salt solution, 0·3 per cent methyl cellulose (15 c.p.s. U.S.P. grade, Fisher Scientific Co., Fair Lawn, New York), and amino-acids and vitamins at a concentration twice that recommended by Eagle[6]. Immediately afterwards and at intervals of 1–2 h, 10 ml. aliquots of infected and uninfected cell suspensions were centrifuged. The sedimented cells were suspended in a medium identical with that already described here except that the unlabelled arginine was replaced with arginine labelled with carbon-14 (0·1 μc./0·73 μg/ml., New England Nuclear Corp., Boston, Massachusetts). After 1 additional hour of incubation at 34° C, the cells were sedimented and washed with medium containing excess unlabelled arginine. They were then suspended in 3 per cent sodium lauryl sulphate solution containing cold arginine and incubated for 30 min at 37° C. At that time, an aliquot was removed for protein determination by the Lowry method; the proteins in the remainder were precipitated on filter paper disks with trichloroacetic acid. The disks were washed with trichloroacetic acid, dried, and then immersed in toluene base scintillation fluid for measurement of carbon-14 disintegrations. For each 1 h pulse labelling, the ratio of:

$$\frac{\text{counts/min/mg protein (infected cells)}}{\text{counts/min/mg protein (uninfected cells)}}$$

was determined and plotted at the mid point of the pulse interval as shown in Fig. 1.

Arginine labelled with carbon-14 was chosen because of the report by Tankersley[7], confirmed in this laboratory, that the amino-acid must be furnished in the medium for Herpes virus multiplication. However, experiments with labelled leucine and with media supplemented with labelled yeast hydrolysate yielded results similar to those recorded in Fig. 1. The pattern of protein synthesis in infected cells as revealed by amino-acid incorporation shows three distinct stages: During the first 3 h after infection, protein synthesis decreased to about 70 per cent of control rate. The decrease was observed in all experiments; the rate of decrease, however, varied with the multiplicity of infection. Between 3 and 6 h after infection, incorporation of amino-acid was generally stimulated. Lastly, between 6 and 10 h after infection, incorporation of amino-acid declined to approximately 60 per cent of that of uninfected cells.

The results presented in Fig. 1 reveal two distinct cycles of inhibition of macromolecular synthesis in infected cells. These cycles occur between 0 and 3 h after infection and from 6 h after infection. It is possible that the first cycle is brought about by a product specified by the virus early in infection, whereas the second cycle is caused by a sub-unit of the capsid or by some other product specified after the onset of DNA synthesis[2]. However, the results are insufficient to determine whether the two cycles are the expression of the same or different viral genes.

Inhibition of host macromolecular synthesis has been observed in animal cells infected with a number of RNA[8–10] and DNA[11,12] viruses. In relation to the data presented in this paper, two comments should be made. First, the inhibition produced by herpes simplex virus takes place much sooner after infection than that produced by vaccinia virus[11,12]. The difference may be due to the fact that vaccinia virus replicates in the cytoplasm, whereas herpes simplex replicates in the nucleus. Secondly, inhibition of host RNA and protein synthesis is not a general characteristic of all viral infections[13]. It is uncertain precisely what selective advantages accrue to the virus which modifies host metabolism over the one which does not. With respect to herpes simplex, the early inhibition of host RNA synthesis may be a prerequisite for the synthesis of viral constituents. Thus, infection of canine cells, under conditions which preclude early inhibition of host RNA synthesis, results in the production of interferon only. Viral constituents but no interferon, on the other hand, are made in cells the RNA synthesis of which is inhibited very early in infection[5].

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PSYCHOLOGY

Cortical Evoked Potentials and Appetite Drive

A NUMBER of investigators have observed the attenuation of evoked potentials during attention and conditioning[1–4].

In each study, the stimulus used has been exteroceptive and capable of producing an 'attentive' state or 'arousal' in the animal. Steiner[5] deprived rats of water for varying lengths of time and demonstrated that appetitive drive states can also produce EEG signs of arousal. In the present experiment, six cats were deprived of food for 30 h, and changes in the amplitude of auditory-evoked potentials and general EEG activity were observed at various times.

The recordings were taken from animals with monopolar stainless steel electrodes (insulated with 'Teflon' except for the very tip) chronically implanted in the auditory cortex. Uninsulated stainless steel wires attached to metal screws in the frontal sinus were used as indifferent and ground electrodes. After the experiment, the cortical electrode placements were verified histologically. One week before testing, the animals were placed on a once-per-day feeding regimen. The animals were placed in the experimental box for 0·5 h during which cat food ('Puss-in-Boots') was given until they stopped eating; they were then removed to the home cages for the intervening 23·5 h. On the testing day the animal was placed in the box and fed. Immediately after the animal stopped eating the first test session (pre-deprivation) was run. There was a total of seven test sessions: pre-deprivation and 3, 6, 12, 24 and 30 h of deprivation; the animal was then fed again until it stopped eating and the final test (post-deprivation) was administered. The animals were kept in the experimental box through the entire test sessions. A test session consisted of three trials. During each trial, 10 clicks (2,500 c.p.s., 30 msec duration) with 1-sec intervals between clicks were presented. These clicks, produced by an audio-oscillator, were of constant intensity and clearly audible to a human. In the six cats used for this report such stimulus produced well-developed evoked potentials in a rather restricted area of the posterior sylvian gyrus All six animals were subjected to this procedure once

One week after the last day of the experiment, two of the animals were tested again under the same procedure with the exception that food was given all through the sessions. The experimental box was sound-proof and had a one-way viewing window; gross behaviour characteristics of animals were noted by the experimenter. Background EEG activities and evoked potentials to the audio signals were recorded on an Offner dynograph. For 3 animals, the evoked potentials and the stimulus marker were recorded on tape ('Mnemotron') and played back on an oscilloscope ('Tektronix 502'). Evoked potentials were evaluated in terms of peak-to-peak amplitude change. The amplitude of evoked potential to each click was measured and summated over each test session which consisted of 10 clicks per trial for three trials.

