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26. The mean values of log β in successive time blocks for the other three conditions were: for the successive-discrimination task, 0.86, 0.95, and 1.04 (low event rate); for the simultaneous-discrimination task, 0.87, 0.96, and 1.07 (low event rate) and 0.98, 1.02, and 1.12 (high event rate).
27. A single response key replaced the four-category rating scale of experiment 1 in order to extend the findings to tasks using this conventional response mode. Previous studies indicate some differences in vigilance performance between the rating scale, yes-no, and single-response procedures [M. J. Guralnick and K. G. Harvey, *Psychonom. Sci.* **20**, 215 (1970)], although they are not marked (*6*).
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29. Delayed-comparison tasks share certain features with successive-discrimination tasks, since both require a target to be discriminated by comparing it to a previously presented standard. In delayed-comparison tasks, d' decreases as the delay interval between the standard and the comparison stimulus increases [R. Kinchla and F. Smyzer, *Percept. Psychophys.* **2**, 219 (1967); W. A. Wickelgren, *Psychol. Rev.* **76**, 232 (1969)]. This result appears to contradict the finding that an increase in the event rate (which corresponds to a decrease in the interstimulus or "delay" interval) reduces d' in successive-discrimination tasks. But this effect interacts with time on task, and is due mainly to the pronounced d' decrement found with a high event rate. Event rate effects are not marked when the subject is alert or at the beginning of the vigilance session (*6*). Also, in delayed-comparison tasks, the decay in d' is much less marked when there is only one standard stimulus [E. G. Aiken and A. W. Lau, *Percept. Psychophys.* **1**, 231 (1966)], as in most successive-discrimination vigilance tasks.
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Emergence of Interoceptive and Exteroceptive Control of Behavior in Rats

Abstract. *The role of exteroceptive and interoceptive aversive stimuli in rats 2 to 14 days old was investigated according to an odor aversion paradigm. Amyl acetate odor was paired with either peripheral shock, intraperitoneal shock, or lithium chloride poisoning. Intraperitoneal shock was an effective unconditioned stimulus at all ages and produced odor aversions comparable to lithium chloride poisoning; peripheral shock, however, was effective only in rats 10 days of age or older. Interoceptive control of aversively motivated behaviors thus seems to develop before exteroceptive control, and the failure of previous studies to find reliable learning and retention of shock-motivated behaviors before 8 to 10 days of age may be attributable to the site to which shock was applied rather than to insensitivity to shock per se.*

To date, attempts to show learning and retention of responses motivated by electric shock or other noxious exteroceptive stimuli have been unsuccessful in rats younger than 8 to 10 days of age (*1*). For example, little evidence has been found for either acquisition or long-term retention of escape or avoidance learning motivated by electric shock (*2, 3*) or cold air (*4*) in rats less than 1 week old. Conversely, young rats can learn odor aversions or simple discrimination for food reinforcement as early as 1 or 2 days of age (*5*). Moreover, long-term retention of odor aversions, lasting a week or more, has been demonstrated in 2-day-old rats (*6*).

Before odor aversion learning by 2-day-old pups was demonstrated, it was possible to entertain the notion that appetitively motivated behaviors were acquired earlier in developmental sequence than aversively motivated behaviors. The odor aversion data reported by Rudy and Cheatle (*6, 7*), however, suggest that such a distinction is inappropriate. Since rats as young as 2 days of age can learn and retain a toxicosis-induced odor aversion response, the difficulty in demonstrating learning and retention of responses motivated by electric shock in rats younger than 8 or 9 days of age remains to be explained. The distinguishing feature of the studies of Rudy and Cheatle (*6, 7*) versus those of Misanin *et al.* (*2*) and Nagy (*1*), and other studies using electric shock, may lie in the nature of the unconditioned stimulus (US) and experimental paradigms. Although it is clear that rats, even when newborn, react to exteroceptively applied shock, the neural mechanisms responsible for the association of peripheral pain and peripheral cues may not mature until later.

