Cerebral Oxygenation During Respiratory Events in Children with Sleep-Disordered Breathing and Associated Disorders

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Objectives To evaluate changes in cerebral oxygenation by means of near-infrared spectroscopy during respiratory events in children with sleep-disordered breathing (SDB) and associated disorders.

Study design Sixty-five children suspected of having SDB underwent a respiratory polygraphy with simultaneous recording of cerebral oxygenation indices. Respiratory events were analyzed by type of event, duration, variations of pulse oximetry (oxygen saturation [SpO_2]), cerebral tissue oxygenation index (TOI), and heart rate. Data were categorized according to the severity of SDB and age.

Results There were 540 obstructive and mixed apneas, 172 central apneas, and 393 obstructive hypopneas analyzed. The mean decreases in SpO_2 and TOI were 4.1 ± 3.1% and 3.4 ± 2.8%, respectively. The mean TOI decrease was significantly smaller for obstructive hypopnea compared with apneas. The TOI decrease was significantly less in children with mild SDB as compared with those with moderate-to-severe SDB and in children >7 years as compared with those <7 years old. TOI decreases correlated significantly with SpO_2 decreases, duration of event, and age, regardless of the type of event. In a multivariable regression model, predictive factors of TOI decreases were the type of respiratory event, SpO_2 decrease, apnea-hypopnea index, and age.

Conclusions In children with SDB and associated disorders, cerebral oxygenation variations depend on the type of respiratory event, severity of SDB, and age. *(J Pediatr 2019;214:134-40)*.

Childhood sleep-disordered breathing (SDB) is associated with neurodevelopmental and behavioral dysfunction which seem to differ according to age.[1,2] Several studies have demonstrated structural brain abnormalities, such as volume reductions in certain cortical areas and changes in brain tissue integrity using magnetic resonance imaging, which correlate with the severity of SDB.[3,4] The mechanisms implicated are hypoxia, alternation of hypoxia-hyperoxia, sleep fragmentation, chronic inflammation, and cerebral blood flow (CBF) variations.[5]

Near-infrared spectroscopy (NIRS) allows a noninvasive monitoring of brain tissue oxygenation by measuring the variations of oxygenated hemoglobin concentration (O_2Hb) and deoxygenated hemoglobin concentration (HHb), allowing the calculation of the tissue oxygenation index (TOI).[6] The TOI reflects the balance between the input and the consumption of cerebral oxygen (O_2) and depends on CBF, hemoglobin rate, and arterial content of O_2 and carbon dioxide.[7]

In adults, several studies have assessed the immediate impact of obstructive events on cerebral oxygenation using NIRS.[8-10] Both amplitude and pattern of hemoglobin variations seemed to be different according to the type of obstructive event.[10] In otherwise healthy children with no comorbidities, both central and obstructive apneas (OA) were found to be associated with a decrease in the TOI.[11] Children with syndromes frequently have sleep disorders that are often severe and one can hypothesize that the underlying pathology may exaggerate the consequences of SDB on the brain.[12] In addition, central and obstructive events differ in terms of both mechanisms and systemic and cerebral hemodynamic consequences.[13] One may, thus, expect that the type of respiratory event may influence changes in cerebral oxygenation. Moreover, cerebral vessels have specific vasoreactivity properties in response to changes in blood pressure, partial pressure of arterial carbon dioxide, and partial pressure of arterial O_2 to modulate CBF to maintain constant nutrient and O_2 supply to the brain.[14] These properties have been shown to be altered in adults and children with obstructive sleep

AHI	Apnea-hypopnea index	OA	Obstructive apnea
CBF	Cerebral blood flow	OSA	Obstructive sleep apnea
HHb	Deoxygenated hemoglobin concentration	$PtcCO_2$	Transcutaneous carbon dioxide pressure
HR	Heart rate	REM	Rapid eye movement
MOA	Mixed and obstructive apnea	SDB	Sleep-disordered breathing
NIRS	Near-infrared spectroscopy	SpO_2	Oxygen saturation
O_2	Oxygen	TOI	Tissue oxygenation index
O_2Hb	Oxygenated hemoglobin concentration		

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apnea (OSA) and in proportion to OSA severity.[15-18] In addition, cerebrovascular reactivity and the autonomic nervous system mature during childhood.[19,20] The impact of respiratory events on cerebral oxygenation may differ according to OSA severity and age. Respiratory events, and in particular OSA, are more common in children with associated disorders, such as craniofacial malformations or Down syndrome, with the possibility that the underlying pathology may also impact changes in cerebral oxygenation.

The aim of the study was to describe changes in cerebral oxygenation during different types of respiratory events—obstructive, mixed, central apneas, and hypopneas in children with SDB and associated disorders, and to evaluate the impact of the type of events, the severity of SDB, and age.

Methods

Consecutive children referred for a suspicion of SDB to the pediatric noninvasive ventilation and sleep unit of Necker University Hospital between February 2017 and June 2018 were included. Exclusion criteria were age <1 year, significant agitation, and prescription of drugs affecting sleep. Data were collected from the patient's medical charts. The study received approval from the ethical committee (CPP Ile de France II, protocol 2014-03-09 SC), and all the parents and/or patients gave their consent.

Sleep Recording

Children underwent a respiratory polygraphy (Cidelec, Ste-Gemmes-sur-Loire, France) with simultaneous recording of O_2 saturation (SpO_2) at a sampling rate of 8 Hz, and transcutaneous carbon dioxide pressure ($PtcCO_2$) (SenTec, Therwil, Switzerland).

Cerebral oxygenation indexes were recorded with a NIRO-200NX spectrophotometer (Hamamatsu Photonics KK, Hamamatsu City, Japan). The analogue signals of TOI, O_2Hb, and HHb were integrated into the Cidelec software. The sampling rate for the signals was 1 Hz.

Overnight Sleep Study

All polygraphy studies were scored by 2 experts in pediatric sleep according to the American Academy of Sleep Medicine recommendations.[21,22] The apnea-hypopnea index (AHI) was defined as the number of apneas and hypopneas by hour of sleep recording. Polygraphy was considered as normal if the AHI was <1 event/hour. Mild SDB was defined as an AHI between ≥1 and <5 events/hour, moderate as an AHI between ≥5 and <10 events/hour, and severe as an AHI of ≥10 events/hour. The O_2 desaturation index was defined as the number of SpO_2 decreases of ≥3% per hour of sleep recording.

Children were grouped by severity of SDB and age (<7 and ≥7 years old) for analysis. This age class was chosen because neurocognitive deficits have been shown to be worse in elementary school aged children compared with preschool aged children.[1,2] AHI, mean TOI, mean and minimum SpO_2, percentage of time with an SpO_2 of <90%, mean and maximum $PtcCO_2$, and percentage of time with a $PtcCO_2$ of >50 mm Hg were compared between SDB severity, age, and associated disorders groups.

Respiratory Events

Respiratory events were retained for analysis if they were free of artifact on NIRO-200NX signals. OAs without O_2 desaturation were excluded. Variation (Δ) in SpO_2, ΔTOI, ΔO_2Hb, ΔHHb, and variation of heart rate (HR) were expressed as absolute values and defined as the difference between baseline value before the respiratory event (the value measured immediately before the onset of the change of the parameter) and subsequent nadir/peak value (**Figure 1**; available at www.jpeds.com). Delay of occurrence of all variations was defined as the time in seconds between the beginning of the respiratory event and the onset of the deflection/increase of the parameter. The interval ΔTOI–ΔSpO_2 referred to the delay in seconds between ΔTOI and ΔSpO_2. Data were then compared according to the type of respiratory event, SDB severity, and age group. For each type of event, groups of SDB severity, and age, we evaluated the correlations between cerebral oxygenation indexes and ΔSpO_2 and event duration.

