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Pulse Transit Time as a Measure of Inspiratory Effort in Children*

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Study objectives: **The current criterion standard for measuring inspiratory effort, esophageal manometry, is an invasive procedure that young patients find intolerable. Inspiratory effort can also be assessed noninvasively by measuring the pulse transit time (PTT). PTT is the time the pulse wave (PW) takes to travel between two arterial sites (normally heart to finger). The speed at which the PW travels is directly proportional to arterial BP. When BP rises, PTT shortens. Conversely, when BP falls, PTT lengthens. In this study, we investigated PTT as a measure for evaluating inspiratory effort in children.**

Participants: **We studied 15 healthy children (age range, 5 to 12 years; mean age [± SD], 8.3 ± 2.74; 9 male children) selected from patients referred to our pediatric center for routine assessment.**

Measurements and results: **We assessed changes in the PTT during breathing against known resistances in awake children. Resistance was applied to the nose and mouth with a modified, two-way, nonrebreathing facemask. Our data show a good correlation between the induced inspiratory effort and the amplitude of PTT variations.**

Conclusions: **PTT should be a useful method for quantifying changes in inspiratory effort due to augmented upper airway resistance in awake children.** ***(CHEST 2003; 124:1487–1493)***

Key words: children; inspiratory effort; obstructive sleep apnea; pulse transit time

Abbreviations: Pdrop = maximal intramask pressure drop; PTT = pulse transit time; ΔPTT = amplitude of pulse transit time variations; PW = pulse wave

Current knowledge suggests that polysomnographic studies should include monitoring of respiratory effort during sleep.[1] In particular, Guilleminault et al[2,3] emphasized the importance of increased upper airway resistance in causing sleep fragmentation and daytime symptoms. These obstructive nonapneic events are difficult to detect without sensitive measures of respiratory effort.[4] The criterion standard for assessing respiratory effort consists of measuring changes in endoesophageal pressure through an endoesophageal balloon catheter.[5] In children, this technique causes some discomfort and can lead to fragmentary sleep.[6,7] Another disadvantage is that the presence of the esophageal monitor can modify airway collapsibility,[8] thereby altering the normal respiratory pattern in children during sleep. Common noninvasive techniques currently used for measuring respiratory effort have various limitations, including high costs, complex measurement procedures, and poor sensitivity in detecting changes in airflow and inspiratory effort.[9]

Studies[10–12] seeking an alternative to esophageal monitoring in adults have validated a noninvasive method that measures respiratory effort from the ECG and pulse oximetry signals in standard polysomnographic recordings. This technique, pulse transit time (PTT), takes its name from the time needed for the pulse wave (PW) to travel from the aortic valve to the periphery, estimated as the delay between the R wave in the ECG and the arrival of the PW at the finger as determined by pulse oximetry.[9]

PTT discloses acute changes in arterial pressure[13] generated by increased oscillations in pleural pressure due to inspiratory effort induced by obstructive

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events.[14] Changes in PTT yield a valid measure of inspiratory effort. Studies[4,10,14] conducted in adult patients with obstructive sleep apnea syndrome have found a significant correlation of variations in endoesophageal pressure (measured by esophageal balloon) induced by an episode of augmented airways resistance, and PTT variations between inspiration and expiration. These observations support PTT as an alternative to esophageal pressure measurement for quantitatively assessing inspiratory efforts in adults.[10] What is now lacking are data on the use of PTT in children. Our aim in this study was to assess the usefulness of PTT as a measure for evaluating inspiratory effort in children.

Materials and Methods

Study Subjects

The 15 children (age range, 5 to 12 years; mean age [± SD], 8.3 ± 2.74; 9 male children) were selected among patients attending our pediatric service for routine assessment. The criteria for inclusion included the absence of active nocturnal and diurnal respiratory symptoms and chronic cardiorespiratory disease. None of the children selected had received medications during the 2 weeks before the study.

