(initial mean weight 409 g), and alcohol infusion to a weight loss of 11.9 percent (initial mean weight 390 g).

The mean amount of alcohol solution drunk over the 14 days by the two groups shows a very large difference (Fig. 1). The group treated with alcohol drank an average 22.22 ml, whereas the group infused with water drank 0.78 ml ($F = 9.24$, $P < .02$ in a repeated measures analysis of variance). When specific comparisons are made within the design of the repeated measures analysis of variance (*5*) between the alcohol rats and the largest drinker in the control group, five rats are significantly different from the largest control ($P < .01$) and two are not significantly different ($P > .05$). There was no significant change in alcohol consumption during the 14 days of observation (repeated measures analysis of variance, $F = 1.19$, $P > .05$). Two of the alcohol drinkers drank 45.9 ml of 10 percent alcohol per day (averaged over 14 days). They had been infused with 45.9 ml per day of the same solution initially.

There is large individual variation among rats in susceptibility to our treatment, which may be related to the difference in the rate at which tolerance to alcohol develops in various individuals. That tolerance to alcohol is apparent on gross observation. While the infusion of 50 ml of 10 percent alcohol initially produces ataxia and sluggishness, with an occasional lapse into unconsciousness, the rats that drink this amount volitionally after they have been treated cannot be distinguished from normal rats in terms of their gait and alertness. We have observed two rats for 11 weeks and, while their daily alcohol intake has averaged 29.8 and 32 ml, respectively, without any sign of diminution, their general health continues to be excellent and their appearance is quite normal. We have also attempted to see if alcohol intake can be diminished by withholding alcohol for a number of days. Five rats, whose average 5-day intake was 31.1 ml before a "drying-out" period of 5 days, averaged 29.9 ml for 5 days after alcohol was again presented. This diminution is not significant ($F = 0.24$, $P \gg .05$ in a repeated measures analysis of variance). Marked restlessness (increased motor activity) was observed during the period of alcohol withdrawal.

The experiment described here, besides showing that alcohol "addiction" (at least in the psychological sense) can be produced without orosensory exposure to the drug, demonstrates a convenient and speedy method for the study of alcohol addiction with a view to its possible pharmacological control.

J. A. DEUTSCH
H. S. KOOPMANS
Department of Psychology, University of California, San Diego, La Jolla 92037

References and Notes

1. R. D. Myers and W. H. Veale, *The Biology of Alcoholism*, B. Kissin and H. Begleiter, Eds. (Plenum, New York, 1972), vol. 2.
2. The gastric cannulas were made from Silastic tubing [inner diameter 0.040 inch (1.016 mm); outer diameter 0.085 inch (2.159 mm)]. A piece of Marlex mesh was attached to the tube about 1/3 inch (0.85 cm) from one end with RTV Silastic glue. A knob of glue was placed between the mesh and the end of the tube. After a midline incision was made the stomach was gently lifted from the peritoneal cavity. A small hole was made in a relatively unvascularized portion of the fundus of the stomach. The tube was inserted through the hole in the stomach until the mesh was flush with the stomach wall. A loop of 5-0 silk thread tied the tissue around the tube. Two anchor stitches were made from the mesh to the stomach wall. The other end of the tube was threaded through the peritoneal muscle near the stomach's normal resting position and under the skin to the back of the neck. Another small piece of Marlex mesh was put around the tube and placed under the skin at the point at which the tube exits. The rats were allowed to recover for at least 5 days. Peritonitis rarely occurred.
3. The Bowman restraining cage is made by connecting stainless steel rods between two Plexiglas endpieces. The rat is enclosed and supported by the rods. The rat cannot move forward or backward but can twist around so that he lies on his back. The cage and a full description are available from Nuclear Supply and Service Co., Washington, D.C.
4. The pump was a ten-veined Buchler Dekastaltic pump.
5. B. J. Weiner, *Statistical Principles in Experimental Design* (McGraw-Hill, New York, 1962), p. 85.
6. This work was supported by grant MH 20996-01 from the Public Health Service. We would like to thank P. Branson and B. J. Shebo for their technical assistance and P. Roll for providing computer programs for the statistics.

