UCLA UCLA Previously Published Works

Title

Identification of risk for severe psychiatric comorbidity in pediatric epilepsy

Permalink

https://escholarship.org/uc/item/2m81k12z

Journal

Epilepsia, 57(11)

ISSN

0013-9580

Authors

Jones, Jana E Siddarth, Prabha Almane, Dace <u>et al.</u>

Publication Date 2016-11-01

DOI

10.1111/epi.13575

Peer reviewed



HHS Public Access

Author manuscript *Epilepsia.* Author manuscript; available in PMC 2018 March 26.

Published in final edited form as:

Epilepsia. 2016 November ; 57(11): 1817–1825. doi:10.1111/epi.13575.

Identification of Risk for Severe Psychiatric Comorbidity in Pediatric Epilepsy

Jana E. Jones, PhD¹, Prabha Siddarth, PhD², Dace Almane, MS¹, Suresh Gurbani, MD, PhD³, Bruce P. Hermann, PhD¹, and Rochelle Caplan, MD²

¹Department of Neurology, University of Wisconsin School of Medicine and Public Health, Madison, WI

²Semel Institute for Neuroscience and Human Behavior, University of California Los Angeles, CA

³Department of Pediatrics, University of California Irvine, CA

SUMMARY

Objective—This study identified items on the Child Behavior Checklist (CBCL) that predict those children and adolescents with epilepsy at highest risk for multiple psychiatric diagnoses.

Methods—328 children, aged 5–18 years, and their parents participated in separate structured psychiatric interviews about the children which yielded Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) diagnoses. Parents completed the CBCL. The sample was divided into a younger (<12 years) (n=214) and older (12–18 years) (n=114) group. This study identified a reduced set of parent-reported CBCL items associated with Multiple Diagnoses vs. Single Diagnosis vs. No Diagnosis using chi-square tests and stepwise logistic regression. We then performed a generalized logistic regression with Multiple Diagnoses vs. Single Diagnosis as the dependent variable and the reduced CBCL set of items as predictors. We calculated the Area Under the Curve (AUC) as a measure of diagnostic accuracy for pairwise comparisons.

Results—For the younger group, 7 items (clingy, cruelty/bullying, perfectionist, nervous; poor school work, inattentive, sulks) had high diagnostic accuracy (AUC=0.88) and for the older group, 3 items (disobedient at school, loner, lies/cheats) (AUC=0.91) when comparing children with multiple psychiatric diagnoses to children with no diagnosis. For both age groups, there was less diagnostic accuracy to identify children with a single vs. no diagnosis [AUC=0.75 (young); 0.70 (older)].

DISCLOSURE OF CONFLICTS OF INTEREST

Suresh Gurbani has no conflicts of interests.

ETHICAL PUBLICATION STATEMENT

Manuscript Correspondence: Jana E. Jones, PhD, Associate Professor, Department of Neurology, University of Wisconsin School of Medicine and Public Health, 1685 Highland Avenue, Room 7229, Madison, WI 53705, jejones@neurology.wisc.edu, Phone: 608-262-5481, Fax: 608-265-0172.

The authors confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Significance—These findings suggest that responses to these two subsets of parent-reported CBCL items should alert clinicians to children and adolescents with epilepsy at risk for multiple psychiatric diagnoses and in need of a psychiatric referral.

Keywords

pediatric epilepsy; psychiatric disorders; risk factors; screening

INTRODUCTION

Epilepsy in childhood and adolescence carries with it a complex interplay among seizures, medication side effects, as well as behavioral, cognitive, and social difficulties. It is well documented that there are higher rates of psychiatric diagnoses and problem behaviors in youth with epilepsy compared to healthy peers and even compared to other youth with chronic conditions like diabetes and asthma.^{1–4} Despite rates of co-occurring psychiatric diagnoses and problem behaviors, ranging from 37% to 77% in youth with epilepsy,^{1; 2; 5} these issues remain under recognized and undertreated with only about a third receiving treatment.^{5–9}

There are a number of barriers that have been identified that may impede the implementation of screening initiatives for psychiatric diagnoses and problem behaviors in youth with epilepsy. They include shrinking resources to conduct the screening,^{8; 10} few recommendations regarding when these screenings should occur,^{11; 12} and which tools are free, can be used easily, and do not require complicated scoring.^{11; 12} Additional barriers to the identification and treatment of the psychiatric comorbidity in pediatric epilepsy are the limited number of mental health professionals with expertise to diagnose and treat children with epilepsy with psychiatric comorbidity as well as limits in insurance coverage for mental health treatment. Given these gaps in mental health resources, medical providers are hesitant to address these problems in youth with epilepsy.^{12; 13}

The goal of this study was to determine if a subset of items from a behavioral screening measure, commonly used in youth with epilepsy (Child Behavior Checklist [CBCL])¹⁴, helps identify those at risk for multiple Axis I Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) diagnoses¹⁵. Further, this study examined the role of chronological age, as well as seizure variables, including seizure control, age of onset, duration, antiepileptic medications (AEDs), number of febrile convulsions and prolonged seizures (i.e., > 5 minutes), as well as seizure type played in the endorsement of the identified items.

