Topic Brief: Anxiety in Adolescents with Epilepsy

Date: 6/27/2022
Nomination Number: 1014

Purpose: This document summarizes the information addressing a nomination submitted on June 5, 2022, through the Effective Health Care Website. This information was used to inform the Evidence-based Practice Center (EPC) Program decisions about whether to produce an evidence report on the topic, and if so, what type of evidence report would be most suitable.

Issue: The nominator of this topic is an individual who is concerned about the lack of guidelines for diagnosis and treatment of anxiety in children and teens with epilepsy. The nominator requests guidance, and insurance coverage of treatment by cognitive behavioral therapists.

Findings: The EPC Program does not develop clinical guidance or determine insurance coverage. We found no relevant systematic reviews, and few relevant research studies. For these reasons the EPC Program will not consider this nomination further.

Background

Epilepsy is a chronic neurological disorder in which abnormal brain activity causes seizures or periods of unusual behavior and sensations. The symptoms of epileptic seizures vary widely, but may include temporary confusion, staring spells, stiff muscles, uncontrolled jerking movements of the limbs, loss of consciousness, and psychological symptoms.[1] Epileptic seizures can be controlled by the appropriate use of seizure medication, and it is possible to diagnose and treat most people with the condition at the primary-care level.[2]

Epilepsy is one of the most common neurological diseases globally, impacting approximately 50 million people worldwide. The vast majority (80%) of people with epilepsy live in low-income countries.[2] The condition affects 0.5 to one percent of children, and is the most frequent chronic neurological condition in childhood, although incidence rates appear to be declining in high-income countries.[3]

In general, patients with epilepsy are more likely to suffer from psychiatric illness, specifically mood disorders, than the general population.[4] The prevalence of anxiety in children with epilepsy is approximately 30 to 35 percent, and the prevalence of depression is around 13 to 37 percent. The Epilepsy Foundation recommends monitoring for and treating mood disorders in children and adults with epilepsy because this can impact daily activities and quality of life of these individuals.[5] In one study at a large tertiary care hospital, a group of children attending an epilepsy clinic without diagnoses of mental health conditions were found to have anxiety (30.2%) and depression (41.2%), while nearly twelve percent answered questions on a structured

tool consistent with suicidal thoughts.[6] The burden of these psychiatric symptoms when combined with epilepsy is significant, and can lead to increased morbidity, impacts patients and their families, and complicates the management of epilepsy.[7]

Scope

1. What is the effectiveness and harms of pharmacologic intervention for treatment of anxiety disorder in children with epilepsy?
2. What is the effectiveness and harms of psychological interventions for treatment of anxiety disorder in children with epilepsy?

Assessment Methods

See Appendix A.

Summary of Literature Findings

We identified no systematic reviews directly related to the key questions.

We identified no primary published research studies in our targeted literature scan relevant to KQ 1. We identified two relevant studies on clobazam (NCT03371836) and cannabidiol (NCT05324449) in ClinicalTrials.gov.

For KQ 2 we identified one study protocol without results on a telephone delivered modular psychological intervention. We also identified two studies on mindfulness (NCT04313686, NCT04687904), though the population was 16 years and older.

We identified too few studies addressing the nomination questions; therefore the EPC Program will not consider this nomination further.

Other Resources

We found the following resources that may be of interest to the nominator, and may answer some of their questions regarding the treatment of psychiatric illness in children and adolescents with epilepsy:

- A 2020 systematic review evaluating the prevalence of anxiety and depression in youth with epilepsy and examining factors that moderate anxiety and depression outcomes.[8]
- A 2020 Cochrane systematic review of psychological interventions to manage anxiety and other psychological symptoms in people with epilepsy. Nine of the 36 included studies were in children and adolescents.[9]
- A 2019 narrative review examining the diagnosis and management of depression and anxiety in pediatric patients with epilepsy.[7]
- Another 2017 Cochrane systematic review looking at psychological (cognitive, behavioral, mindfulness-based, and self-management) interventions for people with epilepsy. Seven of the 24 included studies examined interventions for children or adolescents.[10]

