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HABITUATION: ELECTRICAL CHANGES IN THE VISUAL SYSTEM*

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Abstract—The amplitude of neuroelectric potentials evoked in the visual system by repetitive exposure to a two-second period of light was analyzed. At the optic nerve and lateral geniculate nucleus consistent decrement occurred in two stages. Stage 1 consisted of a sharp decline in amplitude over the first few trials; Stage 2 occurred more gradually over the course of a week of trials. Whenever consistent decrementing occurred it was accompanied by a shift in the power distribution among EEG frequencies. Specifically, a decrease in power of 37–50 and 72–80 Hz occurred. At the striate cortex no such consistent decrementing was found. Instead, while some electrodes did record a decrement, others showed an increment and still others no change in amplitude over the week of testing. Since each electrode recorded reliably and consistently, the conclusion was reached that at the striate cortex, habituation constituted a *pattern* of response. The significance of this finding was discussed in terms of the exquisite specificity of habituation to modality and the neural structures that have been found involved in the habituation process.

INTRODUCTION

THE ORIENTING reaction and its habituation constitute a fundamental adaptive pattern of vertebrates [1, 2]. Over the past decade a number of investigations [3–6] have demonstrated exquisite specificity of this adaptive reaction to the modality and the spatial and temporal configuration of the input. In addition a large number of neural systems, even those of invertebrates [7], have been shown important to the process [8–13]. In view of these findings we deemed it appropriate to once again investigate the course of orienting and habituation of various stations in an input system with the aim of resolving for ourselves some of the discrepancies among the reports of previous research. Specifically, some of these studies [14–16] report consistent decrementing of the amplitude of the neuroelectric response evoked during the orienting reaction with repetitive stimulation; others [17] using carefully controlled procedures find no such consistency.

To this end we implanted small electrodes in the optic nerve, lateral geniculate nucleus and striate cortex and studied the responses evoked by the onset of a two-second period of colored light. Data analysis included the initial responses evoked, the changes in their amplitude over a succession of trials on each day of testing, and the changes that occurred over a week of testing. In addition, for these same trials, power spectra of the possible changes in frequency distribution of the EEG were determined.

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METHOD

Subjects

The subjects were five immature rhesus monkeys. Each subject was chronically implanted bilaterally with 24 bipolar, 300μ nichrome wire electrodes in the following loci: optic nerves, lateral geniculate nuclei, and striate cortices (both with intracortical and epidural electrodes). One subject also had electrodes placed in the superior colliculus. The optic nerve electrodes were positioned by visual inspection after surgical exposure and elevation of the frontal lobe. The depth electrodes were stereotaxically placed and electrode recording sites were selected by monitoring on an oscilloscope to secure the position of maximal response.

Procedure

The fully awake monkeys were placed into a restraining chair and put into a dimly illuminated experimental testing box with a constant low background of white noise for a ten-minute adaptation period prior to testing. The head was secured with a foam padded block to insure that the animal was oriented toward the light. The eyes were approximately 16 inches from the light source and this position was held constant for all animals.

Stimuli were presented on a variable interval schedule with an average intertrial interval of thirty sec (range: 14–54 sec). Each steady light stimulus has two seconds in duration, with an intensity setting of 4.0 on the Grass Model PS–2D photostimulator. An American Electronics Laboratory stimulator was used to control the Grass unit to produce the continuous light stimulus. Colored filters (red and blue) were inserted over the face of the strobe for habituation (Light A) and dishabituation (Light B) presentations. The two filters were equated for lumens per square foot as measured by a Weston Illumination Meter (Model 756). The order of presentation of the colored filters was counterbalanced for different subjects.

Each subject was tested for eight consecutive days at 74 trials per day. The daily testing paradigm was as follows: Light A was presented for 72 habituation trials followed by Light B for two dishabituation trials. The subjects' vocalizations and movements were recorded by hand during every trial.

