Case Sleep and Epidemiology Research Center
MrOS Sleep Reading Center (SRC)
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MrOS Sleep Study
READING CENTER MANUAL OF OPERATIONS

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Dedication

This manual is dedicated to the memory of Kathleen Fisher, who served as Chief Polysomnologist for the Sleep Heart Health Study (SHHS) Reading Center during its formative period. Kathleen's skills in polysomnography and quest for excellence were invaluable in the development of a dedicated Reading Center staff. Her input was also invaluable for the development of detailed methods for dealing with the tremendous amount of polysomnographic data that needed to be processed and analyzed. Kathleen embodied an enthusiasm for research, especially related to the goals of understanding the health impact of sleep-disordered breathing. The Reading Center staff was privileged to have benefited from her generosity, kindness and intelligence.

Acknowledgments

We are deeply indebted to the classic work of Drs. Rechtschaffen and Kales, whose manual of sleep scoring has stood the test of time. We also acknowledge the helpful input of the SHHS Polysomnography Subcommittee (Drs. William Bonekat, Daniel Gottlieb, Conrad Iber, James Kiley, Stuart Quan, David Rapoport, Mark Sanders, and Philip Smith) and to Sonia Ancoli-Israel from the MrOS Sleep Study.

Reading Center Staff and Authors

(*Current staff)

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A Note to Users

The procedures and scoring rules developed and/or adapted for the research studies were done for the purposes of obtaining consistent (reliable), objective data for large numbers of individuals studied with the same equipment in unattended settings for the purposes of developing a large and versatile research database. Records were scored without knowledge of the demographic or clinical history of participants and without any attempt to diagnose clinical disorders. A summary of the ability of these procedures, implemented early in the Sleep Hear Health Study, the first multi-center sleep study that we participated in, to achieve reliable data can be found in *Sleep 21: 749- 758. 1998.* Some of the scoring rules are specific to the use of Compumedics software and may need to be modified when using different systems. The recording montage for MrOS includes: C3/A2 and C4/A1 EEGs; right and left electrooculograms (EOGs); a bipolar submental electromyogram (EMG); thoracic and abdominal excursions (inductive plethysmography bands, with a computerized auto-calibrated summed signal); "airflow" (detected by a nasal-oral thermistor and a nasal pressure cannula; oximetry, ECG and heart rate (using a bipolar ECG lead); body position; and leg movements by piezo sensors. .

SRC MANUAL OF OPERATIONS

1. OBJECTIVES

The Sleep Reading Center (SRC) will:

- Provide centralized training for aspects of MrOS related to the performance of polysomnograms (PSGs).
- Provide ongoing technical support for the performance of sleep studies, providing "second line" advice regarding troubleshooting of problem studies (after consultation with local resources), and acting as a liaison with the equipment supplier to identify equipment problems and solutions.
- Provide timely review (for quality and medical alerts) and scoring of all records, generating reports needed for participant feedback and data files for central (Coordinating Center - CC) processing.
- Provide complete scoring of all sleep studies, with generation of reports that summarize key sleep and respiratory data.
- Participate in on-going quality assurance efforts to maintain high levels of scoring accuracy and technical performance of tests at the field sites. These include assistance in trouble-shooting site-specific and study–wide problems, perform site visits, report generation, perform site visits, and lead regular conference calls with technicians and co-investigators..
- Produce and archive a clean, edited data set of raw and scored poylsomnographs.
- Maintain a data dictionary relevant to polysomnograph variables.

2. STRUCTURE

The Sleep Reading Center (SRC) will be directed by Susan Redline, MD, MPH. She will hire and assist in the training of an Administrative Assistant, a Chief Polysomnologist, and PSG scorers, and be ultimately responsible for all goals specified above.

Physician investigators will assist in the development of scoring procedures. They will participate in weekly staff meetings that discuss issues with scoring and quality control.

The Chief Polysomonologist (CP) will be directly responsible for training and certifying scorers and centrally trained field research assistants. S/he will participate in the development of teaching materials for training and for procedures for certifying scorers and assuring high levels of accuracy and reproducibility of scoring procedures. S/he will review each PSG record within 72 hours of its receipt at the SRC, identifying medical alerts for priority scoring, and providing

feedback on the quality of studies received to field site technicians, and assist in identifying equipment problems. S/he will triage studies for formal scoring to the scorers, monitoring their performance, and providing support for interpreting ambiguous studies. S/he will implement on-going procedures for assuring accuracy and reproducibility of scored procedures.

Three to five scorers will be charged with the responsibility of directly scoring all records. They will be charged with the task of scoring 2-3 records/day and participating in scoring QA procedures.

3. CERTIFICATION AND QA

3.1. Certification of the Chief Polysomnologist.

The CP will be an experienced polysomnologist (>5 years experience in scoring). She will be required to:

- Demonstrate a complete understanding of scoring rules and ability to articulate reasons for assigning epoch by epoch codes for sleep staging and respiratory events scoring.
- Demonstrate a level of agreement (within 10% for summary respiratory disturbance index (RDI) and sleep stages and 15% level of agreement for arousal index) with a second experienced polysomnologist (each scoring the same 10 records "blinded").
- Demonstrate a 5% level of agreement (with-in scorer reliability) by scoring the same 10 records, at least one week apart.

3.2. Certification of Scorers.

Each scorer will be required to demonstrate a complete understanding of scoring rules and ability to articulate reasons for assigning epoch by epoch codes for sleep and respiratory scoring. This will be judged by review of several records with the CP or a physician-investigator.

Each novice scorer will be required to score 50 records under the supervision of a certified scorer. Ten of these records will be selected from a standardized score set. Data from these 10 records must show a 10% level of agreement with the CP or a senior scorer for respiratory events and sleep stages and a 15% level of agreement for arousals.

The CP (or designee) will review (epoch by epoch) the first 10 records scored by each novice scorer after certification. After that she will check score a randomly chosen 20% of the first 100 records

4. QUALITY ASSURANCE AND QUALITY CONTROL

4.1. Weekly QA Exercises at the SRC

Weekly scorers' staff meetings will be conducted at the SRC, with dedication of between 1.5 to 3 hours of time per week for the scorers to meet and discuss scoring issues. The weekly exercises will be organized by the Chief Polysomnologist, with topics that will reflect ongoing needs as identified by the staff or by the CC/PSG Committee. These exercises will include:

- scoring of randomly chosen epochs;
- scoring of problem records/epochs;
- discussions of any problematic rules/examples identified during scoring
- rotating "paired" scoring exercises

Exercises will include individual scoring with follow-up discussion of any discrepancies in assigned scores. A discussion, with participation of SRC investigators, will establish a "consensus" score for discrepant records. Results of any discrepancies between scorers and the Chief Polysomnologist or between any scorers will be reviewed at weekly meetings with investigators. The results of the deliberations will be kept on file. This will include copies of ambiguous records and a summary of any arbitration.

Examples of organized meetings include:

- QA Exercises: At least monthly, individual scorers will score the same 50 epochs from a selected study. Most studies for QA scoring will be chosen randomly; however, scorers also will identify problematic studies that may show useful training/teaching points during QA exercises. Scoring of such designated studies will be recorded on an epoch by epoch basis. Differences in any epoch or event assignment between scorers will be discussed during the weekly QA meeting. Results of this discussion will be noted on the separate form (group consensus). When a group consensus cannot be reached, the epoch or event will be designated "indeterminate". Data will be entered into a database and summarized quarterly for internal QA tracking.

- Scoring Exercises: On the weeks when no QA exercise is performed, 30-60 minutes of paired scoring (one scorer scoring, one watching) or team scoring (with group members acting as a single unit) will be done. Noted differences will be discussed after the scoring exercise. Scorers will rotate roles, partners, and teams so that all interactions occur over any given time period.

- Studies which pose difficulties in scoring or present interesting problems will be reviewed by the entire SRC staff during weekly meetings. Minutes from these meetings and printed copies of problem epochs will be maintained.

4.2. Tracking of QA/QC Data

The Chief Polysomnologist will track two types of data: data from the actual scored SHHS-2 records and data generated during QA exercises. Using actual scored SHHS-2 data, the overall mean RDI, sleep stage values and arousal indexes will be tracked for each scorer. If average values differ by > 15% for any given scorer, those records will be reviewed by the Chief Polysomnologist. The SRC Director will determine whether re-training and re-standardization are required. Using data from the QA exercises, levels of agreement will be determined among scorers and trends tracked over time. Any scorer identified to deviate excessively (>10% from the consensus statement) on 3 consecutive exercises will be "re-trained." "Re-training" will be considered successful if review of at least 5 additional studies demonstrates no deviation from scoring protocol, and the subsequent QA exercises show no deviations in performance compared to scoring assignments made by the other scorers.

At monthly QA meetings, the statistics summarizing inter-and intra-scorer variability will be reviewed by the SRC staff. They will identify any explanations for differences. If differences between scorers can not be explained by real differences in the studies assigned to any given scorer in any given time period, scorers noted to score differently will score together, concentrating on the areas where differences were noted. The Chief Polysomnologist will review consecutive records and reinstruct the scorer. Subsequent scoring will be monitored until conformity is demonstrated.

4.3. Outlier Checks

4.3.1 Study-by-study outlier review

After each study is scored and an initial report is generated, the scorer will use a computer program to identify extreme outliers. These entries will be reviewed and the results of this review will be noted on a PSG scoring form. New reports will be generated if any editing of the record is required.

4.3.2 Batch outlier review

On a weekly basis, prior to sending reports to sites, the reports will be subjected to a secondary review for outliers. Any records with outliers so identified will be checked (QS form/log book) to ascertain that this record was previously identified as containing an outlier, with adequate documentation of the problem.

On a monthly basis, scored PSG data will be imported into a permanent SAS file. Prior to importing these data, it will be subjected to a third check for outliers.

4.4. External Review of Scoring Reliability

The Coordinating Center and Polysomnography (PSG) Committee will establish methods for tracking scoring reliability and drift. This includes re-processing of records for reliability exercises and generation of summary data for each scorer. The overall mean for: RDI, sleep stage percentage, and arousal indexes will be calculated for each scorer over discrete time periods (monthly to quarterly) and reported to the PSG Subcommittee/Coordinating Center (CC). Intra-

and inter-reader differences in the summary data for RDI, sleep stages, and arousal indices will be determined. The same mean values will be calculated for each site in the same periods of the time. The CC will monitor intra- and inter-reader reliability to determine the threshold for requiring remediation, including retraining or removing a reader.

The PSG Committee, in conjunction with the Coordinating Center (CC) may design a formal reliability study of scoring. For example, a sample of previously read PSG studies will be assigned a new "dummy" identification number and be assigned to the scorers for repeat scoring. Scoring of these studies will be integrated into the normal work flow to minimize their likelihood of being identified as a special study. Studies will be assigned to a different reader to define inter-reader reliability. Studies will be also assigned to the same reader at defined time periods to define intra-reader reliability.

Site visits, coordinated by the CC, will occur as directed by the Steering Committee.