Statistical Analyses

Continuous variables were expressed as mean ± SD. Comparisons between variables were performed using the Student *t* test or ANOVA test in case of normal distribution, and with the Mann-Whitney test or Kruskal-Wallis ANOVA on ranks otherwise (Sigma plot, Systat Software, Inc, San Jose, California). Correlations were performed using the Pearson correlation or the Spearman correlation test. Multivariable linear regressions were performed to define predictive factors of ΔTOI. A *P* value of <.05 was considered as statistically significant.

Results

Of the 131 patients who performed a polygraphy with NIRS, 66 were excluded for failure of recordings of polygraphy or NIRS, or artifacts. Of the remaining 65 patients (30 boys, 35 girls) mean age 7.8 ± 4.2 years (range, 1.5-18.6 years), 15 patients (23%) had a normal polygraphy, 24 (37%) patients had mild SDB, 8 patients (12%) had moderate SDB, and 18 patients (28%) had severe SDB. None of the patients had central apnea syndrome defined by a central apnea index of >5 events/hour. The patients had the following associated disorders: constitutional bone disease (n = 13), Down syndrome (n = 10), facio-craniosynostosis (n = 8), maxillofacial abnormalities (n = 7), encephalopathies (n = 7), obesity (n = 5), or others (n = 12) (**Table I**; available at www.jpeds.com). Only 3 patients had isolated tonsillar hypertrophy without any comorbid condition.

Polygraphy findings according to SDB severity are reported in **Table II** (available at www.jpeds.com). For the whole group of patients, the mean AHI was 6.9 ± 9.3 events/hour, the mean SpO_2 was 96.1 ± 1.2%, and the mean nocturnal TOI was 72.3 ± 6.1%. Age did not differ among the SDB severity groups. The mean AHI increased from the mild, moderate, and severe SDB groups, but the AHI differed

statistically only between the mild and severe SDB groups. The mean SpO_2 was significantly higher in the no SDB group compared with the moderate and severe SDB groups. The mean $PtcCO_2$ and mean TOI did not differ among the SDB severity groups. Comparison of polygraphy data, nocturnal gas exchange, and TOI according to age group is reported in Table III (available at www.jpeds.com). The mean nocturnal TOI did not differ according to SDB severity group or age group or associated disorder, and was not correlated with mean nocturnal SpO_2 (r = 0.005; P = .970), AHI (r = 0.038; P = .762), or age (r = 0.06; P = .636).

Respiratory Events

Among the 50 children with SDB, 1105 respiratory events were analyzed: 468 obstructive apneas, 72 mixed apneas, 172 central apneas, and 393 hypopneas. All hypopneas were obstructive. The mean AHI for the patients with SDB was 9.1 ± 9.9 events/hour. Respiratory events had a mean duration of 15.5 ± 8.1 seconds and were followed by a mean decrease of SpO_2 of 4.1 ± 3.1% occurring after a mean of 14.1 ± 6.1 seconds from the beginning of the event. The mean TOI decrease was 3.4 ± 2.8%, occurring after a mean of 2.0 ± 3.2 seconds after the beginning of the event. O_2Hb decreased by a mean of 2.0 ± 1.3 μmol/L and the HHb increased by a mean of 1.4 ± 1.1 μmol/L. The SpO_2 decrease occurred after a mean of 12.1 ± 6.2 seconds after the TOI decrease. Respiratory events were associated with a mean HR decrease of 12.0 ± 10.2 beats/minute.

Type of Respiratory Events. Characteristics of SpO_2, cerebral oxygenation indices, and HR according to the type of respiratory event are reported in Table IV. Mixed and OAs were grouped for analysis because their characteristics were not different (data not shown). The mean duration of central apneas was significantly shorter than the duration of mixed and OAs and obstructive hypopneas. The mean hypopnea duration was about twice the mean duration of apneas. The mean SpO_2 decrease was significantly less for mixed and OAs as compared with central apneas and hypopneas. The mean ΔTOI and ΔHHb were significantly smaller for hypopneas as compared with apneas. The mean ΔHR was significantly smaller for central apneas as compared with mixed and OAs and hypopnea. ΔSpO_2, ΔTOI, ΔO_2Hb, and ΔHR occurred significantly later for central apnea as compared with mixed and OAs and hypopnea. The mean delay between ΔTOI and ΔSpO_2 was significantly longer for central apneas compared with mixed and OAs.

For each type of event, significant correlations were observed between the duration of the event and ΔSpO_2, ΔTOI, ΔO_2Hb, ΔHHb (Figure 2 and Table V; available at www.jpeds.com), between ΔSpO_2 and the variations of cerebral oxygenation indexes (Figure 3, A-C), and between ΔO_2Hb and ΔHR (Figure 3, D-F). Age correlated negatively with ΔTOI, regardless the type of event (Table V).

Effect of Severity of SDB. Characteristics of SpO_2, cerebral oxygenation indices, and HR according to SDB severity are reported in Table VI. Respiratory events had a significantly shorter duration in the mild SDB group as compared with the 2 other groups. The mean ΔSpO_2 did not differ according to SDB severity, but the mean ΔTOI, ΔO_2Hb, ΔHHb, and ΔHR were significantly smaller in the mild SDB group than in the 2 other groups. Regarding the ΔSpO_2, ΔTOI, ΔO_2Hb, ΔHHb, and ΔHR delays, no differences were observed between SDB severity groups.

ΔSpO_2 and ΔTOI correlated significantly for each group of SDB severity, with a stronger correlation in the severe SDB group (r = 0.491; P < .001) (Figure 4, A-C; available at www.jpeds.com). ΔO_2Hb and ΔHR correlated significantly for the 3 SDB groups (Figure 4, D-F). The mean duration of an event was not significantly correlated with ΔSpO_2 and ΔTOI in the mild SDB group (r = 0.139; P = .197 and r = −0.089; P = .291, respectively), contrary to moderate SDB (r = 0.259; P = .003 and r = 0.193; P = .027, respectively) and severe SDB (r = 0.318; P < .001 and r = 0.135; P < .001, respectively) (Table VII; available at www.jpeds.com).

Table IV. Characteristics of peripheral and cerebral oxygenation indexes and HR according to the type of respiratory event

Characteristics	MOA (n = 540)	Central apnea (n = 172)	OH (n = 393)	*P* value
Duration of event (s)	12.9 ± 4.6	9.9 ± 2.7	20.6 ± 10.1	<.001
ΔSpO_2 (%)	3.5 ± 3.0*	4.7 ± 2.6	4.7 ± 3.4	<.001
ΔTOI (%)	3.5 ± 2.1	3.6 ± 1.7	3.2 ± 3.8†	<.001
ΔO_2Hb (μmol/L)	2.1 ± 1.4*	1.6 ± 0.9	1.8 ± 1.4	<.001
ΔHHb (μmol/L)	1.4 ± 1.0	1.4 ± 0.8	1.3 ± 1.2†	<.001
ΔHR (beats/min)	12.7 ± 9.4	5.7 ± 7.1‡	13.7 ± 11.3	<.001
Delay of occurrence (s)				
ΔSpO_2	12.8 ± 4.8	16.2 ± 6.0	14.9 ± 7.3	<.001
ΔTOI	1.4 ± 2.8	3.5 ± 2.2‡	2.2 ± 3.7	<.001
ΔO_2Hb	0.7 ± 3.3	3.1 ± 2.6	1.8 ± 4.5	<.001
ΔHHb	2.3 ± 3.2*	3.3 ± 2.7	3.9 ± 4.0	<.001
ΔHR	1.9 ± 3.1	2.8 ± 3.0	1.8 ± 6.0	<.001
Time interval ΔTOI-ΔSpO_2 (s)	11.4 ± 5.3	12.8 ± 6.1§	12.7 ± 7.2	.002

OH, obstructive hypopnea.
Values are expressed as mean ± SD.
*Significantly different from central apnea and OH.
†Significantly different from central apnea and MOA.
‡Significantly different from MOA and OH.
§Significantly different from MOA.

