Parent and Family Well-Being and Associated Risk Factors as Children with Neonatal Seizures Reach Preschool and School-Age: A Longitudinal Cohort Study

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Objective To assess parent/family well-being when children with neonatal seizures reach 3-8 years of age and examine factors associated with parent/family well-being.

Methods One parent per surviving infant in the Neonatal Seizure Registry-II was invited to complete validated surveys annually when children were between 3 and 8 years of age. Three outcomes were examined: (1) parent well-being (anxiety, depression, and quality of life); (2) parent post-traumatic stress symptoms; and (3) impact on the family. We used mixed model regression with random intercepts and guided backward elimination and included potential predictors that had bivariate associations $P < .10$ in the multivariable analyses.

Results Among 169 parents, 8%-35% experienced symptoms of anxiety, depression, or post-traumatic stress. When children were 8 years of age, about 1 in 3 parents had moderate to severe anxiety symptoms, approximately double the general population, 1 in 5 had post-traumatic stress disorder symptoms and depression symptom frequency was similar to the general population in the final models, only child social communication impairment was associated with poorer parental well-being or post-traumatic stress symptoms. Several child factors, including age at discharge from the neonatal admission, functional impairment at 24 months, social communication impairment, and receiving special services, were associated with greater impact on the family.

Conclusions Child social and functional health challenges following neonatal seizures were associated with poorer parent and family well-being across the preschool and early school years. Longitudinal screening of child social functioning, parent well-being, and family function is indicated for early detection and referral to treatment services. *(J Pediatr 2025;16:200149)*.

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Acute provoked neonatal seizures due to brain injury are associated with a high risk of neurodevelopmental disability.[1] Parents of infants with neonatal seizures are at high risk of adverse outcomes, including poor psychological well-being, in the early months and years following their child's neonatal seizures. Anxiety and depression symptoms, in particular, are prevalent and impact parent and family well-being. In a multicenter prospective cohort of neonates with electroencephalogram-confirmed acute provoked seizures, we pre-

ADHD	Attention deficit hyperactivity disorder
ASD	Autism Spectrum Disorder
HADS	Hospital Anxiety and Depression Scale
IES	Impact of Events
IOF	Impact On Family
PTSD	Post-traumatic stress disorder
SRS-2	Social Responsiveness Scale-2
VABS-3	Vineland Adaptive Behavior Scale-3
WHOQOL-BREF	World Health Organization Quality of Life – Brief Assessment
WIDEA-FS	Warner Initial Developmental Evaluation of Adaptive and Functional Skills

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viously reported that about one-half of parents experience clinically significant anxiety and depression symptoms near the time of discharge from the neonatal hospitalization,[2] and these symptoms persisted for many parents when their child was 24 months of age.[3] Parents of children who experienced neonatal seizures worry about their child's long-term neurodevelopment, such as learning or other disabilities.[4] Long-term mental and physical health problems are common among parents of children with disabilities,[5] and poor parent psychological well-being may undermine family function and a parent's ability to care for a child with medical complexity or cope with uncertainty. However, there has been little research on parent and family well-being for children with neonatal seizures when the children reach preschool and school-age, it is unclear whether the mental and physical health problems are as common among these parents.

Given the strong influence of parent and family well-being on a child's mental health and development,[6] and the potential for stress on the family related to the child's ongoing health needs or uncertainty about the child's long-term prognosis,[7] further examination of parent and family well-being and associated risk factors as children reach school age is warranted. In this study, we aimed to describe parent and family well-being when children with neonatal seizures reach preschool and school age (3 to 8 years of age). We also aimed to generate new knowledge by exploring the relationships between a range of parent and child factors and parent and family well-being. We hypothesized that parent and child risk factors from the neonatal period, at 24 months of age, and contemporary factors are associated with the well-being of parents of children who survived acute provoked neonatal seizures when those children reach 3 to 8 years of age.

