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A Comparison between EEG-Recording and Scoring by QUISI Version 1.0 and Standard PSG with Visual Scoring

A One-Channel Ambulatory EEG Recording Device Using Neural Network Techniques for Automatic Sleep Stage Classification

Ein Vergleich zwischen Aufzeichnung und Auswertung von Schlaf-EEG durch QUISI, Version 1.0 und visueller Auswertung durch PSG

Ein einkanaliges, ambulant anwendbares Gerät zur Aufzeichnung und automatischen Auswertung von Schlaf-EEG mittels Neuronaler Netzwerk-Techniken

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Summary QUISI has been developed as a one-channel, ambulatory EEG recording device with 3 electrodes placed on the forehead close to F_{p1}, F_z and F_{p2}. While F_z serves as ground electrode, the channel F_{p1}–F_{p2} was recorded, filtered and analyzed by Fourier-Transform with the subsequent determination of power spectrum estimates. These variables served as input variables for neural network technique classification, taking 12 input variables, 2 hidden layers and 7 outcome variables for 0 = Movement Time, 1 = Wake, 2 = REM, 3 = S 1, 4 = S2, 5 = S_3 and 6 = S_4. Out of 118 primary values, 12 were selected using evolutionary and genetic algorithms. 8 neural networks were established using 8 different patients. Every 30 s sleep EEG epoch (segment) was subsequently classified 8 times. The final decision for each epoch of 30 s was made taking the median of the 8 classifications. Subsequently smoothing rules were applied in analogy to the Rechtschaffen and Kales smoothing rules. The analysis is fully automated. There is no artefact rejection and no removal of any sleep epoch. Once the rule was established, it was validated by forward classification of 38 sleep disturbed patients, none of whom had been used for the establishment of the classification rule. Every patient had been recorded with polysomnography (PSG) as well according to the standards of the German Sleep Research Society and with the QUISI equipment. The results show an acceptable agreement between PSG with visual scoring and QUISI with automatic scoring. While SPT, TST and SOL showed high correlations, REM and SWS were generally overestimated. Subsequently we evaluated the pathologies in QUISI and PSG. Out of the 38 patients, only 1 patient had a normal profile both in QUISI and PSG. Out of the 37 patients with pathologies, 17 showed exactly the same pathologies in the PSG and QUISI profile. In 1 patient PSG and QUISI showed completely different pathologies. In 10 patients QUISI did not find at least one pathology seen in the PSG, in 4 patients QUISI found more pathologies than were seen in the PSG, in 5 patients both applied. In its current version QUISI often over-estimates SWS and REM in certain patients, as known from other automated scoring methods described earlier in the literature. QUISI is considered as the beginning of a development with the aim of obtaining an affordable and easily self-applicable sleep EEG recording device, which can be applied before a therapy control and after admission to a sleep laboratory. QUISI however can in no way replace sleep laboratory diagnostics.

Key-words Neural network techniques – automated classification – one-channel recording – frontal EEG – QUISI.

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Zusammenfassung QUISI ist ein einkanaliges, ambulant anwendbares Gerät zur Aufzeichnung und automat&hen Auswertung von Schlaf-EEG. Seine erste Validierung erfolgte an 38 Patienten mit Schlafstörungen. Drei Elektroden nahe den Punkten F_{p1}, F_z und F_{p2} werden auf der Stirn angebracht, F_z dient als Erdungselektrode. Der Kanal F_{p1}–F_{p2} wird in Elektrodennähe verstärkt, gefiltert und einer Fourier-Transformation unterzogen. Anschließend werden Power Spektralwerte errechnet. Diese Powerschatzer dienen als Eingangsvariablen für die Schlafstadien-Klassifikation mit Neuronalen Netzen, wobei 12 Eingangsvariablen, 2 Hidden Layers und 7 Ausgangsvariablen vorgegeben wurden: 0 = Movement Time, 1 = Wake, 2 = REM, 3 = St, 4 = S_2, 5 = S3 and 6 = S_4. Mit Hilfe von evolution&-en und genetischen Algorithmen wurden aus 118 Primärvariablen 12 Variablen für die Klassifikation ausgewählt. Mit den parallel aufgenommenen Daten (PSG + QUISI) von acht Patienten (d.h. acht verschiedenen Schlaf-EEG Typen) wurden acht verschiedene Klassifikationsregeln entwickelt. Jede Epoche Schlaf EEG von 30 s wurde achtmal klassifiziert. Dann wurde der Median aus diesen 8 Klassifikationen gebildet und so die Klasse für die Epoche definiert. Anschließend wurden Glattungsalgorithmen in Analogie zu denen von Rechtschaffen und Kales ausgeführt. Die Analyse ist vollautomatisch. Es gibt keinerlei Artefakterkennung des Schlaf EEG, kein Segment wird von der Analyse ausgeschlossen. Nachdem dieses System entwickelt war, wurde es an 38 schlafgestörten Patienten aus unserer Klinik erprobt. Es handelt sich urn eine Vorwartsklassifikation. Keiner der 38 Patienten wurde benutzt, urn die Regeln aufzustellen oder zu modifizieren. Alle Patienten wurden simultan polysomnographisch nach den Empfehlungen der Deutschen Gesellschaft für Schlafforschung und Schlafmedizin abgeleitet, und es wurde jeweils parallel mit QUISI aufgezeichnet. Die Ergebnisse zeigen eine akzeptable Übereinstimmung zwischen beiden Methoden in SPT, TST und SOL, während REM und SWS überschätzt werden. Anschließend haben wir die von der Norm abweichenden Befunde in den Schlaf-EEG Profilen, denen wir pathologischen Wert beimaßen, separat für die PSG und für QUISI visuell beurteilt und verglichen. Das Ergebnis dieses Vergleiches: Von den 38 Patienten hatte nur einer ein völlig normales Profil, sowohl in der PSG und als auch in QUISI. 37 Patienten hatten als pathologisch bewertete Veränderungen in der PSG und in QUISI. Von diesen 37 Patienten zeigten 17 identische pathologische Zeichen und 1 Patient völlig unterschiedliche. Bei 10 Patienten fand QUISI nicht alle pathologischen Zeichen der PSG, bei 4 Patienten fand QUISI mehr pathologische Zeichen, bei 5 Patienten kam beides vor. Von den insgesamt 38 Patienten gab es nur eine wirkliche Fehlklassifikation. QUISI wird als der Beginn einer Entwicklung betrachtet mit dem Ziel, ein preiswertes, selbst applizierbares Gerät zu erhalten, mit dem Arzt und Patient im Vorfeld der klinischen Diagnostik und ggf. zur therapeutischen Nachkontrolle ein Schlaf-EEG-Profil erstellen können. QUISI kann und soll nicht das Schlaflabor ersetzen.

Schlüsselwörter Neuronale Netzwerke – automatische Schlafstadienklassifikation – Ein-Kanal-Aufzeichnung – frontales EEG – QUISI.

Introduction

Visual sleep stage scoring is time consuming, despite accurate rules, and still subjective with only acceptable interrater reliability. Therefore, an extensive search for automatic analysis has already been performed in the 70's and early 80's of our century. A comparison between different methods led to the following results [10] *(a limit of ± 20% in comparison to the Rechtschaffen and Kales Classification [27], called R&K, was determined as "within" tolerable deviations. Beyond that limit, over- or underestimation was assumed):*

sws: 5 of 7 systems overestimated SWS, 2 underestimated the amount.

REM: REM sleep was overestimated by all 7 systems.

WAKE: calculated only by 6 of the 7 systems. 4 overestimated, 2 underestimated WAKE.

Stage 1: 3 systems were within the ± 20% limit, one system over- and 3 underestimated Stage 1.

Stage 2: 3 systems were within the ± 20% limit, 4 underestimated sleep Stage 2.

With the exemption of one system using power spectral values of 4 EEG channels but no other values, all other systems used EOG and EMG channels.