METHODS

Participants

The study included 328 participants, aged 5–18 years, with a mean duration of epilepsy of 2.8 (SD 2.9) years. Participants were recruited from Southern California (e.g., University of California Los Angeles clinics, University of Southern California clinics, and Los Angeles and Anaheim Kaiser Permanente, Los Angeles and San Diego Chapters of the Epilepsy Foundation of America, private practices) and Wisconsin (e.g., University of Wisconsin

Hospital and Clinics, Dean Clinic and Marshfield Clinic). There were 191 (58.2%) participants in the California sample; 49.2% were from tertiary centers (e.g., University of California Los Angeles and University of Southern California clinics) and 50.8% were from community sources (e.g., Los Angeles and Anaheim Kaiser Permanente, Los Angeles and San Diego Chapters of the Epilepsy Foundation of America, private practices). There were 137 (41.8%) participants from Wisconsin; 88.3% were from a tertiary care center at the University of Wisconsin Hospital and Clinics, and 11.6% were from large multispecialty community health networks (Dean Clinic, Marshfield Clinic). A pediatric neurologist at each recruitment site made a diagnosis of focal or generalized epilepsy according to the International Classification of Epilepsy.¹⁶ In order to be included in the study, each participant had to have focal or generalized seizures and clinical manifestations of seizures. One pediatric neurology investigator from the University of California Los Angeles reviewed the history, EEG records, and diagnosis of each epilepsy participant from the California recruitment sites. Two pediatric neurology investigators from the University of Wisconsin reviewed the history, EEG records and diagnosis of each epilepsy participant from the Wisconsin recruitment sites. If there was no agreement with the diagnosis or EEG findings, the child was excluded from the study. The parents' report and children's medical records provided information on seizure frequency, AEDs, age of onset, illness duration, as well as the number of febrile convulsions and prolonged seizures (i.e., > 5 minutes). We excluded children with intellectual disability (IQ <70), other neurological disorders, and bilingual speakers of American English attending non-English speaking schools or not speaking English at home. There were no children with high functioning autism included in this study. Specifics regarding the participant selection process have been described in detail in previous publications.^{7; 17}

In the California sample, EEGs were conducted at the time of the initial epilepsy diagnosis and were reviewed and coded by board certified neurologist. Of the 191 children in this sample, 112 children had focal seizures and 32 had slowing, 79 had generalized seizures and 6 had background slowing.

In the Wisconsin sample, EEGs were conducted at the time of the initial epilepsy diagnosis and were reviewed and coded by board certified neurologists. 65 of the 71 children with focal seizures had a coded EEG record: 43 with recorded epileptic activity; 8 with background slowing. 63 of the 66 children with generalized seizures had a coded EEG record: 49 with recorded epileptic activity; 4 with background slowing.

Procedures

After the procedures were fully explained, written informed consent and assent were obtained from parents and children, respectively. This study was approved by the Human Subjects Protection Committees of the University of California, Los Angeles and the University of Wisconsin School of Medicine and Public Health. All procedures were consistent with the Declaration of Helsinki.¹⁸

Children and parents were scheduled for a study visit, separate from an epilepsy clinic visit. Structured psychiatric interviews were administered separately to each child and parent

about the child, and parents completed the Child Behavior Checklist (CBCL) questionnaire during the same visit.

Psychopathology

Psychiatric Interview—The Kiddie Schedule for Affective Disorders and Schizophrenia– Present and Lifetime Version (K-SADS-PL)¹⁹ was administered by a psychiatrist, psychologist, or trained research assistants separately to each child and parent. A diagnosis was made based on symptom endorsement by child and parent as defined by DSM-IV¹⁵ criteria. In the case of disagreement between the parent and child, differential weighting was given to child-reported mood, anxiety, suicide, and psychotic symptoms and to parentreported externalizing symptoms.²⁰ For reliability purposes, a second clinician reviewed 25% of videotapes of the child interviews. In the case of diagnostic disagreement, a consensus Axis I diagnosis was reached. As a primary indicator of severity of psychopathology and for the purpose of this study, we examined Axis I diagnoses aggregated in the following manner: No Axis I diagnosis (no diagnosis), one Axis I diagnosis (single diagnosis) and more than one Axis I diagnoses (multiple diagnoses).

Problem Behaviors—Parents completed the Childhood Behavioral Checklist $(CBCL)^{14; 21}$ which is comprised of 113 behavioral problem items. The California sample used the 1991 version of the CBCL and the Wisconsin sample used the 2001 version of the CBCL. Items 2, 4, 28, 78, 99 were excluded from the analyses since these items are different in the two versions; all other items remained the same. Since this study did not utilize the normative data to obtain the scaled scores for either version of the CBCL, we were able to combine the samples to conduct the item analyses. CBCL item response choices include 0=Not true, 1=Somewhat or Sometimes True, and 2=Very true or Often True. For the purposes of this study a 1 or 2 response was counted as a Yes response or endorsement of a problem behavior.

Cognition

In the California sample the Wechsler Intelligence Scale for Children-3rd edition (WISC-III)²² and in the Wisconsin sample, the Wechsler Abbreviated Intelligence Scale (WASI),²³ were administered to all study participants to generate a Full Scale IQ (FSIQ). These instruments are highly correlated,²⁴ and there were no significant differences in mean IQ scores between the samples. Cognitive abilities were assessed via WISC/WASI prior to mental health assessment to ensure that IQs were above 70.

