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Tactile Stimulation in Acute Tbi Comas. a Comparative Analysis of Healthy Adults and Children.

Medical Science
KEYWORDS :

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ABSTRACT

The slow C-fiber tactile stimulation induces in healthy adults' limbic system activation was followed by the emotional response. The pleasant touch compared to the other tactile stimuli can be provided by low-threshold mechanosensitive C fibers that innervate the hairy skin and can be used in rehabilitation of comatose patients. 25 healthy adults, 20 children 5–6-years and 19 severely comatose patients were passively touched by soft, rough, and sharp stimuli on the left wrist. EEG was recorded during the resting state and the stimulation using the portable "Entsefalan" device. The spectral analysis showed delta and theta power decrease compared to background level for coma patients with CT stimulation only most pronounced over the right parietal regions.

Introduction

The EEG comatose state patterns are usually described by the absence of sleep and wake cycles, loss of dynamic changes to external stimulation or any commands, and slow wave dominance [13]. Extensive damage to the upper brain stem may appear in the EEG as deep physiological sleep, and can be characterized in the EEG as different reactivity to sensory stimuli: general activation with faster waves or with intervals of slow waves [29], [21]. Damage to the pons usually affects consciousness, characterized by the persistent bilateral rhythmic activity (so-called alpha/theta/alpha-theta coma) [32], [12], [17].

The clinical cases showed that emotional stimulation leads some patients to the path to recovery [3]. For example, relatives' voices and touches were shown to induce a response in comatose patients [26], [27]. The emotional stimulation is effectively applied in rehabilitation programs of TBI patients and even improves cognitive functioning in TBI patients [8]. Stimulation of any sensory modality could improve brain recovery [4]. Our finding is consistent with previous studies by Mitchell et al. [23], [18], [26], who observed that unconscious patients improved faster after applying a sensory stimulation [26].

In our research, we focused on pleasant and unpleasant tactile stimulation, which as previously shown induced statistically significant increases in EEG and EMG parameters in patients with persistent vegetative state [15], [11]. The tactile stimulation can be used in comatose patients, and in our study we investigated what types of these stimuli would be most conducive to recovery for comatose patients [16]. The ERP and MMN studies have shown the predictive value of somatosensory evoked potentials and mismatch negativity in the prognosis for an absence of full recovery [19]. To prevent sensory deprivation after brain injury in unconscious patients, a sensory stimulation program beginning in the early stage of injury may be useful [23]. Frequent sensory stimulation could facilitate dendritic growth, neuronal reorganization, and synaptic reinnervation, and improve the rate of recovery from coma [1], [14], [23], [30].

Meanwhile, according to McGlown, touch plays an important role in many forms of social communication [22] and always includes addictive emotional information depending on the force, velocity, and duration of the touch. This work showed that slow C-fiber stimulation induced in healthy adults' limbic system activation was followed by the emotional response. The pleasant touch can be provided by low-threshold mechanosensitive C fibers that innervate the hairy skin representing the neurobiological substrate for the affective and rewarding properties of touch [22]. In these points of view, soft brush stimulation could be more useful in comatose patients than rough or painful stimulation, because of its links to the limbic system and possible emotional response. In our study, we investigated the brain response of the comatose patients to the different types of tactile stimuli including slow C fibers stimulation, deep sensibility stimulation, painful stimulation, and tactile stimulation with the cognitive component included. Our aim was to confirm that the most important stimulation for unconscious patients is the low-threshold mechanosensitive C fibers.

Subjects:

EEGs were recorded from different groups of subjects, including comatose patients, healthy children, and healthy adults. 1) 25 healthy adults (average age 23.6 years, 18 males). 2) 19 severely comatose patients 2–10 days after coma onset. The outcome was assessed 3 months after coma onset (average age was 21.2 years, 9 males). 3) 20 children 5–6-years (average age 5.6 years, 11 males).

