



Resilience of adolescents and teenagers with self-limited and genetic-generalized epilepsy during the COVID-19 pandemic

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ABSTRACT

Introduction: The study-objective was to determine the emotional impact of the COVID-19 pandemic on children with self-limited and genetic-generalized epilepsy.

Methods: Patients completed the Children's Depression Inventory-2 (CDI-2) and Multidimensional Anxiety Scale for Children 2nd Edition (MASC-2) questionnaires before and during the pandemic. Via tele-visits, a pandemic-lifestyle survey and Obsession with COVID-19 Scale (OCS) was administered.

Results: Fifty subjects with a mean (SD) age of 14.44 (2.97) years and 4.85 (2.97) years of epilepsy were included. Overall, mood (62%), anxiety (61%), sleep (68%) and seizure frequency (88%) were unchanged/improved during the pandemic. There was no significant difference in pre-COVID-19 and during COVID-19 CDI-2 and MASC-2 total *T*-scores. In 24% with a worsening CDI-2 total *T*-score, associations included higher total OCS score ($p = 0.001$), poor sleep ($p = 0.013$) and pre-existing psychiatric history ($p = 0.0450$). In 28% with a worsening MASC-2 total *T*-score, associations included less exercise during the pandemic ($p = 0.028$) and lower maternal education history ($p = 0.022$). On OCS, 6% were in the dysfunctional range.

Conclusions: This cohort demonstrated emotional resilience during the COVID-19 pandemic. However, screening is important, as a subgroup experienced disruptive changes, possibly related to modifiable factors, such as sleep and exercise.

Lay summary: To determine the impact of the COVID-19 pandemic on children with epilepsy (CWE), 50 CWE completed a pandemic-lifestyle survey. Questionnaires for anxiety and depression completed before and during the COVID-19 pandemic were also compared. Overall, there was no worsening of seizures, anxiety, or depression during the pandemic. During the pandemic, 24% had more depressive symptoms (associations: poor sleep and psychiatric history) and 28% had more anxiety (associations: less exercise and lower maternal education). This cohort showed emotional resilience during the COVID-19 pandemic. Regular screening is important, as some CWE experienced disruptive changes, related to modifiable factors, such as sleep and exercise.

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1. Introduction

During the COVID-19 pandemic, many children have experienced significant lifestyle changes, including disruptions in school arrangements and social interactions. In the general population, the impact of the pandemic on mood and anxiety has been variable, with some studies observing no difference [1] and others reporting significant worsening of mood and anxiety [2,3]. To date COVID-19-related lifestyle changes and stressors may lead to additional concerns in children with epilepsy, with distinct impacts on their lives. It is well established that psychiatric comorbidities are

more prevalent in people with epilepsy than in the general population [4,5]. Early detection is important, as comorbidities correlate with poor quality of life [6], seizure severity [7], treatment-resistance [8], and more severe adverse effects of anti-seizure medication (ASM) [9]. Nevertheless, comorbidities are often overlooked; especially in patients with self-limited focal (SLE) or genetic generalized epilepsies (GGE), who often have normal development or well-controlled seizures.

The study was conducted at BC Children's Hospital (BCCH), the only tertiary-care center in British Columbia, serving a population of approximately 5 million people. The first case of community transmission was confirmed in British Columbia in early March 2020. Following, a state of emergency was declared in mid-March and emergency measures were taken in an effort to reduce

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the spread of the virus. The government ordered the province to follow various social distancing guidelines. However, unlike some regions, there were no restrictions to spending time outdoors for fresh air and exercise. All schools halted in-person classes between the middle of March to the end of May. They opened in June with limited hours, then back to full time in September 2020, although many students chose to continue online learning in 2020–2021. At the time of the study, COVID-19 vaccinations were not available for children in British Columbia. From March 2020, clinical care also significantly changed, with the emergence of telemedicine being the primary way to follow patients and to manage non-urgent epilepsy-related problems. During the pandemic, the timing and frequency of follow-up visits with neurologists remained the same as before the pandemic.

Via telehealth visits, the objective of this prospective observational study was to evaluate the impact of the COVID-19 pandemic on children with SLE and GGE, by comparing changes in mood and anxiety before and during the pandemic. A lifestyle questionnaire was developed to garner the views, experiences and possible lifestyle changes due to the COVID-19 pandemic and subsequent restrictions.

