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Behavioral and Neural Correlates of Postnatal Olfactory

Conditioning:

II. Respiration During Conditioning

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Preweanling rats are capable of learning a preference for an odor that has been paired with a variety of stimuli (Brake, 1981; Johanson & Hall, 1982; Johanson & Teicher, 1980; Sullivan, Brake, Hofer, & Williams, 1986; Sullivan, Hofer, & Brake, 1986). This learning is associated with an enhanced ^{14}C 2-deoxyglucose (2-DG) uptake in focal regions of the olfactory bulb glomerular layer in response to presentation of the preferred odor (Coopersmith & Leon, 1984; Sullivan & Leon, 1986; Sullivan & Leon, 1987a). The mitral cells associated with the focal regions of the olfactory bulb also have an altered response pattern to the learned odor (Wilson, Sullivan, & Leon, 1985, 1987; Wilson & Leon, 1988a). These behavioral and neural changes do not occur following experience with only the odor (Sullivan & Leon, 1986; Wilson et al. 1987), are specific to the learned odor (Coopersmith, Henderson, & Leon, 1986; Wilson et al. 1985, 1987, 1988a), persist into adulthood (Coopersmith & Leon, 1986), and are associated with morphological changes within the olfactory bulb (Woo, Coopersmith, & Leon, 1987).

It is unclear how stroking and other stimuli are able to enhance pups' behavioral and neural responsiveness to odors. The purpose of this paper is to assess the role of one possible factor which may influence the acquisition of these behavioral and neural modifications: differential respiration rates between conditioning groups during acquisition.

While the *expression* of the enhanced neural response is not due to differential respiration (Sullivan, Wilson, Kim, & Leon, 1988c), its *acquisition* may be due to increased respiration. The reinforcing tactile stimulation used for early olfactory preference training increases respiration rate (Alberts & May, 1984; Sullivan, Shokrai, & Leon, 1988b). Thus, tactile stimulation in the presence of an odor may increase the amount of odor stimulating the olfactory mucosa compared to control pups receiving only odor. This differential odor exposure between experimental and control pups during training may therefore be an important variable in the acquisition of both the olfactory behavioral and neural responses. To assess the role of respiration during training, we compared stroking with high-humidity as reinforcers, since the latter does not alter respiration rate.

Methods

Subjects

The subjects were 64 male and female rats from 8 litters, born of Wistar (Hilltop Lab Animals, Scottsdale, PA) rats mated in our colony. No more than 1 male and 1 female from each litter were used in a particular training/testing condition. Dams were housed in rectangular

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polypropylene cages (34 × 29 × 17 cm) lined with wood chips in a temperature (22 ± 1°C) and light (0800 to 2000 hr) controlled room. Ad lib food and water was available at all times. Mothers were fed a special diet (Teklad Diet TD69446, Madison, WI) that suppressed their dominant odor to minimize extraneous odor experience by the pups (Leon, 1975). Births were checked at 0800 and 2000 hrs and the day of birth was designated postnatal (PN) day 0.

An additional 128 male and female pups (32/age) from 12 litters were used to assess the effects of reinforcing stimulation on respiration rate at PN 1, 6, 12, and 18. All litters were culled to 8 pups (4 male and 4 female) on PN 1.

Conditioning Procedure

Conditioning was conducted from PN 1 through PN 18 for four training groups: 1) Odor/stroking, 2) Odor/high-humidity, 3) Odor only, and 4) Odor/stroking/high-humidity. Conditioning consisted of 18 training trials. Each training trial lasted 10 min with an intertrial interval of 24 hr. The olfactory conditioned stimulus was peppermint odor delivered by a flow dilution olfactometer in a 1 : 10 dilution of saturated peppermint vapor (Schilling, Baltimore, MD) at a flow rate of 7 L/min. Stroking was done vigorously on all areas of the pup's body with a soft sable hair brush. The high-humidity environment (100% relative humidity) was provided by warm water vapor in an air tight incubator (50 × 26 × 36 cm).

