The effect of adenotonsillectomy for childhood sleep apnea on cardiorespiratory function

Study Enrolment

Details about the original CHAT study enrolment, randomization and follow-up recruitment have been presented previously.[1] A total of 453 children underwent randomization and were assigned to early adenotonsillectomy (eAT) and watchful waiting with supportive care (WWSC). Our per-protocol analysis was based on 194 children who underwent eAT and 181 children who were waiting and participated in both the baseline and follow-up sleep studies and had relevant PSG signals of sufficient quality.

All data of the CHAT study are publicly available at https://sleepdata.org/datasets/chat to other investigators for secondary analyses. In addition to spreadsheets pertaining to the variables and results of the primary analysis, overnight PSG comprising raw data stored in the European Data Format (EDF) as well as scoring information stored in Compumedics output files in Extensible Markup Language (XML) were retrieved.

Respiration and ECG processing

Respiratory analysis was based on the ribcage belt recording of the respiratory inductive plethysmogram (RIP) channel of the PSG. Ribcage RIP signals were visually screened and subjects whose recordings showed noisy, partially recorded or movement artefact dominated breathing signals were excluded (3 from eAT and 7 from WWSC arm at baseline; 9 from eAT and 4 from WWSC arm at follow-up study). The sampling rate varied across recordings ranging from 32, 50, 128, 200 to 256 Hz and was made comparable by up-sampling those signals recorded at 50 Hz and 100 Hz to 200 Hz and up-sampling those recorded at 30 Hz and 128 Hz to 256 Hz. Subsequently, all ribcage RIP signals were low pass filtered at 1Hz, using

a Butterworth zero phase forward and reverse digital filter of order four. Inspiratory onsets were automatically detected by identifying local minima based on first order differences i.e., those points that were lower in magnitude than the preceding and following data points. A threshold – defined as the standard deviation of the respiratory signal within an epoch – was applied to the magnitude of these minima points, exceeding which, the local minima qualify as inspiratory onsets. Furthermore, spurious detections were discarded by estimating the time difference between successive minima and comparing them to an estimate of the respiratory interval made based on the frequency spectra of the epoch being analysed. If the time difference between successive minima fell within 0.5 times to 1.5 times the estimated respiratory interval, the minima were considered to be inspiratory onsets. This way, based on the detected inspiratory onsets, a breath-to-breath time series of respiratory intervals was obtained.

Cardiac cycles were measured based on the R-peaks in the ECG. The vast majority of PSG recordings contained recordings of three ECG leads: ECG1 (below right clavicle), ECG2 (below left clavicle) and ECG3 (left lower rib). Subjects with only one or two ECG leads and those with noisy and/or partial recordings in two or more leads were excluded from this study. Sampling rates of ECG did not vary between channels but varied across recordings between 200 Hz, 250 Hz and 512Hz and hence they were made comparable across the whole data set by down-sampling ECG recordings sampled at 512 Hz to a lower sampling rate of 256Hz. The ECG were subsequently filtered with a pass band of 0.4 to 40 Hz, using Butterworth zero phase forward and reverse low-pass and high-pass digital filters of order 4. The QRS complex of each cardiac cycle was delineated in each ECG channel using appropriate scripts in the Biosig Matlab toolbox.[2, 3] To exclude falsely detected QRS complexes from further analysis, (which might be due to noisy signals), the locations of R-

peaks were compared between all three ECG leads and only those that could be observed in at least 2 out of three ECG leads within a time window of 100ms were included for analysis.

Artefact identification and removal

All 30 second epochs containing discrete respiratory events or signal artefact as manually scored by the sleep technician were removed from subsequent data analysis. Furthermore, any 30 second epoch containing movement-related artefact in the thoracic respiratory signal were automatically detected using the method proposed by Aoude et al., which is based on power spectrum analysis of the RIP signal and were removed from further analysis.[4] RR intervals that were too small or too large maybe due to false or missed R-peaks. To exclude their influence on the analysis, an upper threshold of 1500ms and a lower threshold of 400ms was applied on the RR intervals - the thresholds being based on the normal range of heart rate in young children.[5] RR intervals <400ms and >1500ms were excluded from analysis. Finally, the retained segments of ribcage respiratory signals, their respiratory cycles and the RR interval time series were visually scanned for any evidence of artefacts before being included for further analysis.

Average durations of sleep included in the analyses are summarized in Tab.1.

Calculation of respiratory sinus arrhythmia (RSA)

The pattern of RSA was evaluated by ensemble-averaging of R-R interval changes from multiple respiratory cycles throughout the respiratory phase. For within each respiratory cycle detected from the retained epochs of respiratory signal of each sleep stage, the corresponding R-R intervals were extracted and were interpolated at 50 data points, using cubic spline interpolation. This results in a RSA pattern over the respiratory cycle. This is repeated over all *n* respiratory cycles and an overall RSA pattern within each sleep stage was obtained by

taking the ensemble average of all the RSA patterns. Our parameter of interest, RSA amplitude, was calculated by taking the difference between the maximum and the minimum peak of the overall RSA pattern.

Table 1 Minutes of sleep included in the cardiorespiratory analysis and total time of sleep spent in N2, N3 and REM sleep.

	Early Adenotonsillectomy (N =194)		**Watchful Waiting (N =181)**	
Sleep stage	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**
N2	123.9 ± 42.1 min (27.3 ± 8.1 %)	154.6 ± 43.8 min (32.2 ± 8.3 %)	129.0 ± 42.1 min (28.3 ± 8.6 %)	141.6 ± 41.1min (31.9 ± 8.0 %)
N3	116.8 ± 32.5 min (25.8 ± 7.3 %)	120.0 ± 27.9 min (26.3 ± 6.2 %)	116.7 ± 33.8 min (25.5 ± 7.0 %)	119.6 ± 3.05 min (26.4 ± 6.7 %)
R	35.1 ± 20.3 min (7.5 ± 4.3 %)	51.3 ± 19.2 min (10.5 ± 4.1 %)	36.5 ± 20.7 min (7.9 ± 4.4 %)	42.0 ± 21.2 min (9.7 ± 4.3 %)

References

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