Effect of Age. Characteristics of SpO_2, cerebral oxygenation indices, and HR according to the age groups are reported in Table VIII (available at www.jpeds.com). Respiratory events were significantly shorter (P < .001), but ΔSpO_2 (P < .001), ΔTOI (P < .001), ΔHHb (P < .001), and ΔHR (P < .001) were significantly greater in the <7-year-old group as compared with the >7-year-old group. ΔSpO_2 (P = .003), ΔTOI (P < .001), ΔO_2Hb (P < .001), and ΔHHb (P = .009) occurred significantly later in the <7-year-old group as compared with the >7-year-old group.

In the 2 groups, we observed significant correlations between ΔSpO_2 and ΔTOI, and ΔHHb but these correlations seemed to be stronger in the <7-year-old group (Figure 5, A-F; available

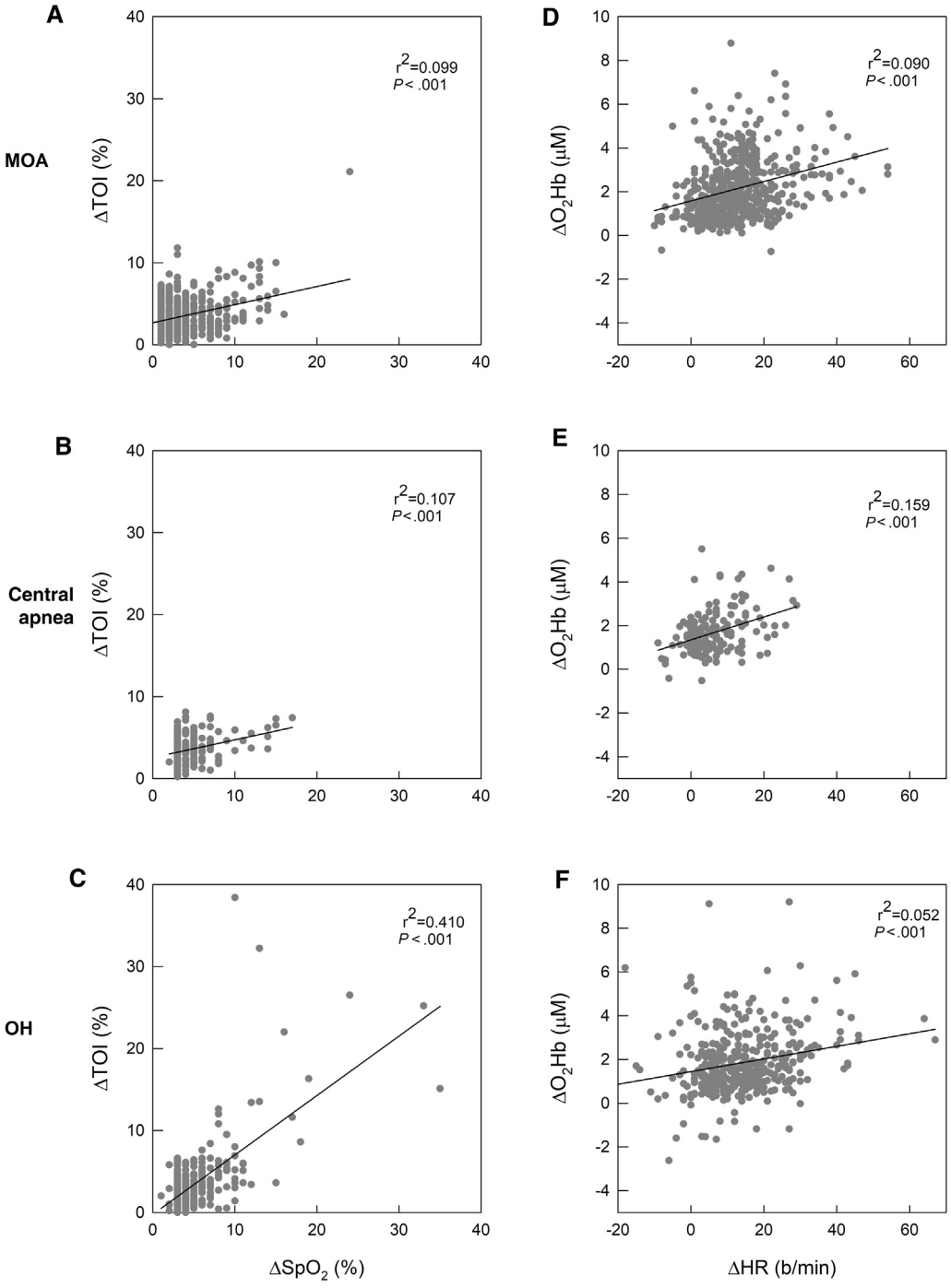

Figure 3. Correlations between changes in TOI and changes in SpO_2, **A-C,** and correlation between changes in oxygenated hemoglobin and changes in HR, **D-F,** in obstructive and mixed apnea, central apnea and hypopnea. *OH*, obstructive hypopnea.

at www.jpeds.com). The duration of an event correlated significantly with ΔSpO_2, ΔTOI, ΔO_2Hb, and ΔHHb for both groups (**Table IX**; available at www.jpeds.com).

Predictive Factors of ΔTOI

In a multivariable regression model, predictive factors of ΔTOI were AHI ($P < .001$), age ($P < .001$), ΔSpO_2 ($P < .001$), and mixed and OAs ($P = .007$), according to the following equation (r = 0.552; $P < .001$): ΔTOI = 1.903 – (0.187 × age) + (0.0365 × AHI) + (0.495 × MOA) + (0.418 × ΔSpO_2), where MOA is mixed and OA (**Table X**).