An update on automatic Sleep EEG Analysis Systems was given by *Penzel et al.* [25]: Spectral analysis using power estimates in predetermined frequency bands, waveform recognition, autoregressive modelling, adaptive segmentation, etc. In 1993 *Kemp* [14] added a model-based sleep analysis which aims at a modification of the R&K. For the first time he added other signals like respiration parameters, ECG, arterial and pulmonal blood pressure, body temperature, body position, and move-

ment for classification. *Kubat et al.* [16] and *Koprinska et al.* [15] presented an artificial intelligence approach based on automatic classification, taking by decision tree-based neural networks. *Nielsen et al.* [21] presented automated sleep stage classifiers using a causal probabilistic network.

If the quality of automated classification, as done earlier as well as in this case, is measured only by fitting the R&K criteria, results will be limited to the time resolution of 20 or 30 s respectively. Many events, however, are in the 1 s range. The main criticism in R&K is the enormous data reduction [9, 14, 20]. Furthermore, the limitation to the central (C3 or C4) EEG channel and the 7.5 μ Volt criteria to recognize Delta-waves for SWS, independent of the wave form, the context and the age of the subject, are subject to criticism.

We have not found in the literature the use of frontal EEG electrodes as the only information input for classification. Only *Werth and Borbély* [31] described a classification based on periorbital skin electrodes (E_1–A_2), compared to one based on C_3–A_2, and found highly corresponding values.

Other attempts using ambulatory equipment and fully automated classification have been made by *Flooh et al.* [7] using the Medilog system. There is quite a lot of literature showing results with the Oxford ambulatory equipment using the Oxford automatic sleep stager [11, 12, 13, 19, 22, 28, 30]. Furthermore, *Pace-Schott et al.* [23] and *Ajilore et al.* [1] have tested equipment called Nightcap. The automatic analysis results were usually compared with visual analysis according to the R&K rules and the agreement between the two methods was in about the 65–80% range.

Obergottsberger et al. [22] described an overestimation of the REM stage (+7,5%) and an underestimation of Stage 2 (–5,2%). *Kubicki et al.* [19] described that with the Oxford automatic stager REM and Wake were overestimated as well as Delta activity, resulting in an increased Slow-Wave-Sleep of 4,4% in comparison to the R&K classification. Not all but most of the literature we reviewed showed an overestimation of REM stage and of Slow-Wave-Sleep if automatic analysis methods were compared with visual analysis according to R&K.

The method presented in this publication conservatively compares a method which could use a time resolution of 1 s with R&K having a 30 s time resolution. The quality of the QUISI system is, therefore, not only limited by the QUISI method alone but also by the limitations of the R&K rules.

The novelty of this method is that only one single EEG channel is used and that the electrodes are self-applicable and placed on the forehead. Therefore, this instrument can be used for pre- and post-sleep laboratory diagnostics.

Rationale of the QUISI development

The rationale of the QUISI development is to have simple, easy, self-applicable equipment with a 24-hour battery supply to record the brain's electrical activity in order to gain an informative EEG-profile of sleep during the night and to determine sleep phases during the day. In order to keep the equipment self-applicable an electrode set is used, which will be applied to the forehead with disposable electrodes as used in ECG. The result is a one-channel EEG recording close to the frontopolar position of the EEG-electrodes F_{p1}–F_{p2}.

Since only EEG is recorded, this equipment is not sufficient to diagnose respiratory-related sleep disturbances as well as other sleep disturbances for which physiological measures other than EEG are required (e.g. restless legs symptom). This equipment cannot replace polysomnographic recording in qualified sleep laboratories, but is intended to help the physicians under ambulatory conditions to pre-diagnose an existing sleep disturbance and to help determine whether a patient complaining of sleep disturbances has to be sent to a sleep laboratory for further diagnostics. With QUISI it is possible to have more detailed information about Sleep-Onset Time, sleep duration and sleep cycles, the percentages of time spent in each stage and about pathological signs in the structure of sleep profiles.

Material and methods

QUISI-Recording Procedures

The recording is done through an electrode band placed on the forehead close to F_{p1}–F_{p2}. The middle electrode serves as a ground electrode. The pre-amplifiers are located close to the electrodes. The QUISI equipment does the final amplification of the signal. The AD conversion rate is 128 Hz, there is filtering with band pass characteristics and a 50 Hz notch filter (Fig. 1) for the off-line mode. The on-line mode allows any later filtering.

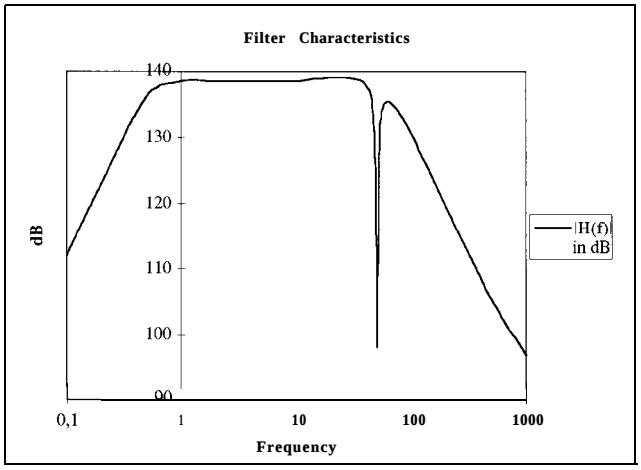


Figure 1. Filter Characteristics of QUISI V 1 .O.

Using the off-line mode with the filter characteristics shown in Figure 1 and using a 128/s AD conversion rate means that frequencies above 64 Hz, especially muscle potential differences between F_{p1} and F_{p2}, are folded (mirrored) into the range below 64 Hz, e.g. a 70 Hz muscle potential is mirrored into 58 Hz after Fourier Transformation. For the off-line mode this was done to keep the economic AD conversion rate of 128 Hz (to enable 24 hours off-line recording) yet still capable of catching some of the signals above 64 Hz signal, where most of the muscle activity is located. This enabled us to better discriminate between wake with **higher** and REM with **lower** muscle activity. Therefore, however, in the off-line mode the range above 20 Hz cannot be interpreted any more as the frequency stated but is contaminated with over 64 Hz activity. Experiments carried out in 5 subjects, where an all-night sleep recording was

performed and 2 AD-conversion rates were used, 128 and 56, showed only very minor and negligible differences. This parallel experiment was done to give us more confidence that the selected 128/s AD conversion rate would be sufficient under off-line conditions.

The all-night EEG recording was taken from all 38 patients without any artefact detection or any segment removal. The clocks of the QUISI and Walter Graphtek equipment to record PSG were set in the evening. However, there was no direct synchronization between PSG and QUISI recordings in this study. Therefore, only the total amount spent for each patient in each of the sleep stages could be calculated and taken for comparisons.

Feature Extraction

In the on-line mode the signal is transferred through an optical fibre cable to any computer to store the original EEG signals. The feature extraction is based on power spectral analysis performed for each second. The results are averaged over 30 s sleep epochs and the mean value of each 30 s epoch was taken as input variable.

Classification using Neuronal Networks

The method of applying Neural Network Techniques in one-channel Sleep-EEG data has been communicated earlier [2, 3, 4]. Several classification procedures have been tested using classical statistics. However the best results could be obtained with neuronal network techniques using 12 input units, two hidden layers and seven output units for the indication of classical sleep parameters: Movement Time (Class 0), Wake (Awake and Sleep Stage 0, Class 1), REM (Class 2), Stage 1 (Class 3), Stage 2 (Class 4), Stage 3 (Class 5), Stage 4 (Class 6).

Since the sleep EEG from various subjects differs entirely, the sleep profiles of eight sleep disturbed patients were taken to develop eight different neural networks. These eight patients had the following diagnoses: 2x Psychophysiological Insomnia (307.42-O), Bruxism (306.8), Depressive Disorder (296.2), 2x Restless Legs Syndrome and Periodic Limb Movement (780.52-5), Primary Snoring (780.53-l) and Sleep State Misperception (307.49-l). The neuronal networks were trained with these eight different sleep EEG recorded by QUISI against R&K classification, done by our senior scoring expert, based on conventionally recorded polysomnography in the sleep laboratory.

