

Behavior of Rat Fetuses Following Chemical or Tactile Stimulation

William P. Smotherman and Scott R. Robinson
Departments of Psychology and Zoology, Oregon State University

The behavior of fetal rats was examined on Day 19 of gestation with procedures that enabled chemical stimulation and direct observation of fetuses. Rat fetuses are sensitive to both tactile stroking and intraoral infusion of chemical solutions, but the pattern and amount of activity depend upon the modality of stimulation. Fetal responsiveness is affected by prior experience with chemical stimuli. Repeated exposure within a 10-min period results in a waning of response, and repeated exposure across a delay of 48 hr results in a different pattern of response than is seen to a novel stimulus. Reexposure to a stimulus experienced earlier in gestation also alters fetal responsiveness to other forms of tactile and chemical stimulation. These findings indicate that the rat fetus exhibits olfactory function in utero and suggest central processing of sensory information, including evidence of habituation, a fetal orienting reflex to novel stimuli, and the existence of prenatal behavioral states associated with different patterns of response.

The fetus develops within a complex intrauterine environment that changes over the course of gestation. Within the uterus fetuses are exposed to a diverse assortment of stimuli, including mechanical stimuli originating in the outside world or maternal physiology and a rich chemical milieu that varies with alterations in maternal diet or environment (Smotherman & Robinson, in press). Because the fetal environment is variable, sensory responsiveness might be anticipated as a normal feature of prenatal behavioral development. Indeed, there is growing evidence that fetuses are sensitive to intrauterine stimuli and can modify their behavior in response to stimulation (Smotherman & Robinson, 1987).

Fetuses are active in utero and exhibit a behavioral repertoire that expands up to the time of birth (de Vries, Visser, & Prechtel, 1982; Robinson & Smotherman, 1987; Smotherman & Robinson, 1986). Fetal activity is both complex and organized, showing temporal patterning (Smotherman & Robinson, 1986), rhythmicity (Robertson, 1985), synchrony (Robinson & Smotherman, 1987), and emergent coordination (Bekoff & Lau, 1980). Fetuses are also responsive to alterations in their immediate physical environment, becoming more active outside the restraining influence of the uterus and amniotic sac than in utero (Smotherman & Robinson, 1986). The behavioral sophistication evident in these findings argues that spontaneous fetal activity cannot be characterized, as it has been in the past, as random motility bearing little relation to postnatal behavior (Hamburger, 1963).

Earnest inquiry into the prenatal roots of responsive behavior began in the 1920s and '30s (Angulo y Gonzalez, 1932; Barcroft & Barron, 1939; Carmichael, 1934; Coghill, 1929;

Windle & Griffin, 1931). These early students were primarily interested in neurological development and exploited fetal behavior as a means of charting the emergence of spinal reflexes. Toward this end, methods were developed for presenting tactile stimulation by probing or stroking fetuses in utero. Probing the skin of fetal rats with a stiff bristle or pin has enabled the mapping of body regions sensitive to punctate tactile stimuli (Narayanan, Fox, & Hamburger, 1971). Fetuses are indeed responsive to tactile stimulation, exhibiting both local reflexes and more general activity. It is interesting that the perioral region is among the earliest to become sensitive to tactile stimulation and remains consistently sensitive throughout gestation.

In contrast to the early investigation of tactile stimuli, prenatal responsiveness to tastes and odors has only recently come under scrutiny with the advent of techniques for delivering chemical solutions into the amniotic fluid of the developing rat fetus (Blass & Pedersen, 1980; Stickrod, 1981). Studies of labeled glucose uptake in the accessory olfactory bulbs of fetal rats indicate that the olfactory system is functional before birth (Mistretta & Bradley, 1986; Pedersen, Stewart, Greer, & Shepherd, 1983). This finding agrees with behavioral evidence that neonatal rats are sensitive to odor cues that they experience in utero (Pedersen & Blass, 1982; Smotherman, 1982a). Early postnatal behavior, such as suckling, seems dependent upon olfactory stimuli. The cue that orients the rat pup to the nipple for the first suckling episode is a substance (olfactorant) present in the amniotic fluid (Pedersen & Blass, 1981).