References

1. Mayo Clinic. Epilepsy: Symptoms and causes. https://www.mayoclinic.org/diseases-conditions/epilepsy/symptoms-causes/syc-20350093. Accessed on 6/29 2022.
2. World Health Organization. Epilepsy. 2022. https://www.who.int/news-room/fact-sheets/detail/epilepsy. Accessed on 06/29 2022.
3. Aaberg KM, Gunnes N, Bakken IJ, et al. Incidence and Prevalence of Childhood Epilepsy: A Nationwide Cohort Study. Pediatrics. 2017 May;139(5). https://doi.org/10.1542/peds.2016-3908. PMID: 28557750.
4. Trivedi MH, Kurian BT. Managing depressive disorders in patients with epilepsy. Psychiatry (Edgmont). 2007 Jan;4(1):26-34. PMID: 20805926.
5. Epilepsy Foundation. Understanding Epilepsy: Moods and Behavior. 2022. https://www.epilepsy.com/complications-risks/moods-behavior. Accessed on 07/01/2022.
6. Dagar A, Anand A, Pestana-Knight E, et al. Screening for suicidality and its relation to undiagnosed psychiatric comorbidities in children and youth with epilepsy. Epilepsy Behav. 2020 Dec;113:107443. https://doi.org/10.1016/j.yebeh.2020.107443. PMID: 33152581.
7. Plevin D, Smith N. Assessment and Management of Depression and Anxiety in Children and Adolescents with Epilepsy. Behav Neurol. 2019;2019:2571368. https://doi.org/10.1155/2019/2571368. PMID: 31191736.
8. Scott AJ, Sharpe L, Loomes M, et al. Systematic Review and Meta-Analysis of Anxiety and Depression in Youth With Epilepsy. J Pediatr Psychol. 2020 Mar 1;45(2):133-44. https://doi.org/10.1093/jpepsy/jsz099. PMID: 31904859.
9. Michaelis R, Tang V, Nevitt SJ, et al. Psychological treatments for people with epilepsy. Cochrane Database Syst Rev. 2020 Sep 7;8:CD012081. https://doi.org/10.1002/14651858.CD012081.pub3. PMID: 35653266.
10. Michaelis R, Tang V, Wagner JL, et al. Psychological treatments for people with epilepsy. Cochrane Database Syst Rev. 2017 Oct 27;10:CD012081. https://doi.org/10.1002/14651858.CD012081.pub2. PMID: 29078005.

Author

Charlotte Armstrong
Christine Chang

Conflict of Interest: None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Acknowledgements

Lisa Winterbottom
Irina Jenkins

This report was developed by the Scientific Resource Center under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. HHSA 290-2017-00003C). The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. No statement in this article should be

construed as an official position of the Agency for Healthcare Research and Quality or of the U.S. Department of Health and Human Services.

Persons using assistive technology may not be able to fully access information in this report. For assistance contact EPC@ahrq.hhs.gov.

Appendix A: Methods

We assessed nomination for priority for a systematic review or other AHRQ Effective Health Care report with a hierarchical process using established selection criteria. Assessment of each criteria determined the need to evaluate the next one. See Appendix B for detailed description of the criteria.

Appropriateness and Importance

We assessed the nomination for appropriateness and importance.