Methods

Design

We conducted this research as part of a larger study to examine the risk factors for developmental disabilities in early childhood in a cohort of children who survived acute provoked neonatal seizures as part of the Neonatal Seizure Registry- Developmental Functional Evaluation (NCT04337697). Longitudinal examination of the well-being of families was a pre-specified secondary aim of the study.

Setting and Sample

Families of children born from July 2015 to March 2018 with neonatal seizures were enrolled at one of nine academic medical centers. The study design, outcome measures, and analyses were informed by a parent advisory panel. Details of the initial cohort recruitment are published elsewhere.[8] Briefly, parents of surviving children without a diagnosis of a congenital or genetic condition known to affect development were eligible. We invited parents/guardians of all surviving children to participate. One parent or other legal guardian per family completed a suite of validated survey instruments annually for a maximum of four years (when children were between 3 to 8 years of age). Parents completed the surveys online or by telephone interview with a trained research assistant. The University of California, San Francisco acted as the central Institutional Review Board. Parental written informed consent was obtained prior to enrollment in the follow-up study.

Measures

Measures of parent and family well-being included well-validated scales. We assessed parental mental health symptoms using the Hospital Anxiety and Depression Scale (HADS)[9] and the Impact of Events (IES) post-traumatic stress symptom scale (revised).[10] We assessed family functioning using the Impact On Family (IOF) scale (revised).[11] We assessed parental quality of life using the World Health Organization Quality of Life – Brief Assessment (WHO-QOL-BREF) scale.[12]

Covariates included potential risk factors that were associated with parent and family well-being at discharge from the neonatal hospitalization and at 24 months corrected age.[2,3] Demographic covariates included caregiver parental role (self-identified as mother or father), highest level of maternal education, public or private health insurance for the child, child's race and ethnicity, family annual income, and receiving public benefits. Neonatal/infant covariates included age at discharge from the neonatal seizure admission, diagnosis of epilepsy or cerebral palsy, functional neurodevelopment as measured with the Warner Initial Developmental Evaluation of Adaptive and Functional Skills (WIDEA-FS),[13] and receiving developmental support services (eg, physical therapy, occupational therapy, or speech therapy) at 24 months corrected age. A child was considered to have functional impairment when their WIDEA-FS total score was more than two standard deviations below the mean for age. Postneonatal epilepsy was defined per International League Against Epilepsy criteria[14] and determined by parent report, corroborated by local study investigator systematic chart review.

Contemporary covariate potential risk factors were ascertained upon enrollment in the follow-up protocol or at the time of the annual follow-up. Because access to diagnostic evaluation is inconsistent, attention deficit hyperactivity disorder (ADHD) symptoms, Autism Spectrum Disorder (ASD) symptoms, and epilepsy diagnoses were based on parent report of diagnoses, electronic medical records, or developmental assessment scores (ADHD: Behavior assessment for children-3 hyperactivity t-score and/or Behavior assessment for children-3 attention problems t-score >60; ASD: Social Responsiveness Scale, 2nd edition [SRS-2] t-score >65[15]). Other contemporary covariates included receiving developmental support services (eg, occupational, physical, speech, vision, feeding, or applied behavioral analysis therapies), adaptive functioning using the composite scores on the Vineland Adaptive Behavior Scales, 3rd edition (VABS-3), parent/caregiver form,[16] and social communication using the SRS-2, which measures presence and severity of social impairment commonly associated with ASD.[17]

Data Analysis

To address issues with multiple tests and to improve interpretability in the final analyses, we conducted a factor analysis to reduce the number of outcomes. We first standardized each scale to have a mean of zero and SD of one (ie, z-scores) across all the time points. We used iterated principal factor analysis with varimax rotation, which identified three distinct factors. Each factor had loadings that were numerically similar, so we explored whether a simple average of the standardized scales contributing to each factor would perform as well as using the factor loadings. They did, with the average scores having a correlation of 0.998 or higher with their respective factors. We therefore used the average summary scales as the outcome variables in subsequent analyses. Since they are averages of standardized scales, these factors can also be interpreted as a z-score to enhance interpretability, ie, they have a mean of approximately zero and a value of 1, for example, indicating a value that is one SD above average.