Study Protocol

Participants were tested in the supine position. Each child was fitted with a custom-designed, nasal and mouth, two-way, nonrebreathing facemask (series 7910; Hans Rudolph; Kansas City, MO) modified to simulate an inspiratory effort. The inhalation valve port of the mask was adapted to lodge three small plastic cylinders (inner diameters, 3 mm, 5 mm, and 8 mm). The openings were gauged to obtain moderate and severe airway resistances (11.3-13.3 cm H_2O/L/s and 85.1 cm H_2O/L/s, respectively) for inspiratory flows ranging from 0.05 to 0.3 L/s.

No extra respiratory resistance was applied to the expiratory port. The mask was also equipped with a transducer for measuring negative pressure generated by inspiratory efforts (Fig 1). After a 3-min trial to stabilize breathing at zero resistance (baseline), the three progressive resistance levels were applied to the inspiratory port, allowing 3 min for each trial and a 2-min recovery period with zero resistance between each trial.

Subjects were asked to breathe normally through the nose, to relax, and to remain still during measurement. Before starting the protocol, all of the children received a short training session. To make sure that sequence had no effect on measurements, resistances were applied in random order. The physiologic variables were recorded with a Grass multichannel instrument (Model Heritage Grass Instruments; Quincy, MA) and sampled at 250 Hz. Polygraphic data included ECG (II lead), arterial blood oxyhemoglobin saturation, and PW recorded with a pulse oximeter (Nellcor NPB290; Nellcor; Pleasanton, CA) at the finger,[15] mask pressure, and abdominal and chest movements (by inductive plethysmography).

PTT Measurement Technique

Data were digitally acquired and transferred to a personal computer. PTT was calculated with software custom designed in our laboratory. R waves were detected according to the methods of Pan and Tompkins.[16] Parabolic interpolation of QRS was used to refine the R-wave detection. After the R wave had been detected, the relative minimum and maximum PWs were identified in the same beat. PTT was calculated as the interval between the ECG R wave and the point at which the PW reached 90% amplitude (PW maximum − PW minimum) [Fig 2, *top*, *A*].

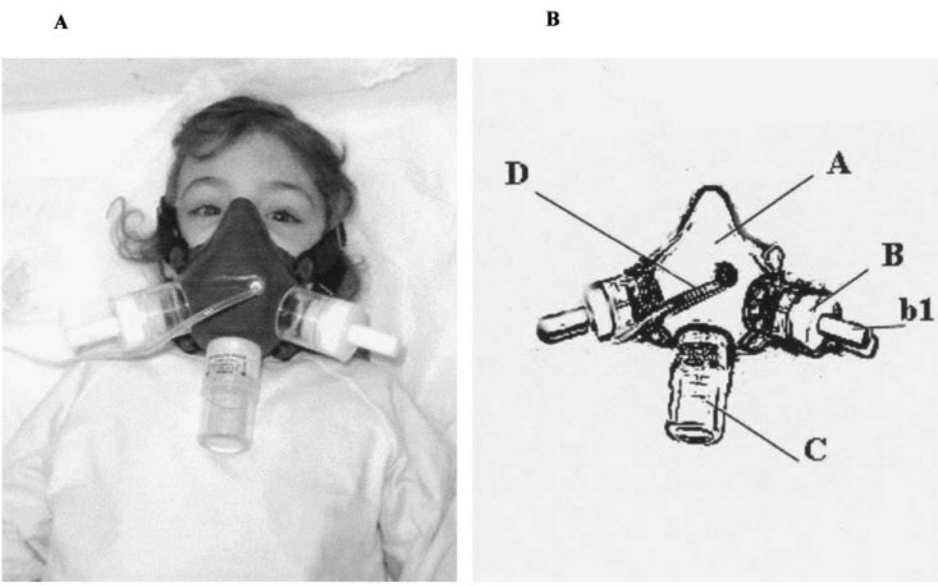

Figure 1. *Left*, *panel A*: Custom-designed nasal and mouth two-way, nonrebreathing facemask modified to simulate an inspiratory effort. *Right*, *panel B*: Facemask (*A*). The inhalation valve port (*B*) was adapted to lodge small plastic cylinders (*b1*). No extra respiratory resistance was applied to the expiratory port (*C*). The mask was also equipped with a transducer for measuring negative pressure generated by inspiratory efforts (*D*).

