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Behavioral predictors of medication adherence trajectories among youth with newly diagnosed epilepsy

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ABSTRACT

Objective: This study aimed to identify psychosocial predictors of two-year antiepileptic drug (AED) adherence trajectories among youth with newly diagnosed epilepsy, controlling for known demographic and medical factors.

Method: This study is part of a large, prospective, longitudinal observational study of AED adherence and medical outcomes in youth with newly diagnosed epilepsy. Parents completed questionnaires of psychosocial and family functioning at one month and one year following diagnosis. Chart review and questionnaires were used to collect medical variables and seizure outcomes. Previously established two-year AED adherence trajectories (Severe Early Nonadherence, Variable Nonadherence, Moderate Nonadherence, High Adherence) were used as the outcome variable.

Results: Participants were 91 parents of youth with epilepsy (7.3 ± 2.8 years of age; 60% male) and their families. Early (one month following diagnosis) predictors of two-year adherence trajectories included socioeconomic status, epilepsy knowledge, family problem-solving, and family communication. Significant predictors one year following diagnosis included socioeconomic status, parent fears and concerns, and parent life stress.

Conclusion: There are modifiable parent and family variables that predict two-year adherence trajectories above and beyond known medical (e.g., seizures, side effects) factors. Psychosocial interventions delivered at key points during the course of epilepsy treatment could have a positive impact on adherence outcomes.

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1. Introduction

Past research has shown that children with epilepsy have difficulties taking antiepileptic drugs (AEDs) as prescribed [1,2]. There are significant health and economic impacts of nonadherence to AEDs, such as poor seizure control [2], uninformed clinical decision-making [3], and increased health-care costs in adults [4].

In an effort to better understand reasons for nonadherence, past research has identified demographic, medical, and psychosocial factors associated with adherence behaviors (e.g., taking medication, clinic attendance). Lower socioeconomic status (SES) is consistently related to [5] and predicts [1] nonadherence across the disease course. Additional demographic and medical predictors of adherence include family composition, family history of epilepsy [6], and seizure control [2,7]. While these factors may help clinicians classify patients most at risk for nonadherence, the identification of modifiable psychosocial factors would more easily lend themselves to intervention and, ultimately, improved adherence. Prior cross-sectional studies have demonstrated that less disease knowledge [8], higher barriers to the medication regimen [9], poorer parent psychosocial status, and poorer family functioning [10] negatively predict AED adherence. However, these studies have methodological limitations which limit generalizability of findings. Specifically, these studies lack an operational definition or evidence-based measure of adherence [6–8,10–12], have small sample sizes [5–7], or assessed patients with chronic epilepsy [10,12]. Additionally, most of the research has identified correlates, rather than predictors, of adherence over the course of epilepsy treatment [7,8,11,12]. Identifying predictors that are amenable to intervention is essential for the prevention or reduction of nonadherence over the course of epilepsy treatment.

This study, which is a secondary data analysis [1], aimed to identify demographic, medical, and psychosocial predictors of previously established adherence trajectories among young children newly diagnosed with epilepsy at two different points in the course of epilepsy treatment. Factors that predict adherence may change over time as the family adjusts to the diagnosis and associated medical management [13]. For example, AED side effects may be highest during the acute period but often dissipate as the patient moves further from diagnosis and treatment initiation [14]. Further, a patient's tolerance for various

Abbreviations: AED, antiepileptic drug; SES, socioeconomic status.

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AED side effects changes over time [15]. However, as the patient and family become more familiar with the condition and AED regimen, other factors, such as lack of resources and parental distress, may contribute to adherence difficulties. These trajectories were initially established to understand the influence of AED adherence on seizure outcomes. The next crucial step is to identify predictors of these trajectories to improve adherence following diagnosis. It was hypothesized that a more favorable (better) adherence trajectory would be predicted by fewer perceived barriers to the medication regimen, greater parent epilepsy knowledge, less perceived social stigma, decreased parent stress, and better family functioning, after controlling for SES, seizure trajectories, and AED side effects both early (one month following diagnosis) and later (one year following diagnosis) in the course of treatment.

2. Methods and materials

2.1. Participants

Participants were recruited from a New Onset Seizure (NOS) Clinic at a Midwestern United States children's hospital from November 2006 through March 2009. Eligibility criteria included: 1) new diagnosis of epilepsy, 2) 2–12 years old, 3) no parent-reported comorbid chronic illnesses requiring routine medications (e.g., diabetes) or significant developmental disorders (e.g., autism), 4) no prior AED treatment, and 5) initiation of carbamazepine or valproic acid monotherapy (which represented standard clinical practice within the NOS Clinic at the time of the study). There were 111 eligible families (children with epilepsy and a parent) that were approached for study participation. Five families declined participation due to time constraints (95% recruitment rate). One participant was found to be ineligible after informed consent was obtained (due to simultaneous diagnosis of a pervasive developmental disorder). Fourteen participants were excluded due to lack of follow-up data after their initial or one-month visit or significant missing adherence data (<90% complete data for all visits, see [16]). Thus, 91 participants were in this study cohort (82% of those initially eligible). The sample size for the one-year analyses was reduced to 73 due to missing adherence data or attrition (e.g., never returned to clinic, family relocated, withdrew) from the study. Participants who withdrew between the one-month and one-year predictor analyses were from lower SES households ($t = 2.51$, $p = .014$). There were no differences in age, sex, epilepsy type, adherence trajectory group, or seizure trajectory group.