These three summary scales were then analyzed using mixed model regression with random intercepts for each child to accommodate the repeated measures. For each scale, the base model was adjusted for time point, site, and caregiver role. We then screened potential predictors related to the child's clinical condition that were found to be significant in previous studies and/or hypothesized to be the most significant (see Table 1): Age in days at discharge from hospital; diagnosed with epilepsy at 24 months; impaired functional development, defined as WIDEA-FS worse than 2 SD below the typically-developing population mean at 24 months; receiving developmental support services at 24 months; receiving developmental support services concurrently; concurrent VABS-3 Adaptive Behavior Scale standard score; SRS-2 t-score at enrollment in the current study. We used the base model and retained any covariate that achieved $P < .10$. Predictors surviving the screen were entered in a multivariable model, and we used guided backward elimination to remove nonsignificant terms, stopping when the first term in the guided elimination had $P < .05$. The order for the guided elimination of the screened-in variables was based on our previous findings of association with parent well-being and temporality (ie, baseline factors, then contemporary factors). The results of the final models are reported in the tables. Residual plots affirmed the assumption of linearity of numeric predictors. Numeric predictors were mean-centered and scaled to help with interpretation. As an exploratory analysis, we redid the screening phase and multivariate model-building using all potential risk factors from Table 1. All analyses were conducted with SAS 9.4 (SAS Software).

Results

Sample Characteristics

Of the 303 children and their families enrolled in the cohort with data from the neonatal admission,[2] 270 had data at the

Table 1. Demographic and Clinical Characteristics of 169 Children who Survived Acute Symptomatic Neonatal Seizures

Parent and child demographic characteristics at enrollment	
Public/private health insurance, n (%)	
Public	50 (30%)
Private	113 (67%)
Unknown/declined/missing	6 (3%)
Identified as mother	150 (89%)
Maternal education, n (%)	
Greater than high school	149 (88%)
High school or less	18 (11%)
Decline/missing	2 (1%)
Total household income, n (%)	
Less than $25,000	18 (11%)
$25,000 to < $50,000	20 (12%)
$50,000 to <$100,000	34 (20%)
$100,000 to <$200,000	42 (25%)
$200,000 or more	37 (22%)
Missing/prefer not to say	18 (11%)
Enrolled in government support programs, n (%)	32 (19%)
Child race/ethnicity, n (%)	
Hispanic, any race	19 (11%)
Asian, non- Hispanic	11 (7%)
Black/African American, non-Hispanic	16 (9%)
Other, non-Hispanic*	4 (2%)
White, non-Hispanic	113 (67%)
Unknown	6 (4%)
Neonatal/infant clinical characteristics	
Age in days at discharge from neonatal hospital admission, median (IQR); range	13 (9, 26); 5 - 210
Epilepsy diagnosis at 24 months, n (%)	20 (12%)
Cerebral palsy diagnosis at 24 months, n (%)	47 (28%)
WIDEA-FS less than 2 SD from mean at 24 months, n (%)	52 (31%)
Child receiving developmental support services at 24 months, n (%)	105 (62%)
Child Characteristics at enrollment in the present study (ages 3 to 5.5 years)	
Age, median years (IQR)	4.3 (3.6, 5.4)
Symptoms of ADHD, n (%)	43 (25%)
Symptoms of ASD, n (%)	24 (14%)
Epilepsy diagnosis, n (%)	23 (14%)
Any developmental support services, n (%)	81 (48%)
Occupational therapy, n (%)	53 (31%)
Physical therapy, n (%)	50 (30%)
Speech therapy, n (%)	62 (37%)
Vision therapy, n (%)	15 (9%)
Feeding therapy	11 (7%)
Applied behavioral analysis, n (%)	5 (3%)
School placement, n (%)	
Not in school	44 (26%)
Home schooled	7 (4%)
Functioning normally in a mainstream classroom without special assistance	65 (38%)
Needs special assistance or part time assistance, but is always in a mainstream classroom	32 (19%)
Part time special education classroom	7 (4%)
Full time special education or full-time 1:1 aide in mainstream class	10 (6%)
VABS-3 scale standard score, mean (SD); range; levels	90 (18); 42 - 129
Average: 86+	97 (57%)
Below average: 71-85	31 (18%)
Low: 70 and below	23 (14%)
SRS-2 t-score, mean (SD); range	51 (11); 35 - 87
Not elevated	124 (73%)
Elevated	20 (12%)

