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Definition of type of physiological activity and pitfalls of current recording methods

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List of abbreviations

ASI	Alpha-/Slow wave Index
BiPAP	Bi-Level Positive Air Pressure
CNS	Central nervous system
cPAP	Continuous Positive Air Pressure
ECG	Electrocardiogram
EDA	Electrodermal Activity
EEG	Electroencephalogram
ELM	Eye Lid Movement
EMG	Electromyogram
EOG	Electrooculogram
HRV	Heart Rate Variability
IAA	Index of Alpha Anteriorization
LOC	left outer cantus
LORETA	Low Resolution Electromagnetic Tomography
MSLT	Multiple Sleep Latency Test
MWT	Maintenance of Wakefulness Test
Non-REM (NREM)	Non REM sleep
OSS	Objective Sleepiness Score
PVT	Psychomotor Vigilance Task
REM	REM sleep
REMs	rapid eye movements
ROC	right outer cantus
SAO ₂	Blood oxygen saturation
SEMs	slow eye movements

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Executive Summary

In numerous studies, physiological signals have been proven to be a sensitive measure for describing human wakefulness and sleep states as well as the transitions between these states. The aim of the current document is to give an overview of the various physiological activities which play a crucial role in monitoring the human sleep-/wakefulness continuum (e.g. brain electrical activity, cardiac activity) on the one hand and furthermore, to identify additional physiological activities and signals, which are necessary for diagnosing several specific sleep disorders (e.g. respiratory parameters).

Accordingly, the methodology currently available to measure these activities (e.g. EEG) is outlined. Special emphasis is put on the insufficiencies of these methods, in order to overcome these shortcomings in future sensor development. Furthermore, thresholds (i.e. the accuracy by which a specific physiological activity has to be measured to adequately reflect a subject's state) was defined to delineate the technical requirements for sensors.

Being a part of the EU funded project SENSATION, the current document draws on several sources of information: it is based on a literature search in scientific databases and textbooks, on interviews with experts by means of an electronic questionnaire, and on the results of a brainstorm meeting which was held in Vienna on May 27, 2004. At this meeting, 23 experts discussed limitations of current recording techniques which resulted in a concrete list of definitions and thresholds with respect to physiological data recording, in order to guide further sensor development.

The first part of this document deals with the states of sleep and wakefulness as well as their transitions and describes their physiological correlates. Special emphasis is put on the fact, that state transitions might occur either voluntarily or involuntarily.

In the second part the changes of physiological activities which are characteristic for specific sleep pathologies are outlined. In the vast majority, patients suffering from sleep disorders differ from a normal population in a multitude of measurable physiological activities. In many disorders, these deviations are even characteristic and specific for a disorder and their objective evaluation is a necessary pre-requisite for diagnosis of these disorders. Sleep related pathologies, their characteristic physiological activities described in literature, and the corresponding sensors to measure these activities are summarized in this part.

In the third part of this document, dealing with physiological data recording, the different kind of physiological activities (central nervous system activity, autonomous nervous system activity, and motor activity) and their correlates and the variety of methods of their measurement are covered. Special emphasis is put on the pitfalls and limitations of the techniques currently used.

Finally, concrete recommendations for the recording relevant are given, in order to establish criteria for optimal recording methods of physiological signals for studying sleep, wakefulness as well as daytime sleepiness and alertness. Again, these recommendations are based on the literature review as outlined above, the survey among sleep experts and the discussions at the brainstorm meeting.

Introduction

In numerous studies, physiological signals have been proven to be a sensitive measure for describing human wakefulness and sleep states as well as the transitions between these states. This report summarizes the state of the art of recording physiological signals needed for identifying the states of wakefulness and sleep as well as their transitions, especially addressing insufficiencies of current recording methods.

The first part of this document deals with the states of sleep and wakefulness as well as their transitions and describes their physiological correlates. Special emphasis is put on the fact, that state transitions might occur either voluntarily or involuntarily.

In the second part the changes of physiological activities which are characteristic for specific sleep pathologies are outlined. In the vast majority, patients suffering from sleep disorders differ from a normal population in a multitude of measurable physiological activities. In many disorders, these deviations are even characteristic and specific for a disorder and their objective evaluation is a necessary pre-requisite for diagnosis of these disorders. Sleep related pathologies, their characteristic physiological activities described in literature, and the corresponding sensors to measure these activities are summarized in this part.

In the third part of this document, dealing with physiological data recording, the different kind of physiological activities (central nervous system activity, autonomous nervous system activity, and motor activity) and their correlates and the variety of methods of their measurement are covered. Special emphasis is put on the pitfalls and limitations of the techniques currently used. The report is limited to non-invasive measurement methods.

Finally, concrete recommendations for the recording relevant are given, in order to establish criteria for optimal recording methods of physiological signals for studying sleep, wakefulness as well as daytime sleepiness and alertness.

Methodology of data retrieval

The present report is part of the EU-funded project SENSATION and is based on a literature search in scientific databases and textbooks, on interviews of experts by means of an electronic questionnaire, and on a brainstorm meeting which was held in Vienna on May 27, 2004. At this meeting, 23 experts discussed definitions of sensors and methods for recording physiological signals. In the acknowledgment, all sleep experts who have completed the questionnaire as well as the participants of the brainstorm meeting are listed.

1. Physiological states and transitions

1.1. Wakefulness

Vigilance, as a hypothetical construct, is often conceived as a state of the nervous system ranging from wakefulness to sleep. In fact Herrmann et al. (37) have proposed to differentiate between: (i) vigilance, expressing the ability of a neural system to perform and (ii) vigility, expressing the state of alertness (from fully alertness to severe drowsiness). Koella (52) stated that vigilance may be regarded as a “readiness to adopt the appropriate behavior in a given situation, which thus finds outward expression through the quality and quantity of the behavior occurring in response to a given (internal or external) stimulus situation”, that is vigilance research would deal with the optimal performance in a specific situation.

The physiological substrates of vigilance have yet to be determined. It is assumed that vigilance is a CNS phenomenon with identifiable neural mechanism and neurochemical correlates. To achieve an optimal state of vigilance and hence an optimal readiness to perform at the behavioral level, various neuronal subsystems have to show a certain level of activation, reactivity, and adaptability, thus enabling specific functional connections. As a rule, this optimum is not maintained permanently, but rather the state of vigilance fluctuates within a physiological area of tolerance. Disturbances of vigilance and hence behavioral deficits occur when the tolerance threshold is transgressed, i.e., when the functional connections of the neuronal subsystems and their interactions deviate greatly from the optimum (14). When dealing with the neural correlates of vigilance it is impossible to avoid referring to arousal and attention. In simple terms arousal can be defined as the state of physiological reactivity of the subjects and attention as the appropriate allocation of processing resources to relevant stimuli. One of the four sub-processes attention is usually fractionated, the so-called sustained attention (attending to one stimulus over an increasing period of time), is often used synonymously with the term vigilance. A more detailed description about arousal and attention in connection with vigilance can be found in Barbanoj et al (12). Functional imaging studies have consistently localized an amodal system for sustained attention in the frontal and parietal lobes, predominantly in the right hemisphere (25). Recent studies using low-resolution brain electromagnetic tomography (LORETA) based on multi-channel EEG recordings have also revealed a right hemispheric vigilance system (7, 8). These cortical areas are activated in response to sustaining attention in visual, somatosensory and auditory modalities. The thalamus has also been implicated in sustained attention. It is possible that the cortical activations are related to the attentional requirements of sustained attention, while the thalamic changes are related to the influence of arousal levels on sustained attention (25). These two distinct networks comprise: (i) thalamus, striatum and anterior cingulate, the predominantly subcortical one; and (ii) right frontal (dorsal and ventral), inferior parietal and mid-temporal, the cortical one. Based on multi-channel EEG recordings at least the cortical network can be investigated also during sleep by means of LORETA (6).

1.2. Sleep

Sleep can be defined at a behavioral level as a “reversible behavioral state of perceptual disengagement from and unresponsiveness to environmental stimuli” (Carskadon and Dement 22). Within sleep, two separate states have been defined on the basis of a constellation of physiological parameters. These two states, non rapid eye movement (NREM) and rapid eye movement sleep (REM) are distinct from one another as each is from wakefulness.

Conventionally, NREM sleep is subdivided into four stages, which are defined relatively precisely, although to some extent arbitrarily (76). These four stages (stage1, 2, 3, and 4) are distinguished from each other principally on the basis of their different patterns of brain electrical activity as measured by the EEG. Thus, the EEG is considered as the “core measurement of polysomnography” (23). The EEG pattern in NREM sleep is synchronous, with characteristic waveforms such as sleep spindles, K-complexes and slow frequency, high-amplitude waves (delta waves).

By contrast, REM sleep is defined by EEG activation, muscle atonia, and episodic bursts of rapid eye movements. REM is generally not subdivided into substates, although tonic and phasic types of REM sleep are often distinguished for research purposes. The tonic versus phasic distinction is based on short, transient events, occurring in clusters separated by episodes of relative quiescence (22).

The sleep recording is performed by collecting a set of established electrophysiological signals recorded with a polygraphic system. The minimum set of signals had been described carefully in the recommendations by Rechtschaffen and Kales (76). The minimum requires one EEG lead with electrode positions either C3-A2 or C4-A1 according to the 10-20 system for placement of electroencephalography electrodes on the skull. It is now well established to have at least one second EEG lead in order to have an alternative signal if one lead loses quality during the night. Two EOG leads are always required, in order to distinguish between eye-movements and prefrontal EEG interference. Often they are abbreviated as ROC (right outer cantus) and LOC (left outer cantus). The electrodes are arranged in a way that the eye ball movements result in signals going in opposite directions whereas head movement and EEG artifacts result in signals going in the same direction. One EMG placed on the chin (mental or submental) is required for detection of REM sleep atonia. Based on these signals a sleep scoring according to the standard criteria can be performed.