5. Data Processing

5.1. Study Receipt

Upon receipt of studies at the Reading Center all CDs will be scanned for viruses. The Study Receipt form will be completed, including the following information: Field Center ID, Participant ID, Alpha Code, Study Date, Zip cartridge number, date received, Monitor/Headbox ID, and Technician ID. If there is a discrepancy between the data contained the Signal Verification Form and the Compumedics Sleep Study recorded file, an e-mail will be sent to the Site Coordinator requesting clarification. If any site is noted to have a significant number of discrepancies in the data submitted, the Coordinator at the site will be contacted by the SRC to request they identify source and report action taken to correct. The data from the study receipt form will be entered into the Receipts table database.

The Signal Verification (SV) Form and Sleep Study Evaluation (SE) form for studies that have been evaluated at the site and determined to be Failed will be sent to the SRC along with the weekly CDs. This data will also be entered into the Receipts table database when received, indicating study was Not Sent and coded with a reason for the failure.

5.2. Offline Automatic Analysis

This Compumedics program must be run prior to review of studies and final scoring to allow visualization of signals and graphic screens. Automatic sleep staging and respiratory scores are generated during the process. These data will not be used as final scores. (Offline Analysis detailed procedures are located in Appendix).

5.3. Preliminary Review

After offline analysis of the record, the CP will then review each study to determine if overall quality is sufficient to be scored (passed/failed), and identify any potential medical alerts (defined as preliminary RDI >45, or extreme heart rate patterns). In addition, the CP will note any signal quality issues, possible monitor malfunctions, and recommendations for electrode replacements on the Receipt form.

Minimal criteria for study acceptability: The record must contain at least 4 hours of scorable EEG, oximetry and respiratory data (either airflow, thoracic or abdomen) between (edited) lights off and lights on (Total Recording Time). Recorded time after final awakening will not contribute to this time. Two continuous blocks of scorable data, each at least 2 hours long are required to consider study acceptable for scoring.

Cropping: Since the units used in MrOS have capabilities of recordings > 18 hours of data, and occasionally units are not turned off after the sleep study, record length can be excessive (containing hours of wake after sleep offset). To conserve storage space for these large data files for archiving, recordings can be cropped using the "Study Crop Option" in Profusion 2. The person reviewing the study will identify the epoch number when participant is clearly awake and the electrodes have been removed (all signals will appear very noisy then flat lines). The end of the recording after removal of the electrodes will be cropped. Therefore, the archived recording will contain signals only while the participant wore the equipment.

5.4. Feedback of Data to the Sites

After preliminary review by the CP is completed, the pass/fail status of the record is entered into the Receipts table database along with any comments and feedback notes regarding quality of the study and equipment troubleshooting. On a weekly basis the following reports are e-mailed to the site coordinator:

> Record of Receipts - Lists Participant ID, Study Date, Date Received at SRC, CD Number, Monitor ID, Headbox ID, Tech ID, and Pass/Fail Status.
>
> Preliminary Study Quality Report - Contains Participant ID, Study Date, Tech ID, Pass/Fail status and Comments from the CP regarding study quality and/or reasons for failure.

The site coordinator is to verify that all information on the Record of Receipts is accurate and notify the SRC of any changes or corrections to be made. The Preliminary Study Quality Report should be made available to the field site technicians and quality issues reviewed and discussed.

Failed studies are archived to CDs for troubleshooting exercises and review.

5.5. Assignment of Studies to Scorers

Potential Medical Alerts - Studies identified as potential medical alerts will be triaged for immediate full scoring (within 48 hours of assignment to scorer). Once fully scored and determined to meet criteria for Medical Alerts (final RDI > 50, time in desaturation of <70% for >10% TST, or average heart rate > 150 BPM or <30 BPM for 2 minutes, atrial fibrillation

(previously unknown, atrial fibrillation-known but with HR < 50 or > 120; or runs of ventricular tachycardia), a physician investigator will be asked to review the study. If the medical alert is ascertained, it will be logged into a Medical Alert Log and the site will receive the Participant Feedback Sleep Report and quality grades (QS form) with the regular weekly reports.

All remaining studies are scored based on date received. Bi-monthly review of scored studies by site by scorer is done to maintain equal distribution of studies from all sites among the scorers.

5.6. Quality Grades (QS Form; Sleep Quality Form)

The quality of each signal and overall study quality will be assessed at the time of scoring of the record. The Scorer will code each channel of information according to the duration of: i) scorable signals; ii) duration of artifact free signals during sleep, and iii) an overall QA grade to each study. The total duration of the study (from the edited lights off to the lights on) and the total duration of sleep will also be indicated. Scoring notes regarding staging, event identification, outliers, and specific physiologic signal issues are also recorded on the QS form. (See Section 7.0 for a more detailed description of criteria for grades and scoring notes. Appendix B contains a sample QS Form.)

All data contained in the QS form (quality grades and scoring notes) will be entered in the QS table database that contains only passed scored studies.

5.7. Scored Sleep Data

After full scoring, the scorer will generate:

- Participant Feedback Report (rtf format – See Appendix C for sample report), contains summary sleep data. Data will include the RDI (the number of apneas and hypopneas per hour of the sleep associated with a desaturation $\geq$ 3%), a summary of the desaturation profile, time in REM/Non-REM sleep, stage distributions, and the arousal index. The report will be used in the Participant Feedback Letters, and can be used in communications with local physicians.

- SAS report containing >760 variables.

- Completed QS form containing all quality grades and scoring notes.

The Sleep Data Summary Report and QS Report are e-mailed to each site on Mondays following the week scored (generally within 12 weeks of receipt of the SRC, except for studies which are triaged as possible Medical Alerts, which will be returned within one to two weeks of receipt).

5.8. Archival of Data

After QS data has been entered and weekly reports are sent to sites, the complete study folder containing the raw data file, scored files, sleep study report, and the SAS report is placed in a site directory for the creation of CDs. When sufficient studies have been scored for a particular site (15-20 studies), they will be archived onto CDs (in triplicate). Copy A will be retained at the SRC, Copy B will be sent to the site, and Copy C will be sent to the Coordinating Center.

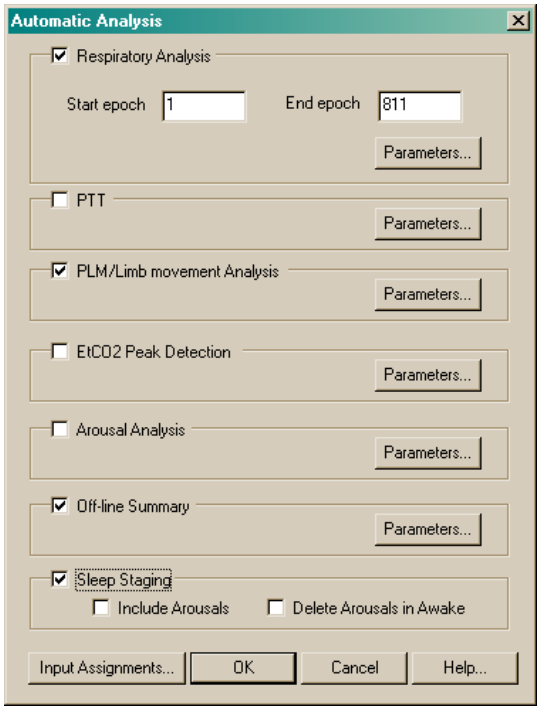
The summary scored data (>760 SHHS variables) are output as individual .txt files. After outlier checks, studies are imported on a monthly basis into a SAS file. This file is sent periodically to the CC for merging with the main SHHS dataset.

5.9. Processing of Sleep Records

The Compumedics Profusion 2 software system will be used to process all the records. To most efficiently utilize the software options and to maximize consistency in viewing and approaching each study, each reading computer needs to be configured comparably with the following procedures need to be followed:

Running Offline analysis- This "pre-processes" every record to allow subsequent epoch by epoch scoring.
On the Offline Analysis window following boxes should be checked:

- Respiratory Analysis
- PLM/Limb movement Analysis
- Off-line Summary
- Sleep Staging



Parameters for the following boxes need to be set:

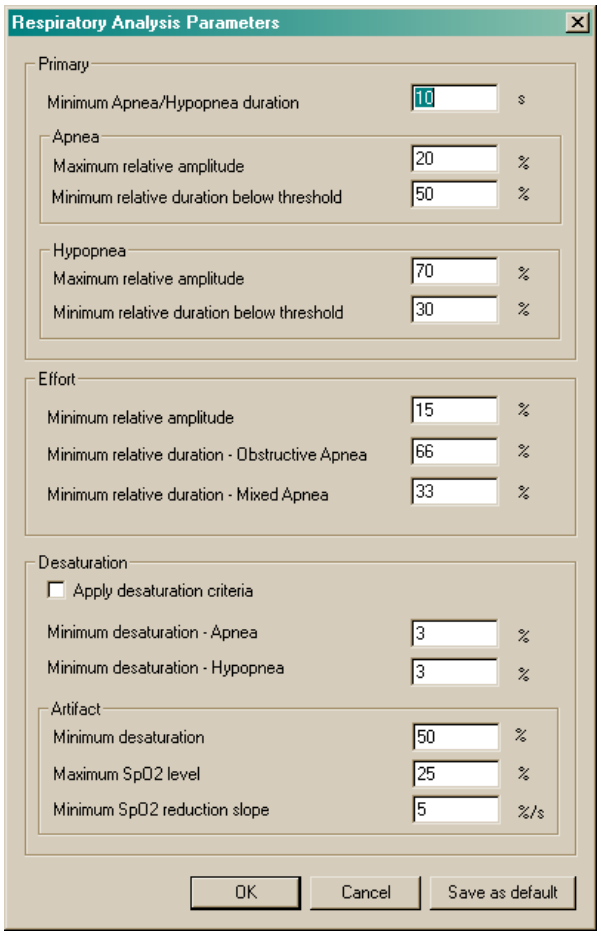
- Respiratory Analysis
- PLM/Limb movements Analysis

Respiratory Analysis – Parameters

The following parameters should be used:

- Minimum Apnea./Hypopnea duration - 10 s
- Apnea : Maximum relative amplitude - 25 %
- Hypopnea: Maximum relative amplitude- 70 %
- Desaturation:
- Apply desaturation criteria box - unchecked

Save these parameters as default (other parameters can be left as they are)



PLM/Limb movements Analysis
The following parameters should be used:

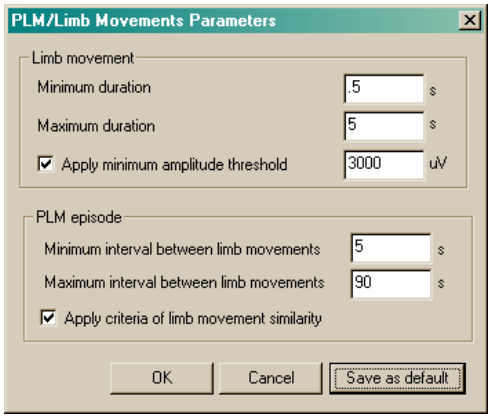
Limb movement:

Minimum duration	-.5 s
Maximum duration	- 5 s
Apply minimum amplitude threshold box	- checked
Apply minimum amplitude threshold	- 3000

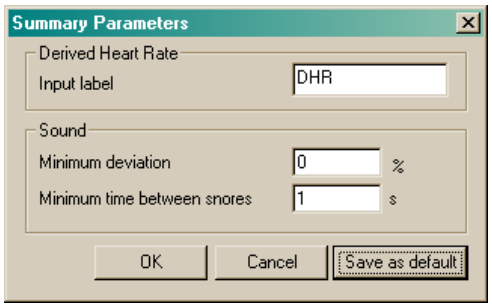
PLM episode

Minimum interval between limb movements	- 5 s
Maximum interval between limb movements	- 90 s
Apply criteria of limb movements similarity box	- checked

If initial analysis of limb movements is not satisfactory PLM analysis can be rerun with the number for minimum amplitude threshold changed (to pick up more or less events) (See Section 6.3). Also Apply criteria of limb movements similarity box can be unchecked.

