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Comparison of five sedation scoring systems by means of auditory evoked potentials

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Abstract *Objective:* To review five sedation scoring systems and to determine their correlation with an objective method for assessing the level of sedation by means of auditory evoked potentials (AEP) in critically ill patients.
Design: Prospective clinical study.
Setting: Multidisciplinary intensive care unit in a university hospital.
Patients: Ninety-five consecutive patients requiring sedation during intensive care therapy.
Measurements and results: Previous studies have shown that auditory evoked potentials, especially latencies of the midlatency component N_b, could serve as an indicator of depth of anaesthesia. In the present study we used this electrophysiological method to evaluate sedation during intensive care therapy. Changes in latency of peak N_b were compared with various levels of sedation assessed by five established sedation scoring systems. As in anaesthesia, latencies of N_b increased with increasing depth of sedation. Among the scoring systems, the one developed by Ramsay correlated best with changes in N_b latency ($r^2 = 0.68$). The coefficient of determination, r^2, of the other scores ranged from 0.56 to 0.61.
Conclusion: For the assessment of sedation, several scoring systems have been introduced into clinical practice, but the differentiation of deeper sedation levels, especially, remains poor. In this study we compared auditory evoked potentials, as an objective method with which to assess the level of sedation, with five different sedation scoring systems. In comparison with changes in latency of the midlatency component N_b, Ramsay's sedation score showed the closest correlation. Objective electrophysiological monitoring is desirable during long-term sedation.

Key words Sedation · Sedation score · Evoked potentials · Intensive care therapy · Monitoring of sedation

Introduction

Previous studies using auditory evoked potentials (AEP) to investigate depth of anaesthesia demonstrated a dose-related suppression of the early cortical auditory evoked response to a variety of anaesthetic agents. An increase in latencies and a decrease in amplitudes of the midlatency auditory evoked waves could be observed with increasing doses of various volatile [1–4] or intravenous anaesthetics [5–7]. Thornton et al. [8] found the latency of the early cortical response N_b to be the best feature for indicating depth of anaesthesia and intraoperative awareness. When N_b latencies decreased in time to less than 44.5 ms during anaesthesia, the incidence of responses to verbal command was high and associated with very light anaesthesia. Further studies showed a similar close relationship between changes of midlatency AEP and several phenomena indicating in-

traoperative awareness, such as purposeful movements [9, 10] or postoperative explicit or implicit memory [11].

Most critically ill patients need sedation and analgesia to tolerate mechanical ventilation or uncomfortable procedures. Each patient has different indications for sedation, and individual requirements will change as the disease process improves or worsens. In contrast to many other drugs, for instance inotropes and vasopressors, which are titrated against the desired effect, sedatives are applied in a rather haphazard way. Effects of undersedation as well as oversedation occur and may be harmful for the critically ill [12]. Scoring systems presently available for assessing the depth of sedation often fail to detect oversedation during the long-term application of sedative drugs.

We investigated AEP as an objective method with which to assess depth of sedation in comparing established sedation scoring systems.

Materials and methods

After approval of the local Ethics Committee, we examined 95 consecutive patients on our intensive care unit who required sedation postoperatively after major surgical procedures or during long-term mechanical ventilation on account of severe acute respiratory distress syndrome (ARDS) of various origins. Most of these critically ill patients received midazolam and fentanyl for sedation and analgesia. Further agents – such as propofol, methohexital, gamma-hydroxybutyrate, ketamine or clonidine – were applied additionally, when midazolam failed to achieve the desired level of sedation.

Auditory evoked potentials (AEP) were recorded by the electrodiagnostic system Pathfinder I (Nicolet Instruments). Corresponding AEP were elicited in response to rarefaction clicks (Amplivox TDH 39 Headphones, 9,3 Hz, 70 dB above the average hearing threshold) and recorded by silver electrodes positioned at Cz and A_1/A_2 with Fpz as earthing according to the international 10–20 system. An epoch of 100 ms was band-pass filtered (1–1500 Hz) with an analogue Butterworth-filter (roll-off 6 dB/Octave). After automatic detection and removal of sweeps containing artefacts or signals greater than 96% of full scale, AEP were averaged over 1000 stimulus presentations. For off-line analysis of the resulting averages, the latency and peak of brainstem peak V and of midlatency peaks Na, Pa, Nb and P_1 were determined. The brainstem-generated response V served as an indicator of correct transmission and transduction of the auditory stimuli, while midlatency AEP were generated in the primary auditory cortex and represented cortical processing. Recordings with missing peak V were excluded from the analysis. AEP were recorded at least twice in each of the 95 patients over a period of 30 min to assure reproducibility. Further stimulation of the patient up to 20 min before measurement of the auditory evoked response was avoided. Measurements took place exclusively in the evening to achieve comparable conditions regarding activity and noise level on our intensive care unit.

