

Normal Neonatal Sleep Defined: Refining Patient Selection and Interpreting Sleep Outcomes for Mandibular Distraction

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Background: Although polysomnography is paramount when evaluating neonatal airway obstruction, “normal” published references do not exist. We present normative polysomnography data for newborns age 0–1 month. We compare this reference to pre and postoperative sleep data from infants undergoing mandibular distraction osteogenesis (MDO) at this same age.

Methods: Following IRB approval, normative subjects were recruited from our neonatal intensive care unit to undergo nap polysomnography. One blinded sleep physician read all studies. From 2016 to 2019, we prospectively collected sleep data for newborns undergoing MDO.

Results: In total, 22 neonates without airway obstruction provided normative sleep data. Median total apnea-hypopnea index (AHI), obstructive apnea-hypopnea index (OAHI), and central apnea index (CAI) were 7.3, 4.9, and 0.7 events/hour. Median O₂ nadir was 91%. Polysomnography for 13 neonates before MDO and during consolidation showed median preoperative AHI was 38.3, OAHI was 37.0, CAI was 1.9, and median O₂ nadir was 83%. Following MDO, median AHI was 6.1, OAHI was 4.0, CAI was 1.3, and median O₂ nadir was 92.5%. Paired t-tests confirmed significant improvements in all indices; when comparing the postoperative group with the normative group, there was no difference in oxygenation nor any respiratory index.

Conclusions: “Normal” neonates have more obstructive events and lower oxygenation nadirs than previously appreciated. We provide normative nap polysomnography values for this age group and encourage centers with multidisciplinary MDO teams to utilize this data to calibrate patient selection algorithms, inform treatment discussions, and better understand surgical outcomes. Limitations include a small sample size and single institution study. (*Plast Reconstr Surg Glob Open* 2022;10:e4031; doi: 10.1097/GOX.0000000000004031; Published online 19 January 2022.)

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INTRODUCTION

Sleep disordered breathing (SDB) has been demonstrated to have a number of adverse effects on children. These include behavior problems,^{1,2} attention deficit disorders,³ decreased quality of life,⁴ and cardiovascular disease. Polysomnography is the gold standard for diagnosis of SDB in children and adults. A variety of parameters are collected during polysomnography, including respiratory effort and airflow channels that allow for the scoring of central, mixed, and obstructive apneas and hypopneas; pulse oximetry; end tidal or transcutaneous carbon dioxide; electroencephalogram/electrocardiogram readings; and measurement of limb movements.⁵ Other methods of studying SDB in children have been explored, including home pulse oximetry monitoring, but were found to be inferior to formal polysomnography.⁶

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In children, polysomnography is done when there is concern for one or more causes of SDB. Most commonly, these include obstruction due to craniofacial anomalies or adenotonsillar hypertrophy,⁷ hypoventilation disorders associated with muscular weakness, chronic lung disease, narcolepsy, and sleep movement disorders.⁵ Polysomnography characterizes the severity of airway obstruction associated with various hypoplasias of the facial skeleton.^{8,9} This includes Pierre Robin sequence (PRS), a causative triad of micrognathia, glossoptosis, and upper airway obstruction (often also with cleft palate).¹⁰ At the authors' institution, polysomnography is used as part of a decision tree model to guide medical and surgical intervention (such as mandibular distraction) in the neonatal population. Still, there has been limited published *normative* data against which physicians can compare respiratory indices and variability in these first days of life.

In 1992, Marcus et al¹¹ performed overnight polysomnography on 50 healthy children and adolescents ranging in age from 1 to 17 years and published recommendations for normal polysomnography values for children. In comparison with adults, they found children had very few apnea events and recommended that more than one obstructive apnea per hour of sleep be considered abnormal for pediatric patients. Infants less than 1 year of age were not included in this study, and normative polysomnography data for a large cohort of infants have never been published. However, there is a growing realization that infants in the first month of life have different respiratory patterns that gradually reach the norms described for children aged 1 year and older. Daftary et al¹² recently reported polysomnography values for healthy term newborns aged 7–31 days, with an average age at the time of study of 19.3 days and average total AHI of 14.9 events per hour. Our study presents nap polysomnography data for an even younger cohort of infants (including infants younger than 7 days) to further define polysomnography norms for those younger than 1 month of age.