Atropine control sessions were carried out on two animals (one a naive monkey and the other a previously tested subject). Topical application of homatropine (5%) and neo-synephrine (0.2%) in the eyes began approximately 45 min prior to testing. To insure maximum dilation of the pupils the drugs were applied every 15 min for a total of three times. Several weeks after initial habituation trials were completed, one monkey was retested as an atropinated control on four successive days at the same time as the naive atropinized animal. The naive monkey had superior colliculus electrodes as well as cortical ones.

Data acquisition and analysis

All analog data were stored on a seven-channel Ampex Model SR-300 tape system. One channel was used to record the stimulus events. On the other six channels, continuous recordings of neuroelectric potentials were taken during the entire testing session. Since the analog data were limited to six channels for each subject, the electrode sites chosen for study were those exhibiting an appropriate latency and well defined potential evoked to flash as determined by a series of twenty pretest stimulation trials. The recording loci were the same for all monkeys: optic nerve, lateral geniculate nucleus, and striate cortex (never less than two striate electrodes per animal).

The evoked potential data were processed by displaying an individual response for each trial on the storage oscilloscope and the baseline-to-peak and peak-to-peak amplitudes measured to the nearest millimeter. Only the primary component was evaluated (as determined by the latency of onset in each station along the visual pathway). This method of analysis was chosen over computer-averaged methods so that variability of response amplitude could be taken into consideration. The *t*-test was used to evaluate changes in amplitude for all data throughout the study unless otherwise noted.

EEG data were processed and analyzed with the PDP-8 computer. Analog to digital conversion proceeded at a sampling rate of 1000 points/sec for a period of five seconds per trial beginning at the onset of the two-second steady light stimulus. The data were stored on digital tape for further processing. A special Digital Spectral Analysis program* was used for the power spectral analysis. The print-out showed the power present for each five-cycle bandpass digital filter, with the center frequencies of each band given in the graphed record. The analyzed output gave a power spectrum for each second of EEG data analyzed. A *t*-test was used to compare the digital data from each frequency band with corresponding frequencies for given blocks of trials.

Day One habituation changes were evaluated in several ways: (1) by comparison of trials 1–5 with late trials, 65–69, to look for amplitude changes in the visual-evoked potential and corresponding changes in the EEG power spectrum; (2) by comparison of the duration of EEG activation over successive trials. The duration of EEG activation for successive trials for Day One of testing was determined by calculation from an ink-written record.

Habituation changes over days of testing were evaluated by comparing the primary evoked response amplitudes for trials 1–30 on Day One with trials 1–30 on Day Eight. Dishabituation trials (#73 and #74)

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and the last habituation trials (#72) for Days One to Eight were compared as blocks for optic nerve, lateral geniculate nucleus and striate cortex electrodes.

Histology

After completion of testing, the brains were sectioned and electrode tip location was determined from histological examination. All striate and geniculate electrode recording tips were verified. Optic nerve electrodes had been inserted by visual inspection and monitored on the oscilloscope at the time of implantation and subsequently, therefore, histological verification was deemed unnecessary.

RESULTS

Short-term habituation—day one

The amplitude of the primary component of the potential evoked to the onset of light showed a statistically reliable decrement for all optic nerve and lateral geniculate responses (except in one electrode) when the first five trials were compared with five later trials on Day One of testing. By contrast, only three of the total nine striate cortex electrodes recorded such a decrease in potentials evoked (see Fig. 1). In fact, some of the potentials recorded from cortex showed a reliable increase in amplitude. This variability between electrodes was obtained even when recordings were from the same subject.