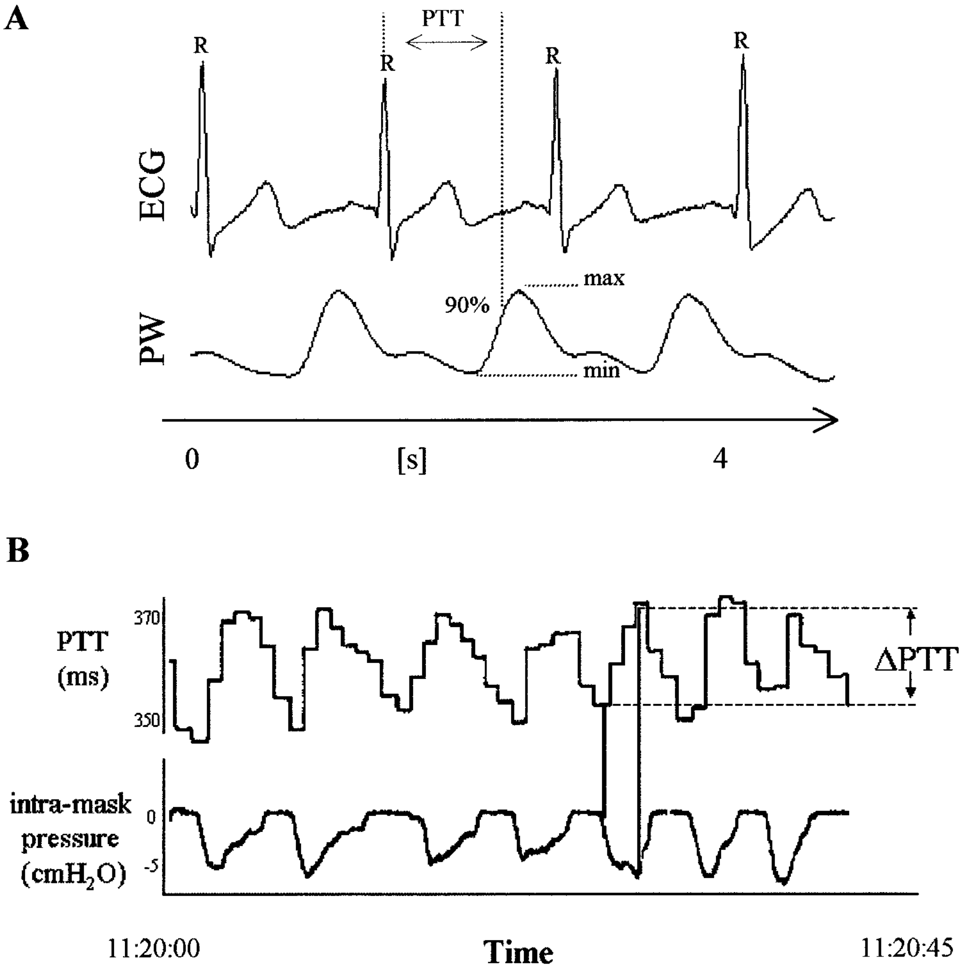

FIGURE 2. *Top*, *panel A*: Fiducial points for PTT estimation. PTT is calculated as the time interval between each R wave of the ECG and 90% of the PW rise, for each beat. *Bottom*, *panel B*: Example of a 45-s section from traces for beat-to-beat (PTT) [*top*] and intramask pressure (*bottom*) traces. The ΔPTT were calculated as the difference between the peak and trough for each breath. Vertical lines indicate the selected breath. max = maximum; min = minimum.

PTT values obtained were automatically converted by the software into a beat-to-beat PTT trace (Fig 2, *bottom*, *B*).

Because individual PTT values correlate poorly with absolute intrathoracic pressure values,[9] to evaluate inspiratory efforts more accurately we also calculated amplitude of PTT variations (ΔPTT), as suggested by Pitson et al.[17] ΔPTT was calculated as the difference between the maximum and minimum PTT values within the same respiratory cycle (Fig 2, *bottom*, *B*).

The maximum and minimum PTTs were detected for every respiratory cycle. For each breathing cycle, we also measured the maximal intramask pressure drop (Pdrop). For each subject, we analyzed 16 consecutive breaths from the second and third minute of each 3-min breathing trial at baseline and against resistance. We calculated the average ΔPTT and Pdrop over 16 consecutive breaths, for each resistance. The local ethics committee approved the study protocol, and all of the children's parents gave their informed consent to the procedures.