In contrast, odor aversion studies suggest that the mechanisms responsible for the association of internal malaise and odor cues are functional by 2 days of age (*6, 7*). In this research we explored the role of interoceptively versus exteroceptively applied aversive stimuli in the learning of odor aversions and addressed the more general issue of the development of exteroceptive control of behavior.

Sprague-Dawley rats ($N = 320$) were used in these experiments. The general design was to condition rats of various ages by pairing an odor conditioned stimulus (CS) with either peripheral shock (PS) or intraperitoneal shock (IPS) and to test for odor aversion on the following day. For the groups receiving interoceptive shock, two copper wire-insulated electrodes with 2-mm exposed tips were inserted into the peritoneal cavity on either side of the stomach (easily visible through the skin). The site of entry of the electrodes was covered with petroleum jelly to prevent leakage of body fluids, and the electrodes were fastened in place with adhesive tape. A subcutaneous indifferent electrode (a wound clip) was implanted in the nape of the neck of each rat that was to receive PS. After the electrode was implanted, the rats were kept in an incubator (34°C, 54 percent relative humidity) and were allowed at least 30 minutes to recover from light ether anesthesia.

The rats were conditioned in a Plexiglas chamber (24 by 15 by 15 cm) containing six compartments separated by nylon mesh cloth. The floor and walls of two of the compartments were made of copper wire mesh, through which the PS was delivered. The rats were placed in the conditioning chamber with one rat per compartment for a period of 30 minutes. Each conditioning session was started by introducing humidified air into the chamber for 40 seconds; odorized air [13 ml of air (per minute) bubbled through amyl acetate mixed with 167 ml of humidified air (per minute)] followed for the next 20 seconds (*8*). The rats receiving shock as the US received a 1-second shock pulse, delivered by constant-current shock generators that terminated with the amyl acetate phase of the cycle. Thus, by the end of the conditioning session, each rat had been exposed to 30 20-second amyl acetate pulses, each ending in shock.

On the conditioning day, the rats were 2, 7, 10, or 14 days old. Five levels and two loci of shock were investigated at each age. The rats received either IPS or PS at 0, 0.1, 0.5, 1.0, or 2.0 mA.

Testing occurred 24 hours later for all but the 2-day-old groups, which were tested when 8 days old to allow them to develop adequate locomotor capabilities. The test chamber consisted of a Plexiglas tray (30 by 20 by 3 cm) and a chamber (30 by 20 by 10 cm) with a copper mesh floor mounted on top of the tray. The tray was divided into two equal

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parts along its longitudinal axis with a Plexiglas barrier 3 cm high. Air bubbled through amyl acetate (13 ml/min) was mixed with fresh air (167 ml/min) and was delivered through the floor of one side of the platform, while air through glacial acetic acid (23 ml/min) was mixed with humidified air (157 ml/min) and was delivered to the opposite side of the platform. The order of testing was randomized, and the test was conducted blind. Each rat was placed in the center of the test platform facing away from the experimenter, and a clock was started. The rat was judged to have made a choice when its snout and one front paw was on one or the other side of a line dividing the two sides of the platform. The test duration was 300 seconds; at the end of each 100-second interval, however, the rat was returned by hand to the center line and allowed to choose again between the two sides. The direction that the rat faced was switched each time it was returned to the center position. Relative preference for one or the other odor was expressed as the percentage of the total test period, minus time spent in the no-choice zone (which never exceeded 30 seconds), that the rat spent over a specific odor (Fig. 1).

