bifrontal injections contained a total of 290 nmole of K^+.

Except for Na^+, the amounts of cations injected intracerebrally were substantial compared to those calculated to be present in the extracellular fluid of the cerebral hemispheres. In these calculations we have used the average weight of 300 mg for the cerebral hemispheres and 10 percent of the volume of the cerebral hemispheres as the extracellular fluid volume; for the concentrations of cations we used those in cerebrospinal fluid (*4*). On this basis, in the bitemporal series the ratios of the amounts of K^+, Ca^{2+}, or Mg^{2+} injected to the amount present in cerebral extracellular fluid was between 4 and 5. The ratio of Na^+ was 0.09, and the ratio for K^+ in the six combined injections was 3.

We have consistently found that bitemporal injection of puromycin dihydrochloride neutralized with NaOH in the amounts used here and the injection at six sites of 30 μg in each site cause loss of recent and longer-term memory, respectively. Nevertheless, because of the nature of our results, the effectiveness in blocking expression of memory of our puromycin dihydrochloride neutralized with NaOH has been checked throughout the experiments. Some of the mice treated in this way also served as controls for other experiments (*5*) that were performed concurrently with ours.

There was substantial variation in the reactions of the mice to injections of puromycin containing the different cations. Mice which receive Na^+ usually lose their excitability and give reliable maze performance 5 days after treatment; this interval between treatment and retention testing was used in the Na^+ series. The group of mice which received Mg^{2+} approached most closely those with Na^+; they were in satisfactory condition for retention testing 7 days after treatment. The effects of injections of puromycin together with K^+, Li^+, or Ca^{2+} were more drastic. Mice which had these injections were highly excitable 1 day after treatment, usually required 10 days to recover sufficiently for reliable testing, and in some cases showed further improvement 14 days later when tested for retention of relearning. The numbers of mice which failed to recover sufficiently for reliable retention testing are given in Table 1.

Table 1 also shows the unique effectiveness of puromycin neutralized with NaOH in blocking memory. Consistent with our previous experience it caused loss of memory, with savings of trials and errors closely approaching zero with a single exception. The number of mice which were tested on their retention in the other 5 groups totaled 58. Of these, 43 retained memory with means savings of trials and errors of about 90 percent, and all but one of the remaining 15 had savings of trials and errors at about 50 percent. There was no significant difference (*t*-test) in savings among the K^+, Li^+, Ca^{2+}, and Mg^{2+} groups in which bitemporal injections were made 1 day after training. The savings for trials and errors (mean ± S.E.) were, respectively: for the K^+ group, 75 ± 5.9 and 79 ± 5.8; for Li^+, 78 ± 7.0 and 74 ± 7.3; for Ca^{2+}, 75 ± 6.5 and 78 ± 5.3; and for Mg^{2+}, 79 ± 6.0 and 86 ± 4.6. Much the same results were obtained 9 days after training with combined bitemporal, biventricular, and bifrontal injections containing these ions. As an example, Table 1 shows the results of such injections of puromycin neutralized with KOH. All but two of the testable mice of Table 1 on second retention testing had high savings of trials and errors consistent with retention of memory; the two exceptions showed moderate impairment.

Table 1. Effect on memory of intracerebral injections of puromycin dihydrochloride neutralized with the indicated bases. All injections were bitemporal and were made 1 day after training except for "KOH" in which combined bitemporal, biventricular, and bifrontal injections were made 9 days after training. Mice too excitable for testing are indicated by not testable. For the mice with retention of memory, the percentage of savings of trials and errors (mean ± S.D.) were, respectively: 89 ± 13 and 91 ± 12; for those with impaired memory, 46 ± 14 and 57 ± 17; and for those with lost memory, 0 ± 2 and 3 ± 6.