Therefore, we obtained eight different classification rules. The forward classification used to classify our 38 patients was done in the following way:

For each 30 s sleep epoch (segment) eight different classifications were done using the eight network rules. In order to determine how to use the eight classification results for a final decision we tried several averaging procedures (modus, mean and median). The best overall reclassification results were obtained using the median, which was then also taken for forward classification. If the median could not be determined, then the segment was classified as non-identifiable (NI). Since in the PSG-based visual analysis NI had a different meaning (e.g. patient went to toilet), the NI segments are identified in the legends of the sleep profiles, are however not taken for any further statistical analysis.

Patients and Polysomnographic Methods

On the validation of the QUISI data, polysomnographical all-night recordings of 38 patients and subjects in the Sleep Laboratory of the Free University of Berlin were used by way of comparison. All consecutive patients of the sleep laboratory were included. The only exclusions were recordings with technical failures, i.e. missing data in the computer of the sleep laboratory. However, overlying muscle potentials did not result in an exclusion. If a patient was in the sleep laboratory for two consecutive nights, one of the nights was – by random selection – excluded. No patient was excluded because of artefacts, nor was any segment removed from the analysis, even if they contained artefacts. Those persons included in the data pool for the neuronal network training were also excluded. The polysomnographic recordings were done according to the rules of R&K, see [26].

The QUISI electrodes were applied in addition (close to F_{p1}, F_{p2}). The evaluation of the EEG data was done by the first author of this paper according to the rules of R&K. The comparison between QUISI classification and R&K classification was done in three different fashions:

1. Comparison of the quantitative sleep parameters (specified below).
2. Qualitative visual inspection of the hypnograms by a Sleep Physiologist.
3. Comparison of the diagnostic parameters shown in both hypnograms.

The pathologies described, were:

a) SWS distribution was not normal (SWS not highest in the beginning of the sleep and then diminished towards the morning),
b) too much stage Wake during the night (more than 3 wake phases of more than 10 min each),
c) fractionized S_2,
d) early awakening and a long wake time before leaving the bed (2 30 min),
f) too much REM (≥ 32%; only in QUISI classification),
g) fractionized REM
h) wrong REM-sleep distribution (REM was not highest in the morning and lowest at the beginning of the sleep),
i) no or not sufficient SWS (≤ 8%),
k) insufficient REM (I 7%),
m) SOL, Sleep Onset Latency too long (≥ 30 min),
n) SOREM, Sleep Onset REM like in Narcolepsy

Results

Descriptive Statistics and Correlations between QUISI and R&K Scoring

The following sleep parameters are selected for statistics:

SPT Sleep Period Time, time between the first epoch of (Sleep Stage 2 (S2) or any other sleep stage except for Stage 1) and the last epoch of sleep (all sleep stages inclusive of Stage 1)
TST Total Sleep Time, all sleep stages without wake times or breaks
SOL Sleep Onset Latency
RLT REM Latency, time from Sleep Onset till the occurrence of the first epoch Stage REM
SLT Slow Wave Sleep Latency, time from Sleep-Onset to the first epoch Sleep Stage 3 (or 4)
SEI Sleep Efficiency Index, TST/TIB X 100
MT Movement Time, body movements longer than 15 s
AWA Wakefulness after Sleep Onset

Table 1. Spearman Rank Correlations between QUISI and R&K Sleep Parameters.

Sleep EEG variable n = 38	Abbr.	Correlation coefficient	p-value*
Sleep Period Time	SPT	0,921	< 0,0001
Total Sleep Time	TST	0,775	< 0,0001
Sleep Onset Latency	SOL	0,705	< 0,0001
Slow Wave Sleep Latency	SLT	0,343	0,0352
REM Latency .	RLT	0,505	0,0012
Sleep Efficiency Index	SEI	0,711	< 0,0001

* Descriptive two-sided a-error.

Table 2. Comparison between QUISI and R&K Estimates of Sleep Parameters.

n = 38	Polysomnography and R&K classification		QUISI and automatic classification		Difference* (Δ)	
EEG Var.	Quartile Range		Quartile Range			
Abbr.	Median	Q1–Q3	Median	Q1-Q3	abs.	%
SPT (min)	461	428-512	470	445-510	9	2.0
TST (min)	385	329–432	403	369–445	18	4.7
SOL (min)	19	13– 35	24	13– 38	5	26.3
SLT (min)	24	15– 35	15	9– 22	–9	37.5
RLT (min)	85	67–115	80	46–118	–5	5.9
SEI (%)	77	68– 86	83	74– 89	6	1.8

* Difference between medians in relation to PSG/R&K median

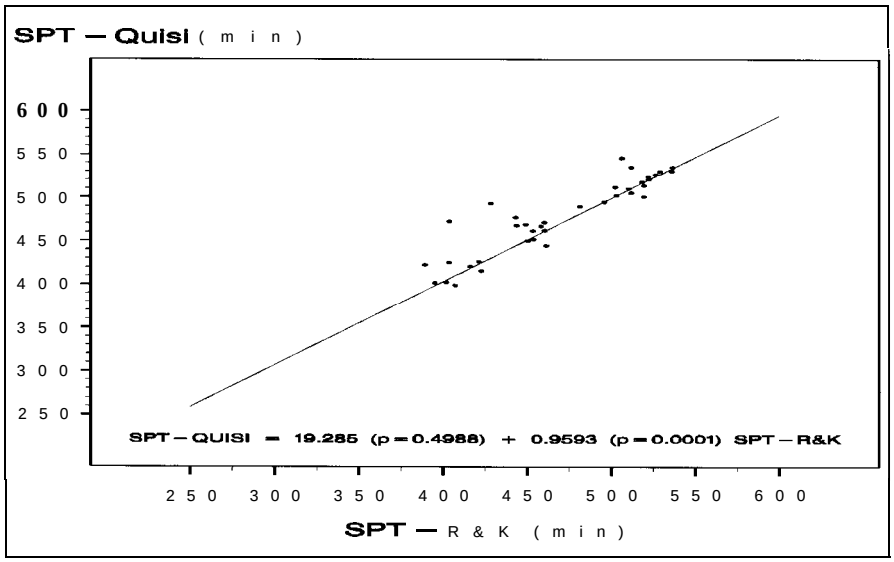


Figure 2. Linear regression of Sleep Period Time (SPT) between QUISI and R&K rules.

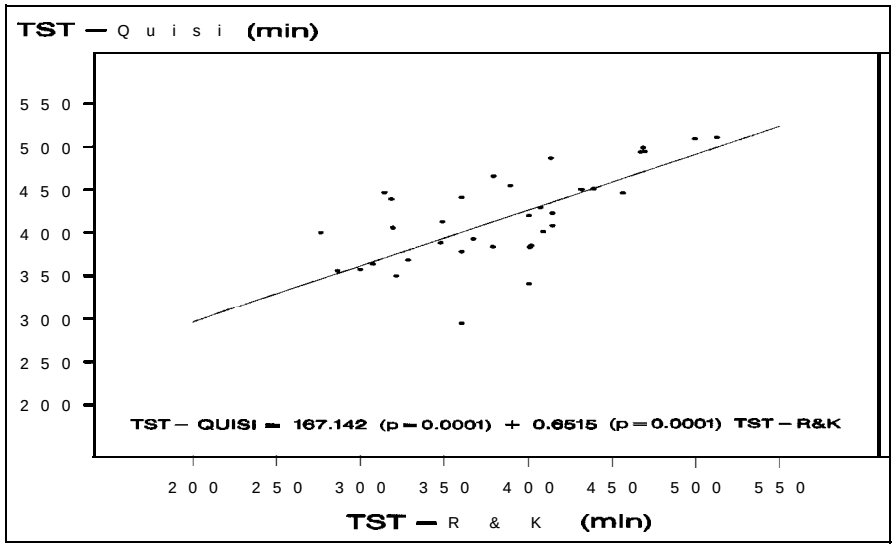


Figure 3. Linear regression of Total Sleep Time (TST) between QUISI and R&K rules.

Since some of the selected sleep variables, especially the latencies, do not follow a Gaussian distribution, but a pattern which includes one or several outliers, the median as robust estimator of the central tendency and the quartile range were used as descriptive statistics instead of means and standard deviations. When the terms average or mean are used in the following, this always refers to the median.