A 3-factor analysis of variance revealed a significant effect of age [F (2, 211) = 16.05, $P < .001$], shock intensity [F (4, 211) = 22.25, $P < .001$], and shock locus [F (1, 211) = 20.25, $P < .001$]. The interactions of age with shock intensity and age with shock locus were also significant ($F > 3.25$, $P < .025$). Because the data from the 2-day-old groups were obtained after a 6-day retention interval, they were not included in this analysis; a separate analysis of variance performed for these data also showed a significant locus effect [F (1, 71) = 5.7, $P < .025$]. The IPS was effective as a US for odor aversion conditioning at all ages; the developmental pattern in the effectiveness of PS as the US was striking, however. Peripheral shock was an ineffective US, irrespective of shock intensity, in rats younger than 10 days of age. At 10 days, PS gained some control over conditioning such that, although there were still absolute differences between rats receiving PS versus IPS at this age, these differences were not significant except when the shock was 1.0 mA (Tukey's tests). By 14 days of age, however, both loci of shock were effective US's for conditioned odor aversion.

Table 1. Preference for amyl acetate (mean percentage of time spent in its presence) in groups of rats conditioned (CS-US) with interoceptive (LiCl and IPS) and exteroceptive (PS) aversive agents. The CS-sham US and no CS-US conditions were controls for nonassociative factors.

US	CS-US	Control groups	
		CS-sham US	No CS-US
LiCl	32.4	64.8	69.5
IPS	30.8	74.4	75.9
PS	51.2	71.4	75.7

The odor aversion produced by IPS compares favorably with aversions produced by LiCl poisoning (*6, 7*). The significant differences found between the IPS and PS suggest that IPS was, in fact, an effective interoceptive US. These differences cannot be attributed to differential sensitivity to shock, since, in an ancillary study, we found no difference in audible vocalizations evoked by IPS or PS (*9*). In addition, intensity had no effect in the PS condition in rats conditioned at 2 and 7 days of age. It is also unlikely that the differences found between IPS and PS conditions are attributable to the IPS's having been administered to the ventral area of the body, whereas PS was administered to the feet. In a second ancillary study conducted with 7-day-old rats, we showed that shock delivered to the pup's ventrum through two surface electrodes was equivalent to PS and differed significantly from IPS.

In experiment 2, the effects of PS and IPS were directly compared with LiCl poisoning in 10-day-old rats. The procedures for conditioning with shock were identical to those described for experiment 1 except that only a single shock intensity of 1.0 mA was used. The procedure for conditioning with LiCl involved administering LiCl (0.15*M* LiCl, 2 percent of body weight) immediately before a 30-minute exposure to amyl acetate delivered in the same conditioning apparatus used for shock conditioning. Six control groups received either the US treatments without the odor pairings or were exposed to the odors but did not receive the US (groups designated as no CS-US and CS-sham US, respectively). All rats were tested 24 hours after conditioning according to the previously described procedures.

Table 1 shows the results of the preference behavior. An analysis of variance revealed a significant effect of conditioning [F (2, 63) = 11.5, $P < .001$], but no significant effect of the US used ($F < 1.0$). Tukey's tests showed that although rats conditioned with IPS and LiCl differed significantly ($P < .05$) from their controls, those rats receiving PS as the US did not differ statistically from

