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Autonomic Responses to Meaningful and Non-Meaningful Auditory Stimuli in Coma

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Summary. In a group of poisoned patients, the lowest MCS (*M*unich *C*oma *S*cale) vigilance grade at which patients responded when called by their names was determined. In 12 patients at this vigilance grade, the extent to which the meaning of the names contributed to their reactions was investigated. Their first name and a control stimulus (name backwards) were repeatedly presented via headphones. Stimulus intensity was 90 dB (A). During stimulus presentation, changes in heart rate, finger pulse amplitude, and electrodermal activity were recorded. A comparison between responses under both stimulus conditions revealed that the first reactions of poisoned patients to their names are primarily elicited by the physical properties of the stimulus.

Key words: Coma – Vigilance – Meaningful vs. non-meaningful stimuli – Autonomic responsiveness.

Zusammenfassung. Mit Hilfe der *M*ünchner *C*oma *S*kala (MCS) wurde im Intoxikationskoma der niedrigste Vigilanzgrad ermittelt, der erste Reaktionen auf Ansprechen mit dem Namen zuläßt. Bei 12 Patienten dieses Vigilanzgrades wurde untersucht, inwieweit die Bedeutung des Namens für die Auslösung von Reaktionen relevant ist. Hierzu wurde ihr Vorname sowie ein Kontrollreiz (Vorname rückwärts) wiederholt über Kopfhörer dargeboten. Die Reizintensität betrug 90 dB (A). Registriert wurden Veränderungen der Herzfrequenz, der Fingerpulsamplitude sowie der elektrodermalen Aktivität. Vergleiche der Reaktionen auf beide Reizbedingungen zeigen, daß die Patienten bei ersten Reaktionen auf den Namen primär auf die physikalischen Stimulusmerkmale reagieren.

Schlüsselwörter: Koma – Vigilanz – Bedeutsame vs. nichtbedeutsame Reize – Autonome Reaktivität.

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Introduction

One of the main stimulus properties which is responsible for the elicitation of a response is the meaning of the stimulus. This is also true during sleep; the first name as a meaningful stimulus provokes more awaking (Langford et al., 1974) and more EEG and electrodermal responses (Oswald et al., 1960) than the name played backwards. According to Fischgold (1960), stimulus meaning is also an important parameter for the elicitation of responses in comatose patients. He describes the case of a comatose child who showed distinct EEG responses when called by its mother, but not when called by a stranger.

Meaningful stimuli are used in the diagnosis of comatose states. The clinician often gets his first impression of the severity of a comatose state by observing the patient's reaction to being called by his name (Jouvet, 1969). In this case, however, it is not clear how much the meaning (in contrast to the physical properties) of the stimulus is responsible for the elicitation of a response. It is possible that it may yield important information for the evaluation of a comatose state by providing an indication of the capacities of sensory discrimination which are still available.

The objective of this study was to investigate the role of stimulus meaning—as compared to the physical stimulus properties—for the elicitation of autonomic responses during the most severe grade of coma in which reactions to meaningful verbal stimuli can still be observed.

To answer this question we studied responses of heart rate, finger pulse amplitude, and palmar skin resistance to stimulation with the first name and a control stimulus lacking personal significance in severely poisoned comatose patients. The grade of impairment was defined according to the MCS (*M*unich *C*oma *S*cale, von Cramon et al., 1975), which has proved useful in measuring drug-induced behavioral deficits (Schulz et al., 1975). The MCS consists of two additive subscales (Guttman scales) of which one measures the degree of differentiation of behavioral responses to different stimuli. Following the concept of Head (1926), this subscale has been interpreted as measuring 'vigilance' (von Cramon, 1978).

The question may be formulated whether the personal significance of the stimulus at the lowest level of vigilance at which responses to the patient's name are recorded contributes to the patient's attaining the threshold of reaction.

Methods

Subjects

Observations of behavioral changes as well as inspection of polygraphic recordings of 36 severely poisoned patients with different vigilance grades indicated that first responses to names can be observed when patients reach the vigilance grade 3 on the MCS (see below). Twelve of the patients with this grade of impairment were studied. Their age, sex, and the ingested drugs are summarized in Table 1. During the examination all patients breathed spontaneously, except patient 8 who received artificial respiration.

Table 1. Description of patients

Patient number	Age	Sex	Drugs ingested
1	25	f	carbromal, diphenhydramine
2	26	f	carbromal, diphenhydramine
3	55	m	methaqualon, carbromal
4	71	f	methaqualon, carbromal
5	29	f	barbiturate
6	43	m	barbiturate
7	26	f	diethylpentenamide, diphenhydramine
8	54	f	methaqualon, oxazepam
9	25	f	methaqualon, lorazepam, clozapin
10	63	f	carbromal
11	49	m	carbromal, diphenhydramine
12	15	f	barbiturate

Stimulus Conditions and Procedure

The patients were studied at bedside in the intensive care unit to which they had been admitted. The examination always began with the assessment of the patient's vigilance grade. This was determined by the differentiation of behavioral responses to four stimuli: (1) optical stimulus (focused flashlight); (2) high intensity acoustic stimulus (siren); (3) tactile stimulation of the face with a flexible nylon hair; and (4) intense electrical stimulation applied to one hand.