IQR, interquartile range; *SD*, standard deviation.
*Other non-Hispanic includes American Indian, Alaskan Native, more than one race and other.

24-month corrected age time point,[3] and 169 caregivers (56% of the initial cohort) completed surveys when their children were between 3 and 8 years of age. There were no differences in demographic, neonatal, or 24-month characteristics between the larger cohort and the families who participated in the 3 to 8-year surveys (See **Supplementary Table 1**). Demographic characteristics of the parents and children and clinical and developmental characteristics of the children at neonatal discharge, 24 months and at enrollment in the present study are shown in **Table 1**.

At enrollment in the present study, the median age of the children was 4.3 years (interquartile range: 3.6, 5.4) and 14% (n = 23) had a diagnosis of epilepsy; 25% (n = 43) had symptoms of ADHD, and 14% (n = 24) had symptoms of ASD. Almost one- half (48%; n = 81) were receiving developmental support services and over one- half of the children were in mainstream classrooms (57%; n = 97).

Parent and Family Well-Being During Preschool and Early School Years

Table 2 provides the mean results for the 6 parent well-being outcome measures total scores and subscales measured when the children were between 3 and 8 years of age. The proportion of parents with borderline or abnormal levels of depression symptoms ranged from 23% at the 3-year assessment to 8% at the 8-year assessment, and the proportion of parents with borderline or abnormal levels of anxiety symptoms ranged from 45% at the 3-year assessment to 34% at the 8-year assessment. Parental health-related quality of life was generally in the top quartile. The proportion of parents with symptoms suggestive or probable for post-traumatic stress disorder (PTSD) ranged from 26% at the 3-year assessment to 18% at the 8-year assessment. The IOF scores were at or below the scale midpoint, varying less than 4 points over the years with wide standard deviations.

Derived Summary Outcomes

Using factor analysis, we assessed the individual outcome scales to derive three, summary scales: (1) Parents' current well-being, comprised of: WHOQOL-BREF: Psychological score, WHOQOL-BREF: Physical Health score, WHOQOL-BREF Overall score, WHOQOL-BREF: Environment score, WHOQOL-BREF: Social Relationships score, HADS: Anxiety score, HADS: Depression score; (2) PTSD symptoms, comprised of: IES: total score, IES: intrusion subscore, IES: hyperarousal subscore, IES: avoidance subscore; and (3) Impact on the family system, comprised of: IOF: overall score and IOF: financial subscale. The IOF: coping subscale did not load onto any factor and was excluded. All scales were converted to z-scores and directionality aligned so that higher scores indicate worse outcomes and factor scores were calculated as the mean of the z-scores. See **Table 3** for details.