30 October 1972; revised 26 December 1972

Camptothecin Blocks Memory of Conditioned Avoidance in the Goldfish

Abstract. *Intracranial injection of 10 to 75 micrograms of camptothecin, a plant alkaloid that blocks RNA synthesis in eucaryotic cells, blocks incorporation of tritiated uridine into RNA in the goldfish brain. Injection of 10 to 50 micrograms of the drug within 1.5 hours of training results in greatly diminished memory, tested 1 week later. Injection of the drug 5 or 24 hours after training produces no measurable effect on retention of the learned response.*

When actinomycin D, an inhibitor of RNA synthesis, is injected intracranially into the pericranial fluid of goldfish immediately after training, retention of a conditioned response is diminished (*1*). While an amnestic effect of intracerebrally injected actinomycin has since been claimed in rodents (*2*) and in chicks (*3*), such injections of the drug into the brain substance can produce morphological (*4*) and physiological (*5*) changes. It also has been reported that actinomycin produces behavioral effects not attributable to a block of memory (*6*). Although the goldfish experiments indicate that intracranially injected actinomycin specifically affected memory formation, the recent availability of a less toxic and more reversible inhibitor of RNA synthesis prompted this further investigation on the putative relation of RNA synthesis and memory in the fish. Camptothecin is a plant alkaloid (*7*) known to possess anticancer activity (*8*) and to inhibit synthesis of high molecular weight nucleic acids (*9*, *10*). In HeLa cell cultures, it inhibits nonmitochondrial nucleic acid synthesis: synthesis of heterogeneous nuclear RNA and of 45*S* nucleolar RNA is blocked as is the appearance of 28*S* and 18*S* ribosomal RNA in the cytoplasm. While the inhibition of synthesis includes messenger-like RNA and DNA, synthesis of 5*S* RNA is not affected by the drug. The DNA isolated from camptothecin-treated cells is of significantly lower molecular weight than control DNA (*10*), but direct addition of the drug to isolated DNA has no effect. Whatever the mode of action of the drug, its effects are rapidly reversed within minutes after removal of camptothecin from a cell culture medium.

We measured the labeling of brain RNA in common goldfish (*Carassius auratus*, 8.5 to 12 g body weight, obtained in weekly shipments from Ozark Fisheries) at various times after the intracranial injection of 50 μg of sodium camptothecin (*11*) dissolved in 10 μl of 0.15*M* NaCl, followed after various intervals by a similar intracranial injection of 15 μc of [5-

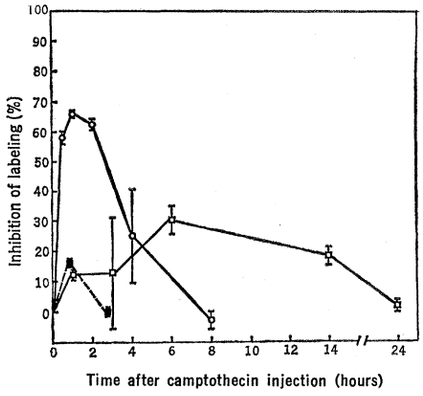

Fig. 1. Effect of intracranial injection of 50 μg of camptothecin on RNA (open circles) and protein labeling (open squares). For RNA studies, 16 fish received camptothecin intracranially at zero time, followed by 15 μc of [^{3}H]uridine at each time point indicated. Fish were killed 1 hour after isotope injection and two pools of eight brains were analyzed. Lines indicate the range of the two determinations. In control groups, the trichloroacetic acid supernatant contained a mean of 1.70×10^6 disintegrations per minute (dpm) per fish and the RNA hydrolysate contained 2.33×10^5 dpm per fish. For protein labeling, 15 μc of [^{3}H]leucine were injected intraperitoneally into two groups of eight fish 1, 3 (one group), 6, 14, and 24 hours after injection of 50 μg of camptothecin or 1 and 3 hours after 25 μg of camptothecin (filled squares, dashed line). Fish were killed 0.5 hour after injection of the isotope. Five groups of eight control fish each received saline intracranially. The trichloroacetic acid supernatant of the control fish contained a mean of 8.63×10^4 dpm per fish and the protein precipitate contained 1.65×10^4 dpm per fish. The drug effect on ratios was in each instance accounted for by reduction of radioactivity in the macromolecular (RNA or protein) fractions, with no effect on the supernatant radioactivity.