In children older than 1 year of age, overnight polysomnography is considered the gold standard for diagnosis of SDB, though nap polysomnography has been suggested as a screening measure.¹³ Due to the different sleep-wake cycles of infants, nap polysomnography has been reported as a valid measure of infant sleep behavior in a variety of studies.^{13–17} For example, nap polysomnography has been used in infants to evaluate the effects of sleep position on circulation and risk for sudden infant death syndrome.^{18,19} This study presents nap polysomnography values for normal neonates and compares this data with that from infants in the same neonatal intensive care unit (NICU) setting who underwent mandibular distraction osteogenesis (MDO) surgery at our institution.

METHODS

Institutional review board approval was obtained for this prospective study. Subjects for the normative data portion of the study were recruited from the NICU to undergo nap polysomnography. Inclusion criteria were infants who were younger than 1 month of age with gestational age 37

Takeaways

Question: This study seeks to define normal reference values for polysomnography in very young neonates and compare these findings with polysomnography values in similar age neonates being evaluated for mandibular distraction surgery.

Findings: Neonates younger than one month of age normally demonstrate median AHI of 7.3, OAHl of 4.9, and oxygen nadir of 91% on polysomnography; similar values are seen in children who underwent mandibular distraction for neonatal airway obstruction.

Meaning: Normal neonates have more obstructive events and lower oxygenation nadirs than previously appreciated; neonates with airway obstruction who undergo mandibular distraction demonstrate significant improvement and "normal" breathing during sleep (no polysomnography differences when compared to the normative cohort).

and 0/7 to 41 and 6/7 weeks at birth. Exclusion criteria were neonates with any of the following conditions: hemodynamic instability, congenital heart disease, upper airway anomalies, requirement of any oxygen or respiratory support for 24 hours, known genetic anomalies, exposure to or treatment with any narcotic medications, or neurological disorders, including seizures, intracranial hemorrhage, or brain malformations. The following data were collected: admitting diagnosis, patient demographics, central, obstructive, mixed and total apnea-hypopnea indices, pulse oximetry, end tidal carbon dioxide, electroencephalogram, and electrocardiogram. All studies were read by one sleep physician masked to all demographic and clinical variables, including gender, age, diagnosis, and reason for admission to the NICU. [Table 1](#) lists admission diagnoses to the NICU for the normative cohort; all acute issues were resolved before nap polysomnography was performed.

Polysomnography data for infants with PRS and neonatal airway obstruction were also prospectively collected before and during consolidation phase of mandibular distraction surgery performed between 2016 and 2019 at the same institution and by the same surgeon. All MDO patients had mandibular osteotomies and internal distractor placement guided by computer-assisted design and modeling. Distractor activation began on postoperative day 1 in all patients and neonates remained intubated in the NICU for 4–7 days after surgery. Rhythm and rate of distraction was generally 0.6 mm twice per day until extubation and 0.3 mm three times per day after. Postoperative

Table 1. Reason for Admission to NICU for Normative Neonates

Reason for Admission	No. Subjects in Normative Group
Hypoglycemia	5
Rule out sepsis	10
Hyperbilirubinemia	1
Meconium delivery	3
Rule out congenital syphilis	1

nap studies were conducted upon completion of the activation phase of mandibular distraction (distraction devices remained in place). All data were collected and analyzed using REDCap databases and SPSS software (IBM). Independent samples Mann-Whitney U tests and chi-square tests were used to compare the normative and MDO populations; Wilcoxon signed-rank tests were used to compare pre and postoperative values for the MDO cohort. Results with a *P* value of less than 0.05 were considered statistically significant.

RESULTS

Twenty-two neonates without airway obstruction provided normative sleep data (Table 2); median age at polysomnography was 5 days (2–29); and median sleep time was 181.5 mins (68–199.5). Median total apnea-hypopnea index (AHI), obstructive apnea-hypopnea index (OAHI), and CAI were 7.3 (2.0–23.0), 4.9 (1.7–19.1), and 0.7 (0.0–12.4) events/hour. The median O₂ nadir was 91% (78–94).

