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Pandemic-associated mental health changes in youth with neuroinflammatory disorders

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ABSTRACT

Background: Children with neuroinflammatory disorders have high rates of anxiety and depression, alongside low rates of physical activity. Given general concerns for mental and physical health in children during the COVID-19 pandemic lockdown, here we sought to understand how sleep, anxiety, depression, and physical activity changed with the lockdown in children with neuroinflammatory disorders. We hypothesized that outcomes would worsen during the lockdown, and that they would differ by underlying disorder category and age.

Methods: Patients attending a specialized neuroinflammatory clinic (n = 314) completed questionnaires (n = 821 responders; Jan 2017-Aug 2020) assessing sleep, anxiety, depression, and physical activity. Respondents had either: childhood-onset chronic or recurrent neuroinflammatory disorders (CRNI), a history of Autoimmune Encephalitis (AE) or Monophasic Acquired Demyelinating Syndromes (monoADS). We performed linear mixed models to examine the association between our outcome measures (sleep, anxiety, depression, and physical activity) and categories of disorder type, sex, age, physical activity, relapses, and time (pre- vs. post- COVID-19 lockdown). Participant ID acted as a random effect, to account for repeated measures.

Results: Sleep significantly increased in the first 6 months of the COVID-19 lockdown (F(1, 544)=56.85, P<0.001.). Across the whole group, anxiety and depression did not change with the pandemic, but we found differing trends by age category. Anxiety decreased in teenagers (≥13y) (Z = 3.96, P<0.001), but not for pre-teens. Depression remained higher in teenagers than preteens across both timepoints (F(1, 597)=6.30, p = 0.012). Physical activity levels did not change with the pandemic in comparison to pre-pandemic (F(1, 629)=1.92, P = 0.166). Anxiety was higher in inactive individuals regardless of timing (F(2, 567)=3.74, p = 0.024).

Conclusion: For youth with neuroinflammatory disorders, the COVID-19 pandemic lockdown resulted in increased hours of nighttime sleep but did not result in significant overall changes in self-reported anxiety or depression. Pre-lockdown, teenagers had higher depression and anxiety scores than preteens. Post-lockdown, anxiety and depression scores decreased in teenagers compared to pre-teens. Physical activity was low both pre- and post-lockdown, and rates of anxiety were higher for inactive participants at both timepoints. Differences based on age suggest that younger children (<13 years) were more negatively affected by the pandemic than older children (≥ 13 years).

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1. Introduction

Mental health challenges are common in children with neuroinflammatory disorders: up to 75% of children with MS suffer from fatigue and depression (Amato et al., 2010; Carroll et al., 2016). Additionally, children with neuroinflammatory disorders have lower rates of physical activity compared to healthy children, and fall below the standards for national physical activity recommendations (Carson et al., 2017; Grover et al., 2016). Reduced physical activity is correlated with higher levels of mental distress in children (Korczak et al., 2017).
This is especially pertinent for children with Multiple Sclerosis (MS) – where increased physical activity has been associated with lower levels of neuroinflammatory disease activity, reduced levels of depression, and reduced fatigue (Grover et al., 2016, 2015).

An important promoting factor for physically active behaviours in children with neuroinflammatory disorders is social connectedness (Ly et al., 2021). Unfortunately, the pandemic lockdown in Ontario, Canada, drove many changes to social structure: in-person school, programs, and sports were all either canceled or switched to virtual environments (Office of the Premier, 2020). In many communities around the world, such COVID-19 pandemic lockdowns brought reports of increased anxiety (Fegert et al., 2020; Marques De Miranda et al., 2020), as well as decreased physical activity (Guerrero et al., 2020; Hemphill et al., 2020) in both healthy children and those with chronic disease. Given these concerns, we sought to understand how the pandemic lockdown specifically affected mental health and physical activity in children with neuroinflammatory disorders. Our second objective was to understand if there were any factors that were associated with mental health and physical activity changes, if present.

We speculated that during the lockdown, for children with neuroinflammatory disorders, anxiety and depression would worsen. We hypothesized that this would be secondary to decreased levels of physical activity juxtaposed with an increased sense of isolation, as links between mental health and physical activity have been established in pediatric MS in our previous research (Ly et al., 2021; Stephens et al., 2019). To evaluate these hypotheses, we compared the levels of sleep, anxiety, depression, and physical activity pre- and post-COVID-19 lockdown in youth with pediatric neuroinflammatory disorders. We also evaluated how these outcomes related to age and disorder category. Our hypothesis was that the outcomes would be worse for younger children and those with chronic and recurrent neuroinflammatory disorders.