2.2. Measures

2.2.1. Demographic and medical characteristics

A demographics questionnaire that assessed child and parent race, sex, age, and SES was obtained at recruitment. Socioeconomic status was assessed with the Revised Duncan, an occupation-based measure ranging from 15 to 97, where higher scores reflect higher occupational attainment [17]. For two-parent households, the higher Duncan score was used. Medical chart review was used to collect epilepsy-related information (e.g., date of diagnosis, epilepsy type, syndrome status, prescribed AED). Previously established seizure trajectories demonstrating the probability of having seizures over a two-year period, including high (26% of participants) and low (74% of participants) [16], were used as the seizure outcome variable. These trajectories are consistent with the broader pediatric literature, which suggests that approximately 30% of children will have intractable seizures [18–20].

2.2.2. Side effects

Antiepileptic drug side effects were assessed with the 19-item Pediatric Epilepsy Side Effects Questionnaire (PESQ) [21] which consists of five subscales (i.e., cognitive, motor, behavioral, general neurological, weight). Each side effect was rated based on degree of severity on a 6-point Likert scale from "not present/not applicable or unable to assess" to "high severity". The PESQ has excellent internal consistency ($\alpha = .90$), test–retest reliability (.91), and construct validity [21].

2.2.3. Barriers to medication adherence

The Barriers subscale (8-items) of the Pediatric Epilepsy Medication Self-Management Questionnaire (PEMSQ) [9], was used to evaluate a parent's perception of factors that interfere with the child's treatment regimen (e.g., forgetting, disliking taste). Items were rated on a 5-point Likert scale from "strongly disagree" to "strongly agree". Internal consistency for the Barriers subscale was adequate ($\alpha = .59$).

2.2.4. Epilepsy knowledge

Knowledge about medical and social aspects of epilepsy was assessed using a modified version of the Epilepsy Knowledge Questionnaire (EKQ) [22]. Items were modified to be consistent with language and medical practice in the United States. The revised 47-item (true/false) version had a reliability coefficient of .58.

2.2.5. Parent functioning and stress

The Concerns and Fears subscale of the Parent Report of Psychosocial Care [23] consists of five items that assess parent concerns regarding whether the child's seizures will result in negative cognitive and health outcomes. Reliability for the current sample was good ($\alpha = .85$). The Family Stress Scale-Seizure Version (FSS-Seizure) [24] is a 14-item epilepsy-specific measure of parenting stress. Reponses were provided on a 5-point Likert scale, ranging from "not at all stressful" to "extremely stressful," with higher scores indicating greater perceived stress. Reliability for the current sample was good ($\alpha = .87$). The Parenting Stress Index (PSI) [25] is a well-established, evidence-based measure of the degree to which stress is related to parent functioning, the behavioral and temperamental qualities of the child, and the parent–child relationship [26].

2.2.6. Social stigma

Each parent's perception of stigma toward his/her child with epilepsy was measured with the Social Stigma Scale [27]. Responses were made on a 5-point Likert scale ranging from "strongly disagree" to "strongly agree", with higher scores indicating greater perceived stigma. Internal consistency for the current sample was .66.

2.2.7. Family functioning

The McMaster Family Assessment Device (FAD) [28] is a 60-item well-established measure of family functioning [26]. Based on a priori hypotheses, we examined the general functioning (overall functioning of family) scale, as well as the problem-solving (ability to resolve problems), communication (exchange of clear and direct verbal information), and behavior control (manner used to express and maintain standards of behavior) subscales. Internal consistencies were excellent for the general functioning scale ($\alpha = .95$) and acceptable for the subscales ($\alpha = .74$–$.77$).

2.2.8. Medication adherence

Adherence to AEDs was assessed on a daily basis with electronic monitors (i.e., MEMS™ TrackCap, Aardex, Sion, Switzerland). These continuous data were used to identify four long-term adherence trajectory groups over the course of two years using latent class growth modeling [16], which include: Severe Early Nonadherence (9%), Variable Nonadherence (15%), Moderate Nonadherence (37%), and High Adherence (39%). These trajectory groups capture patterns of adherence during the two years following epilepsy diagnosis.

2.3. Procedure

This study was approved by the hospital's Institutional Review Board. Written parental consent and verbal assent was obtained during

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