2. Materials and methods

2.1. Study population

Fifty patients, followed at BCCH, 10–19 years of age, with a diagnosis of SLE or GGE were enrolled during August 2020 to April 2021. Eighty-three patients were initially contacted by phone to participate in the study; 16 declined, 15 did not respond, and 2 patients withdrew after consenting, resulting in 50 participants. SLEs included Childhood epilepsy with centrottemporal spikes (CECTS), and self-limited occipital epilepsies of childhood with the early-onset form described by Panayiotopoulos [10] and the late-onset form by Gastaut [11]. The GGEs encompassed four epilepsy syndromes: childhood absence epilepsy (CAE), juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME) and generalized tonic-clonic seizures alone. Patients were included in the study if they completed the Children's Depression Inventory 2 [12] (CDI 2) and the Multidimensional Anxiety Scale for Children, 2nd Edition (MASC 2) [13] questionnaires during an inpatient or out-patient visit in our center from November 2018 to March 2020, prior to the pandemic. Patients were not considered eligible for the study if they had cognitive or behavioural impairment severe enough to prevent engagement or completion of the questionnaires, or if they were not fluent in English. This was determined by a research assistant talking to children and families prior to enrollment.

2.2. Measures

Demographic and clinical data were obtained by review of medical records, including epilepsy diagnosis and syndrome, seizure types, duration of seizures, ASM, other medical conditions and comorbidities. In one follow-up telehealth visit during the pandemic (August 2020 to April 2021), 50 patients retook the CDI 2 and MASC 2 questionnaires, and additionally completed a short survey on lifestyle during the pandemic and the Obsession with COVID-19 Scale (OCS) [14]. All tests and surveys were administered over the phone, with an examiner entering the responses on paper forms. Study data were entered and managed using Research Electronic Data Capture (REDCap) tools hosted at BC Children's Hospital Research Institute. REDCap is a secure, web-based application designed to support data capture for research studies [15].

2.2.1. Children's Depression Inventory 2: Self-Report Long Form [12] (CDI 2)

The CDI 2 is an assessment tool to measure the cognitive, affective and behavioral signs of depressive symptoms in youths ages 7–17 years developed by Kovacs [12]. When results from the CDI 2 are combined with other sources of verified information, the CDI 2 can aid in the early identification of depressive symptoms, the diagnosis of depression and related disorders, as well as the monitoring of treatment effectiveness.

The full-length CDI 2: Self-Report is a 28-item assessment that yields a Total Score, two Scale scores (Emotional Problems and Functional Problems), and four Subscale scores. The items of the CDI 2 are grouped into four factor areas, including Negative Mood/Physical Symptoms, Interpersonal Problems, Ineffectiveness, and Negative Self Esteem. The questionnaire is comprised of statements related to these areas, including sadness, pessimism, self-deprecation, misbehavior, pessimistic worrying, self-hate, self-blame, suicidal ideation, crying spells, irritability and reduced social interest. Raw scores are converted to *T*-scores. A total *T*-score ≥ 65 identifies potentially depressed individuals. A higher score indicates that an individual is experiencing more depressive symptoms. According to the CDI 2 scoring manual, provided at a probability level of $p < 0.10$, a total *T*-score difference of 9 points is required for the change to be considered statistically significant. The test was based on experiences over the past two weeks and the test time was approximately 20 minutes.

2.2.2. Multidimensional Anxiety Scale for Children 2nd Edition Self-Report [13]

The MASC 2 is a self-report measure of anxiety symptoms developed by March [13]. The purpose of the MASC 2 is to assess a broad range of anxiety symptoms in individuals 8–19 years of age. The MASC 2 assesses emotional, physical, cognitive, and behavioural symptoms of anxiety utilizing six scales and four subscales. The MASC 2 measures the range and severity of anxiety symptoms.

Responses on the MASC 2 are combined to create 11 *T*-scores: Total Score, Separation Anxiety/Phobias, Generalized Anxiety Disorder Index, Social Anxiety (Total, Humiliation/Rejection, Performance Fears), Obsessions & Compulsions, Physical Symptoms (Total, Tense/Restless, Panic), and Harm Avoidance. A total *T*-score ≥ 60 indicates increased likelihood of at least one anxiety disorder in an individual. A higher *T*-score over time indicates that the symptoms have become more pronounced across administrations, whereas a decreased score indicates that the symptoms have become less pronounced. For the MASC 2, in order to report at a consistent probability level as the CDI 2, a difference of 7 points in the total *T*-score is required for statistical significance. The test was based on experiences over the past two weeks and the test time was approximately 15 minutes.

2.2.3. Obsession with COVID-19 Scale [14]¹

The OCS is a self-report mental health screener of persistent and disturbed thinking about COVID-19. Because the COVID-19 crisis affects nearly every aspect of a person's life, the OCS was developed to help clinicians and researchers efficiently identify cases of individuals functionally impaired by their COVID-19 related thinking patterns.