Discussion

This study assesses the effect of the type of respiratory event on cerebral oxygenation in children with SDB and associated disorders. ΔSpO_2 and ΔTOI were globally of similar magnitude, with only small differences according to the type of

Table VI. Characteristics of peripheral and cerebral oxygenation indexes and HR according to the SDB severity

Characteristics	Mild SDB (n = 144)	Moderate SDB (n = 132)	Severe SDB (n = 829)	*P* value
Duration of event (s)	11.7 ± 5.7*	15.7 ± 7.5	15.7 ± 8.4	<.001
ΔSpO_2 (%)	3.8 ± 2.4	4.2 ± 2.0	4.2 ± 3.4	.05
ΔTOI (%)	2.4 ± 1.7*	3.4 ± 1.7	3.6 ± 3.0	<.001
ΔO_2Hb (μmol/L)	1.6 ± 1.2*	2.0 ± 1.4	2.0 ± 1.4	<.001
ΔHHb (μmol/L)	1.1 ± 1.0*	1.5 ± 0.9	1.4 ± 1.1	<.001
ΔHR (beats/min)	9.6 ± 9.7*	14.0 ± 12.0	12.1 ± 9.7	.004
Delay of occurrence (s)				
ΔSpO_2	13.8 ± 5.8	14.3 ± 5.3	14.6 ± 6.3	.725
ΔTOI	2.5 ± 2.8	1.9 ± 3.4	1.9 ± 3.2	.088
ΔO_2Hb	2.0 ± 3.4	1.7 ± 4.4	1.3 ± 3.8	.077
ΔHHb	2.5 ± 3.2	2.8 ± 3.5	3.1 ± 3.5	.212
ΔHR	2.1 ± 3.5	2.1 ± 4.0	2.0 ± 4.6	.933

Values are expressed as mean ± SD.
*Significantly different from moderate and severe SDB.

respiratory event, SDB severity, or age group. Interestingly, ΔSpO_2 and ΔTOI were significantly greater in patients with moderate and severe SDB as compared with patients with mild SDB, and in patients <7 years old as compared with older children. MOA, AHI, age, and ΔSpO_2 were found to predict ΔTOI in a multivariable model. Of note, ΔTOI was generally similar to that described in typically developing children by Tamanyan et al.[11]

Studies comparing cerebral oxygenation during the entire night in adults with OSA compared with healthy controls gave inconclusive results. In a group of 33 adults, lower brain SpO_2 in the patients with OSA could be explained exclusively by older age in patients as compared with the healthy controls.[23] However, 3 pediatric studies gave consistent but surprising results. Indeed, SDB was shown to be associated with a decrease in cerebral oxygenation during non REM sleep in 1 study, but with the same magnitude as that in controls.[24] In a recent study that enrolled 159 children, the mean nocturnal TOI was not significantly different between patients with OSA and healthy controls, as in the study by Tamanyan et al who found no differences in mean nocturnal TOI between healthy controls, and children with mild and moderate-to-severe OSA.[25,26] In the present study, the mean nocturnal TOI was also comparable between the SDB groups and those without SDB.

Because SDB is characterized by repetitive episodes of hypoxemia, the analysis of the specific consequences of the different types of respiratory events during sleep on cerebral oxygenation may be more informative. Decreases in cerebral oxygenation have been observed in adult patients during obstructive respiratory events.[8-10] These decreases were significantly greater during REM sleep, longer apneas, more profound peripheral desaturation, and in patients with a higher AHI.[8-10] Children with SDB may have frequent hypopneas and central apnea. The specific consequences of these different types of respiratory events have been reported recently in typically developing children, but not in children with associated disorders which represent the majority of children with moderate and severe SDB.[11] Our results show that mean decreases in SpO_2 and TOI were relatively small and of similar magnitude whatever the type of respiratory event and comparable with the finding of Tamanyan et al in children with no comorbidities.[11] Indeed, even if the mean TOI decrease was found to be significantly less for obstructive hypopnea as compared with apneas, this difference does not seem to be relevant clinically. As observed in adults, the TOI decrease correlated significantly with SpO_2 decrease, duration of respiratory event, and AHI, as well as with age. Interestingly, SpO_2 decreases were greater in adult patients (around 10%) as compared with our population (around 5%), whereas TOI decreases were within the same magnitude (around 3%).[9] In a recent study of adults with severe OSA, the mean decrease in TOI during OAH was 5.4 ± 3.1%, which was less than the corresponding SpO_2 decreases.[27] It is understandable that the mean TOI decrease was greater during apneas as compared with hypopneas, which are less severe respiratory events, but we have no explanation for the lesser SpO_2 decrease observed during MOA as compared with central apnea and obstructive hypopnea.

The variation in cerebral oxygenation parameters during OA appeared almost immediately after the onset of the event as opposed to central apnea. This phenomenon seems to be explained by variation in blood pressure at the initial phase of OA, as a consequence of intrathoracic pressure variation.[13] Moreover, the time interval between ΔTOI and ΔSpO_2 was significantly longer during central apnea as compared with OA. This interval may be considered as a difference of time circulation between the brain and the finger and depends on cardiac output. Also, hemodynamic consequences of obstructive and central events are very different. During OA, blood pressure and cardiac output increase progressively after a short decrease as opposed to central apnea.[13]

Mild SDB was associated with shorter respiratory events, regardless of the type of event, and smaller changes in cerebral oxygenation indices compared with moderate and severe SDB. The similar changes in cerebral oxygenation indices between moderate and severe SDB may be attributable to the similar mean AHI between the groups, but we may be underpowered to compare this with only 8 patients having moderate SDB.

Cerebrovascular reactivity is crucial for the maintenance of normal cerebral metabolism and matures with age.[19] It is, thus, not surprising that changes in cerebral oxygenation during respiratory events during sleep are also affected by age. In the present study, ΔSpO_2, ΔTOI, and ΔHHb were deeper although subsequent to shorter respiratory events in

Table X. Predictive factors of a change of cerebral TOI (ΔTOI) during a respiratory event during sleep

Factors	Regression coefficient	*P* value
AHI	**0.0381**	**<.001**
Age	**−0.184**	**<.001**
ΔSpO_2	**0.419**	**<.001**
Obstructive and mixed apneas	**0.486**	**.007**
Duration of the event	0.00657	.549
Central apneas	0.0172	.946
ΔHR	0.0129	.077
Obstructive hypopneas	–	Colinear

r values associated with statistically significant correlations were presented in bold.

children <7 years old, regardless of the type of respiratory event. Indeed, younger children have a lower functional residual capacity and higher O_2 consumption, a lesser capacity of cerebral vessel autoreactivity, and an immaturity of neural autonomic control compared with older children.[19,20,28,29] More important, the greater correlations between ΔSpO_2 and ΔTOI, ΔO_2Hb, and ΔHHb in younger patients may reflect this maturation of cerebrovascular autoreactivity.

Our study has some limitations. About one-half of the patients who underwent a polygraphy study with NIRS measurements were not included because of technical difficulties or lack of compliance. Patients did not have a full polysomnography, which precludes the analysis of sleep stages. Indeed, it will be interesting to compare non-REM sleep with REM sleep; it has been shown in adults that decreases in cerebral oxygenation were more profound during REM sleep.[8,9] In addition, because we did not have electroencephalographic monitoring, we were not able to score and thus analyze hypopneas associated with an electroencephalographic arousal without desaturation. We were not able to analyze total hemoglobin, which is considered by some authors as a reflection of CBF.[7] This would have allowed us to determine if ΔTOI was related to hypoxemia or hemodynamic consequences, as we hypothesized for OA. The vast majority of our patients had comorbidities or underlying pathologies owing to the specific recruitment of our teaching hospital. Changes in cerebral oxygenation during respiratory events could be impacted by the underlying pathology. For example, patients with Down syndrome have impaired autonomic nervous system functioning, which may contribute to greater side effects of obstructive respiratory events.[30-32] Owing to the heterogeneity of our population, we were not able to analyze the potential effect of the associated disorder. We excluded OAs without peripheral desaturation. Finally, we did not adjust our level of significance for multiple comparisons, which may lead to type I error.

In conclusion, in children with SDB and associated disorders, cerebral oxygenation variations depend on the type of respiratory event, severity of SDB, and age. However, mean decreases in SpO_2 and TOI were relatively small and of similar magnitude whatever the type of respiratory event. Our results concern children with a wide variety of associated disorders, but they are quite comparable with those reported in typically developing children. Importantly, the clinical consequences and significance of iterative TOI decreases are not known. It would therefore be interesting to study the relationships between TOI decreases and neurocognitive and behavioral status in children with SDB, both with and without comorbidities. ■

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50 Years Ago in *THE JOURNAL OF PEDIATRICS*

Polycythemia in Small for Gestational Age Infants

Humbert JR, Abelson H, Hathaway WE, Battaglia FC. J Pediatr 1969;75:812-9.