The rules for sleep scoring are given by the recommendations of Rechtschaffen and Kales. According to this manual it is possible to distinguish wake, REM sleep, non-REM sleep stages 1 to 4 and movement time. Non-REM sleep stages 1 and 2 are regarded as "light sleep" and stages 3 and 4 are regarded as "deep sleep" or "slow-wave-sleep" due to the dominance of slow delta waves in the EEG. This sleep scoring is performed for time episodes of 20 or 30 second duration which are called "epochs". Thus, an 8 hour sleep consists of 960 30-s epochs. Although the visual sleep stage scoring according to these rules has been challenged in recent years (44, 40), it is the only worldwide accepted standard for sleep classification.

Besides the scoring of sleep stages, interruptions of sleep, or central nervous activations, so-called arousal from sleep are evaluated and counted. An arousal is an increase in EEG frequencies for at least 3 seconds and less than 15 seconds. It may occur during any sleep stage. During REM sleep there is an additional increase in EMG muscle tone. A certain

number of arousals often associated with changes in body position is found during normal sleep. An excessive number of arousals is disturbing sleep considerably.

The diagnosis and differential diagnosis of the vast majority of sleep disorders requires the recording of additional biosignals, like cardiac activity, respiration etc. This so-called cardiorespiratory polysomnography requires a minimum of 12 physiological signals.

Further signals may be selected according to the disorders to be diagnosed in a particular patient. Additional EEG leads are useful to evaluate the spatial distribution of sleep related EEG patterns. In the case of sleep related epilepsy or other neurological disorders with associated sleep disturbances additional EEG leads are indispensable.

1.3. Physiological state transitions

1.3.1 From wakefulness to sleep

Transition from wakefulness to sleep may be desired/voluntary (the person is trying to fall asleep and the sleeping environment has been prepared accordingly) or undesired/involuntary (the person is engaged in activity which is abruptly interrupted and the sleeping environment is not adequate). In the latter case and depending on the task the person is engaged in, falling asleep unexpectedly can lead to severe accidents.

Interestingly, there is an ongoing discussion whether falling asleep voluntarily or involuntarily is occurring in a similar manner. While the voluntary transition is facilitated by specific body posture, active eye closure and use of adequate sleeping environment, the involuntary transition will be accompanied by active resistance of the person who will develop any means to fight this transition.

Voluntary transition

In the introduction of their book “The EEG of Drowsiness”, Santamaria and Chiappa (78) mention the following as important features to characterize the gradual progression from wakefulness to sleep (W-S), which were reported in work done before 1987: (1) slowness of the alpha EEG rhythm and reduction of its amplitude, (2) gradual disappearance of occipital alpha and more spatially diffuse alpha presence, moving anteriorly, (3) reduction of rapid eye movements (REMs), (4) appearance of horizontal slow eye movements (SEMs) of 0.2-0.6 Hz frequency, (5) appearance of theta EEG activity bursts, and (6) appearance of vertex EEG waves. In their book they reported own results of trying to establish different levels of the W-S continuum, based on EEG and eye/eye-lid movement measurements. However, these authors caution that there is a great deal of variability in the EEG of drowsiness among different subjects and between consecutive drowsiness periods in the same subject.

Lindsley (1960) described three stages of wakefulness (strong excited emotion, alert attentiveness, relaxed wakefulness) and one stage of drowsiness as a transitional stage between wake and sleep. In comparison, Bente (14) not only determined different stages of drowsiness between relaxed wakefulness (characterised in alpha types by a more or less stable and continuous alpha rhythms in the occipital regions) and sleep, but also sub-classified two different patterns of the change of form of resting wake activity: A stages with synchronised and anteriorized alpha, and B stages with a disintegration of alpha rhythm into theta frequencies with fast superimposed beta waves. Kugler et al. (56) made it possible to subclassify more steps of severe drowsiness and light sleep. A comparison between Lindsley’s classification rule (1960) and that of Bente (14) shows that synchronised optimal alpha rhythm has been interpreted as subvigil A stages [Bente] or relaxed wakefulness [Lindsley].

A further development in the classification of vigilance stages are the automatic procedures for vigilance-indicative EEG staging which have been suggested by several authors (62, 61, 86). It was shown, for instance, that those measures can be used in pharmaco-EEG trials to express sedative or stimulating drug effects. Their systems, however, use only part of the available electrophysiological information and have not all been fitted by mathematical procedures to known EEG parameters expressing the degree of vigilance. Matousek and

Petersen (62) used training material in which they classified the stages “alert” and “drowsy”. Matejcek (61) used the alpha slow wave index (ASI), which is the ratio of the sum of relative α_1 and α_2 to the sum of relative delta and theta, without training material of the visual EEG. Ulrich and Frick (86) based their automatic discrimination on alpha power separating A and B stages according to Bente. A segment with more than 50% of relative alpha power is classified an A stage.

Ott et al (71) linked the two subvigilance factors to Bente’s assumptions that the polyrhythmic decompensation is an expression of a decoupling of two fundamental subsystems co-operating in the macro-state called resting-EEG-rhythm, one seemed to mediate more excitatory, the other more inhibitory influences. It was speculated that the excitatory system could be attributed to the fast alpha-factor because high alpha (10-11 Hz) during resting conditions is closely associated with increased attention in a subsequent condition of performing mathematical tasks. The inhibitory system might be attributed to the slow alpha-factor since it is activated by sedative drugs, especially of the benzodiazepine type (alpha-decrease, beta-increase, theta/delta increase); the blocking reactions, e.g., opening eyes or mental activity, induces alpha-dissolution and beta-increase too.

Streitberg et al (79) have developed what it was called the COMSTAT-rule for vigilance classification, that is a system that could quantify three different vigilance stages of wakefulness (W-1W3: tense wakefulness, alert attentiveness, and relaxed wakefulness) and two stages of drowsiness between awake and sleep (W4-W5: moderate and severe) based on spontaneous EEG-activity. This classification was achieved: (i) by combining different elements and patterns of previously visually analysed EEG [amount of background activity, theta index, alpha index, background rhythm anteriorization index, frontal beta burst, lower/central/upper alpha frequencies, k-complexes and sleep spindles] by means of Latent Class Analysis and (ii) by finding a robust automatic analysis classification procedure based on power spectral estimators that best fits the results of the Latent Class Analysis.

A two dimensional structure of the underlying brain states was also the conclusion of Streitberg et al (79) when using the COMSTAT-rule. They labeled one dimension as “alert vs drowsy” and the other as “neuronal availability”. These two dimensional interpretations corresponds to Kubicki et al (55) hypothesis that the availability of neurons can be low in tense wakefulness and in severe drowsiness, can be higher in alert attentiveness, and is highest in relaxed wakefulness. Thus, vigilance would not indicate performance itself, but the readiness of the system to perform.

Herrmann et al. (39) recorded 65 healthy subjects with an occipital rhythm between 8 and 12 Hz (O_2T_6). The recording lasted for 11 min, 5.5 min under RT (reaction time stimuli), followed by 5.5 min RS (resting): 16 segments of situational vigilance, 40 s each, 8 segments for RT and 8 for RS. Power spectra were estimated between 1.0 and 30 Hz with $\Delta f = 1.0$ Hz steps, calculating the relative power values for 29 spectral estimators (ln transformation was made to approximate multidimensional normality of the distributions). The COMSTAT algorithm for multimodal factor analysis was applied (Röhmel et al., 1983). The vigilance level (VL) according to Matejcek (61) was also calculated.

The frequency (F) mode could be described sufficiently by five factors which were called: δ^F/α_1^F , θ^F/α_2^F , β_1^F/α_1^F , β_2^F , β_3^F . In the situational (V) mode only two factors were extractable, describing the two situations: RT (higher vigilance level) and RS (lower vigilance level). Two

models were used for the description of personal (P) variance: a bimodal model (P x V) [that is, using VL instead of a total power as basic values], and a trimodal model (P x V x F).

A 2-factor solution was extractable when the P-factor structure was described in a bimodal model. One factor contrasted persons with a high versus a low vigilance level, and was therefore called the “*vigilance level factor*”. The other contrasted persons with high versus low vigilance fluctuation during the RT and RS recordings. This factor was called the “*vigilance dynamic factor*”. When the third node (F) was added, the P variance was increased substantially. A four-factor solution was selected for interpretation. The first factor contrasted persons with high versus low α power, and was called the “*a-power factor*”. The second factor contrasted persons with peak at 9-10 Hz, high α , low δ and medium β power versus persons with a peak at 8-9 Hz, medium α , high δ and low β power. Since the contrast persons describe spectral poles also seen as changes in vigilance, this spectral factor was called the “*congruent vigilance factor*”. The third factor contrasts persons with peak at 9-10 Hz, high α , low δ and low β power versus persons with peak 10-11 Hz, medium α , high δ and high β power. Since the contrast persons describe spectral poles, also seen as changes in the so-called dissociative vigilance shift, this factor was called the “*dissociative vigilance factor*”. The fourth factor contrasts persons with high versus low dominant α frequency, and was therefore called the “*a-frequency factor*”.

So, on the basis of these data, the hypothesis has been formulated that the most important P-variance sources on EEG data from subjects with occipital α -EEG and for the occipital lead are: (i) the α power, (ii) the dominant α frequency, and the variance due to dynamic changes which can be caused by a shift in vigilance, either (iii) congruent or (iv) dissociative.

Interestingly, Tsuji and Kobayashi (85) investigating the spatio-temporal organisation of the daytime arousal state found that the diurnal rhythm of the arousal EEG was made up of two ultradian components with periods of about 100 min and 3-8 hours. The shorter component is composed by the slow alpha (8-9 Hz) and beta (12-17 Hz) activities, negatively correlated and was thought to represent the oscillation of vigilance level between mental “rest” and “activity” states in the basic rest-activity cycle (BRAC). The longer component is composed of activity in both the theta (6-7 Hz) and fast alpha (9-12 Hz) bands, these two bands being negatively correlated. It was thought to represent wide variations in levels of consciousness between “wakefulness” and “drowsiness” states. These interpretations suggested that the shorter component is superimposed upon the longer one, that is, the diurnal rhythm of the arousal state would be made up of both vigilance rhythms and variations in consciousness.