Base	Mice with memory (No.)			Mice not testable (No.)
	Retained	Impaired	Lost	
NaOH	0	1	33	3
KOH	9	4	1	5
"KOH"	5	0	0	4
Li_2CO_3	6	3	0	1
$Ca(OH)_2$	10	4	0	1
MgO	13	3	0	2

It is premature to attempt an explanation of these results. They appear consistent with the possibility that K^+, Li^+, Ca^{2+}, and Mg^{2+} protect memory by binding to the anionic sites of neuronal membranes with the resultant exclusion of sufficient peptidyl-puromycin to make it ineffective in blocking memory. If this mechanism is in fact involved, it must be supposed, because of the high concentration of intracellular K^+, that relevant anionic sites are unavailable to intracellular K^+. The experimental situation is, however, complex and demands more direct evidence of exclusion of peptidyl-puromycin from neuronal membranes by the ions we have used.

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Visual Reinforcement of Nonnutritive Sucking in Human Infants

Abstract. *High-amplitude sucking was studied as a conditioned operant response reinforced by visual feedback in 4- and 12-month infants. Typical response acquisition and extinction effects were obtained. With the 12-month infants the conditioned sucking rates were influenced by amounts of redundancy in the visual reinforcers.*

The development of learning tasks for the human infant, in which his behavior is made experimentally effective for producing changes in the exteroceptive environment, may provide important tools for studying the ontogeny of exploratory behavior over the first weeks and months of human life. In experiments with infants from 3 weeks to 1 year of age we began to explore the feasibility of using the sucking response as a conditioned operant to assess the infant's response to visual feedback as a reinforcing event. Sucking is a response that can be reliably elicited in most infants during the first days of life, and studies with newborns have suggested that sucking is a functionally adaptive response that may be influenced by nutritive reinforcement contingencies in the feeding situation (*1*). We created an artificial environment for the infant in which visual feedback was made experimentally contingent upon his emission of high-amplitude nonnutritive sucking responses.

Our apparatus consisted of a nipple and a pressure transducer which provided both polygraphic recordings of all sucking behavior and a digital record of sucking pressure in excess of 18 mm-Hg. Presentation of the projected visual stimulus was automatically programmed. Criterion amplitude sucks activated a power supply which was designed to increase the intensity of a 500-watt light source in a standard 35-mm slide projector. The reinforcing consequence was the opportunity to view on a rear projection screen a 35-mm slide. Transition from no illumination to maximum brightness of the projected visual stimulus occurred gradually, in direct proportion to the infant's sucking rate ["conjugate reinforcement," Lindsley (*2*)].

In the first experiment we studied the effects of visual reinforcement on the acquisition of high-amplitude sucking in 4-month-old infants. Groups of ten infants were randomly assigned to one of three experimental conditions. One group (base-line group) provided base-line reference data for spontaneous changes in the frequency of high-amplitude sucking over 10 minutes of testing in the experimental situation. For the other two groups a 15-minute conditioning procedure consisted of 2-minute base-line, 4-minute conditioning, 2-minute extinction, 4-minute reconditioning, and finally a second 3-minute extinction phase. For the sucking reinforcement group (SR group), presentation of the projected visual stimuli was experimentally contingent upon the occurrence of criterion sucking during each of the two 4-minute conditioning phases. For the last group (SW group) the occurrence of criterion sucking resulted in the discrete withdrawal of the projected visual stimuli, and each high-amplitude suck delayed the presentation of the visual stimulus for 5 seconds. For the last two groups, eight 35-mm chromatic slides (geometric patterns, cartoon figures, and human faces) were presented during each conditioning phase with a change of visual stimuli occurring every 30 seconds. During the base-line and extinction phases, infants sucked in the presence of a constant, dimly illuminated projection screen. All subjects were seated facing the projection screen on the lap of a female research assistant who held the nipple to the infant's mouth for the duration of the experimental procedures. A criterion amplitude suck was a positive pressure response of 18 mm-Hg or greater. Base-line reference data obtained from infants of this age had shown that approximately 35 percent of the infant's normal nonnutritive sucking met our experimental criterion of a high-amplitude suck.

