# CHANGES IN EVOKED POTENTIALS IN THE EEG IN MAN DURING COMBINATION OF TWO INDIFFERENT STIMULI

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Evoked potentials during the formation of a conditioned reflex have been investigated chiefly in animals [1, 2, 3, 7], with highly conflicting results. Some authors [2, 3] observed an increase in the amplitude of the primary response to sound in the course of formation of a conditioned defensive reflex; others [11] observed weakening of the primary response to the sound acting as the conditioned stimulus. The primary response became more marked during acute extinction of the conditioned reflex.

G. D. Kuznetsova [6] investigated evoked potentials in a rabbit during combination of a tone with a flash of light, and found that after repeated application of the acoustic and photic stimuli, the sound alone evoked a variable response in the optic region, resembling in form the primary response to light.

In man, evoked potentials during formation of a conditioned motor reaction to a flash of light were investigated by I. A. Peimer [9]. During the formation of the reflex an increase in the amplitude of the negative phases of the local responses was observed in the region of the thalamus and an increase in the amplitude of the wave of potential in the central region of the cortex. The latent period of the conditioned-reflex reaction corresponded to the interval between the flash of light and the apex of the potential in the central region. L. Kats [5] showed that in the EEG of the human brain the nonspecific response may appear as a conditioned reflex to time.

The object of the present investigation was to study evoked potentials during the formation of a connection between two indifferent stimuli - a tone and a flash of light. Several investigations [5, 14, 19] have shown that a

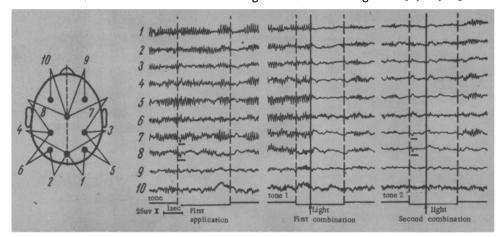


Fig. 1. Restoration of nonspecific response to tone during combination of tone with light. Leads of EEG correspond to positions shown in scheme. Bottom line - marker of stimulation. Moments of switching tone on and off indicated by vertical broken lines, and moments of application of flashes of light by vertical continuous lines, The numbers on the left correspond to the serial numbers of presentation of the tone and the combination of tone with light.

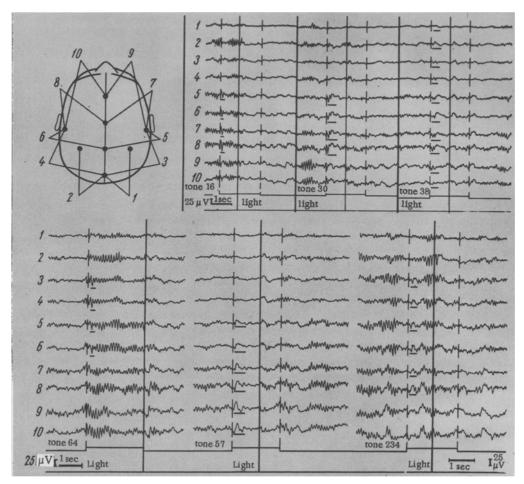


Fig. 2. Variants of localization of nonspecific response to tone in EEG of a human subject during combination of tone with light on the 2nd and 10th days of investigation. Leads of EEG correspond to positions shown on scheme. Bottom line — marker of photic stimulation; second line from bottom — marker of acoustic stimulation (tone 1). The figures on the left are serial numbers of the combination of tone with light.

"nonspecific" response appears in the EEG in response to a tone in the region of the vertex, and disappears when the stimulus is repeated. Besides the nonspecific response in the region of the vertex, a response also develops to light in the occipital region [10, 15, 17, 18, 20]. It is associated with the optic projection zone and is not extinguished during repeated stimulation. This response we call the specific response to light. Hence, during the action of a tone a nonspecific response is recorded in the EEG, and this is extinguished during repetition of the stimulus, and during the action of light there is a nonspecific response, which also disappears, and a specific response which is not extinguished during repeated stimulation. Accordingly, a tone was used as the conditioned stimulus and a light as the unconditioned. Since a nonspecific response may arise when the stimulus is switched both on and off, the flash of light was applied in the middle of the action of the tone, so that the response to switching off the tone did not coincide with the response to the light.