Factors Associated with Parent Well-Being and PTSD Symptoms at Preschool or Early School-Age

Of the potential covariates assessed, five met the threshold for inclusion in the multivariable model of parent well-being: Impaired functional development at 24 months; developmental support services at 24 months; developmental support services currently, the VABS-3 score, and SRS-2 score. Three met the threshold for inclusion in the multivariate model of PTSD: impaired functional development at 24 months; epilepsy diagnosed by 24 months; and SRS-2 score. Adjusting for time-point, study site, and which parent provided the response, only the SRS-2 score was associated with parental well-being and PTSD in the final multivariate models after guided backward elimination. The exploratory

Table 2. Parent and Family Well-Being During Preschool and Early School-Age Years

	Time-point				
Outcome	**3 year n = 43**	**4 year n = 102**	**5 year n = 125**	**7 year n = 78**	**8 year n = 51**
Factor 1					
HADS-D borderline abnormal (8-10)*	6 (14%)	8 (8%)	7 (6%)	7 (9%)	3 (6%)
HADS-D abnormal (>10) *	4 (9%)	3 (3%)	5 (4%)	1 (1%)	1 (2%)
HADS-A borderline abnormal (8-10) *	8 (19%)	22 (22%)	18 (14%)	18 (23%)	11 (22%)
HADS-A abnormal (>10)*	11 (26%)	16 (16%)	18 (14%)	5 (6%)	6 (12%)
WHOQOL-BREF overall (0-100 transformed scale; higher scores indicate better QOL) †	76.2 (22.6)	76.0 (21.4)	79.5 (18.0)	79.7 (17.8)	78.4 (18.4)
Physical†	71.4 (18.7)	76.4 (16.4)	76.8 (16.3)	78.5 (13.0)	77.3 (13.6)
Psychological†	65.6 (18.6)	68.7 (15.7)	69.4 (17.7)	69.6 (14.2)	72.0 (15.7)
Social†	64.7 (22.8)	67.3 (20.3)	68.0 (20.1)	65.9 (18.0)	67.0 (19.0)
Environment†	74.5 (15.4)	77.3 (15.5)	77.2 (14.4)	78.2 (13.5)	79.5 (13.2)
IES suggestive of PTSD (24-32)*	3 (7%)	12 (12%)	13 (10%)	6 (8%)	6 (12%)
IES probable PTSD (>33)*	8 (19%)	9 (9%)	13 (10%)	8 (10%)	3 (6%)
IOF overall (15-60; higher scores indicate greater impact)†	29.3 (11.9)	27.5 (11.5)	27.0 (11.2)	25.1 (10.5)	25.5 (10.6)
IOF financial†	8.5 (3.5)	7.9 (3.5)	8.3 (3.7)	7.7 (3.7)	8.0 (3.6)
IOF coping†	8.7 (2.3)	9.0 (2.4)	9.1 (2.6)	9.6 (2.4)	9.4 (2.5)

m, months.
*n (%).
†Mean (SD).

Table 3. Factor Analysis* to Create Outcome Scales

Varimax rotation pattern (3 factors)

Outcome	Factor 1 (accounts for 45% of variance)	Factor 2 (accounts for 14% of variance)	Factor 3 (accounts for 10% of variance)
Transformed WHOQOL-BREF: Psychological score	0.86589	0.11899	0.12264
Transformed WHOQOL-BREF: Physical health score	0.76864	0.12654	0.21944
Transformed WHOQOL-BREF General score	0.74803	0.14000	0.23184
HADS: Depression score	0.70566	0.24503	0.15820
Transformed WHOQOL-BREF: Environment score	0.65809	0.20043	0.24638
Transformed WHOQOL-BREF: Social relationships score	0.65705	0.08183	0.17796
HADS: Anxiety score	0.57113	0.31465	0.22661
IES: Intrusion subscore	0.18765	0.93776	0.14178
IES: Hyperarousal subscore	0.20145	0.85416	0.14409
IES: Avoidance subscore	0.12997	0.69084	0.09890
IOF: Financial subscale	0.17306	0.16165	0.92192
IOF: Overall score	0.32949	0.24396	0.77464
IOF: Coping subscale	0.27277	0.04009	−0.12340

*Factor analysis performed with data from 3, 4, 5, 7, and 8 years together; Scores were mean-centered by age before factor analysis.

analysis, which included all possible risk factors, rather than the preselected subset, found identical results to the primary analysis, except for a finding of a significant association between child race/ethnicity and parental PTSD. Compared with parents of white non-Hispanic children, those of black non-Hispanic children and other races reported more symptoms of PTSD (β = 0.72 (95%CI 0.19 – 1.26) and β = 2.18 (95%CI 0.30 – 4.06), full results not shown).