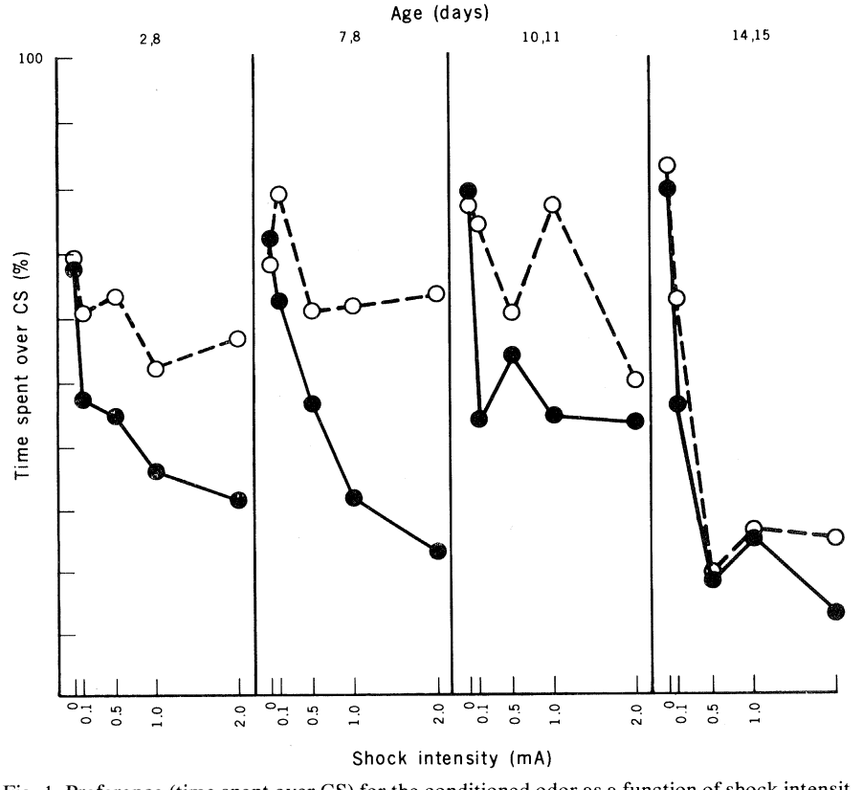

Fig. 1. Preference (time spent over CS) for the conditioned odor as a function of shock intensity and age at conditioning in rats conditioned with either interoceptive peritoneal shock (●) or exteroceptive peripheral shock (○). The first age given is that at conditioning, the second, that at testing.

the US alone or sham-US controls ($P > .05$). The preference behavior of the rats conditioned with PS in this experiment resembled that of their counterparts in experiment 1. These rats did not differ significantly from their controls, nor did they differ significantly from the rats conditioned with IPS or LiCl as the US. Thus PS appears to be of intermediate effectiveness at 10 days of age, ineffective at younger ages, but effective for rats older than 10 days.

The results of these experiments are congruent with studies of odor avoidance learning in adult rats in which both exteroceptive (PS) and interoceptive (LiCl) US's were found to affect behavior (*10*). These results also address the issue of learning and retention of responses conditioned with shock as the US in neonatal rats. It now seems that the failure to obtain reliable conditioning or retention of learned responses based on shock in rats younger than 8 to 10 days of age is related to the locus of application rather than to sensitivity to shock per se. Odors paired with interoceptive US are more easily associated and retained than odors paired with exteroceptive US's, but as the rat matures, exteroceptive aversive stimuli become increasingly effective in establishing associative bonds.

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8. All rats were conditioned against their natural preference for amyl acetate relative to the acetic acid used in testing.
9. In an ancillary study, audible vocalizations were recorded for groups of rats ($N = 4$) receiving either 1.0 mA of IPS or 1.0 mA of PS. There were no significant differences in either the number or the duration of vocalizations. The mean number of vocalizations per blocks of ten trials were 32, 24, and 23 for rats receiving PS and 24, 22, and 16 for IPS.
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Cognitive Deficit Caused by Regional Depletion of Dopamine in Prefrontal Cortex of Rhesus Monkey

Abstract. *Depletion of dopamine in a circumscribed area of association cortex in rhesus monkeys produces an impairment in spatial delayed alternation performance nearly as severe as that caused by surgical ablation of the same area. This behavioral deficit can be pharmacologically reversed with dopamine agonists such as* L-*dopa and apomorphine. These data provide direct evidence that dopamine plays an important role in a specific cortical function.*

