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# Predicting poor school performance in children suspected for sleep-disordered breathing

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#### ABSTRACT

*Objective:* Habitually snoring children are at a greater risk of poor school performance (PSP). We investigated the ability of conventional sleep-disordered breathing (SDB) measures for predicting PSP in habitually snoring children.

*Methods:* The dataset of Hannover Study on Sleep Apnea in Childhood (HASSAC), a large communitybased study in primary school children, was retrospectively analyzed. All habitual snorers were included. Based on their grades, children were grouped into good and poor school performers. SDB measures obtained by a parental questionnaire, a home pulse oximetry, and a home polysomnography were evaluated for their accuracy in predicting poor school performance by calculating receiver operating characteristic curves and area under this curve (AUC). The most predictive single factors were identified and entered into a prediction model.

*Results:* Of 114 habitual snorers (mean age 9.6 years, 51 boys), 59 had PSP. All investigated SDB measures showed low accuracy (ie, AUC <0.8). The highest AUC observed was 0.686 for a questionnaire score, 0.565 for an oximetry factor, and 0.624 for a polysomnography factor. Of 20 single significant predictors for PSP, five were selected for inclusion into a prediction model. The model reached an unadjusted AUC of 0.826 and an adjusted AUC of 0.851.

*Conclusions:* Conventional SDB measures obtained with questionnaire, oximetry, or polysomnography may not be sufficiently predictive of PSP in children suspected for SDB. However, combining factors in a clinical prediction model may improve prediction. Results of such a model may be used to assess the risk of developing neurocognitive impairment and to decide whether a child suspected for SDB might benefit from treatment.

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# 1. Introduction

Sleep-disordered breathing (SDB), among other socioeconomic and biological factors, may be associated with neurocognitive impairment (NCI) as evidenced by poor school performance (PSP) [1,2], inattentive and hyperactive behavior [3,4], and other externalizing behavioral problems in children [5,6]. In 2006, a comprehensive review showed that the overwhelming majority of published studies support a causal association between SDB and NCI [7]. However, convincing interventional data are lacking. Recently, the childhood adenotonsillectomy (CHAT) study found that children with SDB on

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average had largely normal results on neurocognitive tests before, and no significant improvement following, treatment. In contrast to neurocognitive tests, these children showed significantly improved functioning in their school setting on teacher ratings [8]. Thus, PSP may be an SDB-sensitive "real-world" marker of NCI in children.

SDB-associated intermittent hypoxia during sleep and sleep fragmentation has been postulated as mediating factors in the relationship between SDB and NCI [6,9]. Consequently, habitual snoring without intermittent hypoxia and sleep fragmentation (ie, primary snoring) should not be associated with NCI. There is increasing evidence, however, that NCI is more frequent in children with primary snoring compared to never-snoring controls. In these studies, primary snoring was associated with several cognitive impairments [10], problems in memory [3], language, and visuospatial areas [11]. In one study, there was no obvious difference between primary snorers and patients with obstructive sleep apnea (OSA) regarding daytime sleepiness and hyperactive behavior [12]. More recently, children with primary snoring were found to be at higher



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risks for NCI than never-snoring controls, with effects being similar to those in children with upper airway resistance syndrome or OSA [13]. Hence, there is increasing evidence that primary snoring is not a benign condition.

Despite the association between SDB and NCI, there is yet no test available that can accurately predict NCI in children suspected for SDB. This includes sleep-laboratory-based polysomnography (PSG) as the current gold standard for diagnosing SDB. PSG and the PSG-based apnea–hypopnea index (AHI) identify OSA, but the AHI in particular often fails to predict NCI in children suspected for SDB. In one study, a questionnaire score showed better correlations with NCI markers such as hyperactive-inattentive behavior and daytime sleepiness than the simultaneously obtained AHI [14]. Thus, accurate predictors for NCI – PSG and non-PSG-based – are obviously needed.

Medical history, questionnaires, physical examination, oximetry, and home PSG are methods with unknown or insufficient diagnostic test accuracy for diagnosing OSA in children [15,16]. They may be used alone or combined, however, to predict NCI in subjects with SDB. We, hence, set out to identify potential predictors of PSP as one important marker of NCI in childhood. We specifically aimed to investigate the usefulness of easily available clinical information obtained by a parental SDB-questionnaire (SDB-Q), home pulse oximetry (HPO), and home PSG. By using this information, we aimed to create and validate a prediction model for PSP, based on the already published dataset of the Hannover Study on Sleep Apnea in Childhood (HASSAC) (Urschitz et al. 2011).

# 2. Methods

# 2.1. The Hannover study on sleep apnea in childhood

# 2.1.1. Study design

HASSAC was a community-based cross-sectional study on several aspects of SDB in school-aged children conducted between February and December 2001. Methods and main results have been outlined in detail elsewhere [17,18]. HASSAC incorporated a two-phase sequential screening procedure. Participants were screened twice for symptoms and signs of SDB using an SDB-Q and HPO. Children with outlying results on either screening method subsequently underwent home PSG for a final diagnosis of OSA.