According to the slow-wave reactivity of our patients, their response may be related with thalamocortical damage and classified as Grade 2 of Synek's gradation of EEG changes [31]. This suggestion can be supported by the investigation, which showed that full unconsciousness after TBI can be achieved if the thalamocortical interaction was damaged [24]. All of the patients were unable to open their eyes, were unresponsive to the painful, verbal, or other stimuli, and had scores from 3–7 on the Glasgow Coma Scale. The patients were placed in an Intensive Care Unit. Three months later after injury 1 patient died, 4 progressed to a vegetative state, 6 patients were diagnosed with a minimally conscious state, and the other 8 patients began speaking and regained awareness of their surroundings.

Experimental setup

The experiment was conducted in a silent room. Subjects were instructed to keep their eyes closed.

Subjects were passively touched by soft, rough, and sharp stimuli on the left wrist. The choice of the left hand was due to the fact that the right hand was used for acute care procedures (catheters, etc.).**Stimuli**

Subjects were passively touched by 4 types of tactile stimuli on the left wrist. Our stimuli were presented with a velocity of about 3–5 cm per sec. Healthy adults put eye bandages over their eyes and inserted earplugs to block the noise. Soft cosmetic brush

Rough shoe brush Wartenberg neurowheel stimulator

The cognitive tactile stimulation included letters by finger (most of the patient's name and some of the words meaning something pleasant ("happiness").

The tactile stimuli were changed randomly every trial and each trial lasted for 30 seconds. The experiment consisted of 40 trials (10 trials per each stimulus). Every three seconds within the trials a break for 200–500 ms was made to reduce habituation.

The stimuli first past through the approbation procedure using 47 healthy adult experts. The stimuli materials and procedure were chosen for being the most "pleasant," "rough," "thorny," and "recognizable." To designate the moments of the stimuli onset-offset, we marked the moment when the moment of the touch began and ended; the stimulation was manual and synchronization was not precise enough for event-related measures. Before the data analysis, we rejected 200 ms at the beginning and the end of each trial.

Statistical analysis:
A Fourier Transform (FT) is performed on these sections of the EEG data to determine the power content of the frequency bands in order to perform spectrum analysis. The resulting waveforms are displayed as a brain map to show the power distribution within each frequency band. FT is applied to 10 different auditory blocks of the EEG signals (These signals are obtained from the same subject and during the same task and listening). All the windows with EOG artifacts (amplitudes exceeding 80mV) were deleted from further analyses. Artifact-free windows were subjected to a fast Fourier transform (FFT) algorithm, which yielded power in mV2/Hz. Artifact-free windows were subjected to a fast Fourier transform (FFT) algorithm. We have analyzed statistically significant differences of power of the rhythmic activity registered during the presentation of different types of stimuli compared to background using Matlab and Statistica 6.0. :The t-test differences for each type of stimuli compared to the background rhythmic activity were calculated, as well as

The repeated measures ANOVA effects of lateralization, topography, and group (Statistica 6.0.). For statistical analyses, electrode positions were topographically aggregated as follows: Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, Pz, P3, P4, T5, T6, O1, O2.

EEG Recording
EEG data was recorded using the portable "Entsefalan" device with 19 Ag-AgCl electrodes placed on the scalp according to the International 10–20 System (Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, Pz, P3, P4, T5, T6, O1, O2) under the experts' clinical supervision. The EEG data was collected in continuous mode, using a 250 Hz sampling frequency for all the subjects. The EEG recording time for each subject was no more than 45 minutes. The cut-off frequencies for the filters used were 0.15 Hz for the high pass and 100 Hz for the low pass. This range allowed us to eliminate unwanted frequency components and, at the same time, fit our data to the spectrum ranges most common when analyzing EEG signals. Eye movement (electrooculogram, EOG) was recorded from electrodes placed above and below a subject's left eye to allow for the removal of artifacts from the EEG. Another electrode, which was placed at the center of the forehead, was grounded. All the electrodes were maintained below 5000 ohms, and the impedance difference between the left and the right was not allowed to exceed 500 ohms. EEG preprocessing was carried out with MATLAB (The MathWorks) and EEGLAB [20].