Immediately preceding each training session, pups were removed from the dam and placed into individual glass cylinders (1000 mL, 9 cm diameter). Pups were given a 10-min habituation period, followed by the 10-min conditioning procedure. Conditioning took place in an ambient temperature sufficient to mimic nest temperature; 32°, 30°, and 28°C, respectively for pups PN 1-6, 7-12, and 13-18 in both the normal and high-humidity environment.

Testing

On PN 19, pups were given either: 1) a two-odor choice test, or 2) an injection of 2-DG, followed by exposure to the peppermint conditioned odor.

1) Two-Odor Choice Test—Six male and six female pups from each treatment condition were tested for an attraction to the peppermint odor with a two-odor choice test on PN 19. The test apparatus consisted of an (40 × 21 × 15 cm) opaque Plexiglas box with a small grid wire mesh (1 × 1 cm) floor divided in half by a 2 cm wide “neutral zone” which ran the length of the box. Two trays (20 × 20 × 5 cm) containing 500 mL of pine shavings were placed beneath each half of the wire mesh floor. One pan had pine shavings scented with 1 mL of peppermint extract and the other was filled with plain pine shavings. A 1-min trial test began by placing a pup in the neutral zone. When the pup's head and forepaws crossed from the neutral zone into either half of the test box, the experimenter started recording the time. At the end of the test, the total time the pup spent over each of the two odors was recorded by using a microcomputer program. Pups were tested for 5 trials and between each 1-min trial, the pup was taken out of the test box. The direction in which pups were placed into the box was counterbalanced across trials.

2) 2-DG Test—Pups in the 2-DG test were littermates of pups tested in the two-odor choice test. ¹⁴C 2-DG autoradiography has been widely used to analyze differential metabolic activity within the olfactory bulb (Sharp, Kauer, & Shepherd, 1975; 1977; Astic & Cattarelli, 1982; Astic & Saucier, 1982; Jourdan, Duveau, Astic, & Holley, 1980; Greer, Stewart, Kauer, & Shepherd, 1980; Coopersmith & Leon, 1984; Sullivan & Leon, 1986) and is assumed to reflect neural activity (Mata et al., 1980; Yarowsky & Ingvar, 1981). Indeed, within the olfactory bulb, enhanced 2-DG uptake is associated with differential neural activity (Wilson & Leon, 1988a). To assess olfactory bulb 2-DG uptake, five PN 19 pups from each treatment condition

were injected with ^{14}C 2-DG (200 $\mu\text{Ci/kg}$, sc; Pathfinder Laboratories, St. Louis) and then placed in an air-tight glass canister (29×11 cm) followed by odor presentation. Peppermint odor entered the canister in a 1 : 10 dilution at 2 L/min for 1-min periods through a flow-dilution olfactometer. After the odorized air stream ceased, respiratory rate was recorded and sorted into 20 frequency bins for 4.75 min. The cycle was repeated eight times for a total test time of 45 min.

Following odor exposure, pups were decapitated and their brains were quickly removed and frozen in Freon-12 at -40°C . The frozen brain was equilibrated to -17°C in a cryostat for 45 min. The olfactory bulb was cut coronally at 20- μm -thick sections. Each section was immediately picked up on a coverslip and placed on a slide warmer at 60°C for 5-10 min. Coverslips were glued to a sheet of cardboard and exposed to Kodak SB-5 x-ray film for 10 days at 22°C in an exposure cassette. A set of ^{14}C labeled methylmethacrylate standards (Amersham), previously calibrated to ^{14}C uptake in 20- μm brain sections, was exposed with each sheet of film. Autoradiographs were developed using standard techniques.

The autoradiographics were analyzed using a computer-based digital image processor (Spatial Data) that allowed pseudocolor imaging and quantitative optical densitometry. To quantify 2-DG uptake, the computer constructed a calibration curve that related the gray value of ^{14}C standards that were exposed with the brain sections to that of its previously determined ^{14}C tissue equivalent. The computer then linearized this function so that the grey values of the autoradiograph could be translated into ^{14}C levels, and hence 2-DG uptake by the tissue.