Manipulation of the prenatal chemical environment also has provided direct evidence that fetuses are capable of associating neutral chemical cues with aversive stimulation in utero. It is well known that in adult rats the conjunction of a taste or odor with a noxious chemical (ip injection of lithium chloride) leads to the formation of a conditioned aversion (Garcia, Lasiter, Bermudez-Ratoni, & Deems, 1985). Conditioning of this kind can be acquired in utero by the rat fetus and expressed as altered behavior during either the prenatal or the postnatal period. For example, rat fetuses conditioned

This research was supported by National Institute of Child Health and Human Development Grant HD 16102-05 and Research Career Development Award HD 00719-01 to W. P. Smotherman. We thank Patricia La Vallee for technical assistance in this study.

Correspondence concerning this article should be addressed to W. P. Smotherman, Laboratory for Psychobiological Research, Department of Psychology, Oregon State University, Corvallis, Oregon 97331.

to avoid a mint solution on Day 17 of gestation, when reexposed to mint on Day 19, exhibit a conditioned suppression in overall activity (Smotherman & Robinson, 1985). In addition to demonstrating an ability of the fetus to learn, these studies provide direct evidence of fetal chemical competence.

In this report we examine sensory responsiveness in the rat fetus by manipulating the mode of stimulation, the previous experience of the fetus with the test stimulus, and the presence of contextual stimuli prior to the time of testing. Specifically, a series of experiments was conducted to (a) assess the influence of procedures for delivering chemical stimuli to fetuses, (b) compare the effects of tactile stroking and chemical infusion on fetal activity, (c) measure short-term changes in responsiveness to repeated chemical stimulation, (d) assess the influence of prior experience with a chemical cue on subsequent responsiveness to that cue, and (e) investigate the interaction of the mode of stimulation and the contextual stimuli present prior to the time of testing.

General Method

Subjects

Subjects were the progeny of female Sprague-Dawley rats (Simonson Laboratories, Gilroy, California) time-mated to Long-Evans males. Females were housed in groups of three in polycarbonate cages (33 × 38 × 10 cm) until the first day of fetal manipulation/observation. In some experiments fetuses were manipulated on Day 17 of gestation; in all cases fetal behavior was directly observed on Day 19. Cages were kept in a temperature- and humidity-controlled colony room under a 12:12 hr light/dark cycle (lights on at 0700); testing took place between 0900 and 1700. Females were provided with ad lib food and water and at all times maintained in accordance with guidelines for animal care established by the National Institutes of Health, the International Society for Developmental Psychobiology, and the Animal Behavior Society.

Manipulation of the Fetal Environment

In certain experiments it was necessary to manipulate fetal experience with chemical cues through controlled alteration of the intra-uterine environment. This manipulation included injection of taste/odor stimuli into the amniotic fluid and injection of lithium chloride or saline into the peritoneum of individual fetuses. In order to effect these manipulations, pregnant rats were anesthetized with ether on Day 17 of gestation, the ventrum was shaved, and both horns of the uterus were externalized through a midline laparotomy. A 30-ga. needle was inserted through the uterine wall under visual guidance, and 20 μ l of solution was injected into the amniotic fluid that surrounds the fetus. In order to effect conditioning, 20 μ l of LiCl (or isotonic saline) was injected ip. After the last injection, punctures in the uterine wall were sealed with petroleum jelly, the uterus was rinsed with isotonic saline and replaced in the female's peritoneum, and the incision was closed with sutures and stainless steel wound clips. These procedures are not harmful to fetuses and do not interfere with normal fetal development or parturition (Blass & Pedersen, 1980; Stickrod, 1981).

Preparation for Observation

Direct observation of fetal behavior requires surgical preparation of the mother as well as manipulation of the immediate environmen-

tal conditions of the fetus. Pregnant rats were prepared on Day 19 of gestation to eliminate sensation from the lower body while circumventing the suppressive effects of general anesthesia on fetal behavior. Under ether anesthesia, females were prepared by chemomyelotomy, which involved injection of 100 μ l of 100% ethanol into the spinal canal between the first and second lumbar vertebrae, producing irreversible spinal anesthesia posterior to the site of injection (Smotherman, Richards, & Robinson, 1984). Following this treatment, the female was placed in a Plexiglas holding apparatus, her uterus was externalized through a midventral incision, and the uterus and lower body were immersed in a 37.5°C bath containing buffered isotonic saline. The mother and fetuses were allowed to recover from ether anesthesia for 20 min before the onset of behavior observation.