## 2.1.2. Subjects

Twenty-seven of 59 public primary schools located within the city limits of Hannover, Germany, were randomly selected. After approval by the institutional review board and the regional directorate of education, all children attending third-grade classes in these schools were identified and contacted in their classrooms. Of 1760 eligible third graders in classes of the sampled schools, 1144 individuals (65.0%, mean age  $9.6 \pm 0.7$  years) provided parental informed consent, and they were enrolled. Comparisons to the target population of all children of the same grade living in Hannover city (n = 4109) revealed good to excellent representativeness of the study sample in terms of gender distribution, parental education, and the prevalence of childhood asthma [17].

# 2.1.3. Questionnaire

Detailed descriptions of the questionnaire are given elsewhere [17,19]. Briefly, the SDB-Q by Gozal [1] was adjusted to enable the calculation of the OSA score according to Brouillette [20], and it was extended with items on demographic, socioeconomic, and anthropometric characteristics [17], daytime behavior [21], frequent sleep problems [22], and current health status. The OSA score according to Brouillette [20], the SDB score according to Gozal [1], the Snore score according to Gozal [23], and an adapted SDB score according to Paditz [21] were calculated. Details on the calculation of the scores are given elsewhere [17,24]. In short, for the calculation of

scores, arbitrary numerical values were assigned to each of the answers ranging from 0 (never), 1 (rarely), 2 (occasionally), 3 (frequently) to 4 (always/almost always). Missing answers were scored as 0. The adapted SDB score according to Paditz consisted of the items 1–14 and 20–21 of the SDB-Q. In contrast to Gozal's SDB score (13 items), the adapted Paditz score comprised 16 items (including questions on hyperactive behavior, attention deficits, and frequency of respiratory tract infections). In a first comparison, the correlation coefficient for the original Gozal score and the adapted Paditz score was r = 0.931 [17]. The Paditz score was subsequently validated concerning its accuracy in predicting OSA on home PSG [24]. Snoring was assessed with the question "Does your child snore?" and it was rated on a four-point Likert scale. Children were classified as habitual snorers if the answers were "frequently" or "always."

#### 2.1.4. Home pulse oximetry

A detailed description of HPO is presented elsewhere [25,26]. Briefly, recordings of arterial oxygen saturation measured by pulse oximetry (SpO<sub>2</sub>) were performed overnight in the child's home. Data analysis software was used to determine artifact-free recording time and to calculate the mean, standard deviation, median, fifth, and 10th centile SpO<sub>2</sub>, as well as the number of desaturation events of  $\geq$ 4% SpO<sub>2</sub>, the average distance from the optimum of 100% SpO<sub>2</sub>, and a cumulative hypoxemia score [26]. Recordings with artifact-free recording time <5 h were excluded. The nadir SpO<sub>2</sub>, the number of desaturation events to  $\leq$ 92% and to  $\leq$ 90% SpO<sub>2</sub>, as well as desaturation on signal quality, low perfusion, and pulse waveform. Desaturation indices, defined as events per hour of artifact-free recording, were calculated for desaturation events of  $\geq$ 4% SpO<sub>2</sub>, desaturation events to  $\leq$ 92% and to  $\leq$ 90% SpO<sub>2</sub> as well as desaturation events

# 2.1.5. Home PSG

A detailed description of the home PSGs is presented elsewhere [13,28]. Briefly, home PSG was performed overnight in the children's homes. The montage comprised chest and abdominal wall movements, nasal pressure and linearized nasal airflow estimation, oral airflow, snoring, SpO<sub>2</sub>, pulse rate, pulse waveform, body movements and position, and user events. Corrected estimated total sleep time was calculated according to published criteria [28]. Recordings with corrected estimated total sleep time <4 h were excluded. Recordings were manually analyzed for central, mixed and obstructive apneas, hypopneas, and flow limitations based on a guideline by the American Academy of Sleep Medicine [29]. Flow limitations were defined as a reduction of the nasal airflow amplitude by >50% for more than two breathing cycles, not associated with desaturation events of  $\geq 4\%$  SpO<sub>2</sub> [13]. Respiratory event indices, as number of events per hour of corrected estimated total sleep time, were calculated for (i) central, obstructive, and mixed apneas (apnea index); (ii) mixed and obstructive apneas and hypopneas (mixed obstructive apnea-hypopnea index (MOAHI)); (iii) central, obstructive, and mixed apneas and hypopneas (AHI); (iv) central, obstructive and mixed apneas, hypopneas, and flow limitations (respiratory disturbance index); and (v) obstructive and mixed apneas, hypopneas, and flow limitations (obstructive respiratory disturbance index).

# 2.1.6. Assessment of school performance

With parental consent, last term's report form was obtained from the school archive. As usual for the German educational system, the report forms included written ratings on a six-point scale (1 for "outstanding," 2 for "good," 3 for "satisfactory," 4 for "sufficient," and 5 and 6 for "failed") for mathematics, science, spelling, reading, handwriting, ability to study, and attitude toward peers. On an empirical basis, previous studies of this group had suggested that performance in mathematics, science, and spelling may be particularly affected by SDB [2,13]. Thus, PSP was defined for the current study as grade 4 or worse, or requirement for special assistance in at least one out of these three school subjects. Depending on the school subject, the frequency of grade 4 or worse comprised approximately 20% of the total sample, which corresponded to the lower quintile. At the time of study, grade 4 or worse was associated with a low chance for being enrolled in high school (ie, gymnasium) because a grade point average of at least 2.0–2.5 was required in several federal states of Germany (source: http://de.wikipedia.org/wiki/ Lehrerempfehlung).