Before and after recordings of AEP the level of sedation was assessed according to five established sedation scoring systems which are listed in Table 1. Most scoring systems were originally developed during a study of a sedative agent or technique. The one described by Ramsay et al. [13] (Table 2) in 1974 was evolved for evaluation of alphaxalone-alphadolone as a sedative. Six levels of sedation were defined, three for patients who are awake and three for those who are asleep. In the present study we exerted a light glabellar tap to differentiate the asleep levels. This eyeblink-eliciting tap on the glabella (the flat region of skin between the eye-brows) induces a primitive reflex (glabellar or orbicularis oculi reflex) which is processed in the brainstem.

A scoring system developed by Cohen et al. [14] (Table 3) in 1987 to evaluate alfentanil for long-term sedation uses only tolerance of ventilation to assess adequacy of the sedative effect.

The Cambridge sedation score [15] (Table 4) was designed for regular clinical use. To define the fifth level, tracheal suction is used as a painful stimulus. The two final levels describe circumstances when the level of sedation is not assessed: in patients receiving neuromuscular blocking agents and in sleeping patients. No patient examined in the present study belonged to one of these two groups. The Bloomsbury sedation score [16] (Table 5) is part

Table 1 List of the five established sedation scoring systems

Ramsay Sedation Score [13]
Cohen Sedation Score [14]
Cambridge Sedation Score [15]
Bloomsbury Sedation Score [16]
Newcastle or Cook Sedation Score [17]

Table 2 Ramsay Sedation Score [13]

Score	Awake levels	
1	Patient anxious and agitated or restless, or both	
2	Patient co-operative, oriented and tranquil	
3	Patient responds to command only	
	Asleep levels	
4	Brisk response	to a light glabellar tap
5	Sluggish response	or
6	No response	loud auditory stimulus

Table 3 Cohen Sedation Score [14]

Score	Degree of sedation
0	Asleep, no response to tracheal suction
1	Rousable, coughs with tracheal suction
2	Awake, spontaneously coughs or triggers ventilator
3	Actively breathes against ventilator
4	Unmanageable

Table 4 Cambridge Sedation Score [15]

Level	
1	Agitated
2	Awake
3	Roused by voice
4	Roused by tracheal suction
5	Unrousable
6	Paralysed
7	Asleep

Table 5 Bloomsbury Sedation Score [16]

Score	
3	Agitated and restless
2	Awake and uncomfortable
1	Aware but calm
0	Roused by voice, remains calm
–1	Roused by movement or suction
–2	Roused by painful stimuli
–3	Unrousable
A	Natural sleep

Table 6 Newcastle or Cook Sedation Score [17] (*SIMV* synchronized intermittent mandatory ventilation)

Aspects		
Eyes open	Spontaneously	4
	To Speech	3
	To pain	2
	None	1
Response to	Obeys commands	4
nursing	Purposeful movement	3
procedures	Non-purposeful movement	2
	None	1
Cough	Spontaneous strong	4
	Spontaneous weak	3
	On suction only	2
	None	1
Respirations	Extubated	5
	Spontaneous intubated	4
	SIMV/triggering ventilation	3
	Respiration against ventilator	2
	No respiratory efforts	1
Loading for spontaneous communication		2

Score	Grades of sedation	Sum
1	Awake	17–19
2	Sleep	15–17
3	Light sedation	12–14
4	Moderate sedation	8–11
5	Deep sedation	5–7
6	Anaesthesia	4

of a critical care algorithm for sedation, analgesia and paralysis developed in London. The original algorithm combines assessment of sedation, anxiolysis, analgesia, confusion and neuromuscular blockade with management options. The Newcastle sedation score was evolved by Cook et al. [17] (Table 6) for use in both intensive care and anaesthesia. In an attempt to separate different aspects of sedation, this scale was based on the Glasgow Coma Scale [18]. Individual variables, such as response to stimuli and control of ventilation, are scored separately. Four aspects have to be evaluated and the total score which finally indicates the level of sedation calculated from their sum. A further loading for spontaneous communication renders this scale even more complex.