Five grades of vigilance were distinguished:

(0) No behavioral response to any of the four stimuli described above.
(1) Only general motor reactions (movements of the body or head without clear-cut directional components in relation to the stimulus or experimenter).
(2) Grade 1 reactions and orofacial (mimic) reactions such as frowning, eyelid contractions, perioral movements, and those involved in the act of swallowing.
(3) Grade 2 reactions and orienting responses (unequivocal turnings of the head toward or away from the stimulus; opening of eyes or state of open eyes).
(4) Grade 3 reactions and communicative responses (eye contact or verbal utterances).

More detailed information on the vigilance test has been presented elsewhere (von Cramon et al., 1975; von Cramon, 1978). Ten minutes after the assessment of vigilance, autonomic responses to two types of stimuli were studied in patients rated as vigilance grade 3: (1) The patient's first name played forward (F)—which means in its normal direction—from tape (Uher 4200) and (2) the identical stimulus played backward (B) where the familiar phoneme structure and meaning of the stimulus is destroyed. Both stimuli were presented 10 times binaurally via headphones; the order of presentation was random. The interstimulus interval ranged between 20 and 30 s (mean = 25 s). Stimulus intensity was 90 dB (A). This was equivalent to the intensity measured when doctors called comatose patients by name during normal clinical routine.

Physiological Variables

All recordings during stimulus presentation were made on a Beckman model R-611 polygraph and stored on analogue tape (Philips EL 1020).

Heart Rate. An electrocardiogram was recorded from the chest. The 5 R-R intervals prior to each stimulation as well as 30 intervals after stimulus onset were measured by a PDP 11/40 computer and converted into beats/min.

Finger Pulse Amplitude. A photoplethysmogram was recorded from the middle finger of one hand using a Beckman type 9853 coupler with a time constant of 0.1 s. Pulse amplitude (measured in mm) was analysed for 35 consecutive pulses (5 prestimulus and 30 poststimulus).

Electrodermal Activity. Electrodermal activity was measured from the thenar and hypothenar eminences of one hand using Beckman standard biopotential skin electrodes and Hellige GSR-Creme. Recordings were made with a Beckman type 9842 coupler (with 10 μA constant current and a time constant of 10 s). The number of skin resistance responses (SRRs) to the 20 stimuli were counted. A SRR was defined as a change equal to or greater than 500 ohm with a latency of 1 to 5 s.

Results

Finger Pulse Responses

Usable finger pulse (FP) data were obtained from 10 patients. By averaging the 5 prestimulus and 30 poststimulus amplitudes over the 10 trials of each condition, mean individual FP responses for F and B were calculated. For an evaluation of individual-evoked responses, a Wilcoxon test was performed to compare the last prestimulus pulse to the smallest poststimulus pulse. The patient was considered a 'responder' if the value of the test statistic exceeded the critical value for $P = 0.05$ for at least one stimulus condition. Accordingly, there were 9 'responders' and 1 'non-responder' (Patient 3). All FP responses were vasoconstrictions. The average FP changes from the last prestimulus pulse for the 9 'responders' are presented in Fig. 1. There is no indication of stronger responses to the name played forward.

A second method was used for the comparison between both stimulus conditions: The percentage change from the mean of the 3 last prestimulus pulse values to the smallest of the 3–20 poststimulus pulses was calculated. Since it could be possible that distinct responses and differences would only emerge on the first trial(s) or the last trials (due to habituation or sensitization), a comparison between both stimulus conditions was performed separately for responses to the first presentation of F and B[1] as well as the mean responses to stimuli 1–5 and 6–10. The results are summarized in Table 2. There are no significant differences between the stimulus conditions (t-tests for correlated means). The greatest difference between means in the expected direction occurred at the first presentations of F and B. However, responses were highly variable[2].

Heart Rate

Usable heart rate (HR) recordings were obtained from 11 patients. Initially, as for finger pulse, average individual responses were computed and evaluated statisti-

1 In 5 patients the first stimulus was F followed by B and 4 patients started with B followed by F (the same was true for heart rate 'responders')

2 The FPR difference between F and B at trial 1 was also checked with a Wilcoxon test because of the skewed distribution of the data ($\hat{R} = 11$; $P > 0.05$ in a one-tailed test)

