Psychiatric Diagnoses Applied to Children and Adults with Hypothalamic Hamartomas and Refractory Epilepsy

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Records of 57 children and adults with a history of HH and refractory epilepsy were reviewed. The psychiatric diagnoses and behavioral descriptions made by previous examiners were recorded. An attempt was made to relate those diagnostic observations to the patient's level of estimated intelligence when examined. Most patients were described as having a psychiatric or behavioral disorder (47 of 57 patients; 82.5%). The problems were heterogeneous, ranging from mild mood disorders to psychosis; oppositional-defiant disorder and attentional deficit disorder were frequently mentioned. There was, however, no relationship between patients' estimated level of intelligence and their psychiatric diagnosis, except in cases of mental retardation. Patients with estimated normal intelligence tended not to receive a psychiatric diagnosis (5 of 15 patients; 30%).

Key Words: epilepsy, hypothalamic hamartoma, intelligence, psychiatric disorders

Abbreviations Used: HH, hypothalamic hamartoma; IQ, intelligent quotient

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The behavioral and psychiatric disorders associated with HH and refractory epilepsy can be as devastating to patients and families as their cognitive disorders and associated epilepsy. To date, efforts to relate the psychiatric and behavioral disorders of these patients to their seizure history have failed to find any significant relationships.[10] Detailed case analyses of aggressive behavior in HH patients with epilepsy have emphasized the multifactorial nature of the aggressive or angry outbursts of HH patients and the multiplicity of diagnoses that can be applied to a given HH patient.[6] However, most reports explicitly or implicitly suggest that the cognitive limitations of patients underlie their limited coping skills.[2,4,6,10] Thus, there might be a relationship between patients' cognitive status and their psychiatric and behavioral characteristics.

The limited literature on the psychiatric features of HH patients also suggests that the diagnosis of attentional deficit disorder and oppositional-defiant disorder are common in this patient group.[10] Again, however, multiple diagnostic terms have been used to describe these patients.

We recorded the psychiatric diagnostic terms and behavioral descriptions found in the records of 57 children and adults with HH and refractory epilepsy. Our intent was to document the variability of diagnostic terms that previous examiners have applied to this patient population and to determine if a relationship could be established between the psychiatric and behavioral diagnoses applied to these patients and estimates of their current intellectual ability.

Methods

Subjects

Between March 2003 and October 2005, 57 patients with HH and refractory epilepsy were referred for a neuropsychological examination as a part of their preoperative evaluation at our institution. Patients ranged from 5 to 55 years old when examined. An arbitrary cut-off age of 5 years was established so that reliable estimates of intelligence could be obtained on all patients using the same psychometric measures. When evaluated, 32 patients (56.1%) were between the ages of 5 and 14 years old.

Record Review

Before patients underwent neuropsychological testing, their available medical records were reviewed. Psychiatric diagnoses and behavioral disturbances recorded by previous examiners were identified. When records regarding psychiatric history were unavailable or limited, an attempt was made to obtain additional data by obtaining release of information from either the patient or family, as appropriate. Records were available on each patient, but not every patient had a psychiatric diagnosis applied to them. Many patients had more than one psychiatric diagnosis or description of their behavioral abnormalities.

Estimating Level of Intelligence

All HH patients underwent a neuropsychological examination. Many of these patients had significant cognitive and behavioral difficulties that made a lengthy neuropsychological examination impractical, if not impossible.[5] Consequently, an effort was made to administer to each patient at least three subtests of the Wechsler Scale of Intelligence (Wechsler Intelligence Scale for Children-III and IV[7,9] and Wechsler Adult Intelligence Scale-3rd Edition[8] to estimate Verbal Comprehension skills (i.e., Vocabulary), Perceptual Reasoning or Organizational skills (i.e., Block Design), and Processing Speed (i.e., Digit Symbol).

Patients were then classified into three groups. The first group, or Neuropsychology Type 1, were subjects with mean scores on the Vocabulary and Block Design subtests within the average range or higher (e.g., a scaled score of 8 or higher). The second group, or Neuropsychology Group 2, consisted of individuals who had either an average score on Vocabulary or Block Design (i.e., a scaled score of 8 or higher) and a below average score on the other subtest (i.e., a scaled score of 7 or below).