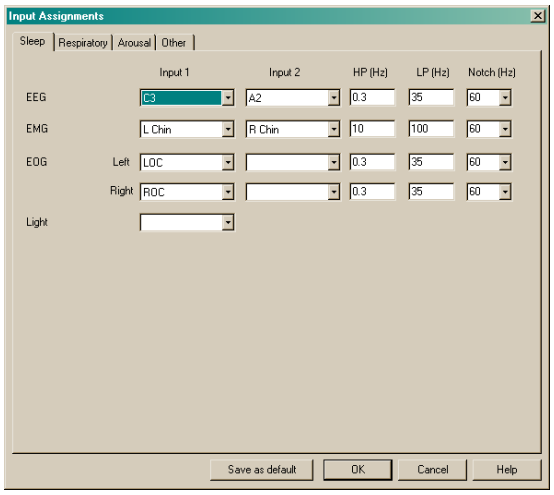


Off-line summary parameters
Once set, these parameters should be maintained without the need to change from study to study. They should be as follows:



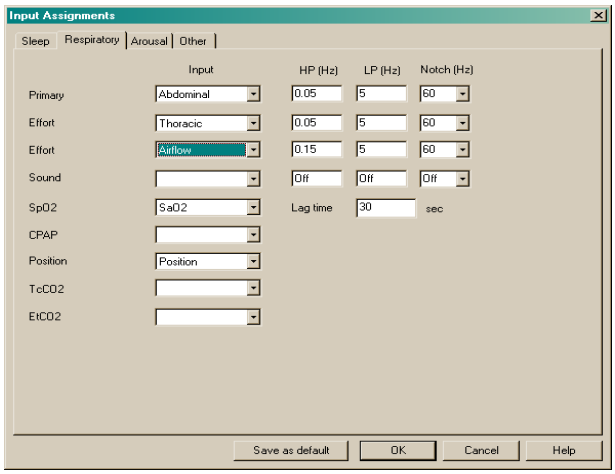
Setting for Input Assignments

Sleep tab

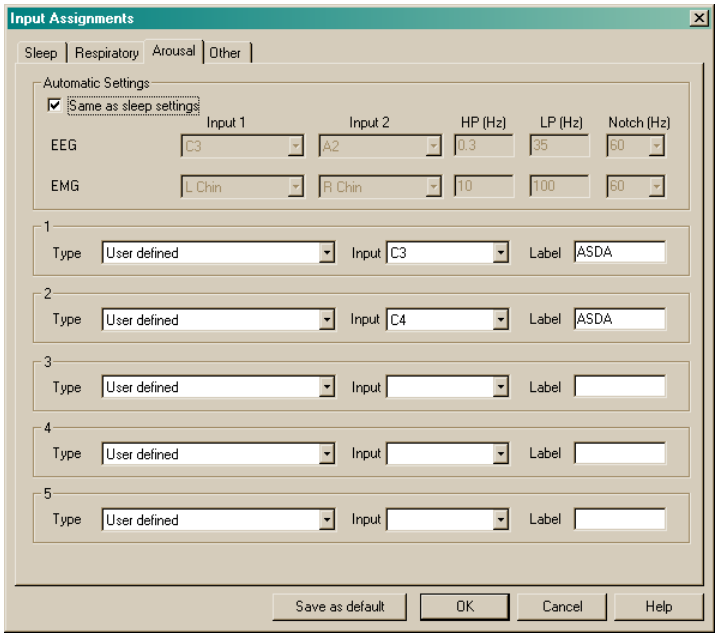


Respiratory tab

Primary and efforts can be changed based on the quality of the signals

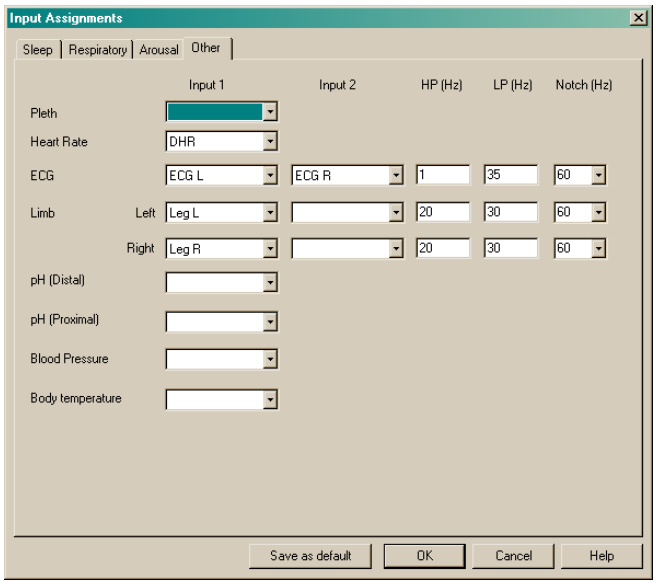


Arousal tab

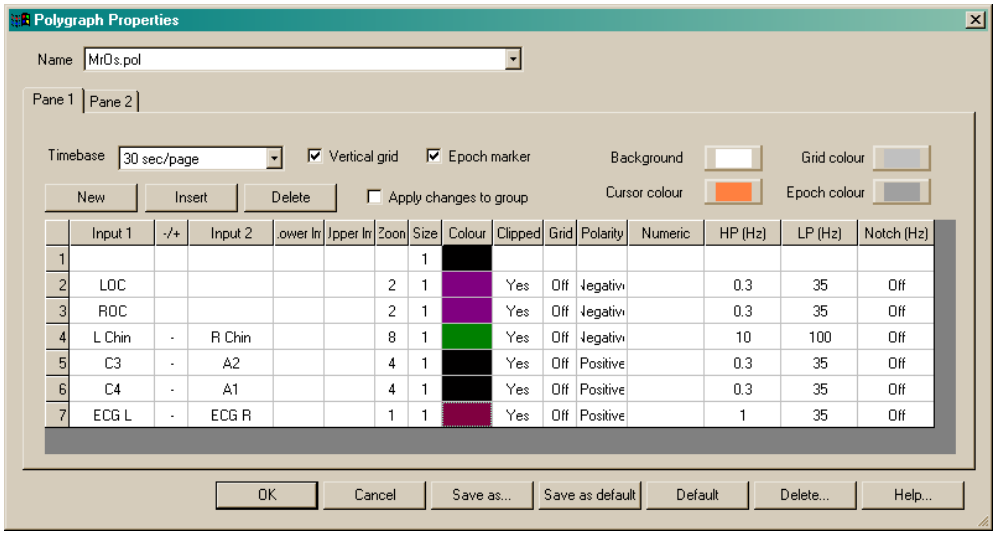


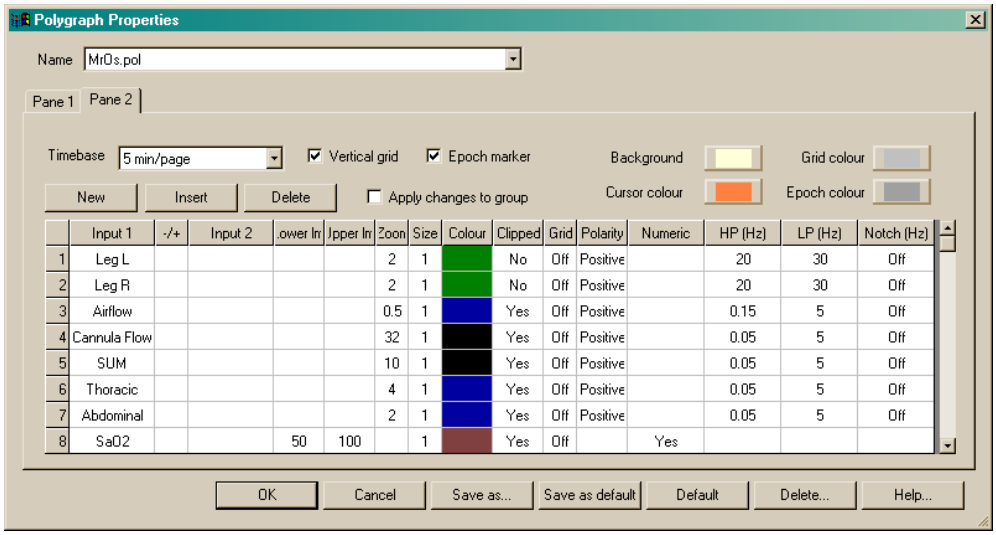
Other tab

Heart Rate has to be changed to DHR after Automatic Analysis is run



<u>The Montage settings for scoring is:</u>





6. SCORING PROCEDURES

6.1. Overview of Scoring

Scorers will review the record using a computer monitor in two passes. First, computer generated scoring of respiratory events during the "offline" processing will be deleted. Then during the first pass, sleep stages and arousals will be marked manually on a (30 s. time base)

epoch by epoch basis. During the second pass, respiratory signals will be displayed (2 or 5 min. time base), respiratory events will be manually marked, and oxygen saturation data edited.

During manual scoring, the following are primary "events" that are identified:

Sleep stages will be identified for each 30 second epoch using Rechtshaffen and Kales criteria (Rechtshaffen A, Kales A. A Manual of Standardized Terminology Techniques And Scoring System for Sleep Stages in Human Subjects. Washington, DC: US Government Printing Office, 1968).

Arousals will be characterized by the American Academy of Sleep Medicine criteria (The Atlas Task Force, EEG Arousals: Scoring Rules and Examples. Sleep 1992: 15:173-84).

Obstructive Apneas will be identified if the amplitude (peak to trough) of the airflow signal is flat or nearly flat. This is noted when amplitude of airflow (by thermister) decreases below at least 75% of the amplitude of "baseline" breathing, i.e. to $\leq$ 25% of the baseline, (identified during a period of regular breathing with stable oxygen levels), and if this change lasts for $\geq$ 10 s. Obstructive apneas cannot be designated in areas of the study where thermistry is missing or uninterpretable.

AASM Hypopneas. Will be identified if $\geq$ 50% reduction of amplitude is visualized on either the respiratory SUM channel OR if the SUM is not present, if a 50% reduction is seen on both belts (thoracic and abdominal). Alternatively, an AASM hyponea may be marked if a clear $\geq$ 50% reduction is seen on a good nasal pressure signal. In considering all available data, greater confidence is given to the SUM than nasal pressure signal. Specifically, when amplitude changes are seen only in the nasal pressure with little or no changes in a sum channel, the event will not be marked. These events are marked independent of whether any associated desaturation is linked with the event.

(Non-AASM) Hypopneas will be identified if the amplitude of any respiratory signal decreases by at least (approximately) 30% of the amplitude of "baseline", i.e. to $\leq$ 70% of baseline, (identified during a period of regular breathing with stable oxygen levels), if this change lasts for $\geq$ 10 s, and if the event does not meet the criteria for the AASM hypopnea. If the observed reduction in amplitude is clear (a clear, discrete beginning and end, but magnitude of reduction is uncertain, then the event will only be marked if there is at least 2% desaturation associated with the event.