Of the 23 neonates who underwent MDO from 2016 to 2019, we excluded four neonates who had preoperative polysomnography performed after 1 month of age (40–116 days) and another six syndromic infants who had a skeletal or airway anomaly beyond isolated micrognathia (three Treacher-Collins, two oculo-auriculo-vertebral spectrum, one CHARGE). This left 13 neonates with PRS who underwent MDO with pre and postoperative nap polysomnography, including at least 120 minutes of sleep in three positions (supine, side-lying, and prone). Figure 1 presents pre (Fig. 1A–C) and postconsolidation (Fig. 1D–F) images of a patient; Figure 2 includes his pre (Fig. 2A) and postoperative (Fig. 2B) CT scans. Median age at preoperative study was 7 days (4–31) and median sleep time was 328 min (180–470). Median AHI was 38.3 (12.4–102.7), OAHI was 37.0 (11.5–75.7), and CAI was 1.9 (0.3–17.8). Median O₂ nadir was 83% (65–91). Positional AHI data were obtained for these patients; median supine AHI was 48.3 (13.5–144.3), side AHI was 41.2 (4.6–102.3) and prone AHI was 32.7 (5.0–79.4) (Table 2). Demographic data for both study groups are presented in Table 3; there were no significant differences between the normative and MDO groups with the exception of birth weight. Both groups had median birth weights within the normal range

for term infants. The most likely explanation for the difference is the five infants born to diabetic mothers who were large for gestational age in the normative cohort. Before undergoing MDO, neonates with airway obstruction had significantly worse AHI, OAHI, and O₂ nadir than normative counterparts (*P* < 0.001). There was no significant difference in CAI (Table 2).

Following completion of the activation phase of MDO, the median age of final postoperative polysomnography was 51 days (32–136) (Table 2). The median sleep time was 343 mins (187.5–490.0). In this group, median AHI was 6.1 (0.7–18.8), OAHI was 4.0 (1.0–10.7), and CAI was 1.3 (0.2–10.5). Median O₂ nadir was 92.5% (85–96). Polysomnography data for all groups are presented in Table 2. Wilcoxon signed-rank tests comparing pre and postoperative data were strongly significant for improvements in OAHI, AHI, and oxygen saturation nadir after MDO (*P* < 0.001). When comparing the normative group with neonates after MDO, there was no significant difference in oxygenation nadir or any of the apnea-hypopnea indices (Table 2). Additional medical co-morbidities for the MDO cohort are listed in Table 4.

DISCUSSION

In pediatrics, OAHI greater than 1 is considered abnormal¹¹; this norm has been extrapolated to neonates. Our study validates the growing realization that existing normative polysomnography values do not apply to infants in the first few months of life. In our study, “normal” neonates had more obstructive and central apneic events than previously appreciated, with a median of 4.9 obstructive and 7.3 total apneic events per hour. Furthermore, newborns without airway obstruction still exhibited a wide range of “abnormal” OAHI values (1.7–19.1) and oxygen saturation nadirs (78%–94%). These findings further validate those of Daftary et al¹² in their older population of 30 neonates (median age 19.3 days, median total AHI of 14.5, range 1.0–37.7, range of oxygen saturation nadir 69%–93%). Similar findings have been reported in an older population of German infants who displayed a wide range of obstructive and central apnea events in their early months, decreasing to nearly zero around 6 months of age.²⁰