2. Methods

2.1. Data collection

This study was approved by the REB at the Hospital for Sick Children (REB #1,000,005,356). After providing informed consent, consecutive patients seen at a specialized pediatric neuroinflammatory clinic at a tertiary regional referral center were provided with questionnaires at the time of their appointment, either online via REDCap (Harris et al., 2019, 2009) or on paper. We assessed sleep using the Children’s Sleep Habits Questionnaire (CSHQ). Depression was evaluated by the Center for Epidemiologic Studies Depression Scale for Children (CES-DC), a 20-item questionnaire with 4-point Likert scale answer choices, a maximum score of 60 and a cut-off for clinically significant depression of scores greater than or equal to 15 (Faulstich et al., 1986; Fendrich et al., 1990). Anxiety was measured using the Screen for Child Anxiety Related Emotional Disorders (SCARED), a 41-question screening tool with 3-point Likert responses, a maximum score of 82 and for which scores greater than or equal to 25 are indicative of an underlying anxiety disorder (Birmaher et al., 1997). The Godin Leisure-Time Exercise Questionnaire, which has been validated in individuals with pediatric MS (Kinnett-Hopkins et al., 2016), was used to examine physical activity behavior. This questionnaire estimates weekly units of time spent in mild, moderate, and vigorous physical activity. We calculated a composite Health Contribution Score (HCS), reflective of the moderate and vigorous physical activity that contributes to health status (Grover et al., 2015).

2.1.1. Inclusion and exclusion criteria

We included participants diagnosed with a neuroinflammatory disorder prior to age 18, who completed questionnaires between January 1, 2017-August 31, 2020. A cut off date of August 2020 was selected due to the change in public health policy to allow for schools to return to in-person learning and to account for regional differences in public health restrictions.

Neuroinflammatory disorders were defined by criteria outlined by the International Pediatric Multiple Sclerosis Study Group (Krupp et al., 2013), and separated into the following categories: 1) Monophasic Acquired Demyelinating Syndrome (MonoADS): which involved events consisting of a single discrete episode of demyelination (e.g., Transverse myelitis (TM), Optic Neuritis (ON)); 2) Chronic and Recurrent Neuroinflammatory Disorders (CRNI): which included NMOSD, recurrent Myelin Oligodendrocyte Glycoprotein Antibody Disorder (MOGAD), Multiple Sclerosis (MS) and other systemic disorders involving CNS inflammation such as Lupus or vasculitis; and 3) Autoimmune Encephalitis (AE) (Graus et al., 2017): including Opsoclonus Myoclonus Ataxia Syndrome (OMAS) (Pranzatelli, 2009), or Anti-NMDAR encephalitis.

We excluded respondents greater than 20 years of age, unknown or non-inflammatory diagnoses, as well as entries completed within 4 weeks of relapse or disease onset.

2.2. Data analysis

The data were divided by date into two time-points (pre versus post-lockdown) with the cut-off of March 17, 2020, representing the start of the pandemic lockdown (declaration of the state of emergency in Ontario, Canada (Office of the Premier, 2020)). For each response, we divided individuals with recurrent conditions into two relapse categories: those with at least two recorded relapses (recurrent), and those without (non-recurrent). Physical activity level was denoted by HCS score, separated into 3 groups: 1) individuals with scores of 23 or less were classified as “inactive” (Amireault and Godin, 2015); 2) individuals between an HCS of 24 and the whole group 75thile (HCS score of 52): denoted as “active”; and 3) and “very active” (HCS of 53 or higher).

2.3. Statistical analysis

We used JASP © (version 0.14.1) to perform our analysis. Descriptive statistics were performed where appropriate. Linear mixed modeling was used to examine the associations with our outcome measures. Anxiety and depression scores were normalized using a cube-root transformation. For each outcome measure (sleep, anxiety, depression, and physical activity), we performed a linear mixed modeling analysis examining the associations with time point (pre-post COVID-19 pandemic lockdown) while adjusting for disorder category (Chronic and recurrent neuroinflammation (CRNI), Monophasic acquired demyelinating syndrome (MonoADS), and Autoimmune Encephalitis (AE)), age category (≥13/<13), relapses (yes/no),). These variables were included as fixed effects in our model (see supplementary material for full model equations). To account for repeated measures within the same individual (i.e., multiple responses at different time-points), participants were treated as a random effect. Post-hoc groupwise comparisons were conducted to identify differences between disease group or age group, and adjusted using the Holm technique. Data are presented as mean (95% Confidence Interval).