#### EXPERIMENTAL METHOD

The tones were produced by a type ZG-10 audio-frequency generator and had a frequency of 500 cps (tone 1) and 1000 cps (tone 2), an intensity of 56-58 dB or, in some experiments, 74 dB over the threshold of audibility, and a duration of 2 or 4 sec. The flash of light was applied by a "Kaiser" photostimulator and a Soviet noiseless FS-1 photostimulator. The intensities of the flashes of light were 0.6 J for the "Kaiser" apparatus and 1000 J for the FS-1, and their duration 75-100  $\mu$  sec. The intervals between the tones were equal (18 or 21 sec).

The EEG was recorded on a 15-channel ink-writing "Alvar" electroencephalograph. Altogether 96 investigations were made on 25 healthy subjects aged 18-35 years.

#### EXPERIMENTAL RESULTS

Nonspecific Response to Tone. In 23 of the 25 subjects a nonspecific response was recorded. In 19 persons the investigation began with extinction of the reaction to the tone; in 17 of these a nonspecific response was observed (well-defined in 10 and ill-defined in 7 persons). The tone was applied repeatedly until the nonspecific response was extinguished. The response to tone 1, after preliminary extinction, was renewed after application of tone 2. Extinction of a well-defined nonspecific response was sometimes unstable, but if it reappeared it was always of lower amplitude and longer duration than formerly. In 16 of 17 persons, when the tone and light were combined, a previously extinguished of weakened response to the tone was restored. An increase in the amplitude of the nonspecific response to the tone during the 2nd or 3rd combination of tone and light, by comparison with the response to the tone in the 1st combination, was observed in 6 persons. Restoration of a previously extinguished nonspecific response to the tone was observed during the 2nd combination in 8 persons, and during the 3rd in 2 persons.

As an example the EEG of subject P may be considered (Fig. 1). During the 1st presentation of the tone a non-specific response was recorded in the parietocentral regions, and it was extinguished fairly quickly. After 9 presentations of the tone combinations of the tone and light were given. During the 1st combination the reaction to the tone was absent, but during the 2nd combination a clear nonspecific response appeared in the same regions, and was also recorded in the posterior divisions of the hemispheres.

In some subjects the reaction to tones 1 and 2 was extinguished at the beginning of the investigation; subsequently the combination of tone 1 with the light was alternated with tone 2. After the first combination of tone 1 with the light the nonspecific response to tone 2 also was restored.

In the course of combination of the tone with the light, the region where a nonspecific response to the tone appeared was changed. At the beginning of the investigation it was recorded in the parieto-central and middle frontal regions. In the occipito-parietal regions a response to the tone during the first presentations of the tone was observed in only one of the 23 subjects investigated. Of the 22 persons in whom a response was recorded in the middle and anterior regions of the hemispheres, 2 were investigated once. Of the 20 persons investigated more than once, in 18 the nonspecific response to the tone was observed to spread or to shift in the course of the combination of the tone with light to the posterior regions of the hemispheres. The nonspecific response to the tone during the combination of tone with light was observed in the posterior regions of the hemispheres on the 1st day of the investigation in 4 persons (in 3 of them the combinations were presented at once, without preliminary extinction of the reaction to the tone), on the 2nd day — in 12, and subsequently (on the 4th and 7th days) — in 2 persons.

The different variants of the localization of the nonspecific response to the tone combined with the light, observed on the 2nd and subsequent days in subject P., are shown in Fig. 2. A nonspecific response to the tone was recorded in the parietal and central regions (16th and 30th combinations), and in the occipital and parietal regions (54th combination); sometimes a response was seen in all regions (38th combination); in isolated cases it appeared in the anterior divisions of the hemispheres (57th combination). On the following days a nonspecific response to the tone was also recorded in the posterior divisions of the hemispheres (234th combination, 10th day of investigation).

Evoked Responses to Light. The nonspecific response to light during application of combinations of the tone with the light appeared more consistently and regularly than the nonspecific response to the tone. With the same number of stimuli, on the 2nd day of the investigation the nonspecific response to light developed much less frequently than on the 1st day, although on the 3rd day it was again recorded regularly. Hence, the nonspecific response to light behaved quantitatively in a periodic manner, for on the 2nd day of the investigation it was recorded very irregularly.

On the 1st day of the investigation a specific response to light was observed in 15 of 25 persons, well-defined in 6 of them an ill-defined or irregular in 9. Of these 25 persons, 14 were investigated once or twice, 9 repeatedly (from 4 to 11 times), and 2 in accordance with a special scheme. Changes in the specific response to light in the course of the combination of tone and light were detected in 9 subjects investigated more than once. In the course of the experiment the response to light became more definite, or appeared for the first time (if absent on the 1st day), i.e., an optimum was observed in the manifestation of the specific response to light. In different subjects this optimum fell on different days. After 1-2 days of optimal manifestation the response disappeared, but sometimes reappeared on the following days.