# 2.2. Measures of SDB and predicting factors

The following common SDB measures were evaluated: the Snore score according to Gozal, the OSA score according to Brouillette, the SDB score according to Gozal, and the adapted SDB score according to Paditz, index of desaturation events by  $\geq 4\%$  SpO<sub>2</sub>, index of desaturation events by  $\geq 2\%$  SpO<sub>2</sub>, index of desaturation events to  $\leq 92\%$  SpO<sub>2</sub>, index of desaturation events to  $\leq 90\%$  SpO<sub>2</sub>, nadir SpO<sub>2</sub>, apnea index, MOAHI, AHI, respiratory disturbance index, and obstructive respiratory disturbance index. Some of these SDB measures have been previously evaluated for their accuracy in predicting OSA [24]. For the prediction model, 65 items and factors obtained with the SDB-Q, the HPO, or the home PSG were evaluated (see Appendix).

# 2.3. Statistical analysis

The predictive accuracy of common SDB measures was investigated using receiver operating characteristic (ROC) curves and the area under the ROC curves (AUCs) [30]. The AUC is equal to the probability that a test will correctly assign disease status to a randomly chosen pair of a diseased and a non-diseased subject. In accordance with previous studies, acceptable predictive accuracy was defined as AUC >0.8 [16]. Classical measures of accuracy such as

#### Table 1

Demographic characteristics of study sample and subgroups.

Characteristic (unit)	Statistics	Total sample N = 114	Without PSP N = 55	With PSP $N = 59$
Age (years) Males Body mass index (kg/m <sup>2</sup> )	Mean ± SD N (%) Mean ± SD	$\begin{array}{c} 9.6 \pm 0.7 \\ 51 \ (45) \\ 18.9 \pm 4.1 \end{array}$	$\begin{array}{c} 9.3 \pm 0.5 \\ 24  (44) \\ 17.9 \pm 3.4 \end{array}$	$\begin{array}{c} 9.8 \pm 0.7 \\ 27  (46) \\ 19.9 \pm 4.5 \end{array}$
Low maternal education	N (%)	39 (34.2)	12 (22)	27 (46)

Abbreviations: PSP, poor school performance; SD, standard deviation.

#### Table 2

Results of the ROC analysis for SDB measures

sensitivity and specificity, as well as positive and negative likelihood ratio (LHR), were calculated for the prediction model. The selection procedure of predicting factors, the construction and validation of the prediction model, and the recommendation for clinical application of the model are presented in the Appendix. Recoding and creation of variables, descriptive statistics and  $2 \times 2$  cross-tabulation, groupwise comparisons, logistic regression analyses, as well as ROC curves and AUC analyses were performed using IBM Statistical Package for Social Science (SPSS) 20.0. For the calculation of classical measures of accuracy, a Microsoft Office Excel 2003 worksheet (German version; service pack 3.0; Microsoft Corporation, Redmond, WA, USA) was used.

# 3. Results

# 3.1. Subjects

Of 1144 children enrolled, 114 (10%) were habitual snorers, and they were included in the present analysis. Of the latter, 59 and 55 were classified with and without PSP, respectively. Demographic characteristics of the study sample and both groups are given in Table 1. SDB-Q and HPO data were available for all 114 children included. However, 16 children had refused to participate in PSG evaluation or had moved out of the study region. Consequently, only 98 PSGs could be conducted. Of these, five were excluded from analysis because of uninterpretable recordings in two and an insufficient corrected estimated total sleep time in three.

# 3.2. Accuracy of measures of SDB

Results of the ROC analysis for SDB measures are given in Table 2. All SDB-Q-based SDB measures had significant AUC results, whereas no HPO-based SDB measure was significant. Of PSG-based SDB-measures, only the MOAHI and obstructive respiratory disturbance index were significant. Of all SDB measures, the adapted SDB score according to Paditz had the highest AUC (0.686). Hence, none of the investigated SDB measures reached the desired level of acceptable accuracy (ie, AUC >0.8).

# 3.3. Prediction model

Of 65 potentially predictive items and factors available, 20 were significantly (*p*-value <0.1) different between PSP groups (Table 3). Starting with a complete model including all significant predictive items/factors, a stepwise conditional backward elimination

SDB measure	AUC	SE of the AUC	Asymptotic P-value	Asymptotic 95% CI	
				Lower limit	Upper limit
Snore score according to Gozal	0.632	0.052	0.015	0.530	0.734
OSA score according to Brouillette	0.621	0.053	0.025	0.518	0.725
SDB score according to Paditz	0.686	0.050	0.001	0.589	0.783
SDB score according to Gozal	0.650	0.051	0.006	0.550	0.751
Index of desaturation events by ≥4% SpO <sub>2</sub>	0.522	0.059	0.705	0.406	0.638
Index of desaturation event clusters	0.522	0.058	0.708	0.407	0.636
Index of desaturation events to ≤92% SpO <sub>2</sub>	0.516	0.059	0.779	0.402	0.631
Index of desaturation events to ≤90% SpO <sub>2</sub>	0.535	0.058	0.552	0.421	0.649
Nadir SpO <sub>2</sub>	0.565	0.058	0.267	0.451	0.679
Apnea index	0.543	0.060	0.475	0.426	0.661
Mixed obstructive apnea-hypopnea index	0.622	0.058	0.042	0.508	0.736
Apnea-hypopnea index	0.568	0.060	0.258	0.451	0.685
Obstructive respiratory disturbance index	0.624	0.059	0.040	0.509	0.739
Respiratory disturbance index	0.572	0.060	0.233	0.454	0.689