Tanaka et al. (81) examined the regulation of the order of appearance and the distribution of duration of typical EEG patterns during the so-called hypnagogic state (relaxed wakefulness to Stage 2 sleep, per R&K criteria). Twenty-three male subjects (20-27 years of age) were studied during the period “lights-off “ until 5 min after the appearance of the first sleep spindle. Thirty-sec EEG epochs from the C3-A1 derivation were scored for nine distinct stages of progressive drowsiness. Accordingly, stage 1 corresponded to relaxed wakefulness. Stages 2 and 3 corresponded to progressive loss of alpha, indicating onset and progression of drowsiness. Stages 4-8 corresponded to the Stage 1 of sleep (R&K), and stage 9 corresponded to the Stage 2 of sleep (R&K). The results indicated that, as far as stage duration is concerned, stages 1, 2, 3, 5, and 9 can be considered to be the “basic” EEG stages during the hypnagogic state, while the others serve the role of “transient” stages, most of them exhibiting durations of less than 30 sec. Interestingly enough, stages 6, 7 and 8 were defined as exhibiting vertex sharp waves mainly. The authors concluded that stage 5 (which relates to an EEG epoch

composed of low-voltage theta waves with burst suppression) is an intermediary stage in the wakefulness-sleep transition, and that this stage appears to be the principal stage of the hypnagogic state, having a duration of up to 2 min, on the average. They also suggested that stages 6, 7 and 8 exist to “enhance the stability of the EEG pattern, especially the theta wave-dominant pattern”.

The same investigators (Tanaka et al., 82) studied the topographic distribution of the EEG during these 9 stages, by using FFT-based spectral analysis. They found that alpha activity in the spectral band of 9.6-11.4 Hz decreased remarkably at the parieto-occipital region in stages 4 and 5, and that, subsequently, from stage 7 on, it increased gradually in the frontal areas. They proposed an anterior/posterior ratio of alpha band power as a possible sensitive index of the hypnagogic state.

Three strategies can be identified when assessing vigilance through neurophysiological recordings. They could be broadly defined, for didactic purposes, as: 1) those trying merely to identify a global appraisal of the phenomenon (yes/no scale); 2) those which allow a classification into different discrete states (ordinal scale); and 3) those leading to an accurate quantification into a theoretical continuous scale (interval scale).

Within the first group the Multiple Sleep Latency Test (MSLT, 21) and the Maintenance of Wakefulness Test (MWT, 64) can be included. The former measures the tendency to fall asleep while lying in a quiet, dark bedroom on repeated opportunities at 2-h intervals throughout the day using standard polysomnographic methods. The latter requires that subjects sit in chairs in a darkened room and remain awake for 40 minutes. Also what is called “Chronospectrogram Analysis” could be included in this category (61). Based on power spectrum analysis the decision about the change in an “initial” state of vigilance is taken when changes in a selected parameter (e.g. percentage power of alpha activity) plotted as a function of time cross a pre-determined confidence limit.

Methods included in the second group follow the common practice used in traditional sleep studies, that is, to segment the recordings and classify each epoch, following pre-defined criteria, into a certain number of pre-determined stages. In sleep studies 30-second epochs are classified into five stages: 4 stages of non-REM sleep and the REM stage (76). When dealing with day recordings different approaches have been undertaken, as for example the one reported by Alford et al (2), who using 16 second epochs define 6 scoring categories while awake which will result in 3 derived stages, that is: waking total (active + quiet waking + quiet waking), drowsiness total (intermittent alpha + continuous alpha + intermittent theta + stage 1 NREM), sedation total (intermittent theta + NREM sleep).

After applying different mathematical and statistical techniques several variables have been derived in order to quantify the vigilance state of the subjects at the discrete time points where the EEG recordings are obtained. They range from simple parameters as Hjorth’s mobility, Hjorth’s complexity, Slow-wave activity, 95% edge frequency, mean frequency; followed by estimated indexes as ASI (Alpha slow-wave index), IAA (index of alpha anteriorization), the alpha quotient (α_1/α_2) or the alpha attenuation test (alpha ratio of eyes-closed to eyes open), up to more sophisticated calculations, as for example the so-called Vigilance Index as the quotient between (tense + alert) wakefulness and (slight + moderate + severe) drowsiness, severe drowsiness being equated to stage 1 NREM (79). Other unusual techniques have also been employed in vigilance research as the bispectral analysis, which is

the estimate of the mutual relationship between different frequency bands within the same time series.

Ogilvie et al. (70) studied SEMs and behavioral response during drowsiness. They confirmed previous observations linking the appearance of SEMs with drowsiness and the disappearance of them with the beginning of behaviorally defined sleep. When SEM activity was almost nonexistent, response to a task was very fast. However, as response times increased, SEM activity increased. Eventually, SEM activity was virtually nonexistent as drowsiness progressed and sleep occurred. The authors concluded that in addition to standard EEG measures, decreases in behavioral response, lengthening of response time, shallow abdominal respiration and SEMs indicate progressive changes from wakefulness to sleep.

Cantero et al. (19) reported on the possibility of detecting drowsiness progression into sleep onset (defined as the first of three consecutive 30-sec epochs of Stage 1 (R&K) without EEG arousals) via eye-lid movement (ELM) measurements. ELM was measured by an adhesive-backed piezoelectric film (22mm x 7mm) attached to the upper eye-lid. The film detected passive deformation of the lid caused by movement of the eyeball as well as movement of the lid produced by contraction of the levator palpebrae muscle. By proper signal processing, the device did not indicate SEMs of drowsiness. Although not explicitly checked by the authors, the results reported indicate that there appears to exist a possible downward trend in ELM density (ELMs/min) during the 90 sec of drowsiness before sleep onset. Such a trend was not obvious in theta or alpha EEG power. The authors concluded that ELM density, but not theta or alpha power, showed a significant shift toward sleep values during the 90 sec before sleep onset, "thus more clearly heralding the impending onset of human sleep". Given the fact that during drowsiness there exists a loss of tonic activation of the levator palpebrae muscle, which normally holds the upper eye-lid open, the authors hypothesized that their procedure (ELM detection) measures this process, which results in a declining number of small eye-lid movements associated with a decrease in tonic activation of the muscle. Thus, their technique could be used as a vigilance monitor.

Atienza et al. (9) have shown that the appearance of SEMs during drowsiness preceding Stage 1 sleep (R&K) could be reliably predicted within a few seconds by a precipitous decline in ELM density. Accordingly, they suggest that ELM density can be a valuable tool for the identification of sudden decreases in alertness.

The same scoring rules as in all-night polysomnography are also used for daytime recordings including Multiple Sleep Latency Test (MSLT) and Maintenance of Wakefulness test (MWT). Harrison and Horne have demonstrated that the sensitivity of MSLT can be increased by using short 5 s epochs as sleep onset criterion in evaluating daytime sleepiness (34). A visual adaptive scoring system has been developed by Himanen (41). It uses 9 stages excluding SWS and 8 additional arousals stages. Beside EEG also EOG and EMG are used. Epoch duration is adaptive with minimum epoch length of 1 s. It has been shown to be sensitive method of scoring at least MSLT.

An automatic adaptive scoring system also exists (42) the MSLT, which has also been correlated to reaction times (50).

Whatever strategy is used, it is faced with the fact that electrophysiological changes related to drowsiness vary rapidly. So duration of the epochs used in the analysis can become a critical point. Different epoch duration has been used in studies dealing with the relationship between

electrophysiological activity, vigilance, alertness, reactivity and performance. Duration as short as 1 sec has been employed but it is not unproblematic. An alternative procedure could be applied, what it is called “adaptive segmentation” (75). When dealing with these approaches there are no distinct epoch lengths but the epoch boundaries have to be determined automatically or visually by properties of the signals. As long as the electrophysiological activity remains constant the same epoch continues and as soon as a change takes place the epoch changes. Adaptive segmentation would include a more detailed division of wakefulness and drowsiness, the records being divided into segments of variable length, with mean of 1.6 sec and range 0.5-14.7 sec.