3. Results

We received a total of 821 responses from 314 individuals who satisfied inclusion criteria (Table 1). Across all respondents, the mean age was 13.5 ± 3.6 years, and 59% were female. Participants with chronic and recurrent neuroinflammation (CRNI) were older than those with Monophasic acquired demyelinating syndrome (MonoADS), and Autoimmune Encephalitis (Table 1). Across both timepoints, questionnaires were completed 3.3 ± 3.1 years after diagnosis.

3.1. Nighttime sleep duration increased with the pandemic

Prior to the pandemic, participants reported an average of 9.4 (9.3–9.6) hours of sleep. This increased significantly with the lockdown...
to 10.7 (10.4–11) hours (Table 2). The increase was greater for teenagers, with a post-lockdown average of 1.7 h longer sleep time than pre-lockdown. For preteens, mean sleep was 0.7 h greater post-lockdown vs. AE, Table 2).

3.1.1. High baseline levels of anxiety remained unchanged in the first 6 months of the pandemic

Nearly one-quarter of our participants met the cut-off for clinically significant anxiety. Raw anxiety scores did not change pre- vs. post-lockdown, after accounting for disorder category, age category, relapse category, and physical activity level (Table 2). Further, there was no difference in anxiety by disorder category (MonoADS vs. CRNI vs. AE, Table 2).

3.1.2. Anxiety decreased in older children with the lockdown

We found an interaction effect between pandemic and age, indicating discrepancies between anxiety scores as they related to the lockdown in pre-teens (<13 years) and teenagers (≥13 years, F(1, 584) = 10.98, p < 0.001). Mean anxiety scores for pre-teens were on average 2.5 points higher after the lockdown than the mean score for pre-teens before the lockdown (z = 0.99, p = 0.324, Fig. 2, Table 2). In contrast, the mean anxiety score for teenagers was 4 points lower post-lockdown than the corresponding pre-lockdown score (z = 3.96, p < 0.001, Fig. 2, Table 2).

3.1.3. Children with higher levels of activity have lower anxiety scores

Both pre- and post-lockdown, respondents who were classified as “inactive” (HCS < 24) reported higher anxiety in comparison to youth who were classified as “very active” (HCS > 52; F(2, 547) = 3.74, p = 0.024; Fig. 3).

3.1.4. High baseline levels of depression remained unchanged in the first 6 months of the pandemic

The proportion of participants meeting the cut-off for clinically significant depression (Fig. 2) did not change after the lockdown. Similarly, whole-group raw depression scores did not change after the lockdown (F(1, 659) = 0.51, p = 0.477) (Fig. 3). Depression scores did not differ by disorder category (F(1, 640) = 0.81, p = 0.447, Table 3).

3.1.5. Teenagers were significantly more depressed than pre-teens

Depression scores were significantly lower for pre-teens than teenagers after adjusting for pandemic onset, disorder category, relapse category, and physical activity level (F(1, 630) = 5.15, p = 0.024). Similar to anxiety, we also found a significant interaction between age category and depression scores pre- vs post-lockdown (F(1, 691) = 4.05, p = 0.045, Fig. 3, Table 3), with the pandemic having a different effect on levels of depression for teenagers versus pre-teens.

3.2. Physical activity levels did not change with the pandemic

Physical activity levels did not change after the lockdown (F(1, 629) = 1.92, p = 0.166, Table 2). Males were more active than females at all time points (Table 2). There were no age or disorder category differences between physical activity, but children with clinically significant anxiety reported significantly less physical activity than children without anxiety (F(1, 641) = 5.15, p = 0.024).

4. Discussion

In this study, we evaluated sleep, anxiety, depression, and physical activity before and after the COVID-19 pandemic lockdown in children with neuroinflammatory disorders. Contrary to our expectations, we did not find any overall change in anxiety, depression, or physical activity.
Table 2
Results by category and timepoint (represented as: mean (95% Confidence Interval per model, calculating using raw scores). Significant results (p<0.05) are represented in bold typeface. Though the means and confidence intervals are all reported per the raw data from the surveys, asterisks (*) indicate that the scores were normalized for statistical analysis in the reported models.

