

Fig. 2. Cumulative number of responses for one fish in the course of the last conditioning session before extinction, and the first extinction session. The subscripts refer to the order in which the fish was run through the three different conditions. Abbreviations as explained in Fig. 1.

extinction data for other animals, perhaps because the fish receives less feedback for responding than the pigeon which at least hears the noise of the peck, or the rat which at least hears the noise of the bar hitting a contact. In our experiments the fish is in a sound-attenuated cubicle, and there is almost no feedback for simply hitting the target except the proprioceptive stimulation from contact with the target.

Three of the fish were run through all three conditions of extinction. They took a mean of 6.7 sessions to extinguish under the condition without feedback, 5.0 sessions with noise reinforcement, and 13.7 sessions with noise and water reinforcement. (The other three fish died before they could be run through the remaining conditions.) The fish were reconditioned after each extinction period for 7 sessions, as in the conditioning sessions. Figures 1 and 2

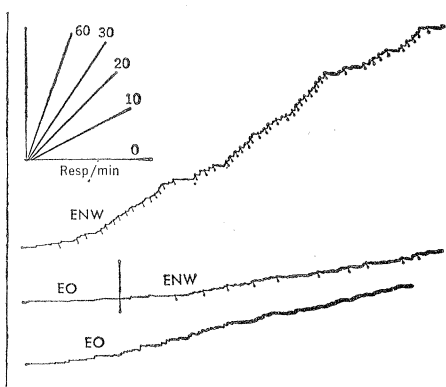


Fig. 3. Cumulative number of responses for a fish starting under conditions of extinction with no feedback at all (EO) and proceeding to conditions in which every tenth response is reinforced by the noise and water (ENW). The delivery of noise and water is indicated by the downward "blips."

show the last conditioning session and the first extinction session for each type of extinction. Although the three conditioning rates ( $C_1$ ,  $C_2$ ,  $C_3$ , Fig. 1) are similar, the rate of extinction is already different in the first extinction session ( $E_1$ ,  $E_2$ ,  $E_3$ , Fig. 1). Figure 2 shows the fish that was extinguished in an order opposite to that of the fish in Fig. 1. The rates of extinction in the different conditions within the fish shown, as well as in the third fish (not shown), are in the same order as the group results presented above.

One fish (Fig. 2) was reconditioned with worm reinforcement and then extinguished without feedback. Subsequently, it was again put into the noise-and-water reinforcement condition. The noise and water (Fig. 3, curves ENW) acted as a reinforcer and gradually increased the rate of response from that achieved after extinction with no feedback (Fig. 3, curves EO).

As a final control, an attempt was made to shape striking of the target in two naive goldfish by using the noise and water stimuli (without the worms) as reinforcers. Neither fish struck the target, a result invalidating the interpretation that the noise-and-water stimulus by itself acts as a sensory reinforcer of some kind.

Our data demonstrate that the goldfish can acquire a conditioned reinforcer by a procedure quite similar to that used with other animals (2). In this respect the goldfish does not differ from other animals higher on the phylogenetic scale.

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#### Dimethyl Sulfoxide: Breakdown of Blood-Brain Barrier?

Brink and Stein (1) have found that the levels of radioactivity in the blood and brain of rats injected intraperitoneally with  $^{14}\text{C}$ -pemoline ( $^{14}\text{C}$ -PIO) dissolved in dimethyl sulfoxide (DMSO) were about twice as high as those given the labeled material suspended in 0.3 percent tragacanth. These authors attributed the increased levels of radioactivity found in the brains of animals treated with DMSO "to a partial breakdown of the blood-brain barrier" induced by DMSO "within the first 30 minutes." However, whether the higher brain levels of radioactivity found in the animals treated with  $^{14}\text{C}$ -PIO in DMSO are anything more than a reflection of the increased blood levels may be questioned on the basis of the data presented.

From the data reported by Brink and Stein it may be calculated that at 30 minutes after injection the radioactivity in the blood of DMSO-treated rats was 25.8 times higher than that found in the brain, whereas the analogous value in the group treated with tragacanth was 31.6 times higher. Since the ratio of the former value (25.8 times) to that of the latter (31.6 times) is less than 1.00, namely 0.817, it seems to take a lower blood level in the group treated with DMSO to achieve a given brain level.

On this basis the authors conclude that "a partial breakdown of the blood-brain barrier within the first 30 minutes" has occurred in the group treated with DMSO. If the ratio between the two groups had been 1.00, one could argue that the brain levels were simply related to the blood values despite the marked differences in brain levels between the two groups. At 60 minutes after injection the relationship between the two groups was reversed, and the ratio of the values in the group treated with DMSO (22.4 times) to that in the group treated with tragacanth (18.4 times) was 1.20, the inverse of the ratio found at 30 minutes. The authors did not conclude from this value, however, that DMSO inhibited transport across the blood-brain barrier at 60 minutes. And at 120 minutes the ratio between the same groups is (16.1 times)/(15.3 times), or 1.05. Thus, an average of the three ratios obtained between the groups treated with DMSO and those treated with

tragacanth at 30, 60, and 120 minutes is 1.02, a value which indicates that DMSO may have had no effect on the blood-brain barrier during this time, and that increased brain levels were due only to facilitated entry of radioactivity into the blood. For the time periods prior to 30 minutes no data are cited for the group treated with tragacanth to support the conclusion of a "a partial breakdown of the blood-brain barrier *within* [italics ours] the first 30 minutes."

