2-1-2011

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Epilepsia, 52(2):316–325, 2011
doi: 10.1111/j.1528-1167.2010.02769.x

FULL-LENGTH ORIGINAL RESEARCH

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

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Summary

Purpose: To examine the impact of maternal depressive symptoms (DS) on health-related quality of life (HRQL) in children with new-onset epilepsy and to identify family factors that moderate and mediate this relationship during the first 24 months after epilepsy diagnosis.

Methods: A sample of 339 mother–child dyads recruited from pediatric neurologists across Canada in the Health-related Quality of Life in Children with Epilepsy Study. Mothers' and neurologists' reports were collected at four times during the 24-month follow-up. Mothers' DS were measured using the Center for Epidemiological Studies Depression Scale (CES-D) and children's HRQL using the Quality of Life in Childhood Epilepsy (QOLCE). Data were modeled using individual growth curve modeling.

Key Findings: Maternal DS were observed to have a negative impact on QOLCE scores at 24 months ($\beta = -0.47$, $p < 0.0001$) and the rate of change in QOLCE scores during follow-up ($\beta = -0.04$, $p = 0.0250$). This relationship was moderated by family resources ($\beta = 0.25$, $p = 0.0243$), and the magnitude of moderation varied over time ($\beta = 0.09$, $p = 0.0212$). Family functioning and demands partially mediated the impact of maternal DS on child HRQL ($\beta = -0.07$, $p = 0.0007$; $\beta = -0.12$, $p = 0.0006$).

Significance: Maternal DS negatively impact child HRQL in new-onset epilepsy during the first 24 months after diagnosis. This relationship is moderated by family resources and mediated by family functioning and demands. By adopting family centered approaches, health care professionals may be able to intervene at the maternal or family level to promote more positive outcomes in children.

KEY WORDS: Depression, Family demands, Family functioning, Family resources, Growth curve modeling, Patient-centered care.

Maternal depressive symptoms (DS) have been linked to a host of child health outcomes. Most commonly, children of mothers with depression are at a significantly higher risk for depression and behavior problems as compared to children of mothers without depression (Weissman et al., 2006; Campbell et al., 2009). In childhood epilepsy, few studies have specifically focused on the impact of maternal DS on child health outcomes. Early work by Hoare (1984) and Hoare and Kerley (1991) demonstrated that psychiatric disturbances in mothers were associated with psychiatric problems in children. These results were verified by more recent work by Adewuya and Ola (2005), which showed that psychiatric morbidity in parents was significantly associated with anxiety and depression in adolescents with epilepsy. Two studies have examined the impact of maternal DS on behavior problems in children with epilepsy and found a positive association between maternal DS and child behavior problems (Rodenburg et al., 2006; Yong et al., 2006). Three studies have assessed the impact of maternal DS on child health-related quality of life (HRQL) and have revealed some support for a negative impact of maternal DS on overall HRQL in children with epilepsy (Adewuya, 2006; Yong et al., 2006; Wood et al., 2008).

Our recent systematic review found that previous studies examining the impact of maternal DS on child outcomes in epilepsy suggested a need for more methodologically robust research (Ferro & Speechley, 2009). Although studies generally reported a negative association between maternal DS and child outcomes, several limitations in study design—including a lack of prospective cohort studies, inclusion of nonrepresentative samples, and sampling

Accepted September 10, 2010; Early View publication November 3, 2010.

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procedures prone to selection bias—make it difficult to reach definitive conclusions. Therefore, there is a need to prospectively assess how maternal DS may impact HRQL in children newly diagnosed with epilepsy.

The objectives of this research were to examine the impact of maternal DS on HRQL in children with new-onset epilepsy and to identify family factors that moderate and mediate this relationship during the first 24 months after epilepsy diagnosis. Given that previous work in this population has shown that, on average, child HRQL improves during the first 24 months after diagnosis (Speechley et al., 2009), it was hypothesized that DS in mothers would negatively impact children's HRQL, such that children of mothers with elevated levels of DS would have poorer HRQL and less favorable rate of change during the 24-month follow-up. In addition, it was hypothesized that the negative impact of maternal DS on child HRQL would be moderated by family resources and maternal perception of the health care received by the child. Finally, it was hypothesized that this relationship would be mediated by family functioning and family demands such that elevated levels of DS would lead to worse family functioning and more family demands, resulting in poorer child HRQL during follow-up.

Methods

Sample and data source

Data for this study came from the Health-related Quality of Life in Children with Epilepsy Study (HERQULES), a prospective cohort study designed to examine the determinants of HRQL in children with epilepsy during the first 24 months postdiagnosis. Participants were recruited primarily from pediatric tertiary-care neurology practices across Canada, with a minority recruited from community-based pediatric neurology practices. The inclusion criteria for patients were as follows: (1) new case of epilepsy (≥2 unprovoked seizures), in whom diagnosis of epilepsy has not been previously confirmed, seen for the first time by a participating pediatric neurologist within the data-collection period; (2) epilepsy diagnosed between the ages of 4 and 12 years; and (3) parent must have been primarily responsible for the child's care for ≥6 months and continue to be for the duration of the study. Children with newly diagnosed epilepsy with a prior history of neonatal seizures were included if medication was removed by 6 weeks of age without recurrence. Patients were excluded from the study if: (1) diagnosis of epilepsy had been previously confirmed by another physician; (2) diagnosed with other progressive or degenerative neurologic disorder (e.g., mental retardation); (3) diagnosed with other major comorbid nonneurologic disorders that would have an impact on quality of life (e.g., asthma requiring daily medication, renal failure); and (4) parent had insufficient English language skills to complete questionnaires.

