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Original Article

# Sleep Problems in Children With Agenesis of the Corpus Callosum

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ABSTRACT

**BACKGROUND:** Very little is known about sleep habits in children with agenesis of the corpus callosum (ACC). The purpose of this investigation was to evaluate sleep problems in children with ACC and examine the association with quality of life. **METHODS:** We performed a cross-sectional, anonymous, internet-based survey offered to parents of children with ACC, aged five to 18 years. The Children's Sleep Habits Questionnaire (CSHQ) and pediatric quality of life (PedsQL) were used to assess sleep habits and quality of life, respectively. Associations between the total and all subdomains of CSHQ and PedsQL were tested. **RESULTS:** The final sample included 66 parents of children with ACC. Overall, 78% of the children had clinically significant sleep problems, using a cutoff score of 41 on the CSHQ. Compared with a prior national sample of typically developing children, children with ACC scored significantly higher overall and in all subdomains of the CSHQ. The overall CSHQ and PedsQL were moderately correlated ($r = -0.485$, $P < 0.001$), indicating that children with more sleep problems had worse quality of life. In addition, the total CSHQ correlated with all subdomains of the pediatric quality of life, including emotional ($r = -0.515$, $P < 0.01$), social ($r = -0.394$, $P < 0.01$), physical ($r = -0.263$, $P < 0.01$), and school ($r = -0.362$, $P < 0.01$). These associations remained statistically significant in multivariable regression models controlling for age and gender. **CONCLUSIONS:** Sleep problems are common and associated with lower quality of life in children with ACC.

***Keywords:*** agenesis of the corpus callosum, sleep habits, quality of life

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## Introduction

The corpus callosum is the largest connective structure in the brain and serves to transfer information between the cerebral hemispheres.[1] As such, the corpus callosum plays an important role in physical and cognitive development. Agenesis of the corpus callosum (ACC) is a common congenital brain malformation, occurring in approximately one in 4000 live births and with a prevalence of 3% to 5% among individuals assessed for neurodevelopmental disorders.[1] ACC may result in physical or cognitive delays, epilepsy, vision impairment, and social challenges.[2] The etiology of ACC is incompletely understood and heterogenous. Many different underlying conditions can result in ACC, and this is reflected in the wide variability in associated additional brain malformations and clinical manifestations.

Although ACC can have substantial impacts on developmental trajectory, it may also be associated with other health issues. Doherty et al.[3] examined a sample of almost 200 children with ACC and compared their health issues with those of their siblings. Although the children with ACC had a variety of health-related issues, sleep was a major problem. Individuals with ACC had significantly more difficulty with getting to sleep, nighttime awakenings, and enuresis. Sleep problems were also found in a sample of children with ACC examined by Badaruddin et al.[4] In fact, on their Child Behavior Checklist, among children aged two to five years, the only behavioral domain in which there was a greater than expected proportion of children exceeding a

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clinical cutoff was in the sleep problems' symptom scale. A subsequent study that included questions related to sleep in children aged five years and older found significantly greater problems with getting to sleep and enuresis compared with their typically developing siblings.[5]

Few prior studies have examined sleep in children with ACC. Children with ACC have been found to have decreased interhemispheric coherence on electroencephalograph during sleep,[6,7] greater percentage of N3, lower percentage of N2, and more frequent but shorter rapid-eye movement (REM) periods.[8] The increased N3 sleep may be related to increased synchronization of neuronal populations within hemispheres.[8] The altered ultradian structure in terms of REM sleep is also interesting because individuals with ACC have been found to recall fewer dreams and have a greater proportion of contentless dreams.[9] In addition, there is a report of an individual with ACC who developed narcolepsy with cataplexy,[10] a disorder of REM sleep intruding into wakefulness.

Although the handful of studies cited previously have found that sleep problems in children with ACC are common, there is a relative paucity of data regarding specific sleep characteristics within this population or possible association with quality of life. Therefore, the purpose of the present investigation was to help more fully elucidate sleep concerns in this population and any possible association with quality of life measures.

## Methods

### Subjects

Participants were recruited by posting a survey invitation on an ACC listserv support group, which serves families of children with ACC and has more than 700 members. In addition, the invitation encouraged others, such as professionals serving families of children with ACC, to inform parents of the survey. The survey was web-based, anonymous with no identifiers collected, and responses were recorded and stored on a secure server in Research Electronic Data Capture (REDCap). Participants were limited to parents aged greater than 18 years having a child with ACC aged between five and 18 years of age. The parent had to have access to the internet. There were no exclusion criteria other than age. There were no direct benefits offered to parents or children for participation.