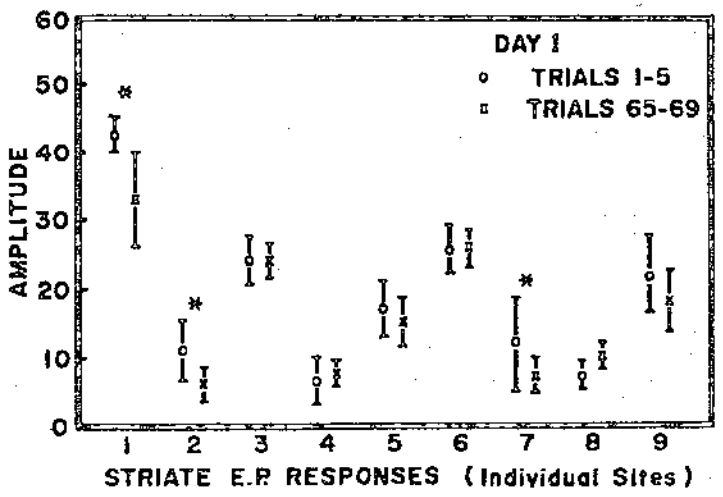

FIG. 1. Amplitude changes in striate cortex evoked potentials showing a comparison of trials 1–5 with trials 65–69 for Day One of testing. (The asterisk denotes amplitude changes which were statistically significant at <0.05 or beyond.)

The frequency changes in the EEG recorded from the striate cortex one second after the onset of stimulus correlated with these variable changes in the striate cortex potential. If there was a statistically significant decrement in the amplitude of the striate cortex evoked potential, there was a corresponding significant decrease in the power of certain EEG frequencies (37–50 Hz and 72–80 Hz). If no reliable change occurred in the evoked potential, no reliable change occurred in the EEG frequencies either.

A reliable decrease in the mean duration of EEG activation in striate cortex occurred between the first five trials of Day One (mean = 7.12 sec) compared with five late trials on the same day of testing (mean = 3.06 sec). Figure 2 shows the means of trial-by-trial duration of EEG activation (pooled data over all subjects) for Day One. The degree to which activation fluctuated over time and trials is reflected in these data.

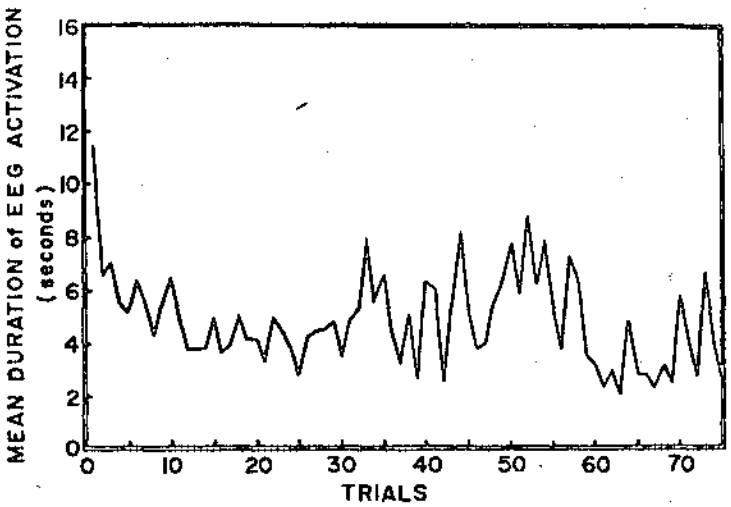

FIG. 2. Trial-by-trial mean duration for striate cortex EEG activation (in seconds) for individual trials of Day One of testing. Data were pooled over all subjects.

Long-term habituation—Day One vs. Day Eight

In all placements which showed a reliable change over days, the habituation of the potential evoked by the light onset exhibited certain characteristics. The most pronounced of these was an oscillation of the response around an over-all baseline (mean amplitude) for any one session of testing. This can best be seen by looking at the individual response amplitudes evoked during the first thirty trials of Day One and comparing them with those evoked during the first thirty trials of Day Eight (Fig. 3). It is obvious that the major decrement is an over-all shift which occurred gradually over daily testing sessions. This was a typical pattern which emerged for all loci that showed a reliable decrease in amplitude.

All leads in the optic nerve showed a statistically reliable (<0.001 level of confidence) attenuation of potentials evoked over successive days. The responses recorded at this location were extremely stable making statistical analysis easy. The lateral geniculate electrodes in all monkeys also yielded statistically reliable amplitude decrements over days (Only one placement had a level of confidence of less than 0.001 and it was 0.01.). The potentials recorded from the lateral geniculate placements were somewhat more variable than those from the optic nerve.