Abbreviations: ROC, receiver operating characteristic; SDB, sleep-disordered breathing; AUC, area under the curve; SE, standard error; CI, confidence interval; OSA, obstructive sleep apnea; SpO<sub>2</sub>, arterial oxygen saturation.

#### Table 3

Significant predicting factors.

Factor	Source	Statistical test	Ν	P-value
Age	SDB-Q	Mann-Whitney U-test	114	0.001
Weight	SDB-Q	Mann-Whitney U-test	101	0.015
Body mass index	SDB-Q	Mann-Whitney U-test	91	0.029
Does your child snore?	SDB-Q	Chi-squared test	114	0.006
If your child snores, how loud is the snore?	SDB-Q	Chi-squared test for trend	113	0.085
Is your child very restless, fidgety, or always in motion during daytime?	SDB-Q	Chi-squared test for trend	113	0.009
Does your child have difficulties concentrating during daytime?	SDB-Q	Chi-squared test for trend	113	< 0.001
Is your child tired during daytime?	SDB-Q	Chi-squared test for trend	113	0.001
Does your child fall asleep while watching television?	SDB-Q	Chi-squared test for trend	111	0.01
Does your child fall asleep at school?	SDB-Q	Chi-squared test for trend	105	0.097
How often did your child have infections during the past 12 months?	SDB-Q	Chi-squared test	109	0.053
How often does your child have a sore throat?	SDB-Q	Chi-squared test for trend	113	0.087
How many cigarettes are smoked in your household per day?	SDB-Q	Chi-squared test for trend	112	0.079
What was your highest graduation from school? (mother)	SDB-Q	Chi-squared test for trend	108	0.017
What was your highest graduation from school? (father)	SDB-Q	Chi-squared test for trend	100	0.018
Snore score according to Gozal	SDB-Q	Mann-Whitney U-test	114	0.007
OSA score according to Brouillette	SDB-Q	Mann-Whitney U-test	114	0.021
SDB score according to Paditz	SDB-Q	Mann-Whitney U-test	114	0.001
Mixed obstructive apnea-hypopnea index	NHPG	Mann-Whitney U-test	93	0.026
Obstructive respiratory disturbance index	NHPG	Mann-Whitney U-test	93	0.034

Abbreviations: OSA, obstructive sleep apnea; SDB, sleep-disordered breathing; SDB-Q, sleep-disordered breathing questionnaire; NHPG, nocturnal home polygraphy.

# Table 4

The final prediction model.

Factor	Beta	SE	Wald's test statistics	Degrees of freedom	P-value
Age	1.364	0.423	10.420	1	0.001
Is your child very restless, fidgety, or always in motion during daytime?	0.886	0.524	2.861	1	0.091
Does your child have difficulties concentrating during daytime?	1.024	0.564	3.291	1	0.070
Does your child fall asleep at school?	1.634	1.257	1.689	1	0.194
SDB score according to Paditz	0.087	0.041	4.429	1	0.035
Constant	-15.407	4.312	12.765	1	< 0.001

Abbreviations: SE, standard error; SDB, sleep-disordered breathing.

procedure was performed in 15 steps, thereby eliminating 15 out of 20 items/factors. Finally, the items/factors age, hyperactive behavior, concentration deficits, falling asleep at school, and the adapted SDB score according to Paditz remained in the model. Hence, these items/factors were, independent of each other, highly predictive of PSP. The final model with estimates for the regression coefficients and their standard errors is presented in Table 4.

# 3.4. Validity of the prediction model

Groupwise comparisons of the probability values delivered by the prediction model showed that children with PSP had higher probability values (median: 0.73, minimum–maximum: 0.17–1.0) than children without PSP (0.33, 0.0–0.88; *p*-value <0.001). The AUC (95% confidence interval [CI]) for the probability values was 0.826 (0.752–0.900); the highest Y-value (ie, 0.497) was obtained with probability value P = 0.620. This cutoff value reached 0.661 sensitivity, 0.836 specificity, 4.040 + LHR, and 0.405 –LHR.

Leave-one-out cross-validation suggested good external validity. The AUC (95% CI) for the leave-one-out cross-validation-adjusted probability values was 0.851 (0.778–0.923); the best performing cutoff value (probability value P=0.504; Y-value = 0.573) reached 0.759 sensitivity, 0.815 specificity, 4.097 + LHR, and 0.296 –LHR. Based on

these results, it is recommended to use a cutoff value of 0.504 for the probability value *P*.