In the absence of population-based registries for epilepsy to facilitate such studies, Speechley et al. (1999) demonstrated that it may be feasible to recruit a representative population-based sample of children with epilepsy by targeting pediatric neurologists. In this study, family physicians practicing in southwestern Ontario reported they would refer between 80% and 99% of their patients with childhood epilepsy (depending on the type of seizure and syndrome) to a pediatric neurologist. Primary caregivers were contacted by telephone to determine participation status and mailed questionnaires for self-administration after diagnosis (baseline), and at 6, 12, and 24 months. A modified version of the Tailored Design Method was used to develop a structured follow-up strategy to enhance retention rates (Dillman, 2007). Of the 456 eligible families approached to participate, 447 (98.0%) verbally consented. Of these, 374 (83.7%) completed the baseline survey. For this analysis, only surveys completed by a child's mother (i.e., biologic, adoptive, foster) were retained and used in the analysis 339 (91.0%). Approval for HERQULES was obtained from all relevant research ethics boards across the country, and parents provided written consent.

Measures

Child HRQL

Child HRQL was reported by mothers using the Quality of Life in Childhood Epilepsy (QOLCE) (Sabaz et al., 2003). The QOLCE is a multifaceted, parent-report, epilepsy-specific instrument for evaluating HRQL of children with epilepsy aged 4–18 years. The QOLCE contains 76 items with 16 subscales spanning seven domains of life function including physical activities, social activities, cognition, well-being, behavior, general health, and general quality of life (Sabaz et al., 2003). Items are rated on a five-point Likert scale, which is used to calculate the 16 subscale scores ranging from zero (low functioning) to 100 (high functioning). The subscale scores are averaged to produce an overall HRQL score. The QOLCE has demonstrated good construct validity, internal consistency reliability, and sensitivity to epilepsy severity (Sabaz et al., 2000). The internal consistency reliabilities were excellent for all measurement occasions in this sample (0.92–0.94).

Epilepsy characteristics

Neurologists completed a questionnaire documenting the clinical factors of each child's epilepsy, including severity of epilepsy, seizure type and frequency, type of epilepsy syndrome, age at onset and diagnosis, medication information, and adverse effects. Neurologists were also asked to rate the presence of comorbidities using single-item measures, specifically, any behavior (0 = none to 3 = severe), cognitive (0 = none to 4 = severe), or motor problems (0 = none to 3 = severe). Severity of epilepsy was classified using the Global Assessment of Severity of Epilepsy

(GASE), a single-item measure developed for HERQULES (Speechley et al., 2008). Using the GASE, neurologists rate the overall severity of each child's epilepsy using a seven-point scale ranging from 1 = extremely severe to 7 = not at all severe. The GASE has demonstrated minimum burden on participants; adequate content, convergent, and construct validity; and high intrarater and interrater reliability (Speechley et al., 2008).

Maternal depressive symptoms

Level of DS in mothers was measured with the Center for Epidemiological Studies Depression Scale (CES-D), a 20-item questionnaire designed to assess depressive symptoms over the past week (Radloff, 1977). The scale includes 20 items that survey mood, somatic complaints, interactions with others, and motor functioning. A four-point Likert scale (0–3) is used to rate the frequency of symptoms experienced. The total score spans from 0–60, with a higher score indicating greater impairment. Individuals with a total score of ≥16 are typically identified as being at risk for clinical depression. In this sample, internal consistency estimates were good, ranging from 0.75–0.80.

Family environment

Three aspects of the family environment (functioning, resources, and demands) were measured based on parent report. The Family Adaptability, Partnership, Growth, Affection, and Resolve (Family APGAR) was used to assess satisfaction with family relationships (Smilkstein, 1978). The Family APGAR is a five-item instrument in which responses are based on a five-point Likert scale, ranging from 0–4 for each item. Higher scores indicate higher satisfaction with family functioning. The Family APGAR has been found to be valid and reliable in both the clinical and research settings with adults and children (Smilkstein, 1978; Smilkstein et al., 1982; Austin & Huberty, 1989). The internal consistency reliabilities in this sample were very good, with Cronbach's α ranging from 0.86–0.89.