Factors Associated with Impact on the Family at Preschool or Early School-Age

Of the covariates assessed, seven met the threshold for inclusion in the multivariable model: Age in days at neonatal hospital discharge, epilepsy diagnosed by 24 months; impaired functional development at 24 months; developmental support services at 24 months; developmental support services currently, VABS score, and SRS-2 score. There were several covariates associated with the impact on the family after guided backward elimination, including age at neonatal hospital discharge that was associated with both the higher level of impact as well as its trend over time. Other covariates that were associated with the impact on the family system were impaired functional development, child receiving special services currently, and SRS-2 scores. (See Table 4 and Figure).

Discussion

Data on parents' long-term psychosocial well-being and family functioning for families of children who experienced neonatal seizures beyond 24 months of age are lacking. Compared with data from our same cohort when the children were 24 months of age,[3] the proportion of parents with high levels of anxiety, depression and PTSD peaked at 3 years of age and then trended down over time. We found that when children reached 8 years of age, almost one-third of parents

Table 4. Factors Associated with Parent and Family Well-Being

Covariate	Parent well-being model	Beta estimate (95% CI) Parent PTSD model	Beta estimate (95% CI) Impact on families model
Length of stay			−0.04 (−0.09 - 0.01)
LOS*timepoint interaction			
3 years	-reference-	-reference-	-reference-
4 years			0.07 (0.02 - 0.12)†
5.5 years			0.06 (0.01 - 0.12)*
7 years			0.05 (−0.01 - 0.10)‡
8 years			0.06 (−0.01 - 0.13)
Epilepsy diagnosed by 24 months		0.39 (−0.17 - 0.94)	0.33 (−0.11 - 0.76)
WIDEA impaired at 24 months	.05 (−0.27 - 0.38)	0.02 (−0.36 - 0.41)	0.47 (0.13 - 0.80)†
Developmental support services at 24 months	.13 (−0.14 - 0.41)		0.18 (−0.08 - 0.45)
Developmental support services currently			0.27 (0.10 - 0.44)†
VABS-3 currently, increase of 10 points	−0.01 (−0.08 - 0.06)		0.04 (−0.02 - 0.11)
SRS-2 at enrollment, increase of 10 points	0.22 (0.09 - 0.35)†	0.16 (0.02 - 0.31)*	0.30 (0.17 - 0.42)†

CI, confidence interval; *LOS*, length of stay.
*$P < .05$.
†$P < .01$.
‡$P < .10$.