Data Analyses

Prior to analyses, all data were inspected for outliers. Responses of all CBCL items were grouped into 'Not True' and 'Sometimes/Often True'. Due to the wide age range of the sample, participants were divided into a younger (12 years) and an older (12–18 years) group in order to examine children prior to adolescence and during adolescence. First, for both of these age groups, each individual CBCL item (grouped into 'Not True' and 'Sometimes/Often True') was examined with respect to the severity of psychopathology (Multiple Diagnoses vs. Single Diagnosis vs. No Diagnosis) using a contingency table and analyzed using chi-square tests of independence. Those CBCL items that were associated at

a significance level of at least 0.2 were then entered into a stepwise logistic regression model, using 0.1 as the significance level required both to allow a variable into the model and for the variable to stay in the model. This allowed us to identify a reduced set of CBCL items for each age group separately. Then a generalized logistic regression was performed, with Multiple Diagnoses vs. Single Diagnosis vs. No diagnosis as the dependent variable and the reduced set of CBCL items as predictors. The model was trimmed using the following procedure: the significance of each CBCL item included in the model was examined, and we also checked for items whose coefficients changed markedly in magnitude when other items were included or excluded. This process of deleting, refitting, and verifying was performed until we obtained a final model that explained the data. A significance level of 0.05 was adopted for all inferences. For all pairwise comparisons (i.e. Multiple Diagnoses vs. No Diagnosis, Single Diagnosis vs. No Diagnosis and Multiple Diagnoses vs. Single Diagnosis), the area under ROC curves (AUC) was calculated as a measure of diagnostic accuracy (the ability of the items to correctly classify cases both with and without the condition). In addition, sensitivity, specificity and false negative rates are also reported for the subset of CBCL items identified by the present method, with the cut-off chosen to maximize the number of cases correctly classified. Additional analyses were conducted to determine if there was an association between illness/seizure variables (age of onset, duration, epilepsy syndrome (focal vs. generalized), AED use, and seizure control) and severity of psychopathology or the endorsement of any of the identified CBCL items.

RESULTS

Demographic and seizure-related variables of children in the younger (12 years) and older (12–18 years) groups are presented in Table 1. There were no differences in gender, ethnicity, Full-Scale IQ, epilepsy syndrome (focal vs. generalized), duration of illness, seizure control, AED use (monotherapy vs. polytherapy) and severity of psychopathology between the two age groups. Among the participants with a single psychiatric diagnosis, 57 (54.3%) had depressive or anxiety disorders and 40 (38.1%) had ADHD, and among participants with multiple psychiatric diagnoses 62 (81.6%) had depressive or anxiety disorders and 52 (68.4%) of those with multiple psychiatric diagnoses had ADHD. When examining the two samples, children in the California sample were significantly younger (10.2 (2.8) years) than children in the Wisconsin sample (12.3 (3.2); t(326) = 6.2, p = .0001);hence the younger age group consisted of 64.5% California participants and 35.5% Wisconsin participants while the older age groups consisted of 46.5% California participants and 53.5% Wisconsin participants. Children in the California sample were more likely to be taking one or more medications compared to the Wisconsin sample (Chi-sq (2) = 27.0, p = . 0001). Additionally, children in the California sample had a longer illness duration compared to the Wisconsin sample (t(323) = 13.6, p = .0001.

Younger Group (<12 years)

In the younger age group, there were 7 items that were found to be significant predictors of the three severity of psychopathology categories Multiple Diagnoses vs. No Diagnosis, Single Diagnosis vs. No diagnosis, and Multiple Diagnoses vs. Single Diagnosis: Items 11, 16, 32, 46, 61, 78 and 88 (See description of items in Table 2). Items 11, 78, and 88 were

Page 6

significant predictors of Multiple Diagnoses vs. No Diagnosis and Single Diagnosis vs. No Diagnosis categories. For Multiple Diagnoses vs. Single Diagnosis, items 16, 46, 61 were identified as significant predictors. Item 32 was found to be predictive of Single Diagnosis vs No Diagnosis.

Area Under ROC Curves (AUC)—As demonstrated in Figure 1, the area under the ROC curve (AUC) for subset of 7 items was as follows: Multiple Diagnoses vs No Diagnosis: 0.88, Single Diagnosis vs No Diagnosis: 0.75, and Multiple Diagnoses vs Single Diagnosis: 0.85 (Table 3).

Seizure Variables—Age of onset, duration, and epilepsy syndrome (Focal vs. Generalized) were not associated with severity of psychopathology in this age group. However, the parents of children taking more than one medication were significantly more likely to endorse item 61 (Poor school work; 64.5% of polytherapy vs. 39.4% of monotherapy and 19.1% of no therapy, p = .003) and significantly more parents of children treated with at least one AED significantly endorsed item 88 (Sulks a lot; 38.7% of polytherapy and 36.8% of monotherapy vs 9.5% of no therapy, p = .04). In terms of seizure control, the parents of children who had uncontrolled seizures were likely to endorse item 78 (Inattentive and easily distracted; 37.9% of not seizure controlled vs. 4.6% of seizure controlled participants p < .0001) and item 88 (Sulks a lot; 43.2% of not seizure controlled vs. 15.9% of seizure controlled participants, p = .0002).

