such disorders include dentatorubro-pallidoluysian atrophy (DRPLA), Lafora body disease, myoclonic epilepsy and ragged red fibers, neuronal ceroid lipofuscinosis, sialidosis, and chorea-acanthocytosis: although, only DRPLA, and as recently found in a family with chorea acanthocytosis [13], are inherited in an autosomal dominant manner. Seventeen (74%) had epileptiform abnormalities. Of 14 patients with onset age between 3 and 12, 10 had seizures and 12 had epileptiform abnormalities [5-8]. The most common seizure type was generalized tonic-clonic seizures, followed by myoclonic and absence seizures. Epileptiform abnormalities included generalized PSW, generalized SW, bilateral synchronous spikes, multifocal spikes and focal spikes. Of the patients whose background

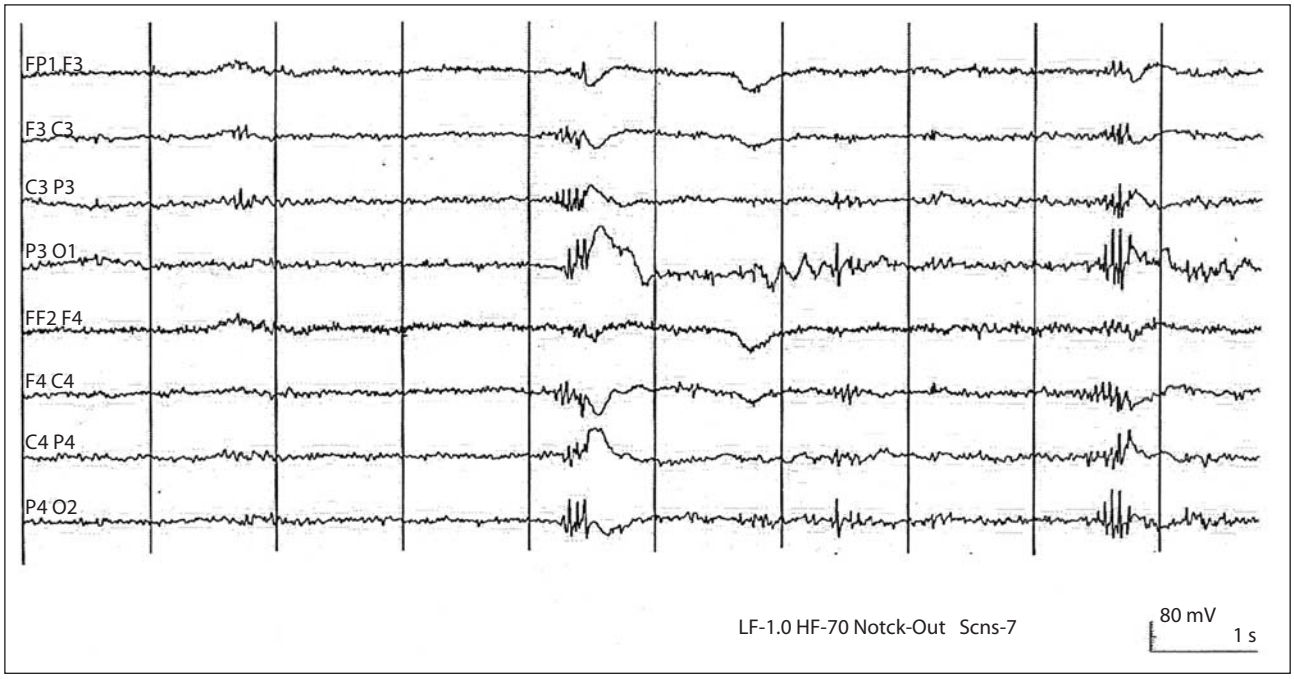

Figure 1. *Electroencephalogram, parasagittal montage. Low frequency filter of 1.0 Hz and high frequency filter of 70 Hz. Generalized, posterior dominant, polyspike and slow-waves of 70-120 μV.*