The Family Inventory of Resources for Management (FIRM) was utilized to assess resources available to aid families' adaptation to stressful events (McCubbin et al., 1996a). For this study, only two subscales (family mastery and health, extended family social support), which have been found to be associated with adaptation to childhood epilepsy, were used (Austin et al., 1992). Scoring procedures for the FIRM involve summing all response values, which range from 0 (not at all) to 3 (very well), to provide a total FIRM score. The FIRM has demonstrated adequate reliability and validity properties (McCubbin et al., 1996a). Internal consistency reliabilities in this sample ranged from 0.91–0.93 for the Family Mastery and Health subscale and 0.44–0.54 for the Extended Family Social Support subscale.

Family demands were quantified using the Family Inventory of Life Events and Changes (FILE), which assesses the pile-up of simultaneous normal and nonnormal life events and changes in life events experienced by a family during the previous year (McCubbin et al., 1996b). There are 71 items in the FILE, with the score computed by giving each ''yes'' response a score of one. Summing responses provides a score for each subscale and the total pile-up score. The reliability and validity of the FILE are well-established (McCubbin et al., 1996b). As measured by Cronbach's α, the overall reliability of the FILE was excellent, ranging from 0.98–0.99 in this sample.

Sociodemographic information was also collected including date of birth (mother and child), child gender, number of children in household, parents' marital and employment status, highest level of completed education, and total annual household income.

Perception of patient-centered care

Based on the Patient-Centered Model of Care, a modified version of the Patient Perception of Patient-centeredness (PPPC) was used to assess mothers' perceptions of the extent to which the health care services their child received were patient-centered (Stewart et al., 2004). Seven of the original 14 items were modified slightly to make them appropriate for parent-report by replacing ''your'' with ''your child's'' and ''you'' with ''your child.'' The PPPC is scored so that low scores correspond to positive perceptions. Interitem reliability has been found to be adequate for the PPPC, and validity was established through a significant correlation with the Measure of Patient-centered Communication (Stewart et al., 2000). In this sample, the internal consistencies were good, ranging from 0.77–0.86.

Statistical analysis

Univariate analyses used to describe maternal DS at baseline included descriptive statistics and frequency distributions. Individual growth curve modeling was used to examine the impact of maternal DS on child HRQL during the 24-month follow-up (Singer & Willett, 2003). A moderation analysis, testing whether family resources or perception of patient-centered care modified the effect of DS on child HRQL was assessed by sequentially examining growth curve models with each potential moderator. The product of coefficients method was used to examine whether family functioning or family demands exist as a mediating variable in the pathway between maternal depressive symptoms and child HRQL as illustrated in Fig. 1 (MacKinnon et al., 2002). Additional details about the statistical analysis are described in the Appendix. Data analysis was conducted with Statistical Analysis Software (SAS, Windows build 9.1.3 Service Pack 4; SAS Institute Inc., Cary, NC, U.S.A.). All hypothesis tests were two-sided with $\alpha = 0.05$.

Missing data

Handling of missing data for children's HRQL followed the strategy described by Wirrell et al. (2005). Briefly, if <20% of subscores in the QOLCE were missing, the child's

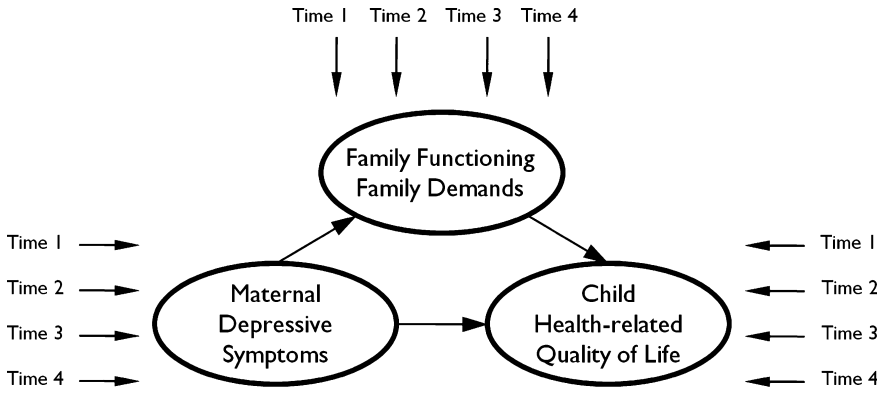

Figure 1.
Hypothesis of the mediational relationship between maternal DS and child HRQL. The illustration represents a dynamic model that incorporates prospective measurements on each variable during the 24-month follow-up.
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HRQL score was calculated by determining the mean for the other subscales, and applying that mean value for the missing subscale(s). If ≥20% of subscales were missing, that participant was excluded from analysis. The number of participants for whom missing data prevented calculation of a QOLCE score was not systematic over the 24-month follow-up (n = 28, n = 28, n = 24, and n = 15 for baseline, 6, 12, and 24 months, respectively). Because of the extensive use of covariates in the models examined in this study, it was assumed that the probability of ''missingness'' was not dependent on any unobserved data and thus, the data did not violate the requirements for data that are missing at random. This is a required assumption for growth curve modeling using PROC MIXED. Participants with at least one measurement occasion were included in the analysis.