| VARIABLE                  | CATEGORY          | PRE-LOCKDOWN MEAN (95% CI) | POST-LOCKDOWN MEAN (95% CI) | STATISTICAL COMPARISON |
|---------------------------|-------------------|----------------------------|-----------------------------|------------------------|
| SLEEP (HOURS)             |                   |                            |                             |                        |
|                           | ALL               | 9.4 (9.3-9.6)              | 10.7 (10.4-11)              | \( F(1, 544) = 56.85, \ p<0.001 \) |
|                           | Pre-teen (<13)    | 10.1 (9.9-10.4)            | 10.8 (10.4-11.3)            | \( z = 3.19, \ p<0.001 \) |
|                           | Teenager (13+)    | 8.8 (8.6-9)                | 10.5 (10.2-10.8)            | \( z = 8.86, \ p<0.001 \) |
|                           | Statistics: Age category |                     |                             |                        |
|                           | Interaction: Age Category/Time Category | \( F(1, 463) = 30.40, \ p<0.001 \) | \( F(1, 360) = 12.69, \ p<0.001 \) |                        |
| ANXIETY (RAW SCORES) SCARED SCALE (0-82) SCORES GREATER THAN 0 TO 25 SIGNIFY CLINICALLY SIGNIFICANT ANXIETY |                   |                            |                             |                        |
|                           | ALL               | 17.3 (15.2-19.3)           | 15.6-13.1-18.2              | \( F(1, 151) = 3.226, \ p=0.073 \) |
|                           | MonoADS           | 15.7 (12.4-18.9)           | 14.0 (10.5-17.5)            | \( z = 0.44, \ p=0.665 \) |
|                           | AE                | 18.9 (15.5-22.3)           | 17.3 (13.5-21.0)            | \( z = 1.57, \ p=0.233 \) |
|                           | GRN               | 17.3 (14.5-20.1)           | 15.7 (12.3-19.0)            | \( z = 1.91, \ p=0.170 \) |
|                           | Statistics: Disorder Category |                     |                             |                        |
|                           | Interaction: Age Category/Time Category | \( F(2, 575) = 3.74, \ p=0.024 \) | \( F(1, 360) = 10.98, \ p<0.001 \) |                        |
|                           | Inactive          | 18.7 (16.5-20.9)           | 17.1 (14.4-19.7)            | \( z = 0.31, \ p=0.757 \) |
|                           | Active            | 17.1 (14.7-19.5)           | 15.4 (12.6-18.2)            | \( z = 1.24, \ p=0.431 \) |
|                           | Very Active       | 16.1 (13.6-18.5)           | 14.4 (11.5-17.4)            | \( z = 1.91, \ p=0.170 \) |
| EDESS (HOURS)             |                   |                            |                             |                        |
|                           | ALL               | 13.5 (12.0-15.0)           | 13.5 (11.3-15.7)            | \( F(1, 151) = 0.51, \ p=0.477 \) |
|                           | MonoADS           | 12.0 (9.5-14.5)            | 12.5 (9.5-15.6)             | \( z = 0.92, \ p=0.373 \) |
|                           | AE                | 14.5 (12.0-17.0)           | 13.4 (9.5-17.2)             | \( z = 0.76, \ p=0.473 \) |
|                           | GRN               | 14.1 (11.9-16.3)           | 14.5 (11.2-17.9)            | \( z = 1.32, \ p=0.556 \) |
|                           | Statistics: Disorder Category |                     |                             |                        |
|                           | Interaction: Age Category/Time Category | \( F(2, 575) = 0.81, \ p=0.447 \) | \( F(1, 360) = 0.045 \) |                        |
|                           | Pre-teen (<13)    | 11.4 (9.4-13.5)            | 12.8 (9.8-15.7)             | \( z = 1.81, \ p=0.140 \) |
|                           | Teenager (13+)    | 15.6 (13.8-17.4)           | 14.2 (11.5-16.8)            | \( z = 0.96, \ p=0.336 \) |
| EDESS (HOURS)             |                   |                            |                             |                        |
|                           | ALL               | 34.5 (31.1-38.0)           | 31.3 (26.3-36.3)            | \( \text{Continued on next page} \) |

(continued on next page)
Table 2 (continued)

| VARIABLE | CATEGORY  | PRE-LOCKDOWN MEAN (95% CI) | POST-LOCKDOWN MEAN (95% CI) | STATISTICAL COMPARISON |
|----------|-----------|-----------------------------|-----------------------------|------------------------|
|          | Male      | 38.8 (34.1–43.5)            | 35.6 (29.7–41.4)            | z = 1.39, p = 0.332    |
|          | Female    | 30.2 (26.3–34.2)            | 27.0 (21.6–32.4)            | z = 1.39, p = 0.332    |
|          | Statistics | Sex Category              |                             | F (1, 278) = 10.41, p = 0.001 |

Fig. 1. Reported number of hours of sleep per night, pre-pandemic and during the pandemic, plotted by age: under-13 years old (blue) and 13-and-over (red).