Results

The smooth brush stimulation showed the delta- and theta-rhythm power reduction in comatose patients, children, and healthy adults in the central, temporal, and left parietal areas (T3, C3, Cz, C4, T4, T5, P3, O1, $p<0.01$) (Pic. 1).

The rough brush stimulation showed the delta-rhythm power reduction in comatose patients and children and the delta- and theta-rhythm power reduction in healthy adults in the central and right temporal areas (T4, Cz, C4, P4, $p<0.01$).

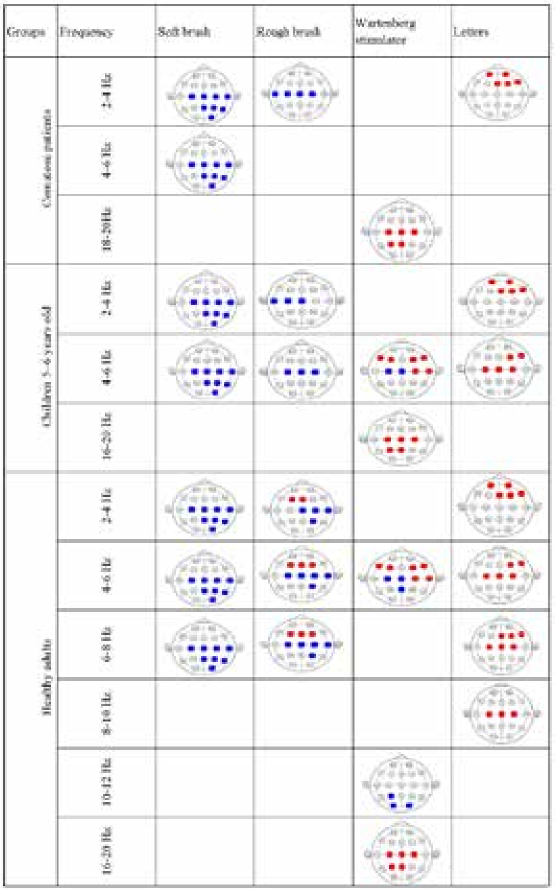
The neurological roller induced in all groups of subjects (patients, children, and healthy adults) the beta-rhythm power acceleration (16–20 Hz, 18–20 Hz in patients) in the central and parietal areas (C3, Cz, C4, P4, Pz). In children and healthy adults the theta-rhythm power reduction was found in the central and frontal areas (C3, Cz) and acceleration in frontal areas (F3, F7, F8, C4, T4, F4). In adults the alpha-rhythm reduction was also found (P4, O1, O2).

The cognitive tactile stimulation induced delta-rhythm power acceleration compared to the background in comatose patients and frontal areas in children (Fp1, Fp2, Fz, F8, F4). In healthy adults and children the cognitive tactile stimulation also induced the theta-rhythm power acceleration in the central and right frontal areas (C3, C4, Cz, F4, F8). In healthy adults the alpha-rhythm acceleration (8–10 Hz) in the central areas (C3, C4, Cz) also was higher.

The EEG rhythm power did not show any significant differences in patients with a different outcome. *The average rhythmic-power reduction and acceleration compared to the background is presented in table 1.*

	Rhythms	Soft brush	Rough brush	Wartenberg stimulator	Letters
Comatose patients	δ	42%	21%		15%
	θ	28%			
	β			3%	
Children 5–6 years old	δ	38%	22%		12%
	θ	31%	12%	7%	8%
	β			12%	
Healthy adults	δ	31%	25%		
	θ	15%	14%	12%	6%
	α			12%	21%
	β			11%	

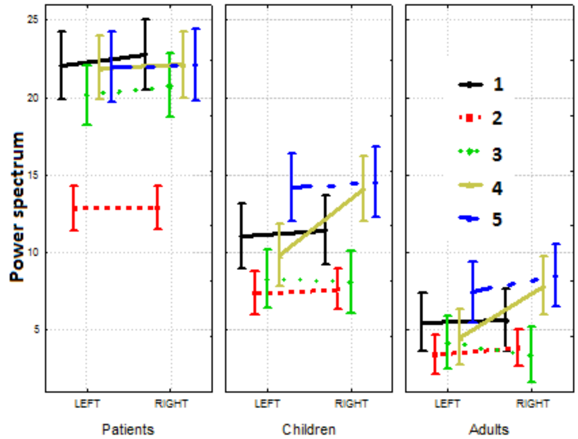
Table 1. The average percentage of *rhythmic-power reduction and acceleration compared to the background.*