The solid line in Fig. 1 represents the averaged amplitude of 30 evoked potentials during each test session for the 6 animals. There were some individual differences in initial responsiveness to the clicks among animals, but the direction of changes with increasing deprivation was uniform. That is, the amount of attenuation of evoked potentials increased as hours of food deprivation increased. At the pre-deprivation session (satiated state), the amplitudes of evoked potentials were about 160 μV. The amount of attenuation increasod sharply by the 6-h session and approached a maximum by the 24- to 30-h session. Following feeding (post-deprivation session) after the 30-h session, the amplitude of evoked potentials returned to the level shown by each animal at the original pre-deprivation session. The dotted line in Fig. 1 presents the average amplitude of 30 evoked potentials during various test sessions for 2 animals which were satiated. There were no significant changes in the averaged amplitude of evoked potentials over the entire test sessions.

Fig. 2 illustrates samples of oscillographic records of 10 superimposed evoked potentials per trial at various deprivation levels for cat S. During the pre-deprivation session, the amplitudes of evoked potentials are high (about 160 μV from peak to peak). The amplitudes decrease at 6 and 30 h of deprivation (70–80 μV). Finally, at the post-deprivation session, after the fast was broken,

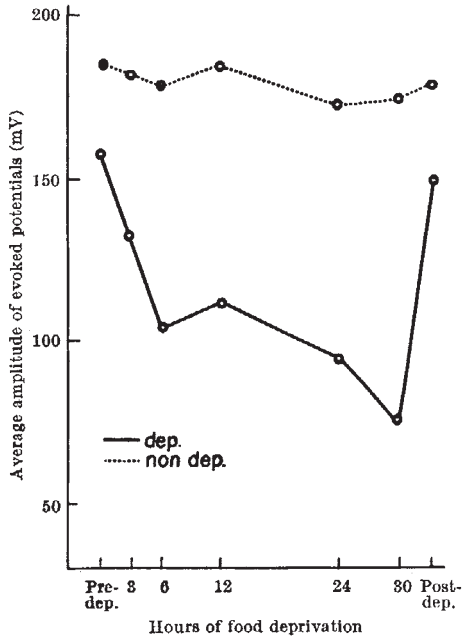

Fig. 1. Average amplitude, peak to peak, of 30 auditory evoked potentials per subject for 6 subjects (solid line) under food deprivation and for 2 subjects (dotted line) under satiated condition plotted against each test session. In the satiated subjects the variations of amplitude of auditory evoked potentials during a 30-h period are insignificant. In the subjects under food deprivation the reduction of amplitude of evoked potentials is maximum at 24–30 h of deprivation. Notice the prompt return to the original amplitude following feeding to satiation (post-deprivation)

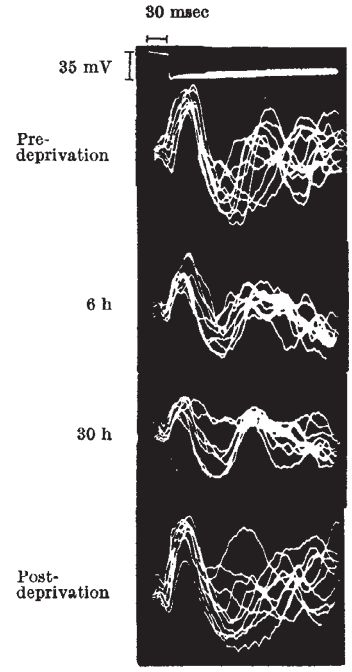

Fig. 2. Oscillographic records of 10 superimposed evoked potentials per trial in one subject during pre-deprivation, 6 and 30 h of food deprivation and post-deprivation (feeding to satiation)

the amplitudes of evoked potentials returned to the pre-deprivation level. The fact that the evoked potentials returned to their original amplitude makes it unlikely that the marked attenuation seen during deprivation can be accounted for by habituation to the clicks. In addition, the two control animals not subjected to food deprivation showed no reduction of amplitude of evoked potentials.

The behaviour of the animals during the entire experimental period showed several characteristic features. Immediately after feeding, the cats tended to groom quietly, sitting or lying down during trials. With increasing hours of deprivation they became more active, restless and started vocalizing.

According to the present data, food deprivation results in increments of EEG indices of arousal with low-voltage desynchronized activity, and in attenuation of evoked potentials to auditory signals with increased behavioural arousal. The EEG arousal is similar to that described by Steiner[5] who found diminution in the synchrony and amplitude of the EEG in rats subjected to increasing levels of thirst. The sensory blockade effects, measured in terms of reduction in amplitude of evoked potentials in the present experiment, are similar to those reported by others under experimental conditions[1,2], in which a stimulus capable of commanding an animal's attention produced a reduction in amplitude of evoked potentials to on-going behaviourally 'neutral' sensory signals. Food deprivation, while not a 'stimulus' in the ordinary sense of the term, is capable of producing a state of heightened EEG arousal, and therefore can result in the attenuation of sensory evoked potentials.

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