Fig. 2. Anxiety and depression (total raw scores for the SCARED and CES-DC questionnaires) plotted by time (pre-lockdown vs post-lockdown) and age category: under-13 years old (blue) and 13-and-over (red). Means and error bars per model, gray shaded regions represent the thresholds for clinically significant scores for Anxiety (SCARED (Birmaher et al., 1997)) and depression (CES-DC (Faulstich et al., 1986)). Note that above data displayed is the raw data, not the cube-root transformed data, for ease of interpretation.
with the lockdown. When the results were analyzed by age group, we found that anxiety decreased in teenagers but remained stable in preteens. Other notable findings include higher levels of anxiety in inactive individuals regardless of timing of questionnaire in relation to the COVID-19 lockdown, and an increase in sleep in all children.

The stability in self-reported mental health in our cohort pre- vs. post-lockdown contrasts with reports of increases in mental health problems in healthy children during the pandemic (Chanchlani et al., 2020; Cost et al., 2021). Notably, however, pre-lockdown rates of clinical anxiety and depression (according to our questionnaires) in our cohort were high – in the range of 25–35% according to clinical cutoffs for the relevant questionnaires (Birmaher et al., 1997; Faulstich et al., 1986) – which is in keeping with previous reports in specific populations with neuroinflammatory disorders such as MS (Parrish et al., 2013; Stephens et al., 2019). These rates are higher than rates of formally diagnosed of depression (3%) and anxiety (7%) seen in healthy children in the United States (Ghandour et al., 2019). Thus, while the early pandemic did not associate with higher rates of mental health problems, it is possible that this is because of the pre-existing high rates of mental health problems in our population. This suggests an urgent need for long term solutions for ongoing mental health issues in children with neuroinflammatory disorders.

Further, our results echo the findings of an Italian study of which found no significant changes in mental health in adults with MS during the early phases of the pandemic (Capuano et al., 2020). In fact, that study showed an increase in self-reported quality of life in adults with MS the early stages of the pandemic. The authors hypothesized that this was secondary to resilience in the population of adults with MS, or to a

Fig. 3. Total depression and anxiety scores plotted by physical activity (all time-points). Red line connects means.
“leveling effect” in the case where adults with MS may have felt less isolated or more socially accepted in their health-related struggles, since the restrictions affected people of all ages and health status (Capuano et al., 2020). We believe that this hypothesis is also relevant with respect to our current findings. It may be that the issues driving anxiety in healthy youth after the start of the lockdown, such as social isolation, were already part of the lived experiences of youth with neuro-inflammatory disorders and therefore did not influence levels of anxiety significantly. Further research is needed to understand whether resilience from experiences related to illness accounts for the lack of change in mental health outcomes.

Importantly, age category was associated with changes in the levels of anxiety and depression level with the pandemic (Fig. 2, Table 2). Teenage children tended to have lower anxiety scores after the lockdown, while pre-teens (<13 years of age), tended to demonstrate higher anxiety scores post-lockdown (Fig. 2). Reasons for this could be that teenagers are more independent in their relationships, their navigation of social media, and schoolwork, whereas pre-teens often rely more on in-person interactions with peers. Teenagers’ use of technology may have allowed them to feel virtually “connected” (James et al., 2017; Wu et al., 2016), despite being at home during the early lockdown. It is also possible that teenagers benefitted from reduced school-related stress, as during the early lockdown, many schools were not fully equipped to transition online—the duration of learning from home was not clear and continued to be graduated extended (Education, 2020). Finally, part of the post-lockdown period under investigation included the summer, a time during which most youth do not attend school. This may have led to improved mood in teenagers due to reduced school-related stress, as during the early lockdown, many schools were not fully equipped to transition online—the duration of learning from home was not clear and continued to be gradually extended (Education, 2020). Finally, part of the post-lockdown period under investigation included the summer, a time during which most youth do not attend school. This may have led to improved mood in teenagers due to reduced school-related pressures. By contrast, pre-teen summer activities often include opportunities for socialization, such as camps and sports, many of which were canceled with the pandemic, potentially leading to worse mental health outcomes.

