Editor's Choice

Routine developmental, autism, behavioral, and psychological screening in epilepsy care settings

SOYONG EOM[1] | BREANNE FISHER[1] | CATHERINE DEZORT[1] | ANNE T BERG[1,2]

1 Epilepsy Center, Ann and Robert H Lurie Children's Hospital of Chicago, Chicago, IL; **2** Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA.

Correspondence to Anne T Berg, Epilepsy Center Ann & Robert H Lurie Children's Hospital of Chicago and Department of Pediatrics, Northwestern University Feinberg School of Medicine, 225 E Chicago Avenue, Chicago, IL 60611, USA. E-mail: atberg@luriechildrens.org

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ABBREVIATIONS

ASQ	Ages and Stages Questionnaire
mCHAT	Modified Checklist for Autism in Toddlers
SCQ	Social Communication Questionnaire
SDQ	Strengths and Difficulties Questionnaire

AIM Screening for cognitive impairment, developmental delay, and neuropsychiatric problems is not always performed in children with epilepsy. The aim of this study was to assess the value of this screening and its validity for determining previously unidentified ('actionable') problems in children with epilepsy.
METHOD New and existing patients with epilepsy were recruited from a hospital-based epilepsy center. The parent of the child completed screening evaluations for development (Ages and Stages Questionnaire [ASQ], 0–66mo), autism (Modified Checklist for Autism in Toddlers [mCHAT], 16–30mo), social communication (Social Communication Questionnaire [SCQ], ≥4y), and psychiatric concerns (Strengths and Difficulties Questionnaire [SDQ], 4–17y).
RESULTS We screened 236 children overall (136 males [58%], 100 females [42%]; mean age [SD] 6y 7mo [4y 6mo]). Of these, 176 children (75%) had established epilepsy diagnoses and 60 (25%) were patients with new-onset epilepsy. Of those with new-onset disease, 22 (37%) were determined not to have epilepsy. Positive findings by test were 82% (ASQ), 54% (mCHAT), 15%, (SCQ), and 58% (SDQ). Findings were actionable in 46 children (20%): 18% of findings in children with established epilepsy and 23% of findings in patients with new-onset epilepsy. Of the 46 children for whom further referrals were made, the parents of 28 (61%) have pursued further evaluations.
INTERPRETATION In this study, children with existing and new-onset diagnoses of epilepsy had actionable screening findings. These findings support the development of systematic screening of comorbidities for children with epilepsy.

Children with epilepsy are at a higher risk of developmental, cognitive, and behavioral difficulties that may have consequences lasting into adulthood.[1]

These problems can be present at onset[2,3] or develop during the course of epilepsy, possibly in association with the occurrence of seizures, the treatment of epilepsy, or the possible comorbidity with epilepsy of cognitive, neurodevelopmental, and psychiatric disorders.[4]

While recommendations exist for routine screening for developmental delay and autism in all infants and toddlers[5] and depression in adolescents,[6] adherence to these recommendations has not been measured. Given that children with epilepsy are at particularly high risk of these difficulties, we sought to assess the value of a routine screening program in our hospital-based epilepsy center.

METHOD

Patients

The parents of all patients seen in either the monitoring unit or the ketogenic diet clinic of the epilepsy center were asked to complete a series of screening questionnaires. The comorbidity screening program has been part of standard care in our center since November 2010. The patients seen in the epilepsy monitoring unit were either established patients of the clinic or new patients who were being evaluated for the first time and had not yet received a diagnosis of epilepsy.

Parents provided written informed consent and the children assented as appropriate for their age and level of development. All procedures were approved by the Ann and Robert H Lurie Children's Hospital of Chicago institutional review board.

Measures

Development was assessed using the Ages and Stages Questionnaire (ASQ, age 1–66mo).[7] Autism screening was performed using the Modified Checklist for Autism in Toddlers ([mCHAT],[8] for age 16–30mo; however, use in this study was extended to 4y) and the Social Communication Questionnaire ([SCQ],[9] age ≥4y). The Strength and Difficulties Questionnaire ([SDQ], age 4–17y) was used to screen for mental health problems.[10] All of the instruments

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selected were available and validated in English and Spanish.

Each screening instrument used took 10 to 15 minutes to complete. Depending on the age of the child, the combination of screening questionnaires took parents 20 to 50 minutes to complete, with the majority finishing within 20 or 30 minutes. There is no financial charge for the mCHAT and SDQ screening questionnaires, as they are freely available on the internet. The ASQ requires a one-time modest payment for the forms and scoring instructions, which can then be used without limitation. The SCQ forms need to be purchased.

