

Interim Findings from the Sibling Voices Survey: Siblings of Epileptic Encephalopathy Patients Are at Risk for Depression and Anxiety

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INTRODUCTION

- Severe epileptic encephalopathies (EEs) of childhood such as Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) are refractory to conventional anticonvulsants and result in developmental delays, neurocognitive impairment, and motor deficiencies¹
- Comprehensive care of these patients places burdens on caregivers and their families in multiple areas, including substantial financial impacts and humanistic burdens²
- In a recent survey, 74% (114/154) of caregivers reported concerns about the emotional impact on siblings of a brother/sister with an EE³; the emotional impact experienced by immediate caregivers may affect the quality of life of the entire family, especially siblings⁴
- Siblings often play a role in caring for EE patients, and the impact on sibling mental health and social development may be under-recognized by the medical community
- Our ongoing Sibling Voices Survey is focusing on the psychosocial impact of growing up with a sibling affected by a severe childhood EE
 - Survey questions are designed to assess risk of depression and anxiety and other aspects that impact sibling mental health

METHODS

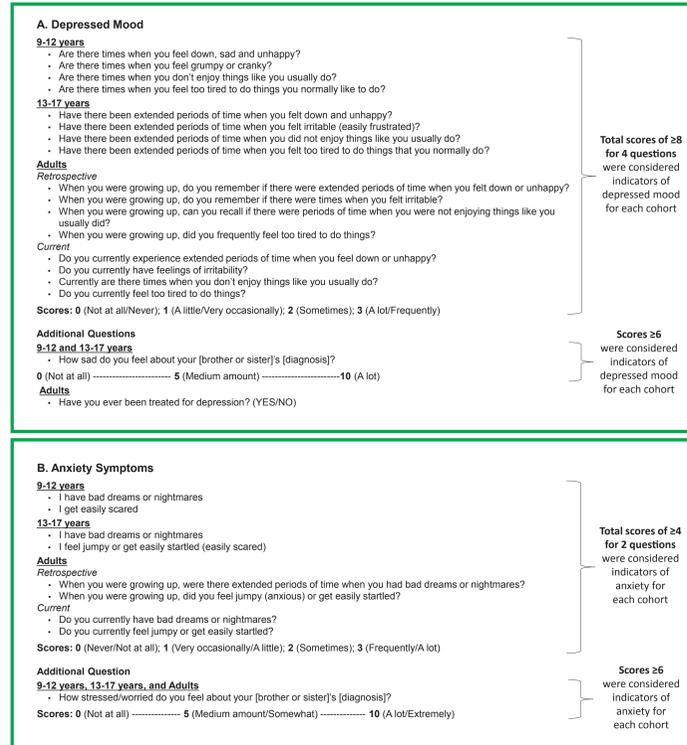
Survey Development and Recruitment

- Online survey questions were developed in consultation with DS and LGS patient communities and healthcare professionals (www.siblingstudy.com)
 - Questions were refined via beta testing in small groups of parents and siblings
 - Age- and role-specific surveys were developed for 4 cohorts: siblings 9-12 years, 13-17 years, or ≥18 years (adults) and parents (not reported here)
- The survey was launched on July 19, 2017 and is currently open for participation
 - Potential participants are being recruited through patient advocacy websites, social media, medical meetings, and patient community events
 - The study protocol was approved by Western IRB (Puyallup, WA) on July 14, 2017

Survey Design

- This interim analysis focused on risk factors for depression and anxiety
- Four questions assessed the potential for depressed mood (Figure 1A)
 - An additional question assessed sadness about their sibling's diagnosis
- Two questions assessed the potential for anxiety (Figure 1B)
 - An additional question assessed stress over their sibling's diagnosis
- Free-form responses were evaluated by indicators of depressed mood and anxiety symptoms

Figure 1. Survey questions and scoring criteria for assessing (A) Depressed mood and (B) Anxiety symptoms.



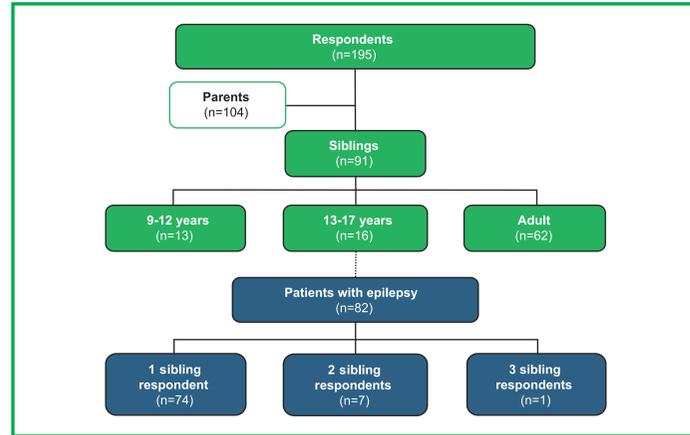
Note: threshold values for indicators of depressed mood and anxiety symptoms were empirically selected.