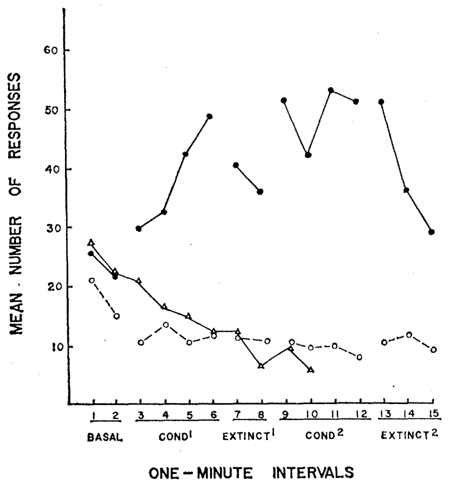

Fig. 1. Mean response rates for the three groups of 4-month infants over conditioning and extinction phases. Solid circles, sucking reinforcement group; open circles, stimulus withdrawal group; open triangles, base-line group.

The mean rate of criterion sucks for each of the three groups in 1-minute blocks over base-line, conditioning, and extinction phases are shown in Fig. 1. The apparent reinforcing effects of visual feedback seen in the performance of the SR group reflect reliable differences ($P < .05$ or less for all comparisons noted; two-tailed tests) between the SR group and the other two groups during the initial 4-minute conditioning and the 2-minute extinction phases. One-way analyses of variance (Kruskal-Wallis) indicated that there were no overall differences between the base-line sucking for the three groups, but highly reliable differences between the sucking rates for these groups were obtained during the initial conditioning and extinction phases. Subsequent individual comparisons between the pairs of groups (Mann-Whitney U-test) indicated that the SR group responded at a higher rate than either of the other two groups during the first conditioning and extinction phases. Reliable differences between the high-amplitude sucking rates of the SR and SW groups were maintained over the reconditioning and final extinction phases of the experiment. A series of Wilcoxon matched-pairs tests were used to determine the statistical reliability of the apparent acquisition and extinction effects for the SR group over the conditioning and extinction procedures. This group demonstrated predictable shifts in sucking rate, indicating response acquisition and extinction effects over each of the two conditioning and two extinction phases of the experiment. Similar statistical tests with the SW group indicated negligible shifts in frequencies of criterion sucking over the conditioning and extinction phases.

The sucking data for the three groups were also analyzed with respect to changes in the proportion of criterion high-amplitude sucks relative to the total number of sucks emitted during each minute in the experimental situation. Selective reinforcement of high amplitude sucking should have resulted in progressively higher proportions of the infant's sucking behavior meeting the criterion for the conditioned operant. This analysis provided clear support for the conclusion that visual reinforcement resulted in a rapid conditioned response differentiation by the SR group. While there were negligible differences in the mean response ratios (the number of criterion amplitude sucks divided by the total number of sucks) for the three groups during base-line measures (range from 0.36 to 0.39), by the 4th minute of conditioning 0.70 of all sucks emitted by the SR group met the criterion of high-amplitude sucking. In contrast to this high proportion of criterion sucking for the sucking reinforcement group, mean response ratios for the base-line and SW groups were 0.30 and 0.24, respectively. By the final minute of the reconditioning phase the SR group had a mean ratio of 0.85 as compared with 0.38 for the SW group. Furthermore, extinction of the acquired response was reflected in the ratio measures with the proportions of high-amplitude sucking for the SR group decreasing from 0.70 to 0.49 and from 0.85 to 0.56 over the respective extinction phases. The other groups showed negligible shifts in their response ratios over the extinction phases. It should be noted that the experimental procedure of withdrawing the projected visual stimuli contingent upon sucking (SW group) failed to produce evidence for an acquired suppression of high-amplitude sucking. However, the performance of this group does provide additional control data indicating that the changes in criterion sucking in the SR group were not attributable to either generalized arousal or specific eliciting effects of visual stimulation per se. Simply presenting infants with a changing pattern of visual stimulation while they were sucking did not result in their response rates differing reliably from those of the base-line control subjects. Only those infants who were specifically reinforced with visual feedback for emitting high-amplitude sucks (SR group) showed evidence of an acquired response differentiation. The reinforcing effectiveness of the visual feedback is seen in the fact that the learned response differentiation occurred quite rapidly, and by the end of 8 minutes of reinforced training these infants showed marked proficiency in their performance with better than 0.80 of their responses meeting the conditioned response criterion.