Central Apneas will be noted if no displacement is seen on either the chest or abdominal inductance channels. Otherwise, events will be noted as "obstructive". Central events cannot be designated if either or both band data are missing or uninterpretable.

Desaturation Events: Profusion2 software has the ability to independently score desaturation events from the oxygen saturation channel.

Computer analysis will link data from varying channels to identify desaturation levels, sleep summary data, and various Respiratory Disturbance Indices (RDIs). The following describe how these data are used:

The desaturation associated with any respiratory event will be based on the nadir desaturation reached within a user defined amount of the time (usually within 30 sec) of the end of the event. The magnitude of the desaturation for an event is the difference between the greatest saturation

level observed during the event and this minimum. The scorer will manually check events to assure that the appropriate desaturation is identified and modify the time lag as needed.

An arousal will be associated with a respiratory event if the arousal begins less than 5.0 seconds after the end of the event (i.e.: 0-4.9 seconds).

RDI (Respiratory Disturbance Index) is defined as the number of respiratory events (apneas and hypopneas) per hour of the sleep. Events will be included in different indices according to level of associated desaturation and/or arousal:

- All events (regardless of desaturation or arousal)
- Summary RDI values, based on events associated with $\geq$ 2%, $\geq$ 3%, $\geq$ 4%, and $\geq$ 5% desaturation levels.
- Summary RDI values based on events associated with > 2%, 3%, 4%, and 5% desaturation levels or associated arousal.
- Summary RDI values based on events associated with arousal regardless of desaturation.\
- Summary events only based on events meeting obstructive apnea and AASM hypopnea criteria.

Time in apnea or hypopnea:

- Percent sleep time in apnea (obstructive or central, with at least a 3% desaturation +/- arousal).
- Percent sleep time in hypopnea (with at least a 3% desaturation +/- arousal).

Oxygen Desaturation Profile:

- Percent sleep time in desaturation (<95%, <90%, <85%, <80%, <75%).
- Number of desaturations/hour of sleep (unlinked with respiratory events) of 2%, 3%, 4%, 5%.
- Average of oxygen desaturation nadirs linked to each respiratory event
- Average of oxygen desaturation nadirs noted from independent desaturation event markings.

Sleep Architecture:

- Time and percent of sleep time in each sleep stage (combine Stages 3 and 4).
- Arousal index.
- Number/hour of upward stage (from deeper to lighter) shifts; wake shifts.
- Sleep efficiency.(sleep time/time in bed – lights off to end of study)
- Sleep latency (lights off to sleep onset); REM latency I (defined as time from onset of sleep to first REM).

Heart Rate data:

- Maximum, minimum and mean heart rate noted during sleep, associated with respiratory events and associated with the arousals (in REM and Non-REM separately).

Following manual scoring of the computer record, the scorer also completes the QS Form to indicate whether unusual patterns describing breathing or EEG are noted or if problems were encountered during the scoring process that could reduce the reliability of the scored data. These include:

- Abnormal Awake EEG
- Alpha intrusion
- Abnormal Eye Movements

- Periodicity
- Periodic large breaths
- Sleep staging/arousal unreliable
- Apneas vs. hypopneas unreliable

Summary of Scoring Process

Each study will be manually scored in the two passes:

During the first pass:
- Review the "lights" channel and manually set time of "lights off" and "lights on."
- The EEG, EMG and EOG signals from each study will be reviewed on an epoch by epoch (30 s.) basis (screen). Each epoch will be assigned a sleep stage. Periods of EEG change that meet the criteria for arousal will be marked.

During second pass:
- Respiratory data (airflow/abdominal/chest/saturation) will be reviewed on 5 minute pages. The saturation channel will be edited for artifact and respiratory events will be marked manually according to the rules stated below.

Finally, the following will be done:
- The QS Form will be completed, indicating unusual patterns, reliability problems, and signal/study QA grades.
- The outlier program will be run, to identify implausible values.
- Participant Feedback Sleep Reports will be generated.
- The raw and scored files and summary reports will be saved, to the scoring hard drive.

6.2. Scoring Rules

Locally introduced rules, based on discussions among the SRC staff and outside consultations are indicated by an (*).

Scoring sleep stages

Scoring sleep stages is based on the guidelines specified by Rechtshaffen and Kales. When guidelines were adopted from other sources, the source is marked in parenthesis. M.C. & A.R refers to Section 7, Chapter 73: Monitoring and Staging Human Sleep, written by M.A. Carskadon and A. Rechtschaffen, in Principles and Practice of Sleep Medicine ed. by M.H. Kryger, T.Roth and W. Dement; W.B. Saunders Co, 1989 (1st edition).

6.2.1 Rules for assigning epoch-specific sleep score:

Epoch-by-epoch approach: The polygraph record is divided into consecutive segments of equal size (30 s., each termed an "epoch"). Each epoch has assigned a single sleep stage score. The epoch duration is maintained for the duration of the recording.

- When more than one stage is present in an epoch, that epoch is assigned a single stage score reflecting the stage that occupied the greatest portion of the epoch.
- When two stages of sleep are evenly distributed on the epoch, and one of these stages was the same stage as in the preceding epoch, then that epoch will be assigned the same sleep stage as the preceding epoch (*).
- Portions of two epochs may not be combined to create a new epoch.
- When an arousal of <15 sec. occurs within an epoch, the time "in arousal" is not counted when determining the predominant sleep stage time in that epoch.

6.2.2 Sleep onset

Sleep onset is defined by three consecutive epochs of stage 1 or one epoch of any other sleep stage.

Caution in interpreting reports: The Compumedics software report identifies sleep onset as three consecutive epochs of sleep regardless of the stage. This may rarely cause a discrepancy between the identity of sleep onset, sleep time, and sleep latency as defined using the conventional approach used by the scorers (sleep onset as 3 epochs of stage 1 or one epoch of any other sleep stages) versus the output of computer generated reports .

6.2.3 EEG arousal

Scoring arousals is based on "A Preliminary Report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association" Sleep, vol. 15, no 2, 1992. (ASDA criteria)

The scoring of EEG arousals is independent from the scoring of sleep stages (i.e. an arousal can be scored in an epoch of recording which would be classified as wake by R & K criteria). An arousal can proceed to the wake stage (by R & K criteria) or can be followed by a return to sleep.

Definition of Arousal:

An EEG arousal is an abrupt shift in EEG frequency, which may include alpha and/or theta waves and/or delta waves and/or frequencies greater than 16 Hz lasting at least 3 s., and starting after at least 10 continuous seconds of sleep. (ArFigures 1a and 1b)

Artifacts, K complexes and delta waves are included in meeting the 3 s. duration criteria only when they occur within the EEG frequency shift (change in frequency must be visible before these waveforms). A "K" complex or spindle occurring immediately prior to the EEG shift or following is not included in the arousal duration. (ArFigures 2a, 2b, 2c and 2d)

Parts of the EEG totally obscured by EMG artifact are considered an arousal if the change in background EEG in addition to the area obscured by EMG is at least $\geq$ 3 sec. (ArFigure 2e)

Alpha activity of less than 3 s. duration in Non-REM sleep at a rate greater than one burst per 10 s. is not scored as an EEG arousal. Three seconds of alpha sleep is not scored as an arousal unless a 10 s. episode of alpha free sleep precedes this.

If both central EEGs are equivalent and interpretable, the arousal (EEG frequency shift) must be observed in both channels. If observed in only one of two equivalent channels, the change in EEG is assumed to be artifact and not an arousal.

Arousals lasting > 15 s. and containing awake EEG within an epoch cause the epoch to be classified as AWAKE.

TIPS for Arousals Generally:

- When unsure if change in background EEG represents an abrupt change, look at a 60 sec epoch and note if there is a discrete change from background EEG.
- Note whether changes were evident on both EEG channels.
- Be careful to distinguish an increase in EEG frequency from EMG artifact (esp. in delta sleep). (ArFigures 3a and 3b).
- Isolated bursts of delta activity or sawtooth-like waves do not constitute an arousal. In contrast, slow waves intermixed with fast activity that differs from background do qualify as arousals. (ArFigures 4a, 4b and 4c.)
- Occasionally, EEG acceleration is superimposed on slower waves. The slowing may be an artifact secondary to movement or burst of delta waves. If there is evidence of embedded EEG acceleration for $\geq$ 3 sec., mark as an arousal. (ArFigures 5a and 5b)

Arousals in REM

In stage REM, an EEG frequency shift must be accompanied by a simultaneous increase in amplitude of the chin EMG (lasting over 0.5 s.). An arousal starts when a definite change in background EEG is visualized. The increase in the chin EMG can occur anytime during the arousal (can be at the end) and is not a marker for the beginning of the arousal However, increased EMG activity without a change in background EEG does not constitute an arousal (ArFigures 6a, 6b and 6c)

TIPS for Arousals in REM:

- If the level of REM EMG appears to be fluctuating, then the increase in EMG in the area of a putative arousal needs to be more than the background level of fluctuations, to identify this as a REM arousal.
- A long period of alpha activity before an EMG increase may mark the beginning of the arousal if the alpha activity represents the change in the background pattern.

Potential Problems:

Some studies with high RDIs have many arousals that may appear to last > 15 sec. within given epochs. If all such epochs were classified as AWAKE, then the respiratory events would not be included in the RDI and the RDI will be underestimated. When faced with this situation, the scorer may attempt to keep the duration of the arousal to as short as feasible (e.g., corresponding to the length of the waking EEG in that epoch.) This will maximize the number of epochs containing arousals that are captured as "sleep".

6.2.4 Rules for assigning sleep stages when arousal is present in the epoch

The following rules were established to maximize the amount of sleep identified and thus the number of respiratory events recorded (*):

Brief arousals (e.g. arousals ≤ 15s. long) do not automatically require a change in sleep stage. The epoch is staged according to the sleep stage in the remaining parts of the epoch (not including the arousal).

If an arousal or an area of increased EMG causing artifact in the EEG channels is followed by Stage wake (W), then the arousal is considered part of the record scored as a stage Wake. If this part is > 15 s. long, then epoch is scored as a Stage Wake.
In Deep Sleep (unequivocal Stage 3/4), when fast frequency waves are visualized as "riding" on the top of the delta waves, and there are no frequencies characteristic of Stage Wake (*):

- If there is any reason to suspect that the fast frequencies are result of artifact (like a sudden increase in EMG bleeding into EEG), an arousal is not scored.
- When the fast frequencies are not the result of artifact, an arousal is scored. Deep Sleep is scored when delta waves persist despite the faster frequencies riding on top, independent of the length of the arousal.

Note for Delta Sleep: When an arousal includes bursts of Delta waves: these waves are not used for meeting Deep Sleep criteria (e.g. Deep Sleep is scored only if there is ≥ 20 % of the epoch covered by delta waves outside of the arousal).

6.2.5 Episodic events in sleep

Sleep spindles: clearly visible, rhythmic bursts of activity 12-14 Hz, duration at least 0.5 s. (one should be able to count 6 or 7 distinctive waves within a half-second period); the amplitude variability appears sinusoidal. (EpFigures 1a and 1b)

Sleep spindle activity occurs in adults with a frequency of about three to eight bursts per minute in Stage 2 sleep. These are absent in wakefulness and Stage 1. Spindles may be rarely observed in Stage REM and 3-4. Spindle rate appears to be a fairly stable individual characteristic. In the elderly and in individuals with various medical conditions, sleep spindles tend to lose their classic morphology and may have a slightly slower frequency, lower amplitude, and shorter duration.