Previous research suggests that mental health in youth can be influenced by physical activity (Korczak et al., 2017) and sleep (El-Sheikh et al., 2019). Our finding of increased sleep was not surprising, given the reduction in organized activities for children and the shift to on-line learning. These findings are in agreement with studies of healthy children, where small increases in sleep were seen in the early pandemic (Gruber et al., 2020; Guerrero et al., 2020), with adolescents seeming to benefit the most (Bruni et al., 2021). Of relevance, however, increased sleep in our cohort did not associate with significantly improved mental health outcomes. This suggests that while poor sleep itself can be associated with poor mental health outcomes, in our study, increases in sleep were either not enough to overcome symptoms of depression or anxiety—or, alternatively, there are other mechanisms that underlie the high levels of anxiety and depression seen in our cohort. These mechanisms may be multifactorial with a biopsychosocial underpinning.

As for physical activity, we again demonstrated an association between greater levels of physical activity and favorable mental health outcomes (Fig. 3, (Korczak et al., 2017; Stephens et al., 2019; Tyson et al., 2010)). In contrast to our hypothesis that physical activity would decrease during the lockdown, we found no overall change in physical activity. Reasons for this may include a very low baseline level of physical activity, as we have previously described (Grover et al., 2015; Ly et al., 2021; Stephens et al., 2019). Canadian movement guidelines for children suggest at least 60 min per day of moderate to vigorous physical activity, with at least 3 days per week being vigorous (Tremblay et al., 2016), corresponding to a HCS score of 188. The mean scores for our sample (in the mid-30s) are far below this, highlighting the marked level of inactivity in our cohort (Fig. 3). Others have shown a reduction in time spent in organized sports during COVID-19 but an increase in habitual physical activity (Schmidt et al., 2020). Previous work from our group has also found an association between physical activity self-efficacy and physical activity level (Grover et al., 2016). Further work has emphasized the centrality of social support and relationships in increases in daily physical activity (Ly et al., 2021). Thus, even though physical activity did not decrease with the pandemic—and many individuals likely engaged in some form of habitual physical activity—the lack of increased daily physical activity in our cohort likely related back to pre-existing low levels of physical activity, self-efficacy and less social support for increased physical activity. This is the subject of future research.

Strengths of our study include a relatively large cohort and longitudinal sample. Limitations include the greater number of pre-lockdown compared to post-lockdown questionnaires which could have modified the outcome. Additionally, there is possible bias introduced by the voluntary nature of questionnaire completion. Children were given questionnaires prior to clinic visits, and the frequency of clinic visits was variable in children. Issues such as socioeconomic status, underling disease state, and underlying anxiety and depression may have influenced participants’ willingness to complete the questionnaires. Other limitations relate to the questionnaires themselves. Some questions in our standardized anxiety questionnaire related to school. As children were no longer required to attend school in person, these questions may have been less relevant/less reflective of their mental health status, particularly in relation to social anxiety. Furthermore, some answers may have been biased towards parental rather than the child’s interpretation. We did not take account of parental assistance with questionnaire completion, but this may have been a factor, particularly for younger children. Other literature has consistently shown discrepancies between parental and child assessments of outcomes such as quality of life in children with demyelinating disorders (Schwartz et al., 2018).

In sum, the early lockdown did not result in increases in the already high rates of mental health problems in children with neuro-inflammatory disorders. It is crucially important to understand the basis of mental health challenges in these youth. Previous work suggests that multiple environmental, social and disease related factors contribute (Ly et al., 2021; Sikes et al., 2019, 2018; Stephens et al., 2019). Studies that further evaluate reasons for the high rates of mental health problems in children with neuroinflammatory disorders, and interventions for improvement, are currently underway.

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Lindsey M Logan: Conceptualization, Methodology, Data curation, Formal analysis, Visualization, Writing – original draft. Samantha Stephens: Conceptualization, Methodology, Formal analysis, Visualization, Writing – review & editing, Supervision. Beyza Ciftci-Kavlioglu: Conceptualization, Methodology, Formal analysis, Writing – review & editing. Tara Berenbaum: Investigation, Conceptualization, Methodology, Project administration. Mina Ly: Investigation, Data curation, Formal analysis, Writing – review & editing, Project administration. Giulia Longoni: Conceptualization, Formal analysis, Writing – review & editing. E Ann Yeh: Conceptualization, Formal analysis, Visualization, Writing – review & editing, Supervision.

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Supplementary materials

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