Statistical Methods

All data are expressed as mean ± SD. A nonparametric, repeated-measures analysis of variance with the Friedman test was used to compare changes in PTT at various inspiratory resistances. A logarithmic correlation was determined between Pdrop and ΔPTT; $p \leq 0.05$ was considered statistically significant. Data were analyzed with a statistical software program (Version 10.1; SPSS; Chicago, IL).

RESULTS

All subjects had normal height and weight for age. Of the 15 participants selected, 13 children completed the trial and 2 children did not because of poor compliance with the procedure.

No significant difference was found for mean PTT values in boys and girls. The various airway resistances applied left the mean, maximum, and minimum PTT values unchanged (Table 1).

As the applied inspiratory resistance increased, the mean ΔPTT increased significantly (from 11.13 ± 1.41 ms at zero resistance to 21.02 ± 3.00

Table 1—*Mean, Maximum, and Minimum PTT Values in the 13 Subjects**

Variables	Boys	Girls	Total
Age, yr	8.41 ± 1.74	9.37 ± 2.98	8.3 ± 2.74
Baseline			
Mean PTT	376.61 ± 20.71	376.94 ± 28.99	376.71 ± 23.03
Mean PTT minimum, ms	368.12 ± 19.96	369.96 ± 33.29	368.83 ± 24.55
Mean PTT maximum, ms	385.11 ± 21.48	381.49 ± 28.39	383.72 ± 23.27
Resistance (11.3 cm H_2O/L/s)			
Mean PTT, ms	382.57 ± 17.96	394.75 ± 12.34	383.01 ± 21.70
Mean PTT minimum, ms	371.25 ± 21.08	375.86 ± 16.12	373.03 ± 18.71
Mean PTT maximum, ms	387.94 ± 21.77	403.17 ± 23.81	393.80 ± 22.91
Resistance (13.3 cm H_2O/L/s)			
Mean PTT, ms	380.96 ± 18.04	397.08 ± 9.69	387.68 ± 15.62
Mean PTT minimum, ms	370.02 ± 20.03	377.65 ± 26.76	372.95 ± 22.08
Mean PTT maximum, ms	385.32 ± 22.46	403.39 ± 17.67	392.27 ± 21.95
Resistance (85.1 cm H_2O/L/s)			
Mean PTT, ms	385.00 ± 19.39	378.19 ± 32.94	382.60 ± 22.56
Mean PTT minimum, ms	372.41 ± 19.12	364.21 ± 36.03	369.25 ± 25.75
Mean PTT, maximum, ms	390.69 ± 21.57	386.02 ± 35.46	388.9 ± 26.38

*Data are presented as mean ± SD.

ms at maximum; analysis of variance, Friedman, $p < 0.05$) [Table 2; Fig 3, *top*, *A*]. No significant differences were found between ΔPTT values according to sex (Table 2). A positive logarithmic correlation was found between Pdrop values and ΔPTT values ($R^2 = 0.544$) [Fig 3, *bottom*, *B*].

Discussion

These results, to our knowledge among the first obtained in healthy awake children and under standardized conditions, indicate that PTT is a sensitive descriptor of inspiratory effort also in children. Our data show a good correlation between the induced inspiratory effort and ΔPTT values. Conversely, the mean, maximum, and minimum PTT values seem unable to evaluate inspiratory effort, as others have reported in adults.[9]

In our study, pressure falls in the mask (− 8.31 ± 3.35 cm H_2O) induced important changes in mean ΔPTT values from baseline (11.13 ± 1.41 ms vs 21.02 ± 3.00 ms, $p < 0.001$). ΔPTT also increased significantly already at a Pdrop of approximately − 1 cm H_2O (Pdrop from − 1.10 ± 0.31 to − 2.42 ± 0.75 cm H_2O, $p < 0.001$; ΔPTT from 11.13 ± 1.41 to 15.82 ± 2.90 ms, $p < 0.001$) [Table

