In Fig. 1 the performance of the four groups is plotted in terms of mean log latency of response over three-trial blocks. (The logarithmic transformation was used to normalize the distributions for statistical purposes.) It seems clear from the curves that the two amounts of reward produced different asymptotic latencies, that a shift from small to large reward produced a gradual improvement in performance, and that a shift from large to small reward produced no deterioration of performance —precisely the pattern of results indicated by the reinforcement principle. A repeated-measures factorial analysis of variance for the postshift data (blocks 11 to 23) shows significant effects of (postshift) amount of reward (F, 11.11; df, 1/44; $P < .01$) and of change in amount of reward (F, 4.76; $P < .05$), as well as a significant interaction of amount with change (F, 30.24; $P < .01$). There are significant differences between groups 4 and 40 (F, 39.01; $P < .01$) and between groups 4 and 4-40 (F, 14.01; $P < .01$), but not between groups 40 and 40-4 ($F < 1$).

These results with goldfish differ from Crespi's results with rats in two respects: One of the differences—the absence of an elation effect in the data for the fish—cannot be given much weight because the effect does not appear dependably even in data for the rat; the conditions necessary to produce it have not yet been clearly defined. The second difference does, however, seem to be of considerable importance. Although the depression effect in the rat is a highly dependable one, the fish not only fails to show it, but also fails to show any decrement in performance whatsoever with a discriminable downward shift in the amount of reward. (The discriminability of the change in amount of reward is shown by the significant difference in the asymptotic latencies of groups 4 and 40, as well as by the postshift decrease in the latency of group 4-40.)

One should consider the possibility, of course, that the results for the fish are the product simply of a rather special set of experimental conditions that happen to differ markedly from those under which the depression effect appeared in the rat (*8*), but that is not very likely. The conditions certainly were similar enough to produce the same preshift pattern. Furthermore, the results for the fish were anticipated on the basis of the results of a series of related extinction experiments.

The simplest interpretation of our results, perhaps, is that the reinforcement principle holds for the fish but not for the rat. Another possibility is that the reinforcement principle holds for both animals, but that its operation in the rat is masked by a contrast mechanism (based on learning about, and anticipation of, reward) which is not present in the fish. Already there is evidence from surgical studies indicating that qualitative differences in the adjustment of the two animals may be due to operation in the rat of second-order processes masking lower-order functional communalities. For example, fish-like behavior is found in adult rats that have been extensively decorticated in infancy (*9*). It will be interesting to see the effects of decortication on performance in a Crespi experiment and in experiments on resistance to extinction as a function of amount of reward.

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15 May 1967

Evoked Potentials: Three-Dimensional Display

Abstract. *Procedures are described for displaying large numbers of evoked potentials. A photographic superposition of average evoked responses, with the concurrent modulation of the brightness of each trace, yields a display having the appearance of a three-dimensional surface formed from hundreds of average responses.*

The study of evoked potentials in the nervous system is a very active field in brain research throughout the world. (We use "evoked potential" to mean the time-locked changes in potential that are recorded with macroelectrodes after presentation of a sensory stimulus.) To a large extent this widespread interest in evoked potentials has been spurred by the advent of computers and the development of averaging techniques (*1*). The summation of potentials evoked by successive stimuli, and the appropriate scaling of these sums to obtain the average evoked response, can now be achieved with a number of special-purpose averaging devices as well as with larger programmable machines.

In many instances average evoked responses have exceedingly complex wave forms; description of these wave forms is seldom simple, and even the variability of average responses may be distressingly large. Summarizing data of this kind has frequently proved difficult, especially for experiments of relatively long duration in which hundreds or even thousands of average responses are obtained from individual subjects. Perhaps the most common way of dealing with these problems has been to present the "typical" average response for some experimental condition; other, more satisfactory, procedures also have been employed. Quantitative measurements of amplitudes or latencies may provide a satisfactory description of some changes in evoked potentials, especially when accompanied by an estimate of variability.