In the 1960s, polycythemia with hyperviscosity became an important diagnosis in neonatology. This interest peaked after an association was shown between hyperviscosity and lower achievement as well as IQ scores at 7 years of age.[1] Therefore, partial exchange transfusion (PET) was a common procedure in the neonatal intensive care unit.

In their observational study on neonatal polycythemia published 50 years ago in *The Journal*, Humbert et al found significantly greater rates of polycythemia in infants born full-term small for gestational age (SGA) (with more symptoms in the male SGA population), compared with infants born full term and with infants born premature appropriate for gestational age. The correlation between neonates born SGA and polycythemia already had been demonstrated by Haworth et al.[2] The diagnosis is established if there is a venous sample hematocrit >65%. Humbert et al did, however, use a venous hematocrit >60% as a diagnosis for polycythemia, which could have led to an increased rate of the diagnosis. The study by Humbert et al highlighted clinically important issues at that time, still of interest 50 years later. However, more recent meta-analyses concluded there are no proven clinically significant short- or long-term benefits of PET in newborn infants with polycythemia who are clinically well or who have minor symptoms related to hyperviscosity; this intervention may lead to an increased risk of necrotizing enterocolitis. Polycythemia is therefore no longer considered of equal interest as before,[3] despite the recent shift in practice with delayed cord clamping, which increases polycythemia.[4]

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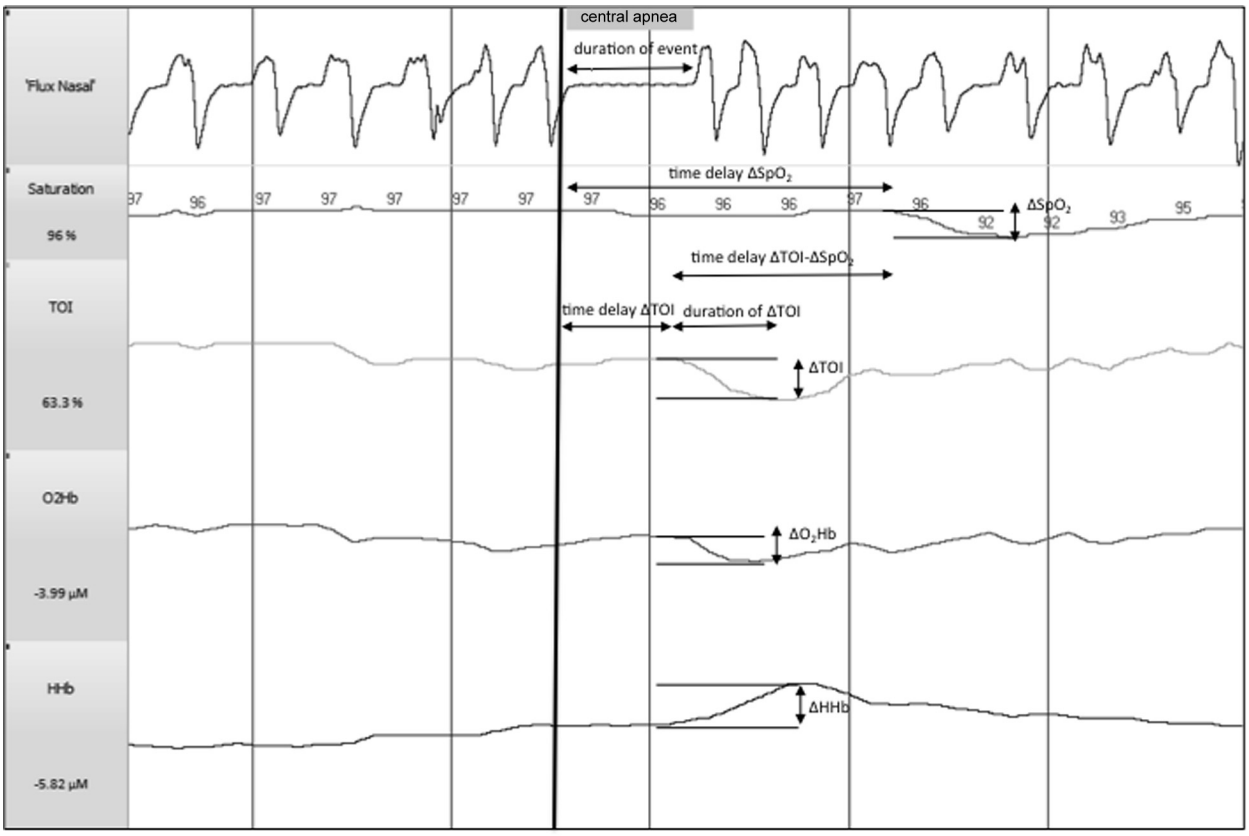

Figure 1. Analysis of nasal airflow, SpO_2, and cerebral oxygenation parameters. First channel: nasal flow cannula, second channel: SpO_2, third to fifth channels: cerebral oxygenation parameters. Time interval between 2 vertical bars equals 10 seconds.