Assessment of the general level of agreement between the statistics derived by both methods was analyzed by means of Spearman rank correlations that are listed in Table 1.

The results show that Sleep Period Time, Total Sleep Time, Sleep Onset Latency and Sleep Efficiency Index have a high correlation and are significant. Even REM Latency is determined with reasonable high correlation while Slow Wave Sleep Latency is correlated only with 0.343 even though statistically significant.

The statistics of the basic quantitative parameters of sleep for the expert rating of the polysomnographic records according to the R&K rules and for QUISI automatic classification are listed in Table 2.

The mean Sleep Period Time (the time from the first Sleep Stage (except S_1) to the last Sleep Stage in the night) was 461 min in the polysomnographic recording in the R&K classification while QUISI recording yielded an SPT of 470 minutes, i.e. a 2% higher mean Sleep Period Time.

Table 2 shows that the median and the upper and lower quartiles for these variables show a good agreement. Sleep Onset Latency (SOL) is overestimated by QUISI by five minutes while Slow Wave Latency (SLT) and REM Latency (RLT) are underestimated on average by nine and five minutes, respectively. The Total Sleep Time is overestimated by QUISI by 18 minutes as an average which is about 4.7%.

The following figures 2, 3, 4 and 5, which show the linear regression between QUISI and R&K estimates, confirm that there is a striking correlation in these parameters. However, if one looks at the quartile ranges, there are also single cases where there are substantial differences between QUISI and the classification based on R&K rules.

The current QUISI rules (taking the median out of eight classifications) lead to a substantial under- as well as overestimation of the duration of S2 in individual cases.

Table 4 shows the medians and quartile ranges of the percentages of each individual sleep stage. Although S2 does not show a statistically significant correlation (Fig. 6) the difference between the

medians which are 44% in R&K classification and 43.8% by QUISI classification is negligible. That means that although overall sample distributions are very similar, there are marked individual differences for this variable.

As can be seen from Table 4 the Awake time as well as St are underestimated by the QUISI classification while both REM Sleep and Slow Wave Sleep (S_3 and S_4) are overestimated substantially.

Slow Wave Sleep is overestimated to a larger amount, **S3** by 4.2% (9.8% instead of 5.6%) and S_4 by 1.5% (3.3% instead of 1.8%). This overestimation is substantial. It might make disturbed Slow Wave Sleep look more normal. We therefore tried to answer the question whether QUISI could lead to misdiagnoses of SWS related sleep profile disturbances. And as we will demonstrate later concerning the SWS distribution, only 1 out of 38 patients would have been misdiagnosed for the SWS distribution (based on sleep profile structure) and only 8 out of the 38 for the amount of Slow Wave Sleep (Table 5 and 6).

Overall, QUISI obviously overestimates SWS, but in 26 cases the result of the visual inspection of both hypnograms is "normal". In 7 cases the overestimation of Slow Wave Sleep by QUISI leads perhaps to a misinterpretation. But looking at the EEG, original data delta waves and a synchronization of EEG can be seen, while the amplitude criterion of R&K does not allow the scoring of deep sleep (see also critical comments on the rules of R&K [18]. Only in one case was SWS detection too low in QUISI and normal in R&K classification (Table 7, patient code # 303). We will reinvestigate the data of the 38 patients and compare QUISI results with those of visual inspection for Z-waves defined as $\geq$ 40 µV on the one hand and $\geq$ 75 µV on the other hand, the latter being the rule according to R&K [6].

Looking at the correlation coefficients for **S3** and S_4 respectively (Table 3), **S3** barely fails the level of statistical significance (p = 0.0677) and S_4 is still significant at the 0.01 level. This indicates that even though Slow Wave is overestimated, this is not by chance but to some extent, systematical.

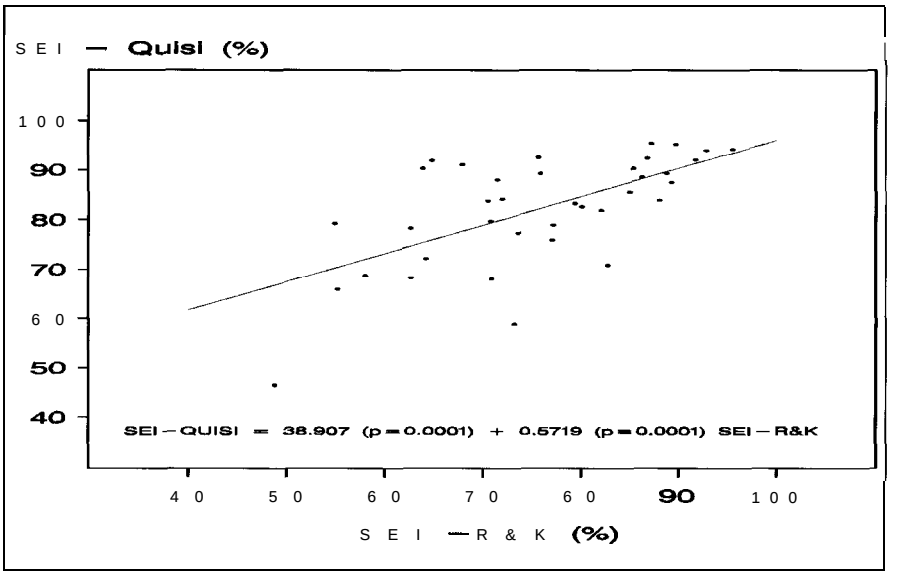


Figure 4. Linear regression of Sleep Efficiency Index (SEI) between QUISI and R&K rules.

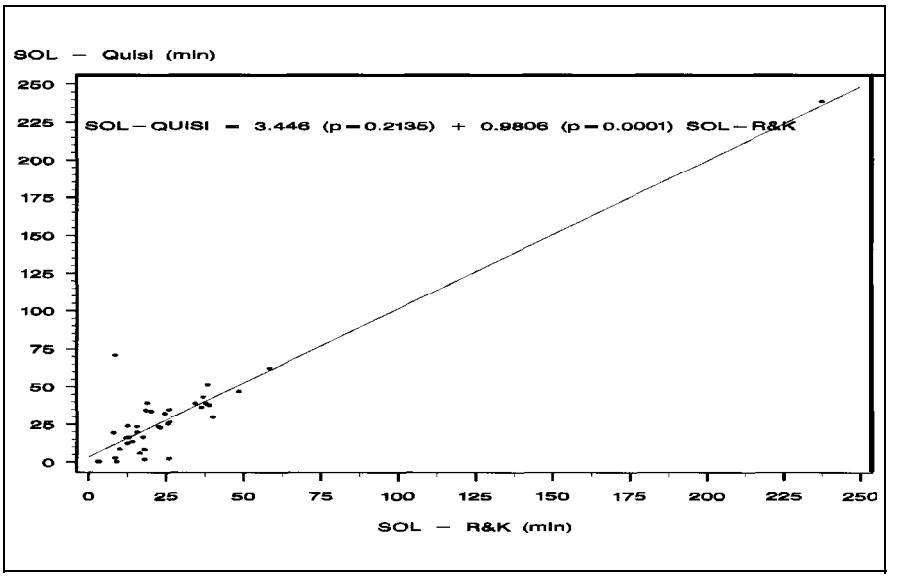


Figure 5. Linear regression of Sleep Onset Latency (SOL) between QUISI and R&K rules.