The results are presented as mean values and standard deviation. Among electrophysiological data, exclusively latencies of the midlatency wave N_b entered the final analysis and were compared between the different groups of each sedation score using the non-parametric Kruskal-Wallis test. Kendall's correlation coefficient τ was calculated to examine the correlation of electrophysiological data and sedation scores. Furthermore, regression analysis was performed for latencies of N_b depending on the different sedation score groups, and tested whether the slopes of regression were different from zero. Finally, the correlation coefficient r was squared to form the coefficient of determination r^2. A probability value less than 0.05 was assumed to be statistically significant. Statistical analysis included Bonferroni × s correction for multiple comparisons.

Results

The final data analysis was made using 190 recordings in 95 patients (double measurements). Agitated patients were excluded on account of a high artefact rate during measurement of the auditory evoked responses due to muscle activation, movement and eye-opening, which rendered any data analysis impossible. The groups within each level of sedation were comparable in terms of sample size, demographic and physiological data. Table 7 gives a summary of patient data divided according to the Ramsay score. In our patient population the desired sedation score depends on the nature and severity of the underlying disease. For instance, at the critical stage of severe ARDS coughing or even spontaneous breathing of the patient has to be avoided by means of deep sedation in order to improve pulmonary gas exchange. Therefore, in this study, patients with higher APACHE II scores ended up in deeper levels of sedation.

As has already been shown for different minimal alveolar concentrations (MAC) of isoflurane during anaesthesia [3], with increasing depth of sedation latencies of the midlatency auditory responses progressively increased and their amplitudes decreased. In contrast, the brainstem response V remained stable (Table 7).

Table 8 lists Kendall's correlation coefficients, τ and the coefficients of determination, r^2, of the midlatency component N_b in dependence on each sedation score. The Ramsay sedation score correlated best with changes in latency of midlatency peak N_b. Its coefficient of determination r^2 came closest to 1 with a value of 0.68. The coefficients of determination of the other scoring systems ranged from 0.56 to 0.61. Interestingly, the r^2 of the Cook sedation score did not differ from that of the Glasgow Coma Scale, which it was based on to create a more useful sedation scoring system. Scatterplots and regression lines for latencies of N_b on the different sedation scores and the Glasgow Coma Scale are presented in Figs. 1A–F. The poor differentiation of the clinical scoring systems to assess sedation in the asleep levels became evident by the widely scattered distribution of N_b latencies with increasing levels of sedation.

Table 7 Demographic and physiological data of the 95 patients, latencies of peak V and N_b as mean values and standard deviation listed according to the Ramsay sedation score. For the APACHE II score the median values and range are indicated

	Ramsay Score				
	2 mean ± sd	3 mean ± sd	4 mean ± sd	5 mean ± sd	6 mean ± sd
Patients [n]	21	19	17	17	21
Gender [f/m]	4/17	8/11	5/12	6/11	14/7
Age (years)	58 ± 18	51 ± 17	46 ± 17	48 ± 17	51 ± 19
Height [cm]	177 ± 8	173 ± 11	175 ± 11	172 ± 10	165 ± 9
Weight [kg]	81 ± 15	75 ± 19	79 ± 17	83 ± 21	71 ± 16
MAP [mm Hg]	99 ± 14	92 ± 14	91 ± 17	88 ± 10	84 ± 11
Heart rate [bpm]	91 ± 16	87 ± 21	87 ± 26	94 ± 17	93 ± 24
Temp [°C]	37.2 ± 0.6	37.3 ± 0.5	37.5 ± 0.8	37.5 ± 1.0	36.7 ± 1.4
V [ms]	6.1 ± 0.91	6.5 ± 0.75	7.0 ± 0.68	7.1 ± 0.84	6.9 ± 0.70
N_b [ms]	*51.1 ± 2.41	*58.9 ± 6.31	*69.8 ± 12.56	*85.9 ± 14.06	90.6 ± 12.70
	Median (range)	Median (range)	Median (range)	Median (range)	Median (range)
APACHE II [points]	7 (4–13)	11.5 (5–25)	17 (9–20)	19 (13–26)	20 (14–27)

