and vice versa, and subsequently, that it was possible not only to reinforce drinking with running, but also to reverse the reinforcement relation in the same subjects merely by changing from one set of parameters to the other (*5*).

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4. D. R. Williams and P. Teitlebaum [*Science* **124**, 1294 (1956)] have reported the negative reinforcement of drinking—drinking turning off electric shock—but I can find no report of the positive reinforcement of eating and drinking responses.
5. This report is based on a paper read at the meeting of the Psychonomic Society, New York, 1961. This work was aided by grant M-3345 from the National Institute of Mental Health and by grant G-19574 from the National Science Foundation.

20 December 1961

Enhancement of Cesium-137 Excretion by Rats Treated with Acetazolamide

Abstract. Acetazolamide (10 mg/kg, intraperitoneally) increases the urinary excretion of cesium-137 in the rat. Meralluride (6.8 mg of Hg per kilogram, subcutaneously) blocks the effect of acetazolamide on the cesium-137 excretion without any influence on the urine volume and *p*H of the urine. This indicates that acetazolamide increases the urinary excretion of cesium-137 by increasing its secretion through the renal tubule in the same manner as it increases the excretion of potassium and rubidium-86.

As Cs^{137} forms in large quantities during uranium and plutonium fission and ranks high on the list of hazardous by-products of various uses of nuclear energy, we have attempted to find methods of increasing the excretion of this isotope from animals. The agents which have been tested previously include certain diuretics (*1*), steroids (*1, 2*), vitamins (*2*), hormones (*2, 3*) and ion exchange resins (*4*). As Cs is closely related to K in its physicochemical properties, and as acetazolamide increases the excretion of K by increasing its secretion in the renal tubule (*5, 6*), we have studied the influence of acetazolamide on the urinary excretion of Cs^{137} in the rat.

Male white rats of Sprague-Dawley strain weighing between 250 and 260 g were used in these studies. The animals were fed on "Purina Chow" until the day of experiment. The plan of the experiment was to observe the excretion of Cs^{137} during the first 6 hours. This time period was chosen because the duration of action of acetazolamide was about 6 hours ("drug phase") (*7*). A total of 24 animals were divided into four groups and treated as follows: group A, meralluride (6.8 mg of Hg per kilogram, subcutaneously) at 0 hours, acetazolamide (10 mg/kg intraperitoneally) at 2 hours; group B, meralluride (6.8 mg of Hg per kilogram, subcutaneously) at 0 hours; group C, acetazolamide (10 mg/kg, intraperitoneally) at 2 hours; group D, control. All animals received Cs^{137} (11.35 μc/kg, intraperitoneally in normal saline) at 2 hours 10 min. The urine samples were collected at 8 hours 10 min for radio-assay. The Cs^{137} in the urine samples was estimated by standard radiometric methods.

Table 1. Influence of acetazolamide (AZ) and meralluride (ML) on the urinary excretion of Cs^{137} in the rat*. Values are means (of six observations on six rats) ± standard error.

Group	Cs^{137} excreted in 6 hours (% of dose)	Urine volume (ml)	*p*H of urine
Group A (ML + AZ + Cs)	3.98 ± 0.70	10.7 ± 1.3	7.7 ± 0.2
Group B (ML + Cs)	3.28 ± 0.51	9.1 ± 1.3	6.8 ± 0.4
Group C (AZ + Cs)	6.68 ± 1.25	9.7 ± 1.3	8.4 ± 0.2
Group D (Cs only)	2.33 ± 0.27	5.1 ± 0.6	6.6 ± 0.2

*Statistical analysis:

Column	*Mean differences*	*Reliability by t-test* (P *values*)
2	C – D	< 0.01
	B – D	> 0.05
	A – D	> 0.05
3	C – D	< 0.01
	A – D	< 0.01
	B – D	< 0.02, > 0.01
4	C – D	< 0.01
	A – D	< 0.01
	B – D	> 0.05

The results in Table 1 indicate that group C, treated with acetazolamide, excreted two to three times more Cs^{137} than did the control group, D. Acetazolamide increased the urine volume and raised the *p*H of the urine. Meralluride did not increase the excretion of Cs^{137} (compare groups D and B). It did increase the volume of urine without altering the *p*H of the urine. The effect of acetazolamide on the urinary excretion of Cs^{137} was blocked by meralluride, but the effect of acetazolamide on the urine volume and *p*H of the urine (compare groups A and B) was not influenced.