Results

Sample characteristics

A total of 339 mothers were included in the study. Mothers had a mean age of 37.7 years (standard deviation 5.8) years at baseline. Approximately half of the children were male (52.2%). Children had a mean age of seizure onset of 6.9 (2.5) years and a mean age of 7.4 (2.4) years at baseline. Children had a mean score of 70.4 (13.4) on the QOLCE and the majority of children (58.7%) had ''a little severe'' or ''somewhat severe'' epilepsy using the GASE score. Mean scores on family environment measures were as follows: Family APGAR 14.0 (3.8); FIRM 50.1 (11.1); and FILE 9.6 (6.5), indicating that families were functioning well, had adequate resources, and had relatively few demands on them. Additional baseline and 24-month characteristics of the study sample are shown in Table 1. At baseline, 38% of mothers scored above the cut-point for risk of depression (i.e., CES-D ≥16). This proportion decreased to 30% at 24 months.

Impact of maternal depressive symptoms on child HRQL

Growth curve models for changes in child HRQL over time are shown in Table 2. Potential confounders were tested a priori to fitting the growth curve models and none met the criterion for inclusion; therefore, unadjusted models are presented. There was significant improvement in model fit between each step in the modeling strategy ($\chi^2 = 86.3$, d.f. = 2, $p < 0.0001$; $\chi^2 = 114.5$, d.f. = 1, $p < 0.0001$). In the first model, a mean score of 73.1 on the QOLCE was observed for the unconditional means model, which assumes static HRQL over time. The unconditional growth curve model, which includes a linear function of time, shows that QOLCE scores increase significantly during the 24-month follow-up ($\beta = 1.17$, $p < 0.0001$). The final model includes mothers' CES-D scores in predicting child QOLCE scores over time. Maternal DS were observed to have a negative impact on both QOLCE scores at 24 months ($\beta = -0.47$, $p < 0.0001$) and on the rate of change in QOLCE scores during follow-up ($\beta = -0.04$, $p < 0.0250$).

Results from each model suggest a need for additional time-varying and time-invariant predictors of child HRQL, given by the significant amount of residual variation in the intra- and interindividual components of the growth curve models. Interestingly, there was significant covariance observed between the intercept and slope in the growth curve models, indicating that children with higher QOLCE scores also had greater rates of change over time. Trajectories for mothers with high and low CES-D scores based on results from the conditional growth curve model are illustrated in Fig. 2.

Moderating effects of family resources and perception of patient-centered care

The potential moderating effects of family resources and perception of patient-centered care were examined by including an interaction term between mothers' CES-D scores and the moderator in the growth curve model. Results from the two models are show in Table 3. Family resources moderated the impact of maternal DS on child HRQL ($\beta = 0.25$, $p < 0.0243$), and the magnitude of the moderating effect varied over time ($\beta = 0.09$, $p < 0.0212$). This moderating effect is illustrated in Fig. 3. In contrast, perception of patient-centered care was not observed to

Table 1. Description of maternal, child, and family characteristics

	Baseline (N = 339)	24 Months (N = 257)
Maternal characteristics		
Age, years	37.7 (5.8)	40.4 (5.5)
Marital status, %		
Not married	19.8	18.1
Married[a]	80.2	81.9
Employment status, %		
Not employed	9.5	6.6
Employed	66.1	77.7
Homemaker	22.9	15.2
Student	1.5	0.4
Education, %		
Primary school	11.5	5.0
High school	20.9	19.2
Technical training	13.6	11.9
College/University	54.0	63.9
Number of children	2.3 (0.9)	2.3 (0.9)
Depressive symptoms, CES-D	14.6 (10.6)	12.0 (10.0)
Child characteristics		
Age, years	7.4 (2.4)	9.4 (2.4)
Age at onset, years	6.9 (2.5)	6.8 (2.5)
Sex, %		
Male	52.2	51.6
Female	47.8	48.4
Seizure type, %		
Generalized	38.6	37.3
Partial	61.4	62.7
Antiepileptic drugs, %	68.2	76.8
Health-related quality of life, QOLCE	70.4 (13.4)	75.9 (13.9)
Epilepsy severity, GASE	5.4 (1.2)	6.3 (1.0)
Comorbidities, %		
Behavior problems	14.1	20.0
Cognitive disability	13.6	17.5
Motor dysfunction	6.3	5.7
Family characteristics		
Functioning, APGAR	14.0 (3.8)	14.1 (3.8)
Resources, FIRM	50.1 (11.1)	50.7 (11.5)
Demands, FILE	9.6 (6.5)	7.9 (5.8)
Perception of patient-centered care, PPPC	1.6 (0.5)	1.6 (0.6)
Annual household income, %		
<$20,000	7.7	4.0
$20,000–39,999	13.5	10.0
$40,000–59,999	21.2	18.8
$60,000–79,999	18.2	18.4
≥$80,000	37.2	44.0
Unknown	2.2	4.8

Data reported as mean (standard deviation), unless stated otherwise.
[a]Includes mothers in married and common-law relationships.