Table 1. EEG characteristics of patients with early onset Huntington's disease

Patient [reference]	Age of onset	Seizures	EEG Background	Epileptiform elements
1 [5]	9	GTC	5-6 Hz	Bilateral synchronous spikes
2 [5]	6	GTC	2-3 Hz	Biphasic spikes
3 [5]	5	GTC	3-4 Hz	Random spikes
4 [5]	3	GTC	2-3 Hz	Multiple spikes
5 [6]	5	myoclonic	Irregular sharp	Diphasic spikes
6 [6]	5	GTC	Irregular	Generalized spikes
7 [6]	5	GTC	Poorly sustained; random 3-4 Hz	SW in left hemisphere
8 [7]	8	GTC, absence	3-5 Hz	SW, PSW, + IPS
9 [7]	8	Staring, jerks	Not stated	PSW, + IPS; Right > Left posterior spikes
10 [7]	4	none	Not stated	Right occipital > Left temporal spikes
11 [7]	3	none	Not stated	Right posterior spikes; 2 Hz S/W
12 [7]	10	none	Normal	None
13 [8]	12	none	Flat 12 Hz	None
14 [4]	6	GTC	Normal	Gen. SW; IPS negative; sharps R > L, frontocentral regions
15 [9]	22	none	Normal	None
16 [9]	32	none	Normal	None
17 [9]	26	none	Normal	None
18 [9]	22	none	Normal	None
19 [10]	24	GTC	Regular and irregular synchronous 2.5-5 Hz	Spike content; + IPS
20 [10]	24	GTC	4-5 Hz	Spike; polyspike; + IPS
21 [11]	21	GTC	Low voltage; poor organization	Gen PSW + IPS
22 [12]	26	none	Not stated	PSW; + IPS
23 [12]	28	none	Not stated	PSW; + IPS
24	14	GTC	5-6 Hz	PSW; SW

IPS – Intermittent photic stimulation; **GTC** – generalized tonic-clonic seizure; **Hz** – hertz
PSW – polyspike and wave; **SW** – spike and wave

rhythm was stated, 81% (9/11) were abnormal. See *table 1* for details. There were no cases with disease onset between 12 and 22 years of age. Of the nine patients who had onset between the ages 22 and 32, five had abnormal EEGs [9-12]. Of these five, three had generalized tonic-clonic seizures and the other two had myoclonus. PSW were seen in four of five. Exacerbation of abnormalities with intermittent photic stimulation was noted in all five. The background rhythms were reported in only three of these five, and all were abnormal.

J-HD is more commonly associated with epilepsy than the adult-onset variety. A literature survey in 1980 found epilepsy in 90% (27/30) of patients with onset prior to the age of five, in 80% (32/40) with onset between the ages of six and ten, and in 52% (24/46) with onset between the ages of 11 and 20 [2]. A high incidence of epileptiform abnormalities on EEG is therefore an expected finding. The EEG characteristics in J-HD clearly differ from adult-onset HD. In 1972, the EEG findings in 95 patients with a mean age of 47 years were reported [14]. A low amplitude tracing, defined as all electrical activity less than 10 microvolts, was noted in 33% (31/95). Three patients in this series had seizures and only one had epileptiform abnormalities on the EEG.

The most remarkable EEG findings in our patient were the PSWs. Although not the majority, PSWs were the most frequently represented epileptiform abnormality in our review. PSW are detected in diseases associated with myoclonic epilepsy and some evidence suggests that frontal cortex may be the generator [15, 16]. It is not clear why J-HD should be more prone to seizures and epileptiform activity. HD is a prototypic subcortical neurodegenerative disorder, and there are ample data supporting the role of subcortical nuclei in seizure generation [17]. Comparing HD to J-HD, different populations of striatal projection neurons are preferentially effected [18-20]. How this plays a role is unknown. □

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