In our center, the screening program was carried out by advanced practice nurses, and positive findings were reviewed by an attending neurologist, pediatrician, or psychiatrist. If the screening measures detected previously unidentified concerns or problems for which a child was not receiving services, a referral was made to psychiatry, educational services, or specific therapeutic interventions as appropriate. Other health professionals in the healthcare setting, such as advanced practice nurses, physician's assistants, social workers, and psychologists, can also perform screening. Referrals can be made by appropriate providers. Patient medical records were subsequently reviewed for evidence that the parents followed through with the referral recommendations.

Statistical analysis

The data were analyzed using SPSS software, version 20.0 (IBM SPSS Statistics, IBM Corp, Armonk, NY, USA). Bivariate analyses were conducted with the χ^2 test, Student *t*-test, or Mann–Whitney *U* test (for non-parametric ordinal data), as appropriate for the data.

RESULTS

Sample characteristics

A total of 236 children and adolescents (136 males, 100 females) were screened in the period between November 2010 and April 2013. Of these, 176 (75%) were patients with an established diagnosis of epilepsy or seizures and 60 children (25%) were new, screened in the new-onset epilepsy clinic. After full evaluations were complete, 16 of the 60 patients in our new-onset clinic were determined not to have epilepsy, but were found to have another disorder. In six patients with new-onset events, the evaluation was inconclusive. Finally, 14 children had seizures but did not meet conventional criteria for epilepsy (recurrent unprovoked seizures). These children had all experienced at least one seizure (n=6 single unprovoked seizure, n=7 recurrent febrile seizures, and n=1 prolonged febrile seizure) and were considered at high risk of epilepsy, as a result of a strong family history or a neurological insult. All of these patients were kept in our sample, as they were evaluated for epilepsy and represented an important segment of the children regularly seen in an epilepsy service.[11]

The mean age (SD) at the time of screening was 6y 7mo (SD 4y 6mo), range 1mo–18y. Children with established epilepsy were slightly older than those seen in the new-onset clinic (6y 11mo [SD 4y 7mo] vs 5y 6mo [SD 4y 3mo], p=0.03) but were similar in distribution of sex (60% and 52% male, p=0.28). Of the 214 children with diagnosis of epilepsy or at 'high risk' for seizures, the mean age at onset was 3 years 5 months (range 0–17y).

Of the children with seizures (epilepsy or high risk), 96 out of 214 (45%) had non-syndromic forms of epilepsy. The clinical characteristics of the group, including specific epilepsy syndromes, are provided in Table I.

What this paper adds

- Actionable results were found in 20% of children with epilepsy who were screened.
- Routine screening should be offered to all children with established or new-onset epilepsy.
- Screening should be done in conjunction with a capacity for referral, in order to interpret and act on the results.

Screening results

Overall, of the 236 children participating in this program, 100 were assessed using the ASQ, 69 using the mCHAT, 139 using the SCQ, and 96 using the SDQ. Positive screening results were obtained for developmental delay (ASQ) in 82 out of 100 (82%), for autism in 37 out of 69 (54%) on mCHAT and 21 out of 139 (15%) on SCQ, and for behavioral and psychiatric concerns (SDQ) in 56 out of 96 (58%) patients. The screening results and their association with clinical characteristics of the children are presented in Table I.

Patients with established epilepsy were more likely than new-onset patients (all combined) to screen positive for developmental delay (88% vs 65%, p=0.01), autism (62% vs 29%, p=0.02 for mCHAT, 20% vs 0%, p=0.002 for SCQ), and behavioral–psychiatric concerns (64% vs 39%, p=0.03).

Among children aged 4 years and older, the patients with established epilepsy were more likely than those with new-onset epilepsy to show evidence of autism on the SCQ (77% vs 23%, p<0.001), and similarly for behavioral–psychiatric concern on the SDQ (76% vs 24%, p=0.03; see Table II). The SDQ was completed for 96 children (73 with established epilepsy, 23 with new-onset epilepsy). In each of the six domains, established patients had the highest yield (Table III).

Autism screening results relative to developmental, behavioral, and psychiatric screening

Positive autism screening results were associated with a clinical diagnosis of autism more often for screening performed with the SCQ (12 out of 21 patients, 57%), than with the mCHAT (3 out of 37 patients, 8%; p<0.001).

Cognitive and developmental disabilities were also more common in children who screened positive for autism than in those who did not (57% vs 19%, p<0.001). Of the children who screened positive and were actually diagnosed with autism (n=15), 12 also had developmental delays or intellectual disability.