Older Group (Age >12–18 years)

In the older age group, there were a total of 3 items that were associated with the three severity of psychopathology categories Multiple Diagnoses vs. No Diagnosis, Single Diagnosis vs. No diagnosis, and Multiple Diagnoses vs. Single Diagnosis: Items 23, 42, 43 (See description of the items in Table 4). Items 23 and 42 were significant predictors of Multiple Diagnoses vs. No Diagnosis and Multiple Diagnoses vs. Single Diagnosis categories. Item 43 significantly predicted of Multiple Diagnoses vs. No Diagnosis and Single Diagnosis vs. No Diagnosis categories.

Area Under ROC Curves (AUC)—As demonstrated in Figure 2, the area under the ROC curve (AUC) for this subset of items was as follows: Multiple Diagnoses vs. No Diagnosis: 0.91, Single Diagnosis vs. No Diagnosis: 0.70, and Multiple Diagnoses vs. Single Diagnosis: 0.83 (Table 3).

Seizure Variables—Unlike the younger group, none of the seizure variables were associated with severity of psychopathology or with any of the above identified CBCL items in the older age group.

Site and Gender Effects

Both severity of psychopathology and endorsement of the reduced subset of CBCL items did not differ by site (UCLA vs. Wisconsin) for both age groups. Gender, on the other hand, was associated with severity of psychopathology. In the younger group, more females had a single diagnosis compared to multiple diagnoses or no diagnosis; in the older group, more

males had a single diagnosis compared to multiple diagnoses or no diagnosis. The two final models (generalized logistic regressions) examining the association of the CBCL items with severity of psychopathology for the two age groups were re-estimated controlling for gender. All the findings remained the same, with comparable OR's and 95% CI's.

DISCUSSION

This study determined if yes/no answers on a subset of CBCL items identified youth with epilepsy who meet diagnostic criteria for multiple DSM-IV-TR Axis I diagnoses. It demonstrated an age-related effect in that different CBCL items identified children with epilepsy under age 12 with multiple psychiatric diagnoses than those aged 12 - 18. Seven CBCL items (clingy, cruel/bully, perfectionist, nervous, poor school work, inattentive, and sulks) correctly (AUC = 0.88) identified the younger children with epilepsy and multiple psychiatric diagnoses compared to those with a single or no psychiatric diagnosis. Three items (disobedient at school, loner, dishonest) had high diagnostic accuracy (ACU = 0.91) for the adolescents with epilepsy with severe psychopathology compared to those with a single or no psychiatric diagnosis.

In contrast to the good diagnostic accuracy of the two CBCL item subsets for participants with multiple psychiatric diagnoses, this was not the case for the single to no psychiatric diagnosis comparison [AUC=0.75 (younger); AUC= 0.70 (older)]. Whereas parents might be unaware of the internalizing symptoms of youth with depression or anxiety disorders, this is not the case for the observable externalizing behavior problems of children with ADHD.²⁰ Among the single psychiatric diagnosis participants, 54.3% had depressive or anxiety disorders and 38.1% had ADHD. However, 68.4% of those with multiple psychiatric diagnoses had ADHD. Therefore, the good diagnostic accuracy for the multiple vs. no psychiatric diagnosis comparison but poor diagnostic accuracy for the single vs. no psychiatric diagnosis comparison might reflect the combined effect of a qualitative and a quantitative factor. The qualitative factor is parents' lack of awareness about internalizing symptoms in the subjects with a single depression or anxiety disorder diagnosis. The quantitative factor is the relatively large ADHD sample size in the multiple psychiatric diagnosis group but small ADHD sample size in the single psychiatric diagnosis group and the associated difference in the number of parent CBCL ratings of problem behaviors. Replication of our findings using youth self-report on problems behaviors is needed to confirm this explanation.

Evidence for good diagnostic accuracy of each of the CBCL item subsets is particularly important because, as demonstrated in the general child/adolescent population, an increased number of psychiatric diagnoses place youth at higher risk for chronic mental health problems, functional impairments, and suicidal behavior.^{25–27, 30, 31} Children with more than one psychiatric diagnosis are also more likely to carry these diagnoses into young adulthood.²⁶ Given the association of psychiatric comorbidity with poor quality of life in children and adolescents with epilepsy, it is important to identify those youth at highest risk and need for psychiatric intervention.²⁸

Unlike two recent large screening initiatives conducted in the field of pediatric epilepsy,^{29; 30} the current study utilized a semi-structured psychiatric interview and obtained information separately from each child and from parents about the child. In addition to this comprehensive diagnostic assessment, by using a developmental approach, we found two different subsets of items on the well-established, commonly used, broad based CBCL that identified children and adolescents with epilepsy at highest risk for multiple Axis I diagnoses. Furthermore, the study included a large representative sample of children and adolescents with epilepsy only." Hesdorffer et al.,²⁹ however, reported low diagnostic sensitivity of both parent- and youth-reported total CBCL scores, administered 9 years after onset of childhood epilepsy, for young adults using the telephone administered Diagnostic Interview Survey-IV (DIS-IV)³¹ to diagnose DSM-IV-TR Axis I disorders at the 15-year follow-up. But Reilly et al.³⁰ found good sensitivity for the total parent score of the easily administered, brief Strength and Difficulties Questionnaire³² in 69 children with epilepsy with IQ scores above 34 and in 16 with IQ <34, 62% of whom had a consensus clinical diagnosis based on the DSM-IV-TR.