The potentials evoked from the striate cortex were the most variable. The long term changes in striate placements which occurred between Day One of testing and Day Eight yielded mixed results (Fig. 4). Some of the electrode placements showed a statistically reliable decrease in amplitude (<0.001 level of confidence), while responses from other sites were either essentially unchanged or actually showed a reliable (<0.001) *increase*. As in the case of short term habituation this variability was not just across animals, but was evident within a single animal.

Spectral analysis of EEG activity present in the optic nerve and lateral geniculate one second after the onset of the stimulus indicated that these loci did not exhibit a reliable change in power distribution among frequencies over days of testing. Again, however, EEG changes in striate cortex correlated with reliable changes in the potentials evoked. If there was an absence of change in the amplitude of the evoked potential, there was little change in

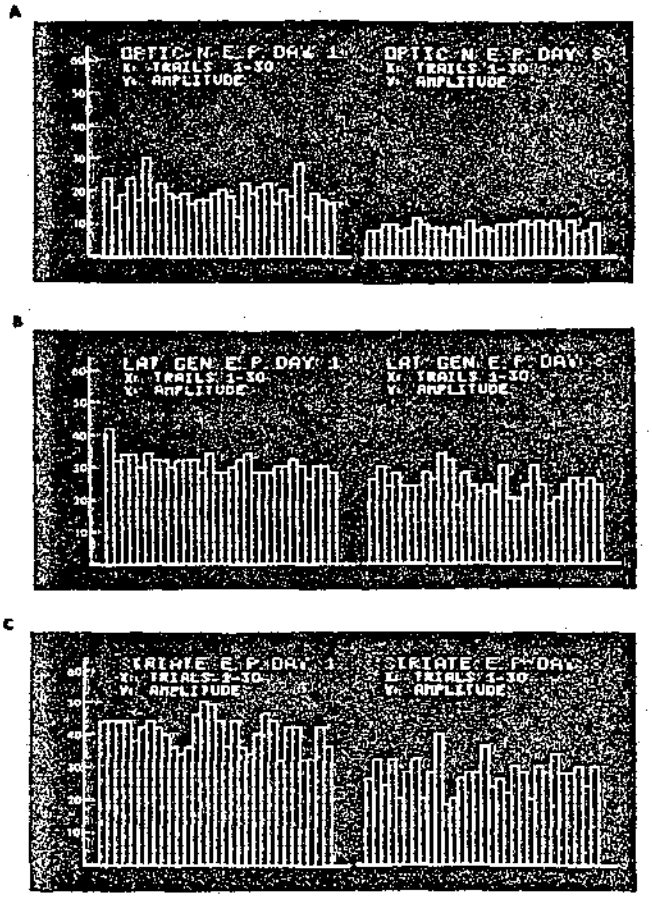

FIG. 3. Individual trials on Day One and Day Eight showing the variability observed in the amplitude of the primary component of the evoked potential for the optic nerve, lateral geniculate and striate cortex. Note the attenuation in amplitude in all leads for Day Eight trials.

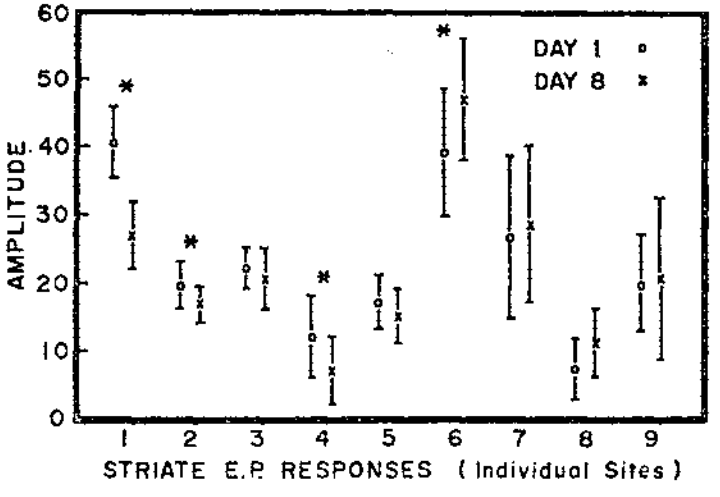

FIG. 4. Amplitude changes as shown in striate evoked potentials for trials 1–30 of Day One compared with trials 1–30 of Day Eight of testing. The asterisk denotes those changes which were statistically significant at <0.01 or beyond.