In order to explain and predict variations in alertness mathematical models of alertness have been proposed (29, 15, 48). Folkard and Akerstedt (29) constructed a quantitative model that uses sleep/wake timing to predict alertness, that is, a model using sleep data as input: times of rising and going to bed for the period investigated. The work was inspired by the two-process model of sleep regulation, which had shown that sleep length and slow-wave activity could be described by a combination of homeostatic (prior time awake or amount of prior sleep) and a circadian influence (15). Using subjective alertness data from a number of experiments of altered sleep/wake patterns, it was found that alertness was also predictable from a homeostatic and a circadian component in combination with a component for sleep inertia, that is alertness was predictable from three parameters: S, C and W. The output of the model yield predicted alertness on a scale between 1 and 16. In practice 3 corresponds to extreme sleepiness, 14 to high alertness and 7 to a sleepiness threshold, that is levels ≤ 7 on the 16-point scale were defined as critically low alertness. The model has been validated against subjective rating of sleepiness (Karolinska Sleepiness Scale), performance, electrooculogram (EOG) and EEG parameters (alpha [8-12 Hz] power density). Process S is an exponential function of the time since awakening; it is high on awakening, falls rapidly initially and gradually approaches a lower asymptote. At sleep onset Process S is reversed and called S'; recovery occurs in an exponential fashion that initially increases very rapidly but subsequently levels off toward an upper asymptote. Total recovery is usually accomplished in 8 hours. In humans and other mammals EEG slow-wave activity (EEG power in the 0.75-4.5 Hz range) seems determined by the duration of prior waking and sleep. Slow-wave activity is assumed to represent the homeostatically regulated sleep process, being a marker of Process S. Process C, controlled by the circadian pacemaker, represents sleepiness due to circadian influences and has a sinusoidal form with an afternoon peak. It has been suggested that endogenous circadian performance rhythms are controlled by the same pacemaker that drives the endogenous circadian rhythm of other physiological rhythms (i.e. body temperature, plasma cortisol and melatonin). However, only one recent study has looked at how performance rhythms are correlated with other physiological ones (65). Results showed predominantly positive correlations between good performance and higher temperatures and better subjective alertness and predominantly negative correlations between good performance and higher plasma levels of cortisol and melatonin. However, while all three physiological rhythms were reasonably well correlated with performance, the parallelism was far from compelling (mean intrasubject correlations accounting for $< 10\%$ of variance). Thus, it has been asserted that performance rhythms would be driven independently by the “Circadian Timing System” (and time since awakening / sleep inertia) with a pattern that happens to yield a positive relationship with temperature and a negative one with cortisol and melatonin, without necessarily being directly mediated (causal relationship) by any particular physiological rhythm (20). It is interesting to notice that mathematical models of the effects of light on the human circadian pacemaker have been proposed. These enable to predict the effects of intensity (bright-light or light of moderate intensities), timing and duration

(extended –5h- or brief pulses) of light stimuli on the phase and amplitude of the human circadian pacemaker (53). Process W or inertia process on transitions between sleep and waking states (sleep inertia alone or sleep and wake inertia) is the third component of the model (49). It has been documented that alertness and performance are impaired immediately upon waking from sleep.

While some models imply that the homeostatic and circadian processes are independent and additive (29, 1), the model of Jewett and Kronauer (48) implies a non-linear interaction between the homeostatic and the circadian processes. They based their assumption on detailed analysis of forced desynchrony data. Those results have shown that the amplitude of the circadian modulation on both alertness and cognitive throughput (number of mathematical additions performed) fluctuates with the amount of hours since awake. According to these results, the circadian influence on alertness and performance is low on awakening, increases during the first 15 h of wakefulness, and remains quite constant up to 50 h of sleep deprivation. It has been suggested, however, that possible nonlinearity in the neurobiological metrics used (e.g., floor or ceiling effects) can explain such an interaction (1, 26). This latter argument points out the importance of testing these models with different performance tasks. In that vein, Owens et al. (72) examined the hypothesis that alertness can be used to predict time-of-day effects of performance between 08:00 and midnight. While alertness was a reasonably good “predictor” of the simple perceptual-motor speed measures in this study, it predicted less well some of the other performance measures, like accuracy from a low and high memory search task. The conclusion was that the three-process model of alertness could not be generalized to predict successfully all measures of mood and performance.

Moreover, although in all current alertness and performance models, sleep inertia (W) acts independently of S and C, it is quite possible that S and W may also interact in a non-linear manner. For example, the magnitude of W at waketime and/or the time constant of the dissipation of W may increase when subjects have been previously sleep deprived (so that S is low). Similarly, C and W may interact such that sleep inertia is worse at some circadian phases than at others. Clearly, further studies are needed in which the time course of sleep inertia dissipation is measured at different circadian phases and when subjects are carrying various sleep debts.

The understanding of the mechanisms underlying different diurnal fluctuations during waking hours (without suspending the sleep/wake cycle) will require, apart from controlling sleep inertia, the dissection of the individual effects of homeostatic and circadian influences on performance efficiency. Some experimental and mathematical approaches have been proposed (e.g., forced desynchrony, mathematical removal of data trends), with each of these having underlying assumptions and limitations. Unless a study adopts a specific approach to separate homeostatic and rhythmic factors, it is not possible to know how they are interacting to influence the observed fluctuations in performance.

It is emphasized that factors outside the model parameters will influence alertness greatly. One such factor is the ultradian rhythm, which causes a bimodal sleep pattern with an increased sleep tendency during the afternoon (17). To account for the post lunch dip phenomenon, the existence of a circasemidian rhythm of vigilance and slow-wave sleep propensity having 12 h and 24 h components was initially proposed. In a new model of sleep/wake cycle regulation, it was proposed that the afternoon nap zone was due to increasing homeostatic sleep propensity after morning awakening (Process S) being overwhelmed by a circadian arousal process that would become maximal later in the evening.

Another influence is individual differences such as “diurnal type” (45, 84), age and gender. Modifying the model for such influences will make it possible to predict individual data and not only group mean data. Other influencing factors are monotony, stress, sleep conditions, drugs, health status, etc. These do not, however, belong in a general model of alertness and sleep regulation, but would have to be considered when interpreting output from the model.

Involuntary transition

As an example, car driving is a task where involuntary transition from wakefulness to sleep should be particularly avoided. Nevertheless, we know that a quite large percentage of car accidents are related to driver’s drowsiness. In a recent study, Muzet et al. (68) have proposed the use of an Objective Sleepiness Score (OSS) which was measured through the use of electrophysiological methods: electrical brain activity (EEG) and electrical eye activity (EOG), combined with video recording of the driver’s face. The diagnosis of objective sleepiness score (OSS) was based on visual analysis using defined criteria in a five-level scale. Visual scoring was preferred to spectral analysis in the present study due to the fact that body movements of the driver produce abundant EEG artifacts and lead sometimes to elimination of large portions of records, creating discontinuity in the analysis of the data.

1.3.2. From sleep to wakefulness

The particular case of sleep inertia

Sleep inertia of lowered arousal occurs immediately after awakening from sleep and produces temporary decrement in subsequent performance (83). Many factors are involved in the characteristics of sleep inertia. The duration of prior sleep can influence the severity of sleep inertia. Although most of the studies focused on sleep inertia after short naps, its effects can be shown also after a normal 8-h sleep period. One of the most critical factors refers to sleep stage prior to awakening. Abrupt awakening during a slow wave sleep (SWS) episode produces more sleep inertia than awakening in stage 1 or 2, REM sleep being intermediate. Therefore, prior sleep deprivation usually enhances sleep inertia since it increases SWS. There is no direct evidence that sleep inertia exhibits a circadian rhythm. However, it seems that sleep inertia is more intense when awakening occurs near the trough of the core body temperature as compared to its circadian peak. The more controversial issue concerns the time course of sleep inertia. Depending on the studies, it can last from 1 min to 4 hours. However, in the absence of major sleep deprivation, the duration of sleep inertia rarely exceeds 30 min. But all these results should be analyzed as a function of type of task and dependent variables. Different cognitive functions are probably not sensitive to the same degree to sleep inertia and special attention should be provided to dependent variables as a result of the cognitive processes under review. Finally, sleep disorders represent risk factors which deserve new insight in treatment strategies to counteract the adverse effects of sleep inertia.

2. Pathological states

In the vast majority, patients suffering from various sleep disorders differ from a normal population in a multitude of measurable physiological activities. In many disorders, these deviations are even characteristic and specific for a disorder and their objective evaluation is a necessary pre-requisite for diagnosis of these disorders. This was also a result of the expert's survey.

Detailed Recommendations on measurement techniques for detecting sleep related breathing disorders have been outlined by the American Academy of Sleep Medicine Task force (3).

In the following table, sleep related pathologies, their characteristic physiological activities described in literature, and the corresponding sensors to measure these activities are listed:

Physio-logical activity	Measure-ment sensor	Physio-logical event	Sleep pathology	References
Brain activity during sleep	EEG	Frequent or high number of awakenings	OSA, central sleep apnea syndrome, PLM, RLS, panic disorder	209, 132, 148, 190, 194, 195, 193, 228, 229,235
	EEG	Arousals	OSA, central sleep apnea syndrome, primary snoring, PLM, RLS	118, 121, 136, 144, 165, 177, 190, 193, 194, 195, 196, 228, 232, 233
	EEG	Prolonged sleep latency	psychophysiological insomnia, idiopathic insomnia, delayed sleep phase syndrome, hypomania and mania, anxiety disorders, parkinsonism	98, 103, 107, 125, 131, 133, 243, 157, 185, 199, 226
	EEG	Shortened total sleep time	stimulant-dependending syndrome, depression, hypomania and mania, chronic obstructive pulmonary disorder	122, 137,156, 175, 183, 197, 198
	EEG	Reduced sleep efficiency	PLM, RLS, altitude insomnia, depression,	169, 170, 184, 190, 191, 193, 194, 195, 197, 198
	EEG	Deviations in sleep stage 1	enviromental sleep disorder, RLS, PLM, depression, sleeping sickness	105, 118, 130, 141, 187, 190, 191, 194, 198, 201, 216, 217
	EEG	Deviations in sleep	PLM, RLS, depression, dementia, sleeping	141, 190,193, 194, 197, 198

		stage 2	sickness,	
	EEG	Deviations in sleep stage 3/4	REM sleep behavior disorder, infant sleep apnea, , depression, fatal familiar insomnia	101, 102, 106, 139, 149, 181, 203, 205, 206, 227
	EEG (EOG, EMG)	Deviations in sleep stage REM	narcolepsy, stimulant-dependent syndrome, REM sleep behavior disorder, depression, sleeping sickness	101, 102, 116, 119, 126, 135, 142, 146, 150, 151, 156, 166, 179, 183, 222
	EEG	Fragmented sleep architecture	OSA, central sleep apnea syndrome, sleep terror, dementia, chronic obstructive pulmonary disorder	108, 112, 122, 134, 196, 197, 200, 229, 235
	EEG	Deviations in background activity	psychophysiological insomnia, fatal familiar insomnia	104, 124, 139, 147, 180
	EEG	Deviations in microstructures (KC, SS, Vertex waves)	OSA, dementia, parkinsonism	103, 125, 127, 128, 134, 197
	EEG	Spike-slow wave activity	Sleep-related epilepsy, status epilepticus of sleep.	140
Brain activity during day	EEG	Tiredness, sleepiness, daytime naps	Idiopathic hypersomnia, OSA, PLM, RLS, primary snoring	136, 165, 190, 192, 194, 196, 220, 234
	EEG	Vigilance decrement	OSA	136, 192, 196
Blood gases	Pulse oximetry	Oxygen desaturation	OSA, central sleep apnea syndrome, infant sleep apnea, nocturnal cardiac ischemia, chronic obstructive pulmonary disorder	100, 117, 122, 123, 137, 176, 182, 207, 212, 218, 219, 224, 225, 227, 229, 232, 234, 236
	Capnography trans-cutaneous measurement	Increased PCO2	OSA	114, 122
Cardio-vascular function	ECG	Bradycardia	OSA	100, 186, 232
	ECG	Tachycardia	OSA, nightmares, acute alcohol abuse before bed, sleeping sickness	100, 162, 171, 179, 186, 232