Table 2. Polysomnography Data for All Groups

Polysomnography Variable	Normative Cohort	MDO Preoperative	<i>P</i>	MDO Postoperative	<i>P</i>
Total sleep time (min)	181.5 (68.0–199.5)	333.0 (180.0–470.0)	<0.001	343.0 (187.5–419.0)	<0.001
Sleep efficiency (%)	70.5 (27.4–84.9)	70.7 (59.8–88.3)	0.873	73.7 (61.1–88.4)	0.657
% Time in REM sleep	49.3 (20.8–73.0)	47.6 (30.8–66.9)	0.585	45.0 (31.7–65.6)	0.363
OAHI	4.9 (1.7–19.1)	37.0 (11.6–75.7)	<0.001	4.0 (1.0–10.7)	0.468
CAI	0.7 (0.0–12.4)	1.9 (0.3–17.8)	0.126	1.3 (0.2–10.5)	0.309
Mixed AHI	0.0 (0.0–0.0)	0.7 (0.0–9.2)	0.286	0.2 (0.0–0.7)	0.500
Total AHI	6.9 (2.0–23.0)	38.3 (12.4–102.7)	<0.001	6.1 (0.7–18.8)	0.569
Supine		48.3 (13.5–144.3)		6.7 (0.7–18.8)	
Side		41.2 (4.6–102.3)		3.6 (0.2–27.6)	
Prone		32.7 (5.0–79.4)		4.7 (0.0–13.4)	
O ₂ Nadir (% saturation)	91 (78–94)	83 (65–91)	<0.001	92.5 (85–96)	0.157
% Time O ₂ saturation < 90%	0.0 (0.00–24.0)	1.9 (0.00–13.0)	0.001	0.0 (0.00–1.4)	0.618
EKG sleep minimum (BPM)	98 (63–139)	110 (71–148)	0.305	117 (95–151)	0.089
EKG sleep maximum (BPM)	169 (136–225)	194 (180–218)	0.001	189 (147–228)	0.015
EKG sleep average (BPM)	131 (101–162)	142.5 (134–170)	0.002	139 (115–171)	0.058

Values represent median (range). *P* values compare MDO and normative groups.



Fig. 1. Neonate before and after mandibular distraction osteogenesis. Preoperative OAHl = 67, oxygen nadir = 74%; Postoperative OAHl = 4, oxygen nadir = 92%. Preoperative (top row, A-C) and postoperative (bottom row, D-F) frontal, profile, and submental views.

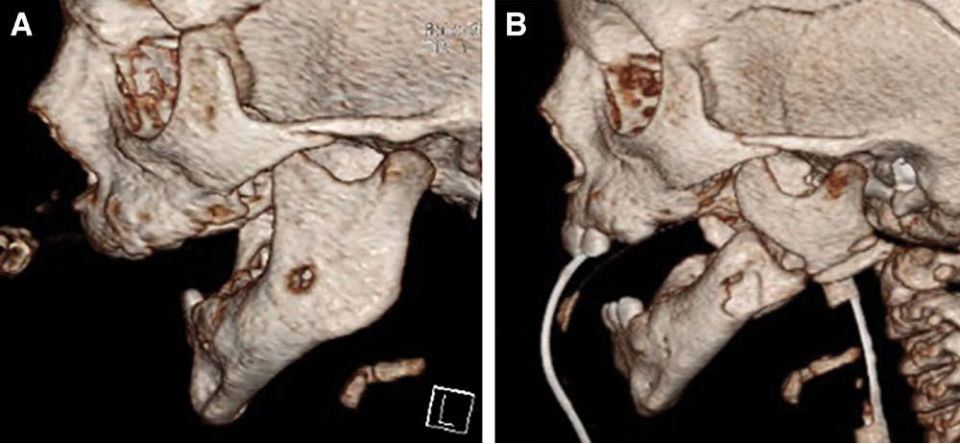


Fig. 2. CT scan of same infant pictured in Figure 1. Preoperative anatomy (A), postoperative anatomy (B).

Table 3. Demographic Data Comparison between Normative and MDO Groups

	Normative Cohort (n = 22)	MDO Cohort (n = 13)	P
Gender			P = 0.829
Male	50.0%	41.7%	
Female	50.0%	58.3%	
Race			P = 0.260 (Fisher exact test)
White	33.3%	41.7%	
Hispanic	23.8%	50.0%	
Black	9.5%	0.0%	
Asian	19.0%	0.0%	
Other	14.3%	8.3%	
*Age at first PSG examination: median (range)	52–29	74–31	P = 0.110
Gestational age at first PSG examination: median (range)	2 (–13 to –17)	4 (–39 to –21)	P = 0.231
Median birth weight (g)	4005 (2210–5320)	3070 (2120–3880)	P = 0.008
Median gestational age (w.d)	39.0 (37.0–41.0)	39.0 (33.0–41.3)	P = 0.231