# 3.5. Recommendations for clinical application

Linear regression analysis revealed the following cutoffs for age and SDB score according to Paditz: 9.54 years and 20.2 score points, respectively. Above these cutoff values, the corresponding probability values were >0.504, hence, suggesting an increased risk of PSP. For the three predictive items of the SDB-Q, each "problempresent" category was associated with a probability value of >0.504.

# 4. Discussion

The present study aimed at predicting PSP in habitually snoring children using standard SDB measures based on a questionnaire, HPO, and PSG, as well as a newly developed prediction model. Therefore, data on a community-based sample of third graders were reanalyzed. The prevalence of habitual snoring was 10% in this sample, which was in line with international studies [31]. The results showed moderate but significant predictive accuracy for SDB-Q and PSG-based SDB measures and weak and non-significant predictive accuracy for HPO-based SDB measures. In addition, a newly developed prediction model for PSP, whose variables were selected and weighted using logistic regression analysis, performed better, and it reached a desired predictive accuracy of AUC >0.8, even following cross-validation. Standard SDB measures alone – HPO-based measures in particular – may be poor predictors of PSP in habitually snoring children.

In the present study, all investigated SDB-Q-based SDB measures showed, on their one, only insufficient predictive accuracy, which prevents recommendation for clinical use. There are only few studies investigating the capability of questionnaires to predict NCI in snoring children. In 2007, Chervin et al. analyzed the usefulness of a questionnaire in predicting hyperactive behavior, attention deficits, and daytime sleepiness in a cohort of 105 children [14]. The questionnaire score showed a good correlation with hyperactive behavior (ie, 0.65), a weak correlation with daytime sleepiness (ie, -0.25), and no significant correlation with attention deficits (ie, -0.16). The same figures for the AHI were 0.18 for hyperactive behavior, -0.19 for daytime sleepiness, and 0.03 for attention deficits (all non-significant). The authors concluded that this questionnaire score was at least as predictive as the AHI for NCI. However, this questionnaire was not used in the present study, because it was not available in 2000 when HASSAC was designed. However, the predictive capability of Chervin's questionnaire seems promising, should be evaluated in future studies, and may be more accurate than the SDB measures investigated here.

No HPO-based SDB measure showed a significant AUC for predicting PSP. This is of interest as intermittent hypoxia was postulated to be one of the most important explanations why SDB may lead to significant NCI [32]. Furthermore, a systematic review found quite convincing evidence for a causal relationship between hypoxia and NCI in SDB subjects [33]. In a study from our group, nadir SpO<sub>2</sub> was significantly related to PSP [26]. Mild (ie, nadir SpO<sub>2</sub> 91–93%) and moderate hypoxia (ie, nadir SpO<sub>2</sub>  $\leq$  90%) showed odds ratios of 1.65 and 2.28, respectively, for the association of PSP in mathematics [26]. On the other hand, intermittent hypoxia may not be the only cause for NCI in SDB subjects. Frequent arousal or sleep disturbance, triggered by snoring or apnea, is suspected to be the other causal mediators [32]. This was supported by studies of our group, where habitually snoring children with intermittent hypoxia did not differ from habitually snoring children without intermittent hypoxia regarding their risk of PSP [2] and behavioral disturbances [19]. Hence, in the population-based sample of HASSAC, snoring was the main predictor for PSP, and intermittent hypoxia did not alter or modify this relationship. The results of the current study are in line with these observations, and they suggest that HPO-based SDB measures may not provide additional information for the prediction of PSP in children suspected for SDB.

Two PSG-based SDB measures, the MOAHI and the obstructive respiratory disturbance index, were significantly related to PSP according to AUC results. Although statistically significant, AUC levels were low (<0.8), and they did not reach an acceptable accuracy. Several studies have failed to demonstrate clinically relevant and statistically significant correlations between PSG indices and NCI [5,34,35]. In one study, the correlation between PSG and NCI variables was investigated in children with attention-deficit hyperactivity disorder (ADHD) [34]. PSG variables accounted only for a negligible proportion of the variance in several neurocognitive test results. Rapid eye movement (REM) sleep total percentage and REM sleep latency, but not the AHI, were the only variables that correlated with test results. In another study, Beebe et al. performed several neuropsychological tests, and they compared them with 17 PSG variables derived from sleep architecture, sleep disruption, respiratory events, and hypoxic events. No PSG variable showed significant correlations with any neuropsychological test [5]. This was later confirmed by Chervin et al., where the AHI was related neither to hyperactive behavior nor to daytime sleepiness or attention deficits [14]. Other studies, however, have shown at least weak relationships between the AHI and some neurocognitive variables [12,36]. In one study, an obstructive PSG index was significantly related to parent- and teacher-reported behavioral disturbances and school grades, but not to office-based neuropsychological tests [36]. The present study concurs with all these findings, and it confirms two repeatedly made observations: PSG indices are only weakly related to NCI, and among all candidate indices, the "obstructive" indices such as MOAHI and obstructive respiratory disturbance index show the best performance. However, it seems that conventional PSG indices are not helpful, and there is obviously a need for better predictive methods and markers.

