

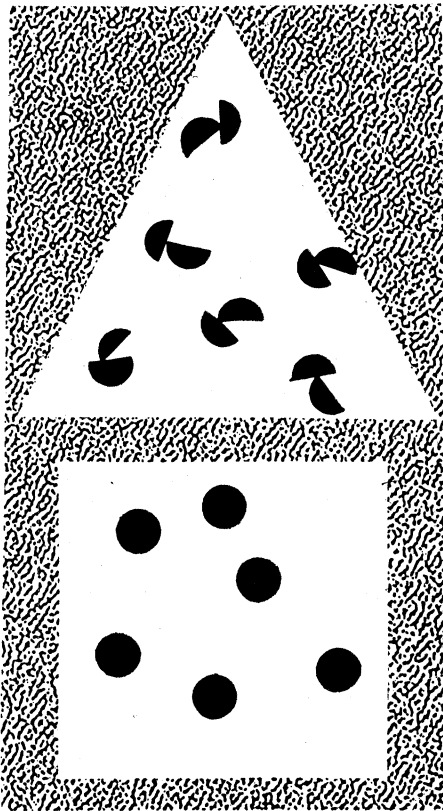


Fig. 1. Two stimuli used in avoidance training and test for interocular transfer. The square stimulus was 1.5 in. high.

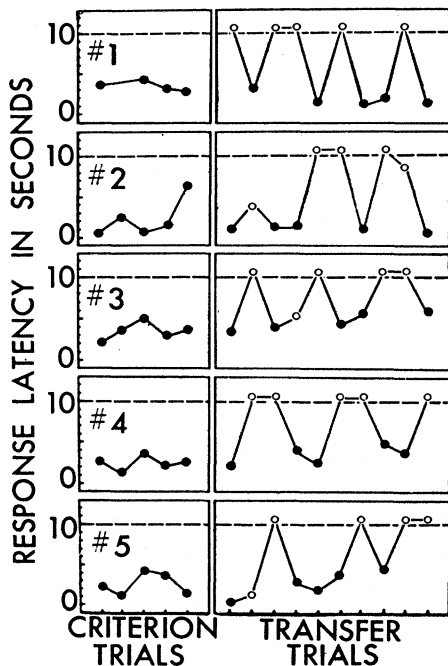


Fig. 2. Avoidance response latencies of five fish during criterion trials for "trained" eye (shown for positive stimulus only) and during test of the contralateral "naive" eye for interocular transfer. Solid circles, responses to positive stimulus; open circles, responses to neutral stimulus. With a 10-second limit on each trial, points above the dashed line represent the absence of a response.

in binocular vision. In order to preclude the possibility of a brightness discrimination, the two stimuli were constructed so that both contained the same amounts of black and white. Three of the five fish were trained with the triangular pattern as positive; the square stimulus was positive for the remaining two. Previous experience with pattern discrimination in fish suggests that the small, black dots and half-dots contributed the important differential characteristic to the stimuli.

The results are shown in Fig. 2. Quite clearly, interocular transfer of a pattern discrimination is immediately present when the naive eye is tested. Considering all five fish together, there were 25 positive trials and 25 neutral trials. In these 50 trials, there were only four occasions when a fish responded incorrectly, always by responding inappropriately to the neutral stimulus.

As far as this simple vertebrate animal is concerned, the results clearly demonstrate that prior binocular experience is not a necessary prerequisite for successful interocular transfer. However, Hebb's concern was with the proposed importance of past perceptual experience for the development of neocortical neural circuits (that is, cell assemblies). The fish has no neocortex. It could still be, for animals with neocortex, that prior perceptual experience does indeed play either a crucial or ancillary role in shaping adult perceptual abilities. There are a number of quite convincing experiments (4) to suggest that this is the case. On the other hand, an alternative interpretation of the results of these experiments is possible (2).

There are already numerous ethological studies showing that the vertebrate nervous system is innately capable of responding appropriately to the relative configuration of a stimulus. Further, recent electrophysiological findings also indicate that the adult nervous system, as far peripheral as the retina, is able to respond differentially to the configurational aspects of a stimulus (5). The present results demonstrate that this innate characteristic of the nervous system is also at work when an organism has learned a new response to a new stimulus (6).