Table I: Positive findings on screening instruments for patients with established and new-onset epilepsy and the results of epilepsy diagnosis by screening results and by age of the child (<5y vs ≥5y)

	Ages and Stages Questionnaire (*n*=100), *n* (%)	Modified Checklist for Autism in Toddlers (*n*=69), *n* (%)	Social Communication Questionnaire (*n*=139), *n* (%)	Strengths and Difficulties Questionnaire (*n*=96), *n* (%)
Overall (*n*=236)	82 (82)	37 (54)	21 (15)	56 (58)
Established epilepsy (*n*=176)	65/74 (88)	32/52 (62)	21/106 (20)	47/73 (64)
New-onset epilepsy (*n*=60)	17/26 (65)	5/17 (29)	0/32 (0)	9/23 (39)
p	0.014	0.021	0.002	0.029
Male (*n*=136, 58%)	62 (62)	43 (62)	79 (57)	51 (53)
Female (*n*=100, 42%)	38 (38)	26 (38)	60 (43)	45 (47)
p	0.433	0.439	0.226	0.127
Type of epilepsy				
Non-syndromic epilepsy with focal features (*n*=60, 25%)	9 (15)	10 (17)	49 (82)	21 (35)
Non-syndromic epilepsy with generalized features (*n*=36, 15%)	7 (19)	6 (17)	30 (83)	13 (36)
Infantile spasms (*n*=29, 12%)	28 (97)	18 (62)	2 (7)	1 (3)
Epileptic encephalopathies[a] (*n*=16, 7%)	12 (75)	10 (63)	6 (38)	5 (31)
Absence epilepsy[b] (*n*=14, 6%)	6 (43)	3 (21)	10 (71)	3 (21)
Myoclonic absence epilepsy (*n*=15, 6%)	0	6 (40)	6 (40)	1 (7)
Benign seizure susceptibility syndrome (*n*=20, 9%)	1 (5)	2 (10)	16 (80)	5 (25)
Epilepsy not otherwise specified[c] (*n*=3, 1%)	1 (33)	1 (33)	–	1 (33)
High risk[d] (*n*=14, 6%)	7 (50)	7 (50)	5 (36)	2 (14)
Non-conclusive[e] (*n*=6, 3%)	2 (33)	2 (33)	3 (50)	1 (17)
Not epilepsy[f] (*n*=16, 7%)	6 (35)	3 (18)	9 (53)	1 (6)
Subgroup by age				
<4y (*n*=78)	63/67 (82)	29/58 (50)		
≥4y (*n*=157)	19/23 (83)	5/11 (46)	26/132 (19)	56/96 (58)
p	0.601	0.521		0.303

[a]Including Lennox–Gastaut syndrome. [b]Including childhood absence epilepsy. [c]Including unclassified. [d]Patients with a history of unprovoked single or several seizures, such as febrile seizure, that had not developed as epilepsy yet. [e]Examinations for diagnosis are still ongoing and not proved yet. [f]Diagnosis could not be determined.

'Actionable' findings

Overall, tests revealed evidence of problems that required additional referral or evaluation ('actionable'; see Table IV) in 46 (20%) of the 236 patients who were screened. Actionable findings occurred in comparable proportions of established patients (*n*=32, 18%) and patients seen in the new-onset clinic setting (*n*=14, 23%, *p*=0.26).

Actionable findings were found in 21 children (21%) who were screened for developmental delay using the ASQ. The comparable figures for the other questionnaires were 15 (22%) on mCHAT and 25 (18%) on SCQ for autism, and 18 patients (19%) on the SDQ for behavioral–psychiatric concerns. The proportion of patients with actionable findings was similar in the subgroup of children who were found not to have epilepsy (*n*=5, 23%) and in the subgroup of children with 'high risk' of seizures (*n*=2/14, 14%).

Types of referral made for children with actionable findings

Of the 46 children with actionable screening results, 44 (19%) were referred to psychiatric, psychological, or educational specialists, five (2%) were referred back to the neurologist or pediatrician, and 21 (7%) were referred to specific therapeutic interventions (e.g. physical, speech, or occupational therapy, or early intervention programs). Some children received multiple referrals (Table SI, online supporting information). To date, and based on the records available, at least 28 children (61%) have followed through on referral recommendations (Table IV).

DISCUSSION

In our hospital-based epilepsy center, we found a very high yield of developmental and behavioral concerns as assessed by standard screening tools. Furthermore, screening revealed evidence of problems that had not been previously recognized in some children. These resulted in referrals to a variety of resources in one of every five patients screened in our program. This report, which covers children and adolescents from 0 to 18 years of age, provides a substantial update from a previous preliminary report carried out at the center of the first 66 young patients in our program.[12] The wider sample of patients obtained means that this research also includes children aged 4 years and older, which the previous study did not.