The OCS was developed on two large samples of adults ($n = 775$; $n = 398$) residing across the United States. Each item of the OCS is rated on a 5-point scale, from 0 (not at all) to 4 (nearly every day). An OCS total score ≥ 7 indicates probable dysfunctional thinking about COVID-19. Elevated scores on a particular item or a high

¹ There is no need to abbreviate 2.2.2 and 2.2.3 and the rereferences "[14] and [15]" can be deleted since they have already been referenced.

total scale score (≥ 7) may indicate problematic symptoms for the individual that might warrant further assessment and/or treatment. Clinical judgement should guide the interpretation of the OCS results. The test was based on experiences over the past two weeks and the test time was approximately 5 minutes.

2.2.4. Phone survey: Lifestyle questionnaire

To garner the impact of COVID-19 pandemic and related restrictions, a lifestyle questionnaire was created. Patients were asked during a telehealth visit about the following issues: epilepsy (changes in seizure frequency, administration of ASM), social networks (changes in time spent with family and friends), school arrangement (including virtual classes), impact on the patient's and parents' jobs, concern regarding finances, exercise, sleep disturbance, screen time (the amount of time spent using a device with a screen such as a smartphone, computer, television, or video game console) and time spent specifically on COVID-19-related news. Patients were also asked specifically if they felt that epilepsy limited their activities during the pandemic compared to peers or if they felt that hospital visits were perceived to impact the risk of COVID-19 infections. This questionnaire is attached in the [supplementary material](#).

2.2.5. Analysis

Statistical analysis was performed using R statistical software (R Core team 2021, Austria). Descriptive statistics were used to characterise the cohort based on the demographic data and questionnaires. Categorical variables were summarised using counts and percentages while continuous variables were summarised with median and interquartile ranges. Associated factors were initially assessed univariately by categorising the patients as having an increase or decrease in total *T*-score, after which responses for these classes were compared via chi-squared tests or *t*-tests. To assess the mean difference in pre-COVID-19 and during COVID-19 total *T*-scores, a mixed effects model was fit with a random effect for each subject ID, as well as adjusting for relevant demographic factors. All model estimates were reported with 95% confidence intervals and *p*-values < 0.05 were considered significant. The study was approved by the institutional ethics board and informed consent (patients < 19 years of age) and assent (patients ≤ 18 years of age) was obtained for all patients.

3. Results

3.1. Demographics

A descriptive analysis of sociodemographic and clinical history data of the overall population is reported in [Table 1](#). Fifty patients were included in the study, of which 28 (56%) were female. The patients had a mean (SD) age of 14.44 (3.23) years, a mean (SD) of 9.22 (3.13) years of education and 4.85 (2.97) years of epilepsy. Patients with the following epilepsy syndromes were included: CECTS (26%), CAE (26%), JAE (18%), JME (18%) and other GGE (12%). A history of convulsive seizures was present in 27 (54%) patients. In the 3 months prior to taking the questionnaires, seizure frequency was reported as daily (4%), weekly (2%), monthly (6%), less than monthly (16%) and none in the past 3 months (72%) ([Table 2](#)). There was no significant association between epilepsy syndrome, seizure type or frequency with pre-COVID-19 and during COVID-19 CDI 2, MASC 2 or OCS scores. Regarding pre-existing conditions, 9 had a history of depression (2 had contemplated suicide at one point), 15 had anxiety disorders, 7 had sleep disorders and 22 had difficulties with school performance, requiring additional assistance.

Table 1
Summary of clinical and demographic data.