Medication effects can introduce beta range activity that may be confused with spindles.
Tips to alert to the presence of drug effects mimicking spindles are two or more of the following: (EpFigures 2a and 2b)

- Increased beta activity (spindle like) in well defined REM sleep and wakefulness.
- Increased spindle duration (often > 1 sec.)
- Increased frequency of spindles per epoch (>5/epoch).
- Spindle like activity with amplitude variability that is NOT sinusoidal.
- Fast frequencies (often > 13 Hz).

- When identifying atypical "spindle activity," review previous epochs to ascertain if stage was properly scored.

- When atypical spindle like activity is observed, then such activity cannot be used to distinguish Stage 2 from other sleep stages. This may lead to some underscoring of Stage 2 from 1.

K-complex: EEG waveforms having a well-outlined negative sharp wave, immediately followed by a positive component. Total duration of the K complex should exceed 0.5 s. Waves of 12-14 Hz (sleep spindles) may or may not constitute part of K complex. K complexes can occur as a response to sudden auditory stimuli. K complexes may be reflected on the EOG channels. When in doubt about whether a particular polyphasic wave is a "true" K complex, record is scanned for clear Stage 2 sleep. Questionable K complexes are only designated as K complexes if their morphology closely matches those seen in unequivocal Stage 2 sleep. (EpFigures 3a-d)

Caution!
On the Compumedics system used in SHHS 1, with correct electrode placements, the first, negative part of K complex should be down going and subsequent positive component up (as seen with some traditional polygraphs). If the K complex is reflected on the EOG channels, it will usually appear to be in the opposite phase as that seen on the EEG channel. Sometimes K complexes on EEG are in the same phase as on EOG channels (EEG tracing is upside down). This may be caused by erroneous electrode placement (switching the reference with the C_3 or C_4 electrode). If this happens on the channel used for scoring sleep stages, the computer will not recognize K complexes during automatic analysis.

Hypersynchrony: bursts of high voltage delta (< 4 Hz) or theta (4 - 7 Hz) waves lasting 2-3 s. with a comb-like morphology with a positive polarity (points up going). Hypersynchrony is not considered an arousal. May need to be distinguished from seizure discharges. (EpFigures 4a-d) In children, this actually may be exaggerated. It is relatively more common during the transition from wakefulness to sleep.

Seizures: This is manifest by an abrupt change in background EEG. This usually requires a wider sampling of areas of the brain than is provided with our montage. Two patterns are commonly seen: 1) High voltage, rhythmic activity in the 2-6 Hz range, or 2) Diffuse sustained beta activity. A seizure is often accompanied by prominent muscle artifact. A seizure is usually followed by low to moderate voltage irregular slowing. On the 10 s. screen, characteristic 'spikes and wave' pattern may be seen. If a possible seizure is identified, a physician investigator will be immediately asked to review the study. (EpFigures 5a-e)

6.2.6 Rules for assigning sleep stages

EEG frequencies are divided into following bandwidths:

	β (beta)	> 13 Hz
13 Hz	≥ α (alpha)	≥ 8 Hz
8 Hz	> θ (theta)	≥ 4 Hz
4 Hz	> δ (delta)	

An alpha wave is any wave that has the frequency in alpha range.
Alpha rhythm (also known as posterior background rhythm) has the following characteristics:

1. Is seen in the relaxed waking state with the eyes closed.
2. Attenuates with eye opening, anxiety or mental activity such as mental calculations
3. Slows in drowsiness (occasionally <8 Hz) and then disappears in sleep. The slowing may be so brief as to be unnoticed.
4. Generated by occipital lobes and has a broad reflection to temporal and mastoid areas.

An illustration of the differences in alpha with open and closed eyes is shown in (SsFigures 1a-d).

Stage W - Waking State

Stage W, when eyes are open, is defined by low voltage, mixed frequency EEG in the alpha and beta ranges (> 8 Hz). When eyes are closed, wake is defined by the presence of the alpha rhythm. There is usually (but not necessarily), a relatively high tonic EMG. Waking shows frequent eye movements and eye blinks. Some subjects may have virtually continuous alpha activity, others may show little or no alpha activity in the waking record.

Stage 1 sleep

Stage 1 sleep occurs most often in transition from wakefulness to other sleep stages.

Stage 1 is defined by a background of relatively low voltage, mixed frequency EEG activity with noticeable activity in the 2-7 Hz range with no clearly defined K complexes or sleep spindles. Faster frequencies are mostly lower voltage (amplitude). High voltage (50-75 μV) 2-7 Hz activity tends to occur in irregularly spaced bursts mostly during the later portions of the stage. There are slow eye movements, each of several seconds duration, usually most prominent during early portions of the stage. No rapid eye movements or blinks are present. During the latter portion of the stage, vertex sharp waves, occasionally as high as 200 μV, are often seen in conjunction with high amplitude 2-7 Hz activity. The amount of alpha activity combined with low voltage activity comprises less than half of the epoch. Finally, the tonic EMG level may be lower than observed during relaxed wakefulness. (SsFigures 2a-d)

Traces of low voltage activity at 12-14 Hz may begin to appear as the transition to Stage 2 approaches, but this activity is not defined as a sleep spindles until the rhythmic bursts are clearly visible for at least 0.5 s.

Intervals of > 3 minutes between K complexes or spindles (and which do not meet criteria for REM of delta sleep or Wake) are staged as Stage 1 ("3 minute rule").

Stage 2 sleep

Stage 2 is defined by a background similar to Stage 1 sleep with the presence of the K complexes and/or sleep spindles. It is impossible to define the difference between Stage 1 and Stage 2 sleep on the basis of background activity alone. Bursts of other polymorphic high voltage slow waves, which do not have the precise morphology of K complex, are also frequently seen. Delta waves: high amplitude (> 75 μV), slow (≤ 4 Hz; duration 0.5 s. and longer) activity occupy no more than 19% of the epoch. At the beginning of the Stage 2, slow eye movements may infrequently, and only briefly, persist after the appearance of sleep spindles and K complexes. (SsFigures 3a-c)

Relatively long periods may intervene between K complexes and/or sleep spindles without a background change in the EEG. Regardless of the presence of the arousal:

- If there is <3 minutes of the low voltage, mixed frequency EEG between sleep spindles and/or K complexes, this portion of the record is scored as Stage 2.
- Otherwise if > 3 minutes, this portion of the record is scored Stage 1.

K complexes may be imbedded within an arousal and nonetheless constitute evidence of Stage 2. (SsFigure 4a)

Deep Sleep (Stage 3 and 4)

In SHHS, no attempt is made to distinguish Stage 3 from Stage 4 which are combined into a single category: Deep Sleep.

Deep Sleep is scored when 20% or more of the epoch consists of delta waves which are $\leq$ 2 Hz (duration 0.5 s.) and have an amplitude greater than 75 μV. The 20% criteria refers specifically to the time occupied by the high amplitude, slow waves, and does not include intervening waves of higher frequency and lower amplitude or K complexes. To fulfill the criteria for Deep Sleep, one should be able to find at least 5-6 high voltage delta waves in the 30second sleep epoch (SsFigures 5a-b). Delta waves embedded in increased frequency activity (an arousal) do not contribute to the calculation of time in delta sleep. (SsFigure 5c)

Sleep spindles and K complexes may or may not be present in Deep Sleep (SsFigure 5d). Eye movements do not occur in Deep Sleep, although the EOG may reflect the high voltage slow wave activity. The EMG is tonically active, although the tracing may achieve very low levels, indistinguishable from that of REM sleep.

Note: In the Compumedics software Stages 2, 3/4 are assigned based on the amount of the "delta-H" waves. K complexes and all the waves from the delta range (< 2 Hz) are considered by the computer algorithm in the count of these waves. The computer based calculation of delta sleep can be used to help determine % of slow waves when there are K complexes or events or other artifact. When any ambiguity exists, the scorer must quantify the percentage of time delta waves occupy within the epoch. Any questionable areas should be re-measured, subtracting time occupied by K complexes and other waveforms.

An attempt should be made to distinguish between spontaneous K complexes and delta waves, although this distinction is not always easy. When a K complex distinction is in doubt, comparison should be done with the K complex in unambiguous Stage 2.

Stage REM sleep

Stage REM is defined by a background of relatively low voltage, mixed frequency EEG with accompanying episodes of REMs (Rapid Eye Movements). The EEG pattern resembles Stage 1, except that vertex sharp waves are not readily noticeable. Bursts of characteristic "sawtooth" waves may appear, appearing as notched waves in the theta range. Alpha activity is usually more prominent than in Stage 1 and its frequency is 1-2 Hz slower than the alpha rhythm in wakefulness. The EMG reaches its lowest levels (it cannot be higher than the level during the preceding stage). Phasic twitches and intermittent increases of EMG activity may be observed but intervening baseline must remain low. Phasic twitch (EMG) defined as: short (no longer than .10

sec burst of EMG activity superimposed on suppressed muscle tone which physically manifests as a twitch (contraction) of a muscle or jerk of a limb. In REM such muscle contractions may be isolated or become repetitive, but they remain distinctive. Periods of the relatively low voltage, mixed frequency EEG and EMG at Stage REM level but without eye movements may follow unambiguous stage REM and is considered Stage REM unless criteria for a state change are met. (SsFigures 6a-e)

The EOG shows bursts of rapid eye movements; often the density of such bursts increase as sleep progresses. Thus, earlier Stage REM episodes usually contain fewer REMs than later episodes.

Rarely delta waves may be observed in an epoch that is within a period of REM (SsFigures 7a and b). If occurring within period of REM, a low EMG, continue to score as REM. Large sawtooth waves also may be confused with hypersyncrony (SsFigure 7c).

Note: Excessive beta activity may be observed in REM and should not be confused with spindles. Medications (benzodiazepine or barbiturate ingestion) may induce excessive beta activity in both REM and Non-REM sleep. This beta activity can mimic sleep spindles. Their frequencies often are faster than those seen with the true sleep spindles (see above Stage 2 sleep section for guidance on identifying spindles). Rarely, sleep spindles can be seen in REM in subjects with substantial sleep deprivation (SsFigures 7d-f).

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Start of the Stage REM:

At the start of Stage REM, K complexes, sleep spindles and delta waves end, characteristic sawtooth waves can appear. EMG levels tend to be the lowest after eye movements begin. The fall in EMG may not coincide with the EEG changes.

- If the EMG drops before the last sleep spindle, K complex or delta wave: Score Stage REM from the point the last sleep spindle, K complex or delta wave was seen. (SsFigure 6a).
- Otherwise: Score Stage REM from the point where EMG drops. The period of the record before the EMG drop is scored according to the rules for NREM sleep. (SsFigure 8a).

Periods of elevated sustained EMG during Stage REM sleep:

When EMG is elevated above the REM level for longer than .5 sec, then this portion of the record is scored as a Non-REM sleep or WAKE. If phasic twiches or sawtooth waves are seen, but intervening EMG is low, the epoch remains REM (SsFigure 6e).