	BP	High BP, elevation	OSA, central sleep apnea syndrome,	137, 207, 224, 232, 234
	ECG, pulse measurement	Frequent pulse rate changes, heart rate variations , acceleration	OSA, nightmares, nocturnal paroxysmal dystonia, sudden infant death syndrome, Nocturnal cardiac ischemia	123,141, 160, 168, 172, 174, 208, 214, 218, 219, 232, 236
	ECG	Sinus arrest, arrhythmias,	REM-related sinus arrest, sudden unexplained nocturnal death syndrome,	115, 129, 151, 168, 173
	ECG	Asystoles	REM-related sinus arrest	115, 129, 151
	ECG	Ischemic episodes	Nocturnal cardiac ischemia	146, 174, 178, 182
Skin resistance	Electro-dermal activity	Skin resistance, skin response,	sleep terrors, nocturnal paroxysmal dystonia, fatal familial insomnia,	139, 160, 188
Respiratory events	respiration	Apneic episodes	OSA, alcohol-dependent syndrome, nocturnal paroxysmal dystonia, infant sleep apnea, sudden infant death syndrome	117, 123, 137, 160, 176, 207, 219, 227, 229,232, 234, 236
	Respiration, EEG	Respiratory effort related arousal	OSA, central sleep apnea syndrome	121, 196, 233
	respiration	Periodic breathing	altitude insomnia	215
	Tracheal sound/ sound recording	Snoring	OSA, alcohol-dependent syndrome, pregnancy-associated sleep disorder	117, 120, 136, 165
	Respiration	Tachypnea	sleep terrors, nightmares	112, 171
	respiration	Dyspnea	panic disorder	132, 148, 209
Thermo-regulation	Body temperature	Deviations in body temperature	Psychophysiological insomnia, depression	104, 157
Movements	Body motility, body posture	Periodic movements; rhythmic movements	Nocturnal eating syndrome, body rocking	231, 204
	Body motility, body posture	Increased movements	RLS, PLM, sleep walking, REM sleep behavior disorder	145, 163, 164, 190, 193, 194, 195, 202, 203, 205, 206, 230
Muscle tone	EMG	Increased PLM; phasic contractions,	PLM, RLS, sleep starts, nocturnal leg cramps, bruxism, fragmentary	109, 110, 111, 118,138, 144, 153, 154, 155, 158, 159, 161, 189,

		bursts in muscles	myoclonus	211,221, 223
Circadian rhythm	Actigraphy	Disrupted sleep/wake pattern	non-24 hours sleep-wake disorder, fatal familiar insomnia	131, 181

3. Physiological data recording

3.1. Central nervous system activity

3.1.1. Brain electrical activity

Electroencephalography (EEG):

The electroencephalogram (EEG) measures non-invasively the spontaneous electrical activity of the brain collected through several layers of biological tissues and liquid, including the skull bone. The first description of EEG recording was made by Caton (24). The potentials can vary in frequency from less than 1 to over 50 Hz, with amplitude between 20 to 200 μV . Some predominant activities can be recognized such as delta waves (0.5-3.5 Hz, 75-200 μV), theta waves (4-7 Hz, 20-120 μV), alpha waves (8 to 12 Hz, 25-100 μV), beta waves (faster than 13 Hz and below 40 μV). Other patterns are specific to sleeping EEG, such as spindles (12-16 Hz, 20-100 μV) and a synchronous high-amplitude irregular slow-wave pattern called K-complex. As described in detail previously, the EEG is the most important biosignal for determining and modeling sleep and wakefulness.

Pitfalls: There is broad agreement, that one of the most crucial pitfalls of measuring brain electrical activity by means of EEG is its vulnerability to technical and biological artifacts. Artifacts in the EEG can be defined as any potential difference due to an extracerebral source. The importance of dealing with artifacts effectively, both in visual and in quantitative EEG analysis, is unequivocally accepted, as artifacts can mimic almost any kind of EEG pattern (13, 51) and artifacts included in automatic analysis can seriously affect the results. Brunner et al. (1996) for instance demonstrated that rejection of short-lasting muscle bursts significantly reduced power spectral density in all frequencies from 0.25 Hz to 32 Hz, most prominently of course in the faster frequency bands. Thus the careful handling of artifacts is of utmost importance for EEG data processing and reliability and validity of the artifact processing strategy used should be reported. Of course, artifacts themselves may contain valuable information. In sleep analysis for instance, eye movement and muscle artifacts in the EEG recordings might facilitate classification of sleep stages. Nevertheless, if the aim of the analysis is to quantify patterns of cerebral activity (e.g. sleep spindles, K-complexes etc.) or to describe the behavior of the brain during sleep, only artifact-free epochs should be included in the analysis. In addition to technical and movement artifacts, ocular, electromyographic, electrodermal, electrovascular, and respiratory signals can interfere with the EEG as artifacts. Although there is a variety of procedures for artifacts minimization and identification (for a review see Ref. 5), the best way of dealing with the problem of artifacts is to avoid their occurrence when recording the EEG. This goal can be achieved by using high-quality EEG recording techniques.

Ocular activity: Ocular artifacts either result from eye movements, which change the external electrical field of the cornea-retinal dipole, or from movements of the eyelids (blinks), which have a shunting effect on this field. While blink artifacts may only occur during the wake periods, SEMs and REMs can contaminate the sleep EEG. For EEGs recorded with symmetrical reference (e.g. versus the average of left and right mastoids), maximal interference due to vertical eye movements is found at frontopolar sites, with an exponential decrease towards occipital sites. Maximal interference due to horizontal eye movements is at

frontotemporal sites, with opposite signs for the left and the right hemisphere and a linear slope between these two extremes (4).

Muscle activity: Electromyographic artifacts often appear in combination with swallowing or body movements. Muscle artifacts can range from single spikes separated from each other to a continuous interference, and from rather small to relatively large amplitudes. Brunner et al. (18) reported short-lasting muscle artifacts in the sleep-EEG more frequently towards the end of non-REM sleep periods. EMG arousals were uniformly distributed within REM sleep but concentrated at the beginning and the end of non-REM periods (18). Moreover, a close correspondence between transient EMG activity and changes in EEG activity has been reported (74).

Movements: Body and head movements may induce not only muscle artifacts but also slow potential shifts, which can be misinterpreted as delta activity (35). The occurrence of body movements during sleep was shown to be related to the sleep cycling (43) and was found to decrease progressively from waking to stages 1, REM, 2, 3 and 4 (88).

Cardiac activity: The electrical field generated by the heart can directly interfere with the EEG. This ECG interference is dependent on the orientation of the electrical dipole of the heart and is seen in several leads simultaneously. Pulse artifacts on the other hand usually affect only one lead as they are due to pulsating scalp arteries lying directly under the electrode.

Electrodermal activity: Electrodermal artifacts can originate from changes in the electrolyte concentration of the EEG electrodes due to sweat secreted from the sweat glands. Phasic electrodermal artifacts can occur upon sudden arousal from light sleep stages.

Respiration: Chest movements due to respiration may induce movement of the head and thus of the electrodes against the pillow resulting in rhythmic slow potential shifts in these electrodes.

Technical artifacts: Finally, technical artifacts may arise anywhere in the recording system, e.g. electrodes, leads or EEG instrument. Electrode artifacts may result from a sudden change in the DC potential between the electrode and the skin, resulting in a sharp rise of variable amplitude and an exponential decay depending on the time constant used. Moreover, movement of the leads can electrostatically induce slow-wave artifacts. Thus an appropriate environment for sleep recordings should include a high quality and short wiring with shielding from electromagnetic fields. Electromagnetic interference and changes in impedance throughout can also distort an EEG recording.

Apart from the frequent occurrence of artifacts, the following pitfalls of current EEG recording techniques have been also mentioned by the experts:

- Electrode leads (cables) constrain the patient's freedom to move and thus, may disturb his sleep.
- Currently, relatively large-sized electrodes are used and thus, reduce specificity to the location, increase the contact problem due to the curvature of head, increase surface cross-talk and increase the effects of sweating, ECG, pulse, etc.
- The procedure of skin preparation and electrode application is very time consuming.
- Furthermore, it may lead to skin irritation,

- In ambulatory recording systems, the high battery power consumption is still a limitation for sampling rate, number of channels and recording time.

3.1.2. Ocular activity:

Electrooculography (EOG):

In sleep recordings, EOG is used to detect characteristic eye movement patterns in order to discriminate between the different sleep stages. While rapid eye movements, resembling the saccades in wakefulness, are a hallmark of stage REM, slowly rolling eye-movements are characteristic for the transition from wakefulness to sleep and occur predominantly during sleep stage 1. Eyeball movements are detected by measuring the external electrical field of the cornea-retinal dipole. Two EOG leads are always required. Usually, they are abbreviated as ROC (right outer cantus) and LOC (left outer cantus). Rechtschaffen and Kales 1968 recommend an electrode montage in a way that the eye ball movements result in signals going in opposite directions whereas head movement and EEG artifacts result in signals going in the same direction. In this montage, both electrodes are referenced to same electrode. A related electrode montage was recommended by Hakkinen, Hirvonen et al (33): due to the fact that the amplitude of the EOG signal is sensitive to relatively small differences in electrode position, larger and more symmetrical EOG amplitudes could be obtained by placing the electrodes more medially (P8, P18) than in the conventionally used system. This EOG montage was also used in the EU-project SIESTA (<http://www.ai.univie.ac.at/siesta/>).