The third group, or Neuropsychology Type 3 patients, were patients who obtained scaled scores of 6 or below on the Vocabulary and/or Block Design subtests. This group performed at a level compatible with at least mild mental retardation. The cognition of an additional group of patients was so severely impaired that they could not adequately take these three subtests. The "testable" mentally retarded patients were identified as Type 3a. The "untestable" mentally retarded patients were identified as Type 3b.

Statistical Analyses

If multiple diagnoses were applied to a given patient, all terms were included in the analysis. A frequency table, which listed the diagnostic and descriptive terms for patients falling within the different neuropsychological types noted above, was established.

A qualitative analysis of descriptive and diagnostic terms that clustered with one another was then performed to determine if there was a relationship between a general class of psychiatric and behavioral disturbances and patients' overall cognitive status. Finally, the frequency that a diagnostic term was applied relative to all of the diagnostic terms was calculated, as well as the frequency with which that diagnostic term was applied to the 57 patients.

Results

Demographic and Clinical Features of Neuropsychology Types

Table 1 summarizes the demographic and selected clinical features of the three neuropsychology types. The three groups did not differ in terms of age, ratio of males to females, handedness, age of seizure onset, duration of epilepsy, or seizure type. However, children with mental retardation had a significantly higher incidence of precocious puberty and larger preoperative HHs than patients with normal intelligence.

Psychiatric and Behavioral Disorders as a Function of Neuropsychology Type

Table 2 lists verbatim the psychiatric terms and behavioral descriptions applied by previous examiners to each of the 57 patients studied. Forty-seven patients (82.5%) had one or more psychiatric and/or behavioral disturbances noted. Only 10 of 57 patients (17.5%) had no psychiatric or behavioral difficulties listed in their medical records. Of these 10 patients, 5 had estimated average intelligence. Multiple terms were applied to this patient group (Table 2), only some of which could be classified using the DSM-IV Manual.[1]

Table 3 summarizes the relative frequency of the diagnostic and descriptive terms that were recorded. Almost half of the sample was described as having mental retardation/developmental delay or borderline intellectual functioning (45.61%). Of 30 patients who were classified as having mental retardation based on current IQ testing, 21 had been classified by previous examiners as showing mental retardation or borderline intellectual functioning.

About one-third of the patients were described by previous examiners as having problems with anger control, episodic dyscontrol, or oppositional behavior (36.84%). These descriptive terms were applied across all levels of intellectual functioning (i.e., neuropsychology types).

The diagnostic terms that indicated attentional deficit/hyperactivity disorder and autistic spectrum disorder also applied across all levels of intellectual functioning. Approximately 16% of the sample were described as having attentional deficit/hyperactivity disorder and 14% as having autistic spectrum disor-

der. Diagnoses seemed to be independent of the patient's current level of intellectual test performance.

More than one-third of the patients were described in behavioral terms that did not easily lend themselves to psychiatric classification. Some of these terms included feeding disorders, self-injurious behavior, stuttering, and unspecified emotional and behavioral problems.

Discussion

This brief report documents that numerous psychiatric and behavioral difficulties have been applied to children and adults who have an HH and refractory epilepsy. Furthermore, more than 82.5% of the patients studied were described as having some form of psychiatric or behavioral disturbance.

As would be expected in children and adults who have an HH syndrome,[3] the diagnostic impression of mental re-

Table 1. Demographic and Clinical Characteristics of HH Patients by Neuropsychological Type