WAKE-REM Transition:

When one epoch or more of Stage Wake slows into a low voltage, mixed EEG pattern before REMs or sawtooth waves begin: Score Stage 1 until the EMG drops to REM level and Stage REM afterwards. (*) (SsFigure 8a)

When Stage Wake (> 15s.) interrupts Stage REM (i.e., REM-> WAKE): (*)

If the EEG background of the epochs between the intervening waking epoch and the appearance of REMs (eye movements) is ambiguous (i.e. the EEG background is compatible with either REM or Non-REM sleep), then

- Score as Stage 1 if the EMG is elevated (SsFigure 8a).
- Score as Stage REM when EMG is at the Stage REM level (SsFigures Series 9a-e).

However, if a sleep spindle or K-complex appears prior to the appearance of REMs, then the waking epochs are considered the end of the Stage REM (SsFigures Series 9f-k).

When arousals (< 15 sec) interrupt REM:

The occurrence of an arousal in REM does not automatically change sleep state. However, if the EMG increases after the arousal, REM is considered terminated by the arousal. The following epoch is non REM.

Note: Often a single K complex may be seen in REM after an arousal, with subsequent REMs. This per se does not change REM state. In particular, K complexes do not change REM state if intervening eye movements are seen following the K complex or the interval between the first K complex and the subsequent K complex is > 3 minutes (SsFigure 7f). In contrast, a K-complex occurring after a period of wake interrupting REM does change the state (beginning with Stage 2 at the first K-complex, and Stage 1 between the end of wake and the next K-complex) (SsFigures 9f-k).

End of the Stage REM

Stage REM is scored until a clear evidence of sleep stage change is visualized:

- Appearance of K complexes or sleep spindles without presence of eye movements or sawtooth waves between them, or at intervals of < 3 minutes (SsFigures 10a-d).
- Transition to Stage Wake (SsFigures 9b-c).
- Sustained, increased EMG (SsFigures 11a-d).

When K complexes or unquestionable sleep spindles are seen in the Stage REM:

An isolated K complex may be seen in REM. When K complexes or unquestionable sleep spindles (as compared to Stage 2) are present in stage REM, then an interval between two K complexes or sleep spindles is scored as Stage 2 only if there are no REMs (eye movements) or sawtooth waves in this interval and it is less than 3 min. long. Otherwise the interval is scored as Stage REM (SsFigure 7f).

Scoring REM when there are problems with REM related atonia or the EMG is difficult to interpret.

Identification of the Stage REM is may be difficult when there are prolonged bursts of elevated EMG seen during eye movements or the EMG increases with snoring. In such cases:

> EMG increases clearly related to snoring (changing with breathing) may be ignored, as long as intervening EMG is low (SsFigure 12a).
>
> The portion of the record with unquestionable Stage REM should be reviewed to provide a visual reference of the characteristic Stage REM EEG pattern. Stage REM is scored when EEG pattern changes to the pattern characteristic for Stage REM regardless of the level of the EMG (SsFigures 12b-c). When EEG is consistent with Stage REM, and there is no evidence of wake (blinking), no evidence of Stage 1 (vertex waves, slow rolling eye movements), or the presence of REMs, then score stage Stage REM from the last K complex, sleep spindles or delta wave. Distinguishing between Stage 1 and Stage REM is unreliable and noted as such on the PSG scoring notes form.

6.2.7 Scoring respiratory events

SHHS will identify the following categories of discrete breathing events: obstructive apneas, central apneas, and hypopneas. Additionally, periodic breathing and periodic large breaths will be identified. No attempt will be made to distinguish mixed apneas from obstructive apneas. This decision was based on previous data that indicated mixed events cannot be reliably identified. Central hypopneas and increased upper airway resistance (RERAs) will not be identified because of controversies in the defining these events and the probable need to use invasive monitoring to identify these accurately (ResFigures 1a-d).

Obstructive Apneas are identified when the amplitude (peak to trough) of the airflow signal decreases to a flat or almost flat signal (showing a 75% reduction of the amplitude of "baseline" breathing) if this change lasts for $\geq$ 10 s. *Baseline breathing* is defined as a period of regular breathing with stable oxygen levels (ResFigures 2a-d).

Hypopneas are distinguished as AASM hypopneas or non-AASM hypopneas, as follows:

AASM Hypopneas. Will be identified if $\geq$ 50% reduction of amplitude is visualized on either the respiratory SUM channel OR if the SUM is not present, if a 50% reduction is seen on both belts (thoracic and abdominal). Alternatively, an AASM hyponea may be marked if a clear $\geq$ 50% reduction is seen on a good nasal pressure signal. In considering all available data, greater confidence is given to the SUM than nasal pressure signal. Specifically, when amplitude changes are seen only in the nasal pressure with little or no changes in a sum channel, the event will not be marked. These events are marked independent of whether any associated desaturation is linked with the event.

(Non-AASM) Hypopneas will be identified if the amplitude of any respiratory signal decreases by at least (approximately) 30% of the amplitude of "baseline", i.e. to $\leq$ 70% of baseline, (identified during a period of regular breathing with stable oxygen levels), if this change lasts for $\geq$ 10 s, and if the event does not meet the criteria for the AASM hypopnea (ResFigure 3a-b).. Sometimes more subtle changes in breathing are observed (not clearly reduced by 30% or more from baseline). These require at least a 2% desaturation (ResFigure 3c).

Distinguishing Between Hypopneas and Apneas. This distinction only can be made for events in which airflow by thermistry is interpretable. (If airflow is uninterpretable, the event-based on inductance data is considered by default to be a hypopnea.) (ResFigure 4a). Apneas are marked if > 50% of the event shows absent or nearly absent airflow on the thermister channel (and this reduction is 75% the amplitude of the surrounding breaths). (ResFigures 4b-c)

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Variation in signal amplitude on airflow, thoracic and abdominal channels: In some studies, information appears qualitatively different from different channels. Scoring will be done from the channel that correlates the best with the changes in the oxygen saturation (ResFigure 4d). If there are no changes in O_2 saturation, scoring will be done from the channel that shows the clearest amplitude variation (ResFigure 4e). In cases where the thermister or nasal pressure varies from the inductance channels, and the inductance channels appear mostly artifact free, the inductance channels will be used for event identification and classification (ResFigure 3b, 4f). For example, sometimes the airflow channels will suggest prolonged periods of "no flow", but changes in inductance and oxygen saturation suggest that breathing is occurring. When in doubt, use data from the inductance and saturation channels to identify/classify events.

A **Central apnea** event is scored if NO displacement is noted on both chest and the abdominal inductance channels (ResFigures 5a-b). Otherwise, events are noted as "obstructive."

Distinguishing Between Central and Obstructive Events. " Only events in which there is clear data from both the abdominal and chest signals can be distinguished as "central" or "obstructive". (Events where one or both of these channels are missing or contain artifact are considered "obstructive.") (ResFigure 5c).

Often determining whether an event is central or obstructive is influenced by where the event is noted to begin and end. Sometimes, small efforts are seen following a completely flat area, followed by a large ("breaking") breath. If a single small breath is seen at the beginning or the end of the period of flat signal, the event will be marked as "central." (This recognizes that shortening the event slightly would make it a central event) (ResFigure 6a). However, if 2 or more consecutive small breaths are seen in the period in question, the event is marked as "obstructive." Many of these events would be noted as "mixed" by non-SHHS scorers (ResFigures 6b-c).

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Determining whether an event is central or obstructive in areas of periodic breathing can be difficult because of uncertainties in deciding when to start and end such events. Often, these areas contain breaths that gradually increase and decrease, sometimes decreasing to an imperceptible level. Marking "longer" events in these areas would result in identifying "obstructive" events; "shorter" events are more likely to appear "central." When it is unclear as to when to start an event, look for evidence of paradoxical breathing. Change in phase angle between thoracic and abdomen is an indicator of upper airway obstruction (such events will be designated as obstructive) (ResFigure 6d). When still unclear, the event duration will be marked using the airflow channel. Identify the areas where airflow stops and starts, then assess whether the period is also associated with effort on either channel/band. Then, the inductance channels will be visualized to decide whether during this period, any effort occurred. If any effort was visualized, the event will be considered "obstructive", otherwise, "central." (ResFigures 6e-g).

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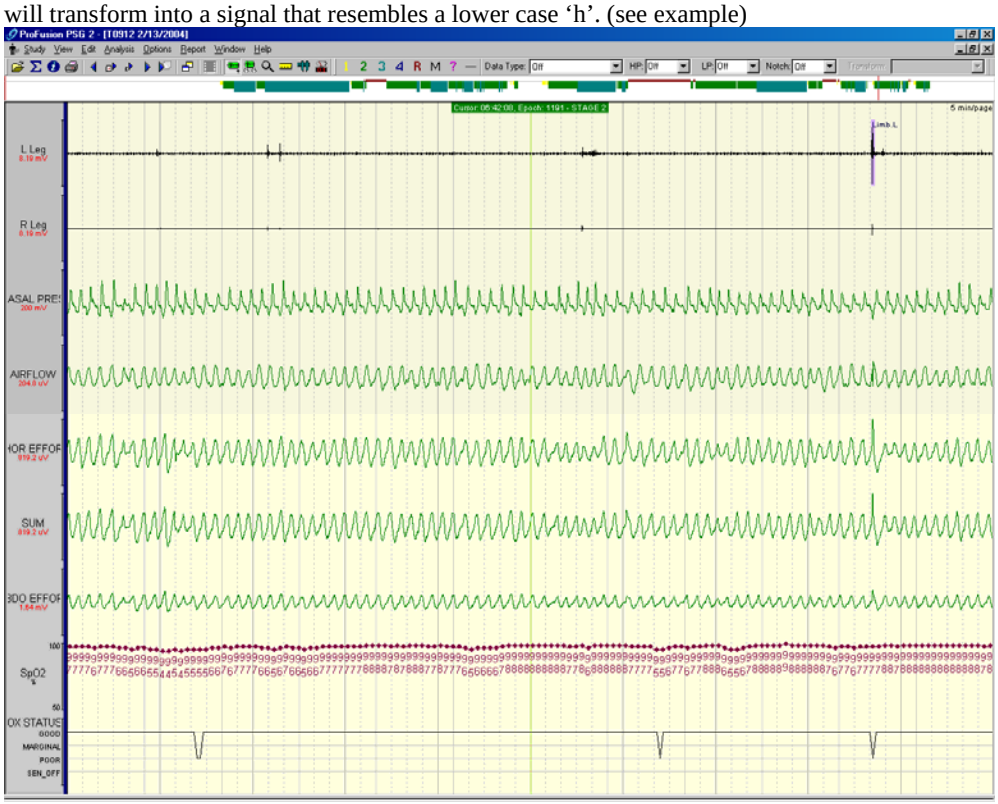
Duration criteria: The beginning of an Apnea/Hypopnea is marked at the end of the last "normal" breath; the end of the event is identified as the beginning of the first breath that exceeds the amplitude of the first reduced breath used to mark the beginning of the event. Duration is based on a "trough to trough" marking (ResFigures 6h-j).