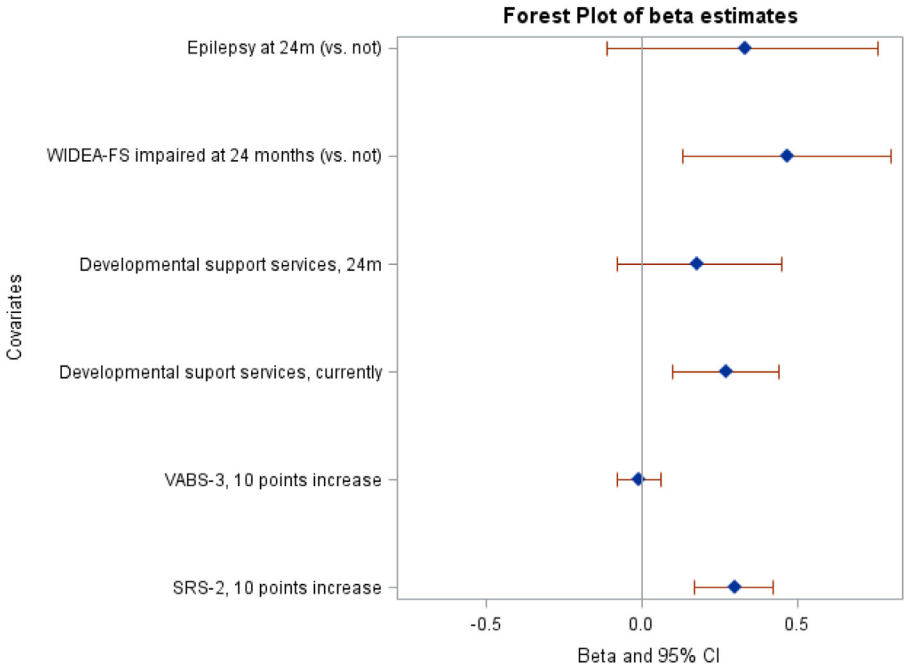

Figure. Factors associated with impact on the family. *m*, months.

were experiencing symptoms of anxiety and nearly 1 in 5 were experiencing symptoms of PTSD. Despite the downward trends, the proportion of parents of children with neonatal seizures experiencing moderate to severe anxiety was approximately double that of the general population[18] and approximately triple that of the civilian population,[19] although similar to the general population for depression.[18] Our findings affirm existing data that major childhood illness increases the risk of adverse caregiver mental and physical health symptoms, including anxiety, depression, and PTSD.[20–22] These findings clearly indicate the need for early and ongoing routine screening to identify families who need further assessment and supportive services.[23]

Among the demographic and clinical factors we examined, only the preschool or school-aged child's social communication functioning was associated with all parental well-being (including anxiety, depression, and health-related quality of life) measures, PTSD symptoms, and family functioning. Our findings differ from a study of school-aged children who had experienced perinatal stroke that found that severity of the child's impairment as well as parental emotional distress were associated with parental depression.[24] Although our findings of association between racial identity and parental PTSD symptoms should also be interpreted with caution as they arose from an exploratory analysis. It is consistent with our prior findings from this same cohort at 24 months of age, and another other study that found higher rates of PTSD for African American and Latinx adults[25] suggesting further research is needed to confirm our findings and examine the social determinants of health, risk, and protective factors for mental health for socially-constructed racial and ethnic groups in the U.S.[26]

While it was beyond the scope of this investigation to explore the causal mechanisms of associations between child clinical and behavioral characteristics and parent and family well-being, qualitative data from our cohort[27] and that of others[28] suggest the importance of addressing the challenges of managing children's behavior and social engagement and the uncertainty of the child's long-term prognosis and developmental capabilities, as each of these factors is known to cause considerable stress for parents and the family as a whole.[27,28] Moreover, our findings suggest that studies of long-term outcomes in neonatal neurologic conditions should include attention to a child's social functioning in addition to the more traditionally measured motor and cognitive outcomes. This is especially salient since the child's social responsiveness challenges may not meet the threshold for an ASD diagnosis yet still have a significant negative impact on parental well-being and family functioning. Poor parent and family function may in turn increase the risk for the child to experience adverse health and developmental outcomes.

We found that family functioning was also associated with the length of the neonatal hospitalization, impaired functional development at 24 months corrected age and receiving developmental supportive services during the preschool or early school-age years. This further emphasizes the need for longitudinal screening of parental well-being and family function during the toddler, preschool, and school-age years to facilitate early detection and referral to treatment. Families who experienced long neonatal stays or with children who have significant functional impairment at 24 months should receive anticipatory guidance and appropriate psychological support

services. While the primary aim of this study was not designed to assess the frequency of parent well-being screening, the relatively high rates of symptoms of poor well-being across all time points suggest that at least annual screening may be necessary to identify parents with clinically meaningful symptoms of anxiety, depression, and PTSD. Effective interventions to promote the mental health of parents of children with a range of chronic, uncertain, or life-limiting conditions include peer-to-peer support and should be offered to families of children with neonatal seizures.[29] Finally, the work of caregiving for children with complex health care needs by parents and family members must be acknowledged and supported through programming to address loss of income, and coverage to address the additional costs of the child's health care and special education, preventative mental and physical health care access, respite care, and supportive services for siblings.[30,31]