* $p < 0.05$ versus next group

Table 8 Kendall's correlation coefficients, τ, and coefficients of determination, r^2, for N_b latencies in dependence on each sedation score. The Ramsay sedation score correlated best with changes in N_b latencies (*GCS* Glasgow Coma Scale)

Sedation score	τ	r^2	p
Ramsay	0.71	0.68	< 0.05
Cohen	–0.62	0.56	< 0.05
Cambridge	0.68	0.61	< 0.05
Bloomsbury	–0.62	0.57	< 0.05
Cook/Newcastle	–0.64	0.59	< 0.05
GCS	–0.65	0.59	< 0.05

Discussion

Our findings, concerning auditory evoked potentials (AEP) as an objective method for assessing depth of sedation, are in line with those noted in previous studies of AEP during anaesthesia. While patients were awake, AEP exhibited a periodic waveform. Early cortical waves showed an increase in latency and an attenuation of amplitude with increasing depth of sedation. Brainstem waves were not affected significantly. Since Thornton et al. [8] defined a threshold N_b latency of 44.5 ms below which intraoperative awareness occurred during anaesthesia maintained by nitrous oxide in oxygen, it is noteworthy that N_b latencies of more than 50 ms could be observed even in the awake levels in our patient population. This may be due to the only weak hypnotic effects of nitrous oxide which lead to smaller changes in the auditory evoked responses, compared with a more potent hypnotic agent like isoflurane [19]. To elucidate this aspect further investigations are necessary, focusing on the central nervous effects of one particular sedative drug.

A major problem of long-term sedation during intensive care therapy is the occurrence of oversedation which leads to a delayed arousal of the patient, unnecessarily prolonged weaning from the ventilator and, in the end, to a considerable increase in costs. There are some electrophysiological measurements, such as the electroencephalogram and power spectral analysis, auditory evoked, visual evoked and somatosensory evoked responses, which are helpful in evaluating the neuronal function of the brain under sedation, in coma or other neurological disorders. All of these techniques have in common that their use requires time and special training. Furthermore, basic knowledge of the electroencephalogram is mandatory. But, as clinical sedation scoring systems often fail to detect oversedation, we selected five established sedation scales to determine their correlation with changes in N_b latency of AEP as an objective parameter to assess the level of sedation.

The scoring system designed by Cohen [14] in 1987 to evaluate alfentanil as a sedative showed the poorest correlation with a coefficient of determination, r^2, of 0.56. It considered only tolerance of mechanical ventilation to assess the adequacy of the sedative effect. Despite discrimination of eight sedation levels, the Bloomsbury sedation score [16] came up with a comparably low r^2 of 0.57. The Newcastle sedation score developed by Cook [17] was based on the Glasgow Coma scale (GCS). Increasing the number of defined points should add to the accuracy of this score, but enhanced its complexity. In comparison with the original GCS used as a sedation scoring system, it achieved an identical r^2 of 0.59. Disregarding the two final levels "paralysed" and "asleep" in the present study, the Cambridge sedation score reached a slightly better r^2 of 0.61.