^{3}H]uridine (25.7 c/mmole). Fish were decapitated 1 hour after the second injection, and groups of eight brains were pooled and were rinsed thoroughly, then homogenized in 5 ml of water. The RNA was hydrolyzed from a washed trichloroacetic acid precipitate by heating and stirring for 4 hours at 37°C in 1*N* KOH (*1*). After acidification and precipitation of DNA and protein with 6*M* perchloric acid, 0.5 ml of the supernatant was added to 12 ml of a scintillation counting fluid containing 26 percent Triton X-100 in toluene, 2,5-diphenyloxazole, and 1,4-bis-[2-(4-methyl-5-phenyloxazolyl)]-benzene. A 0.5-ml portion of the original trichloroacetic acid supernatant was counted under the same conditions. The RNA synthesis was calculated as the ratio of radioactivity in the RNA hydrolysate to that in the trichloroacetic acid supernatant, and the inhibition was calculated from this ratio compared with one obtained after a similar labeling for 1 hour in control fish that had been injected intracranially with saline. Injection of 50 μg of camptothecin inhibited RNA labeling very rapidly, but substantial recovery occurred within 4 hours, and by 8 hours the rate of RNA labeling had returned to control levels (Fig. 1). This rapid inhibition and recovery of RNA synthesis in brain is consistent with the reported activity of camptothecin in cell cultures and is in contrast to the protracted course of inhibition achieved with actinomycin in the goldfish brain (*1*).

To explore the possible effect of camptothecin on protein labeling, fish were injected intracranially with 50 μg of the drug and at various times later with 15 μc of L-[4,5-^{3}H]leucine (35.5 c/mmole) in 50 μl of 0.15*M* NaCl administered intraperitoneally (*12*). Fish were decapitated 30 minutes later, and eight brains were pooled and were homogenized in water. A portion was dried on a filter paper disk, and protein was precipitated with 10 percent trichloroacetic acid. Disks were washed with 5 percent trichloroacetic acid at 80°C, then ethanol and ether prior to scintillation counting (*13*). Protein labeling and its inhibition were calculated from the ratio of radioactivity in the precipitated protein to radioactivity remaining in the trichloroacetic acid supernatant in drug-injected fish compared with the ratio in control fish injected intracranially with saline (*12*). Inhibition of protein labeling after a 50-μg dose of camptothecin was greatest (31 percent) 6 hours later, whereas the block in RNA labeling developed much more rapidly and was more profound (Fig. 1). However, while RNA labeling rapidly returned to control levels, protein labeling remained depressed for more than 14 hours. The relation between the two curves suggests, as has been concluded from studies in cell cultures (*9, 10*), that the effect of camptothecin on protein synthesis is secondary to the disruption in RNA metabolism. A dose-response study (Fig. 2) showed a measurable decrease of RNA labeling (32 percent) with as little as 10 μg of camptothecin and that 77 percent inhibition could be produced with 75 μg of the drug. A higher dose, 100 μg, produced no additional inhibition of RNA labeling.

Having established the efficacy of camptothecin as an inhibitor of brain RNA labeling, we examined its effects on retention of a conditioned avoidance response when injected after training. Goldfish were conditioned to avoid a shock, administered through the water, by swimming across a barrier after presentation of a light stimulus on the same side of a two-way shuttlebox (*1, 14*). Each 60-second trial consisted of 20 seconds of light presentation followed by 20 seconds of light and shock

Table 1. Effect of camptothecin on retention of a conditioned avoidance response in goldfish; A, achieved; P, predicted; S.E., standard error.