Nasal Flow Limitation

Nasal flow limitation is derived from the nasal cannula signal. A normal flow signal will present a regular sinus rhythm and curve. Flow limitation may occur with increase upper airway resistance, not sufficient enough to cause discrete apneas and hypopneas. A regular sinus curve will transform into a signal that resembles a lower case 'h'. (see example)



6.2.8 Dealing with ambiguous respiratory events:

<u>If changes in amplitude are reduced by < 30%,</u> but a <u>≥</u> 10 s. period of a clearly discernible reduction in the amplitude of respiratory signals from baseline is observed, then score events when:

- they occur as part of a series of events (that do meet the 30% reduction criteria) (ResFigures 7a, 7n-o).
- they are associated with desaturations of at least 2% (ResFigures 7b, 7m, 7p).

Apneas/hypopneas immediately following large breaths or movements are not scored, unless they are part of the cycle (there are other respiratory events before and following). Such isolated events may be "sighs" or artifact (ResFigures 7c). When such an event is noted after a movement/large breath and appears to "trigger" a series of events, the first respiratory event is not scored (unless apneas/hypopneas were scored *before* the movement/large breath) (ResFigure 7d,e).

Determining whether to score one long event or two short events *(i.e., after an initial decrease in amplitude of a breathing signal, there is some increase, but not to baseline, and then a fall again*): In these cases, the oxygen saturation channel will be checked to determine whether one or more than one event should be marked. If the event is punctuated by a clear decrease in oxygen saturation followed by a rise or a stabilization, and then a decrease again, two events are marked; otherwise if the event is characterized by one steady progressive fall in desaturation, than one event is scored (ResFigure 7f-j).

Periods of hyperventilation followed by long periods of hypoventilation: If periods of hypoventilation have clearly visible beginnings and endings (i.e., are "discrete") and are associated with at least 2% desaturation, score as hypopneas regardless of their length (they can last up to a few min.). *(Note: This is commonly observed in REM.)* (ResFigure 7k-l).

Deciding Between an AASM and non-AASM hypopnea: The AASM hypopnea is designated as the event that most specifically reflects reduced amplitude ($\geq$ 50%) as its central criterion. According to the 1999 AASM recommendations, the primary signal used is the SUM channel, and if this is unavailable, from each of the band channels. However, also consistent with the growing appreciation for the "sensitivity" of data from the nasal pressure flow signal, we will also consider that data in this designation. However, many times, the nasal pressure signal may appear to be 50% reduced with very little evidence of reduction in other channels. When little change is seen in the band channels that otherwise appear to be functioning well, the event should not be scored as an AASM hypopnea. Also, if it unclear whether a 50% reduction in amplitude has been achieved, the event should be scored as a non-AASM hypopnea (assuring that all AASM hypopneas are specific to this level of amplitude reduction.)

6.3 Scoring Periodic Leg Movements

A. PLMS DEFINTION

1."PLMS is a series of four or more consecutive movements lasting 0.5 to 5.0 seconds with an interimovement interval of 4 to 90 seconds."(Coleman RM: Periodic movements in sleep (nocturnal myoclonus) and restless legs syndrome. In Guilleminault C (ed) Sleeping and Waking Disorders: Indications and Techniques. Menio Park, CA, Addison-Wesley, 1982, pp265-295.)

2.Events that occur simultaneously or within one half second on both limb traces will be reported as one event.

3.Intervals between limb movement events are measured between the end of the previous limb movement event and the commencement of the next limb movement event.

4.Minimum peak to peak amplitude for a Limb Movement to be detected and marked. This applies when using EMG electrodes to measure limb movements.

5. Leg movements that are exclusively associated with the termination of respiratory events will not be considered in the PLMI. (Will be deleted if occurring in clusters.)

B. **Limitations of PLM Recordings.** Sensors used in MrOS are piezo sensors that detect gross movement, not EMG that detect muscle activity. Therefore, we will apply the following modifications to the above rules:

- If any movement occurring in a characteristic PLM cluster approximates classical leg movements (LM), but lasts for 6-7 seconds, that movement will be considered as a LM.
- Analysis software will be adjusted to maximize automatic detection of leg movements. This will require adjusting the amplitude/gain settings to maximize correct identification of events.

C. **Scoring Leg Movements**

- Run automatic LM and PLM analysis. Adjust gain (see above) to maximize correction automatic detection of leg movements that meet
- DO NOT DELETE ANY Limb movement automatically scored in AWAKE. (Will make subsequent editing easier).
- Delete LMs that exclusively occur at the end of specific respiratory events if these occur as part of clusters where failure to delete these will inflate the PLMI.
- Add any LMs not recognized by automatic scoring that meet criteria above.
- Enable the software's PLM episode detection after limb movement's manual editing (check the box with this name found it under Preferences),
- To have all qualifying LMs correctly associate as PLMs or PLM clusters, add one more limb movement. This will activate the software's automatic detection system to mark all LMs that occur in characteristic clusters as PLMs.
- Briefly check through the study if the system picked up all PLMs. (It sometimes is necessary to add or delete some of the automatic PLM association made by the
- Delete all the PLMs in awake.
- **RULE for the studies, which have a mixture of PLMs and Respiratory events:**

Delete all clusters of 4 or more leg movements in row, if all of them clearly terminate a respiratory event. However, when a mixture of LMs are seen where some occur at the termination of a respiratory event and others appear unrelated temporally to a respiratory event, retain such events other than ones where a sequence of 3 occur associated with respiratory termination.

Identifying Abnormal Leg Movements in Wake (possibly associated with RLS):

Note on the QS form (Q 23) if there is a pattern of periodic leg movements that occurs over a minimum period of least 10 min of quiet awake in the study, and occupy at least 75% of the awake time and is not movement artifact. *Hint: look especially carefully at studies with abundant PLM's in sleep.*

7. QS FORM - SCORING NOTES

See Appendix B for sample QS form

The following are coded on the QS Form during the scoring of each study:

Lights out time, Sleep onset time, and Lights on time: Lights When using the Safiros or Siesta monitors (no light sensors), the Staged Lights must be manually set by the scorer and will be based on participant reported time to bed (from SE forms). The time of lights out, sleep onset and lights on are recorded by the scorer on the QS form to assist in analysis of accuracy of reported time to bed and sleep latency.

Setting Lights ON/OFF: The default for the Staged Lights is OFF for the entire study. If sleep onset occurs before the "Participant Reported Time to Bed", then the Staged Lights are marked ON from epoch one to the first epoch of sleep. If sleep onset occurs after the "Participant Reported time to Bed", then the Staged Lights are marked ON from epoch one to this reported time. At the end of the study, the Staged Lights are marked ON after the last epoch of sleep until the last epoch of the recording.

Sleep latency will be considered reliable when onset of sleep occurs after the "Participant Reported Time to Bed".

Position changing during study: This sensor will be considered to have been calibrated appropriately if changes in position are visualized during the recording.

QA Grade Review

The QA grades of the signal and study are assigned at the time of scoring. It is recognized that the scorer, who spends a longer time with each study, may disagree with the preliminary pass/fail review of the Chief Polysomnologist. This will be re-reviewed with the Chief Polysomnologist and final determination made. Unusual signals, questions not addressed in manual of operations will be addressed at weekly scoring meeting

In addition to quality grades for each signal, the scorer will indicate if they needed to re-reference electrodes to obtain a quality EEG signal. Box will be checked for A1, A2 and/or Ground/Reference if this re-referencing was required for more than one hour.

Studies with limited sleep data

The following codes and guidelines are used to maximize the use of the respiratory data even when the sleep data are limited. These codes also provide a means for subsetting analyses according to the perceived levels of reliability of the scored data. Some studies will undergo only limited scoring (sleep-wake), as described below.

Limited Scoring:

Study is scored sleep - wake only when the technical quality of the EEG does not allow distinction between sleep stages, but allows a differentiation between sleep and wake. The time considered sleep will be marked as Stage 2. No arousals will be scored for these studies. Respiratory events will be scored as usual. Scoring a study "sleep-wake" requires approval by the CP. Any study scored sleep - wake only will be given grade Fair regardless of the hours of scorable signal.

Arousals are not scored when the technical quality of the EEG does not allow differentiation of background changes in EEG from discrete periods of EEG acceleration.
Studies may still be of sufficient quality to stage sleep.

Urgent Referrals/Medical Alerts:

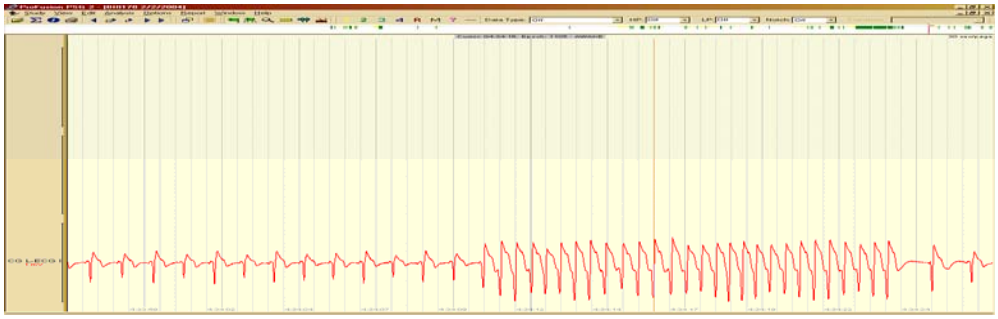
Will be checked "yes" if any criteria for urgent alert as listed below are met:

- Heart rate > 150 bpm for $\geq$ 2 min
- Heart rate < 30 bpm for $\geq$ 2 min.
- Fib/flutter noted with no known diagnosis (as recorded at the clinic and communicated to RC) or known fib/flutter occurred with HR exceeding limits (>120 or <50).
- Ventricular tacycardia (NSVT) observed
- Oxygen Saturation < 75% for >10% TST.
- RDI > 50.

Heart Rate Extremes are further coded as follows with immediate email notification by RC investigator (who will review all alerts) to site investigator as follows:
0= No Abnormalities are seen.
1 = Abnormalities seen and are not clinically significant.
2 =A-fib/flutter noticed, HR within limits (50-120), and it is a known diagnosis.
No further action will be taken.
3 = A-fib/flutter noticed, HR exceeds limits (>120 or <50), and/ or it is not a known diagnosis; Site will be notified.
4 = HR >150 or <30 for 2 consecutive minutes, or NSVT (3 beats duration at a rate $\geq$ 120) or any other abnormality necessitating action. Site will be notified.