RESULTS

Sibling Voices Survey Respondents

- Responses received from July 19 to August 31, 2017 were analyzed
- Most of the respondents were adults (Figure 2)
- The 91 sibling respondents represented 82 families of patients with epilepsy; between 1 and 3 siblings responded per family (Figure 2)

Figure 2. Sibling Voices Survey respondents, overall and by patient.



Respondent Demographics

- Demographic characteristics of sibling respondents and EE patients are presented in Table 1 (sibling characteristics) and Table 2 (patient characteristics)

Table 1. Demographic Characteristics of Sibling Survey Respondents (n=91)

Characteristic	Age Group			All
	9-12	13-17	Adult	
N	13	16	62	91
Sex, n (%)				
Male	6 (46)	11 (69)	14 (23)	31 (34)
Female	7 (54)	5 (31)	48 (77)	60 (66)
Twin sibling, n (%)	1 (8)	0 (0)	1 (2)	2 (2)
Age, years, mean±SD (range)	10±1 (9-12)	14±1 (13-15)	27±8 (18-63)	22±10 (9-63)
School grade, mean±SD (range)	5±1 (3-7)	9±1 (8-11)	NA	NA
Family size, mean±SD (range)	5±1 (4-8)	6±2 (4-10)	5±4 (1-30)	5±3 (1-30)
No. of children/family, mean±SD (range)	3±1 (2-6)	4±2 (2-8)	3±2 (0-10)	3±2 (0-10)

SD, standard deviation; NA, not applicable.

Table 2. Demographic Characteristics of EE Patients (n=82)

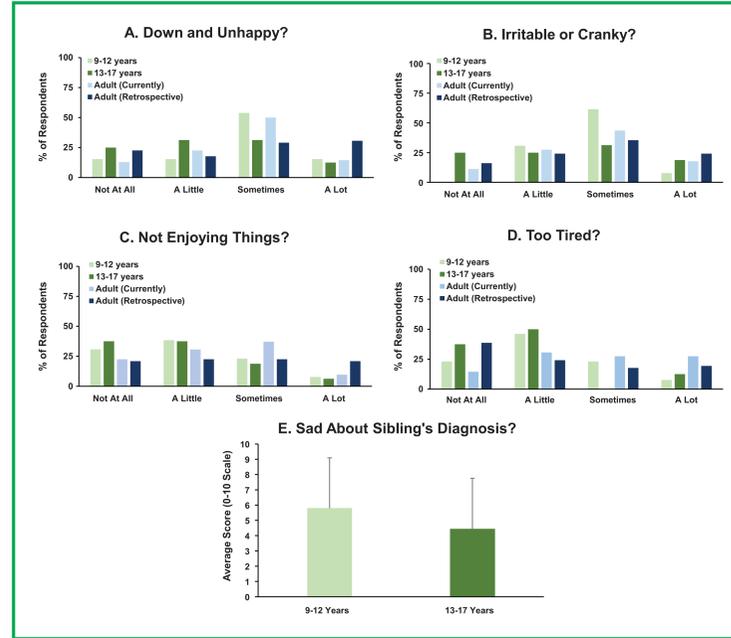
Characteristic	
N	82
Patient sex, n (%)	
Male	33 (40)
Female	49 (60)
Patient age, years, mean±SD (range)	19±11 (1-61)
Epilepsy diagnosis, n (%)	
Dravet syndrome	29 (35)
Lennox-Gastaut syndrome	11 (13)
Other epileptic encephalopathy	42 (51)

SD, standard deviation.

Depressed Mood

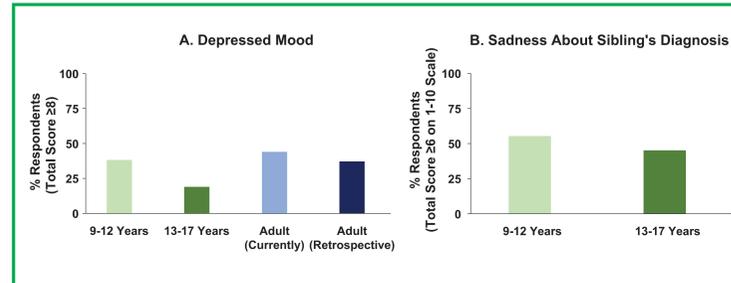
- Sibling responses to questions assessing the potential for depressed mood are shown in Figure 3 (individual questions) and Figure 4 (composite scores)
 - The 13-17 age group scored lowest of all cohorts on the 4 indicators of potential depression (Figure 3)
- Composite scores for depressed mood were approximately 2-fold higher in the other age groups (Figure 4A)
 - Most of the adult siblings and siblings 9-12 (≥50%) reported experiencing feelings of unhappiness "sometimes" or "a lot," vs 44% of siblings 13-17 (Figure 3A)
 - In all cohorts, ≥50% of siblings reported feelings of irritability or anger "sometimes" or "a lot" (Figure 3B)
 - In adult siblings, 37% reported a history of treatment for clinical depression

Figure 3. Responses to questions assessing the potential for depressed mood.



Error bars represent standard deviation of the mean.

Figure 4. Composite scores for questions assessing the potential for depressed mood.