The final prediction model included variables such as age, hyperactive behavior, concentration deficits, falling asleep at school, and the SDB score according to Paditz [21]. Hence, no objectively obtained predictor was strong enough to be maintained in the final model. The importance of behavioral factors such as attention deficit, hyperactive behavior, and sleepiness for the evolution of PSP is in line with the literature [19,37,38]. ADHD is per se and independent of the presence of SDB associated with PSP [39], in particular

in the presence of davtime sleepiness [40]. SDB, in turn, is associated with attention deficits and hyperactive behaviors, which leads to interactions and mixed effects between SDB and ADHD, if both are present in a child. However, ADHD was not evaluated in this study, and children with ADHD were not excluded. Thus, some of the associations reported here may be mediated solely by ADHD. A conservative interpretation of our findings could be that SDB adds at least some additional effect to the effect of ADHD in predicting PSP. To some extent and for some children, attention deficits and hyperactive behaviors could be due to, or exacerbated by, SDB. However, if a child suffers from both SDB and ADHD, the risk of PSP may be elevated markedly. The precise mechanism of how SDB affects PSP is unknown. Several factors such as verbal and nonverbal intelligence [7], executive functioning [41], and working memory [6] are likely related to PSP, and these may be impaired by SDB. Obviously, the effect of SDB seems to be embedded in a complex arrangement of genetic and environmental factors that together influence school performance in the end [7].

In our model, age was also related to PSP. In detail, the risk of PSP increased with age. Biological age may be correlated to the cumulative exposure time for snoring. In other words, older children may have already snored for a longer time period (ie, long-term habitual snoring) compared to younger children. If the risk of PSP increases with exposure time for snoring, PSP will be more prevalent among long-term habitual snorers and, thus, older children. Longitudinal data from the Avon Longitudinal Study of Parents and Children (ALSPAC) study suggest that nearly 4% of 2-6-year-old children snore always and retain their snoring over years [42]. Unfortunately, risk factors for long-term habitual snoring were not addressed. In an authors' study [43], children with long-term snoring differed significantly from ex-habitual snorers in maternal education, household smoking, snoring loudness, and prior ear, nose, and throat surgery. It is likely that long-term snoring may be an important predictor of PSP, and biological age - as in the present study - may be a proxy for this predictor. The role of long-term snoring in the evolution of PSP should be evaluated in future longitudinal studies.

Incorporating five variables into a prediction model, weighting them with estimates obtained from logistic regression, and calculating probability values achieved an acceptable accuracy of >0.8 AUC. To our knowledge, this is the first prediction model for PSP in primary school children with SDB. The model has the advantage that it is based on factors that can be easily obtained by filling out a 16-item questionnaire. This can be performed in primarycare settings, schools, or even at home. With the widespread use of electronic devices (eg, smartphones), the prediction model could easily be integrated into software for clinical use. Based on this model, older children (>9.5 years), those with a high SDB score (>20), and those demonstrating hyperactive behavior, concentration deficits, and daytime sleepiness in school are likely at an increased risk of PSP. This may be considered in clinical decision making, and this may be particularly important for children with primary snoring, who are often not treated for their snoring. The proposed prediction model may be of help to identify those children who may benefit from early treatment, an approach that has been demonstrated to improve several neurocognitive domains in school children [8].

Complete sleep-laboratory-based PSG is the accepted gold standard for diagnosing OSA in children [15], but in HASSAC, home PSG without electroencephalography was used, and an arousal index could not be calculated. Validation studies on home PSG have shown conflicting results [44–47]. One concern with omitting sensors to record sleep is a possible loss of accuracy. This is based on the assumption that if the detection of REM sleep (when OSA is most likely or most severe) is not possible, OSA cannot be ruled out. However, as previously discussed by Morielli [48] and Jacob [45], there is invariably REM sleep present in an all-night recording, even though it may not be possible to determine which specific epochs are included. One study showed a high correlation (ie, r = 0.9) between PSG-derived and polygraphy-derived AHI indices, although the polygraphic recording was obtained in a sleep laboratory and not at home [47]. The lack of an arousal index is a clear limitation of this study, because various types of arousals from sleep (ie, cortical and subcortical) are suspected somehow to account for NCI in pediatric SDB [49–51].

The main outcome of the present study was PSP, based on the last school term's report form. PSP was defined as grade 4 or worse, or requirement for special assistance. This definition was somewhat arbitrary; however, it roughly corresponds to the lowest quintile of a school class. No specific cognitive tests were performed in this study, and we are aware that school grades only provide a rudimentary assessment of cognitive, behavioral, and learning capabilities. In addition, teachers likely vary in their criteria used to assign grades, and assessing school performance is of course not an objective and reproducible procedure. However, there are several aspects voting for the use of grades: (1) the use of teacher ratings is justified by past studies that have found relationships between biological risks and similar teacher ratings [1,23]; (2) school grades are the most important "real-life" indicators for school success in children; (3) due to the unawareness of teachers to the study goals at the time of assigning grades, this assessment was, in any case, a fairly unbiased process; and (4) office-based tests of attention and executive functioning have the limitation of correlating poorly with actual functioning in the daily life of a child. The latter is supported by a recent study showing close relationships between SDB measures and academic grades but not with office-based neuropsychological tests [36]. The authors concluded that office-based tests may not be sufficiently accurate to detect real-life relevant PSP.

