Prefrontal lesion effects on suppression of open-field activity in young and adult rats

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A total of 108 rats, 18-20, 30-32, or 100-130 days of age, received dorsomedial, orbital prefrontal, or sham lesions. After recovery, the subjects were assigned to one of three Pavlovian training conditions. Thirty-six subjects of each age level and surgical treatment received 2 days of 20 presentations of a 30-sec, 3,000-Hz tone, during which inescapable shock of .5 sec duration was administered. The same number of subjects received the same treatment but without the shock, while the remaining subjects were simply placed in the apparatus with no stimuli presented. Four hours after Pavlovian treatment on both days, the subjects were placed in the open field for baseline measurement of ambulations and rearings. On 3 successive days after Pavlovian training and baseline activity measurement, the subjects were tested for suppression of activity by alternating intervals of tone/no tone in the open field. The results of baseline activity measures showed decreasing activity with increasing age, and both surgical groups were more active than the shams, with lateral subjects most active. During suppression testing, activity in the laterals given tones and shocks was most disrupted by tone presentations; shams showed least suppression. The lateral suppression tended to be greatest in the youngest subjects. The data were considered in terms of Pavlovian extinction processes and the maturation of inhibitory centers.

Age comparisons in aversively motivated behavior have indicated deficits in acquisition and retention of task-specific responses on the part of immature rats. Task requirements involving response-inhibition reflect performance deficiencies in weanlings compared to adult rats (Fiegle & Spear, 1970; Schulenburg, Riccio, & Stikes, 1971). Age-related deficiencies in acquisition of active avoidance emerge with a stringent criterion (Egger & Livesey, 1972), and differential extinction of active avoidance has been shown with response-produced punishment (Riccio & Marrazo, 1972), after conditioned stimulus (CS) habituation (Wilson, Phinney & Brennan, 1974) or with a complexity of CS cues (Brennan & Barone, 1976). While comparable gradients of stimulus control of active avoidance in young and adult rats have been reported (Brennan & Riccio, 1972), Brennan (1975) found age differences in the generalization of a response-inhibiting, Pavlovian safety signal. Aversive effects on general activity in young and adult rats are relatively unexplored. Changes in ongoing running wheel and stabilimeter activity have been examined across ages (Campbell, 1967; Campbell, Misanin, White, & Lytle, 1974). One study by Candland and Campbell (1962) found that spontaneous open-field ambulations increased from age 18 days to

age 54 days, when asymptotic levels were reached. Nevertheless, little is known of the relationship between aversively motivated conditioning and open-field activity.

Through anatomical studies (Domesick, 1972; Leonard, 1969, 1972) and more recently by the use of the horseradish peroxidase technique (Divac, Kosmal, Bjorklund, & Lindvall, 1978), the prefrontal cortex of the rat has been described in terms of the dorsomedial and ventrolateral projection sites of nucleus medialis dorsalis. Corresponding dissociated behavioral functions have been reported after selective lesions in these prefrontal subfields (e.g., Divac, 1971; Kolb, Nonneman & Singh, 1974; Lukaszewska, 1975). Examinations of prefrontal damage on activity include a study by Lynch (1970), who found a greater increase in running-wheel activity following lateral orbital damage than after medial lesions. Kolb (1974) replicated Lynch's findings, and also noted that although lateral lesions produced more heightened activity than medial damage, the latter lesions nevertheless resulted in consistently elevated activity levels compared to normals.

The importance of the prefrontal cortex in understanding the ontogeny of conditioning has been noted by Campbell and Spear (1972), who stressed the striking parallel between behavioral deficits and cortical growth up to 60 days of age. A study by Brennan, Powell, and Vicedomini (1977) compared retention of active and passive avoidance in young and adult rats after medial prefrontal damage. The

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behavior of the young rats was more susceptible to lesion disruption, and age differences in active avoidance were related to both the time of initial learning and surgical intervention. Variability in passive avoidance retention was more directly related to age only. The purpose of the present experiment was to determine whether dissociated prefrontal effects would emerge in rats of varying ages at the time of surgery. Accordingly, prefrontal effects on spontaneous activity as well as on defensive, Pavlovian conditioned suppression were assessed in rats of three age levels.