Several study limitations and strengths should be considered to provide context for our findings. First, there are several demographic characteristics of the cohort that limit the generalizability of our findings. Children were receiving follow-up care from large tertiary urban medical centers and, therefore, the sample may not be representative of all families of children with neonatal seizures. The cohort was comprised mostly of mothers, had a relatively high level of education, private insurance, and family income, and self-identified as white and the findings may not be generalizable to other groups. Although we included a broad range of medical and sociodemographic predictors, other unmeasured characteristics, such as additional measures of socioeconomic status or caregiver coping style, may also influence parental well-being and impact on the family. For example, one recent study of parents of children with drug-resistant epilepsy at two years of age found that family financial resources were associated with stable or lesser parental anxiety and depression.[32] As is typical with longitudinal follow-up studies, there was attrition in the cohort over time, which also affects the generalizability of the findings. Given that recruitment for this study occurred during the COVID-19 pandemic, more robust retention was not feasible. Finally, we did not measure family access to or uptake of mental health or other developmental support services, and these unmeasured interventions may have influenced the findings. Strengths of the study include the large, geographically diverse sample, the longitudinal design, and the multivariate analyses that enabled simultaneous consideration of multiple predictors, outcomes, and interactions.

In summary, we found that parents of infants with neonatal seizures experienced persistent mental health symptoms during their child's preschool and school-age years, and child social and functional health challenges following neonatal seizures were associated with poorer parent and family well-being in the early school years. Longitudinal screening of parental well-being and family function during the preschool and early school years is indicated for early detection and referral to treatment services. ■

CRediT authorship contribution statement

Linda S. Franck: Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. **Monica E. Lemmon:** Writing – review & editing, Methodology, Investigation, Data curation. **Lisa Grossbauer:** Writing – review & editing, Methodology, Conceptualization. **Kamil Pawlowski:** Writing – review & editing, Methodology, Conceptualization. **Julie S. Sturza:** Writing – review & editing, Visualization, Methodology, Formal analysis, Data curation. **Courtney J. Wusthoff:** Writing – review & editing, Investigation, Data curation, Conceptualization. **Shavonne L. Massey:** Writing – review & editing, Investigation, Data curation, Conceptualization. **Catherine J. Chu:** Writing – review & editing, Investigation, Conceptualization. **Janet S. Soul:** Writing – review & editing, Investigation, Data curation. **Adam L. Numis:** Writing – review & editing, Investigation, Conceptualization. **Cameron Thomas:** Writing – review & editing, Investigation, Data curation. **Giulia M. Benedetti:** Writing – review & editing, Investigation, Data curation. **Tayyba Anwar:** Writing – review & editing, Investigation, Data curation. **Madison M. Berl:** Writing – review & editing, Investigation, Data curation. **Jennifer C. Gidley Larson:** Writing – review & editing, Investigation, Data curation. **Elizabeth E. Rogers:** Writing – review & editing, Investigation, Data curation. **Carmen Chen:** Writing – review & editing, Investigation, Data curation. **Charles E. McCulloch:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Hannah C. Glass:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition, Conceptualization. **Renée A. Shellhaas:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Funding acquisition, Conceptualization.

Declaration of Competing Interest

H.C.G. has shares in Elemeno Health; they report financial support was provided by National Institutes of Health. R.A.S. receives a stipend for her role as President of the Pediatric Epilepsy Research Foundation, serves as a consultant for the Epilepsy Study Consortium, and receives royalties from UpToDate for authorship of topics related to neonatal seizures. C.J.W. receives an honorarium as an associate editor for Neurology. The remaining authors have no conflicts of interest relevant to this article to disclose.

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