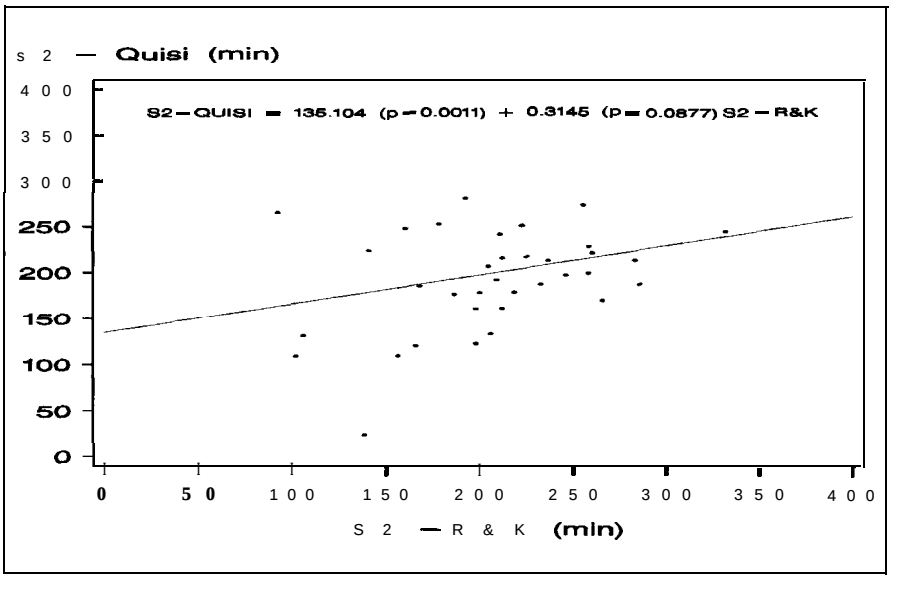


Figure 6. An Example of Non-Significant Correlation. Linear regression of Sleep Stage 2 (S_2) between QUISI and R&K rules.

Table 3. Spearman Rank Correlations between QUISI and R&K Sleep Parameters based on values in minutes.

Sleep EEG variable n = 38	Abbr.	Correlation coeffkient	p-value*
Movement Time	MT	0.432	0.0068
Awake during SPT	AWA	0.678	< 0.0001
Rapid Eye Movement Sleep	REM	0.580	< 0.0001
Sleep Stage 1	S_1	0.187	0.2615
Sleep Stage 2	S_2	0.257	0.1199
Sleep Stage 3	S_3	0.300	0.0677
Sleep Stage 4	S_4	0.413	0.0100

* Descriptive two-sided a-error

The correlations between the QUISI and Rechtschaffen and Kales estimates for single sleep stages (see Table 3) demonstrate that for MT, AWA, REM and S_4 the correlation is statistically significant, while for St, S_2 and S_3 it is not.

Table 4. Comparison between QUISI and R&K Estimates of Duration Sleep Stages in Percent of SPT (Based on Individually Calculated Percent).

n= 38		Polysomnography and R&K Classification		QUISI and Automatic Classification		Difference*
		Quartile Range		Quartile Range		
Sleep EEG variable	Abbr.	Median	Q1–Q3	Median	Q1–Q3	abs.
Movement Time	MT (%)	0.9	0.5– 1.4	1.0	0.4– 2.8	-0.1
Awake during SPT	AWA (%)	15.6	8.1-22.6	10.1	5.1-17.1	-5.5
REM Sleep (%)	REM	13.9	9.3-16.6	16.3	8.4–23.4	2.4
Sleep Stage 1 (%)	St	12.0	8.4-14.9	8.3	5.3-12.1	-3.1
Sleep Stage 2	S_2 (%)	44.0	37.6–52.5	43.8	36.0–51.4	-0.2
Sleep Stage 3 (%)	S_3	5.6	1.7– 7.6	9.8	6.3-13.6	4.2
Sleep Stage 4 (%)	S_4	1.8	0.0- 4.5	3.3	1.1– 6.5	1.5

* Simple difference between medians (median R&K – median QUISI)

Table 5. SWS Distribution (Visual Inspection).

		QUISI	
		normal	not normal
PSG/R&K	Normal	**25**	**1**
	Not Normal	0	**12**

n = 38 forward classified patients

The *sensitivity* of QUISI to recognize the disturbance of SWS-distribution is 0.923, the specificity is 1.000.

Table 6. SWS Amount (Visual Inspection).

		QUISI	
		normal	not normal
PSG/R&K	Normal	**26**	**1**
	Not Normal	**7**	**4**

n = 38 forward classified patients

The *sensitivity* of QUISI to recognize the disturbance of SWS-amount is 0.800, the *specificity* is 0.788.

Comparisons of Sleep Profiles in Patients Evaluated by Polysomnographic Recordings Using Rechtschaffen and Kales Rules with the Automated Classification Using QUISI Recording and Equipment

Profiles with good similarities (16 out of 38)

In Figures 7-9 profiles with good agreement between R&K and QUISI classifications are shown.

Patient # 412 (Fig. 7) shows some difficulties falling asleep as well as early awakening and a well-organized SWS, again demonstrated by both profiles.

In patient # 193 (Fig. 8) the greatest block of slow-wave Sleep is in the early morning, as demonstrated by both profiles.

The hypnogram of patient # 134 (Fig. 9) shows five NREM/REM-cycles in both profiles. Wake phases during the night are obvious.

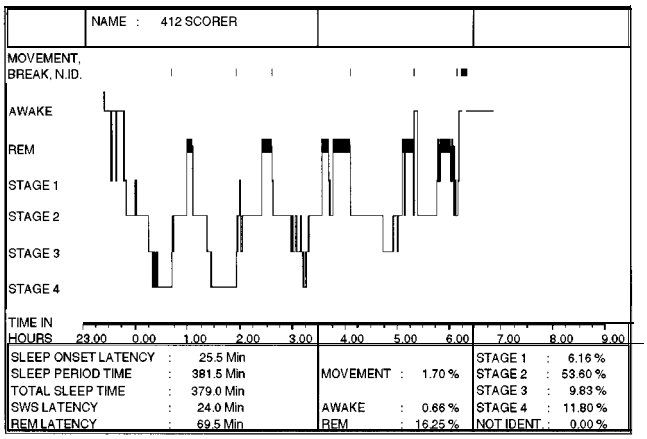
Profiles with some differences, however, still acceptable **(I 7** *out* **of 38)**

Such profiles are shown in Figures 10-12.

Patient # 453 (Fig. 10) has been suffering from a Restless Legs Syndrome and shows difficulties in both profiles with falling asleep as well as very long wakeful times during the night due to the Restless Legs Syndrome. In addition, this patient shows early awakening in both profiles. However, QUISI did not detect the first REM-period.

As shown in Figure 11, patient # 582, suffering from Periodic Limb Movement Disorder and fragmentary myoklonus shows the typical fractionized stage 2 in the profiles as well as the difficulty of falling into Slow Wave Sleep. QUISI, in this

Visual analysis



Automatic analysis

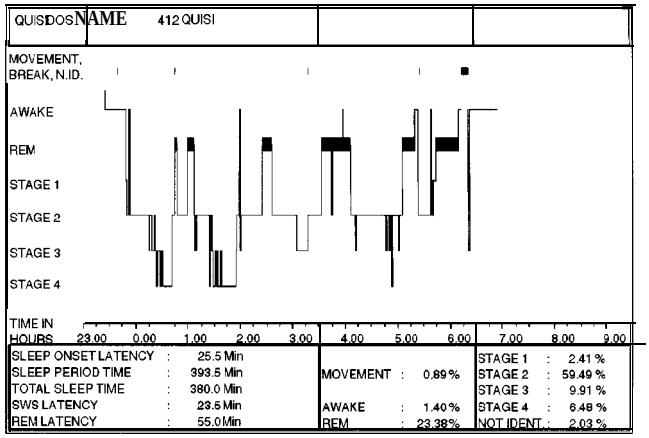


Figure 7.

case, shows more stage REM than would have been classified according to R&K.

As can be seen from Figure 12, in patient # 512, who suffered from Restless Legs Syndrome as well as Periodic Limb Movement Disorder, there is a long wakeful phase in the morning and a long wakeful phase during the night.