The autoradiographs were then optically scanned for areas of relatively high 2-DG uptake and sections in this area were analyzed. In every analyzed section, five readings (each 40 pixels) were taken within the previously identified peppermint responsive areas of the glomerular layer which are 1.5-2.2 mm from the rostral pole of the olfactory bulb. Five readings were taken from the rest of the glomerular layer, and five additional readings were taken in the periventricular core of the olfactory bulb. The 2-DG uptake in the identified areas of the glomerular layer were calculated relative to the 2-DG uptake in the periventricular core because the latter has consistently low levels of 2-DG uptake in response to odor presentation (Jourdan et al., 1980). Thus, differences in thickness and in nonuniformity of background illumination within a section are eliminated by this procedure.

Respiration Rate during Training

Respiration rate in response to: 1) stroking, 2) high-humidity, 3) high-humidity while stroking, and 4) no stimulation was assessed at PN 1, 6, 12, and 18. These pups were not used in the conditioning experiment. Pups were removed from the nest and placed in an air-tight glass canister (12×12 cm), the lid of which held a pressure-sensitive transducer which fed into a respiration monitor (Columbus Instruments). Respiration rate was displayed continuously on a pen recorder (Fisher Recordall, Series 5000). Pups were placed in the test cylinder for a 10-min adaptation period prior to recording respiration. Prestimulation respiration baselines were then recorded for 1 min, following by a 10-min period in which respiration was recorded while pups received stimulation. Stroking consisted of vigorously stroking all surfaces of the pup's body with a sable hair brush that had been flexibly sealed into the lid of the canister. Pups were stroked every min for 30 sec. Although respiration was recorded continuously, respiration data was not used during tactile stimulation because stimulation itself produces changes in pressure which may produce artifacts in the respiration readings of the pressure-sensitive transducer. Respiration in the high-humidity group and in the no-stimulation groups was continuously recorded but their respiration was scored every other 30 sec to coincide with that of the two stroked groups.

Results

Behavior

Both odor/stroke and odor/high-humidity training were sufficient to produce a behavioral odor preference ($F = 7.26, p < 0.01$). As illustrated in Figure 1, the Odor/high-humidity treatment group spent significantly more time over the conditioned odor than the Odor/stroke/high-humidity group (post hoc test, $p < 0.05$). No significant differences were found between the Odor/stroke and Odor/high-humidity groups, nor between the Odor/stroke/high-humidity and Odor-only treatment groups.

2-DG Autoradiography

Both Odor/stroke and Odor/high-humidity training produced an enhanced uptake of 2-DG within the foci of the glomerular layer ($F = 3.96, p < 0.05$). As is illustrated in Figure 2, the Odor/stroke treatment group was significantly different from both the Odor stroke/high-humidity and Odor-only treatment groups (post hoc test, $p < 0.05$). No significant difference was found between the Odor/stroke and Odor/high-humidity groups, nor between the Odor/stroke/high-humidity and Odor-only groups.

The 2-DG uptake differences appear to be limited to the odor-specific foci since the glomerular areas adjacent to the odor-specific foci of 2-DG uptake did not differ between groups. Baseline 2-DG uptake within the periventricular core of the bulb, as well as the size and location of the odor-specific areas, did not differ among treatment conditions. The differential 2-DG uptake can not be accounted for by respiration differences during testing; respiration rates during the odor test did not differ among the treatment groups. Additional analysis indicated no significant difference in the pattern of respiratory frequencies throughout the test odor exposure.

Respiration during Training

As is illustrated in Figure 3, stroking, with or without high humidity, produced an increase in respiration rate throughout development. Analysis of respiration rates during stimulation indicated a significant age effect ($F = 16.77, p < 0.01$), treatment effect ($F = 21.01, p < 0.01$) and age $\times$ treatment interaction ($F = 3.49, p < 0.05$). Post-hoc analysis revealed that the treatment effect was due to stroke only and stroke/high-humidity groups, at each age, having higher respiration rates than high-humidity and no-stimulation groups. No significant differences were found between stroke-only and stroke/high-humidity groups, nor between high-humidity and no-stimulation groups. Additional analysis revealed that the significant age effect was due to older pups' having a higher overall respiration rate than the younger pups (prestimulation baseline; $F = 3.48, p < 0.05$). Baseline respiration rates were 87, 95, 87, and 116 cpm in PN 1, 6, 12, and 18, respectively. However, older pups do not appear to have a significantly more robust respiration response to tactile stimulation than younger pups. When the respiration data were analyzed in ratios to equalize the age differences (ratio of during stimulation/prestimulation + during stimulation) only the treatment effect remained significant ($F = 53.15, p < 0.01$).