Clinical Implications

The findings of this study have several clinical implications. Screening for psychiatric diagnoses and problem behaviors in youth with epilepsy is important particularly as evidenced by the literature that many youth with epilepsy with this comorbidity otherwise escape their clinicians' attention.^{6–9; 33} To address this gap in quality care, clinicians need quick and effective ways to identify children and adolescents with epilepsy who are at risk for severe psychopathology and need treatment.

Additionally, barriers to the identification and treatment of psychiatric and behavior problems in pediatric epilepsy include high clinical demands for neurologists/ epileptologists, few mental health professionals who treat children with epilepsy, and limited insurance coverage for diagnosing and treating the psychiatric comorbidity of pediatric epilepsy. However, easy identification of children and adolescents with epilepsy most at risk for this comorbidity is an important first step towards addressing this unmet mental health care need. The results of our study are applicable to diverse health care settings due to the inclusion of children from large community based multispecialty clinics, health maintenance organizations (HMOs) and tertiary care centers.

Identification of children and adolescents with epilepsy at highest risk for severe psychopathology through the use of this screening approach will ultimately highlight the need for professionals with mental health expertise to work with children with epilepsy. This, in turn, will underscore the requirement for insurance coverage for these services as part of the management of pediatric epilepsy. This is particularly relevant since in the general pediatric population there is a push to screen youth for psychiatric and problem behaviors in order to reduce the related mortality and morbidity. More specifically, in 2008 the state of Massachusetts mandated that all children in the Medicaid program participate in mental health screenings.^{34; 35} It is becoming quite clear that mental health problems, including suicidality, are a significant concern and unmet health care need in pediatric epilepsy.³⁶

From both the clinical and psychometric perspectives, however, it is important to remember that completion of the entire CBCL in conjunction with the screening items will help to obtain a comprehensive assessment and understanding of the type and range of problem behaviors reported by the parents. Whereas a positive screen of patients with the validated CBCL items necessitates administration of the entire CBCL to confirm the extent of problem behaviors, this is not the case for a negative screen.

The study's positive AED and poor seizure control findings in the younger participants also underscore the importance of carefully assessing parents' reports about their young children's poor school work (Item 61), sulking (Item 88), and inattention (Item 78). Lacking information on stress, anxiety, and depression in the mothers of the children in the study, it is unclear if these results were related to parents' increased concerns or worry about their young children's AEDs or seizure frequency or if participants were indeed displaying more difficulties with school, attention and mood due to medication side effects (See review in Caplan³⁷) and poor seizure control.^{38; 39} However, several recent studies have demonstrated the role of parent stress, anxiety,⁴⁰ and depression^{41; 42} in how mothers code quality of life measures and report behavior problems in children with epilepsy (See review in Austin & Caplan⁴³). In contrast to the findings in the younger patients in our study, the lack of an association of seizure variables with the 3 adolescent CBCL items might suggest that parents are unable to closely observe the behavior of their adolescent children. Alternatively, it might also reflect that the significantly larger and younger subsample was on AED polytherapy (Table 1). It will be important to replicate these age-related findings and tease out their underlying mechanisms.

Limitations

There are several limitations of this study. First, the inclusion of only children with IQs above 70 with relatively uncomplicated epilepsy and recruitment mainly from tertiary centers limit generalizability of the study's findings. Second, CBCL parent rather than youth self-report report might have skewed the findings towards easily observed externalizing behaviors, such as cruelty and bullying; nervousness and twitching movements; poor school work, and inattentiveness in the younger children and disobedient at school, lying and cheating, as well as loner behavior in the older participants. If the study included youth selfreport, we might have identified more CBCL internalizing items associated with multiple psychiatric diagnoses. Third, parent's lack of awareness about internalizing symptoms among the single psychiatric diagnosis participants with depression or anxiety disorder and the relatively small number of participants with a single ADHD diagnosis might underlie the lack of differentiation between the one vs. no psychiatric diagnosis groups. Fourth, we did not measure parent stress, anxiety, and depression, variables that play a role in how parents report behavior problems in children with epilepsy.^{40–42; 44} Finally, for clinical and copyright issues, it is recommended that the CBCL be completed in its entirety, and these screening items be reviewed in this context. The study's seizure variable findings might reflect the significant differences in the number of participants on AED polytherapy in the Wisconsin and California samples.

Conclusion

Given the high rate of unmet mental health care in youth with epilepsy, this study provides clinicians with a clinically applicable, brief, and easy method for identifying patients at highest risk for severe psychopathology. This is an important interim goal in improving the quality of care and addressing the psychiatric comorbidity of pediatric epilepsy.

Acknowledgments

The authors would like to thank Thomas Achenbach, PhD, for his thoughtful review of this paper and comments related to the use of the CBCL and potential copyright issues to be avoided. Additionally, the authors would like to thank the support of Kate Young, MEd, Melissa Hansen, Erin Lanphier, PhD, Amy Mo, Caroline Bailey, PhD, Kimberly Smith, MA, Joanna Wu, and Sona Hovsepian. This study was supported by NIH grants NS32070 (R Caplan) and 5R01NS044351-09 (BP Hermann).

Rochelle Caplan and Prabha Siddarth have received support from NIH RO1 NS32070.