At our institution, neonates being evaluated for MDO undergo a standardized multidisciplinary preoperative evaluation to determine optimal surgical candidacy. This includes nap polysomnography with 2 hours in each the supine, prone, and side-lying positions, nasoendoscopy to assess severity of glossoptosis, maxillofacial CT scan to visualize the relaxed airway and operative anatomy, capillary blood gas, continuous pulse oximetry, and evaluation of gastroesophageal reflux. This is similar to protocols reported by other institutions^{21–23}. Before this study, our decision tree model for management of neonatal airway obstruction classified an OAHl greater than 15 severe enough to prompt surgical intervention. Many institutions categorize an OAHl greater than 10 (or even less) as abnormal and an indication for surgical intervention.^{21,24,25} In our normative cohort, four of 22 patients (18%) had an OAHl in that range. As our normal infants demonstrated a range of OAHl from 1.7 to 19.1, we have subsequently modified our decision tree model such that an OAHl greater than 20 is considered abnormal; longitudinal monitoring and possible repeat testing are indicated in patients with borderline values. In evaluating for surgery, the whole patient must of course be considered. This includes a comprehensive analysis of patient anatomy, comorbidities, quality/severity of airway obstructions, social situation, and more. In our reported cohort, there was one patient with an OAHl of 11.6 who underwent MDO. This is the only patient in our cohort, with an OAHl less than 20 who underwent surgery, and this was because each of this patient’s apneas and hypopneas were associated with dangerously severe desaturations/bradycardias. Once MDO activation was completed, OAHl was

2.21 and this patient avoided tracheostomy. This again underscores that while our new data are extremely helpful for physicians who are using evidence-based metrics for patient selection, no isolated clinical metric is sufficient to solely rely upon in choosing surgery over nonsurgical management. Polysomnography is a well-tolerated procedure, and its resulting metrics have been well studied, validated, and clinically applied. It is our goal that this study helps guide the clinical applicability of this important tool and refine evidence-based selection of neonatal candidates for MDO.

This study demonstrates that newborns with Pierre Robin sequence (micrognathia, glossoptosis, and airway obstruction) have significantly worse OAHl/AHI and O₂ saturation nadirs than their nonobstructed counterparts. Those who underwent mandibular distraction for PRS exhibited improvement to our newly described normative neonatal sleep values. It is interesting to note that such values might have previously been interpreted as residual neonatal airway obstruction. In longer-term studies of children who underwent MDO as infants,^{26,27} respiratory gains have been sustained. Limitations of this study include the small sample size for the normative population, the single center site, and use of nap polysomnography instead of full overnight polysomnography. In addition, although the sleep studies for the control patients were shorter, they were still of appropriate length for a nap study. Our polysomnography studies were longer in our MDO group only due to evaluation of subjects in various positions (supine, side, and prone); these positional changes were not performed in our control cohort. The percentage of time during each sleep study subjects spent in REM sleep (Table 2) is remarkably consistent between our study and control groups. Because of the nonconsolidated nature of sleep in infants, this consistency is a strong indicator of overall polysomnography consistency despite shorter study times in our normative cohort. The finding that normal early neonatal sleep is not the same as normal infant or pediatric sleep should encourage each center with a multidisciplinary MDO team to consider collecting or studying existing normative neonatal sleep data to reflect their regional population and sleep laboratory. This will enable calibration of existing patient selection algorithms and further inform important discussions with anxious parents.

Table 4. Medical Comorbidities for MDO Cohort

Additional Diagnosis	No. Subjects in MDO Group
Gastroesophageal reflux	5
Anemia	4
Atrial or ventricular septal defect	3
Ventriculomegaly	1
Congenital hip dysplasia	1
Femur micromelia	1
Umbilical hernia	1
Inguinal hernia	1
Club foot	1
Infantile hemangioma	1

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PATIENT CONSENT

Parents or guardians provided written consent for the use of the patient's image.

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