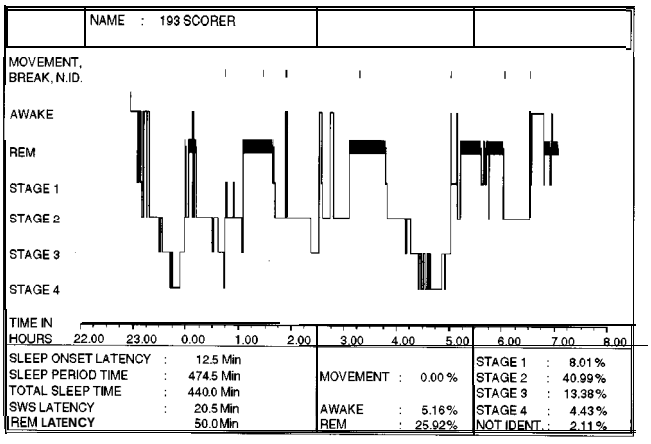
At the beginning of the sleep QUISI alternates between Awake and S_1, which shows the difficulty of falling asleep as well as in the R&K scoring. This would not lead to misclassification because the first sleep is determined to be first segment with S_2. When the subject goes to bed and tries to sleep, there is a long wakeful time according to the R&K classification, which is transformed by QUISI into occasional S_1 periods. The Sleep Period Time is overestimated by QUISI because S_1 is counted as sleep in the morning. During the night the long wake phase between 02.00 and 03.00 o'clock is transformed by QUISI into a mixture of wake, S_1 and REM, so REM in this case is falsely allocated. This, however, would not lead to a misinterpretation. SWS is overestimated by QUISI, but the SWS distribution is the same in both profiles.

Profile with major differences, which are not acceptable (5 out of 38)

Such a profile is shown in Figure 13.

As can be seen in Figure 13, patient # 303 was suffering from REM Sleep Behavior Disorder, Periodic Limb Movement Disorder and Narcolepsy. In both cases the Sleep-Onset-REM has been detected. However, the Slow-

Visual analysis



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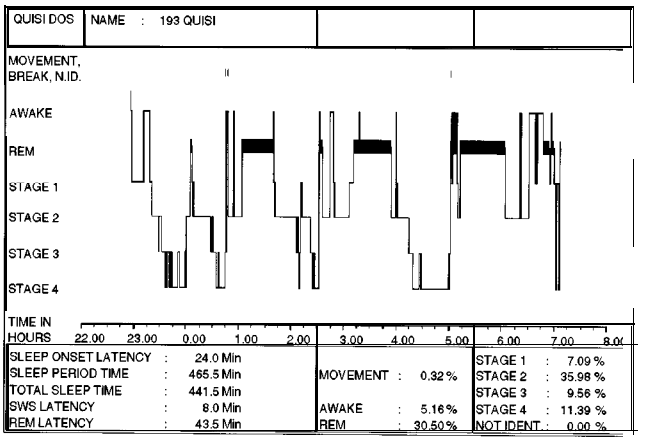
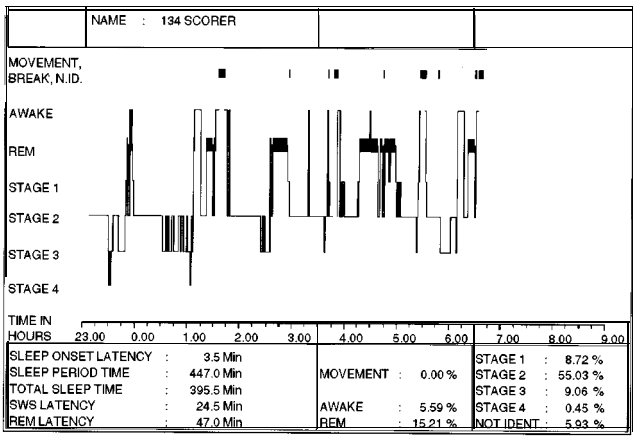


Figure 8.

Visual analysis



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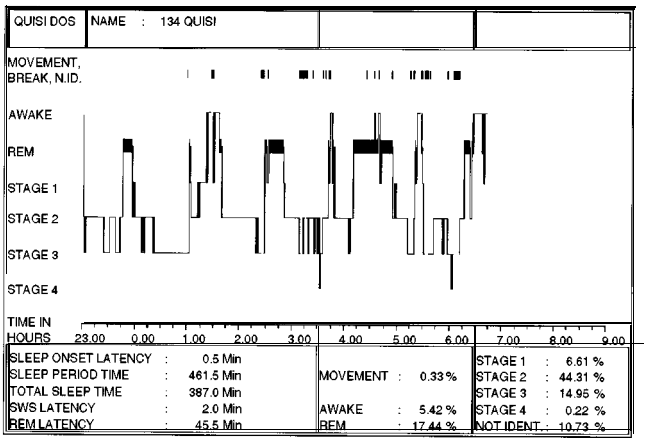
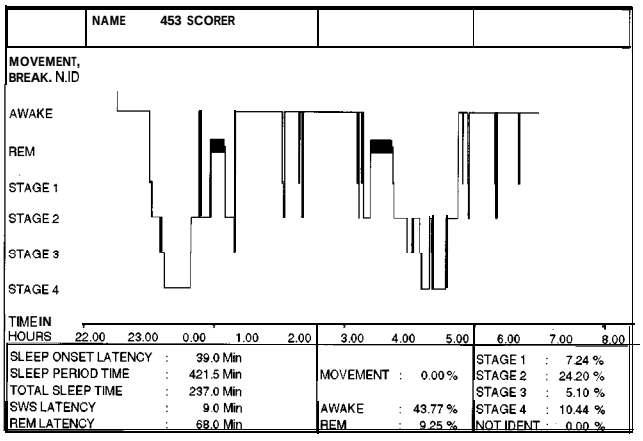


Figure 9.

Visual analysis



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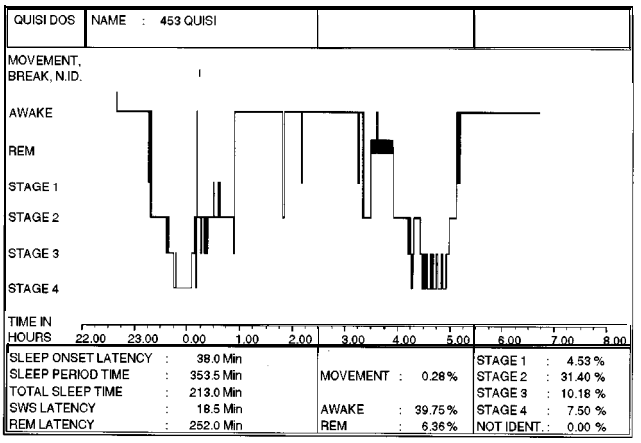
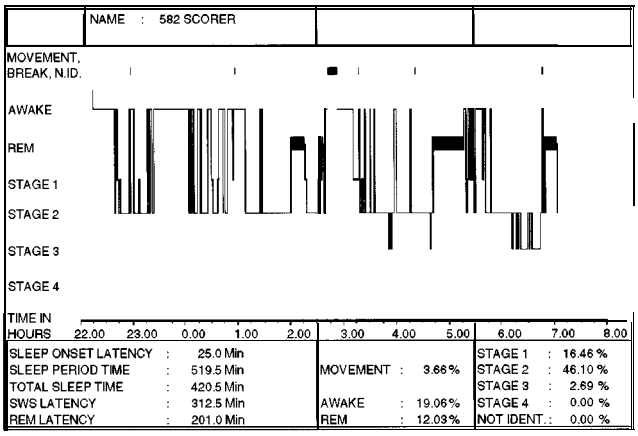


Figure 10.

Visual analysis



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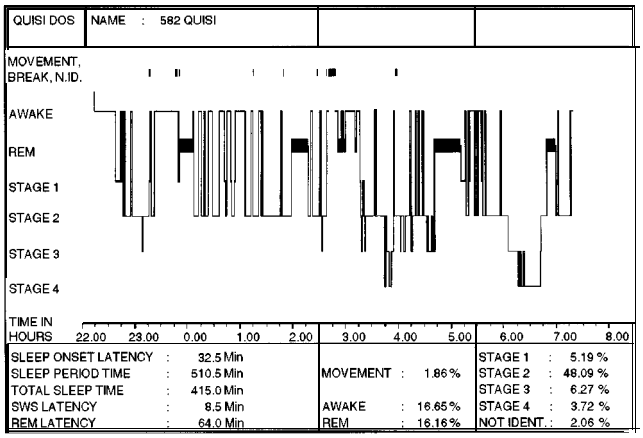


Figure 11.

Wave Sleep cycle is insufficiently described by QUISI. This is also true for the amount of deep sleep in the first cycle and in the early morning. REM is not sufficiently described during the night. This profile is not adequately identified by QUISI.

