Reports

Harmonic Oscillation as Model for Cortical Excitability Changes with Attention in Cats

Abstract. A single shock to the prepyriform cortex with implanted electrodes caused a damped, sinusoidal oscillation in potential. The root-mean-square amplitudes of potentials evoked by short trains of stimuli, when plotted against the frequency of stimulation, fitted the equation for forced harmonic oscillation when the cat was attentive to the stimuli.

An attentive animal is necessarily awake and will respond to some events in its environment but not to others. The pattern of excitability for each animal is variable and can be modified systematically by learning. A relevant response to a particular stimulus does not necessarily imply attention, since there is always some level of probability that the response occurs accidentally in conjunction with the stimulus. By increasing the complexity of choice or the number of choices, this probability can be reduced to any selected level. In this case, attentiveness may be defined as a state of selective excitability to a patterned stimulus over a predetermined number of trials, without resort to anthropomorphic interpretation of what an animal is "thinking." On the other hand, failure of an animal to respond to a particular stimulus does not necessarily imply inattention, although concomitant responsiveness to other stimuli gives a strong possibility of this.

Recent work on the phenomenon of attention has centered on modification of cortical electrical activity by manipulations of behavior involving perception, often in conjunction with localized electrical stimulation of the diencephalon and brain stem. Basically, the same technique was used here in a form first employed by Nielson, Doty, and Rutledge (*1*). Cats were trained to perform a response upon receipt of an electrical stimulus to the cortex. Changes in the electrical potential evoked in the cortex by that stimulus were then correlated with changes in overt responsiveness.

Two or more pairs of electrodes were implanted in the prepyriform cortex of each of six cats, one pair for stimulation and the other for recording. Three of the cats were trained to proceed down a runway to reach food upon receipt of an electrical stimulus to this cortex. Training was in three stages: (i) An electrical stimulus was delivered at sufficiently high intensity to elicit an orienting response (sniffing, erection of the ears, turning of the head and eyes, and so forth), which occurred at stimulus intensities just below threshold for convulsions. (ii) Standard operant conditioning was carried out with the high-intensity electrical stimulus as the signal and milk as the reward. (iii) After establishment of the response, the stimulus intensity was reduced to a level 1.3 times that of the threshold for the behavioral response. In this circumstance the threshold intensities for both the electrical and behavioral responses were approximately the same. The other three cats were stimulated electrically in identical fashion but not in association with a reward.

The parameter of electrical change chosen for study was the graphic curve relating the root-mean-square amplitude of evoked potential to the frequency of electrical stimulation. Previous studies of the prepyriform-evoked potential (*2*) had shown that, when short bursts of electrical stimuli were delivered to the cortex at different frequencies, the maximum peak-to-peak transcortical amplitudes of response occurred at stimulus frequencies approximating the commonest frequencies of spontaneous cortical activity. The resemblance of this relationship to that inherent in harmonic oscillation, together with the sinusoidal nature of the spontaneous activity, suggested that the degree of peaking (Q) of the amplitude-frequency curve might change with fluctuations in attention. This was further substantiated by the facts that the potential evoked by a single shock delivered to the cortex strongly resembled damped sinusoidal oscillation; that the degree of apparent damping diminished when the cats became attentive to the stimulus and increased with habituation to the stimulus; and that both evoked and spontaneous wave forms were commonly seen at frequencies approximately one-half that of the dominant frequency, especially after training to respond to the stimulus.

In the present study (*3*) the root-mean-square amplitude of evoked potential was used in preference to peak-to-peak amplitude. The electronic techniques and the methods for determination of stimulus parameters will be described elsewhere (*4*). An important condition of measurement was

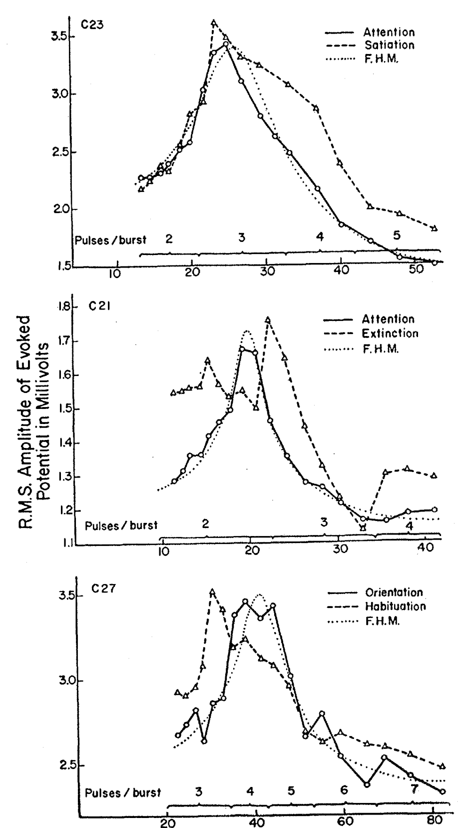

Fig. 1. Response amplitude-stimulus frequency curves from attentive and inattentive cats, compared with curves derived from the equation for forced harmonic motion (F.H.M.).

that the duration of recording of bursts of potentials was fixed, so that with changes in stimulus frequency the number of stimuli in each burst also was changed.