Dace Almane, Jana E. Jones and Bruce P. Hermann have received support from NIH 5R01NS044351-09

References

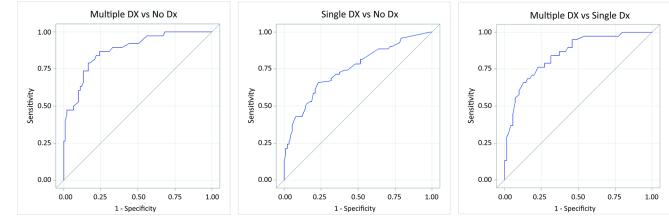
- Rodenburg R, Stams GJ, Meijer AM, et al. Psychopathology in children with epilepsy: a metaanalysis. J Pediatr Psychol. 2005; 30:453–468. [PubMed: 16055484]
- 2. Davies S, Heyman I, Goodman R. A population survey of mental health problems in children with epilepsy. Dev Med Child Neurol. 2003; 45:292–295. [PubMed: 12729141]
- Austin JK, Dunn DW, Huster GA. Childhood epilepsy and asthma: changes in behavior problems related to gender and change in condition severity. Epilepsia. 2000; 41:615–623. [PubMed: 10802769]
- Wagner JL, Smith G, Ferguson PL, et al. Preliminary Psychometrics of the Neurological Disorders Depression Inventory for Epilepsy-Youth. J Child Neurol. 2013; 28:1392–1399. [PubMed: 23576412]
- 5. Reilly C, Atkinson P, Das KB, et al. Neurobehavioral comorbidities in children with active epilepsy: a population-based study. Pediatrics. 2014; 133:e1586–1593. [PubMed: 24864167]
- Russ SA, Larson K, Halfon N. A national profile of childhood epilepsy and seizure disorder. Pediatrics. 2012; 129:256–264. [PubMed: 22271699]
- 7. Caplan R, Siddarth P, Gurbani S, et al. Depression and anxiety disorders in pediatric epilepsy. Epilepsia. 2005; 46:720–730. [PubMed: 15857439]
- Ott D, Siddarth P, Gurbani S, et al. Behavioral disorders in pediatric epilepsy: unmet psychiatric need. Epilepsia. 2003; 44:591–597. [PubMed: 12681010]
- Roeder R, Roeder K, Asano E, et al. Depression and mental health help-seeking behaviors in a predominantly African American population of children and adolescents with epilepsy. Epilepsia. 2009; 50:1943–1952. [PubMed: 19260941]
- Shore CP, Buelow JM, Austin JK, et al. Continuing psychosocial care needs in children with newonset epilepsy and their parents. J Neurosci Nurs. 2009; 41:244–250. [PubMed: 19835237]
- Kerr MP, Mensah S, Besag F, et al. International consensus clinical practice statements for the treatment of neuropsychiatric conditions associated with epilepsy. Epilepsia. 2011; 52:2133–2138. [PubMed: 21955156]
- Barry JJ, Ettinger AB, Friel P, et al. Consensus statement: the evaluation and treatment of people with epilepsy and affective disorders. Epilepsy Behav. 2008; 13(Suppl 1):S1–29. [PubMed: 18502183]
- 13. Kanner AM. When did neurologists and psychiatrists stop talking to each other? Epilepsy Behav. 2003; 4:597–601. [PubMed: 14698691]
- 14. Achenbach, TM., Rescorla, LA. Manual for the ASEBA School-Age forms and profiles. University of Vermont, Research Center for Children, Youth and Families; Burlington, VT: 2001.