Table 2. Growth models for the impact of maternal depressive symptoms on child health-related quality of life

	Model A	Model B	Model C
Fixed effects			
Final status			
Intercept	73.14 (0.67)[d]	76.09 (0.85)[d]	75.88 (0.72)[d]
CES-D			−0.47 (0.06)[d]
Rate of change			
Time		1.17 (0.19)[d]	0.99 (0.15)[d]
CES-D × time			−0.04 (0.02)[a]
Variance components			
Level 1			
Intraindividual	56.26 (2.88)[d]	41.32 (2.62)[d]	41.89 (2.70)[d]
Level 2			
Final status	129.31 (11.74)[d]	166.62 (17.86)[d]	133.99 (15.64)[d]
Linear		4.22 (0.90)[d]	2.79 (0.82)[c]
Covariance		12.36 (3.22)[c]	8.95 (2.90)[b]
Goodness-of-fit			
Deviance	8,224.5	8,138.2	8,023.7

Values denote β-coefficient (standard error). Model A is the unconditional means model; Model B is the unconditional growth model; Model C is the growth model conditional on maternal depressive symptoms.
[a]$p < 0.05$, [b]$p < 0.01$, [c]$p < 0.001$, [d]$p < 0.0001$.

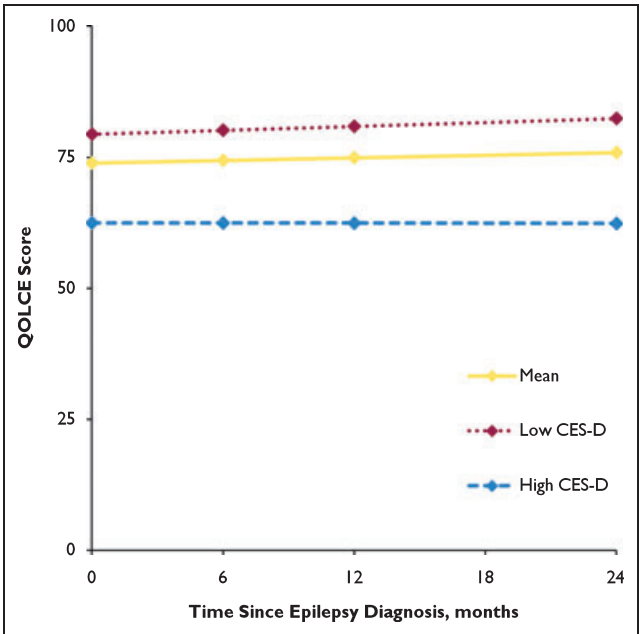

Figure 2.
Change in child HRQL over 24 months. Child HRQL was measured using the QOLCE. The solid yellow line represents the trajectory for children of average mothers; the dotted red line represents the trajectory for children of mothers with a CES-D score in the bottom 5%; and the dashed blue line represents the trajectory for children of mothers with a CES-D score in the top 5%.
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significantly moderate the relationship between maternal DS and child HRQL ($\beta = 3.48$, $p = 0.1281$).

Mediating effects of family functioning and family demands

The product of coefficients method was used to examine the potential mediating effects of family functioning and family demands in two sets of growth curve models during

Table 3. Moderating effects on the relationship between maternal depressive symptoms on child health-related quality of life

	Estimate	Standard error	p-Value
Model A			
Final status			
Intercept	77.05	0.81	<0.0001
CES-D	−1.43	1.38	0.3016
Family resources	0.41	0.06	<0.0001
CES-D × family resources	0.25	0.11	0.0243
Rate of change			
Time	1.43	0.20	<0.0001
CES-D × time	0.18	0.46	0.6976
Family resources × time	0.02	0.02	0.2565
CES-D × family resources × time	0.09	0.04	0.0212
Model B			
Final status			
Intercept	76.19	0.85	<0.0001
CES-D	−5.62	1.32	<0.0001
Perception of patient-centered care	−2.00	1.19	0.0933
CES-D × perception of patient-centered care	3.48	2.28	0.1281
Rate of change			
Time	1.30	0.20	<0.0001
CES-D × time	−0.57	0.45	0.1983
Perception of patient-centered care × time	0.01	0.39	0.9758
CES-D × perception of patient-centered care × time	1.52	0.84	0.0710

Model A includes family resources as the moderating variable and Model B includes perception of patient-centered care as the moderating variable.