METHOD

Subjects

A total of 108 naive male Sprague-Dawley albino Wistar rats served as subjects. At the time of surgery, 36 subjects were 18-20-day-old weanlings, 36 were 30-32 days of age, and the rest were 100-130-day-old adults. During the experiment, the subjects were housed singly and food and water were always available in the home cage.

Apparatus

Subjects received Pavlovian tone and shock pairings or related control procedures in a 30-cm-square acrylic chamber. The floor of the chamber consisted of steel rods spaced 1 cm apart through which scrambled shock of 170 V from a matched impedance source (Campbell & Teghtsoonian, 1958) was delivered. Campbell (1967) has reported shock-induced activity data showing that match-impedance shock of moderate intensities is equally aversive across ages in rats. A 10-cm, 6- Ω speaker was attached to the acrylic lid of the chamber and delivered a tonal frequency of 3,000 Hz from a Heathkit audio generator. The intensity of the tone was measured at 78 dB (.0002 dyne/cm²) by a sound-level meter (General Radio Corp. Model 551-C). The order of presentation of experimental events was automatically programmed. Open-field testing was done in a circular chamber, 90 cm in diameter and with walls 60 cm high, manufactured by Lehigh Valley Electronics, Model 1497. Photocells provided automatic recording of ambulations, while rearings were recorded by two observers and subsequently averaged. During tests of activity suppression, tones were delivered from a speaker suspended over the center of the apparatus. The same tone generator delivered the 3,000-Hz tone to the open-field chamber. During Pavlovian training and open-field measurements, the only source of room illumination was provided by a 15-W bulb suspended 90 cm above the center of each apparatus. For surgery, subjects were mounted in a stereotaxic frame manufactured by Knopf. Skull holes were made using an Emesco dental drill. A radio frequency lesion generator (Model FR G-4), manufactured by Radionics, activated a temperature-sensing insulated electrode with 1 mm exposure.

Procedure

The subjects were assigned to one of three surgical procedures. Within each age level, 18 of the subjects received bilateral lesions of the medial prefrontal cortex, 18 additional subjects were administered bilateral lesions of the orbital frontal aspect of the prefrontal area, and the remaining 18 subjects served as operated sham controls. All subjects were anesthetized with an IP injection of sodium pentobarbital (Nembutal 50 mg/kg) at a dosage level determined by weight. For the medial lesions, trephin holes were drilled 2 mm bilaterally from the midline suture at bregma and 2.3, 3.4, and 4.0 mm anterior to bregma in the 18-20, 30-32, and adult subjects, respectively. The electrode was lowered 1.0 mm from the dura in the two younger age groups, and 1.5 mm in the adults. For the orbital groups, the lateral cranium

was removed bilaterally and the individual hemispheres were retracted. Then, for 18-20-day-old subjects, the lesioning electrode was lowered 3.4 mm from the dura at a point 2.6 mm anterior and 4.3 mm bilateral to bregma; for the 30-32-day-old subjects, the electrode was lowered 4.00 mm at a point 2.8 mm anterior and 4.5 mm bilateral to bregma; and for the adults, the electrode was lowered 6 mm at a point 3 mm anterior and 5 mm bilateral to bregma. Both types of lesions were made at all age levels by maintaining the tip temperature at 70°C for 60 sec. Nine sham subjects at each age level received the same procedure as their appropriate lesioned counterparts, except that the lesioning electrode was simply lowered but not activated. The sham subjects were arbitrarily assigned to the various Pavlovian treatments subsequently administered. The subjects recovered for 5 days in the home cage.