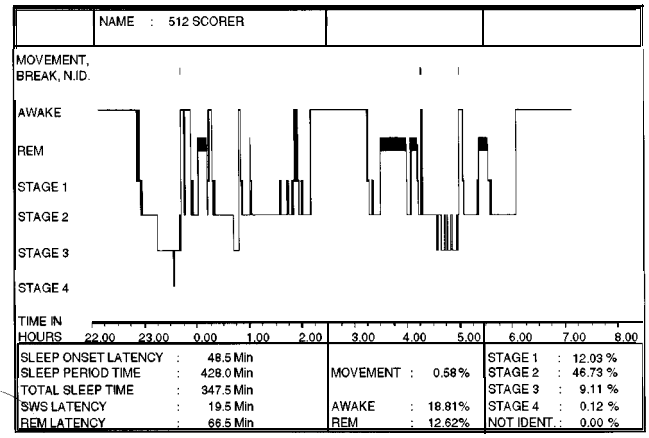
This patient has a non-Alpha EEG with very low amplitude and high frequencies, which also overlay the Sleep Stages 3 and 4. This shows that non-Alpha, low amplitude EEG with a high Beta portion cannot be classified by the current QUISI algorithm.

On the use of QUISI as a pre-clinical ambulatory diagnostic tool

In order to find out whether QUISI can be used as a pre-clinical, ambulatory, diagnostic tool, pathologies in the EEG-profiles were estimated independently for the QUISI generated profiles and the profiles generated that were based on visual classification according to R&K. Table 7 shows the results of the 38 patients who were classified. It shows the ICSD code, if available, and the final diagnosis.

There was only one patient with none of these pathologies as can be seen in Table 8. 37 profiles showed pathologies. Such pathologies can be seen in Table 7. The summary table shows that 37 profiles with pathologies, according to the R&K classification after polysomnographic recording, also show pathologies based on the one-channel QUISI recording and the automatic classification. Out of the 37 patients, in 19 patients there were exactly the same type and number of pathologies with

Visual analysis



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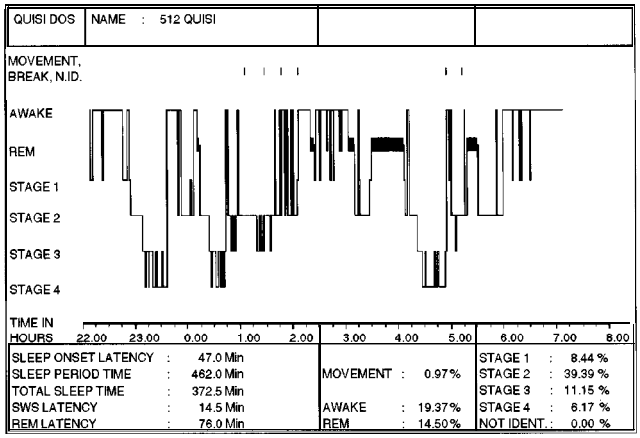
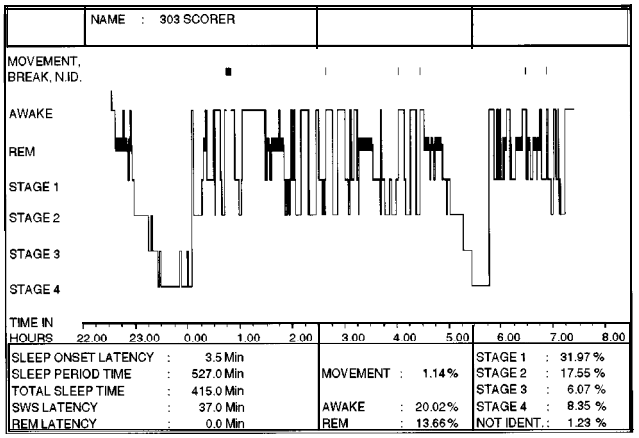


Figure 12.

Visual analysis



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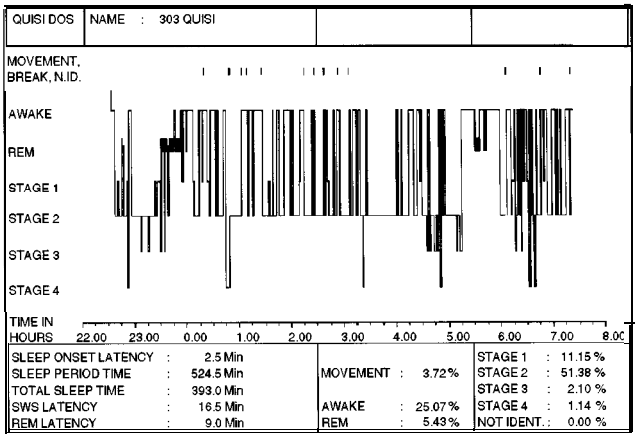

Figure 13.

Table 7. A Table of 38 Patients who were used for Forward Classification.

#	Patient Code	QUISI Pathological	QUISI Pathologies	R&K Pathological	R&K Pathologies	Diagnosis	Fig.
1	134	+	a b	+	a b	780.52-4 Periodic Leg Movement Disorder	9
2	172	+	b a	+	b a	780.52-o Restless Legs Syndrome	
3	184	+	g n	+	c g	347 Narcolepsy	
4	193	+	a	+	a	780.59-o REM Sleep Behavior Disorder	8
5	202	+	b	+	b i	307.45-3 Irregular Sleep-Wake Pattern	
6	222	+	i	+	i c	780.53-I Primary Snoring	
7	244	+	b g n	+	b g n	347 Narcolepsy	
8	252	+	b g c	+	b g c	307.42-o Psychophysiological Insomnia	
9	262	+	c	+	c	No typical ICSD diagnosis	
10	272	+	b c	+	b c i	780.52-0 Hypnotic-dependent Sleep Disorder	
11	303	+	n b c g i	+	n b c g	347 Narcolepsy 780.59-o REM Sleep Behavior Disorder 780.52-4 Periodic Limb Movement Disorder	13
12	312	+	b c	+	b c i	780.52-5 Restless Legs Syndrome	
13	324	+	b c a	+	b c a	780.52-4 Periodic Limb Movement Disorder 307.52-o Hypnotic-dependent Sleep Disorder	
14	334	+	b g	+	c g	780.54-7 Idiopathic Hypersomnia	
15	352	+	b g a c	+	b a c	780.53-1 Primary Snoring 780.52-4 Periodic Limb Movement Disorder	
16	362	+	b c i	+	b c i	307.49-l Sleep State Misperception 307.42-o Psychophysiological Insomnia	
17	382	+	b a	+	b a	307.42-0 Psychophysiological Insomnia	
18	402	+	b	+	b g	780.53-1 Primary Snoring	
19	412	—	e	—	e	No typical ICSD diagnosis	7
20	453	+	a b d m	+	a b d h m	780.52-5 Restless Legs Syndrome	10
21	512	+	b a m d	+	b a m d	780.52-5 Restless Legs Syndrome 780.52-4 Periodic Limb Movement Disorder	12
22	552	+	b c m	+	b c m i	780.52-5 Restless Legs Syndrome	
23	572	+	m	+	m b	Sleep Disorder caused by Hyperthyreosis	
24	582	+	b a c	+	b a c	780.52-4 Periodic Limb Movement Disorder 780.59-7 Fragmentary Myoclonus	11

Table 7. Continue.