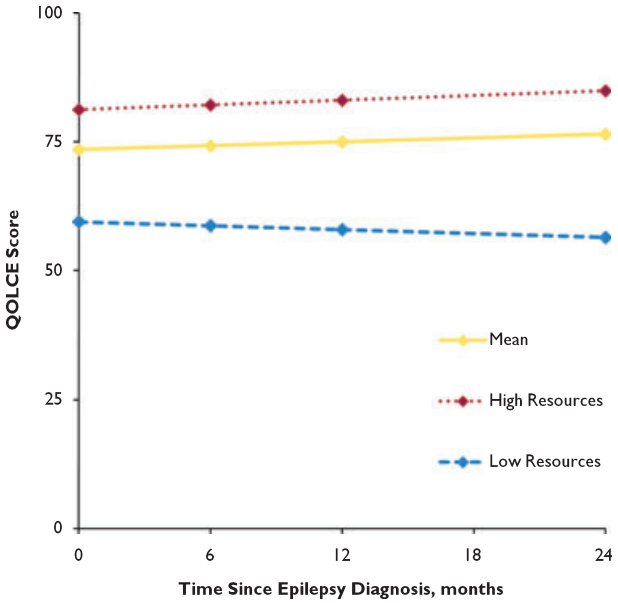

Figure 3.
Moderating effect of family resources on the relationship between maternal DS and child HRQL over 24 months. The solid yellow line represents the trajectory for children with mothers with average levels of DS and average family resources; the dotted red line represents the trajectory for children in the bottom 5% for family resources; and the dashed blue line represents the trajectory for children of mothers in the top 5% for family resources.

the 24-month follow-up. Results from the mediation analyses are shown in Table 4. Family functioning was observed to partially mediate the impact of maternal DS on child HRQL ($\hat{ab} = -0.07$, $p = 0.0007$). The proportion of the total effect of maternal DS on child HRQL mediated by family functioning was 20%. In comparison, family demands were also observed to partially mediate this relationship ($\hat{ab} = -0.12$, $p = 0.0006$). The proportion of the total effect mediated by family demands was 29%.

In a post hoc analysis examining the mediating effect of family functioning and family demands simultaneously in a two-mediator model, the proportion of total effect mediated was 45% ($\hat{ab} = -0.19$, $p < 0.0001$). There was no significant difference between the family functioning- and family demands-specific effects ($\Delta\hat{ab} = 0.05$, $p < 0.8708$).

Discussion

Approximately one-third of mothers of children with new-onset epilepsy are at risk for clinical depression. This proportion is much higher compared to mothers in the general population, where previous research suggests that about 17% are considered at risk for depression (Horwitz et al., 2007). When assessed over the first 24 months after diagnosis of epilepsy, maternal DS appeared to have a significant negative impact on child HRQL. This result is consistent with previous estimates from cross-sectional studies that included samples of children with more established epilepsy (Adewuya, 2006; Yong et al., 2006; Wood et al., 2008). However, none of these studies focused specifically on mothers of children with new-onset epilepsy and none followed participants prospectively over time. Not only do children of mothers with elevated levels of depressive symptoms have poorer HRQL compared to mothers with low levels of depressive symptoms, but their rate of change is also significantly less favorable during the first 24 months after diagnosis. Whereas children of mothers with lower levels of depressive symptoms have improved HRQL scores over time, children of mothers with elevated symptoms show no evidence of improvement.

Results from this study also demonstrated that family resources, but not perception of patient-centered care, moderated the impact of maternal depressive symptoms on child HRQL. Children of mothers experiencing DS, but having more family resources, including social support systems, had significantly improved HRQL during the first

Table 4. Mediating effects on the relationship between maternal depressive symptoms on child health-related quality of life

	Equation 1	Equation 2	$\hat{a}\hat{b}$	95% CI	Z-value	p-Value
Mediator: family functioning						
Intercept	76.20 (0.76)[b]	14.00 (0.20)[b]	−0.07	−0.11, −0.03	3.39	0.0007
Time	1.08 (0.18)[b]	−0.02 (0.05)[c]				
CES-D	−0.30 (0.06)[b]	−0.11 (0.01)[b]				
APGAR	0.64 (0.17)[a]					
Mediator: family demands						
Intercept	76.14 (0.77)[b]	7.98 (0.28)[b]	−0.12	−0.19, −0.05	3.44	0.0006
Time	1.09 (0.19)[b]	−0.25 (0.08)[a]				
CES-D	−0.29 (0.07)[b]	0.27 (0.02)[b]				
FILE	−0.45 (0.12)[a]					

Values denote β-coefficient (standard error).
[a]$p < 0.001$, [b]$p < 0.0001$, [c]not significant.

24 months after diagnosis, compared to child of mothers with fewer family resources. The children in this latter group actually experienced declines in their HRQL over time. The moderating effect of family resources on child health outcomes in epilepsy has been observed in previous cross-sectional studies. Baum et al. (2007) reported that family resources moderated the relationships between temperament and internalizing and externalizing behavior problems in children with epilepsy, and Fastenau et al. (2004) noted a moderating effect of family resources on children's academic achievement. Interestingly, the magnitude of the moderating effect of family resources on maternal depressive symptoms on child HRQL varied significantly over time. Larger effects were observed at later measurement occasions during the 24-month follow-up. This is consistent with the Convoy Model proposed by Kahn and Antonucci (1980). The Convoy Model offers a framework within which to understand how an assembly of family and friends are available as resources to an individual in times of need. Convoys are dynamic across time and situations, whereby each life change brings with it the potential to reconstitute the convoy as the individual seeks to construct a network of resources that meets her support needs (Levitt, 2005). In this sample, mothers may observe improvement in their child's HRQL with the addition of supportive resources, which may in turn lead mothers to acquire additional resources, resulting in further improvements in child HRQL over time. Therefore, it appears that the accumulation of resources is the driving force for the dynamic moderating effect observed over time. The fact that perception of patient-centered care did not moderate the impact of maternal DS on child HRQL was unlikely to be the result of missing important effects, since the study was adequately powered to detect statistically significant interactions, as described by McCarthy (2007).