Berliner and his coworkers (*5*) have demonstrated that acetazolamide modifies the excretion of potassium in the dog by increasing its secretion into the renal tubules; and this effect of acetazolamide is blocked by mersalyl. Recently, Kunin *et al.* (*8*) found that acetazolamide increases the excretion of Rb^{86} by the dog, and this effect of acetazolamide can be blocked by meralluride. Our experiments suggest that acetazolamide increases the excretion of Cs^{137} in the rat by increasing its secretion in the renal tubule in the same manner as it increases the excretion of K and Rb^{86} (*9, 10*).

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7. The effect of acetazolamide on urinary composition during the first 6 hours was striking and was termed "drug phase" by Maren *et al.* [T. H. Maren, B. C. Wadsworth, E. K. Yale, L. G. Alonso, *Bull. Johns Hopkins Hosp.* **95**, 277 (1954)].
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9. There seems to exist a relationship between the activities of the structural analogs of acetazolamide (2-acetylamino-1,3,4-thiadiazole-5-sulfonamide) to inhibit carbonic anhydrase and their efficacies to increase the urinary excretion of Cs^{137}. Ethoxzolamide (6-ethoxybenzothiazole-2-sulfonamide) (10 mg/kg, intraperitoneally) during its "drug phase" of 6 hours and chlorothiazide (6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1,1-dioxide) (500 mg/kg, intraperitoneally) during its drug phase of 1 hour increase the urinary excretion of Cs^{137}.

Further work is in progress to explore the relationship between the carbonic anhydrase inhibition and Cs^{137} excretion.

10. This investigation was supported by American Cancer Society grant IN-25A, Army contract No. DA-49-007-MD-995, and a grant from Squibb Institute for Medical Research. We thank Dr. Allen D. Bass and Dr. George R. Meneely for their interest in the work.

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Double Visual Learning in Split-Brain Monkeys

Abstract. Split-brain monkeys (with forebrain divided) were trained to perform two contradictory visual tasks simultaneously, one task being presented to each eye. Usually one cerebral hemisphere dominated, but in some cases the two halves of the brain learned simultaneously. Contradictory color discriminations showed interference or transfer of learning until mid-brain commissures were also sectioned. The more extensive surgery failed to prevent transfer of simple brightness discriminations.

Recent experiments have shown that split-brain cats and rhesus monkeys, with midline section of the optic chiasm, corpus callosum, and hippocampal and anterior commissures, learn pattern discriminations presented to one eye but subsequently fail to remember them when the patterns are presented to the other eye (*1–3*). When successive monocular learning curves were compared, there was no indication that the learning with the second eye could benefit from the learning with the first eye (*4*). Animals sectioned in the optic chiasm and corpus callosum have also been found able to learn an opposite discrimination habit with the second eye without any sign of confusion or retardation of learning (*2*). They have been trained to perform two contradictory tasks concurrently by switching from eye to eye every few trials during training, and there has been no evidence of interaction between the processes of learning (*3, 5*).