#	Patient Code	QUISI Pathological	QUISI Pathologies	R&K Pathological	R&K Pathologies	Diagnosis	Fig.
25	592	+	m	+	m	780.52-4 Periodic Limb Movement 780.53-O Obstructive Sleep Apnea Svndrome	
26	612	+	b	+	b	307.42 Sleep Choking Syndrome	
27	622	+	b	+	b c	780.52-4 Limit Setting Sleep Disorder 780.52-5 Sleep-Onset Association Disorder	
28	642	+	b c a	+	b c i a	307.46-O Sleepwalking	
29	662	+	(m) d	+	(m) d c i	780.52-5 Restless Legs Syndrome	
30	1562	+	a b	+	a b	780.52-7 Idiopathic Insomnia	
31	1592	+	b	+	b c	780.52-5 Restless Legs Syndrome 780.53-l Primary Snoring	
32	1613	+	f	+	b d	780.53-l Primary Snoring 307.41-l Inadequate Sleep Hygiene	
33	1642	+	b i	+	b i k	780.52-4 Periodic Limb Movement 780.53-O Obstructive Sleep Apnea Syndrome 780.53-O Obstructive Sleep Apnea Syndrome	
34	1692	+	b g a c n	+	b g a c n	347 Narcolepsy	
35	1702	+	b f m	+	b m	780.52-5 Restless Legs Syndrome	
36	1713	+	b k	+	b	780.52-4 Periodic Limb Movement Disorder	
37	1722	+	c a	+	c i	780.53-l Primary Snoring	
38	1732	+	b f	+	b c	780.52-5 Restless Legs Syndrome	

Explanations:

Pathologies:

a) SWS distribution was not normal (SWS not highest in the beginning of the sleep and then diminished towards the morning),
b) too much stage Wake during the night (more than 3 wake phases of more than 10 min each),
c) fractionized S_2,
d) early awakening and a long wake time before leaving the bed (≥ 30 min),
f) too much REM (± 25%; only in QUISI classification),
g) fractionized REM
h) wrong REM-sleep distribution (REM was not highest in the morning and lowest at the beginning of the sleep),
i) no or not sufficient SWS (≤ 8%),
k) insufficient REM (≤ 7%),
m) SOL, Sleep Onset Latency too long (≥ 30 min),
n) SOREM, Sleep Onset REM like in Narcolepsy

both classifications. Only one patient showed completely different reasons. This patient would have been sent to the laboratory based on the QUISI pre-laboratory recording but then did show different pathologies. This was patient # 32 (patient code 1613) who showed too much REM in the QUISI profile and then showed too much Stage Wake and early awakening in the R&K profile. This is a typical patient, in whom awakening during the night had been turned into sleep, favoring REM Sleep and S_1, by QUISI.

Table 8. Comparison of the Visual Recognized Pathologies seen in the QUISI-Sleep Profiles and in the PSG Sleep Profiles.

		QUISI	
		n disturbed profile	, p r o f i l e
PSG/R&K	Disturbed Profile	37 n = 17 same reasons n = 19* partly same reasons n = 1 different reasons	0
	Normal Profile	**0**	**14**

n = 38 forward classified patients
* In 10 patients QUISI did not find all pathologies (/), in 4 patients QUISI found more pathologies than described by R&K (\), in 5 patients both applied ("I").
The sensitivity of QUISI to recognize the disturbance of sleep profiles is 1.000, the specificity is 1.000.

In the remaining 19 patients, as can be seen from Table 7, QUISI and R&K showed the same reasons,

QUISI, however, showed in some cases additional reasons or none of the reasons recognized by R&K. Therefore, in interpreting Table 8, we think that there is only one misclassification out of 38 classifications. However, this one patient would have been sent to the sleep laboratory anyway, but for different reasons.

Discussion

Even though one lead analysis of Sleep EEG has been described earlier, we did not know a classification based only on one frontal lead when we started our work. *Werth and Borbély* [31] were able to obtain reasonable classification results when they compared periorbital skin electrodes (El-A2) with C_3–A_2, using an automated detection routine. Therefore, it is understandable that the information derived from F_{p1}-F_{p2} can result in a reasonable classification when compared to C_3–A_2. The frontal bipolar lead F_{p1}-F_{p2} does not show eyelid blinks and parallel vertical eye movements, while horizontal are shown, not as in a classical EOG but still in a way that Rapid Eye Movements can usually be discriminated from other eye movements.

The frontal leads react to any muscle movement. Even movement of the lips or minor chewing movement results in a substantial over 40 Hz activity. We therefore believe that a single frontopolar EEG lead (F_{p1}–F_{p2}) is a better parameter than C_3–A_2 without information about EMG and EOG.

The frontal, self-applicable electrodes do not limit the further development of QUISI-like equipment. On the contrary, we have reason to believe that frontal coherence may allow us to better distinguish REM from Wake and St. Therefore, QUISI should be modified to allow coherence measures. The question whether Neural Network techniques finally led to our favourable results cannot be answered until a direct comparison with discriminant function or cluster analysis or other methods is done. Such investigations are underway. We would not expect much worse classification results, however, that these classical methods – being less adaptive – would be more sensitive towards artefacts. The fact that our results were done without removal of any artefact is seen as major progress for ambulatory and fully automated usage.

QUISI is the smallest equipment available so far and much smaller than Medilog 9000 or Medilog 4-24. The results obtained with Medilog are in the range of 71–89% agreement when manual classification was compared with automated classification [5, 12, 22].

As described by *Obergottsberger et al.* [22] REM was overestimated by 7,5% with the Oxford Medilog 9000 recorder and automated analysis, while Stage 2 was underestimated by 5,2%. With QUISI, REM was overestimated by 2,4% (16,3% with QUISI; 13,9% with manual classification according to R&K). Stage 2 was underestimated with QUISI by 0,2% as an average. In another comparison between two visual raters and the Oxford Sleep Stager, *Kubicki et al.* [19] found less REM and less Stage 2 with the automated method, but more SWS. In our own comparison of 7 different systems used for one sleep night we found that REM was overestimated by all 7 systems, while Stage 2 was underestimated by 4 systems and SWS was overestimated by 5 of the 7 systems but underestimated by 2 [10].

The fact that QUISI is obviously in line with other automated analysis systems when compared to R&K classification based on polysomnographic recordings lets us hypothesize that eye movements in Awake Stages during the night, in phases with low muscle potentials may be falsely recognized as REM. On the other hand, the overestimation of SWS may be solely due to the 75 µV criteria of R&K. Most methods use power spectral analysis and the power of a Delta wave is a product of the amplitude, the frequency and the total number of δ-waves.

Kubicki et al. [19], when testing the Oxford Stager, compared two visual raters and described differences.

Table 9. Interrater comparison (from [19]).

Stage	# of epochs First rater	Differences of the Second rater	
		Number of epochs	%
Awake	**678**	**55**	8,1
REM	2533	101	4,0
Stage 1	952	422	44,3
Stage 2	7999	215	2,7
Stage 3	1072	253	23,6
Stage 4	351	143	40,7

The optimized results of both raters were compared with the results of the automated sleep stager.

Table 10. Comparison with the automatic sleep stager (from [19]).

Stage	Optimized results of 2 raters	Differences by	Automated Classification	
	# of epochs	# of epochs	%	Automated vs R&K
Awake	838	602	72	↓
REM	2532	544	22	↓
Stage 1	747	414	55	
Stage 2	8070	1370	17	↑
Stage 3	1068	478	45	↑
Stage 4	313	97	31	↑

If we compare these results with our own findings shown in Table 4 we can see that the overall results (median of 38 patients) are much closer than in the case described by *Kubicki et al.* [19].

So far the forward classification was done in patients, not in healthy volunteers. This is one of the next steps necessary. However, from a few comparisons we have done in our laboratory, we expect a reasonably higher agreement between R&K and QUISI classification.

Non-alpha, low amplitude, high frequence EEG was not included in the classification rule and QUISI cannot be used for such subjects. This is mainly because some subjects maintain high frequencies during all sleep stages.

The patients included had no respiratory related sleep disturbances but we believe that QUISI can be utilized also for those patients if another channel and an oxygen saturation sensor were included.

Since the QUISI equipment can record 24 hours EEG without recharging the batteries, it could also be validated against performance and mood parameters during the day. Such a study is in progress.

QUISI is an affordable, self-applicable, small, ambulatory sleep EEG recording and analysis device, which seems to be a useful addition to the existing ambulatory devices.

With the current first results in 38 patients we would like to ask our colleagues to use and test QUISI as a

pre-sleep lab, ambulatory, diagnostic' tool. Then during an all-night sleep recording in the laboratory the results of QUISI and R&K classification should be compared. Depending on the results of this comparison it may then be decided whether this particular patient would be suitable for an ambulatory follow-up using the QUISI device.

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