Alternatively, EOG can be recorded using bipolar montages, measuring horizontal and vertical components separately. This montage has the advantage that EOG artifacts can be removed from the EEG computationally; this is not possible with the standard montage for sleep recording. Nevertheless, one has to keep in mind that the eye movements are not necessarily synchronized and thus separate measurements for both eyes may be indicated (16). Saccade velocity can be used to indicate alertness (47).

Longer eye-blinks are associated with greater sleepiness measure by MWT (32). Disappearance of blinks can also be used to indicate sleep periods (58).

Pitfalls: Similar to the EEG recording, EOG leads can be contaminated by various artefacts of biological and technical origin (see above). Furthermore, electrode cables and large electrodes are disturbing for the patient and thus, may exert a negative influence on his sleep. The procedure of skin preparation and electrode application may lead to skin irritation.

3.1.3. Muscle Tone:

Electromyography (EMG):

Surface EMG is recorded routinely from the chin (mental or submental). Since the decrement of the tonic EMG-level during REM sleep may be very slight ($< 0.1 \mu\text{V}$), these electrodes have to be applied carefully at a preferably shaved skin with 1 cm inter-electrode distance

Pitfalls: Similar to the EEG recording, EMG leads can be contaminated by various artefacts of biological and technical origin (see above). Furthermore, electrode cables and large electrodes are disturbing for the patient and thus, may exert a negative influence on his sleep. The procedure of skin preparation and electrode application may lead to skin irritation.

3.2. Autonomic nervous system activity

3.2.1. Cardiac activity, sympathetic and parasympathetic components

ECG:

The gold standard for cardiovascular signals is the recording of at least one lead of ECG during cardiorespiratory polysomnography. One lead of ECG can be used to derive heart rate and may give indications of arrhythmias. ECG and heart rate are also used to investigate changes during sleep which go along with transient tachycardia or bradycardia. Some arrhythmias may be associated to specific sleep stages e.g. REM sleep. Heart rate changes are very characteristic for sleep apnea. Along with each apnea event a relative bradycardia followed by a relative tachycardia is observed. This pattern has been described as a cyclical variation of heart rate. Changes in heart rate are also associated with arousal from sleep. Central nervous activations cause an increase in heart rate. While there are guidelines for normal ECG- and Holter-ECG recordings (a sampling frequency of at least 500 Hz, which may also be the result of interpolation), there are no established evaluation guidelines for ECG recordings during sleep. However it is possible to refer to the recommendations for general long term ECG analysis, if sampling rate (at least 250Hz) and leads are chosen according to those criteria. This would require the recording of at least two leads of ECG. Amplitude resolution should be $5\mu\text{V}$, the amplitude range $\pm 2\text{mV}$. The diagnosis of cardiac pathologies (which have a high co-morbidity with sleep apnea) definitely require more ECG channels (9-12).

Pitfalls: Electrode leads (cables) constrain the patient's freedom to move and thus, may disturb his sleep. Artifacts such as main interference, changes in impedance, sweat or movement artifacts or even electrode detachment can spoil ECG measurement. Determining heart rate variability (HRV) requires high sampling rates.

Pulse Transit Time and Peripheral Arterial Tonometry

The pulse transit time (PTT) determines the time delay between ECG and the resulting peripheral pulse wave. PTT is reverse proportional to arterial blood pressure and changes in amplitude of the PTT signal do correlate well with intra-thoracic pressure changes (73). The peripheral arterial tonometry (PAT) determines the peripheral arterial vascular tone using a plethysmographic method. The peripheral arterial tone is modulated by sympathetic and parasympathetic activity, by peripheral blood pressure, and by the peripheral resistance of the vessels. Both signals are non-invasive methods to assess changes of autonomous nervous function and allow to detect sub-cortical arousals.

3.2.2. Blood Pressure

The recording of blood pressure has major importance for sleep recordings because high blood pressure presents the direct link to cardiovascular consequences of sleep disorders. Several studies did prove that obstructive sleep apnea is an independent risk factor to develop daytime hypertension with an increased morbidity and mortality. Blood pressure shows immediate rises with events of apnea and shows prominent changes with sleep stages. There are reports on REM sleep associated hypertension with sudden nose bleeding.

Pitfalls: Unfortunately most methods either disturb sleep or are invasive and therefore no method has been established as a gold standard for sleep. The method most commonly used is blood pressure readings using periodic arm cuff inflations. These arm cuff inflations disturb sleep quite often. As a consequence these blood pressure readings do present more often readings for nocturnal awakenings than for sleep. Also the arm cuff cannot keep track of such rapid blood pressure changes as they are observed in sleep apnea and during arousals. The method of finger-photoplethysmography provides a continuous blood pressure signal derived from one (e.g. Finapres) or two inflated finger cuffs (e.g. Portapres). In order to obtain valid pressure traces it is extremely important to apply the finger sensors carefully and then cross check with arm cuff pressure readings. This signal proved to have high reliability but the finger cuffs also create some discomfort because the venous return of blood flow is reduced and this may disturb sleep as well. The gold standard for blood pressure is the invasive arterial line pressure recording. This requires intensive care-like settings and it is used in few and very specific sleep laboratory studies only.

3.2.3. Respiration

The diagnosis as well as the evaluation of therapeutic outcome of sleep related breathing disorders requires the recording of respiratory signals. Respiration is evaluated by measuring respiratory effort and airflow through nose and/or mouth.

3.2.3.1. Respiratory effort

Usually two sensor locations – one over the chest wall and one over the abdominal wall – are used. Kumar and Hofman (57) demonstrated – irrespective of the type of sensors – that thoracic-abdominal asynchrony can be used as an index of upper airway obstruction.

Strain gauges:

A strain gauge consists of an elastic tube filled with an electrical conductor (usually mercury) through which an electrical current is passed. Stretching in length, due to inspiration, changes the length and cross-sectional area of the volume conductor, resulting in proportional increases in resistance. Kryger (54) suggests that an unstretched gauge should be at least 20% smaller than the circumference of the torso. In practice, two strain gauges (thoracic, abdominal) are used.

Pitfalls: The optimal working range of a strain gauge sensor is very narrow: understretching or overstretching will not produce reliable signals. Due to the constant current through the conductor, there is deterioration in function over time. Changes in body position may cause artifacts.

Inductance plethysmography:

Transducers, consisting of insulated wires sewn into an elastic band, are placed around the chest and abdomen. Breathing movements alter the diameter and self-inductance of each transducer.

Pitfalls: Changes in body position may cause artifacts. As changes in body position can lead to sudden changes in signal amplitude, these changes can be misinterpreted as respiratory events (i.e. apneas and hypopneas).

Impedance pneumography:

Impedance is measured by passing a small current across the thorax using a pair of electrodes placed at the site of maximal thoracic excursion. Increased air in the lung increases impedance, while increased fluid (blood, lymph, etc) decreases impedance.

Pitfalls: During apneas, the negative intrathoracic pressure pools blood into the pulmonary circulation. Both air volume related and fluid related changes are measured. Therefore, a precise measurement of respiratory patterns may not be possible (54).

Static charge sensitive bed:

The transducer is part of a thin mattress that responds to very slight movements from the person lying on it (80).

Pitfalls: The amplitude of the respiratory signal varies with body position but otherwise is stable.

Diaphragmatic EMG:

Diaphragm EMG is an indirect measurement of respiratory effort.

Pitfalls: It is a difficult signal to record reliably and continuously, and there is no direct way to correlate it with reference measures as upper airway resistance. At present, there are no data on accuracy, reliability, or correlation with long term outcome in relation to this technique. Therefore, the APSS concluded that this method is not valid for diagnosing obstructive sleep apnea. There are limited data regarding using diaphragm EMG to distinguish central from obstructive sleep apnea (3).

3.2.3.2. Nasal and oral airflow

Apnea is defined as the cessation of airflow. Airflow can be evaluated directly by using a pneumotachograph or by detecting chemical or physical differences between expired and ambient air.

Pneumotachography:

This is the most accurate means of assessing the volume of airflow. In sleep research applications, the pneumotachograph is usually connected to a face mask. Some newer BiPAP and cPAP devices have in-built pneumotachographs. Cardiogenic oscillations, which are markers of central apnea, can be detected with these systems (10).

Pitfalls: The face mask needed is relatively uncomfortable, especially in sleep studies.

Thermistors:

There is a temperature difference between expired and inspired air. Thus, measuring temperature in front of the nose and the mouth can be used to evaluate airflow. A thermistor is a thermally sensitive resistor: expired air heats the sensor and thus increases its resistance, while inspired air cools the sensor, resulting in a relative decrease in resistance. Thermistors are designed to maximize the sensing area while minimizing the size of the sensor (54).

Pitfalls: Since thermistors cannot reliably differentiate between a prolonged inspiration and cessation of breathing, they have to be combined with a device measuring sensitivity to respiratory effort.

Nasal airway pressure:

Airway pressure is negative relative to atmosphere during inspiration and positive during expiration. These pressure changes can be used to estimate airflow. (11, 66, 69) The obtained signal is comparable to that of a pneumotachograph and more sensitive in detecting limitations of airflow than thermistors (38, 46). Furthermore, also snoring events can be detected by measuring nasal airway pressure (38). The optimal signal is obtained using a DC amplifier; a short time constant will result in artifacts.