Additional evidence for the reinforcing effects of visual feedback on sucking behavior in human infants was obtained in a subsequent experiment with 12-month infants. While the first experiment showed that visual reinforcers could be employed to modify the topography of sucking in 4-month infants, the second experiment was designed to determine whether similar reinforcement procedures could be effectively employed to reestablish sucking in infants for whom nonnutritive sucking was no longer a stable response in their behavioral repertoire. Attempts to obtain base-line reference data on nonnutritive sucking with 12-month infants indicated that better than 60 percent of the infants actively rejected the experimental nipple prior to completing a 5-minute base-line measure of sucking. The apparent aversiveness of the sucking task for these infants was reflected in the high frequency of such behaviors as "crying," "fussing," and attempts by subjects to push away the nonnutritive nipple. Thus, in the second experiment we studied the effectiveness of visual reinforcers in reestablishing sucking with 12-month infants. A second variable studied in this experiment was the effect of varying the amount of redundancy in the array of visual reinforcers on the reinforcing effectiveness of the visual feedback. Studies with infrahuman organisms have indicated that instrumental exploratory behavior increases with increasing amounts of change in the visual reinforcing event (*3*, *4*). Briefly, the second experiment compared the conditional sucking rates for two groups of ten 12-month infants who received visual reinforcers varying in the amount of redundancy. Both groups were presented with conditioning and extinction procedures similar to those employed with the SR group in the previous experiment. One group (high-redundancy group) received three replications of four chromatic stimuli as reinforcers over the two 4-minute conditioning phases (with a stimulus change each 30 seconds). The second group (low-redundancy group) was presented with a single replication of eight visual stimuli as reinforcers over these conditioning phases. The results showed that when sucking was made functional for visual feedback, both groups showed rapid acquisition of conditioned sucking during the initial 4-minute conditioning phase.

In contrast to a base-line reference group of 12-month infants, who averaged less than 15 sucks per minute over a 5-minute sucking measure, both of the experimental groups averaged better than 40 sucks per minute during the 4th minute of the initial conditioning phase. Although the two groups did not differ in their conditioned sucking rates during the initial 4-minute conditioning and 2-minute extinction phases, the effects of stimulus redundancy on the reinforcing effectiveness of the visual feedback was seen during the reconditioning and second extinction phases, with the high-redundancy group sucking at reliably higher levels than the low-redundancy group during both these phases. In contrast to the apparent satiation effects due to reinforcement which are reflected in the decreasing sucking rates for the former group during reconditioning (third and fourth replication of the set of four stimuli), infants receiving only the second replication of the set of eight stimuli during reconditioning (low-redundancy group) maintained highly stable rates of conditioned sucking. These results supported the prediction that the reinforcing effectiveness of visual feedback was reliably influenced by the amount of stimulus redundancy.

Our experiments provide support for the conclusion that effective reinforcement of motivated behavior in the young human infant is not limited to a restricted class of stimuli in his environment. In addition to nutritive reinforcers, there are other classes of stimuli, possibly in each of the sensory modalities, that are effective in strengthening instrumental behaviors in infants. Berlyne (*5*) has suggested that any stimuli that are effective in "capturing the subject's attention" can have reinforcing value in suitable circumstances. The important developmental problem is the specification of stimulus parameters which distinguish positive and negative stimuli, and distinguish reinforcing and nonreinforcing stimuli for the developing infant in each of the sensory modalities. In subsequent experiments with infants we have found that visual feedback of the type employed in these experiments was effective in supporting motivated exploratory behavior with infants as young as 3 weeks of age. Furthermore, acquisition of conditioned sucking has been demonstrated when heterogeneous auditory feedback in the form of music and human voices was employed for reinforcement.

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Tryptophan Pyrrolase Induction in Patients with Manic Depression

Mandell and Spooner (*1*) presented a graph of some biochemical data gathered from a manic-depressive patient. The authors' discussion of these data is inconsistent with the graph, and therefore is misleading. They stated that after intravenous administration of ^{14}C-tryptophan during the different clinical phases, the turnover of radioactive tryptophan to kynurenine during depression was "significantly in-