Variable	Type 1 (n = 15) mean (SD)	Type 2 (n = 12) mean (SD)	Type 3a (n = 21) mean (SD)	Type 3b (n = 9) mean (SD)	F/χ^2	*p*
Demographic Variables						
Age when tested (yrs)	17.60 (11.10)	14.33 (7.27)	17.64 (10.09)	12.13 (7.62)	0.51	0.61
Gender (% males)	46.7 (-)	58.3 (-)	68.2 (-)	87.5 (-)	5.77	0.22
Handedness (% right)	73.3 (-)	91.7 (-)	81.8 (-)	100 (-)	3.43	0.33
Seizure History						
Age at onset of any form of seizure	16.20 (26.42)	6.73 (8.88)	11.27 (14.59)	16.75 (28.28)	0.87	0.43
Epilepsy onset before 1 mo of age (n)	7	5	10	2	2.52	0.64
Epilepsy onset before 1 mo age (%)	46.7	45.5	45.5	25.0		
Duration of epilepsy (mos)	206.36 (128.11)	143.55 (62.61)	200.81 (130.56)	133.25 (91.85)	1.08	0.35
Seizure Type						
Gelastic only (n)	2	1	2	2	10.16	0.25
Gelastic only (%)	13.3	8.3	9.1	25.0		
Mixed (n)	12	10	20	6		
Mixed (%)	80.0	83.3	90.9	75.0		
Precocious puberty						
n	1	3	13	4	12.16	0.02
% present	6.7	27.3	59.1	50.0		
Pallister-Hall syndrome						
n	1	1	1	1	8.76	0.72
% present	6.7	8.3	4.5	12.5		
Hypothalamic hamartoma						
Presurgical size (cm)	1.29 (1.76)	1.31 (1.16)	5.72 (6.55)	4.41 (4.77)	5.69	0.01
Attachment						
Right						
n	6	5	6	3	6.11	0.64
% present	40.0	41.7	27.3	37.5		
Left						
n	7	3	7	2		
% present	46.7	25.0	31.8	25.0		
Bilateral						
n	1	1	1	1		
% present	13.3	33.3	40.9	37.5		

Table 2. Verbatim Descriptions of the Psychiatric and Behavioral Disorders of HH Patients with Refractory Epilepsy Found in Patients' Records as a Function of Neuropsychology Type

Neuropsychology Type 1	Neuropsychology Type 2†	Neuropsychology Type 3a†	Neuropsychology Type 3b†
Adjustment reaction with anxious mood	Anger problems	Adjustment disorder with depressed mood	Attention deficit hyperactivity disorder
Anorexia	Asperger's disorder	Attention deficit hyperactivity disorder	Autistic disorder
Asperger's disorder	Attention deficit hyperactivity disorder	Autistic spectrum disorder, probably Asperger's disorder	Behavioral problems
Attention deficit hyperactivity disorder	Attention deficit hyperactivity disorder NOS	Behavioral dyscontrol	Developmental delay
Autistic disorder	Behavioral dyscontrol	Borderline intellectual functioning	Episodic dyscontrol syndrome
Borderline traits	Borderline intellectual functioning	Cognitive disorder	Intermittent explosive disorder
Cognitive disorder NOS	Cognitive deficits	Cognitive disorder secondary to Asperger's	Learning disability
Cognitive dysfunction	Cognitive disorder due to medical condition	Cognitive dysfunction	Mental retardation
Depression NOS	Cognitive disorder NOS	Dementia secondary to seizure disorder	Obsessive compulsive disorder (features)
Developmental delay	Developmental delay	Developmental retardation	Oppositional behaviors
Dysthymic disorder	Emotional/behavioral disturbance	Developmental delay	Pervasive developmental disorder NOS
Major depressive disorder	Feeding problems	Emotional/behavioral disturbance	
Mood disorder	Impulse control disorder due to medical condition	Learning disability NOS	
Mood disorder secondary to HH	Learning disability	Major depressive disorder	
Oppositional defiant disorder	Learning disability NOS	Mental retardation	
Psychosis	Major depressive disorder	Obsessive compulsive disorder	
Self-injurious behavior	Mental retardation	Oppositional defiant disorder	
Temper outbursts	Mood instability with anxiety and depression	Pervasive developmental disorder	
Unspecified emotional and behavioral problems	Oppositional behavior	Psychosis	
	Paranoid disorder	Stuttering	
	Pervasive developmental disorder due to medical condition	Tourette's disorder	
	Poor impulse control		
	Sensory integration disorder		
	Schizoid personality traits		
	Specific language delays		

HH = hypothalamic harmatoma, NOS = not otherwise specified; †Five Type 1 patients, 2 Type 2 patients, and 3 Type 3a patients had no psychiatric diagnosis or behavioral disorder listed in their medical record.