The action postulated for DMSO in promoting transport across the blood-brain barrier would seem to be most readily demonstrated when DMSO is injected intravenously as a vehicle for drugs acting on the central nervous system. We (2) found, however, that when DMSO was administered intravenously as a vehicle for barbitol or phenobarbital sodium in various experiments, either there was no difference between the use of DMSO or saline as a vehicle, or it took mice significantly longer to lose their righting reflex with DMSO.

This would indicate that DMSO either had no effect or that it may actually have decreased transport across the blood-brain barrier. Earlier Dixon *et al.* (3) had found that the use of DMSO as a vehicle (i) did not affect the penetration of intravenously administered  $^{14}\text{C}$ -*p*-aminohippuric acid into the brain or cerebrospinal fluid in dogs, nor (ii) did it affect the time required for intraperitoneally administered phenobarbital to cause a loss of the righting reflex in mice.

Thus, there does not appear to be any substantial evidence showing that DMSO exerts any general action in promoting transport across the blood-brain barrier, and we believe that it remains to be demonstrated that DMSO affects the brain uptake of pemoline specifically.

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Although the comments of Kocsis, Harkaway, and Vogel are valid in the restricted sense that elevated plasma levels of pemoline- $\text{C}^{14}$  will increase brain levels of this compound, the authors appear not to consider tissue to plasma ratios as being important to an interpretation of possible changes in transport phenomena. If the ratios at different times in animals injected with pemoline and tragacanth are used as criteria, then averaging the ratios for animals treated with pemoline and dimethyl sulfoxide (DMSO) over time to give a value approximating that of the former group does not necessarily mean that no change in the transport process had occurred within this period, regardless of direction. The authors' proposal that "transport across the blood-brain barrier would seem to be most readily demonstrated when DMSO is injected intravenously as a vehicle for drugs" has recently been used by Thompson and Hart (1) to study the effects of DMSO on the transport of sucrose- $\text{C}^{14}$  and urea- $\text{C}^{14}$  into the brain. Under the conditions employed, DMSO facilitated penetration by urea- $\text{C}^{14}$  but had no effect on the uptake of sucrose- $\text{C}^{14}$ . It appears that DMSO may have differential effects on the blood-brain barrier, depending on the type of compound used to evaluate the effect of this vehicle on the brain transport process. The citation of Dixon's findings by these authors could represent a case in which DMSO does not affect brain penetration by *p*-aminohippurate, whereas it may well facilitate uptake of pemoline.

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#### Venus: Ice Sheets

Libby (1) suggests that the polar regions of Venus may be covered with ice sheets despite the fact that the Cytherean surface is very hot in the equatorial region. His revival of this old hypothesis stems from the difficulty in accounting for all the water on Venus.

It is reasonable to assume that almost as much water has escaped from the interior of Venus as from the interior of Earth.

I point out that if the amount of water on Venus is of the same magnitude as that on Earth (2), about  $1.5 \times 10^9 \text{ km}^3$ , then the Cytherean ice sheets must extend into low latitudes indeed if they are to lock up all the water. Since the equatorial region is very hot it does not appear realistic to postulate that the missing water on Venus is all contained in polar ice sheets.

The profile and thickness of an active ice sheet are almost uniquely determined once its horizontal dimensions are specified (3, 4). The profile of a circular ice sheet, centered on a pole of a planet, is given approximately by the equation

$$h^2 = (3\tau R/\rho g)(\theta - \theta_0)$$

where  $h$  is the thickness of the ice sheet at latitude  $\theta$  (measured in radians),  $\theta_0$  is the latitude of the edge of the ice sheet,  $R$  is the radius of the planet,  $\rho$  is the density of ice,  $g$  is the gravitational acceleration at the planet's surface, and  $\tau$  is the average shear stress at the bottom of the ice sheet—

$$\tau \approx - (2\rho gh/3R)dh/d\theta = -\rho gh\alpha$$

where  $\alpha$  is the slope of the upper surface. This profile equation is derived under the assumption that an ice sheet sinks isostatically into the crust to the extent of  $1/3$  the total thickness of ice. (Note that the density of surface rocks is about three times greater than the density of ice.) The curvature of the surface of the planet is taken into account in this equation, but surface relief in the form of mountain chains or "ocean basins" is ignored.

The total volume  $V$  of ice in two sheets, one centered at each pole, is

$$V = (4\pi R^2)(3\tau R/\rho g)^{1/2} \int_{\theta_0}^{\pi/2} (\theta - \theta_0)^{1/2} \cos \theta \cdot d\theta$$

The integral in this equation is equal to the series

$$(\pi/2 - \theta_0)^{3/2} \{ [2^2(\pi/2 - \theta_0)^2/3 \cdot 5] - [2^4(\pi/2 - \theta_0)^4/3 \cdot 5 \cdot 7 \cdot 9] + [2^6(\pi/2 - \theta_0)^6/3 \cdot 5 \cdot 7 \cdot 9 \cdot 11 \cdot 13] - \dots \}$$

For the typical value of  $\tau \approx 0.5 \text{ bar}$ , we find  $\theta_0 \approx 27^\circ$  when  $V$  is set equal to the volume of water on Earth. If  $\tau \approx 1 \text{ bar}$ ,  $\theta_0 \approx 36^\circ$ . Therefore the Cytherean ice sheets must extend to quite