- American Psychological Association. Diagnostic and Statistical Manual of Mental Disorders. Washington, DC: 1994.
- Shorvon SD. The etiologic classification of epilepsy. Epilepsia. 2011; 52:1052–1057. [PubMed: 21449936]
- 17. Hermann B, Jones J, Sheth R, et al. Children with new-onset epilepsy: neuropsychological status and brain structure. Brain. 2006; 129:2609–2619. [PubMed: 16928696]
- World Medical Association Declaration of Helsinki. The Journal of Law, Medicine & Ethics. 1991; 19:264–265.
- Kaufman J, Birmaher B, Brent D, et al. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry. 1997; 36:980–988. [PubMed: 9204677]
- Grills AE, Ollendick TH. Issues in parent-child agreement: the case of structured diagnostic interviews. Clin Child Fam Psychol Rev. 2002; 5:57–83. [PubMed: 11993545]
- 21. Achenbach, T. Manual for the Child Behavior Checklist and revised Child Behavior Profile. Department of Psychiatry, Unviersity of Vermont; Vermont: 1991.
- Wechsler, D. Wechsler Intelligence Scale for Children. The Psycholocal Corporation; San Antonio, TX: 1991.
- 23. Wechsler, D. Wechsler Abbreviated Scale of Intelligence. The Psychological Corporation; San Antonio, TX: 1999.
- Scott WC, Austin DW, Reid DS. Investigation of the WISC-III and WASI in Clinical Child Populations: A Framework for Further Exploration. Canadian Journal of School Psychology. 2007; 22:249–254.
- 25. Costello EJ, Mustillo S, Erkanli A, et al. Prevalence and development of psychiatric disorders in childhood and adolescence. Arch Gen Psychiatry. 2003; 60:837–844. [PubMed: 12912767]
- Copeland WE, Shanahan L, Costello EJ, et al. Childhood and adolescent psychiatric disorders as predictors of young adult disorders. Arch Gen Psychiatry. 2009; 66:764–772. [PubMed: 19581568]
- 27. Nock MK, Green JG, Hwang I, et al. Prevalence, correlates, and treatment of lifetime suicidal behavior among adolescents: results from the National Comorbidity Survey Replication Adolescent Supplement. JAMA Psychiatry. 2013; 70:300–310. [PubMed: 23303463]
- Baca CB, Vickrey BG, Caplan R, et al. Psychiatric and medical comorbidity and quality of life outcomes in childhood-onset epilepsy. Pediatrics. 2011; 128:e1532–1543. [PubMed: 22123895]
- 29. Hesdorffer DC, Baldin E, Caplan R, et al. How do we measure psychiatric diagnoses? Implications of the choice of instruments in epilepsy. Epilepsy Behav. 2014; 31:351–355. [PubMed: 24230987]
- 30. Reilly C, Atkinson P, Das KB, et al. Screening for mental health disorders in active childhood epilepsy: population-based data. Epilepsy Res. 2014; 108:1917–1926. [PubMed: 25454504]
- Robins, L., Cottler, L., Bucholz, K., et al. Diagnostic interview schedule for DSM-IV (DIS-IV). St. Louis: Washington University School of Medicine; 1997.
- 32. Goodman R. The Strengths and Difficulties Questionnaire: a research note. J Child Psychol Psychiatry. 1997; 38:581–586. [PubMed: 9255702]
- 33. Reilly C, Atkinson P, Das KB, et al. Parent- and Teacher-Reported Symptoms of ADHD in School-Aged Children With Active Epilepsy: A Population-Based Study. J Atten Disord. 2014
- Hacker KA, Penfold RB, Arsenault LN, et al. Effect of Pediatric Behavioral Health Screening and Colocated Services on Ambulatory and Inpatient Utilization. Psychiatr Serv. 2015; 66:1141–1148. [PubMed: 26129994]
- 35. Romano-Clarke G, Tang MH, Xerras DC, et al. Have rates of behavioral health assessment and treatment increased for Massachusetts children since the Rosie D. decision? A report from two primary care practices. Clin Pediatr (Phila). 2014; 53:243–249. [PubMed: 24220574]
- 36. Book Epilepsy across the spectrum: Promoting health and understanding. Institute of Medicine Committee on the Public Health Dimension of Epilepsies; Washington DC: 2012. Epilepsy across the spectrum: Promoting health and understanding.
- Caplan R. Psychopathology in pediatric epilepsy: role of antiepileptic drugs. Front Neurol. 2012; 3:163. [PubMed: 23233847]

- Ferro MA, Boyle MH, Scott JG, et al. The child behavior checklist and youth self-report in adolescents with epilepsy: testing measurement invariance of the attention and thought problems subscales. Epilepsy Behav. 2014; 31:34–42. [PubMed: 24333500]
- Oostrom KJ, Schouten A, Kruitwagen CL, et al. Epilepsy-related ambiguity in rating the child behavior checklist and the teacher's report form. Epileptic Disord. 2001; 3:39–45. [PubMed: 11313222]
- 40. Wu YP, Follansbee-Junger K, Rausch J, et al. Parent and family stress factors predict health-related quality in pediatric patients with new-onset epilepsy. Epilepsia. 2014; 55:866–877. [PubMed: 24673687]
- 41. Ferro MA, Avison WR, Campbell MK, et al. The impact of maternal depressive symptoms on health-related quality of life in children with epilepsy: a prospective study of family environment as mediators and moderators. Epilepsia. 2011; 52:316–325. [PubMed: 21054352]
- Ferro MA, Speechley KN. Depressive symptoms among mothers of children with epilepsy: a review of prevalence, associated factors, and impact on children. Epilepsia. 2009; 50:2344–2354. [PubMed: 19694788]
- 43. Austin JK, Caplan R. Behavioral and psychiatric comorbidities in pediatric epilepsy: toward an integrative model. Epilepsia. 2007; 48:1639–1651. [PubMed: 17565593]
- 44. Sherman EM, Brooks BL, Akdag S, et al. Parents report more ADHD symptoms than do teachers in children with epilepsy. Epilepsy Behav. 2010; 19:428–435. [PubMed: 20926354]

Key Points

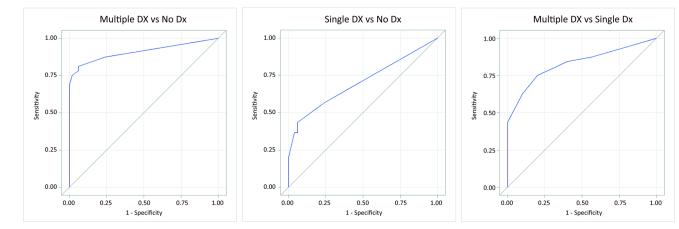
- Parent responses to a subset of Child Behavior Checklist (CBCL) items identify children at risk for multiple psychiatric diagnoses.
- There are 7 items for children under age 12 and 3 items for children over age 12.
- Parent responses to these questions help identify children who will benefit from a psychiatric referral.