	Overall
<i>n</i>	50
Pre-COVID-19 CDI 2 total <i>T</i> -score, mean (SD)	58.1 (11.0)
During COVID-19 CDI 2 total <i>T</i> -score, mean (SD)	57.4 (12.6)
Pre-COVID-19 MASC 2 total <i>T</i> -score, mean (SD)	60.2 (11.4)
During COVID-19 MASC 2 total <i>T</i> -score, mean (SD)	59.6 (11.1)
CDI 2 score difference, adjusted mean (95% CI); <i>p</i> -value	-0.62 (-3.13, 4.38); 0.106
MASC 2 score difference, adjusted mean (95% CI); <i>p</i> -value	-0.70 (-3.33, 4.73); 0.115
OCS score, mean (SD)	2.20 (2.68)
Age at enrolment, mean (SD), years	14.44 (3.23)
Duration of epilepsy, mean (SD), years	4.85 (2.97)
Education, mean (SD), years	9.22 (3.13)
Female, <i>n</i> (%)	28 (56.0)
Mother's highest level of education, <i>n</i> (%)	
High school graduate	5 (10.0)
< 1 year of college (no degree)	1 (2.0)
1–2 years of college (no degree)	7 (14.0)
3 years of college (no degree)	2 (4.0)
Associate degree	5 (10.0)
Bachelor's degree	17 (34.0)
Master's degree	8 (16.0)
Professional degree	2 (4.0)
Unknown	3 (6.0)
Type of epilepsy, <i>n</i> (%)	
Self-limited epilepsy with Centrottemporal Spikes	13 (26.0)
Childhood Absence Epilepsy	13 (26.0)
Juvenile Absence Epilepsy	9 (18.0)
Juvenile Myoclonic Epilepsy	9 (18.0)
Genetic Generalized Epilepsy with Generalized Tonic-Clonic Seizures	6 (12.0)
History of convulsive seizures, <i>n</i> (%)	27 (54.0)
Diagnosis of ADHD, <i>n</i> (%)	8 (16.0)
Number of ASMs, mean (SD)	0.98 (0.68)
Psychiatric History, <i>n</i> (%)	
Depression	9 (18%)
Suicidal ideation	2 (4%)
Anxiety disorder	15 (30%)
Other pre-existing conditions, <i>n</i> (%)	
Sleep disorder	7 (14%)
School performance difficulties, requiring assistance	22 (44%)
Number of psychiatric medications, <i>n</i> (%)	
SSRI/SNRI	4 (8.0)
Anti-psychotic	1 (2.0)
Stimulant	3 (6.0)

ASM, anti-seizure medication; CI, confidence interval; SD, standard deviation; SNRI, serotonin and norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

3.2. Lifestyle questionnaire

The lifestyle questionnaire is provided in the [supplementary material](#) and results are summarized in [Table 2](#). The majority reported mood (62%), anxiety (61%), and stress level (82%) as unchanged or improved during the pandemic. Most patients had well-controlled seizures, with only 14 (28%) having seizures in the 3 months preceding the pandemic phone visit. At the time of the phone visit, 38 (76%) patients were on ASMs and the mean (SD) number of ASMs was 0.98 (0.68). Regarding the timing of taking ASMs, 23 (61%) were taking ASMs at regularly prescribed times prior to the pandemic and during the pandemic. As for compliance with ASMs, 26 (68%) missed ASM doses at least once per month prior to the pandemic and 22 (58%) during the pandemic. Only 6 (12%) had a worsening of seizure frequency during the pandemic and 13 (26%) believed that COVID-19 impacted their feelings about making changes to their ASMs.

With regards to school and other activities of daily routine, 41 (82%) patients were in school at the time of the survey with 36 (97%) switching to virtual classes as part of the public, private,

Table 2
Summary of COVID-19 Lifestyle Questionnaire responses.

Lifestyle during COVID-19 pandemic	Participant (n = 50)
Education	
Currently in school	
Yes	41 (82%)
No	9 (18%)
Type of school ¹	
Public	23 (56%)
Private	5 (12%)
Homeschool	4 (10%)
Post-secondary	9 (22%)
Grade ¹	
4	1 (2%)
5	5 (12%)
6	5 (12%)
7	5 (12%)
8	3 (7%)
9	4 (10%)
10	2 (5%)
11	1 (2%)
12	6 (15%)
First year post-secondary	9 (22%)
Virtual classes ²	
Not at all	1 (3%)
Part of the time	14 (38%)
Full time	22 (59%)
Preference of virtual or in-person classes ²	
No preference	12 (32%)
Learn from home	7 (19%)
Attend school in-person	18 (49%)
Finance	
Paid employment	
Yes, part time	14 (28%)
Yes, full time	2 (4%)
No	34 (68%)
Pandemic affected employment opportunities ³	
Yes	8 (50%)
No	6 (38%)
Not applicable	2 (13%)
Parents work	
Yes	49 (98%)
No	1 (2%)
Parents work from home due to pandemic ⁴	
Mom only	9 (18%)
Dad only	6 (12%)
Both	10 (20%)
No	24 (49%)
Concern about money	
Very unconcerned	4 (8%)
Unconcerned	22 (44%)
Average concern	17 (34%)
Concerned	6 (12%)
Very concerned	1 (2%)
Social Interactions	
Communication with friends	
Much less	9 (18%)
Less	11 (22%)
Same	17 (34%)
More	1 (2%)
Much more	12 (24%)
Epilepsy prevent activities during pandemic compared to peers	
Not at all	37 (74%)
Small degree	5 (10%)
Medium degree	4 (8%)
Large degree	4 (8%)
Time spent with family	
Much less	5 (10%)
Less	6 (12%)
Same	17 (34%)
More	7 (14%)
Much more	15 (30%)
Screen Time	
Time per day in the past 3 months	
<1 hour	2 (4%)
1–3 hours	11 (22%)
3–6 hours	20 (40%)