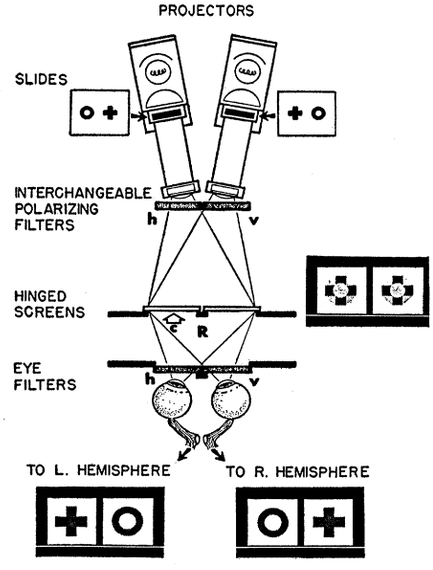

Fig. 1. Plan of the projection apparatus, with horizontal (*h*) and vertical (*v*) polarizing filters arranged to project +o to the left eye and o+ to the right eye. A correct response (*c*) to the left screen leads to automatic delivery of a reward at *R*. Diagrams of the screens as they appear without polarizing filters are shown to the right, and below they are shown as seen by left and right eyes through their respective filters. Intertrial reversal of the side of reward was accompanied by exchange of the filters in front of the projector.

The object of my study was to carry the analysis a step further. Can the concurrent learning of contradictory tasks proceed under conditions where both eyes receive the contradictory information simultaneously in each trial of training?

To test this question, a training apparatus was designed in which plane-polarized light and polarizing filters were used for the separation of stimuli to the two eyes. This apparatus, and the method of its use, are diagrammed in Fig. 1. Of the two pairs of patterns, one was polarized vertically, the other horizontally, and one pattern of each pair was rewarded consistently for a given eye throughout training, the rewarded figure for one eye being always the reverse of that for the other eye. The subject was trained to place its head in position at the sound of an alerting tone, and to respond by pushing one of the stimulus-bearing screens by hand.

Learning was allowed to proceed with both eyes open until a reliable criterion of learning (*6*) had been attained; then each eye was tested separately. When the performance with one eye did not show complete retention, training was continued with this eye alone until the criterion of learning was again satisfied.

Two subjects, with optic chiasm, corpus callosum, and anterior and hippocampal commissures cut (*7*), showed double learning, as in Fig. 2*A*, when presented with a black circle and a black cross equated for brightness. Both eyes retained knowledge of the discriminations as if there had been simultaneous learning of the contradictory choices. Moreover, as training proceeded, there was no sign of interference between rival learning processes. A normal control, in contrast, would not attend and showed signs of extreme

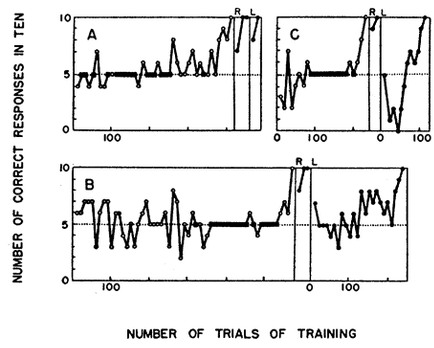

Fig. 2. Sample learning curves for three different tasks. *A*, Simultaneous learning of contradictory "circle vs. plus" discriminations by the two eyes. *B*, Monocular learning of another task, and interference of performance with the other eye. *C*, Monocular learning and interocular transfer of learning with contradictory brightness discriminations. Each hollow circle (binocular learning) or solid circle (monocular tests) represents ten trials. R = right eye test, L = left eye test. Position habits by which all ten trials of a group were made to one response screen, are shown by black horizontal bars.

frustration when confronted with the two overlapping pairs of stimuli after being trained to choose with reference to only one of them.

However, in 12 out of 14 tasks given these animals the retention was not equal in the two halves of the brain. In these instances one eye learned ahead of the other, as if the latter had been somewhat inattentive during binocular training, even though it was open and directed to the screens in each trial. An example of this asymmetric performance is shown in Fig. 2*B*, which gives the learning of contradictory choices between two complex colored figures. In a series of nine pattern-discrimination tasks there appeared to be no simple correlation between the nature of the patterns and the restriction of learning to one eye, although variations in the learning were closely similar in the two subjects.

An expected preference for the use of eye and hand connected with the same hemisphere appeared with the asymmetric learning. As a rule, it was the eye contralateral to the limb chosen for response which was superior. Furthermore, when vision was subsequently restricted to the unpreferred eye, there often resulted, after 10 to 20 trials, a spontaneous exchange of hands. Nevertheless, preferences for using motor and visual areas of the same hemisphere were not invariable. An eye and a hand of the same side would occasionally be chosen for execution of previously