Pitfalls: Nevertheless, some patients may not breathe via the nose. Thus, ideally nasal airway pressure measurement should be combined with a thermistor measuring oral airflow.

Measurement of expired CO₂:

Expired air has a higher concentration of CO₂ than ambient air. An infrared sensor, placed in front of the nose and mouth can be used to measure the CO₂ concentration and thus, detect expiration.

Pitfalls: Like thermistors, these sensors cannot reliably differentiate between a prolonged inspiration and cessation of breathing.

CPAP and BiPAP as a diagnostic tool:

If the cardiorespiratory study is conducted as a ventilation therapy control study using CPAP, BiPAP or other modes of ventilation, it is useful and interesting to record the applied air pressure through the mask. The fluctuations observed in the air pressure signals can serve as a valid alternative to a thermistor or thermocouple respiration signal. If the pressure transducer has a rapid pressure response which allows the detection of high frequency pressure fluctuations then these can be evaluated in terms of persistent snoring under ventilation therapy.

3.2.3.3. Blood gas measurements

The effect of respiration is reflected by changes in blood gas concentrations. Apneas and hypopneas, for instance, are usually followed by subsequent drops in oxygen saturation of arterial blood (“desaturations”).

Pulse Oximetry:

Non-invasive techniques allow the continuous measurement of oxygen saturation of arterial blood (SaO₂). Pulse oximeters determine SaO₂ from a two-wavelength light emitter and a corresponding sensor located on either side of a pulsating artery. Digit and ear are commonly used sites for sensor placement. The amplitude of light detected by the sensor is dependent on the magnitude of change in arterial pulse and the SaO₂ of the arterial haemoglobin. Pulse oximeters are only sensitive to pulsating tissues and minimal pulse amplitude must be detected to obtain reliable measurements.

Pitfalls: If the sensor is placed on a digit, bending might restrict its ability to detect pulse, and therefore spoil the measurement. Therefore, it is sometimes recommended to immobilize the digit. Unfortunately in a considerable number of patients the interpretation of oxygen saturation is limited. Due to the oxygen binding curve oxygen saturation may not show clear drops with apnea or hypopnea events if the patient has a healthy lung and a very high blood gas baseline. In patients with additional lung diseases (e.g. chronic obstructive pulmonary disease) the baseline oxygen saturation may be low even when awake. In these patients it is hard to detect apnea related events based on the analysis of oxygen desaturations. Most oximeters low-pass filter the SaO₂ signal. The greater the filtering, the less likely brief, mild hypoxic episodes are detected (28). In heavy smokers, SaO₂ will be overestimated, due to the presence of carboxyhaemoglobin.

Transcutaneous CO₂ (TcCO₂)

There are two methods of measuring TcCO₂. The first is based on a silver chloride electrode which measures CO₂ that has diffused from the skin through a gas permeable membrane into solution. The second utilizes an infrared capnometer that analyzes CO₂ in a gas phase. The response time of the first method is quicker (< 1 minute) than the second (> 2 minutes). Many studies have reported the results of TcCO₂ measurements in patient populations known to hypoventilate. Increases in TcCO₂, especially in REM sleep, are commonly reported, as are reductions in TcCO₂ with treatment (3).

Pitfalls: There is a large discrepancy in many instances between arterial carbon dioxide (PaCO₂) and TcCO₂ measured simultaneously. It is not clear at this time whether in the future TcCO₂ can be shown to be accurate during sleep in some circumstances. Before used routinely to diagnose sleep hypoventilation, further research is needed (3).

Expired End tidal CO₂ (ETCO₂)

Continuous measurement of CO₂ in expired air shows a gradual increase until near the end of a complete expiration when there is a plateau in the CO₂ level. This ETCO₂ measurement reflects PACO₂. ETCO₂ has been used in several clinical scenarios as a measurement of

PACO₂ including patients weaning from mechanical ventilation, anesthesia, exercise and sleep (3).

Pitfalls: There are several potential limitations to the practical measurement of ETCO₂ including the inability to measure ETCO₂ during CPAP or bilevel pressure therapy to assess response to treatment. The only study that has compared ETCO₂ to the reference standard found poor accuracy in sleeping patients under conditions of spontaneous breathing, nasal prong oxygen, and positive pressure therapy. Patients with underlying lung disease are unlikely to have uniform ventilation-perfusion ratios, which will further affect the accuracy of ETCO₂. Furthermore, as tidal volume decreases, the ability to identify an alveolar plateau and thus infer alveolar gas concentration becomes increasingly difficult. For all these reasons it is unlikely that this technology will be useful for non-invasive measurement of PaCO₂ during sleep (3).

3.2.3.4. Snoring:

Snoring microphone:

A tracheal microphone or as a less favorable alternative a room microphone to pick up snoring noise serves as an indirect way to detect partial upper airway obstruction during sleep. A complete obstruction cannot be detected because then no sound is produced. Simple piezo microphones are sufficient to pick up snoring noise. For subsequent interpretation the microphone recordings are only interpreted in terms of relative loudness and therefore the recording of this signal does not need to preserve sound signal characteristics. As a consequence a low sampling rate of 100 Hz which is severe undersampling is still sufficient. A better analysis of tracheal sounds would evaluate the proportion of low frequencies (below 800Hz) on total signal power with the use of a hardware filter to discriminate snoring from general breathing noise. To preserve the full frequency content of snoring noise a sampling rate of 5000 Hz would be needed.

Pitfalls: Vibration, sound and noise intertwiningly mixed and thus, create unclarity and factual errors.

3.2.4. Gastrointestinal parameters

Some patients mention complaints about gastroesophageal reflux events during the night. In these patients it is useful to record the esophageal pH in order to see whether more gastric acid reflux events occur during the night and whether they are related to nocturnal awakenings. A reflux event is defined as a drop in esophageal pH below a value of 4 for at least 30 seconds duration. It is common to find nocturnal reflux events in patients with such complaints. Few patients without complaint of esophageal reflux do have such events during the night. The majority of the nocturnal gastroesophageal reflux events are observed during awakenings from sleep or are associated with an arousal event during sleep. Very few events are found during undisturbed sleep without any arousal. The potential danger of nocturnal reflux events is that the natural esophageal clearance during sleep is much slower due to reduced motor activity of the esophagus and due to lying horizontal.

3.2.5. Electro dermal activity

Electro dermal activity (EDA) is a general term for electrical activity of the skin and eccrine sweat glands. The galvanic skin response, where an external current is passed through the skin, gives an insight on exo somatic EDA through skin resistance and skin conductance. Spontaneously occurring electrical potentials of the skin refers to endo somatic EDA. EDA is larger in NREM than in REM sleep and peak activity occurs in Stage 4 (63).

3.2.6. Core temperature

Body temperature is a sensible marker for a subject's circadian synchronization. It varies across the day and night period in a regular rhythmic pattern within a narrow range. The normal difference between maximum and minimum body temperature in the diurnal rhythm is close to 1 °C. This circadian rhythm in humans normally shows a maximum in the middle to late afternoon while the minimum is visible in the early morning hours. The rather high stability in core temperature in mammals reflects the thermoregulation mechanisms keeping a balance between heat production and heat loss. However, these mechanisms are also depending on the wakefulness/sleep alternation and they are not active the same way depending on sleep stages (59, 67). Thermoregulation and sleep onset are closely related and interactive (30).

If disorders of the circadian rhythm are investigated the recording of core body temperature can give insights on the actual circadian phase of the patient. Core body temperature is closely linked to the circadian system and its recording will allow conclusions on jet-lag, delayed or advanced sleep phase problems. Rectal or ear temperature probes are most appropriate.

Pitfalls: Body temperature depends much on physical activity, postural changes, psychological excitement, type of food, and environmental conditions. Therefore a scientifically correct and undisturbed recording of body temperature requires extremely standardized settings which are not available in a sleep laboratory with settings for clinical routine. High quality body temperature recording require a "constant routine" protocol with a well defined reduction of all external "zeitgebers". This means a constant low level of light, a protein reduced food given at fixed intervals during day and night, isolation from external light and external sound sources, lying in bed for at least 26 hours without any activities beside questionnaires and psychophysiological tests. This kind of recording condition for circadian phase is a special variant of sleep laboratories and it is conducted by a few specialized circadian sleep laboratories.

3.3. Motor activity

3.3.1. Body posture

Body position sensors:

The recording of body position is essential because body position may modify many sleep disorders. In a considerable percentage of patients sleep related breathing disorders do occur in one body position exclusively. Therefore it is very useful to keep track of this modifier and include the results in the sleep lab report. Simple sensors make use of a weight and a circular resistor to code the angle of the body into a continuous voltage. Other transducers use miniature contacts in a small housing to convert the angle of the body into a voltage or a digital code. Switch or contact based sensors are usually able to code not only the angle but also upright or supine position. This is very useful in order to have an indirect indication for patient behavior based on a bio-signal.

Pitfalls: Some sensors can only differentiate between four positions (left, right, front, back) and cannot detect the upright position.

3.3.2. Body movements

Actigraphy:

The number of body movement per a certain time interval (e.g. 30 s) varies within the sleep-wake cycles and even between sleep stages. Therefore, recording movements by portable devices allows a rough scoring of sleep-wake states.

Pitfalls: The correlation of body movements with sleep-wake behavior is systematically altered in some sleep disorders. The estimates given by actigraphs are rather coarse.

3.3.3. Limb movements

EMG:

For limb movement recording the gold standard is to record the EMG at the tibialis muscle with two ECG electrodes placed 5 cm apart on the skin of the lower leg where the m. tibialis is found. Usually both legs will be recorded with two bipolar EMG leads. The required minimum is one EMG leg recording.

Pitfalls: (see above).

3.3.4. Eyelid closure

PERCLOS:

Most studied eyelid closure measure is PERCLOS, which defines proportion of time in a minute that the eyes are at least 80 percent close (87). It has been correlated to Psychomotor Vigilance Task (PVT) (27) and also computerized (31).