Table 3. Summary of Psychiatric and Behavioral Disorders of HH Patients with Refractory Epilepsy as a Function of Neuropsychology Type

Psychiatric and Behavioral Disorder	Type 1 (n = 15)	Type 2 (n = 12)	Type 3a (n = 21)	Type 3b (n = 9)	Total (n = 57)	% of all diagnostic terms applied	% of patients having the term applied
Attention deficit/hyperactivity disorder	2	4	1	2	9	7.83	15.79
Oppositional defiant disorder and problems with behavioral dyscontrol/anger management					21	18.26	36.84
Oppositional defiant disorder	1	0	1	0	2	1.74	3.51
Temper outbursts	1	0	1	0	2	1.74	3.51
Anger problems	0	1	0	0	1	0.09	1.75
Impulse control problem	0	2	0	0	2	1.74	3.51
Behavioral dyscontrol/labile	1	1	3	3	8	6.96	14.04
Episodic dyscontrol	0	0	0	2	2	1.74	3.51
Oppositional behavior	0	1	0	1	2	1.74	3.51
Intermittent explosive disorder	0	0	1	1	2	1.74	3.51
Autistic spectrum disorder and other pervasive developmental disorders (PDD)					8	6.96	14.04
Asperger's disorder	1	1	1	0	3	2.61	5.26
Autistic disorder	1	0	0	1	2	1.74	3.51
PDD NOS	0	1	1	1	3	2.61	5.26
Psychosis, schizoid, or borderline traits	2	2	1	0	5	4.35	8.77
Mood disorder (major and minor)	5	3	3	0	11	9.57	19.30
Mental retardation/developmental delay/borderline intellectual functioning	1	4	14	7	26	22.61	45.61
Cognitive disorder/dysfunction	2	3	3	0	8	6.96	14.04
Learning disorder	0	3	1	2	6	5.22	10.53
Adjustment disorders	1	0	1	0	2	1.74	5.26
Other	4	4	7	4	19	16.52	33.33

HH = hypothalamic hamartoma, NOS = not otherwise specified

tardation was the most common term encountered. In the present study, however, fewer than 50% of the patients were described as having oppositional-defiant disorders or attentional deficit disorders. These findings contrast with those of Weissenberger et al.[10] who systematically studied 12 children with psychiatric comorbidities associated with HH and seizure disorder. In their small sample of patients, 83.3% were diagnosed as having an oppositional-defiant disorder, 75% were diagnosed as having attentional deficit/hyperactivity disorder, 33.3% were described as having a conduct disorder, and 16.7% were described as having an anxiety or mood disorder.

Our clinical impression is that a higher percentage of our patients showed oppositional-defiant disorders than was captured in the medical records. However, the percentage was less than 50% of our sample. Moreover, several children showed features indicative of an autistic spectrum disorder. Many behavioral terms were applied to these children, including problems in relating to others emotionally, having difficulties with social relationships, and early problems with feeding and with relating to early caregivers emotionally. We were impressed that most of the HH patients examined had subtle-to-obvious difficulties with social interaction, even if their intelligence was judged to be within the normal range.

Of the 10 HH patients who did not receive a psychiatric diagnosis or who were not described as having behavioral difficulties, 5 were estimated to have normal intelligence. This finding suggests

that there may be a relationship between normal intelligence and the absence of psychiatric/behavioral problems. Once a psychiatric and/or behavioral problem is present, estimates of IQ per se do not seem to relate to the diagnosis. However, other underlying neuropsychological deficits that do relate to the psychiatric diagnosis may be present. For example, neuropsychological impairments suggestive of a disorder of the frontal lobe system may be related to diagnoses such as attentional deficit/hyperactivity disorder or autistic spectrum disorder. This issue should be explored in future studies.

The present findings do not provide definitive estimates of the incidence of different types of psychiatric disorders observed in HH patients with refractory epilepsy. We also did not systematically assess the neurocognitive impairments underlying these disorders. However, our findings do suggest that numerous psychiatric problems may emerge in relationship to HH and untreatable seizure disorders. It is unlikely that a single variable (e. g., size of HH, mode of attachment, history of seizure disorder, cognitive strengths and weaknesses) can explain the varied psychiatric disturbances observed in this patient population. It is probable that the psychiatric and behavioral difficulties of HH patients represent complex interactions among their underlying brain disorder, seizure history, and their cognitive strengths and limitations (Prigatano GP, unpublished data, 2006). Furthermore, the role of medications and environmental factors contributing to the psychiatric difficulties of these patients cannot be excluded. Further studies should systematically assess these and other variables to help explain the various psychiatric disturbances seen in HH patients with refractory epilepsy.

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