Pic.1. The t-test for significant differences in the rhythmic power to the tactile stimuli compared to background for each EEG channel for each group separately, p<0.01

Discussion

The present results demonstrate that tactile stimulation causes delta-, theta-, and beta-band power changes in comatose patients. The most pronounced response was aroused by the soft brush stimulation and consisted of the theta-rhythm power significant regression. The other tactile stimulation showed significant theta-band power changes in children and healthy adults, but not in comatose patients (Pic. 2). According to our hypothesis, the most significant response in unconscious patients was prevented for the stimulation of the low-threshold mechanosensitive C fibers, and we registered the theta-rhythm power deceleration to the soft brush. These data are comparable to the previous studies investigating the rhythmic modulations induced by tactile stimulations and showed that the theta-rhythm power depends on the roughness of the tactile stimulation. The theta oscillations showed to be sensitive to physical properties of tactile stimuli (low, mid, and high levels of roughness) and were higher for high roughness tactile stimulation compared to the low [25]. The other data showed similar differences in theta-rhythm oscillations for two types of stimuli – smooth and rough. During stimulation, theta wave activities under smooth stimuli were significantly lower than those under rough stimuli [10],[16]. Therefore, we should find the theta-rhythm power acceleration to the rough stimuli as we see in healthy adults and children, but not in comatose patients.



Pic.2. Theta power (4-6 Hz) for C3-C4 electrodes for resting baseline (black) and for different tactile stimulations. 1 (Black) – resting baseline condition, 2 (Red) – soft brush stimulation, 3 (Blue) – rough brush stimulation, 4 (Dark yellow) – sound of coughing, and 5 (Wine) – wide Wartenberg neurowheel stimulation. The whiskers are SDs.

We compared the EEG response of comatose patients with the EEG responses of healthy adults and preschool children. According to the studies in patients with brain impairments, there is a kind of recurrence of the electrical activity that is more similar to the electrical activity of preschool children than healthy adults [9]. The data shows that unconscious patients' electrical activity can be characterized by slow-oscillation prevalence with specific wave localization similar to small children EEG [6]. In our research, the comatose patients' response to the tactile stimulation was similar to the preschool children's EEG changes when compared to the healthy adults. In healthy adults alpha-rhythm power changes were found during thorny roller and written letter tactile stimulations; these changes were not registered in children or comatose patients. Moreover, the theta-rhythm acceleration to the rough brush stimulation was found only in healthy adults, but not in comatose patients and children.

For the soft brush, rough brush, and written letter stimulation we found the delta-rhythm power changes: for the soft and rough brush stimulation the delta power regression was registered. Electrical activity observed in comatose patients can be characterized by slow frequency bands [33], [2], increased delta-rhythm, and decreased alpha-rhythm in TBI patients [7]. Thus, the delta-rhythm power reduction can be suggested to be the brain activity increase.

Our data also showed that thorny roller stimulation induced toe beta-rhythm power acceleration in all groups of subjects; the changes in beta-rhythm were not found in response to the smoother stimuli. The previous data showed that the beta wave activity under smooth stimuli was also significantly lower than those under rough stimuli [10]. According to our data, the beta-rhythm power changes were accompanied with alpha- and theta-rhythm power changes in healthy subjects and were the only changes in comatose changes. Therefore, we suggest these beta-rhythm power accelerations may just be the effect of muscle irritation during painful stimulation.

Conclusions

Prominent delta and theta power decrease compared to background level for coma patients with CT stimulation only (Condition effect p<0.0001)

Most pronounced over the right parietal regions
Similar but less pronounced effect for both preschool children and healthy adults

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