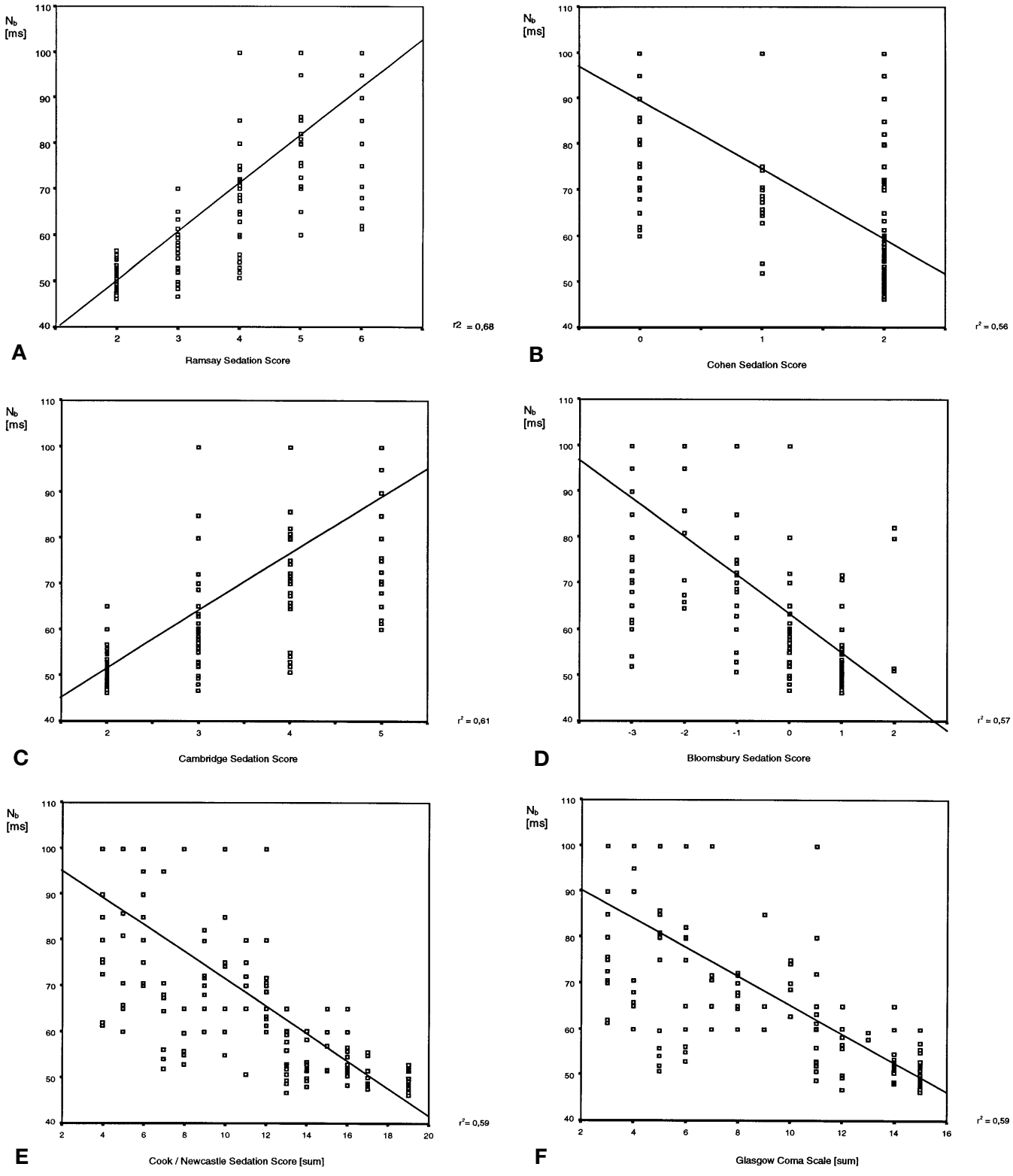

Fig. 1 A–F Scatterplots and regression lines for N_b latencies on the different sedation scores and the Glasgow Coma Scale with coefficients of determination r^2. In the asleep levels the differentiation of the sedation scoring systems is weak

The Ramsay sedation score, which is a widely accepted scoring system on intensive care units, showed the closest relationship with changes in N_b latency. Its r^2 came closest to 1, with a value of 0.68. This finding may be due to the inclusion of a primitive reflex in order to discriminate the asleep levels. The glabellar or blink reflex is elicited mechanically by a tap on the flat region of skin between the eye-brows, processed in the brainstem and evokes eyelid movements by contraction of the orbicularis oculi muscles. Adults exhibit robust reflex inhibition to repetitive stimuli, while neonates and patients with Parkinson's disease lack habituation [20, 21]. The amplitude of the blink reflex increases as a function of an increased tap [22]. As with every other clinical sedation scale, the differentiation of the asleep levels remains unreliable.

In comparison with other sedation scoring systems, the Ramsay score showed the best correlation to AEP as an objective measurement to assess depth of sedation. However, in cases where deeper levels of sedation are required over a longer period of time, objective electrophysiological monitoring of sedation is desirable.

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