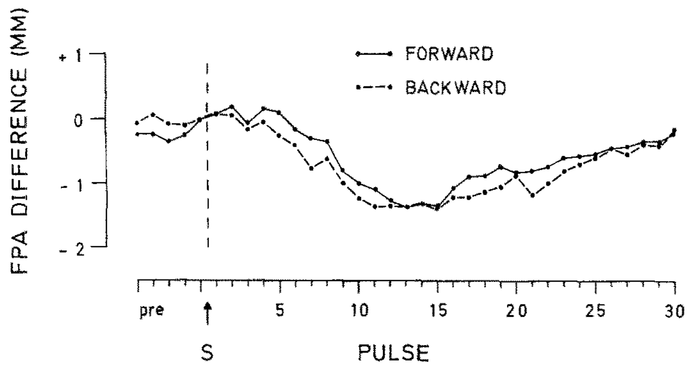

Fig. 1. Average changes of finger pulse amplitudes (FPA), referred to the last prestimulus pulse in 9 'responders' at vigilance grade 3

Table 2. Mean finger pulse and heart rate responses (FPR, HRR) to the name played forward (F) and backward (B) at trial 1 and for mean responses of trials 1–5 and 6–10

Stimuli		FPR (%) ($N=9$)			HRR (bpm) ($N=9$)		
		$\bar{x}$	SD	t*	$\bar{x}$	SD	t*
Trial 1	F	23.11	16.53	1.26	4.75	2.78	1.07
	B	11.22	18.53		4.13	2.97	
Trial 1–5	F	16.78	5.04	0.55	4.65	2.57	0.74
	B	15.13	7.27		4.39	2.10	
Trial 6–10	F	15.33	7.50	−1.33	4.72	2.52	1.60
	B	20.38	8.50		4.26	2.04	

* For $t=1.86$, $P=0.05$ (in one-tailed test)

cally. There were 9 'responders' and 2 'non-responders' (Patients 3 and 8). Three of the 'responders' showed accelerations, four reacted with a deceleration, and one showed a bidirectional response (deceleration followed by acceleration). Because of the interindividual variation in response shape, no average responses for 'responders' were calculated.

To test the differences between F and B for their significance, the ranges of the 5, 10, and 20 poststimulus beats (fastest minus slowest) were separately compared. As for FP, an analysis was performed for trial 1, trials 1–5, and trials 6–10. Differences between F and B were most frequently seen when 20 poststimulus beats were analysed. These results are shown in Table 2. The range tended to be higher after the name was played forward, but the difference between both conditions for 'responders' was not found to be significant when tested with a t-test for correlated means.

Electrodermal Responses

Electrodermal recordings were obtained from 9 patients. There was a high interindividual variability in skin resistance levels. The measurements taken before presentation of the first stimulus ranged between 25 and 380 kohm · cm^2 with a median of 205 kohm · cm^2.

There were 8 'responders' (who reacted to at least 1 of the 20 stimuli) and 1 'non-responder' (Patient 5). The total number of SRRs of all 8 'responders' to F was 27 and to B 24. The number of total individual responses to F ranged between 1 and 9 (median = 1.5) and to B between 0 and 9 (median = 2.0). Thus, no noteworthy difference between stimulus conditions was found, although the name played forward tended to elicit a few more responses[3].

Discussion

The lowest MCS vigilance grade (von Cramon, 1978) of severely poisoned patients at which somator-motor and/or autonomic responses to their names can be observed is vigilance grade 3. At this level of impairment patients are able to react with turnings of the head toward or away from a stimulus or to open their eyes when stimulated with the MCS stimuli. However, no communicative responses (eye contact or verbal utterances; grade 4) are observed. Is the feature of stimulus meaning of major importance for the elicitation of autonomic responses to the patient's name at this level of impairment? The data do not provide evidence that the reactions of poisoned patients (of this vigilance grade) when called by name depend on the meaning of the stimulus. There were no significant differences between cardiovascular and electrodermal responses to the name and a control stimulus lacking personal significance for the patient. Thus, caution should be exercised when interpreting an opening of the eyes in response to calling a comatose patient by his name as a sign of his cognitive capacity.

Responses were rather small as compared, for example, with responses of healthy subjects to less intense, nonsignificant auditory stimuli during sleep (Baust and Marbaise, 1971). Thus, it cannot be argued that strong responses to both stimulus conditions possibly mask the effect of stimulus significance.

Variability was high in electrodermal measures, with the median number of responses being low and the median tonic level being high. This is consistent with results from previous reports on electrodermal activity in coma from drug overdose (Schuri and von Cramon, 1979) and in comatose patients with brain lesions (Bjornaes et al., 1977). For the evaluation of these results disturbed peripheral mechanisms must be considered. There were patients exhibiting dehydration (which results in high skin resistance levels). Furthermore, it is known that necrosis of sweat glands can occur in acute poisoning (Brehmer-Andersson and Pedersen, 1969).

The rise of vigilance from severe coma to full attention is accompanied by increasing differentiation of behavioral responses (von Cramon, 1978). With

3 Due to the high interindividual variability of electrodermal measures which may partly be due to disturbed peripheral mechanisms (Bremer-Andersson and Pedersen, 1969), no attempt was made to evaluate exact amplitude information

increasing vigilance, the physical properties of stimulus should therefore evoke a response before this response is influenced by the personally significant information of the stimulus, the latter including a more complex processing of information. At a higher level of vigilance we should expect a stronger effect of the feature of stimulus meaning.

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