### Measures

Basic demographic information was elicited, including age, gender, country of residence, and which parent completed the survey. Parents were asked if their child had any of the following comorbidities or characteristics: well-controlled seizures, not well-controlled seizures, gastroesophageal reflux disease (GERD), hydrocephalus requiring surgery, partial or total blindness, congenital heart disease, autism spectrum disorder, and developmental delay. Complete versus partial ACC, as well as other potential associated brain malformations, were queried. Finally, parents were asked if their child had ever had an overnight sleep study, been diagnosed with sleep apnea, had surgery to remove tonsils, or used a continuous positive airway pressure machine.

Sleep characteristics were measured via the Children's Sleep Habits Questionnaire (CSHQ), which measures the eight sleep domains of bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep-disordered breathing, and daytime sleepiness.[11] The CSHQ is a comprehensive, parent-report sleep questionnaire that has been demonstrated to have adequate internal consistency, test–retest reliability, and validity across community and clinical samples.[11] Each question within subdomains asks about the frequency of a specific sleep habit for more than the course of a week; some items require reverse scoring, and all are summed to obtain total and subdomain scores. A total CSHQ score is calculated, with higher scores indicating more sleep problems and a cutoff of 41 considered as indicative of clinical sleep problems.[11] This instrument has previously been used in studies examining sleep characteristics of children with neurodevelopmental disorders, such as autism spectrum disorders,[12,13] fetal alcohol syndrome,[14] and Down syndrome.[15]

Quality of life was assessed via the pediatric quality of life (PedsQL) survey. The PedsQL is a short survey instrument that has been used extensively to assess parents' perceptions of health-related quality of life in children with a variety of chronic health conditions. This questionnaire is widely used in quality of life outcomes research and has demonstrated good reliability, internal consistency, and construct validity.[16] Furthermore, the PedsQL has previously been used as an important clinical outcome in major clinical trials assessing the impact of interventions for sleep problems on quality of life in children.[17,18] Parents are asked how frequently their children have a problem with individual items during the last one month. Items are reverse scored and transformed to a 0 to 100 scale, with higher scores indicating better quality of life. A total score and scores in individual domains of physical, emotional, social, and school functioning are calculated.

### Analysis plan

Results were summarized with mean and standard deviation for continuous variables and frequencies for categorical variables. Total and subscale scores on the CSHQ were compared between children aged five to 12 and 13 to 18 years via independent samples $t$ test to assess for developmental differences. Although there was no comparison group of typically developing children in the present study, the younger age group of children from the present study was compared with a previous large national sample of typically developing children in the United States[19]; published means, standard deviations, and sample size made summary-independent samples $t$ tests possible. A total CSHQ score of 41 was chosen as a cutoff to indicate clinically significant sleep problems. Possible associations between sample characteristics and CSHQ scores were explored.

To assess the relationship between sleep habits and quality of life Pearson correlations were calculated between CSHQ and PedsQL scores. To control for any effects of age and gender, multivariable ordinary least squares regression models were built with PedsQL as the outcome, and CSHQ, age, and gender as predictors. Regression models assessed the relationships of total and subscale scores between CSHQ and PedsQL. Standardized regression coefficients and statistically significant relationships were reported.

Statistical tests were two-sided with results considered statistically significant at $P < 0.05$ level. This study was approved by the institutional review board at Children's Mercy Hospital. All data analyses were performed in SPSS (IBM Corp Released 2014. IBM SPSS Statistics for Windows, Version 23.0. IBM Corp, Armonk, NY, USA).

## Results

### Sample characteristics

Of the 86 respondents, 66 completed the survey and were included in analysis. Most (60 of 66, 90%) of the respondents were mothers. Responses were international, with 50 from the United States, eight from Canada, three from Britain, two from Australia, and one each from Brazil, the Netherlands, and Sweden. There were slightly more male than female children with ACC (54%, 36/66), and the average age was 10.89 (S.D., 4.10; range, five to 18) years. Comorbidities and other clinical characteristics of the sample of children are summarized in Table 1.