Discussion

Increased respiration rate during training is not necessary for the acquisition of either the behavioral or olfactory bulb neural modifications expressed by infant rats following olfactory classical conditioning. Odor/high-humidity pups had the same neurobehavioral response as the Odor/stroking pups during testing, without an increase in respiration rate during training. Indeed, the ability of high humidity to function as a reward appears as robust as that of stroking.

The olfactory bulb modifications were only evident following training which also produced a learned odor preference. Thus, these data support the notion that the olfactory bulb modifications represent processing of the “value” of an odor. Similarly, odors which have acquired significance or biological significance for adults alter their olfactory bulb responses (Astic & Catarelli, 1982; Catarelli, 1982; Freeman, 1982;Pager, 1974).

Odor/stroking/high-humidity pups did not learn a conditioned odor preference nor was there an increase in 2-DG uptake in the odor-specific foci of the glomerular layer in response to that odor. It seems possible that the combination of high humidity with stroking blocks the neurobehavioral response to the exposed odor due to what has been called “overstimulation.” Similar demonstrations of “overstimulation” in the acquisition of an odor preference by pups have been reported. Pups develop an odor preference when that odor is paired with either stroking or an injection of isoproterenol (Sullivan & Leon, 1987b) or amphetamine (Pedersen et al. 1982). However, when the odor is paired with both stroking and the drug injection, pups do not develop a preference for the odor. Thus, it appears that pups must receive an optimal level of stimulation for learning to occur.

The present result suggest that “overstimulation” not only blocks the acquisition of an odor preference, it also blocks the acquisition of the olfactory bulb modifications. Indeed, these results are consistent with the results when odor, stroking and isoproterenol were combined; these pups did not exhibit the enhanced olfactory bulb 2-DG uptake (Sullivan & Leon, 1986). These results emphasize the “learned” nature of the enhanced focal 2-DG uptake response to attractive odors.

The ability of high-humidity to support the behavioral and neural changes expressed by pups following olfactory conditioning suggests that high humidity may be added to the increasing list of stimuli which appear to possess reinforcing value to pups. The list includes: stroking (Pedersen, Williams, & Blass, 1982;Sullivan, Brake, Hofer, & Williams, 1986a;Sullivan, Hofer, & Brake, 1986b;Wilson & Leon, 1988b; Wilson et al., 1986, 1987), opiate injection (Kehoe & Blass, 1986), tailpinching (Sullivan et al., 1986b), milk ingestion (Brake, 1981;Johanson & Hall, 1982;Johanson, Polefrone, & Hall, 1984;Johanson & Teicher, 1980;Sullivan & Hall, 1988;Sullivan, McGaugh, & Leon, 1988a), norepinephrine injection (Pedersen et al., 1982;Sullivan & Leon, 1987b), suckling (Amsel, Letz, & Burdette, 1977;Kenny & Blass, 1977) and brain stimulation (Moran, Lew, & Blass, 1981). The ability of such a diverse group of stimuli to function as a reward in infant rats suggests that these stimuli share a common, perhaps nonspecific basis (Sullivan et al., 1986a,1986b). The present experiments permit us to exclude increased olfactory sensation, produced by increased respiration, as that common factor.

We can also exclude another possible common nonspecific basis for the reward value of stimuli in infant rats, based on the above data. Many of the stimuli which function as a reward in infant rats produce a decrease in both body (Barnett & Walker, 1974;Sullivan et al., 1988b) and brain temperature (Sullivan et al., 1988d). Thus, it is possible that a reaction to a temperature decrease underlies the ability of stimuli to function as a reward. Indeed, the fact that Odor/stroke pups learn is consistent with this notion.