In primates, including humans, the dorsolateral convexity of the frontal lobe plays a selective role in mediating mnemonic, attentional, and spatial capacities (*1*). In infrahuman primates this region of the cerebral neocortex has high catecholamine levels and synthesis rates, particularly for dopamine (DA), whereas serotonin (5-HT) content and activity in the same cortical tissue is relatively low (*2, 3*). The combination of distinctive behavioral function and differentiated monoamine chemistry makes the frontal association cortex of the rhesus monkey highly suitable for analyzing the role of the putative monoamine neurotransmitters in behavioral processes. We now report that a substantial depletion of DA, along with a more modest depletion of norepinephrine (NE), in the cortex of the principal sulcus on the dorsolateral prefrontal convexity produces a selective impairment of delayed alternation performance similar to that produced by surgical ablation. Moreover, the behavioral deficit resulting from this biochemi-

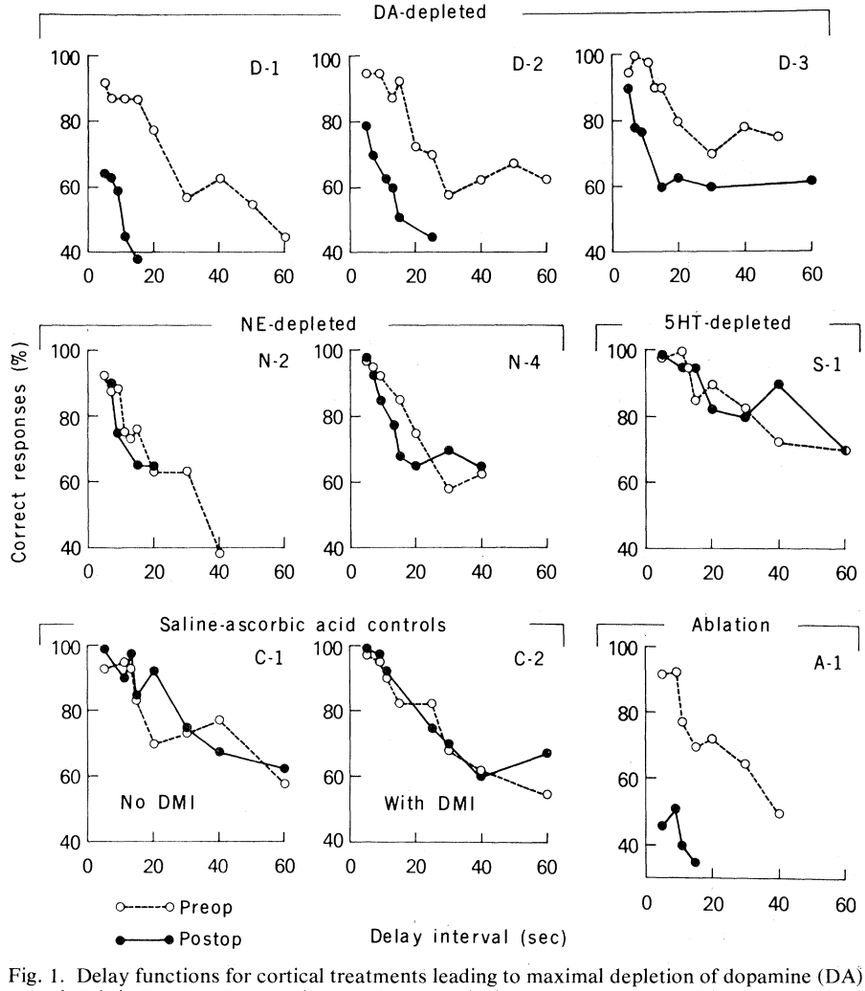

Fig. 1. Delay functions for cortical treatments leading to maximal depletion of dopamine (DA), norepinephrine (NE), or serotonin (5-HT) in the principal sulcus and for ablation. Each point is based on a minimum of 40 test trials at each delay value. Delay values were tested in nonsystematic series with replication in counterbalanced order. Differences between pre- and postoperative functions were significant only for the DA-depleted ($t = 7.94$, d.f. = 57, $P < .001$) and ablated animals ($t = 9.19$, d.f. = 9, $P < .001$). Animals N-2 and N-4 show the deficit range for NE depletion. The 5-HT-depleted (S-1) and ablated (A-1) animals are representative.

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