Table 2 (continued)

Lifestyle during COVID-19 pandemic	Participant (n = 50)
6–9 hours	15 (30%)
>9 hours	2 (4%)
During pandemic vs. 3 months before pandemic	
Much less	0 (0%)
Less	7 (14%)
Same	9 (18%)
More	21 (42%)
Much more	13 (26%)
Mood and Sleep	
Mood during past 3 months	
Much worse	3 (6%)
Worse	16 (32%)
Same	24 (48%)
Better	3 (6%)
Much better	4 (8%)
Anxiety during past 3 months	
Much worse	6 (12%)
Worse	15 (30%)
Same	18 (39%)
Better	6 (12%)
Much better	5 (10%)
Sleep during past 3 months	
Much worse	7 (14%)
Worse	9 (18%)
Same	21 (42%)
Better	9 (18%)
Much better	4 (8%)
Stress during past 3 months	
Much worse	5 (10%)
Worse	4 (8%)
Same	19 (38%)
Better	17 (34%)
Much better	5 (10%)
Seizure Frequency	
During past 3 months	
None	36 (72%)
Less than monthly	8 (16%)
Several/month	3 (6%)
Several/week	1 (2%)
Daily	2 (4%)
During pandemic vs. 3 months before pandemic	
Much worse	4 (8%)
Worse	2 (4%)
Same	40 (80%)
Better	2 (4%)
Much better	2 (4%)
Antiseizure medication (ASM)	
On AEDs for seizures	
Yes	38 (76%)
No	12 (24%)
Frequency of missed ASM doses in 6 months before pandemic⁵	
Never	12 (32%)
Less than 1/month	13 (34%)
Few times per month	13 (34%)
Few times per week	0 (0%)
Most days of the week	0 (0%)
Frequency of missed ASM doses in past 3 months during pandemic⁵	
Never	16 (42%)
Less than 1/month	10 (26%)
Few times per month	11 (29%)
Few times per week	1 (3%)
Most days of the week	0 (0%)
Frequency of taking ASM at regular times in 6 months before pandemic⁵	
Never	1 (3%)
Not most days/month	0 (0%)
Half the time	4 (11%)
Most days/month	10 (26%)
Always	23 (61%)
Frequency of taking ASM at regular times in 3 months during pandemic⁵	
Never	1 (3%)
Not most days/month	0 (0%)
Half the time	2 (5%)
Most days/month	12 (32%)
Always	23 (61%)

(continued on next page)

Table 2 (continued)

Lifestyle during COVID-19 pandemic	Participant (n = 50)
Pandemic affect feeling on making changes to ASM	
Not at all	37 (74%)
Small degree	5 (10%)
Medium degree	4 (8%)
Large degree	4 (8%)
Exercise and Outdoors	
Exercise level	
Much less	10 (20%)
Less	14 (28%)
Same	15 (30%)
More	7 (14%)
Much more	4 (8%)
Time spent outdoors	
Much less	6 (12%)
Less	16 (32%)
Same	8 (16%)
More	10 (20%)
Much more	10 (20%)
Access to outdoor spaces (e.g., parks, backyard)	
Rarely	1 (2%)
Sometimes	9 (18%)
Most of the time	7 (14%)
Always	31 (62%)
COVID-19 Risks	
Know any COVID-19 cases	
Yes	12 (24%)
Suspected	1 (2%)
No	37 (74%)
Worry about contracting COVID-19	
Very unconcerned	4 (8%)
Unconcerned	12 (24%)
Average concern	16 (32%)
Concerned	9 (18%)
Very concerned	9 (18%)
Attention spent per day on COVID-19 updates	
<1 hour	45 (90%)
1–3 hours	5 (10%)
3–6 hours	0 (0%)
6–9 hours	0 (0%)
>9 hours	0 (0%)
Concern epilepsy may increase COVID-19 risk	
Very unconcerned	22 (44%)
Unconcerned	14 (28%)
Average concern	12 (24%)
Concerned	1 (2%)
Very concerned	1 (2%)
Feel hospital visits increase risk of contracting COVID-19	
Not at all	4 (8%)
Very small risk	6 (12%)
Small risk	26 (52%)
Large risk	10 (20%)
Very large risk	4 (8%)

¹ n = 41.² n = 37.³ n = 16.⁴ n = 49.⁵ n = 38.

and post-secondary school system. Of the children who experienced virtual classes, seven (19%) preferred remote classes, 18 (49%) preferred in-school classes and the remainder had no preference of school format. The majority (68%) reported sleep quality as unchanged or improved during the pandemic. Fifty-two percent exercised the same or more and only 1 (2%) had reduced access to outdoor space during the pandemic. Screen time was increased in 34 (68%) patients during the pandemic, with 17 (34%) having 6 or more hours of screen time per day.