# 4.1. Conclusions

Using standard SDB measures, PSP can only poorly be predicted in children suspected for SDB. By contrast, a prediction model based on a simple parental questionnaire showed acceptable accuracy for such a prediction. This model may be used for deciding whether a child with habitual snoring should be treated for his/ her snoring. The use of the model may be particularly relevant to primary snorers, who – by convention – would otherwise not get any treatment. Future studies evaluating prediction models in prospective cohorts and elaborating further predictive factors for PSP in snoring children are necessary.

# **Conflict of interest**

The authors declare no conflicts of interest.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2015.03.021.

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# **Appendix: Supplementary material**

Supplementary data to this article can be found online at doi:10.1016/j.sleep.2015.03.021.

#### References

- [1] Gozal D. Sleep-disordered breathing and school performance in children. Pediatrics 1998;102:616–20.
- [2] Urschitz MS, Guenther A, Eggebrecht E, et al. Snoring, intermittent hypoxia and academic performance in primary school children. Am J Respir Crit Care Med 2003;168:464–8.
- [3] Blunden S, Lushington K, Kennedy D, et al. Behavior and neurocognitive performance in children aged 5–10 years who snore compared to controls. J Clin Exp Neuropsychol 2000;22:554–68.
- [4] Huang YS, Guilleminault C, Li HY, et al. Attention-deficit/hyperactivity disorder with obstructive sleep apnea: a treatment outcome study. Sleep Med 2007;8:18–30.
- [5] Beebe DW, Wells CT, Jeffries J, et al. Neuropsychological effects of pediatric obstructive sleep apnea. J Int Neuropsychol Soc 2004;10:962–75.
- [6] O'Brien LM, Gozal D. Behavioural and neurocognitive implications of snoring and obstructive sleep apnoea in children: facts and theory. Paediatr Respir Rev 2002;3:3–9.
- [7] Beebe DW. Neurobehavioral morbidity associated with disordered breathing during sleep in children: a comprehensive review. Sleep 2006;29:1115–34.
- [8] Marcus CL, Moore RH, Rosen CL, et al. A randomized trial of adenotonsillectomy for childhood sleep apnea. N Engl J Med 2013;368:2366–76.
- [9] Gozal D, Daniel JM, Dohanich GP. Behavioral and anatomical correlates of chronic episodic hypoxia during sleep in the rat. J Neurosci 2001;21:2442– 50.
- [10] Kennedy JD, Blunden S, Hirte C, et al. Reduced neurocognition in children who snore. Pediatr Pulmonol 2004;37:330–7.
- [11] O'Brien LM, Mervis CB, Holbrook CR, et al. Neurobehavioral implications of habitual snoring in children. Pediatrics 2004;114:44–9.
- [12] Melendres MC, Lutz JM, Rubin ED, et al. Daytime sleepiness and hyperactivity in children with suspected sleep-disordered breathing. Pediatrics 2004;114:768–75.
- [13] Brockmann PE, Urschitz MS, Schlaud M, et al. Primary snoring in school children: prevalence and neurocognitive impairments. Sleep Breath 2012;16:23–9.
- [14] Chervin RD, Weatherly RA, Garetz SL, et al. Pediatric sleep questionnaire: prediction of sleep apnea and outcomes. Arch Otolaryngol Head Neck Surg 2007;133:216–22.
- [15] American Academy of Pediatrics, Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome. Clinical practice guideline: diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 2002;109:704–12.
- [16] Brockmann PE, Schaefer C, Poets A, et al. Diagnosis of obstructive sleep apnea in children: a systematic review. Sleep Med Rev 2013;17:331–40.
- [17] Schlaud M, Urschitz MS, Urschitz-Duprat PM, et al. The German study on sleep-disordered breathing in primary school children: epidemiological approach, representativeness of study sample, and preliminary screening results. Paediatr Perinat Epidemiol 2004;18:431–40.
- [18] Urschitz MS, Brockmann PE, Schlaud M, et al. Population prevalence of obstructive sleep apnoea in a community of German third graders (letter). Eur Respir J 2011;37:975–6.
- [19] Urschitz MS, Eitner S, Guenther A, et al. Habitual snoring, intermittent hypoxia, and impaired behavior in primary school children. Pediatrics 2004;114:1041– o
- [20] Brouilette R, Hanson D, David R, et al. A diagnostic approach to suspected obstructive sleep apnea in children. J Pediatr 1984;105:10–14.
- [21] Paditz E, Gräther M, Koch R, et al. Häufigkeit von OSAS-Symptomen im Kleinkindesalter - Vorstudie, Multizenterstudie der AG Pädiatrie DGSM. Somnologie 1999;3:313–18.
- [22] Paavonen EJ, Aronen ET, Moilanen I, et al. Sleep problems of school-aged children: a complementary view. Acta Paediatr 2000;89:223–8.
- [23] Gozal D, Pope DW Jr. Snoring during early childhood and academic performance at ages thirteen to fourteen years. Pediatrics 2001;107:1394–9.
- [24] Urschitz MS, Brockmann PE, Schlaud M, et al. Population prevalence of obstructive sleep apnoea in a community of German third graders. Eur Respir J 2010;36:556–68.
- [25] Urschitz MS, Wolff J, Von Einem V, et al. Reference values for nocturnal home pulse oximetry during sleep in primary school children. Chest 2003;123:96– 101.
- [26] Urschitz MS, Wolff J, Sokollik C, et al. Nocturnal arterial oxygen saturation and academic performance in a community sample of children. Pediatrics 2005;115:e204–9.
- [27] Brouillette RT, Morielli A, Leimanis A, et al. Nocturnal pulse oximetry as an abbreviated testing modality for pediatric obstructive sleep apnea. Pediatrics 2000;105:405–12.
- [28] Moss D, Urschitz MS, von Bodman A, et al. Reference values for nocturnal home polysomnography in primary schoolchildren. Pediatr Res 2005;58:958–65.
- [29] Iber C, Ancoli-Israel S, Chesson A, Quan SF, for the American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated event: rules, terminology and technical specifications. 1st ed. Westchester (IL): American Academy of Sleep Medicine; 2007.
- [30] Pepe MS Atkinson AC, Pierce DA, Schervish MJ, et al., editors. The statistical evaluation of medical tests for classification and prediction. New York: Oxford University Press Inc.; 2003.
- [31] Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. Proc Am Thorac Soc 2008;5:242–52.