In addition, the study demonstrated that family functioning and family demands partially mediated the impact of maternal DS on child HRQL during the 24-month follow-up. This result is consistent with previous research, which has shown that current and past DS in mothers are significant predictors of lower family functioning (Herr et al., 2007) and that family functioning (as measured by parental behavior), mediates the relationship between maternal depression and child health outcomes in both healthy and chronically ill pediatric populations (Burke, 2003; Elgar et al., 2007; Lim et al., 2008). Elgar et al. (2007) showed that the quality of the child's rearing environment mediated the impact of maternal DS on child and adolescent maladjustment over a 2-year period. In comparison, Lim et al. (2008) showed that parenting quality partially mediated the relationship between maternal depression and child internalizing behavior problems.

Being mindful of the mental state of caregivers and the climate of the family environment is an important component of family-centered care, and may present avenues for intervention that can potentially improve child outcomes (Smith et al., 2002). Family-centered care has been shown to be associated with an increase in parents' satisfaction with health care services, lower parent stress, and with positive child health outcomes (Law et al., 2003). Detection and treatment of maternal depression have been shown to have immediate significant benefits. Recently in the health economics literature, Perry (2008) demonstrated that treatment of maternal depression resulted in a reduction of health care costs in the 6 months after having a child diagnosed with asthma. This result supports health policy to invest in training pediatric health care professionals to detect DS in adults. Such a policy can lead to more efficient use of limited health care funds.

This study has several strengths. First, to our knowledge this is the only study to prospectively document the DS of mothers of children with epilepsy. In addition, the relatively large sample and strong response and retention rates increase the external validity of findings. Second, this study utilized the CES-D, a well-validated and reliable instrument to measure maternal DS. Third, the potential for bias in

mothers' reports associated with depression distortion (Richters, 1992) was investigated in this study, and no evidence of informant discrepancy was found in this sample of mothers (Ferro et al., 2010). If it was the case that depressed mothers' reports were negatively biased, this bias should be detected by comparing mothers' and neurologists' reports of children's HRQL. That is, the association between mothers' and neurologists' reports would vary significantly when stratified by level of maternal DS, if mothers' reports are biased by symptoms of depression. Interactions, depicted as product terms between CES-D scores and neurologist-reported measures, were used to determine the presence of depression distortion. There was a lack of evidence to support depression distortion in this sample (Ferro et al., 2010). Fourth, this study focused on incident rather than prevalent cases of childhood epilepsy. Results may be useful for health care professionals as part of the initial consultation when diagnosing childhood epilepsy so as to prevent any potential negative impact of maternal depressive symptoms on child health outcomes.

Results from this study are tempered by a few limitations. First is the fact that mothers with higher levels of DS and other risk factors for clinical depression (Lehtinen & Joukamaa, 1994) were less likely to complete the 24-month follow-up compared to mothers who did not exhibit such traits. A similar trend has been observed in other research of mothers with DS (de Graaf et al., 2000; Avison, 2010). Bias due to losses during follow-up may underestimate the proportion of mothers at risk and limit the external validity of results. Second, although there was no evidence to suggest that mothers were not valid informants, concerns regarding the accuracy and acceptability of parent-proxy ratings of children's HRQL continue to be raised, because research has shown that children and parents do not necessarily share similar views about illness (Harding, 2001). Although not feasible in the current study, the young patient's perspective on the experience with illness should also be incorporated in future investigations. Third, this sample may not be completely representative of the Canadian population (Statistics Canada 2006). Compared to women in the general population, this sample of mothers had a larger proportion with a college or university education (54.5% vs. 45.9%), income ≥$80,000 (37.2% vs. 28.3%), and married (80.2% vs. 46.4%). The fact that this sample had a larger proportion of married women compared to the general population was expected, since this study focused on mothers of children with epilepsy.

Conclusion

The negative impact of maternal DS on HRQL in children with new-onset epilepsy is significant during the first 24 months of diagnosis. This research has demonstrated that children of mothers with elevated levels of depressive symptoms have poorer HRQL over time and that this relationship is moderated by family resources and partially mediated by family functioning and family demands. It is important for health care professionals caring for children with epilepsy to be aware of how diagnosing epilepsy in a child can impact the mothers' mental health status and the family environment. By adopting a family-centered approach, health care professionals may be able to intervene at the maternal or family level to in turn promote more positive outcomes in children with epilepsy.