Table 2—*Mean ΔPTT Values and Mean Pdrop**

		Baseline		11.3 cm H_2O/L/s		13.3 cm H_2O/L/s		85.1 cm H_2O/L/s	
Patient No.	Sex	Mean ΔPTT, ms	Pdrop, cm H_2O	Mean ΔPTT, ms	Pdrop, cm H_2O	Mean ΔPTT, ms	Pdrop, cm H_2O	Mean ΔPTT, ms	Pdrop, cm H_2O
1	M	12.11 ± 1.32	− 1.27 ± 0.22	17.90 ± 2.97	− 1.25 ± 0.20	19.83 ± 2.95	− 1.45 ± 0.24	21.55 ± 2.83	− 4.63 ± 0.10
2	M	10.93 ± 1.44	− 1.23 ± 0.21	16.08 ± 3.34	− 1.92 ± 0.59	16.86 ± 2.12	− 2.35 ± 0.24	18.42 ± 1.04	− 8.89 ± 0.33
3	M	11.16 ± 2.34	− 1.59 ± 0.33	17.53 ± 2.01	− 2.43 ± 0.28	17.31 ± 0.95	− 2.81 ± 0.11	21.05 ± 1.72	− 9.35 ± 0.26
5	M	13.61 ± 1.35	− 1.27 ± 0.18	17.25 ± 1.50	− 2.26 ± 0.05	17.87 ± 2.20	− 3.14 ± 0.27	26.00 ± 3.15	− 12.12 ± 0.26
6	M	10.47 ± 1.42	− 1.25 ± 0.22	18.21 ± 2.19	− 2.57 ± 0.32	19.68 ± 1.21	− 3.71 ± 0.13	21.89 ± 3.18	− 13.32 ± 0.20
7	M	11.64 ± 1.22	− 0.79 ± 0.11	12.56 ± 0.76	− 2.41 ± 0.16	15.20 ± 1.97	− 2.65 ± 0.07	22.22 ± 1.92	− 11.80 ± 0.20
8	M	11.55 ± 2.64	− 1.08 ± 0.09	13.18 ± 2.30	− 2.65 ± 0.17	15.87 ± 0.64	− 3.7 ± 0.14	20.44 ± 2.10	− 5.27 ± 0.22
14	M	13.17 ± 1.78	− 0.72 ± 0.27	16.02 ± 1.78	− 1.11 ± 0.22	15.01 ± 1.65	− 1.66 ± 0.17	20.97 ± 2.03	− 8.61 ± 1.45
Mean	(M)	11.83 ± 1.08	− 1.15 ± 0.28	16.09 ± 2.14	− 2.07 ± 0.59	17.20 ± 1.85	− 2.68 ± 0.84	21.56 ± 2.13	− 9.24 ± 3.14
4	F	8.53 ± 2.89	− 1.36 ± 0.26	15.87 ± 3.23	− 3.77 ± 0.12	16.39 ± 1.63	− 4.34 ± 0.19	21.24 ± 3.71	− 13.62 ± 0.34
10	F	11.5 ± 2.14	− 1.11 ± 0.38	14.89 ± 1.79	− 2.64 ± 0.29	17.39 ± 1.57	− 3.5 ± 0.23	20.94 ± 2.28	− 7.23 ± 0.32
11	F	10.92 ± 1.85	− 1.38 ± 0.02	22.08 ± 2.98	− 2.24 ± 0.04	21.57 ± 3.07	− 2.64 ± 0.57	26.09 ± 3.12	− 6.26 ± 0.53
12	F	9.3 ± 1.18	− 0.83 ± 0.07	12.77 ± 1.32	− 2.59 ± 0.89	11.22 ± 2.15	− 3.59 ± 0.74	15.08 ± 2.68	− 5.09 ± 1.53
13	F	9.91 ± 2.05	− 0.48 ± 0.14	11.44 ± 2.37	− 3.62 ± 0.23	11.23 ± 0.98	− 3.84 ± 0.15	17.42 ± 1.96	− 9.35 ± 0.15
Mean	(F)	10.03 ± 1.19	− 1.03 ± 0.3	15.41 ± 4.11	− 2.97 ± 0.6	15.56 ± 4.40	− 3.58 ± 0.61	20.15 ± 4.19	− 8.31 ± 3.35
Mean total		11.13 ± 1.41	− 1.10 ± 0.3	15.82 ± 2.90	− 2.42 ± 0.75	16.57 ± 3.03	− 3.02 ± 0.86	21.02 ± 3.00	− 8.68 ± 3.32

*Data are presented as mean ± SD. M = male; F = female.