the power of EEG frequencies. On the other hand, a reliable increase in total power was found whenever there was an increase in the amplitude of the potentials evoked.

The potentials evoked in the optic nerve and lateral geniculate nucleus by the dishabituating stimulus showed no consistent pattern; the amplitude decreased in one animal, it increased or remained unchanged in others. The striate cortical electrodes, however, presented a consistent picture: a reliable decrement occurred in the amplitude of the response evoked by the first dishabituating stimulus. Further, the response amplitude of the second dishabituation trial showed a definite increase over that of the first dishabituation trial. Thus the mean response amplitude for all first dishabituation trials in all cortical leads was always less than the baseline mean response amplitude for the preceding last habituation trials. In addition, the mean response amplitude for the second dishabituation trials showed a partial restitution toward the baseline.

Atropine control

The results obtained in the atropinized monkeys were no different from those obtained in the experimental groups. Optic nerve and lateral geniculate responses in the atropinized animal showed a significant decrement (<0.001 level of confidence) in amplitude by the fourth day of testing. Two of the striate placements (in the previously habituated monkey) were also decreasing in amplitude and showed reliability at the 0.05 level. The relative amount of over-all change between Day One and Day Eight correlated with that in the initial habituation trials. Two other cortical electrodes (in the naive monkey) showed an increase in amplitude; one of these increases was reliable at the 0.001, the other at the 0.01 level. The naive animal also had statistically reliable (<0.001 level) amplitude attenuation in the superior colliculus responses with habituation.

DISCUSSION AND CONCLUSION

The results of the current experiments show that repeated stimulation produces a decrement in the amplitude of the evoked potential in the optic nerve and lateral geniculate nucleus of monkeys. This decrement has two distinct time courses: One occurs over the first few trials of the initial day; the other is more gradual and is manifest over a week to ten days. The potentials recorded from the striate cortex, though they show the same time course, do not simply decrease, however. Some potentials decrease, others increase, and some remain unchanged in amplitude. This pattern of change is similar to that reported in some previous investigations [18, 19], but differs from that of others who did report a consistent decrement to occur *throughout* primary sensory systems with habituation [14–16]. Since in the present study very small electrodes were used, it is likely that finding a pattern of response depends on sampling with any one electrode a sufficiently small population and that grosser recording washes out the differential effects.

The changes observed in the power distribution of EEG frequencies recorded from the striate cortex paralleled those obtained for the discrete potentials evoked and thus indicate that the effect of the stimulus extends beyond the duration of the distinct potential. Evidence from several sources (5, 6, 20, 21) suggests that these extended effects are more readily related to psychological variables than the initial deflections of potentials evoked.

In addition there is a distinct decrease in the *duration* of the EEG activation in striate cortex during the intial trials (see Fig. 2). This "low voltage-fast frequency" activity has been associated with "arousal" in a number of now classical studies [18, 22, 23]. All vertebrates appear to exhibit this arousal response which occurs with orienting regardless of

the sense modality involved. It is this lack of modality specificity which has led to the suggestion that the orienting response be attributed to influence of the reticular formation. According to such views, the finding that the duration of EEG activation decreases with habituation therefore implies that the reticular formation is a site of habituation [2].