Acknowledgments

The authors would like to thank the families for their participation in this study and gratefully acknowledge the participation of the following physicians: British Columbia: Coleen Adams, Bruce Bjornson, Margaret Clark, Mary Connolly, Kevin Farrell, Juliette Hukin, Steven Miller, Elke Roland, Kathryn Selby, Katherine Wambera; Alberta: Karen Barlow, Lorie Hamiwka, Jean Mah, Bev Prieur, Lawrence, Richer, Barry Sinclair Elaine Wirrell, Jerome Yager; Saskatchewan: Richard Huntsman, Noel Lowry, Shashi Seshia; Manitoba: Fran Booth, Charuta Joshi, Mubeen Rafay, Michael Salman; Ontario: Craig Campbell, Pam Cooper, Asif Doja, Pierre Jacob, Daniel Keene, Betty Koo, Wayne Langburt, Simon Levin, Robert Munn, Minh Nguyen, Narayan Prasad, Sharon Whiting, Conrad Yim; Quebec: Lionel Carmant, Paola Diadori, Marie-Emmanuelle Dilenge, Albert Larbrisseau, Alison Moore, Chantel Poulin, Bernie Rosenblatt, Michael Shevell, Michel Vanasse; New Brunswick: David Meek; Nova Scotia: Carol Camfield, Peter Camfield, Joe Dooley, Kevin Gordon, Ellen Wood; Newfoundland: Muhammad Alam, David Buckley. Mark A. Ferro is the recipient of a Canadian Institutes for Health Research, Frederick Banting and Charles Best Canada Graduate Scholarship Doctoral Award. Kathy N. Speechley is the recipient of a Canadian Institutes for Health Research operating grant for HERQULES (MOP-117493).

Disclosure

We 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. None of the authors has any conflict of interest to disclose.

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Appendix

Individual growth curve modeling was used to examine the impact of maternal depressive symptoms on child HRQL during the 24-month follow-up (Singer & Willett,

2003). Such an approach can handle designs with repeated measures. The models were built following the guidelines suggested by Singer (2002). In particular, time since child was diagnosed with epilepsy and maternal depressive symptoms as time-varying predictors of child HRQL. Both the model intercept and slope were specified as random effects (i.e., differing for each individual in the sample). An unstructured variance-covariance matrix was specified, which is the most heterogeneous type and requires estimation of several parameters, thus additional degrees of freedom, but does not constrain any pairwise comparisons within the matrix, allowing for additional flexibility (Weiss, 2005). Variables were centered on their respective sample means at 24 months to improve interpretation of results.

Potential confounders were tested a priori to the growth curve modeling. The variables tested were child age, child sex, epilepsy severity, seizure type, age of onset, severity of co-morbidities, antiepileptic drug use, maternal age, education, employment status, parity, marital status, and family income. Confounding was determined by adding the variable to the model to examine the change in the effect estimate. For the purposes of this study, a collapsibility criterion was used to operationally define confounders as those variables, when entered in the model resulted in a ≥10% change in the effect estimate of maternal depressive symptoms on child HRQL (Rothman & Greenland, 1998).

Moderation was examined by sequentially testing growth curve models of child HRQL regressed on maternal depressive symptoms in the presence of each potential moderator using a product interaction term (Aiken & West, 1991). To examine whether family resources or perception of patient-centered care moderated the impact of maternal depressive symptoms on child HRQL at the 24-month follow-up, a two-way interaction between maternal depressive symptoms and the moderator was entered in the model. A three-way interaction between maternal depressive symptoms, the moderator, and time was entered to examine whether the magnitude of the moderating effect varied over time. The moderation analyses conformed to Kleinbaum's Hierarchy Principle such that maternal depressive symptoms and moderator main effects were included in the model assessing the interaction term (Kleinbaum & Klein, 2002).

The product of coefficients method described by MacKinnon et al. (2002) was used to examine the potential mediating effects of family functioning and family demands on the relationship between maternal depressive symptoms and child HRQL as illustrated in Fig. 1. The product of coefficients method has been shown to have more accurate type I error rates and greater statistical power compared to the more traditionally employed causal steps described by Baron and Kenny (1986). Instead the product of coefficients approach involved estimating two growth curve models: (1) $Y = i_1 + c'X + bM + e_1$ and (2) $M = i_2 + aX + e_2$, and computing the product of $\hat{a}$ and $\hat{b}$ to form the mediated or indirect effect. The rationale behind this approach is that mediation is dependent upon the extent to which the predictor impacts the mediator, a, and the extent to which the mediator impacts the outcome, b. The proportion of the total effect that is mediated was calculated using a ratio of the indirect effect, $\hat{a}\hat{b}$, divided by the total effect, $\hat{a}\hat{b} + \hat{c}'$. Significance of the mediated effect was tested by dividing the product by its standard error and compared to the standard normal distribution and by construction of confidence intervals. The standard error of $\hat{a}\hat{b}$ was calculated using the method described by Sobel (1982). The Sobel method is the most commonly used approach to calculating the standard error and has been shown to produce unbiased and statistically robust results (MacKinnon et al., 2002). Growth curve models used in the mediation analysis were adjusted for potential confounding factors using the methods described by Li et al. (2007) in order to obtain unbiased estimates of effect.