DX: Diagnosis



Area Under the ROC Curves for Younger Group (12 years old) Area Under the ROC curves for Multiple Diagnoses vs. No Diagnosis, Single Diagnosis vs. No Diagnosis, Multiple Diagnoses vs. Single Diagnosis



Dx: Diagnosis



Area Under the ROC Curves for Older Group (Age >12–18 years) Area Under the ROC curves for Multiple Diagnoses vs. No Diagnosis, Single Diagnosis vs. No Diagnosis, Multiple Diagnoses vs. Single Diagnosis

Table 1

Demographic Characteristics of Children with Epilepsy in Younger and Older Groups

	Younger Group (12 years &under) (N=214)	Older Group (>12–18 years) (N=114)
Site		
California (n, %)	138 (72.3)	53 (27.8)
Wisconsin (n, %)	76 (55.5)	61 (44.5)
Age (years; mean, SD)	9.1 (1.6)	14.7 (1.8)
Gender (n, %)		
Male	107 (50.0)	58 (50.9)
Female	107 (50.0)	56 (49.1)
Full Scale IQ (mean, SD)	98.6 (15.0)	100.2 (13.3)
Ethnicity (n, %)		-
Caucasian	131 (61.2)	82 (71.9)
Non-Caucasian	83 (38.8)	32 (28.1)
Epilepsy Variables		
Age at Seizure Onset (mean, SD)	6.5 (2.8)	11.6 (4.5)
Seizure Duration (mean, SD)	2.7 (2.4)	3.2 (3.7)
Focal Seizures (n, %)	121 (56.5)	63 (55.3)
Generalized Seizures (n, %)	93 (43.5)	51 (44.7)
Seizures Controlled (n, %)	68 (32.2)	28 (24.8)
Seizures Uncontrolled	143 (67.8)	85 (75.2)
AED Use (n, %)		
No AEDs	21 (9.8)	12 (10.5)
Monotherapy	160 (74.8)	82 (71.9)
Polytherapy	33 (15.5)	20 (17.6)
Psychiatric Diagnoses (n, %)		
No Diagnosis	96 (44.9)	51 (44.7)
Single Diagnosis	75 (35.0)	30 (26.3)
Multiple Diagnosis	43 (20.1)	33 (28.9)

Author Manuscript

Author Manuscript

Table 2

Individual Predictor Items for Younger Group (12 years old)

Item Number	Item Description	Multiple vs. No Diagnosis OR [95% CI]	P value	Single vs. No Diagnosis OR (95% CI)	P value	Multiple vs. Single Diagnosis OR (95% CI)	P value
11	Clings to adults or is too dependent	2.7 [1.0, 7.4]	0.05	2.9 [1.4, 6.1] 0.005	0.005	0.9 [0.4, 2.5],	6.0
16	Cruelty, bullying or meanness to others	6.8 [2.0,22.5] 0.002	0.002	0.7 [0.2, 2.4]	0.6	9.18 [2.7, 0.1]	0.0003
32	Feels he/she has to be perfect	.7 [0.3, 2.0]	0.5	2.8 [1.4, 5.7]	0.004	$0.3\ [0.1,0.7]$	0.008
46	Nervous movements or twitching	4.3 [1.5,12.4] 0.008	0.008	2.8 [1.4, 5.7]	0.9	3.9 [1.4,11.1]	0.01
61	Poor school work	3.7 [1.4,9.9]	0.008	1.2 [0.6, 2.5]	0.6	3.1 [1.2, 8.2]	0.02
78	Inattentive or easily distracted	2.7 [0.9, 7.8] 0.06	0.06	3.3 [1.5, 7.5] 0.004	0.004	0.8 [0.3, 2.2]	0.7
88	Sulks a lot	3.7 [1.4, 10.2]	0.01	2.6 [1.2, 5.7]	0.02	1.4 [0.5, 3.8]	0.5

Table 3

Predictive Ability of CBCL 7- and 3-Item Screening Tool

CBCL Screener	AUC*	False Negative	Sensitivity	Specificity
Your	iger Grou	p (12 years))	
Multiple vs. No Diagnosis	0.88	16.0	60.5	86.8
Single vs. No Diagnosis	0.75	28.7	58.6	79.1
Multiple vs. Single Diagnosis	0.85	20.7	55.3	92.9
Old	er Group	(>12 years)		
Multiple vs. No Diagnosis	0.91	11.3	81.3	94.0
Single vs. No Diagnosis	0.70	26.6	43.3	94.0
Multiple vs. Single Diagnosis	0.83	21.7	84.4	60.0

Table 4

ars
ye
18
4
$\overline{}$
∆ge
A)
dno
Gro
er
ld
r O
s for
Items
tor
dic
Pre
ual]
'idu
Indi

Item Number	Item Description	Multiple vs. No Diagnosis OR [95% CI]	P value	Single vs. No Diagnosis OR (95% CI)	P value	Multiple vs. Single Diagnosis OR (95% CI)	P value
23	Disobedient at school	28.7 [2.9, 281.1]	0.004	28.7 [2.9, 281.1] 0.004 5.4 [0.5, 54.3]	0.2	0.2 5.3 [1.4, 20.4],	0.02
42	Would rather be alone than with others	5.1 [1.3,19.9]	0.02	0.9 [0.3, 2.9]	0.8	5.9 [1.7, 20.5]	0.005
43	Lying or cheating	24.1 [4.2, 138.5] 0.0004 11.6 [2.3, 59.3] 0.003 2.1 [0.6, 7.4]	0.0004	11.6 [2.3, 59.3]	0.003	2.1 [0.6, 7.4]	0.3