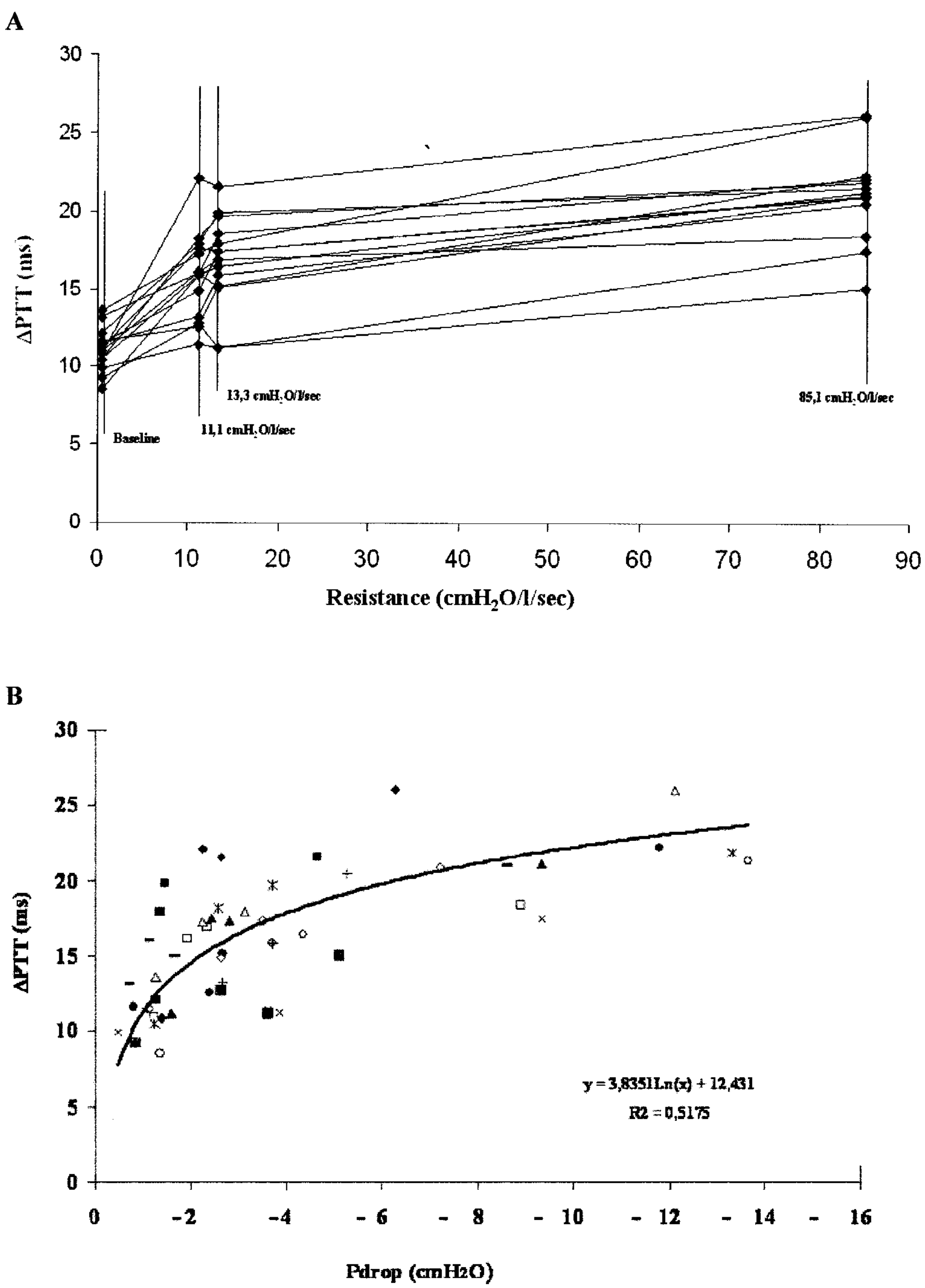

FIGURE 3. *Top, panel A*: ΔPTT (difference between the maximum and minimum PTT values within the same respiratory cycle) at the various airway resistances applied. *Bottom, panel B*: Positive logarithmic correlation ($R^2 = 0.544$) between Pdrop values (maximal intramask pressure drop) and ΔPTT values. Each child is represented by a different symbol.