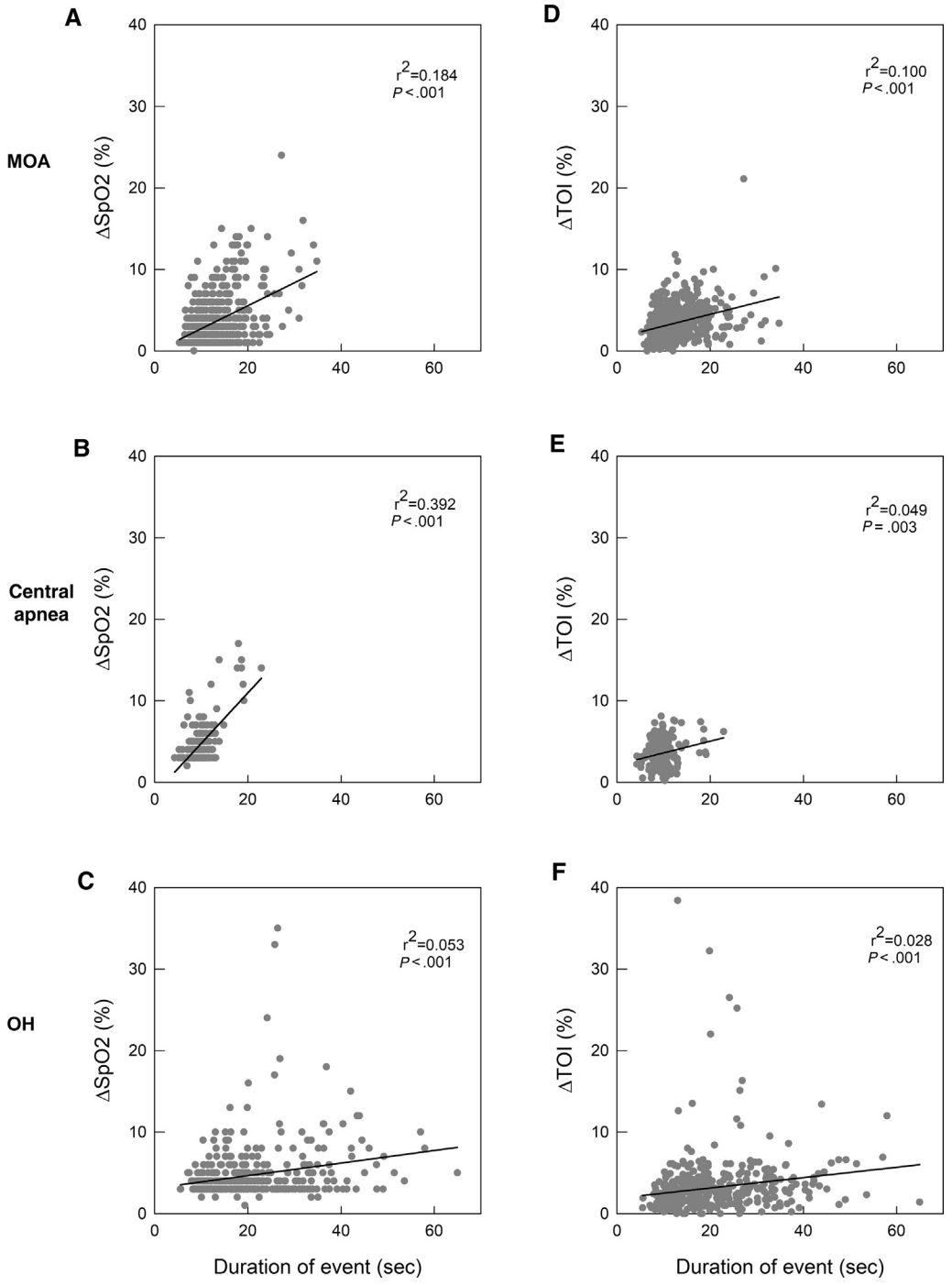

Figure 2. Correlations between changes in SpO_2 and event duration, **A-C,** and TOI and event duration, **D-F,** in obstructive and mixed apnea, central apnea and hypopnea. *OH*, obstructive hypopnea.

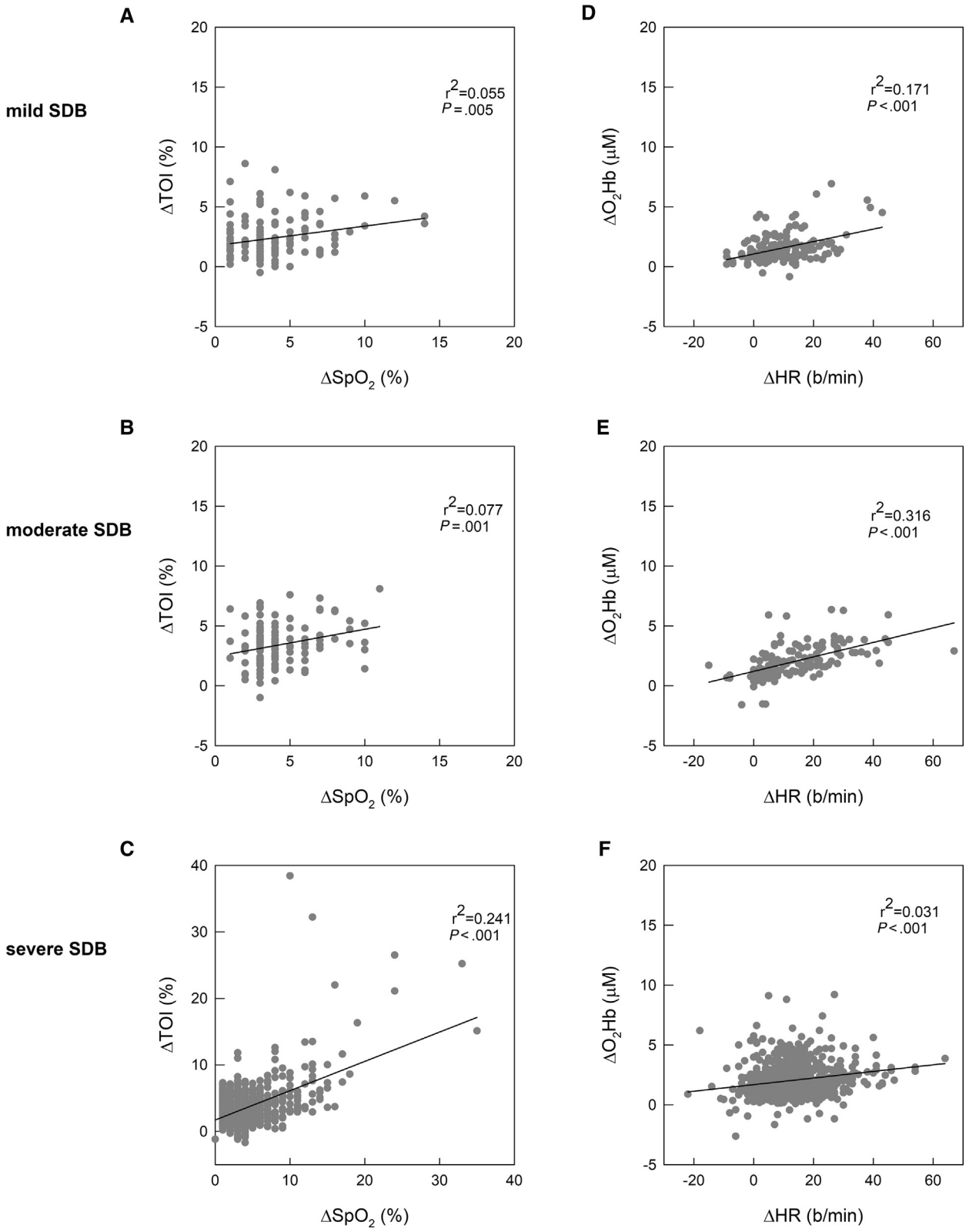

Figure 4. Correlations between changes in TOI and changes in SpO_2, **A-C,** and correlation between changes in oxygenated hemoglobin and changes in HR, **D-F,** according to the SDB severity group.