The mechanism for this decrease in temperature appears to be an increase in respiration during stimulation which cools pups by evaporative and conductive heat loss (Sullivan et al., 1988b, 1988d). The temperature decrease can be prevented by placing pups in a high-humidity environment, a procedure that blocks evaporative heat loss. Indeed, the fact that Odor/stroke/high humidity pups do not learn is consistent with the notion that decrease in temperature may be an important variable in pups’ response to a reinforcing stimulus. However, the fact that

odor/high-humidity pups learn without a decrease in temperature argues against this hypothesis.

This paper has delineated stimulus characteristics which are not important in defining reinforcing properties of stimuli. However, it has left unanswered the question of why stroking, high-humidity and other stimuli are reinforcing to infant rats. Although, it is likely that a stimulus possesses many characteristics which enable it to have reinforcing value, recent work has begun to define these variables. Exogenous norepinephrine (NE), when paired with an odor, is sufficient to produce both the learned behavioral (Pedersen, Williams, & Blass 1982; Sullivan, Wilson, & Leon, 1987) and olfactory bulb neural (Sullivan et al., 1987) responses. Moreover, the acquisition of both the behavioral and neural responses can be blocked by injecting an NE receptor antagonist prior to the training trial (Sullivan et al., 1988a; Sullivan & Leon, 1987b).

Interestingly, stroking and other nonspecific sensory stimulation results in activation of the locus coeruleus (lc) in both adult (Foote, Bloom, & Aston-Jones, 1983) and infant rats (Kimura & Nakamura, 1985; Kimura, Nakamura, & Sakaguchi, 1987). This suggests that stimuli which possess reinforcing properties to pups activate endogenous NE (Leonard, 1981). Indeed, at least in the adult, over 40% of lc neurons terminate directly in the olfactory bulb (Shipley, Halloran & de la Torre, 1985). Furthermore, the pup olfactory bulb appears to have high levels of NE very early in the postnatal period (Brunjes 1985; McLean & Shipley, 1987) and the NE system is capable of modulating olfactory bulb excitability as soon as the first postnatal week (Wilson & Leon, 1988b). Thus, NE may, at least in part, underlie the learned behavioral and olfactory bulb modification associated with early olfactory learning.

In conclusion, the present study indicates that changes in respiration and temperature during early olfactory conditioning do not mediate the ability of stimuli to function as a reward. Moreover, these results support the notion that the concomitant changes in the olfactory bulb, may participate in the neural representation of the "value" of an odor.

References

- Alberts JR, May B. Development of nasal respiration and sniffing in the rat. *Dev. Psychobiol* 1980;17:161–181. [PubMed: 6538526]
- Amsel A, Letz R, Burdette DR. Appetitive learning and extinction in 11-day-old rat pups. Effects of various reinforcement conditions. *J. Comp. Physiol. Psychol* 1977;91:1156–1167.
- Astic L, Catarelli M. Metabolic mapping of functional activity in the rat olfactory system after a bilateral transection of the lateral olfactory tract. *Brain Res* 1982;245:17–25. [PubMed: 7116189]
- Astic L, Saucier D. Ontogenesis of the functional activity of rat olfactory bulb: Autoradiographic study with the 2-deoxyglucose method. *Dev. Brain Res* 1982;2:243–256.
- Barnett SA, Walker KZ. Early stimulation, parental behavior, and temperature of infant mice. *Dev. Psychobiol* 1974;7:563–577. [PubMed: 4448307]
- Brake SC. Suckling infant rats learn a preference for a novel olfactory stimulus paired with milk delivery. *Science* 1981;211:506–508. [PubMed: 7192882]
- Brunjes PC, Smith-Craft LK, McCarthy R. Unilateral odor deprivation: Effects on the development of olfactory bulb catecholamines and behavior. *Dev. Brain Res* 1985;22:1–6.
- Coopersmith R, Henderson S, Leon M. Odor specificity of the enhanced neural response following odor experience in rats. *Dev. Brain Res* 1986;27:191–197.
- Coopersmith R, Leon M. Enhanced neural response to familiar olfactory cues. *Science* 1984;225:849–851. [PubMed: 6474157]
- Coopersmith R, Leon M. Enhanced neural response by adult rats to odors experienced early in life. *Brain Res* 1984;371:400–403. [PubMed: 3697770]