Following recovery from surgery, subjects of each level and surgical condition were assigned to one of three Pavlovian treatment groups for 2 successive days of training: (1) Tone/shock pairings (T/S)—Four medial, lateral, and sham subjects at each age level received 20 presentations of the 3,000-Hz, 78-dB tonal CS, and tonal duration on each trial was 30 sec. The inescapable shock unconditioned stimulus (US) of .5 sec duration was randomly distributed during the first, second, or third 10-sec block of the total CS duration. Trials were separated by varying intervals, averaging 30 sec. (2) Tone only (TO)—Twelve subjects of the three surgical procedures at each age level were treated the same as the T/S groups, except that the shocks were omitted. (3) No tone (NT)—The remaining medial, lateral, and sham groups at each age were placed in the chamber used for Pavlovian conditioning for approximately 20 min with neither tones nor shocks presented.

Four hours after each of the conditioning sessions, spontaneous activity in each subject was measured by recording the numbers of ambulations and rearings in the open-field chamber for a period of 20 min. That is, the subjects were placed in the center of the open-field apparatus and the total number of movements transversing the apparatus was automatically tallied for the 20-min period. Two observers independently recorded the number of times a subject's frontpaws were lifted from surface contact with the floor of the chamber during the 20-min duration.

After the 2 days of conditioning and subsequent spontaneous activity measures, the subjects were given 3 consecutive days of testing for activity suppression to tonal presentations in the open-field chamber. Tests of 20 min duration in the open field involved recording of ambulations and rearings for each 30-sec period of alternating intervals of tone on and no tone.

The subjects were administered a lethal dose of sodium pentobarbital and intracardially perfused with a 10% Formalin solution. The brains were removed from the cranium and stored in 30% Formalin solution for 4-6 days. Each brain was blocked at the angle of lesioning, frozen, and serially sectioned at 100 μ m throughout the extent of the lesion. The details of this procedure, which account for different brain sizes at each age level, are reported by Brennan et al. (1977). Mounted sections were stained with cresyl violet.

RESULTS

Histology

Figure 1 shows reconstructions of the extent of the smallest, median, and largest lesions. Dorsomedial damage was largely confined to the neocortex and a small portion of the corpus callosum. Ventrolateral lesions damaged the orbital frontal cortex and a portion of the anterolateral caudoputamen. It should be noted that subjects of the youngest group were at least 29 days old when sacrificed. Examination of

Figure 1. Reconstruction of coronal composites of the largest, median, and smallest lesion extent for lateral (right) and medial (left) prefrontal damage. The labels refer to drawings of König and Klippel (1963).

the variability in lesion placement did not indicate any unique effects due to age.

Behavior

Spontaneous activity. Examination of the baseline open-field activity levels revealed differences that were attributable to age, surgical treatment, or Pavlovian training procedures, and successive days of observation. Table 1 shows the mean numbers of ambulations (left) and rearings (right) for the 2 days of open-field activity that followed Pavlovian training. Analyses of both measures indicated significant effects of Pavlovian training [$F_A(2/81) = 11.99$, $p < .001$; $F_R(2/81) = 8.82$, $p < .001$], age [$F_A(2/81) = 19.27$, $p < .001$; $F_R(2/81) = 13.52$, $p < .001$], and their interaction [$F_A(4/81) = 8.67$, $p < .001$;

$F_R(4/81) = 12.77$, $p < .001$]. Subsequent examination of these effects (Newman-Keuls, all $ps < .01$) indicated that both ambulations and rearings were greater after tone/shock pairings than after either TO or NT control procedures. Moreover, both ambulations and rearings decreased with increasing age, and the decrease in activity within age levels was sharpest after the T/S Pavlovian treatment, compared to activity differences for age levels after the TO and NT treatments.

A significant effect of surgery emerged for both activity measures [$F_A(2/81) = 23.42$, $p < .001$; $F_R(2/81) = 21.25$, $p < .001$]. The Surgery by Pavlovian Training interaction was significant in the ambulations measure [$F_A(4/81) = 4.71$, $p < .005$], and the Surgery by Pavlovian Training by Age interaction approached acceptable confidence in the number of rearings [$F_R(8/81) = 1.99$, $p < .10$]. Under both measures, the laterals were most active and the shams least, and differences between surgical treatments were most apparent in the number of ambulations after tone and shock pairings than after either of the Pavlovian control treatments.