- [32] Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. J Sleep Res 2002;11:1–16.
- [33] Bass JL, Corwin M, Gozal D, et al. The effect of chronic or intermittent hypoxia on cognition in childhood: a review of the evidence. Pediatrics 2004;114:805– 16.
- [34] O'Brien LM, Holbrook CR, Mervis CB, et al. Sleep and neurobehavioral characteristics of 5- to 7-year-old children with parentally reported symptoms of attention-deficit/hyperactivity disorder. Pediatrics 2003;111:554– 63.
- [35] Kaemingk KL, Pasvogel AE, Goodwin JL, et al. Learning in children and sleep disordered breathing: findings of the Tucson Children's Assessment of SleepApnea (tuCASA) prospective cohort study. J Int Neuropsychol Soc 2003;9:1016–26.
- [36] Beebe DW, Ris MD, Kramer ME, et al. The association between sleep disordered breathing, academic grades, and cognitive and behavioral functioning among overweight subjects during middle to late childhood. Sleep 2010;33:1447– 56.
- [37] Karande S, Kulkarni M. Poor school performance. Indian J Pediatr 2005;72:961– 7.
- [38] Dewald JF, Meijer AM, Oort FJ, et al. The influence of sleep quality, sleep duration and sleepiness on school performance in children and adolescents: a metaanalytic review. Sleep Med Rev 2010;14:179–89.
- [39] Molina BS, Hinshaw SP, Swanson JM, et al. The MTA at 8 years: prospective follow-up of children treated for combined-type ADHD in a multisite study. J Am Acad Child Adolesc Psychiatry 2009;48:484–500.
- [40] Langberg JM, Dvorsky MR, Becker SP, et al. The impact of daytime sleepiness on the school performance of college students with attention deficit hyperactivity disorder (ADHD): a prospective longitudinal study. J Sleep Res 2014;23:318–25.

- [41] Barnes ME, Gozal D, Molfese DL. Attention in children with obstructive sleep apnoea: an event-related potentials study. Sleep Med 2012;13:368– 77.
- [42] Bonuck KA, Chervin RD, Cole TJ, et al. Prevalence and persistence of sleep disordered breathing symptoms in young children: a 6-year population-based cohort study. Sleep 2011;34:875–84.
- [43] Urschitz MS, Guenther A, Eitner S, et al. Risk factors and natural history of habitual snoring. Chest 2004;126:790–800.
- [44] Brouillette RT, Jacob SV, Morielli A, et al. There's no place like home: evaluation of obstructive sleep apnea in the child's home. Pediatr Pulmonol Suppl 1995;11:86–8.
- [45] Jacob SV, Morielli A, Mograss MA, et al. Home testing for pediatric obstructive sleep apnea syndrome secondary to adenotonsillar hypertrophy. Pediatr Pulmonol 1995;20:241–52.
- [46] Zucconi M, Calori G, Castronovo V, et al. Respiratory monitoring by means of an unattended device in children with suspected uncomplicated obstructive sleep apnea: a validation study. Chest 2003;124:602–7.
- [47] Alonso Alvarez ML, Teran Santos J, Cordero Guevara JA, et al. [Reliability of respiratory polygraphy for the diagnosis of sleep apnea-hypopnea syndrome in children]. Arch Bronconeumol 2008;44:318–23.
- [48] Morielli A, Desjardins D, Brouillette RT. Transcutaneous and end-tidal carbon dioxide pressures should be measured during pediatric polysomnography. Am Rev Respir Dis 1993;148:1599–604.
- [49] Lopes MC, Marcus CL. The significance of ASDA arousals in children. Sleep Med 2007;9:3–8.
- [50] Bruni O, Kohler M, Novelli L, et al. The role of NREM sleep instability in child cognitive performance. Sleep 2012;35:649–56.
- [51] Brockmann PE, Urschitz MS, Noehren A, et al. Risk factors and consequences of excessive autonomic activation during sleep in children. Sleep Breath 2010;15:409–16.