Desirability of New Review/Absence of Duplication

We conducted a search for existing systematic reviews. We searched for high-quality, completed or in-process evidence reviews published in the last three years June 2019 to June 2022 on the questions of the nomination from these sources:

- AHRQ: Evidence reports and technology assessments
    - AHRQ Evidence Reports https://www.ahrq.gov/research/findings/evidence-based-reports/index.html
    - EHC Program https://effectivehealthcare.ahrq.gov/
- US Department of Veterans Affairs Products publications
    - Evidence Synthesis Program https://www.hsrd.research.va.gov/publications/esp/
    - VA/Department of Defense Evidence-Based Clinical Practice Guideline Program https://www.healthquality.va.gov/
- Cochrane Systematic Reviews https://www.cochranelibrary.com/
- PROSPERO Database (international prospective register of systematic reviews and protocols) http://www.crd.york.ac.uk/prospero/
- PubMed https://www.ncbi.nlm.nih.gov/pubmed/

Impact of a New Evidence Review

The impact of a new evidence review was qualitatively assessed by analyzing the current standard of care, the existence of potential knowledge gaps, and practice variation. We considered whether it was possible for this review to influence the current state of practice through various dissemination pathways (practice recommendation, clinical guidelines, etc.).

Feasibility of New Evidence Review

We conducted a limited Medline search of primary literature published within the last five years from July 2016 through July 2022.

Feasibility Search Anxiety Tx in Childhood Epilepsy

Ovid MEDLINE(R) ALL <1946 to July 06, 2022>

1	exp Drug Therapy/ or drug therapy.fs.	3295431
2	pharmacologic treatment.mp.	5334
3	selective serotonin reuptake inhibitors.mp. or exp Serotonin Uptake Inhibitors/	48539
4	(SSRI or SSIRs).m_titl.	975
5	Citalopram.mp. or exp Citalopram/	7513

6 Escitalopram.mp. or Escitalopram/ 2985
7 Fluoxetine.mp. or Fluoxetine/ 15112
8 Fluvoxamine.mp. or exp Fluvoxamine/ 3180
9 Paroxetine.mp. or exp Paroxetine/ 6661
10 sertraline.mp. or exp Sertraline/ 5722
11 (serotonin and norepinephrine reuptake inhibitor).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms] 975
12 (SNRI or SNRIs).m_titl. 165
13 Desvenlafaxine.mp. or exp Desvenlafaxine Succinate/ 503
14 Duloxetine.mp. or exp Duloxetine Hydrochloride/ 3077
15 venlafaxine.mp. or Venlafaxine Hydrochloride/ 4793
16 Benzodiazepines.mp. or exp Benzodiazepines/ 77736
17 Alprazolam.mp. or exp Alprazolam/ or exp Anti-Anxiety Agents/ 73461
18 clonazepam.mp. or exp Clonazepam/ 4818
19 Tricyclic antidepressants.mp. or exp Antidepressive Agents, Tricyclic/ 35212
20 Amitriptyline.mp. or exp Amitriptyline/ 9703
21 clomipramine.mp. or exp Clomipramine/ 4084
22 Bupropion/ or Buproprion.mp. 3298
23 Mirtazapine.mp. or exp Mirtazapine/ 2595
24 or/1-23 3393207
25 separation anxiety.mp. or exp Anxiety, Separation/ 3228
26 social anxiety disorder.mp. or exp Phobia, Social/ 3479
27 panic disorder.mp. or exp Panic Disorder/ 11660
28 generalized anxiety disorder.mp. 8237
29 anxiety disorder.mp. or exp Anxiety Disorders/ 95495
30 or/25-29 97521
31 exp Epilepsy/ or epilepsy.mp. 161578
32 24 and 30 and 31 299
33 limit 32 to ("preschool child (2 to 5 years)" or "child (6 to 12 years)" or "adolescent (13 to 18 years)") 75
34 limit 33 to "reviews (maximizes sensitivity)" 35
35 limit 33 to clinical trial, all 5
36 33 not (34 or 35) 38

Reviews N=35 ris(18).ris
Clinical Trials N=5 ris(19).ris
Other N=38 filename ris(20).ris