- Footo SL, Bloom FE, Aston-Jones G. Nucleus locus coeruleus; New evidence of anatomical and physiological specificity. *Physiol. Behav* 1983;63:844–914.
- Freeman WJ. Changes in spatial patterns of rabbit olfactory EEG with conditioning to odors. *Psychobiology* 1982;19:44–56.
- Greer CA, Stewart WB, Kauer JS, Shepherd GM. Topographical and laminar localization of 2-deoxyglucose uptake in rat olfactory bulb induced by electrical stimulation of olfactory nerves. *Brain Res* 1981;217:279–293. [PubMed: 6265036]
- Johanson IB, Hall WG. Appetitive conditioning in neonatal rats: Conditioned orientation to a novel odor. *Dev. Psychobiol* 1982;15:379–397. [PubMed: 7106397]
- Johanson IB, Polefrone JM, Hall WG. Appetitive conditioning in neonatal rats: Conditioned ingestive responding to stimuli paired with oral infusions of milk. *Dev. Psychobiol* 1984;17:357–381. [PubMed: 6745498]
- Johanson IB, Teicher MH. Classical conditioning of an odor preference in three-day-old rats. *Behav. Neural Biol* 1980;29:132–136. [PubMed: 7387583]
- Jourdon R, Duveau A, Astic L, Holley A. Spatial distribution of I4C 2-deoxyglucose uptake in the olfactory bulbs of rats stimulated with two different odours. *Brain Res* 1980;188:139–154. [PubMed: 7370749]
- Kenny JT, Blass EM. Suckling as incentive to instrumental learning in preweanling rats. *Science* 1977;196:898–899. [PubMed: 860121]
- Kimura F, Nakamura S. Locus ceruleus neurons in the neonatal rat: electrical activity and responses to sensory stimulation. *Dev. Brain Res* 1985;23:301–305.
- Kimura F, Nakamura S, Sakaguchi T. Postnatal development of electrical activity in the locus ceruleus. *J Neurophysiol* 1987;58:510–524. [PubMed: 3655880]
- Leon M. Dietary control of maternal pheromone. *Physiol. Behav* 1975;14:311–319. [PubMed: 1169786]
- Leonard, C. Some speculations concerning neurological mechanisms for early olfactory recognition. In: Aslin, RW.; Alberts, JR.; Pedersen, MR., editors. *Development of Perception: Psychobiological Perspectives*. 1. Academic Press; New York: 1981.
- Mata M, Fink DJ, Gainer H, Smith CB, Davidson L, Savaki H, Schwartz W, Sokoloff L. Activity-dependent energy metabolism in rat posterior pituitary primarily reflects sodium pump activity. *J. Neurochem* 1980;34:213–215. [PubMed: 7452237]
- McLean JH, Shipley MT. Postnatal development of noradrenergic afferents to the olfactory bulb. *Assoc. Chemorecep. Sci. Abst* 1987:169.
- Moran TH, Lew MF, Blass EM. Intracranial self-stimulation in 3-day-old rat pups. *Science* 1981;214:1366–1368. [PubMed: 6975999]
- Pager J. A selective modulation of olfactory input suppressed by lesions of the anterior limb of the anterior commissure. *Physiol. Behav* 1974;13:523–526. [PubMed: 4445272]
- Pedersen PE, Williams CL, Blass EM. Activation and odor conditioning of suckling behavior in 3-day-old albino rats. *J. Exp. Psychol.: Anim. Behav. Proc* 1982;8:329–341.
- Sharp F, Kauer J, Shepherd GM. Local sites of activity related glucose metabolism in rat olfactory bulb during olfactory stimulation. *Brain Res* 1987;98:596–600. [PubMed: 1182541]
- Shipley MT, Halloran FJ, de la Torre J. Surprisingly rich projection from locus coeruleus to the olfactory bulb in the rat. *Brain Res* 1985;329:294–299. [PubMed: 3978450]
- Sullivan RM, Brake SC, Hofer MA, Williams CL. Huddling and independent feeding of neonatal rats can be facilitated by a conditioned change in behavioral state. *Dev. Psychobiol* 1986;19(a):625–635. [PubMed: 3803730]
- Sullivan, RM.; McGaugh, J.; Leon, M. 1988.
- Sullivan RM, Hall WG. Reinforcers in infancy: Classical conditioning using stroking or intra-oral infusions of milk as UCS. *Dev. Psychobiol* 1988;21:215–223. [PubMed: 3371554]
- Sullivan RM, Hofer MA, Brake SC. Olfactory-guided orientation in neonatal rats is enhanced by a conditioned change in behavioral state. *Dev. Psychobiol* 1986;19(b):615–623. [PubMed: 3803729]
- Sullivan RM, Leon M. Early olfactory learning induces an enhanced olfactory bulb response in young rats. *Dev. Brain Res* 1986;27:278–282.