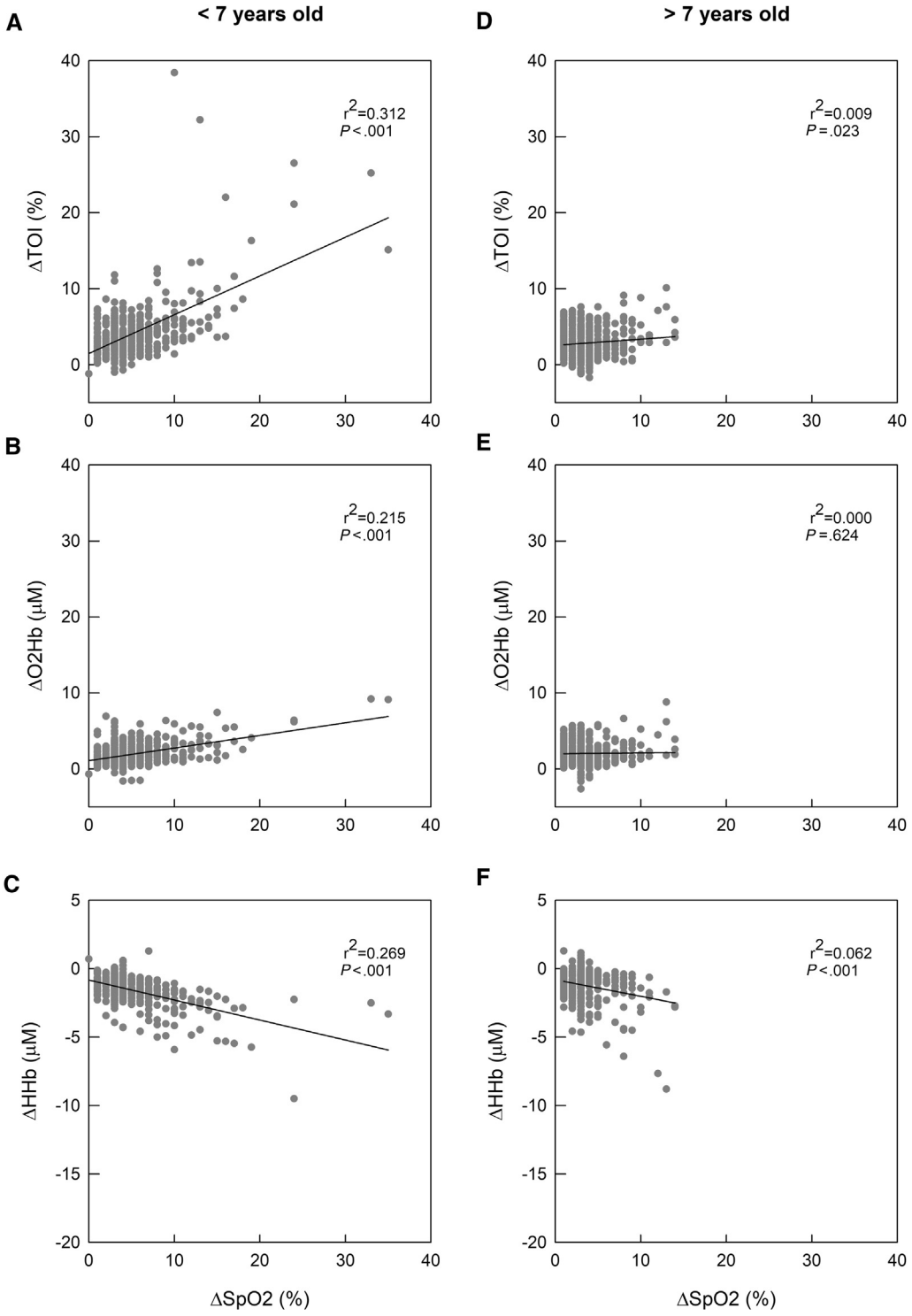

Figure 5. Correlation between changes in cerebral oxygenation indexes and changes in SpO_2 in children **A-C,** under 7 years of age, and **D-F,** children above 7 years old.

Table I. Description of the associated disorders

Associated disorders	No.
Constitutional bone diseases	13
Achondroplasia	6
Pycnodysostosis	2
Metatropic dysplasia	2
Osteogenesis imperfecta	2
Bone dysplasia	1
Down syndrome	10
Craniofaciostenosis	8
Craniostenosis	4
Crouzon	4
Maxillofacial abnormalities	7
Treacher-Collins	1
Pierre Robin sequence	3
Other mandibulomaxillary abnormalities	3
Encephalopathies	7
Genetic	4
Sequel of premature birth	1
Undetermined etiology	2
Obesity	5
Tonsil hypertrophy	3
Others	12
Syringomyelia	1
Chiari	2
Pontine cavernoma	1
Ectodermic dysplasia	1
Sickle cell disease	1
Morquio syndrome	1
Wiedmann-Beckwith	1
Velopharyngeal insufficiency	1
Inter-auricular communication and pulmonary arterial hypertension	1
Amelogenesis imperfecta	1
Arthrogryposis	1

Table II. Polygraphic findings, nocturnal transcutaneous gas exchange, and mean TOI across the night of the sleep study according to the severity of SDB

Characteristics	No SDB (n = 15)	Mild SDB (n = 24)	Moderate SDB (n = 8)	Severe SDB (n = 18)	Total (n = 65)	*P* value
Age (years)	10.1 ± 4.0	7.2 ± 4.2	6.0 ± 3.6	7.4 ± 3.9	7.8 ± 4.2	.067
AHI (events/h)	0.1 ± 0.2*	2.0 ± 0.9†	6.7 ± 1.5	19.1 ± 9.5	6.9 ± 9.3	<.001
MOAI (events/h)	0.03 ± 0.11*	0.73 ± 0.70†	1.9 ± 1.5	7.3 ± 7.4	2.5 ± 4.9	<.001
CAI (events/h)	0.02 ± 0.09*	0.47 ± 0.40	0.7 ± 0.9	2.2 ± 4.5	0.9 ± 4.0	<.001
HI (events/h)	0.01 ± 0.04‡	0.74 ± 0.64‡	4.1 ± 1.0	9.5 ± 6.5	3.4 ± 5.2	<.001
Mean SpO_2 (%)	96.9 ± 0.9‡	96.2 ± 1.0	95.6 ± 1.0	95.6 ± 1.5	96.1 ± 1.2	.002
Minimum SpO_2 (%)	94.9 ± 1.4‡	89.4 ± 4.4§	85.9 ± 3.5	80.7 ± 10.8	87.9 ± 8.2	<.001
% time with SpO_2 ≤90 (%)	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	2.0 ± 5.1	0.6 ± 2.8	.074
ODI (events/h)	0.7 ± 1.3‡	3.6 ± 2.6‡	13.3 ± 6.3	17.9 ± 9.6	7.9 ± 9.0	<.001
Mean $PtcCO_2$ (mm Hg)	41.6 ± 3.0	40.6 ± 3.7	41.2 ± 2.9	42.6 ± 3.8	41.5 ± 3.5	.374
Maximum $PtcCO_2$ (mm Hg)	44.5 ± 3.3	44.5 ± 3.7†	45.0 ± 2.6	48.2 ± 4.5	45.6 ± 4.1	.020
% time with $PtcCO_2$ ≥50 mm Hg (%)	0.0 ± 0.0	0.5 ± 1.5	0.0 ± 0.0	1.2 ± 2.9	0.5 ± 1.8	.273
Mean TOI (%)	73.1 ± 7.6	71.5 ± 6.8	73.3 ± 2.8	72.2 ± 4.8	72.3 ± 6.1	.839

CAI, central apnea index; *HI*, hypopnea index; *MOAI*, MOA index; *ODI*, O_2 desaturation index.
Values are expressed as mean ± SD across the night of the sleep study.
*Significantly different from mild, moderate and severe SDB groups.
†Significantly different from severe SDB group.
‡Significantly different from moderate and severe SDB groups.
§Significantly different from normal and severe SDB groups.

Table III. Polygraphic findings, nocturnal transcutaneous gas exchange, and mean TOI across the night of the sleep study according to the age groups

Characteristics	Age <7 years old (n = 34)	Age >7 years old (n = 31)	*P* value
Age (years)	4.5 ± 1.4	11.4 ± 3.1	<.001
AHI (events/h)	6.6 ± 8.0	7.2 ± 10.7	.304
MOAI (events/h)	2.1 ± 3.1	3.0 ± 6.4	.150
CAI (events/h)	1.5 ± 5.5	0.2 ± 0.3	.022
HI (events/h)	3.0 ± 3.7	3.9 ± 6.6	.516
Mean SpO_2 (%)	96.2 ± 1.2	96.1 ± 1.2	.956
Minimum SpO_2 (%)	86.2 ± 8.8	89.7 ± 7.3	.031
% time with SpO_2 ≤90% (%)	0.4 ± 1.3	0.7 ± 3.8	.496
ODI (nb/h)	9.3 ± 7.0	6.5 ± 8.6	.092
Mean $PtcCO_2$ (mm Hg)	40.0 ± 3.3	43.1 ± 3.1	<.001
Maximum $PtcCO_2$ (mm Hg)	44.5 ± 4.1	46.7 ± 3.8	.018
% time with $PtcCO_2$ ≥50 mm Hg (%)	0.3 ± 1.8	0.7 ± 1.8	.164
Mean TOI (%)	71.6 ± 6.6	73.0 ± 5.5	.173

Values are expressed as means ± SD across the night of the sleep study.