(Child[Mesh] OR Adolescent[Mesh]) AND **Anxiety Disorders[Mesh]** AND Epilepsy[Mesh] AND (Psychotherapy[Mesh] OR Motivational Interviewing[Mesh] OR “problem solving therapy”[tiab]) – *1 result (didn’t include Anxiety[mesh])*

~~~~~~

(Child[Mesh] OR Adolescent[Mesh]) AND (Anxiety Disorders[Mesh] OR **Anxiety[Mesh]**) AND Epilepsy[Mesh] AND (Psychotherapy[Mesh] OR Motivational Interviewing[mesh] OR "problem solving therapy") – *3* results (added OR Anxiety[mesh])
~~~~~~

~~~~~~

(Child[Mesh] OR Adolescent[Mesh]) AND (Anxiety Disorders[Mesh] OR Anxiety[Mesh]) AND Epilepsy[Mesh] AND (**psychotherapy** OR Motivational Interviewing[Mesh] OR "problem solving therapy" OR **"motivational interviewing" OR therapy OR "cognitive behavioral")** - *50 results*

~~~~~~

((child*[tiab] OR pediatric*[tiab]) AND epilepsy[ti] AND (anxiety OR panic) AND (therap*[tiab] OR psychotherapy[tiab] OR "cognitive behavioral"[tiab] OR mindfulness[tiab] OR "problem solving"[tiab] OR "motivational interviewing"[tiab])) NOT Medline[sb] – *5 results (to retrieve citations not yet indexed with Mesh terms)*

https://clinicaltrials.gov/ct2/results?cond=epilepsy&term=anxiety&cntry=&state=&city=&dist=

Appendix B. Selection Criteria Assessment

Selection Criteria	Assessment
1. Appropriateness	
1a. Does the nomination represent a health care drug, intervention, device, technology, or health care system/setting available (or soon to be available) in the U.S.?	Yes.
1b. Is the nomination a request for an evidence report?	The nominator is interested in guidance to assist in healthcare decision-making. Such guidance would ideally be supported by an evidence review.
1c. Is the focus on effectiveness or comparative effectiveness?	Yes. The nominator is interested in effectiveness and harms of treatment.
1d. Is the nomination focus supported by a logic model or biologic plausibility? Is it consistent or coherent with what is known about the topic?	Yes.
2. Importance	
2a. Represents a significant disease burden; large proportion of the population	Anxiety disorders are the most common psychiatric disorder in childhood and are often underdiagnosed in typically developing children and in those with epilepsy. Studies in the US have found rates of anxiety disorders in pediatric epilepsy as high as 35.8%.
2b. Is of high public interest; affects health care decision making, outcomes, or costs for a large proportion of the US population or for a vulnerable population	
2c. Incorporates issues around both clinical benefits and potential clinical harms	Yes. The nominator is interested in both benefits and harms, especially interaction with epilepsy treatment.
2d. Represents high costs due to common use, high unit costs, or high associated costs to consumers, to patients, to health care systems, or to payers	Yes.
3. Desirability of a New Evidence Review/Absence of Duplication	
3. A recent high-quality systematic review or other evidence review is not available on this topic	We did not identify relevant high-quality systematic reviews related to the nomination questions.
4. Impact of a New Evidence Review	
4a. Is the standard of care unclear (guidelines not available or guidelines inconsistent, indicating an information gap that may be addressed by a new evidence review)?	We identified no guidelines specific to treatment of anxiety in children with epilepsy. We identified 2018 information sheet from the American Epilepsy Society, which indicated that guidance was based on studies of children without epilepsy.
4b. Is there practice variation (guideline inconsistent with current practice, indicating a potential implementation gap and not best addressed by a new evidence review)?	Yes. There is a practice variation. In a 2021 survey of health professionals less than half of respondents felt adequately resourced to manage depression and anxiety. There was a lack of consensus about which health professionals were responsible for screening and management. 38% respondents noted that the lack of standardized procedures was a common barrier.
5. Primary Research	
5. Effectively utilizes existing research and knowledge by considering: - Adequacy (type and volume) of research for conducting a systematic review	Too few studies are available to inform a new systematic review. We identified two in-process studies in Clinicaltrials.gov relevant to KQ 1; and two in-process studies relevant to KQ 2.

- Newly available evidence (particularly for updates or new technologies)	