- Free-form responses suggestive of depression are shown in Table 3

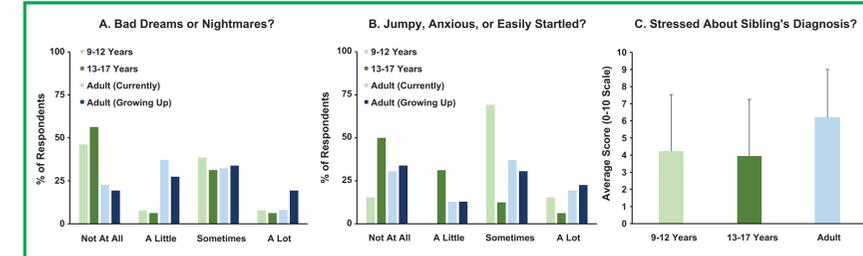
Table 3. Free-Form Responses Suggestive of Depression

Age Group	Response
13-17	"When I think about it sometimes I start to cry and it makes me upset."
	"I feel guilty because I am the older sibling for him and a role model but I don't think I'm doing a good job."
Adults	"I have had a lot of difficulty dealing with guilt associated to my feelings towards her situation. I sometimes would get upset because I would feel that it was unfair but I also thought it was horrible for me to feel this way and the conflicting feelings are not easy to deal with."
	"...makes me feel guilty and also angry that I have to feel like this."
	"I feel like I feed off my mum's mood a lot so if she was negative or stressed because of my brother's Dravet, my concern for this this would affect me – often caused arguments or lowered my mood."
	"I felt terrible they [my parents] had to go through so many traumatic events and felt their sadness."
	"It's scary at times and sad that I can't see that side of my family at times especially when sometimes I'm not always informed when my brother is in the hospital because of his epilepsy."

Anxiety Symptoms

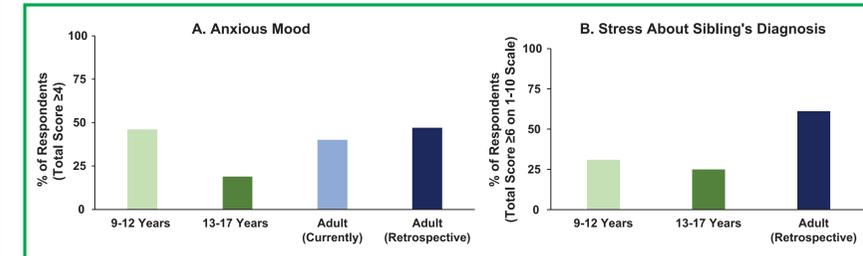
- Sibling responses to questions assessing the potential for anxiety are shown in Figure 5 (individual questions) and Figure 6 (composite scores)
 - Feeling jumpy or easily startled was more frequently reported "sometimes" or "a lot" in the 9-12 age group than the 13-17 age group or in adult siblings (Figure 5B)
- The 13-17 age group scored lowest of all cohorts on the 2 composite indicators of anxiety (Figure 6)

Figure 5. Responses to questions assessing the potential for anxiety.



Error bars represent standard deviation of the mean.

Figure 6. Composite scores for questions assessing the potential for anxiety.



- Free-form responses suggestive of anxiety are shown in Table 4

Table 4. Free-Form Responses Suggestive of Anxiety

Age Group	Response
13-17	"I try spend some time reading or listening to music to calm me down."
	"I love doing sports to get my mind away from all the drama at home."
Adults	"It scared me and caused me a lot of stress that I did not believe I should share with others. I kept it to myself and it made me shut people out."
	"Their stress and frustration are contagious and it sits like a dark cloud above our heads."
	"Made me worry that I will soon have to take on this responsibility and I feel uncertain that I would be able to take on this task as well as my parents have."
	"My concern for my parents has caused a lot of stress on me."
	"I was left with family a lot because they were in/out of hospitals I worried all the time what was going on are they telling me everything and their stress was usually taken out on me."
	"As the oldest sibling, I feel it is my responsibility to care for my parents. Because I can't actually do anything to alleviate their stress, it only stresses me out as well."
	"Always seeing them stressed out about his health and feeling like I'm not doing enough to help or not being supportive enough."

CONCLUSIONS

- This interim analysis of the Sibling Voices Survey suggests that siblings of children with DS, LGS, and other EEs may be at risk for depression and anxiety
- A substantial portion of respondents reported sadness and stress over their sibling's epilepsy, including responses suggestive of depressed mood and anxiety
- In adult siblings, 37% reported receiving treatment for clinical depression
- This study confirms and extends previously reported findings suggesting that caring for a child with DS, LGS, or other severe EEs adversely affects the entire family unit⁴⁻⁶

Future Directions

- Siblings of children with EE may represent an "at risk" population who warrant assessment, monitoring, and potential intervention for depression and anxiety
- Clinicians should discuss the potential for sibling depressed mood and anxiety with parents
- Further research is warranted to better understand how to identify those siblings exhibiting signs suggesting depression and/or anxiety and the best methods for intervention

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DISCLOSURE

LDB, ARG, BSG, CS: Employee, Zogenix; Stock ownership, Zogenix. LS: Consultant, Zogenix.

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