Changes in complex wave forms do not always lend themselves, however, to descriptions by a few specific meas-

urements; instead they are often summarized best by presentation of a significant number of successive average responses. In fact, the technique to be described is an extension of this method, one that provides for the display of a large number of average responses in a relatively small space. The display also has other features that appear to be very useful.

The display (Fig. 1) shows the click-evoked cortical potentials recorded from a rat to be appreciably altered by administration of a drug (chlorpromazine) at the time indicated by the arrow. The display was generated by the photographic superposition of 512 average evoked responses. The responses were displayed sequentially on an oscilloscope in the conventional way, except that the amplitude of the responses also modulated the intensity of the oscilloscope beam. Deflections in the evoked responses in the downward direction decreased the intensity of the beam, and deflections in the upward direction increased the intensity. The first average obtained from this recording period is shown at the bottom of the photograph, and succeeding averages are displaced upward and to the right. The effect of these procedures is to produce a display clearly having the appearance of a three-dimensional surface. The display is quite similar to one developed by Webb (*2*) for the electrocardiogram, except for the horizontal displacement. Inversion of the polarity of the averaged potentials produces a complementary display in which the "peaks" of the surface become "valleys," and vice versa; thus potential changes in both directions can be portrayed with reasonable clarity.

Each of the average responses contained in the display (Fig. 1) was computed from 120 evoked potentials. A sliding or moving average was employed, providing a "smoother surface" than that obtained from averages of successive blocks of evoked potentials. In this case each average of 120 responses is displaced by only 15 responses from the preceding average, so that 105 of the evoked potentials included in each average also entered into the computation of the adjacent one. These cortical potentials were evoked by click stimuli presented continuously at a rate of one per second. Almost 8000 evoked potentials entered into this display—all the evoked potentials recorded during a period longer than 2 hours of the experimental session.

In another example of the display (Fig. 2), the average evoked responses were computed from acoustically evoked potentials recorded from the scalp of a human subject during a night of normal sleep. Each average in the display was computed from 140 evoked potentials, and a sliding average was employed in which successive averages are displaced by ten responses. To the left of the photographic display, the course of sleep during the 7-hour period is shown graphically. The several stages of sleep and wakefulness were determined from ink recordings of the electroencephalogram, eye movements, and activity of facial muscles (*3*).

It is apparent (Figs. 1 and 2) that the photographic display contains a wealth of information and provides an overview of rather large amounts of evoked-potential data. It is not a sub-