The evidence that, at the striate cortex, a *pattern* of response change occurs with habituation, argues against any hypothesis that considers the reticular formation as the sole or even the primary locus involved in habituation. The work of THOMPSON [8, 9], BURES [10], and HOMSKAYA [24] and of PRIBRAM [2] has amply demonstrated that habituation is a property of neural systems such as spinal cord, colliculus, amygdala and frontal cortex as well as of the brain stem reticulum. The results of the current study, by showing a consistent decrementing at subcortical stations and the development of a pattern at cortex, suggest that, in fact, populations of cortical cells can and do habituate. This suggestion can readily be checked by unit recording.

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REFERENCES

1. PRIBRAM, KARL H. Comparative neurology and the evolution of behavior. In *Behavior and Evolution*, A. ROE and G. G. SIMPSON (Editors). Yale University Press, New Haven, 1958.
2. PRIBRAM, KARL H. *Languages of the Brain*. Prentice Hall, Englewood Cliffs, New Jersey, 1971.
3. SOKOLOV, E. N. Neuronal models and the orienting reflex. In *The Central Nervous System and Behavior*, M. A. B. BRAZIER (Editor). Josiah Macy, Jr., Foundation, New York, 1960.
4. PRIBRAM, K. H. The limbic systems efferent control of neural inhibition and behavior. In *Progress in Brain Research*, W. R. ADEY and T. T. TOKIZANE (Editors), pp. 318–336. Elsevier, Amsterdam, 1967.
5. HAIDER, M., SPONG, P. and LINDSLEY, D. B. Attention, vigilance and cortical evoked-potentials in humans. *Science, N.Y.* **145**, 180–182, 1964.
6. SPONG, P., HAIDER, M. and LINDSLEY, D. B. Selective attentiveness and cortical evoked responses to visual and auditory stimuli. *Science, N.Y.* **148**, 395–397, 1965.
7. KANDEL, E. R. and SPENCER, W. H. Cellular neurophysiological approaches in the study of learning. *Physiol. Rev.* **48**, 65–134, 1968.
8. THOMPSON, R. F. and SPENCER, W. A. Habituation: A model phenomenon for the study of neuronal substrates of behavior. *Psychol. Rev.* **73**, 16–43, 1966.
9. GROVES, PHILIP M. and THOMPSON, RICHARD F. Habituation: a dual process theory. *Psychol. Rev.* **77**, 419–450, 1970.
10. GERBRANDT, K., BURES, J. and BURESOVA, O. Investigations of plasticity in single units in mammalian brain. In *Biology of Memory*, K. PRIBRAM and D. BROADBENT (Editors), pp. 223–235. Academic Press, New York, 1970.
11. VINOGRAVADA, O. S., SEMYONOVA, T. T. and KONOVALOV, V. PH. Trace phenomena in single neurons of hippocampus and mammillary bodies. In *Biology of Memory*, K. H. PRIBRAM and D. BROADBENT (Editors). Academic Press, New York, 1970.
12. HORN, G. Neuronal mechanisms of habituation. *Nature, Lond.* **215**, 707–711, 1967.
13. PRIBRAM, K. H. The four R's of remembering. In *On the Biology of Learning*, K. H. PRIBRAM (Editor). Harcourt Brace and World, New York, 1969.
14. HERNANDEZ-PEON, R. Central mechanisms controlling conduction along central sensory pathways. *Acta Neurol. Latino-Am.* **1**, 256–264, 1955.
15. HERNANDEZ-PEON, R., SCHERER, H. and JOUVET, M. Modification of electrical activity in cochlear nucleus during "attention" in unanesthetized cats. *Science, N.Y.* **123**, 331, 1956.
16. GALAMBOS, R., SHEATZ, G. and VERNIER, V. G. Electrophysiological correlations of a conditioned response in cats. *Science, N.Y.* **123**, 331–332, 1956.
17. WORDEN, F. G. and MARSH, J. T. Amplitude changes of auditory potentials evoked at cochlear nucleus during acoustic habituation. *Electroenceph. Clin. Neurophysiolog.* **15**, 866–881, 1963.
18. SHARPLESS, S. and JASPER, H. Habituation of the arousal reaction. *Brain* **79**, 655–680, 1956.
19. MARSH, J. T., MCCARTHY, D. A., SHEATZ, G. and GALAMBOS, R. Amplitude changes in evoked auditory potentials during habituation and conditioning. *Electroenceph. clin. Neurophysiol.* **13**, 224–234, 1961.
20. HAIDER, M. Vigilance, attention, expectation and cortical evoked potentials. *Acta Psychologica* **27**, 245–252, 1967.