- Sullivan RM, Leon M. One-trial olfactory learning enhances olfactory bulb responses to an appetitive conditioned odor in 7-day-old rats. *Devel. Brain Res* 1987;35(a):307–311.
- Sullivan RM, Leon M. NE modulation of one-trial olfactory conditioning and olfactory bulb neural responding to an attractive odor. *Assoc. Chemorecep. Sci. Abst* 1987;(b):121.
- Sullivan RM, Shokrai N, Leon M. Physical stimulation reduces the body temperature of infant rat. *Dev. Psychobiol* 1988;21(b):225–235. [PubMed: 3371555]
- Sullivan RM, Wilson DA, Leon M. Norepinephrine influences early olfactory learning: Single-unit, metabolic and behavioral responses to learned odor cues. *Internat. Soc. Devel. Psychobiol. Abst.* 1987
- Sullivan RM, Wilson DA, Kim MH, Leon M. Behavioral and neural correlates of postnatal olfactory conditioning: I. Effect of respiration on conditioned neural responses. *Physiol. Behav.* 1988;(c)in press
- Sullivan RM, Wilson DA, Leon M. Physical stimulation reduces the brain temperature of infant rats. *Dev. Psychobiol* 1988;21(d):237–250. [PubMed: 3371556]
- Wilson DA, Leon M. Postnatal development of noradrenergic modulation of olfactory bulb excitability. *Soc. Neurosci. Abst* 1987;13:1402.
- Wilson DA, Leon M. Spatial patterns of olfactory bulb single-unit responses to learned olfactory cues in young rats. *J. Neurophysiol* 1988;59(a):1770–1782. [PubMed: 3404204]
- Wilson DA, Leon M. Noradrenergic modulation of olfactory bulb excitability in the postnatal rat. *Dev. Brain Res.* 1988;(b)in press
- Wilson DA, Sullivan RM, Leon M. Odor familiarity alters mitral cell response in the olfactory bulb of neonatal rats. *Dev. Brain Res* 1985;22:314–317.
- Wilson DA, Sullivan RM, Leon M. Single-unit analysis of postnatal olfactory learning: Modified olfactory bulb output response patterns to learned attractive odors. *J. Neurosci.* 1987;7:3154–3162. [PubMed: 3668621]
- Woo CC, Coopersmith R, Leon M. Localized changes in olfactory bulb morphology associated with early olfactory learning. *J. Comp. Neurol* 1987;263:113–125. [PubMed: 3667967]
- Yarowsky PJ, Ingvar DH. Neuronal activity and energy metabolism. *Fed Proc* 1981;40:2353–2362. [PubMed: 6265285]

Fig 1.
Mean time ($\pm$ SE) spent over peppermint odor in the two-odor choice test for pups in each of the conditioning groups.

Fig 2.
Mean relative 2-DG uptake (+SE) in the spatially odor-specific focal areas of the olfactory bulb during test exposure to peppermint odor for each of the conditioning groups.

Fig 3.

Mean respiration rate ($\pm$ SE) in response to stroking, stroking in high humidity, high humidity and no stimulation control for 1-, 6-, 12-, and 18-day-old pups. No change in respiration rate is indicated by 0.5, an increase is greater than 0.5, and a decrease is less than 0.5.