The overall number of ambulations [$F_A(1/81) = 18.50$, $p < .001$] and rearings [$F_R(1/81) = 138.32$, $p < .001$] decreased from the 1st to the 2nd day of spontaneous activity observation. In the rearings measure, a significant interaction of Days by Training by Age [$F_R(4/81) = 4.83$, $p < .01$] was also found. This interaction was largely due to shifts in rearings from the 1st to the 2nd day of observation by age levels within the TO and NT control treatments. Thus, the observation of spontaneous activity revealed general consistency between ambulations and rearings in that lateral effects were most pronounced, especially at the youngest age levels. Both surgery and age effects were differentially influenced

Table 1
Number of Ambulations and Rearings for Each Age Level and Surgical Treatment During Spontaneous Activity Measurement After Pavlovian Tone and Shock Conditioning (T/S), Tone Presentations Only (TO), and No Tones (NT)

Age at Surgery	Ambulations			Rearings		
	Medial	Lateral	Sham	Medial	Lateral	Sham
T/S Pavlovian Training						
18-20	830.13	913.00	539.88	50.00	62.50	30.25
30-32	606.38	740.13	446.50	47.00	48.75	39.38
100-130	431.50	510.00	293.88	31.58	34.38	21.25
T/O Pavlovian Training						
18-20	530.75	576.63	520.50	46.00	47.13	44.00
30-32	443.13	530.88	327.25	42.25	40.38	24.88
100-130	532.88	589.63	362.00	55.00	60.13	36.63
NT Pavlovian Training						
18-20	441.88	509.63	400.25	43.38	49.50	29.25
30-32	390.13	642.50	609.38	37.63	47.50	40.25
100-130	290.38	426.13	341.00	13.13	26.75	18.25

by Pavlovian treatments, which reflected a strong residual transfer from conditioning sessions to spontaneous activity.

Suppression of activity. Tests of suppression of open-field activity were conducted on the 3 days following Pavlovian training and spontaneous activity measurement. The number of ambulations and rearings of each subject during 30-sec blocks were converted to measures of suppression by the ratio: tone on/tone off + tone on (Annau & Kamin, 1961; Church, 1969), and Table 2 shows the mean suppression ratios for ambulations (left) and rearings (right) across the three testing days for groups of each Pavlovian training condition, treatment, and age.

Analyses of activity suppression in both measures revealed highly significant effects from Pavlovian training [$F_A(2/81) = 48.69$, $p < .001$; $F_R(2/81) = 55.81$, $p < .001$], which reflected greater overall suppression in subjects after the Pavlovian pairings than the two control treatments that did not differ from each other. The interaction of Pavlovian Training by Age [$F_A(4/81) = 5.75$, $p < .001$; $F_R(4/81) = 5.48$, $p < .001$] indicated greater suppression in the two younger T/S age groups than in the adults. However, in the TO groups, only the adults showed any activity suppression to the tones, while none of the groups suppressed after prior experience with the apparatus (NT treatment) and the 18-day and adult ages showed highly elevated ratios compared to the 30-day subjects. From the ambulations measure, a marginally significant interaction of Surgical Treatment by Age [$F_A(4/81) = 2.26$, $p = .07$] suggested more pronounced suppressive effects in the 30-day medial and 18-day lateral ages than the other surgical age groups, while the shams were relatively similar.

In the ambulations measure, the effect of successive testing days [$F_A(2/162) = 27.15$, $p < .001$] indicated generally elevated ratios as testing days progressed. Moreover, the significant interaction of Testing Days