Research has demonstrated that developmental attainment is maximized and can have lifelong benefits when intervention is initiated earlier, and that such programs are

cost-effective.[13] Randomized evaluations of early intervention programs have demonstrated the beneficial impact of such interventions in children who are socially or biologically at risk of developmental delay, especially in traditional measures of development, such as cognitive, motor, and social–emotional skills.[14–16]

This has led professional societies, such as the American Academy of Pediatrics (AAP), to recommend that screening be performed for all young children at risk using screening instruments such as those used in this study (mCHAT and ASQ).[5] The American Academy of Neurology and the Child Neurology Society also recently published recommendations for developmental screening tools with good sensitivity and specificity to be used at every preventive visit.[17,18] In the case of older children (12–18y), the US Preventive Services Task Force (USPSTF) recommends screening for depression.[6] Such a recommendation is especially important given the evidence concerning the higher risk of psychiatric disorders in children with epilepsy.

In light of the well-known burden of cognitive, behavioral, and psychiatric disorders in children with epilepsy, and given the recommendations for screening in primary care from various professional groups,[5] it is noteworthy that so many children in our study had actionable findings. This raises the question of whether these children had previously received routine screening in either the primary or neurological care settings. Even if they had, there may be a need for repeated screening over time to monitor for changes in behavior or development.

There has been much concern regarding the association between epilepsy and autism.[19,20] A previous report found a high yield of autism using the mCHAT in children with refractory epilepsy. This study is sometimes used as evidence of the high prevalence of autism in children with epilepsy; however, it did not report on actual autism diagnosis or take into account level of intellectual disability.[20] Autism screening is not the same as diagnosis. Autism is a complex disorder and the diagnostic evaluation requires assessment of the individual's cognitive and adaptive levels, as well as the features of autism.[21] The mCHAT, in particular, while a popular and helpful screening tool, must be interpreted very carefully, as many of the items used to indicate autistic features, including the critical items, are also signs of neurological impairment (e.g. vision or hearing impairment), and others are non-specific symptoms of global delay.[22]

Thus, any positive autism screening result must be interpreted in light of the child's developmental and neurological status. Although screening of children for developmental delay, autism, and other behavioral difficulties is increasingly accepted as a core element of general pediatric practice,[5] it may not always be feasible. Developmental screening programs take time and effort to administer. A recent cost–benefit analysis of developmental

Table II: Positive screening results on the Social Communication Questionnaire and Strengths and Difficulties Questionnaire and clinical variables for children aged ≥4 years or more (*n*=157)

	Social Communication Questionnaire (*n*=139), *n* (%)	Strengths and Difficulties Questionnaire (*n*=96), *n* (%)
Overall positive screening	26 (19)	56 (58)
Sex		
Male (*n*=89)	78 (57)	51 (53)
Female (*n*=68)	60 (44)	45 (47)
p	0.226	0.127
Type of patient		
Established (*n*=121)	106 (77)	73 (76)
New-onset (*n*=36)	32 (23)	23 (24)
p	<0.001	0.029
Type of epilepsy		
NSE with focal features (*n*=52)	49 (94)	36 (69)
NSE with generalized features (*n*=29)	29 (100)	19 (66)
Infantile spasms (*n*=4)	2 (50)	1 (25)
Epileptic encephalopathies[a] (*n*=8)	6 (75)	5 (63)
Absence epilepsy[b] (*n*=12)	10 (83)	9 (75)
Myoclonic absence epilepsy (*n*=10)	6 (60)	5 (50)
BCSSS (*n*=18)	16 (89)	9 (50)
Epilepsy NOS[c] (*n*=3)	0 (0)	1 (33)
High risk[d] (*n*=5)	5 (100)	3 (60)
Non-conclusive[e] (*n*=3)	3 (100)	2 (67)
Not epilepsy[f] (*n*=9)	9 (100)	4 (44)
Age at onset (y)		
<10 (*n*=94)	18/79 (23)	31/50 (62)
≥10 (*n*=63)	8/59 (14)	25/46 (54)
p	0.124	0.290

[a]Including Lennox–Gastaut syndrome. [b]Including childhood absence epilepsy. [c]Including unclassified. [d]Patients with history of unprovoked single or several seizures, such as febrile seizure, but who had not developed as epilepsy yet. [e]Examinations for diagnosis are still ongoing and not proved yet. [f]Diagnosis could not be determined. NSE, nonsyndromic epilepsy; BCSSS, benign childhood seizure susceptibility syndrome; NOS, not otherwise specified.