N	Day 1, number of avoidance responses (± S.E.) during acquisition			Treatment after acquisition		Day 8, correct responses		Retention deficit A − P
	Trials 1 to 10	Trials 11 to 20	Trials 21 to 30	Delay (hr)	Camptothecin (μg)	A, trials 31 to 40	P, trials 31 to 40	
85	1.04 (± .15)	2.66 (± .32)	4.55 (± .34)			6.41 (± .27)	*	
38	1.00 (± .22)	3.16 (± .39)	5.21 (± .52)	0	50	3.42 (± .45)	6.23 (± .18)	− 2.81 (± .45)‡
24	1.58 (± .34)	4.50 (± .62)	6.62 (± .68)	1.5	50	5.46 (± .58)	6.66 (± .20)	− 1.20 (± .52)†
35	1.31 (± .24)	3.60 (± .59)	6.00 (± .58)	5	50	5.60 (± .51)	6.38 (± .20)	− 0.78 (± .52)
34	1.03 (± .24)	3.09 (± .55)	4.60 (± .57)	24	50	6.65 (± .50)	6.33 (± .18)	0.31 (± .40)
23	0.78 (± .24)	1.44 (± .38)	3.78 (± .69)	0	25	3.30 (± .69)	5.75 (± .26)	− 2.45 (± .68)‡
20	0.80 (± .26)	1.45 (± .39)	3.60 (± .60)	0	10	4.10 (± .58)	5.19 (± .27)	− 1.09 (± .43)†

* The multiple regression values obtained from this group were used to predict the number of correct responses for other groups in this experiment (*15*). † $P < .05$, one-tailed *t*-test. ‡ $P < .005$, one-tailed *t*-test.

and 20 seconds of darkness. Crossing the barrier was detected by photocells and terminated the trial. If the fish crossed during the light-only presentation, an avoidance response was recorded, whereas if fish crossed the barrier after the intermittent electrical shock was presented, an escape response was recorded. The sequence was controlled and recorded by means of a PDP-8S computer that also recorded latencies (*14*). Fish were given 30 trials on day 1 of an experiment and then were returned to home storage tanks. Retention was tested during ten trials administered 7 days later. Memory deficits were calculated as the difference between the achieved scores on day 8 and a predicted score obtained from multiple regression analyses based on control animals run during the 5-week period during which the experimental animals were trained (*15*).

When 50 μg of camptothecin were injected intracranially immediately after training on day 1, a mean deficit of −2.81 avoidance responses was observed on retraining on day 8 (Table 1). Fish that were returned to their home tanks after training and then given 50 μg of camptothecin 90 minutes later had a considerably smaller deficit on retraining. When the interval between the end of training and injection was 5 or 24 hours, significant memory loss did not occur. As has been observed with inhibitors of protein synthesis (*14*), as well as with actinomycin (*1*), memory of the shock avoidance response was resistant to disruption a few hours after the acquisition trials. Injection of as little as 10 μg of camptothecin immediately after trial 30 resulted in a measurable retention deficit and 25 μg seemed almost as effective as 50 μg. When 75- and 100-μg doses were administered 24 hours after training, residual effects of the drug injection on performance were assumed to be present on retraining, since these animals showed decreased responding. In contrast, delayed injection of lower doses produced no effect.

From this study, it would appear that camptothecin is a suitable drug for investigation of the role of RNA in brain function. Although actinomycin had been shown previously to produce an effect on retention of conditioned avoidance in fish, the confirmatory effect with camptothecin, a drug having a completely different molecular basis of action (*9, 10*), is useful.

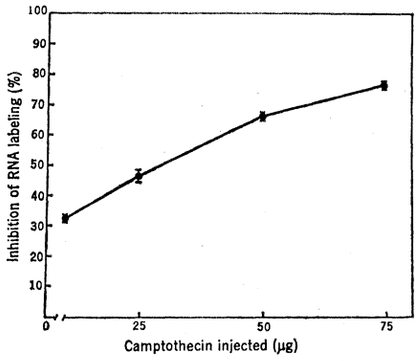

Fig. 2. Dose response of RNA labeling to camptothecin. Camptothecin (10, 25, 50, or 75 μg) was injected intracranially 1 hour prior to injection of [^{3}H]uridine. One hour later the fish were killed, and two pools of eight fish brains each were analyzed as in Fig. 1.