by Pavlovian Training [$F_A(4/162) = 7.97$, $p < .001$] showed that suppression recovered as testing days in Pavlovian extinction increased, whereas the Pavlovian control treatments resulted in less systematic fluctuations in ratios over testing days. The interactions of Testing Days by Pavlovian Training by Age [$F_A(8/182) = 3.85$, $p < .001$] and Testing Days by Pavlovian Training by Surgical Treatment [$F_A(8/162) = 3.08$, $p < .01$] support the indication of differential processes of Pavlovian extinction on the part of the T/S groups. Specifically, the former interaction suggested that in the T/S groups suppression was initially greater and recovery more dramatic than with the other age levels under that Pavlovian training condition. The latter interaction reflected the greatest suppression and progressive recovery in the lateral T/S groups. Again, the Pavlovian control conditions at all age levels, and especially for the sham-operated subjects, tended to produce little suppression and overall enhancement of responding during tone presentations by the 2nd day of testing. These findings are supported by the Days by Pavlovian Training by Surgical Treatment by Age interaction that approached acceptable significance [$F_A(16/162) = 1.65$, $p = .06$].

The results of repeated measurement of rearings suppression over testing days [$F_R(2/162) = 20.81$, $p < .001$] and the interactions of testing days with the other variables were clearer than the analysis of ambulations ratios. That is, the two-variable interactions of Days by Pavlovian Training [$F_R(4/162) = 21.45$, $p < .001$] and Days by Age [$F_R(4/162) = 2.57$, $p < .05$] were significant. Together with the significance of all of the triple interactions: Days by Training by Surgery [$F_R(8/162) = 2.05$, $p < .05$], Days by Training by Age [$F_R(8/162) = 3.30$, $p < .01$], and Days by Surgery by Age [$F_R(8/162) = 2.64$, $p < .01$], the rearings suppression ratios support the interpretation offered for ambulations. That is, rearings suppression was evident after the T/S training

Table 2
Mean Ratios of Suppression of Ambulations and Rearings for Each Age, Surgical Treatment, and Pavlovian Training Condition

Age at Surgery	Ambulations			Rearings		
	Surgical Treatment			Surgical Treatment		
	Medial	Lateral	Sham	Medial	Lateral	Sham
T/S Pavlovian Training						
18-20	.4192	.3158	.4375	.2964	.2903	.3733
30-32	.3933	.4133	.3583	.2933	.3217	.3450
100-130	.5017	.4542	.3267	.3050	.2742	.3333
TO Pavlovian Training						
18-20	.4958	.5250	.4842	.4800	.4358	.5000
30-32	.5367	.5275	.5908	.5542	.5050	.3867
100-130	.4542	.5067	.4367	.2392	.4283	.3617
NT Pavlovian Training						
18-20	.6517	.5683	.5692	.6567	.6133	.6117
30-32	.4967	.5433	.5083	.5333	.5708	.4225
100-130	.7042	.6283	.5925	.6600	.6442	.5867

only. Within that condition, initial suppression and subsequent recovery were most dramatic at the younger levels and especially in the laterals.

DISCUSSION

The inverse relationship between age and both activity measures during baseline measurement was most pronounced after tone and shock pairings. This evidence is consistent with ontogenic studies of behavioral arousal (Campbell & Mabry, 1972), which reported peak arousal at 15 days of age followed by a decline to an adult level by 30 days. Campbell and Raskin (1978) examined this phenomenon under several conditions and concluded that fear in a novel environment is critical. The present findings of a strong transfer effect from Pavlovian conditioning suggest that the circumstances for the emergence of differential arousal among ages were met. It may be that the absence of a control procedure giving unpaired or randomly determined tone and shock presentations limits the interpretation of the T/S effects in this experiment. However, comparisons of spontaneous activity in the surgical sham subjects of each conditioning treatment with each other and with their lesioned counterparts (Table 1) indicate that only the lesioned groups under the T/S treatment produced heightened activity. The heightened ambulations and rearings in the lateral subjects and the similar, although not as pronounced, increased activity in the medials support the results of Kolb (1974).