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5 June 1961

Radar Observation of Venus

Abstract. Radar observations of Venus during the last close approach have resulted in a value of solar parallax of 8.79460 seconds of arc, corresponding to a value for the astronomical unit of 149,596,000 km. This is in satisfactory agreement with the determinations made, during the same close approach of Venus, at the Millstone Hill Radar Observatory and at Jodrell Bank, which are 149,597,700 km and 149,601,000 km, respectively. The size of the astronomical unit heretofore generally accepted as most authoritative is based upon a 1950 determination by Rabe, and is 149,532,200 km.

The R.C.A. BMEWS pulsed tracking radar system at Moorestown, New Jersey, was employed during the last close approach of Venus in an attempt to measure the size of the astronomical unit. The radar is provided with an antenna 84 feet in diameter; other parameters of the system cannot be stated here because of security classification.

Transmission periods alternated with reception periods, the transmission period in each case being several seconds less than the expected signal travel time to Venus and return, and the reception period being several seconds greater. The target was expected to introduce random depolarization of the signal, so reception was accomplished separately for both vertical and horizontal polarization, the separate wave forms being added after square law detection.

The processing of the received wave form was accomplished by analog methods up to the addition of the two detected wave forms and was then converted to digital form. In processing the data, account was taken of the

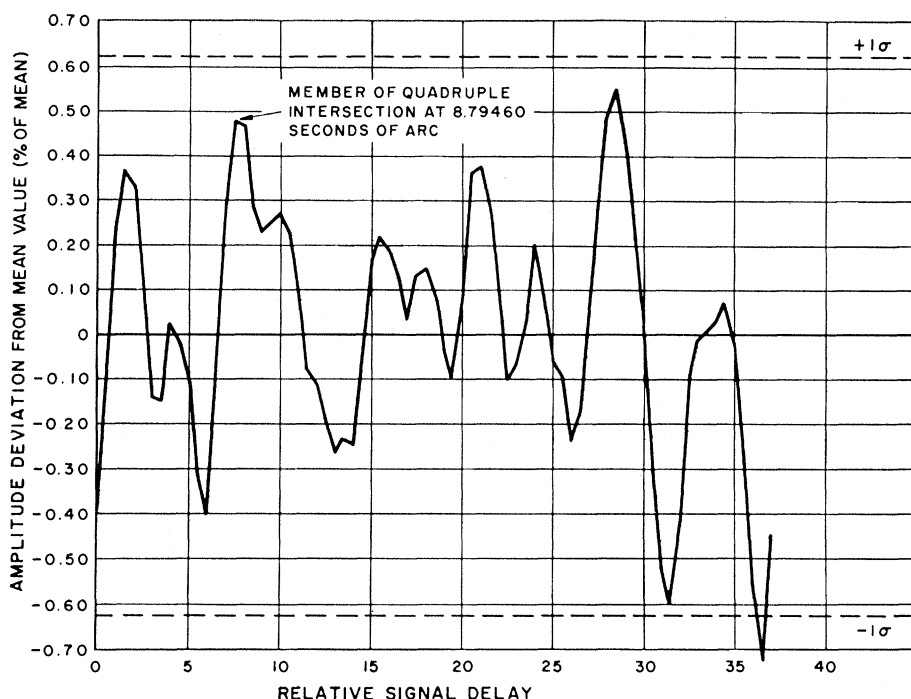


Fig. 1. Integrated data from 0.53 hour of transmission on 8 April 1961.

gradual change in range and of the effect of the rate of change of range upon the signal. The magnitudes of these effects were computed from the heliocentric spherical coordinates of the Earth and Venus as derived from the tabulations of the *American Ephemeris and Nautical Almanac* for 1961. The distance of the radar from the center of the earth, the diurnal rotation of the earth, and the finite velocity of light were taken into account in determining the best estimates of the astronomically predicted ranges and range rates for the times of the experiment.