Although we have not measured the effect of camptothecin on DNA synthesis in the goldfish brain, we previously found that a DNA synthesis inhibitor, arabinosyl cytosine, had no measurable effect on retention of shock avoidance conditioning in the goldfish (*16*). The small but prolonged effect of camptothecin on protein synthesis, rather than the block of RNA synthesis, could mediate the observed effect on memory. However, studies with puromycin and acetoxycycloheximide indicate that low levels of inhibition, such as were observed in our study with camptothecin, do not produce effects on retention (*17*). Furthermore, 25 μg of camptothecin produced a retention deficit (Table 1) when RNA labeling was depressed 47 percent, while the block in protein synthesis was even smaller and more transient than that observed with 50 μg.

It remains possible that the effect of camptothecin on retention is not specifically related to memory but to some other neurological or behavioral parameter affecting performance on the retraining day. For example, Nakajima (*6*) has indicated in maze training of rats that a delayed proactive effect of actinomycin can explain a performance decrement. It is extremely unlikely, however, that proactive effects play a role in our experiments with the goldfish treated with either actinomycin or with camptothecin, since the inject-retrain intervals are very long compared with the rate of development of drug insusceptibility (consolidation).

The significance of this first report of an effect of camptothecin on the nervous system may reside as much in differences between the mode of action of this drug and actinomycin as in their similarities. Camptothecin appears more selective than actinomycin in its action on nuclear RNA species, is rapidly reversible, and does not significantly affect purified *Escherichia coli* or crude eucaryotic RNA polymerases (*9, 10*). Also, we found that camptothecin was less toxic (*18*). Whether camptothecin exerts its effect by blocking an inductive process such as growth, by lowering the level of a rapidly turning over macromolecule, or by some other mechanism, its effect on behavior, on the basis of present knowledge, suggests a role for the cell nucleus in long-term memory formation.

J. H. NEALE
P. D. KLINGER
B. W. AGRANOFF
Mental Health Research Institute and *Neurosciences Laboratory, University of Michigan, Ann Arbor 48104*

References and Notes

1. B. W. Agranoff, R. E. Davis, L. Casola, R. Lim, *Science* **158**, 1600 (1967).
2. L. R. Squire and S. H. Barondes, *Nature* **225**, 649 (1970); D. Daniels, *ibid.* **231**, 395 (1971).
3. S. D. Codish, *Physiol. Behav.* **6**, 95 (1971).
4. A. Torvik and A. Heding, *Acta Neuropathol.* **9**, 146 (1967); H. Koenig, C. Y. Lu, S. Jacobson, P. Sanghavi, R. Nayyar, in *Protein Metabolism of the Nervous System*, A. Lajtha, Ed. (Plenum, New York, 1970), p. 491.
5. S. Nakajima, *J. Comp. Physiol. Psychol.* **67**, 457 (1969).
6. ———, *Physiol. Behav.* **8**, 1063 (1972).
7. M. E. Wall, M. C. Wani, C. E. Cook, K. H. Palmer, A. T. McPhail, G. A. Sim, *J. Amer. Chem. Soc.* **88**, 3888 (1966).
8. J. L. Hartwell and B. J. Abbott, *Advan. Pharmacol. Chemother.* **7**, 137 (1969); L. G. Hart, J. B. Call, V. T. Oliverio, *Cancer Chemother. Rep.* **53**, 211 (1969); J. A. Gottlieb, A. M. Guarino, J. B. Call, V. T. Oliverio, J. B. Block, *ibid.* **54**, 461 (1970).
9. H. B. Bosmann, *Biochem. Biophys. Res. Commun.* **41**, 1412 (1970); D. Kessel, *Biochim. Biophys. Acta* **246**, 225 (19[illegible] → R. S. Wu, A. Kumar, J. R. Warner, *Proc. Nat. Acad. Sci. U.S.A.* **68**, 3009 (1971); R. C. Gallo, J. Whang-Peng, R. H. Adamson, *Fed. Proc.* **30**, 627 abstract (1971); H. T. Abelson and S. Penman, *Nature New Biol.* **237**, 144 (1972).
10. M. S. Horwitz and S. B. Horwitz, *Biochem. Biophys. Res. Commun.* **45**, 723 (1971); S. B. Horwitz, C.-K. Chang, A. P. Grollman, *Mol. Pharmacol.* **7**, 632 (1971).
11. The sodium salt of camptothecin (NSC-100880) was graciously supplied by Dr. H. B. Wood, Jr., of the Cancer Chemotherapy Service Center, National Cancer Institute, National Institutes of Health.
12. R. Lim and B. W. Agranoff, *J. Neurochem.* **16**, 431 (1969).
13. R. J. Mans and G. D. Novelli, *Arch. Biochem.* **94**, 48 (1961).
14. B. W. Agranoff, in *Animal Memory*, W. K. Honig and P. H. R. James, Eds. (Academic Press, New York, 1971), p. 243.
15. To reduce individual as well as group-to-group (including seasonal) variability, a regression equation based on control fish from the same shipment was used (*14*). For most of the study, for trials 31 to 40, the predicted number of avoidance responses, $P = 7.00 + .108\ A_1 + .155\ A_2 + .0048\ A_3 - .012\ S_1 - .0066\ S_2 - .0096\ S_3$, where A_1, A_2, and A_3 are the number of avoidance responses observed on day 1 during trials 1 to 10, 11 to 20, and 21 to 30, respectively, and S_1, S_2, and