21. DONCHIN, E. and COHEN, L. Averaged evoked potentials and intramodality selective attention. *Electroenceph. clin. Neurophysiol.* **22,** 537–546, 1967.
22. HERNANDEZ-PEON, R. Neurophysiological correlates of habituation and other manifestations of plastic inhibition (internal inhibition). *Electroenceph. clin. Neurophysiol.*, Suppl. **13,** 101–114, 1960.
23. SOKOLOV, Y. N. *Perception and the Conditioned Reflex.* (Trans. by S. W. WAYDENFELD). Pergamon Press, Oxford, 1963.
24. LURIA, A. R., PRIBRAM, K. H. and HOMSKAYA, E. D. An experimental analysis of the behavioral disturbance produced by a left frontal arachnoidal endothelioma (meningioma). *Neuropsychologia* **2,** 257–280, 1964.

Résumé—On a analysé l'amplitude des potentiels neuroélectriques évoqués dans le système visuel par exposition répétée à une période de deux secondes de lumière. Au niveau du nerf optique et du corps genouillé latéral survenait une réduction en 2 stades. Le stade 1 consistait en un busque déclin d'amplitude des les premiers essais, le stade 2 survenait plus graduellement pendant l'évolution d'une semaine d'essai. Lorsque cette réduction survenait, elle était accompagnée par un déplacement de la distribution de puissance parmi les fréquences EEG. Spécifiquement une diminution de puissance 37–50 et 72–80 Hz survenait. Au niveau du cortex strié, on ne constatait pas une telle réduction. A la place tandis que sur certaines électrodes, on enregistrait une certaine réduction, d'autres montraient une augmentation et d'autres encore aucun changement d'amplitude dans la semaine pendant laquelle étaient passés les tests. Puisque l'enregistrement de chaque électrode était régulier et fiable, on en conclut qu'au niveau cortex stré, l'habituation représentait un *pattern* de réponse. On discute la signification de cette constatation en terme de spécificité quasi absolue de l'habituation à la modalité et d'après les structures nerveuses impliquées dans le processus d'habituation.

Zusammenfassung—Untersucht wurde die Amplitude der elektrischen Aktionspotentiale im visuellen System bei wiederholten Lichtdarbietungen von jeweils 2 Sekunden Dauer. Im N. opticus und im Geniculatum laterale fand sich dabei eine regelmäßige Abnahme und zwar in zwei Stufen. Stufe I bestand in einem raschen Abfall der Amplitude während der ersten paar Darbietungen. Die Stufe II bestand in einer allmählichen Änderung über eine ganze Woche hinweg. Immer, wenn ein klarer Abfall der Amplitude auftrat, kam es gleichzeitig zu einer Verschiebung im Power-Spektrum der EEG-Frequenzen. Die Abnahme im Power fand sich spezifisch für Frequenzen von 37-50 und 72-80 Hz.

In der Area striata des Cortex fand sich keine derartige regelmäßige Amplitudenabnahme. Hier zeigte sich während der Testwoche an manchen Elektroden eine Abnahme, an anderen eine Zunahme und an wieder anderen keine Änderung in der Amplitude. Da jede Elektrode verläßlich und gut registrierte, ergab sich als Schlußfolgerung, daß in der Area striata des Cortex Habituation in einem strukturierten Antwortmuster bestand.

Die Bedeutung dieses Befundes wurde diskutiert hinsichtlich folgender Punkte: 1. daß die Habituation außerordentlich spezifisch ist für die jeweils untersuchte Sinnesmodalität und 2. bezüglich der neuralen Strukturen, die bei der Habituation beteiligt sind.