Social interactions and finances were also impacted for some individuals during the pandemic. Thirty-nine (78%) spent the same or more time with family during the pandemic and 30 (60%) talked to friends the same or more during the pandemic. Of the parents who were working, half (50%) of parents were working from home for the first time during the pandemic. Concerns about money and finances were present in 24 (48%) families.

In relation to COVID-19 risks, only a small subset (28%) felt that epilepsy increased the risk of COVID-19, and 13 (26%) felt that epi-

lepsy prevented them from doing certain activities during COVID-19 compared to other kids their age. However, 46 (92%) felt that coming to the hospital would increase their risk of contracting COVID-19. Twelve (24%) patients knew someone with a confirmed COVID-19 infection and one (2%) knew someone with a suspected infection. Five (10%) children spent at least 1 hour per day on COVID-19 updates specifically.

3.3. OCS

Thirty-six percent reported above average concern about contracting COVID-19 and the mean (SD) OCS total score was 2.20 (2.68), suggesting that most did not have excessive persistent disturbing thoughts about COVID-19. Three patients' total scale score were ≥ 7 , which indicates probable dysfunctional thinking about COVID-19. On sub-analysis, for a period of several days or more, 8 (16%) had disturbing thoughts that people they saw may have the virus, 13 (26%) could not stop thinking about the virus and 3 (6%) dreamed about the virus.

3.4. CDI 2 and MASC 2 questionnaires

The median pre-COVID-19 CDI 2 total *T*-score was 55.5 [Interquartile Range (IQR) = 49.50, 64.8] (consistent with average functioning) and the median pre-COVID-19 MASC 2 total *T*-score was 58.0 [IQR = 52.8, 69.0] (consistent with high average functioning) (Fig. 1). Pre-COVID-19-pandemic, 13 (26%) had a CDI 2 total *T*-score ≥ 65 , indicative of potentially depressed individuals. Twenty-one (42%) had a MASC 2 total *T*-score ≥ 60 , indicative of increased likelihood of an anxiety disorder. There was no significant difference in the pre-COVID-19 and during COVID-19 total *T*-scores for either test (Fig. 1); the adjusted mean difference for CDI 2 was -0.62 (CI: $-3.13, 4.38$); $p = 0.106$ and for MASC 2 was -0.70 (CI: $-3.33, 4.73$); $p = 0.115$ (Table 1).

For the CDI 2 total *T*-score, 13 (26%) patients had a decrease (improvement) in score, 12 (24%) had an increase (worsening) in score, and 25 (50%) had no change. For the MASC 2 total *T*-score, 13 (26%) patients had a decrease (improvement) in score, 14 (28%) had an increase (worsening) in score, and 21 (42%) had no change. Of the 12 (24%) patients with a worsening CDI 2 total *T*-score, associated factors included a higher total OCS score ($p = 0.001$). Specifically, on the OCS, this group indicated that for several days or more over the course of 2 weeks, they had "disturbing thoughts that [they] may have caught the coronavirus" ($p = 0.045$), "disturbing thoughts that certain people [they] saw may have the coronavirus" ($p = 0.047$) and "[they] could not stop thinking about the coronavirus" ($p = 0.01$). Other associated factors include poor sleep during the pandemic ($p = 0.013$) and previous psychiatric history ($p = 0.045$). Of the 14 (28%) patients with a worsening MASC 2 total *T*-score, associated factors included lower levels of maternal education ($p = 0.022$), less exercise during the pandemic ($p = 0.028$) and "not being able to stop thinking about the coronavirus" on the OCS ($p = 0.008$). For both questionnaires, patients with higher total *T*-scores before the COVID-19 pandemic were associated with resilience (unchanged or improved scores) ($p < 0.001$).

4. Discussion

4.1. Mood/anxiety

Pandemic-related depression and anxiety have been studied in epilepsy populations with heterogeneous ages, geography, lockdown measures, seizure types, comorbidities and screening tools. Some studies have shown moderate to high proportions of mood

disorders, including new onset anxiety, depressive symptoms and increased psychological distress in people with epilepsy during the pandemic [16–20]. However, a survey-based study found depression rates were similar in people with and without epilepsy; reported in 19% of people with epilepsy compared to 17% of controls [18]. The timing of assessing symptoms may also be of importance. One group compared the initial peak of COVID-19 and mid-pandemic and noted that depression rates increased significantly after the first wave [22]. Our questionnaires were administered once, at variable times over a 1-year period, and therefore the time of testing was not standardized in each patient and there may have been variability of symptoms at different time points during the pandemic.