The interpulse period employed was less than the time required for the electromagnetic energy from the radar to traverse the region of space which, from a priori position information, was expected to encompass the true location of the reflecting surface of Venus. It was originally planned to counter the resultant range ambiguity by employing a pseudorandom pulse code (as in 1). A statistical analysis of the predicted performance of the system indicated that satisfactory results could be expected from this approach for observations of at least 2 hours duration (that is, 1 hour of transmission and 1 hour of reception). Unfortunately, an extremely high local noise environment reduced the efficacy of the coded transmission method below the point of usefulness and another method was em-

ployed to resolve the range ambiguity. This was accomplished by taking advantage of the fact that the change in the range of Venus from experiment to experiment causes all the possible ambiguous range values that result from an uncoded transmission to intersect only at the true radar range. To make use of this characteristic, the detected wave form resulting from each (nominally, 2-hour) observation was integrated over a single interpulse period (applying corrections for the slow variation of the period due to the relative motion of Venus), and the four most likely locations for the return energy were selected in accordance with the four highest peaks of the resultant integration. (The expected height of a peak corresponding to signal was approximately one-half the standard deviation of the noise amplitude. See Fig. 1.) The various possible values of solar parallax in the range 8.79250 to 8.80350 seconds of arc were computed for each of the four highest peaks obtained from a total of eight observations amounting to 6.18 hours of transmitted signals. This range of values encompasses the various determinations of solar parallax made since 1950 (including the 1961 U.S.S.R. determination reported in the press).

There were a number of intersections of values from three observations, as was to be expected, since the probability

of a triple intersection due to noise alone is about 0.44. However, the results from *four* of the eight observations intersected at a common value of solar parallax at only one point (within the precision of the radar system, which is ± 0.00001 seconds of arc of solar parallax). The common intersection occurred at 8.79460 ± 0.00001 seconds, which is therefore taken to be the value of solar parallax determined by the experiment. The probability that this fourfold intersection out of eight observations resulted from noise alone is 0.0736, while the probability that the intersection resulted from signal is 0.913. Thus, the likelihood that the observation is a valid one is 12.4 times as great as the likelihood that the observation is invalid.

The size of the astronomical unit corresponding to this measured value of solar parallax, assuming the adopted value of 6378.388 km for the radius of the earth, is $149,596,000 \pm 200$ km, where the limits define the precision of the measurement. This is in satisfactory agreement with the determinations made, during the same close approach of Venus, at the Millstone Hill Radar Observatory and at Jodrell Bank. These measurements, converted to values of the astronomical unit by utilizing the adopted value of the earth's radius, are $149,597,700 \pm 1400$ km and $149,601,000 \pm 5000$ km, respectively (2), where the limits are indicative of accuracy, not precision. The size of the astronomical unit heretofore generally accepted as most authoritative is based upon a 1950 determination by Rabe, and is $149,532,200 \pm 6600$ km.

The observations that contributed to the fourfold intersection of values at 8.79460 ± 0.00001 seconds of arc were made on 21 March, 7 April (two experiments), and 8 April, and consisted of 3.34 hours of data in total. The target reflectivity (ratio of scattered energy to incident energy) corresponding to the results of the 21 March observation is approximately 0.26. Similar computations were not practical in the case of the other observations because of the nature of the local noise.

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18 September 1961

On the Site of Action of Amethopterin

Abstract. In the liver of the intact mouse, the conversion of exogenous folic acid to compounds with citrovorum-factor activity is inhibited completely by an amount of amethopterin similar to that bound to the enzyme folic acid reductase in vitro. Because this amount of amethopterin is several thousand times smaller than the LD₅₀, the toxic effects produced by the larger doses must be mediated via some additional mechanism.

Both folic and folinic (5-formyl-5,6,7,8-tetrahydrofolic) acids can protect mice from aminopterin toxicity (1). While folinic acid is effective when given simultaneously or even after the drug, folic acid must be given about 1 hour before aminopterin in order to provide any protection. During the period of 1 hour after the administration of folic acid, the folic acid is converted to compounds with citrovorum-factor activity, which can then serve to protect against aminopterin (2). A priming dose (nontoxic) of aminopterin abolishes the protection afforded by folic acid by preventing its reduction to more active materials. Folinic acid, because it is already reduced, is unaffected by prior administration of

aminopterin and can substitute for the biologically active derivatives of folic acid. The measurement of liver citrovorum factor after the administration of folic acid provides an in vivo assay of the enzymes responsible for this conversion.