Table III: Screening yield for the Strengths and Difficulties Questionnaire

No. of positive results per domain	Total patients (*n*=96), *n* (%)	Established patients (*n*=73), *n* (%)	New-onset patients (*n*=23), *n* (%)	*p*
Overall stress	35 (37)	30 (41)	5 (22)	0.073
Emotional distress	23 (24)	18 (25)	5 (22)	0.508
Behavioral difficulties	20 (21)	17 (23)	3 (13)	0.228
Hyperactivity/attention difficulties	31 (32)	27 (37)	4 (17)	0.064
Difficulty getting along with other children	27 (28)	23 (32)	4 (17)	0.147
Kind and helpful behavior	33 (34)	28 (38)	5 (22)	0.111

Table IV: Proportion of children for each screening instrument whose results required further evaluation (actionable)

	Actionable Total (*n*=236), *n* (%)	Ages and Stages Questionnaire (*n*=100), *n* (%)	Modified Checklist for Autism in Toddlers (*n*=69), *n* (%)	Social Communication Questionnaire (*n*=139), *n* (%)	Strengths and Difficulties Questionnaire (*n*=96), *n* (%)	Follow-through *n* (%)
Overall (*n*=236)	46 (20)	21/100 (21)	15/69 (22)	25/139 (18)	18/96 (19)	28/46 (61)
Diagnosis of epilepsy						
Established (*n*=176)	32 (18)	14/75 (19)	11/52 (21)	19/107 (18)	13/73 (18)	–
New-onset (*n*=60)	14 (23)	7/25 (28)	4/17 (24)	6/32 (19)	5/23 (22)	–
p	0.257	0.066	0.539	0.541	0.441	–
Age at onset						
<4y (*n*=78)	15/65 (23)	15/77 (20)	11/58 (19)	–	–	9/15 (60)
≥4y (*n*=157)	31/78 (40)	6/23 (26)	4/11 (36)	25/138 (18)	18/96 (19)	19/31 (61)
p	0.489	0.514	0.354	–	–	0.542

screening approaches, including costs of administration, interpreting results, diagnostic testing, and treatment, showed that the use of parental reports was by far the most efficient approach.[23] Advanced practice nurses, physician's assistants, social workers, and psychologists, as certified professionals, can perform a screening program and appropriate providers can make referrals in other healthcare settings. Other considerations also play a role, including the parent's time, parent's health literacy, scoring and reporting, and referral resources when further evaluations are needed.

Our study has several limitations. As we screened patients in the epilepsy monitoring unit and ketogenic diet clinic, parents were often at the hospital for prolonged or multiple appointments and had time to complete the screening questionnaires. Implementing our program more broadly, including in the outpatient setting, may require more modifications.

Our findings may over represent the yield of screening in children with epilepsy, as our study was based in a tertiary center. While that may be the case, population-based studies all demonstrate a very high level of intellectual disability (20–25%) in children who developed epilepsy within the first 15 years of life.[24,25] Among patients who develop epilepsy at a younger age, the proportion is even higher.[24] Thus, regardless of whether or not the yield might be somewhat lower in the general population, we have good reason to believe that it is still relatively high and warrants a systematic approach to identify these difficulties at the earliest possible opportunity. We also had limited ability to determine whether parents had followed through on referral recommendations. Thus, it is likely that our finding that 61% parents followed through with referrals underestimates how many really did pursue further evaluations.

Our study lays the foundation for future studies to continue to improve the early identification of epilepsy and its comorbid health conditions.[26] The implementation of screening will require an understanding of the reasons why children do not currently receive routine screening. Solutions will need to be identified to overcome those barriers. An alternative briefer screening approach is one strategy that we are currently developing. Systems that would allow parents to directly input information and then score the survey and provide a report for staff would make screening far more feasible and greatly reduce the time and resources required from physicians and staff. We are aware of one such system, the Child Health and Development Interactive System (CHADIS; www.chadis.com), which provides these services for an annual fee. Other possibilities include designing, building, and maintaining an internal system. In any case, it is likely that quality of care indicators would encompass measures such as developmental, behavioral, and psychiatric screening in the near future. The yield in children with epilepsy certainly warrants that screening be adopted. Whether screening should be done in the primary care or the neurology setting may not always be clear; however, this is certainly an issue that would benefit from discussion among the interested parties.

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SUPPORTING INFORMATION

The following additional material may be found online:

Table SI: Types of referral made for children with actionable findings and follow through with referred recommendations.

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