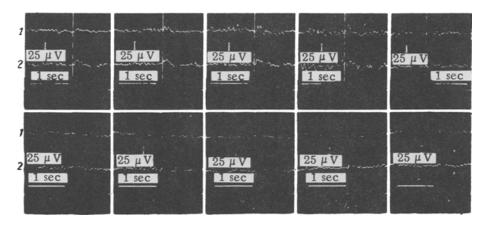


Fig. 3. Changes in the specific response to light in the EEG of a human subject during a combination of tone with light. Serial numbers denote days of investigation. Leads correspond to 1-2 on the scheme in Fig. 2. Vertical line - marker of photic stimulation. Downward deviation - positivity, upward - negativity.

In accordance with the intensity of the specific response to light on the 1st day of the investigation, these 9 persons fell into 3 groups:

- 1) In 3 persons a clearly defined specific response was observed; in one of these the optimum of manifestation of the response fell on the 4th-5th day and in another on the 6th day. In one subject the response developed more or less uniformly and no clear optimum was observed;
- 2) In 3 persons the response developed irregularly. In 2 of them it became regular on the 2nd-3rd day; in 1 person no changes in the nature of the response were observed;
- 3) In 3 persons there was no response. It appeared in the course of the investigation in one person on the 2nd day, in one on the 4th, and in the third on the 6th day.

Hence, in 7 of the 9 subjects an optimum of manifestation of the specific response to light was observed in the course of the combination of the tone with the light, while in 2 persons no optimum was recorded. On the 2nd-3rd day an optimum was observed in 3 persons, on the 4th-5th day - in 2, and on the 6th day - in 2.

In some subjects, on the day that the specific response to light was optimal, it became well-defined in form and its amplitude increased. As an example we give the EEG in subject Sh (Fig. 3). Optimal intensity of the response was observed on the 4th and 5th day of the investigation. The response on these days was well defined and increased in amplitude (No. 4-5). A sharp fall in the number of specific responses on the 6th day of the investigation was combined with marked weakening of the response (No. 6). On the 7th day the number of responses again increased, and the response became more clearly defined (No. 7). On the 8th day the number of responses again fell, but in the cases in which a response developed it was very clear (No. 8).

The dynamics of the nonspecific response to the tone during application of the tone alone and during the first combinations of the tone with the light corresponded to the dynamics of extinction and subsequent restoration of the orienting reflex, which it evidently reflects. This hypothesis appears very probable, for both the nonspecific response and the orienting reaction have recently been associated by many authors with the same structures of the brain [19, 21]. Direct measurement of the excitability of individual regions of the brain [8] has shown that a stimulus of signal value causes increased excitability in a focus of reinforced stimulation, and with consolidation of the conditioned reflex the possibility of stimulation attaining signal value at a particular point is increased. Electrophysiological findings [4] indicate that foci of high-amplitude activity may arise in zones adequate in relation to the stimuli during the formation of a conditioned reflex. The spread or shift of the nonspecific response to the tone into the posterior divisions of the hemispheres is evidently associated with increased excitability in the occipital regions. This is also demonstrated by the shift of the nonspecific response to the tone, presented against the background of rhythmic flashes of light, into the posterior divisions of the hemispheres, which we observed in some subjects. This phenomenon will be examined in detail in a special communication.

It has been found [12] that a stimulus with signal value causes a change in the level of the constant potential in the cerebral cortex. It is also known [16] that the character of the manifestation of evoked potentials is dependent on the level of the constant potential. The changes which we have observed in the manifestation of the specific response to light may well be associated with these phenomena.

#### SUMMARY

A study was made of induced potentials in the EEG of man following combination of a tone with a flash of light. In most of the persons examined, a nonspecific response to a preliminarily extinguished tone was reproduced after its very first combination with light. On the 2nd day of investigation the area of its manifestation was shifted to the posterior portions of the hemispheres. During subsequent days the response came irregularly sometimes in the anterior and sometimes in the posterior portions of the hemispheres. Nonspecific response to light, combined with the tone, appeared irregularly from one experiment to another; during the second day (as compared to the first) its manifestations were very irregular.

On certain days of the investigation the specific response to light had an optimal intensity, the number of reactions subsequently declining, down to complete disappearance of the response.

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