Pitfalls: Reliability and validity of this method need further experimental support.

3.3.5. Pupil size fluctuations

Pupillometry:

The size of the pupil is considered as a useful indicator of sleepiness or alertness. Generally, alertness is associated to a large pupil while sleepiness is accompanied with a small and unstable diameter. Changes in pupil size reflect the balance between the sympathetic and parasympathetic influences. Spontaneous pupil size fluctuations in darkness indicate subject's level of sleepiness (89, 90).

Pitfalls: Reliability and validity of this method need further experimental support.

3.3.6. Videometry

In addition to the physiological signals a sleep laboratory for clinical diagnosis and treatment of sleep disorders should provide the possibility for audiovisual recording of the sleeping subject. Video recording is useful to document sleep apnea events, movement disorders, or REM sleep behavior disorders with uncontrolled movements during sleep. Usually patients are not aware of any of the events occurring during sleep. Talking during sleep can be recorded using an additional audio channel in this way. The presentation of these recorded events to the patient by the physician the next morning may be very helpful to explain the disorder to the patient and to educate him about the need to use the optimal therapy as recommended. This education improves acceptance of therapy in patients.

Pitfalls: none. Videometry is only used as a complementary tool and is used only in combination with other methods.

4. Conclusions

Based on the literature – as summarized above – as well as on the discussions with experts at the workshop on definitions of characteristics of transducers and methods for recording physiological signals, held in Vienna on May 27, 2004 and on the comments of the experts, who completed the electronic questionnaires on data acquisition techniques and their improvement for developing new sensors and on pathological sleep states, the following recommendations for acquisition of physiological signals were made, in order to guide further sensor development. For each of the following physiological signals, the number and - if applicable – location are defined. In order not to introduce any constraints, minimal as well as optimal requirements are given. Furthermore, the technical signal characteristics (noise level, amplitude resolution, temporal resolution), existing pitfalls and potential improvements of the listed methods are included.

Signal	
EEG	<p><i>Number of channels:</i> Min: 3, Opt: 6; For topographic and tomographic analysis: Min: 19, Opt: 48</p> <p><i>Location:</i> At least central, occipital and frontal or frontopolar</p> <p><i>Reference:</i> Unipolar versus a common reference electrode</p> <p><i>Noise level:</i> Opt: $< 1\mu\text{V}_{\text{pp}}$ or $< 0.1\mu\text{V}_{\text{eff}}$ within the frequency band 0.1-20 Hz</p> <p><i>Amplitude range:</i> $\pm 1000\mu\text{V}$ in connection with 16 bit A/D</p> <p><i>Frequency range:</i> Opt: 0.01 Hz – 90 Hz with a sampling frequency = 300 Hz (Opt. 500 Hz); Min: 0.1 – 40 Hz with a sampling frequency = 200 Hz</p> <p><i>Pitfalls:</i> Electrode leads (cables), time consuming electrode application, skin preparation, skin irritation, large electrode size, changes in impedance, electromagnetic interference, sweat and movement artifacts, high battery power consumption.</p> <p><i>Potential Improvements:</i> Wireless recording, dry electrodes with permanent good electrical contact, avoidance of skin preparation</p>
EOG	<p><i>Number of channels:</i> Min: 2</p> <p><i>Location:</i> Either according to R&K (unipolar versus common reference) or vertical and horizontal (bipolar). Sensors as close as possible to the eyeball.</p> <p><i>Noise level:</i> Opt: $< 2\mu\text{V}_{\text{pp}}$ or $< 0.2\mu\text{V}_{\text{eff}}$ within the frequency band 0.1-20 Hz</p> <p><i>Amplitude range:</i> $\pm 2000\mu\text{V}$ in connection with 16 bit A/D</p> <p><i>Frequency range:</i> Opt: 0.01 Hz – 90 Hz with a sampling frequency = 300 Hz</p>

	<p>(Opt. 500 Hz); Min: 0.1 – 40 Hz with a sampling frequency = 200 Hz; for determination of eye position: DC</p> <p><i>Pitfalls:</i> Electrode leads (cables), time consuming electrode application, skin preparation, skin irritation, large electrode size, changes in impedance, electromagnetic interference, sweat and movement artifacts, high battery power consumption, EEG interference.</p> <p><i>Potential Improvements:</i> Wireless recording, dry electrodes with permanent good electrical contact, avoidance of skin preparation</p>
EMG (sub) mental	<p><i>Number of channels:</i> Opt: 1</p> <p><i>Location:</i> submental (1 cm interelectrode distance)</p> <p><i>Noise level:</i> Opt: < 1μVpp or < 0.1μVeff within the frequency band 0.1-20 Hz <i>Amplitude range:</i> \pm 1000μV in connection with 16 bit A/D</p> <p><i>Frequency range:</i> 15-2000Hz (no anti-aliasing filter!) with a sampling rate = 200 Hz</p> <p><i>Pitfalls:</i> Electrode leads (cables), skin preparation, skin irritation, changes in impedance, electromagnetic interference, sweat and movement artifacts, high battery power consumption, beard can grow during the night.</p> <p><i>Potential Improvements:</i> Wireless recording, dry electrodes with permanent good electrical contact, avoidance of skin preparation</p>
EMG anterior tibialis	<p><i>Number of channels:</i> Min: 1 (averaged left and right leg), Opt: 2</p> <p><i>Location:</i> Anterior tibialis</p> <p><i>Noise level:</i> Opt: < 1μVpp or < 0.1μVeff within the frequency band 0.1-20 Hz <i>Amplitude range:</i> \pm 1000μV in connection with 16 bit A/D</p> <p><i>Frequency range:</i> 15-2000Hz (no anti-aliasing filter!) with a sampling rate = 200 Hz, low pass filter at 2000Hz is needed for elimination of not relevant spectral components, e.g. clock rate of signal processor.</p> <p><i>Pitfalls:</i> Electrode leads (cables), skin preparation, skin irritation, changes in impedance, electromagnetic interference, sweat and movement artifacts, high battery power consumption.</p> <p><i>Potential Improvements:</i> Wireless recording, dry electrodes with permanent good electrical contact, avoidance of skin preparation</p>
ECG	<p><i>Number of channels:</i> Min: 1, Opt: 2, Max: 9</p>

	<p><i>Location:</i> At least 1 bipolar derivation at the chest</p> <p><i>Noise level:</i> Opt: $< 5\mu\text{Vpp}$ or $< 0.5\mu\text{Veff}$ within the frequency band 0.1-20 Hz</p> <p><i>Amplitude range:</i> $\pm 2000\mu\text{V}$ in connection with 16 bit A/D</p> <p><i>Frequency range:</i> 0.1-100 Hz with a sampling rate = 300 (opt. 500 Hz) (optimal frequency range for RR analysis up to 500Hz)</p> <p><i>Pitfalls:</i> Electrode leads (cables), skin preparation, skin irritation, changes in impedance, electromagnetic interference, sweat and movement artifacts, high ECG input impedance is needed for dry electrodes and reduction of sweat artifacts.</p> <p><i>Potential Improvements:</i> Wireless recording, dry electrodes with permanent good electrical contact and low impedance, avoidance of skin preparation</p>
Temperature	<p><i>Number of channels:</i> Min 1</p> <p><i>Location:</i> Rectal, esophageal</p> <p><i>Amplitude resolution:</i> 0.1°C</p> <p><i>Amplitude range:</i> 2°C for body temperature; 10°C for skin temperature</p> <p><i>Sampling frequency:</i> 1/min</p> <p><i>Pitfalls:</i> Rectal as well as esophageal sensors are inconvenient</p> <p><i>Potential Improvements:</i> smaller probe and stable fixation for rectal temperature measurement, wireless solution for recording of body temperature.</p>
Body position	<p><i>Number of channels:</i> 1</p> <p>Sensor which can differentiate 5 positions (left, right, front, back, upright)</p> <p><i>Potential Improvements:</i> one sensor placed on the chest which avoids displacement or placement with wrong directions.</p>
Respiratory effort	<p><i>Number of channels:</i> Min 2</p> <p><i>Location:</i> thorax, abdomen</p> <p>Inductance plethysmography (6 electrodes for 2 locations, the same electrodes may be applicable for ECG), respiratory belts</p>

	<p><i>Pitfalls:</i> belts are inconvenient for the patient</p> <p><i>Potential Improvements:</i> elastic bands which avoid slippage during night</p>
Respiratory flow	<p><i>Number of channels:</i> Min: 1 (nasal pressure), Opt: 2 (nasal pressure + oral thermistor)</p> <p><i>Sampling frequency:</i> 200 Hz (snoring)</p> <p><i>Pitfalls:</i> High costs, blocking of sensors (slime), artifacts due to lying on the tube, sensors and tubes are inconvenient</p> <p><i>Potential Improvements:</i> measurement of nasal airway pressure should be combined with measurement of a thermistor (oral airflow).</p>
Snoring	<p>Can be derived from nasal pressure, alternatively: snoring microphone</p> <p><i>Potential Improvements:</i> a small wireless tracheal microphone, a sampling rate of 5000 Hz would be useful.</p>
Blood oxygen saturation	<p><i>Number of channels:</i> 1</p> <p><i>Location:</i> finger or ear</p> <p><i>Potential Improvements:</i> Combined sensors for O₂ and CO₂ saturation and resolution above 1 % of current systems are appreciated. A finger ring sensor for different finger sizes would be useful.</p>
Blood pressure	<p>Magnetoelastic bending sensors</p> <p>More sophisticated and validated models for continuous non-invasive measurement are necessary</p> <p><i>Potential Improvements:</i> a robust finger ring sensor which is able to produce a subdiastolic pressure when applied.</p>
Additional signals	<p>Eye lid movement, ambient light</p> <p><i>Potential Improvements:</i> small cameras with large dynamics are needed.</p>

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