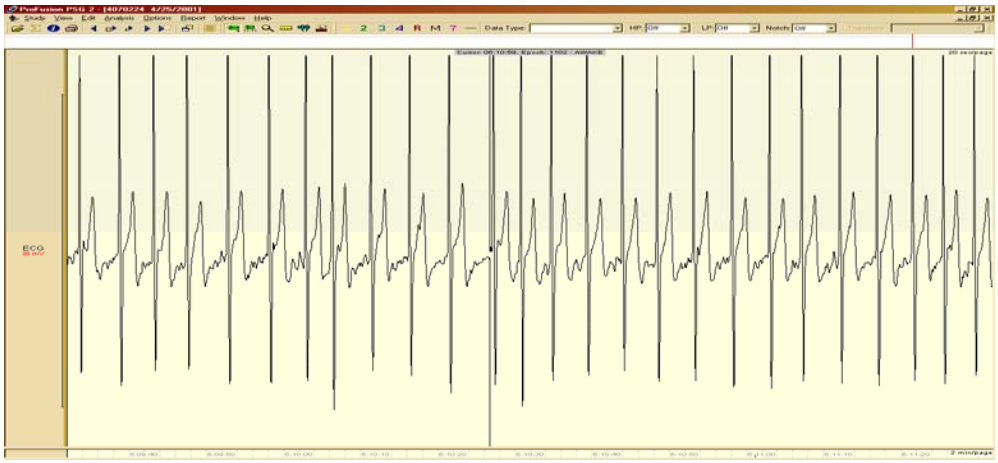
Examples of heart rate extremes to be identified:

NSVT Non Sustained V Tachycarda (rate$\geq$ 120)

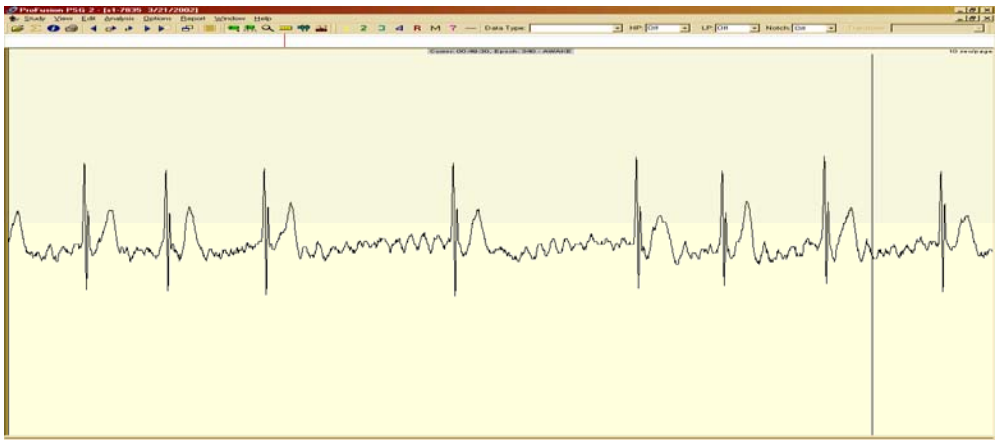


Atrial Flutter, Rate within Limits

Atrial fibrillation, rate >120



Atrial Fib/Flutter, rate<50



Scoring Limitations or Unreliability

Was the study scored with the minimal problems? The following boxes are checked when the scorer is unsure approximately 20% of the time (1 in 5) about classifying epochs/events when making a decision regarding each of the following

- Wake - Sleep unreliable: when the clarity of the EEG makes distinguishing the transition from Stage Wake to sleep uncertain.
- Stage 1/Stage 2 unreliable: when K-complexes and sleep spindles do not have show their classical morphology and distinction between Stage 1 and Stage 2 is doubtful (characteristic for the studies with low voltage EEG).
- Stage 2/Deep Sleep unreliable: when distinction between Stage 2 and Deep Sleep is unreliable because of EEG artifact (usually due to the respiratory artifact on the EEG).
- REM/NonREM unreliable: when identification of Stage REM is unreliable (usually due to poor or missing EMG or when both EOGs are absent).

- Arousals unreliable: when the technical quality of the study does not allow one to distinguish discrete increases in EEG frequency from background changes in EEG. EEG still may be of sufficient quality to score stages. Studies with the physiological alpha intrusion will have arousals scored regardless of difficulty, Checking the "arousal unreliable" box requires approval by the CP.
- Arousals in REM unreliable: when EMG is artifactual or absent during all or REM portion of the study.
- Respiratory events/RDI unreliable: when due to the technical quality of the respiratory signals, distinctions between hypopneas and normal breaths are equivocal in over 20 % of scored events ; also when the quality of the oximetry signal raises doubts about actual magnitude of desaturation linked with over 20 % of respiratory events (unstable baseline).
- Apnea/hypopnea unreliable – when airflow signal is artifactual or absent for over 20 % of scored respiratory events.

Unusual occurrences during sleep

The following patterns are also noted on the QS form:

- Abnormal Awake EEG: when the waking EEG background rhythm consists of waves in the theta range. This should be distinguished from presence of theta waves as a result of excessive sleepiness, which will disappear after some period of sleep, and may indicate a neurological disorder or toxicity (QSFigure 1a-b).

- Physiologic alpha intrusion - when alpha rhythm is present in more than 40% of Non-REM sleep, Alpha delta sleep (QSFigure 2a-c).

- Alpha artifact-when alpha range activity is seen throughout all periods of sleep, does not vary with eye closure, may be evident on non-cerebral channels (i.e., EOG) (QSFigure 2d).

TIP:

Alpha artifact was more likely than alpha intrusion when the activity in question:

- Occurs across most sleep stages, and does not vary by sleep state;
- The activity is fairly similar in amplitude throughout the study
- Often is superimposed on top of the EEG signal

Alpha intrusion is more likely when:

- Varied by sleep stage
- Displayed a fluctuating amplitude

- Abnormal Eye Movements: presence of the rhythmical lateral eye movements in Non-REM sleep, or asymmetrical or disconjugate movements (QSFigure 3a-f).

- Periodic breathing ≥ 10 minutes: when the airflow or inductance channels are increasing and decreasing at least 50 % from the maximum, in a periodic (cyclic waxing and waning or "sinusoidal") manner, for a consecutive period of at least 10 min. Examples of this pattern will be printed and attached to the scoring form. Periodicity is noted independently from scoring apneas and hypopneas (QSFigures 4a-d).

- Periodic large breaths: when very large breaths (one or two) occur periodically (mostly on the inductance channels) between runs of fairly normal breaths for a duration of at least 10

minutes. Examples of this pattern will be printed and attached to the scoring form (QSFigures 5a-c).

Before the QS form is marked for the presence of abnormal events, such events will be reviewed with the CP and physician investigator (abnormal awake EEG, alpha intrusion) or other scorers (periodicity and periodic large breaths). Any study with abnormal events or problems with scoring will be discussed at the weekly QA meetings.

Any problems with the staging or marking arousals will be marked on the QS scoring notes form by checking appropriate boxes and/or by placing notes in the Notes section. All studies so marked will be reviewed with a physician investigator or other scorers.

Was any data lost?

Some studies do not contain usable signals for the entire recording time or include only a portion of the sleep period.

- Recording ended before participant awoke - the last epoch of the study is any stage of sleep; or when an arousal is seen in the last few epochs of the study and there is a question if the participant actually awoke or would have returned to sleep (i.e., lack of sustained activity indicating "out of bed.").
- Loss of the data at the beginning, end or during study - indicates a loss of the data due to poor technical quality of the signals for >30 minutes.

Flow Limitation Flow limitation, as seen by the nasal cannula, which is not associated with respiratory events, and occurs in more than 10% of sleep time. On the QS Form, iff 10% or more of the PSG contains nasal flow limitation, answer 'yes' to question 20 on the QS form. If it is less than 10%, answer 'no' to this question.

Leg Movements in Wake - Study must have at least 10 minutes of wakefulness on the record. Leg movements not associated with obvious movement or artifact must be present during majority of wakefulness (more than 75%). This notation may be used to explore potential associations of Restless Legs Syndrome symptoms, PLMs, and this pattern.

Study-by-Study Outlier Identification

The Outlier program will be run after each study is scored and a report generated. The presence of the following potential outliers will be identified immediately after each study is scored and a report is generated

- 0 % of the any sleep stage
- 90 % of any Non-REM sleep stage
- >60 % of Stage REM
- RDI3P = 0 or RDI3P > 160
- Obstructive apnea index > 80
- Central apnea index > 40

- Minimum desaturation < 40 %
- AI (Arousal Index) < 3
- Apnea or hypopnea duration < 10 s.
- Oxygen saturation = 0.
- PLM Index > 100

If any of the outliers will be found, the scorer will review the study and identify the source. Any errors in scoring or editing will be corrected. New Short and Full reports will be generated and saved. The identification of outliers and the results of the review process (with corrections) will be noted on the QS Form.

Scoring respiratory events/RDI unreliable: "Yes" will be checked when, due to the technical quality of the respiratory signals, over 20 % of scored events distinctions are equivocal; also when quality of the oximetry signal raises doubts about the actual magnitude of desaturation linked with over 20 % of respiratory events (unstable baseline).

Scoring apnea/hypopnea unreliable: "No" will be checked when airflow signal is bad or missing for over 20 % of scored respiratory events.

Summary of Procedures to Follow With Problematic Signals:

EMG artifactual (does not show discernible amplitude variations): may result in difficulty distinguishing REM from non-REM and identify REM- associated arousals. Indicate limitations on form.

EEG artifactual: may result in unreliable or impossible staging and/or arousal identification. Indicate limitations and approaches on form.

Airflow signal poor: Results in all respiratory events defaulting to hypopneas (none qualify as apnea). Indicate limitations.

- Exception to identifying central events when airflow is poor: An exception occurs when both inductance channels (thoracic and abdomen) are flat for > 10 s. Then the event will be marked as a central apnea.

Thoracic or/and abdominal channel poor: Results in events defaulting to "obstructive" (none qualify as "central").

Situations when staging or scoring respiratory events are impossible during some portion of the study: If this occurs at the beginning or end of the study, this period will be scored as stage Wake and edited lights will be set as "On" during this period (sleep latency will be unreliable if it is on the beginning). This action may result in artificially shortened sleep time. The appropriate box will be checked on PSG scoring form (Data Lost – Other)

If periods of data loss occurs in the middle of the study:

- if periods are < 30 min. long:
  - on the O_2sat signal: period will be marked as a O_2 sat artifact
  - on airflow and both inductance channels: no respiratory events will be scored during this period
  - on both EEGs: period will be scored as a stage Wake
- if periods are ≥ 30 min. long then period of unscorable data will be marked as Stage Wake and on the PSG scoring form appropriate box ("Intervening period of bad EEG" or "Intervening period of bad Resp/Oximetry") will be checked. This action may result in artificially shortened sleep time.

APPENDIX A – TABLE OF CONTENTS

Staging screens reflect 30 sec/page timebase, unless otherwise stated.
Respiratory screens reflect 5 minute/page timebase, unless otherwise stated.

FIGURES (Examples of Signals)

Arousal Examples

Episodic Event Examples

Sleep Stages

Respiratory Events

ResFigures 1c-d - Periodic large breaths
ResFigures 2a-d - Obstructive Apneas
ResFigures 3a-c - Hypopnea
ResFigures 4a-c - Distinguishing between Hypopneas & Apneas
ResFigures 4d-f - Variation in signal amplitude on airflow, thoracic, abdominal
ResFigures 5a-c - Central Apneas
ResFigures 6a-c - Distinguishing between Central and Obstructive Apneas
ResFigures 6d- Paradoxical breathing
ResFigures 6e-g –When to start/stop events
ResFigures 6h-j – Trough-to- trough marking of respiratory events
ResFigures 7a-b – Respiratory events in a series
ResFigures 7c-e – Marking respiratory events after large breaths
ResFigures 7f-j - Marking one long event vs. two short events
ResFigures 7k-l- Periods of hyperventilation followed by hypoventilation
ResFigures7m-p - Scoring respiratory events in series, ambiguous amplitude changes

QS FORM

Unusual occurrences during Sleep

QSFigures 1a-b - Abnormal wake EEG
QSFigures 2a-c - Physiologic alpha intrusion
QSFigures 2d - Alpha-like artifact
QSFigures 3a-f - Abnormal eye movements
QSFigures 4a-d - Periodic breathing in sleep
QSFigures 5a-c - Periodic large breaths