The citrovorum-factor content of the livers of (C57 × DBA)F₁ male mice was determined by incubation of acetone powders with ascorbate and histidine and subsequent microbiological assay with *Pediococcus cerevisiae* (ATCC No. 8081), as described elsewhere (2). The influence of amethopterin (0.05 mg/kg) on the liver citrovorum factor after administration of folic acid (25 mg/kg) on the days indicated is presented in Fig. 1. In the animals that received no amethopterin (day 0), liver citrovorum factor increased from 50 to 140 μg/g in the first 3 hours after folic acid was given. On subsequent days, after administration of amethopterin, this response was abolished and had not been completely re-established by day 4, the last day of observation. Thus, in this experiment, the conversion of folic acid to citrovorum factor was inhibited completely by a very small dose of amethopterin.

The degree of inhibition of the conversion of folic acid can also be determined by observing the protective effect of previously administered folic acid on the toxicity of amethopterin. The data summarized in Table 1 show that administration of folic acid (25 mg/kg) 1 hour before administration of amethopterin increased the LD₅₀ from 200 to 350 mg/kg. The administration of amethopterin (0.1 mg/kg) 24 hours before the LD₅₀ injections abolished this protective effect.

Inhibition of the conversion of folic acid to liver citrovorum factor was produced by administration of 0.05 mg of amethopterin per kilogram of mouse, or 1 μg for a 20-g mouse. If all of the drug were localized in the liver, the concentration would be 2 mμmole/g of liver. Since the amount of folic acid reductase in 1 g of mouse liver can bind 0.8 mμmole of amethopterin in vitro (3), these results suggest that at this low dose of amethopterin most of the drug was bound to this enzyme. The disappearance of the protective action of previously administered folic acid after such a small dose of amethopterin further demonstrates the effectiveness of amethopterin in inhibiting the action of this enzyme.

Table 1. Protective effect of previously administered folic acid on the toxicity of amethopterin.

Prior treatment	Time before amethopterin administration (hr)	Amethopterin LD ₅₀ (mg/kg)
None		200
Folic acid (25 mg/kg)	1	350
Amethopterin (0.1 mg/kg) and folic acid (25 mg/kg)	24	180
	1	

If doses of amethopterin several thousand times smaller than the LD₅₀ completely inhibit the conversion of folic acid to citrovorum factor in the intact mouse, larger doses cannot increase the degree of inhibition and therefore must produce toxicity via some additional mechanism. It is not possible to account for all the effects of the folic acid antagonists solely on the basis of inhibition of this conversion process. Because all these effects can be reversed by administration of folinic acid, the additional sites of action may involve the further metabolism of tetrahydrofolic acid and its derivatives (4, 5).

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5. This work was supported in part by grant No. T-118 and by a Florence L. Fenton memorial grant for cancer research from the American Cancer Society. Able technical assistance was provided by Kay Barrick and Germaine Petty.

13 June 1961

An Overview of Sleep as an Experimental Variable (1940–1959)

Abstract. Less than one half of 1 percent of the psychological literature relates to sleep. Although there has been a relative decline in such research, the central nervous system and pathological aspects have recently received increased attention. The United States is producing less than 17 percent of the research on sleep.

In a recent review of the research literature on sleep, some statistics of interest regarding this research area were assembled. The review covered the primarily psychological research since 1941, since Kleitman's book, pub-

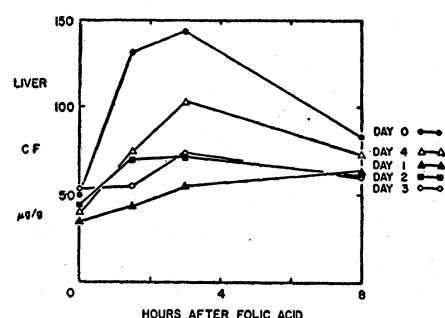


Fig. 1. The effect of amethopterin (0.05 mg/kg) on liver citrovorum factor derived from folic acid (25 mg/kg). Folic acid was given without amethopterin (day 0) and after amethopterin (days 1, 2, 3, and 4). Each point represents the mean for two mice. Amethopterin and folic acid were given subcutaneously.

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