Given the lateral performance in the T/S condition on the baseline activity measures, the extent of their suppression on the subsequent tests is somewhat surprising. That is, on the basis of their hyperactivity, it might be expected that they would show least suppression relative to the other groups with Pavlovian fear conditioning. It should also be noted that the hyperactivity in the laterals during baseline observation may have subsequently distorted the suppression ratio measurement. However, given the sensitivity of the ratios in the overall results, which reflected both suppression and enhancement of response levels, it appears that the laterals' suppression was not artifactual. Accordingly, within the T/S groups, ambulation suppression was greatest for the 18-day laterals. It appears that Pavlovian extinction influences in the young T/S lateral subjects were minimal. This finding is consistent with a report of heightened activity and an inability to discriminate appetitively motivated extinction from acquisition following lateral prefrontal lesions in dogs (Brennan, Kowalska, & Zielinski, 1976). If the ratios of the laterals in the Pavlovian controls are compared, it may readily be seen that without the aversive Pavlovian experience, the laterals showed little suppression and some enhancement of responding as did subjects of the

other surgical treatments that responded to the eliciting capacity of the novel tone during testing.

The question remains of why the suppression was greatest in the youngest T/S group with lateral lesions. That is, despite the youngest group being tested at ages where they should emulate adults, some heightened activity, in contrast to suppression, should be present. However, the complexity of the present assessment of Pavlovian suppression of activity provides some insight. Specifically, the age-related deficit in inhibiting systems may be interacting with the lesion effects to produce the persistence of suppression in the young, T/S lateral subjects. If spontaneous performance of the young subjects reflects characteristic response-inhibiting deficits, and the lateral lesions interfere with subjects' inability to extinguish, the net result of these joint processes would be a perseveration of the learned Pavlovian response. Such is the case presently, and these data are consistent with interpretations of behavioral ontogeny that stress the sequential maturation of excitatory and inhibiting centers in forebrain activity (Campbell & Spear, 1972; Mabry & Campbell, 1974). Moreover, the results suggest that the selectivity of cortical action (e.g., Larsen & Divac, 1978) may be differentially affected by this sequential maturation due to age.

REFERENCES

- ANNAU, Z., & KAMIN, L. J. The conditioned emotional response as a function of intensity of the US. *Journal of Comparative and Physiological Psychology*, 1961, **54**, 428-432.
- BRENNAN, J. F. Differential response gradients to a Pavlovian safety signal following active avoidance training in young and adult rats. *Animal Learning & Behavior*, 1975, **3**, 277-281.
- BRENNAN, J. F., & BARONE, R. J. Effects of differential cue availability in an active avoidance CS for young and adult rats. *Developmental Psychobiology*, 1976, **9**, 237-244.
- BRENNAN, J., KOWALSKA, D., & ZIELINSKI, K. Auditory frequency generalization with differing extinction influences in normal and prefrontal dogs trained in instrumental alimentary reflexes. *Acta Neurobiologiae Experimentalis*, 1976, **36**, 475-516.
- BRENNAN, J. F., POWELL, E. A., & VICEDOMINI, J. P. Differential effects of dorsomedial prefrontal lesions on active and passive avoidance in young and adult rats. *Acta Neurobiologiae Experimentalis*, 1977, **37**, 151-177.
- BRENNAN, J. F., & RICCIO, D. C. Stimulus control of shuttle avoidance in young and adult rats. *Canadian Journal of Psychology*, 1972, **26**, 361-373.
- CAMPBELL, B. A. Learning in infra-primate mammals. In H. W. Stevenson, E. H. Hess, & H. L. Rheingold (Eds.), *Early behavior: Comparative and developmental approaches*. New York: Wiley, 1967.
- CAMPBELL, B. A., & MABRY, P. D. Ontogeny of behavioral arousal: A comparative study. *Journal of Comparative and Physiological Psychology*, 1972, **81**, 371-379.
- CAMPBELL, B. A., MISANIN, J. K., WHITE, B. C., & LYTLE, L. D. Species differences in ontogeny of memory: Indirect support for neural maturation as a determinant of forgetting. *Journal of Comparative and Physiological Psychology*, 1974, **87**, 193-202.
- CAMPBELL, B. A., & RASKIN, L. A. Ontogeny of behavioral