In a multi-country study exploring the prevalence of anxiety and depression in patients with epilepsy during the pandemic, 50.4% had anxiety symptoms and 39.8% had depressive symptoms [21]. However, no comparison was made to pre-pandemic scores. In a study similar to ours, comparing emotional and lifestyle changes before and during the COVID-19 pandemic, respondents reported statistically significant higher levels of anxiety, weakened social support network strength and perceived isolation during the pandemic than pre-pandemic [23]. Our results may differ due to the fact that most subjects continued to have the same or more interaction with family and friends. In addition, we specifically studied a group with SLE and GGE, as opposed to a heterogeneous epilepsy population. In addition, our patients had regular virtual follow-up appointments, were treated in one tertiary care center in a high-income country and had high levels of maternal education, which may have impacted comorbidities. The degree of regional pandemic-related restrictions may also lead to differences amongst studies. For example, our cohort continued to have access to outdoor spaces and exercise.

It has been suggested that people with previous psychological disorders are more vulnerable to depression, anxiety disorders, post-traumatic stress disorder, psychotic disorders and suicide due to fear of COVID-19 [16,18,24]. The majority in our group did not have severe pre-existing psychiatric disorders. However, we observed that a pre-existing history of psychiatric disorders was associated with a higher COVID-19 CDI 2 total *T*-score.

Seizure control can also impact comorbidities. Hao et al. reported that patients with epilepsy, especially drugological-resistant epilepsy, reported more psychdistress than healthy controls [26]. The no change in mood and anxiety in our population may be due to the fact that most patients in our cohort had well-controlled or infrequent seizures.

4.2. Pandemic-related anxiety

New pandemic-related anxieties also emerged in a subset of patients. The majority (92%) were worried that hospital visits increase COVID-19 infection risk. However, positive findings are that only a minority (26%) had concerns to making changes to ASMs during the pandemic and only 6% had an OCS score in the dysfunctional range, which is consistent with general population studies ranging from 5.5 to 10.5% [27,28]. Previous COVID-19 studies found that fears regarding epilepsy in general were present in 19.6–23.9% of respondents [16,20]. Although not addressed in our study, another study noted that people with epilepsy reported moderated to severe worries concerning lack of professional consultation (41.2%), and medication supply (48.62%) [20].

4.3. Seizures and ASM

Only 6 (12%) of our patients noted an increase in seizure frequency during the pandemic. Our finding corresponds with the literature, where seizure exacerbation rates varied between

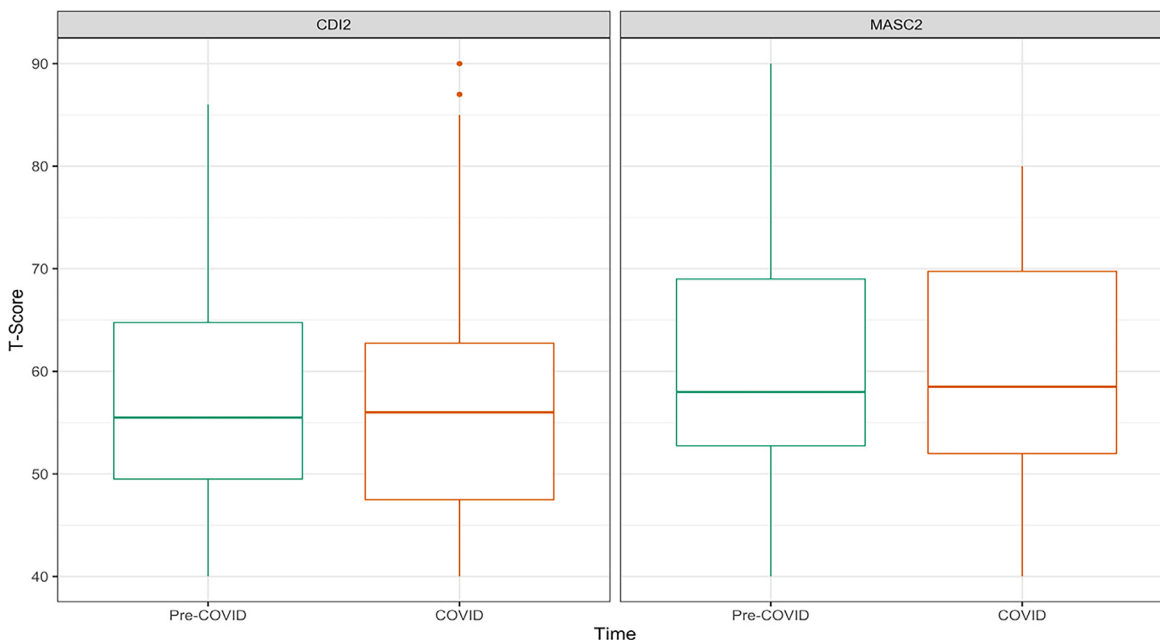


Fig. 1. Comparison of pre-COVID-19 (green) and COVID-19 (orange) CDI 2 and MASC 2 median total T-scores in 50 patients. There was no significant difference in pre-COVID-19 and COVID-19 CDI 2 and MASC 2 median total T-scores.