S_3 are escape latencies measured as the number of shocks (40 per minute) administered during trials 1 to 10, 11 to 20, and 21 to 30. One-half of the fish receiving 25 μg of camptothecin and all of the fish receiving 10 μg of camptothecin were from a group of fish in which the control animals had low responding rates. For these fish, $P = 4.518 + .233\ A_1 - .409\ A_2 + .573\ A_3 - .0198\ S_1 - .0013\ S_2 + .0118\ S_3$. Fish that failed to show an avoidance response during acquisition training or had more than five avoidances or failures to escape during the first ten trials (about 20 percent of the animals) were excluded from further study.

L. Casola, R. Lim, R. E. Davis, B. W. Agranoff, *Proc. Nat. Acad. Sci. U.S.A.* **60**, 1389 (1968).

B. W. Agranoff, R. E. Davis, J. J. Brink, *Brain Res.* **1**, 303 (1966); J. J. Brink, R. E. Davis, B. W. Agranoff, *J. Neurochem.* **13**, 889 (1966).

18. Eighteen of 20 fish injected intracranially with 2 μg of actinomycin died between 11 and 20 days of the injection, while two fish survived. In 20 fish injected intracranially with 50 μg of camptothecin, there were no deaths.

19. J.H.N. was supported by NIMH training grant 07417. Supported by NIMH grant MH-12506 and NSF grant GB-5125X.

3 November 1972

Analgesic Strength of 33 Percent Nitrous Oxide: A Signal Detection Theory Evaluation

Abstract. *Radiant heat stimulation was applied to volunteers and rating scale responses were obtained to assess the analgesic properties of 33 percent nitrous oxide. The methodology of signal detection theory was applied to the data to demonstrate that nitrous oxide reduces both sensitivity to pain and willingness to report pain. This method is superior to threshold estimation for the evaluation of analgesics.*

The efficacy of analgesic agents for pain in humans has been studied extensively in the laboratory by using the sensory threshold as an index of sensitivity to pain, but, as in other areas of behavioral research, this index has proved to be unreliable. As Goldiamond (*1*) noted, the threshold reflects both sensory sensitivity to stimulation and response bias (willingness to report the experience of the stimulation). Thus, an elevated pain threshold following drug administration may reflect changes in either or both of these factors. Recently, an alternative methodology based on signal detection theory (SDT) has been applied to the problems of quantifying human pain in the laboratory in terms of sensory and response factors (*2*). Our purpose in this report is to demonstrate the usefulness of SDT methodology in assessing the analgesic effects of agents commonly used to relieve pain. We chose nitrous oxide because in a concentration of 33 percent, its analgesic effects are well documented (*3*) and it still permits subject control and cooperation.