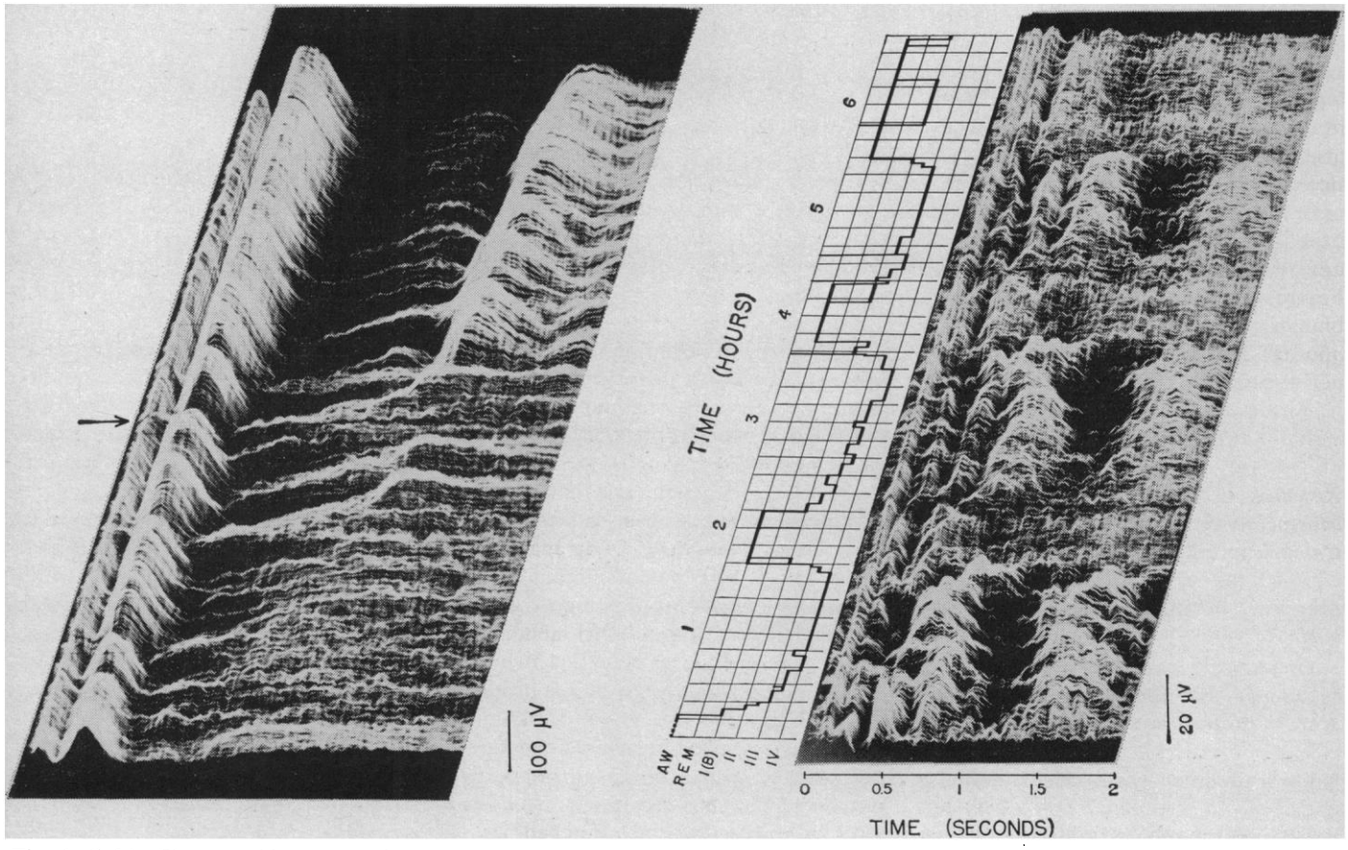

Fig. 1 (left). Photographic superposition of 512 average click-evoked cortical potentials recorded from a partialy restrained rat before and after intraperitoneal administration of chlorpromazine (10 mg/kg) at time indicated by arrow. Total sweep time, 240 msec. Fig. 2 (right). Sliding averages of click-evoked potentials recorded at vertex with scalp electrodes from a sleeping human subject. Clicks presented continuously every 3 seconds. State of sleep is indicated at left of average-response display. Double lines in these graphs indicate periods when stage could not be determined unambiguously.

stitute for quantitative measurements of specific attributes of responses, but it can point the way to attributes that deserve more detailed study. The display also presents a very reasonable, though qualitative, estimate of the variability in average evoked responses.

A PDP-4 computer (*4*), with a digital magnetic tape unit, was used to obtain the sliding averages shown in Figs. 1 and 2. The large storage capacity provided by the digital tape offered a number of conveniences that made the computations rather easy, but so much storage is not necessary for such computations. The sliding average itself is not a requisite for use of the photographic display, although it appears to have several advantages over averages computed from nonoverlapping, contiguous blocks of evoked potentials. The additional "smoothing" that it provides may in some instances yield a more satisfactory display. Transient phenomena and transitional forms of evoked potentials may be given added weight, an advantage in studies in which such phenomena are of interest.

The analog outputs from the PDP-4 were used as the inputs to a special-purpose digital-display device that added a small d-c voltage to the *X* and *Y* inputs of the oscilloscope with each sweep, and modulated the *Z* axis in accordance with the amplitude changes in evoked responses. The device, which also performs other operations, will be described in detail elsewhere (*5*); its resolution is sufficient to permit the superposition of as many as 256 average responses in a single photograph. Figures 1 and 2 were obtained by combining two (Fig. 1) or three (Fig. 2) photographs, each containing 256 average responses.