- arousal: The role of environmental stimuli. *Journal of Comparative and Physiological Psychology*, 1978, **92**, 176-194.
- CAMPBELL, B. A., & SPEAR, N. E. Ontogeny of memory. *Psychological Review*, 1972, **79**, 215-236.
- CAMPBELL, B. A., & TEGHTSOONIAN, R. Electrical and behavioral effects of different types of shock stimuli on the rat. *Journal of Comparative and Physiological Psychology*, 1958, **51**, 185-192.
- CANDLAND, D. K., & CAMPBELL, B. A. Development of fear in the rat as measured by behavior in the open field. *Journal of Comparative and Physiological Psychology*, 1962, **55**, 593-596.
- CHURCH, R. M. Response suppression. In B. A. Campbell & R. M. Church (Eds.), *Punishment and aversive behavior*. New York: Appleton-Century-Crofts, 1969.
- DIVAC, I. Frontal lobe system and spatial reversal in the rat. *Neuropsychologia*, 1971, **9**, 175-184.
- DIVAC, I., KOSMAL, A., BJORKLUND, A., & LINDVALL, O. Subcortical projections to the prefrontal cortex in the rat as revealed by the horseradish peroxidase technique. *Neuroscience*, 1978, **3**, 785-796.
- DOMESICK, V. Thalamic relationships of the medial cortex in the rat. *Brain Behavior and Evolution*, 1972, **6**, 457-483.
- EGGER, G. J., & LIVESEY, P. J. Age effects in the acquisition and retention of active and passive avoidance learning by rats. *Developmental Psychobiology*, 1972, **5**, 343-351.
- FEIGLEY, D. A., & SPEAR, N. E. Effect of age and punishment conditions on long-term retention by the rat of active-passive avoidance learning. *Journal of Comparative and Physiological Psychology*, 1970, **73**, 515-526.
- KOLB, B. Dissociation of the effects of lesions of the orbital or medial aspect of the prefrontal cortex of the rat with respect to activity. *Behavioral Biology*, 1974, **10**, 329-343.
- KOLB, B., NONNEMAN, A., & SINGH, R. Double dissociation of spatial impairments and perseveration following selective prefrontal lesions in rats. *Journal of Comparative and Physiological Psychology*, 1974, **87**, 772-780.
- KÖNIG, J. F. R., & KLIPPEL, R. A. *The rat brain: A stereotaxis atlas of the forebrain and lower parts of the brain stem*. Baltimore: Williams and Wilkins, 1963.
- LARSEN, J. K., & DIVAC, I. Selective ablations within the prefrontal cortex of the rat and performance of delayed alternation. *Physiological Psychology*, 1978, **6**, 15-17.
- LEONARD, C. The prefrontal cortex of the rat. I. Cortical projection of the mediodorsal nucleus. II. Efferent connections. *Brain Research*, 1969, **12**, 324-343.
- LEONARD, C. The connections of the dorsomedial nuclei. *Brain Behavior and Evolution*, 1972, **6**, 534-541.
- LUKASZEWSKA, I. Delayed responses of kinesthetic type following frontomedial lesions in rats. *Acta Neurobiologiae Experimentalis*, 1975, **34**, 351-360.
- LYNCH, G. S. Separable forebrain systems controlling different manifestations of spontaneous activity. *Journal of Comparative and Physiological Psychology*, 1970, **70**, 48-59.
- MABRY, P. D., & CAMPBELL, B. A. Ontogeny of serotonergic inhibition of behavioral arousal in the rat. *Journal of Comparative and Physiological Psychology*, 1974, **86**, 193-201.
- RICCIO, D. C., & MARRAZO, M. S. Effects of punishing active avoidance in young and adult rats. *Journal of Comparative and Physiological Psychology*, 1972, **79**, 453-458.
- SCHULENBURG, C. J., RICCIO, D. C., & STIKES, E. R. Acquisition and retention of a passive avoidance response as a function of age in rats. *Journal of Comparative and Physiological Psychology*, 1971, **74**, 75-83.
- WILSON, L. M., PHINNEY, R. L., & BRENNAN, J. F. Age-related differences in avoidance behavior in rats following CS pre-exposure. *Developmental Psychobiology*, 1974, **7**, 421-427.

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