The Hardy-Wolff-Goodell dolorimeter was used to deliver potentially painful intensities of radiant heat ranging from 0 to 500 mcal sec^{-1} cm^{-2} to ink-blackened spots on the skin for 3-second periods. We defined four intensities for each subject: zero (stimulus 1), pain threshold minus 60 mcal sec^{-1} cm^{-2} (stimulus 2), pain threshold (stimulus 3), and pain threshold plus 60 mcal sec^{-1} cm^{-2} (stimulus 4).

Fourteen male subjects participated individually in two 1-hour sessions on different days (*4*). Each subject was randomly assigned to one of two groups to determine whether he would receive 33 percent nitrous oxide in the first or the second session. Before the first session, we introduced the dolorimeter and explained its function as we blacked five areas (each about 3 cm in diameter) on the volar surface of each of the subject's forearms. An estimate of the subject's pain threshold was obtained by using the method of limits, and the heat and pain stimuli were calculated on the basis of this estimate.

Before the first experimental session, subjects were instructed to assign each stimulus experienced to one of six categories: nothing, warm, hot, faint pain, moderate pain, and strong pain. We did not restrict how often each category could be used, nor did we say how many heat intensities would be employed or that one intensity was zero.

During each session, 200 stimuli were delivered sequentially: 50 trials were given at each intensity level with the levels interspersed according to a random schedule. We introduced a brief rest and measured the subject's skin temperature after every 50 trials.

The supine subject wore an airtight anesthesia mask in each testing session, breathing a mixture of 33 percent nitrous oxide with oxygen in one session and room air in the other (*5*). He indicated responses on the rating scale by finger signals. Before the session involving 33 percent nitrous oxide, the gas was administered for a 15-minute period to ensure that the subject was at a stable level of intoxication (*6*).

The methodology of SDT (*7*) may be used as an alternative to the unreliable pain threshold employed in early work with the dolorimeter. While the threshold provides a single index of sensitivity to stimulation, SDT methods yield two dependent variables: (i) a relatively pure index of perceptual sensitivity, *d'*, and (ii) an index of response bias which reflects the willingness of the observer to categorize the stimulation in a certain way, for example, as painful. It is the uncontrolled interaction of these two factors which led to the unreliability of the older dolorimeter research. We used the threshold only to adjust the demand characteristics of the experimental task to each subject.

A discrete stimulus experience is represented in SDT as a sensory event, *x*, along a hypothetical subjective continuum such that the intensity of the stimulus determines the location of *x*

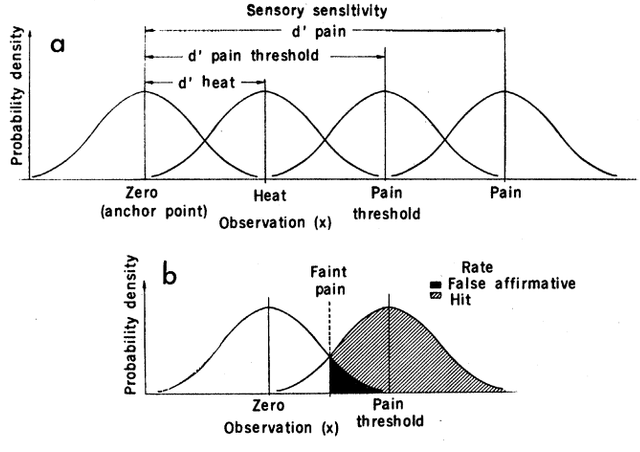

Fig. 1. (a) Representation of sensory events that occur in response to stimuli along the hypothetical subjective continuum. (b) Location of a simple response criterion corresponding to a rating scale category along the hypothetical continuum.