Three types of results are shown in Fig. 1. The points in C23 connected by the heavy line represent values of the amplitude of potentials evoked at each of a range of frequencies, in a cat which gave a response at each presentation of the electrical stimulus, there being no more than one false-positive response in each ten trials and no negative responses. The points connected by the broken line represent values obtained from the same cat and with the same stimulus parameters after free feeding, until the animal no longer responded to the electrical stimulus, but did so to other events in its environment, for example, the approach of another cat. The demonstrated change in the form of the curve did not take place immediately after satiation but rather after an additional half-hour of repeated negative trials.

The points in C21 connected by the heavy line represent values of amplitude from another cat in the same circumstances as in C23. The points connected by the broken line represent values obtained after extinction of the response by omitting the reward. Again, this change did not follow immediately upon cessation of response but after repeated negative trials.

The points in C27 connected with the solid line represent values from one of the control cats after elicitation of the orienting response with a strong electrical stimulus, the stimulus intensity thereafter having been reduced to 1.3 times threshold for the electrical response. The points connected by the broken line represent values obtained after 6 days of repeated electrical stimulation with habituation; that is, the cat was in the same environment as C23 and C21 but with no significance being attached to the stimulus.

The dotted curve in each of the three examples was derived from the equation describing forced harmonic motion in a system driven by a sinusoidal force:

$$m\frac{d^2x}{dt^2} + r\frac{dx}{dt} + kx = F\cos\omega t$$

As applied to an electronic oscillator, the constant m would represent inductance, r resistance, and k the reciprocal of capacitance. Although each of these elements has been described in squid axon (*5*), no physical meaning was assigned to them in the present study. The equation was used in one of its integrated forms:

$$E = \frac{F}{\omega\{r^2 + [(k/\omega) - \omega m]^2\}^{\frac{1}{2}}} + C$$

where E represents amplitude, F the driving force (dependent only in part on stimulus intensity), ω the stimulus frequency times 2π, and C an arbitrary constant of unknown significance. Use of the equation in this form implied two approximations: (i) that despite the shortness of the bursts (115 msec) the amplitude represented predominantly the steady state rather than the transient response; and (ii) that the driving force was sinusoidal, whereas in actuality it was impulsive. By these assumptions calculations were avoided, which were prohibitively complex for this preliminary stage of analysis.

These results show that the empirically derived relationship between the amplitude of evoked potential and the frequency of electrical stimulation corresponds to the analytical function describing forced harmonic motion, in states wherein the stimulus influences overt behavior at intensities well below convulsion levels. It may be inferred that when the cat is attentive to a stimulus, the cortex upon which it falls becomes (in a formal sense) resonant to that stimulus. In states of habituation, satiation, extinction, and also sleep, which alike imply the probability of inattention, the correspondence is not apparent. The change in form of the curves is compatible less with increased damping than with some disorganization of the cortex manifested by the appearance of two peaks of amplitude in the place of one.

The agreement between the observed and calculated data implies that the periodic activity of the cortex is harmonic, but it does not specify the mechanism, that is, whether the property of oscillation is inherent in the physicochemical structure of single neurons or in chains of neurons forming reverberating circuits. However, it does specify the need for further studies of the resistive and reactive properties of neurons and neuroglia, as well as comparison of the frequency-specificity of the excitability change with amplitude changes previously found to accompany changes in attention (*6*).

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References and Notes

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Isolation of Viruses from Children with Infectious Hepatitis

Abstract. Cytopathologic agents were isolated from 14 of 22 Indian children involved in an outbreak of infectious hepatitis in Arizona. Isolation was made in a serially transplantable cell line originating from human embryonic lung. Efforts to identify these agents as known viruses, by utilizing standard techniques, have been unsuccessful.

A serially transplantable cell line highly susceptible to viral infections was isolated from human embryonic lung during studies on the etiology of viral gastroenteritis. The superiority of these cells over established lines in primary isolation of enteroviruses (*1*) prompted attempts to isolate viruses from the feces of patients with clinical symptoms of infectious hepatitis.

In October 1959 an epidemic of infectious hepatitis was observed on an Indian reservation in eastern Arizona. There were 22 hospitalized cases of this disease in children varying in age between 20 mo and 3 yr. The course of the disease was severe, and protracted hospitalization was required in a majority of the cases. Scleral icterus was noted in all cases, although dermal icterus was not pronounced because of dark pigmentation. All urines were strongly positive for bile pigments, serum icterus indexes were elevated, and stools usually were clay colored. The clinical diagnosis of all 22 children was infectious hepatitis.

Tissue cultures were prepared as outlined previously (*1*) and changed to a maintenance medium of 2 percent calf serum and M199 prior to inoculation of the fecal specimens. Twenty percent fecal suspensions were prepared for inoculation into tissue culture according to methods described by Paul (*2*). One-tenth of a milliliter of 20 percent fecal suspension and 0.9 ml of maintenance medium were