2]. This finding shows that ΔPTT is a sensitive indicator capable of describing even small changes in inspiratory effort.

In some of the children we studied, we found no correspondence between Pdrop values in the mask and ΔPTT. For example, at maximum resistance, child 1 and child 3 had distinctly different Pdrop values (− 4.63 ± 0.10 cm H_2O vs − 9.35 ± 0.26 cm H_2O) but similar ΔPTT (21.55 ± 2.83 ms vs 21.05 ± 1.72 ms, respectively) [Table 2]. This finding could have several explanations. One is that emotional factors induced variations in arterial pressure and heart rate.[18] Nonetheless, this hypothesis receives no support from the mean heart rate data in our patients, insofar as heart rates remained appreciably unchanged throughout the test. An alternative, more likely explanation is that our subjects differed in vascular compliance.

Interestingly, as the pressure exerted on the respiratory airways increased, ΔPTT increased not linearly but in a logarithmic manner, thus tending to saturate. Again, this behavior may have arisen from cardiovascular factors such as elasticity and compliance of the arterial vascular tree that prevented the PTT velocity from increasing or slowing down beyond a certain limit. Nevertheless, because we compared inspiratory effort evaluated by PTT with Pdrop at the mouth, mouth pressure was not linearly related to intrapleural pressure. This finding may also explain the nonlinear relationship between Pdrop and ΔPTT.

Although esophageal balloon measurement would probably have yielded a better correlation of the data for inspiratory force and changes in ΔPTT, unfortunately this study protocol failed to receive ethics committee approval; however, the Pdrop values at which ΔPTT tended to saturate in our study exceeded – 8 cm H_2O. In children during sleep, even these subatmospheric mouth pressures are probably sufficient to cause complete upper airway occlusion.[19] This observation implies that the mouth Pdrop values at which ΔPTT values tend to saturate are at the limits of the maximal respiratory effort induced by transient upper airway obstructive events, such as sleep apneas.[20,21]

Hence, because the ΔPTT reached a plateau at high subatmospheric mouth pressures, our patients were presumably already at their maximum tolerable resistance. Augmenting resistance would therefore have left esophageal pressure unchanged.

Two findings are of importance in judging the clinical value of the method we propose. First, the significant increase in absolute values began at relatively low applied resistances (and hence Pdrop) [resistance, < 14 cm H_2O/L/s; Pdrop, < 3 cm H_2O]. Second, the nonlinear relationship is a problem if ΔPTT is to be used as a quantitative measure of changes in respiratory effort when children are close to the maximum resistance they can tolerate. ΔPTT could nonetheless be useful as a qualitative measure for identifying obstructive events associated with increased respiratory effort. Last, for clinical application, the normalized values we obtained from baseline suggest that the method needs to be calibrated for each patient.

Our results imply that ΔPTT will detect even moderate inspiratory efforts in children. ΔPTT measurement could provide a valid noninvasive alternative to the endoesophageal balloon technique for measuring inspiratory effort during sleep study. Only few published data are available on the use of PTT in children during sleep.[22] These data indicate that, as happens in the adult,[4,9,10] the minor changes in pulmonary dynamics during sleep are unlikely to alter the ability of PTT to detect inspiratory effort. For these reasons, PTT could have a clinical application in polysomnographic studies for the diagnosis of upper airways resistance syndrome and obstructive sleep apnea syndrome in children. Software based on ΔPTT measurement might also help to simplify portable polysomnographic systems.

In conclusion, techniques based on the detection of ΔPTT values may be useful for evaluating increased inspiratory resistance in children. The PTT technique we propose for measuring changes in inspiratory effort in children merits further validation in a sleep laboratory.

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