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LSD: Injection Early in Pregnancy Produces Abnormalities in Offspring of Rats

Abstract. *One of five rats given a single subcutaneous injection of lysergic acid diethylamide (LSD) early in pregnancy appeared to abort early; two delivered stunted stillborn offspring at term, one delivered a littler of seven healthy and one underdeveloped young, and the last one delivered an apparently normal litter. All five matched controls, given saline injections, went to term and delivered healthy litters of 11 to 16 offspring; there were no abortions and no stillbirths. In a replicate experiment, one of five rats given LSD on the 4th day of gestation aborted, two delivered some stillborn offspring, one gave an abnormally small litter of four, and the last one produced an apparently normal litter of ten. All matched controls delivered healthy litters, totaling 66. Some surviving offspring treated with LSD failed to develop as well as control animals. Treatment of five additional rats with LSD late in pregnancy had no obvious effect on the offspring.*

As part of a continuing investigation of toxic effects of psychotropic drugs (*1*), we have studied the influence of subcutaneous injections of "psychedelic" doses of lysergic acid diethylamide (LSD) on the course of pregnancy. Here are some preliminary results.

Obtained several years ago (*2*), the LSD was kept dry in the dark pending solution in saline at 5 μg/ml. Ultraviolet and fluorescence analyses revealed no significant degree of oxidation of the material. Healthy female rats, Wistar strain, 250 g, were mated with selected healthy males weighing 450 g. Pregnant females were divided into matched groups: one group received saline subcutaneously; the other, LSD at 5 μg/kg of body weight. This dosage was selected to correspond in rats to the human hallucinogenic dose which is said to range from 100 to 400 μg pr person—1.7 to 6.7 μg/kg for a person weighting 60 kg (*3*).

In the first experiment five rats received a single injection of LSD on the 4th day of pregnancy, with no further treatment (Table 1). Of these, one produced no young; autopsy showed that pregnancy had presumably terminated in abortion; ovaries and uterus were somewhat irregular and enlarged, one horn of the uterus being markedly constricted, with no trace of fetuses. Two rats that received LSD on the 4th day of pregnancy produced abnormal young: six of a litter of 13 were stillborn, as were all nine of the second litter. One rat injected with LSD delivered a litter of eight of which seven appeared normal, one being definitely stunted. The last injected rat delivered a normal litter of 16. Matched controls, given saline, delivered 11, 11, 13, 13, and 16 offspring, all apparently normal and healthy.

In the second experiment one animal that received LSD on the 4th day of gestation did not come to term. The weight curve indicated that pregnancy was interrupted during the 3 days following treatment with LSD. Another treated animal delivered a litter of 14, three of which were stillborn, with one more dying within 24 hours. A third rat delivered a litter of 11 including one stillborn. A fourth animal gave an unusually small litter of four normally appearing offspring. The last one delivered a healthy litter of ten. Again, matched controls produced apparently healthy normal litters averaging 13.

In the third experiment, five animals received similar single injections of LSD late in pregnancy (Table 1). There was no obvious effect on the apparently healthy offspring totaling 51—against 65 for the controls.

Table 1. Effects of prenatal treatment of rats with LSD. Each rat had a matched control, which was injected with saline; all controls delivered normal litters of 8 to 17 offspring. The day of gestation on which each rat was treated appears in parentheses.

Rat (No.)	Offspring	
	In litter (No.)	Nature
	Experiment 1	
2-3-2 (4)	0	Fetuses resorbed
2-5-2 (4)	9	All stillborn (2 stunted)
2-2-1 (4)	13	Six stillborn, remainder normal
2-6-2 (4)	8	Seven normal, one small
2-1-2 (4)	16	Normal
	Experiment 2	
1-2-1 (4)	0	Presumed abortion
2-6-1 (4)	14	Three stillborn, one died within 1 day
2-4-2 (4)	11	One stillborn
1-1-1 (4)	4	Normal; litter unusually small
2-4-1 (4)	10	Normal
	Experiment 3	
1-3-2 (7)	10	Normal
1-4-2 (8)	11	Normal
1 2-5 (10)	13	Normal
1-1-5 (13)	9	Normal
1-1-4 (16)	8	Normal