Table V. Correlations for each type of event

Variables	ΔTOI (%)	ΔO_2Hb (μmol/L)	ΔHHb (μmol/L)	ΔHR (b/min)	Age (years)	ΔSpO_2 (%)
MOA						
Duration of event (s)						
r	**0.319**	**0.401**	**−0.476**	0.075	**0.143**	**0.431**
P value	<.001	<.001	<.001	.083	<.001	<.001
ΔSpO_2 (%)						
r	**0.319**	**0.151**	**−0.438**	0.025	−0.042	–
P value	<.001	<.001	<.001	.567	.326	
Age (years)						
r	**−0.136**	0.043	**0.146**	−0.070	–	–
P value	.002	.328	.001	.107		
ΔHR (b/min)						
r	**0.184**	**0.306**	−0.057	–	–	–
P value	<.001	<.001	.209			
Central apnea						
Duration of event (s)						
r	**0.220**	**0.348**	**−0.362**	**0.189**	**0.225**	**0.626**
P value	.003	<.001	<.001	.013	<.001	<.001
ΔSpO_2(%)						
r	**0.327**	**0.380**	**−0.523**	0.138	−0.111	–
P value	<.001	<.001	<.001	.075	.145	
Age (years)						
r	**−0.282**	0.097	**0.390**	0.129	–	–
P value	<.001	.206	<.001	.09		
ΔHR (b/min)						
r	0.082	**0.399**	−0.012	–	–	–
P value	.281	<.001	.877			
OH						
Duration of event (s)						
r	**0.168**	**0.243**	**−0.349**	0.096	**−0.193**	**0.231**
P value	<.001	<.001	<.001	.057	<.001	<.001
ΔSpO_2 (%)						
r	**0.640**	**0.464**	**−0.488**	0.035	**−0.243**	–
P value	<.001	<.001	<.001	.487	<.001	
Age (years)						
r	**−0.338**	**−0.216**	**0.373**	**−0.140**	–	–
P value	<.001	<.001	<.001	.005		
ΔHR (b/min)						
r	−0.017	**0.229**	0.002	–	–	–
P value	.734	<.001	.968			

OH, obstructive hypopnea.
r values associated with statistically significant correlations were presented in bold.

Table VII. Correlations for each group of SDB severity

Variables	ΔTOI (%)	ΔO_2Hb (μmol/L)	ΔHHb (μmol/L)	ΔHR (b/min)	Age (years)	ΔSpO_2 (%)
Mild SDB						
Duration of event (s)						
r	−0.089	0.030	−0.013	**0.207**	**0.211**	0.139
P value	.291	.724	.882	.013	.011	.097
ΔSpO_2 (%)						
r	**0.235**	0.044	**−0.411**	**−0.186**	−0.221	–
P value	.005	.604	<.001	.026	.008	
Age (years)						
r	**−0.295**	−0.013	**0.405**	0.161	–	–
P value	<.001	.880	<.001	.054		
ΔHR (b/min)						
r	**0.221**	**0.414**	−0.037	–	–	–
P value	.008	<.001	.667			
Moderate SDB						
Duration of event (s)						
r	**0.193**	0.145	**−0.288**	0.067	**0.204**	**0.259**
P value	.027	.098	<.001	.443	.019	.003
ΔSpO_2 (%)						
r	**0.278**	**0.323**	**−0.624**	**0.243**	−0.117	–
P value	.001	<.001	<.001	.005	.180	
Age (years)						
r	0.022	−0.041	0.163	−0.092	–	–
P value	.802	.642	.062	.293		
ΔHR (b/min)						
r	**0.381**	**0.560**	**−0.263**	–	–	–
P value	<.001	<.001	.002			
Severe SDB						
Duration of event (s)						
r	**0.135**	**0.237**	**−0.302**	**0.167**	−0.010	**0.318**
P value	<.001	<.001	<.001	<.001	.766	<.001
ΔSpO_2 (%)						
r	**0.491**	**0.289**	**−0.302**	0.0186	**−0.125**	–
P value	<.001	<.001	<.001	.594	<.001	
Age (years)						
r	**−0.308**	**−0.086**	**0.291**	−0.061	–	–
P value	<.001	.014	<.001	.077		
ΔHR (b/min)						
r	−0.019	**0.198**	0.055	–	–	–
P value	.588	<.001	.157			

r values associated with statistically significant correlations were presented in bold.

Table VIII. Characteristics of peripheral and cerebral oxygenation indexes and HR according to age groups

Characteristics	<7 years old (n = 568)	>7 years old (n = 537)	All (n = 1105)	*P* value
Duration of event (s)	14.3 ± 8.4	16.1 ± 7.6	15.5 ± 8.1	<.001
ΔSpO_2 (%)	4.8 ± 3.7	3.5 ± 2.3	4.1 ± 3.1	<.001
ΔTOI (%)	3.9 ± 3.3	2.8 ± 1.9	3.4 ± 2.8	<.001
ΔO_2Hb (μmol/L)	1.9 ± 1.3	2.0 ± 1.4	2.0 ± 1.3	.07
ΔHHb (μmol/L)	1.6 ± 1.0	1.2 ± 1.1	1.4 ± 1.1	<.001
ΔHR (beats/min)	11.9 ± 12.2	12.1 ± 7.6	12.0 ± 10.2	<.001
Delay of occurrence (s)				
ΔSpO_2	14.7 ± 6.8	13.5 ± 5.3	14.1 ± 6.1	.003
ΔTOI	2.5 ± 3.2	1.5 ± 3.1	2.0 ± 3.2	<.001
ΔO_2Hb	2.2 ± 3.7	0.7 ± 3.8	1.5 ± 3.8	<.001
ΔHHb	3.3 ± 3.4	2.6 ± 3.5	2.9 ± 3.5	.009
ΔHR	1.9 ± 3.4	2.1 ± 5.2	2.0 ± 4.4	.821

Values are expressed as mean ± SD.

Table IX. Correlations by age group

Variables	ΔTOI (%)	ΔO_2Hb (μmol/L)	ΔHHb (μmol/L)	ΔHR (b/min)	ΔSpO_2 (%)
<7 years old					
Duration of event (s)					
r	**0.196**	**0.260**	**−0.337**	**0.266**	**0.401**
P value	<.001	<.001	<.001	<.001	<.001
ΔSpO_2 (%)					–
r	**0.559**	**0.464**	**−0.553**	0.027	
P value	<.001	<.001	<.001	.525	
ΔHR (b/min)				–	–
r	0.035	**0.387**	**−0.142**		
P value	.412	<.001	.002		
>7 years old					
Duration of event (s)					
r	0.138	0.175	−0.317	−0.011	0.230
P value	.001	<.001	<.001	.796	<.001
ΔSpO_2 (%)					–
r	**0.098**	0.021	**−0.249**	0.033	
P value	.023	.624	<.001	.439	
ΔHR (b/min)				–	–
r	**0.103**	**0.151**	**0.114**		
P value	.017	<.001	.013		

r values associated with statistically significant correlations were presented in bold.