populations; however, the majority of people surveyed reported unchanged seizure frequency during the pandemic. In most populations, seizures worsened during the COVID-19 pandemic in a minority (<10% in people with epilepsy) [16,17,20,24,25,29], a finding that may also reflect the natural fluctuations of epilepsy itself.

In studies that demonstrate worsening of seizures during the pandemic, worsening was significantly associated with several seizure and epilepsy factors: drug-resistant epilepsy [16,20], number of ASMs [16,18], not being seizure-free [18] or having more seizures at baseline [16,20]. In one study, tonic-clonic seizures during the COVID-19 pandemic [18] and tumor-related etiology [16] were associated with worsening. The fact that a minority of our patients experienced seizure worsening could be related to the fact our patients had overall well-controlled seizures and few ASMs.

Others have also noted that seizure worsening was associated with a history of depression, anti-depressant use, and more severe depression and anxiety symptoms [18]. Again, our population differs, as they did not have severe baseline depression and anxiety (8% were on an antidepressant and 2% on an antipsychotic medication).

4.3. Sleep, social interaction and exercise

In our Previous COVID-19 pandemic studies show significant sleep disruption in epilepsy patients, which can be associated with worsening of seizures [16–18]. In our study, one third of our cohort reported worse sleep during the COVID-19 pandemic. However, there was no association between sleep disruption and seizure exacerbation. However, patients with a worsening CDI 2 total T-score had a higher incidence of sleep disturbances.

In a study exploring psychological resilience during the pandemic, more time spent outdoors, exercise, sleep, prayer, and perception of social support from family and friends were associated with resilience [30]. In our cohort, the majority did not have a decline in interactions with family and friends, had regular Neurology follow-up visits, exercised the same or more than before the pandemic and had access to outdoor spaces. These factors may

contribute to our patients' resilience. Notably, decreased exercise during the pandemic was associated with a worsening MASC 2 total T-score in our cohort.

Limitations of this study include a small sample size of patients followed at a single tertiary care center. A control group of patients without epilepsy would have strengthened the study. There may have been selection bias, where participants choosing to join the study differ from those that chose not to. Most patients in the study had well-controlled seizures, came from families with overall high maternal education, and had regular medical care during the pandemic, which may have impacted the incidence of comorbidities. Patients with newly diagnosed epilepsy were not included, affecting generalizability of this cohort. In addition, the questionnaires were administered once over a 1-year period and symptoms may vary over time.

5. Conclusions

No worsening in mood, anxiety or seizure frequency were observed in patients during the COVID-19 pandemic compared to before the pandemic. Furthermore, the majority of patients did not have dysfunctional thinking about COVID-19. Therefore, as a whole, this cohort was resilient to COVID-19-related changes and threats. Based on our results and review of the literature, in the majority, high maternal education, maintenance of sleep quality, exercise, access to outdoor space, social interactions with friends and family during the pandemic, and relatively low pre-existing psychiatric disease and seizure burden might be contributing factors to this resilience. Regular screening of emotional comorbidities and lifestyle changes in this population are still of upmost importance during the pandemic, as some individuals are more psychologically resilient to adversity than others. In addition, some factors for emotional resilience or dysfunction in the face of the pandemic may be related to modifiable factors, such as exercise and sleep.

6. Ethical Statement

The study was approved by the institutional ethics board and informed consent (patients < 19 years of age) and assent (patients ≤ 18 years of age) was obtained for all patients. The authors confirm that we have reviewed the Journal's position on issues involved in ethical publication, and the work is in compliance. H20-02049.

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Statement of Authorship

SK participated in identifying eligible patients. She administered the questionnaires and helped to analyze the data. She reviewed, and edited the manuscript for important intellectual content. JE provided guidance in study design and analysis and reviewed, and edited the manuscript for important intellectual content.

AD developed the original concept and study design of the manuscript. She helped to analyze the data, drafted the manuscript, and then reviewed, and edited it for important intellectual content. All authors gave approval to the final version of the manuscript to be submitted and all authors are in agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ebr.2021.100520>.

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