In most experiments (Experiments 1-3), a single fetus was observed from each mother. In Experiment 4, 2 fetuses were selected as subjects from each mother, with the treatment and order of fetal observation counterbalanced. All subject fetuses were selected from the ovarian end of a uterine horn. In some experiments fetuses were reexposed to a chemical stimulus by intra-amniotic injection 2 min prior to observation. Immediately before observation, the subject fetus was carefully delivered from the uterus and amniotic sac into the saline bath, with care taken to maintain the integrity of the umbilical circulation and the placental-uterine attachment. Because all behavioral observations were conducted after delivery from the uterus and amnion, fetuses were not tested in the presence of chemical stimuli within the amniotic fluid. All fetuses included in this study were unremarkable and remained well oxygenated (pink coloration) throughout the observation.

Presentation of Stimuli

During a 10-min period of observation, each subject fetus was exposed to either tactile or chemical stimulation. In order to maintain the subject fetus in an observable position, its uterine horn was gently repositioned. All fetuses received minimal handling. Tactile stimulation was provided by gently stroking the fetus from head to rump three times in quick succession with a soft, camel-hair brush (total duration of stroking = 1-2 s).

Controlled presentation of chemical stimuli into the mouth of the fetus was made possible through the use of an intraoral cannula, adapted from procedures developed for rat pups (Hall & Rosenblatt, 1977). The cannula, which consisted of a length of PE-10 polyethylene tubing (diameter = 0.61 mm), was inserted through the fetus's lower jaw with the flanged tip resting on the dorsal surface of the tongue. The free end of the cannula was connected to a length of PE-50 tubing, which in turn attached to a 23-ga. needle on a microliter syringe. During installation, care was exercised to maintain the fetus under the surface of the water, to avoid crimping or pulling the umbilical cord, and to provide enough tubing so as not to restrict fetal movement. This system enabled precise infusion ($\pm 1 \mu$ l) of a chemical solution to the fetus without otherwise interrupting ongoing fetal activity. Infusions were delivered in a 1-2-s pulse consisting of 20 μ l of the test solution.

Chemical solutions consisted of lemon or mint extract presented in an isotonic saline carrier, or isotonic saline. Solutions were prepared by mixing one part of pure lemon or mint extract (Schilling brand) in three parts saline (v/v), centrifuging, and removing the supernatant oil. The remaining solutions were presented to fetuses by intra-amniotic injection (mint or saline) or intraoral infusion (lemon, mint, or saline). Although both lemon and mint solutions are distinct and strong to the human nose, lemon solution has been found to elicit greater activity than mint following infusion to fetal rats (Smotherman & Robinson, 1987).

Behavioral Observation

Each subject fetus was observed for 10 min, during which stimuli were presented on a regular schedule (described below for each experiment). Each instance of fetal movement was entered into a microcomputer serving as a real-time event recorder, thereby preserving a continuous sequential record of movements in temporal relation to the presentation of stimuli. Following observation these movement events were tallied to provide a measure of overall fetal activity. We have found this procedure to be highly reliable in recording the occurrence of fetal movements (Smotherman & Robinson, 1985). After data were collected, the female and fetus(es) were humanely sacrificed.

Experiment 1: Response to Tactile Stroking

Previous studies of evoked activity in rat fetuses have employed various forms of tactile stimulation, such as vibration, pin point, or brush stroke, to elicit fetal responses (Angulo y Gonzalez, 1932; Narayanan et al., 1971). Unlike in those studies, which were primarily concerned with the development of reflexes during the prenatal period, the focus here was to investigate the effect of tactile stimulation on overall fetal activity. Therefore, an area-directed mode of stimulation—brush stroking—was applied repeatedly to the fetus's dorsal surface.

Method

A total of 20 fetuses were observed, all from different mothers. Each subject fetus was delivered from the uterus and amniotic sac into the water bath, and tactile stimulation was applied by gently applying three strokes from head to rump with a soft brush. Stroking was applied five times at 2-min intervals during each 10-min observation period. A series of matched-pair *t* tests ($df = 19$) was used to compare fetal activity during the 1-min interval before and after each application of stroking. Overall fetal activity during the ten 1-min intervals of the observation period was analyzed in a one-way repeated measures analysis of variance (ANOVA).

Results and Discussion

The behavior of fetuses over the 10-min observation period in which stroking was applied is depicted in Figure 1. Stroking increased fetal activity after the first ($t = 1.8, p < .05$) and second ($t = 1.9, p < 0.5$) applications but had no significant effect on fetal activity thereafter. In 64 of 100 observations (64%), fetal activity showed an increase after stroking. The ANOVA comparing the ten 1-min intervals indicated an overall increase in fetal activity over the observation period, $F(9, 171) = 2.8, p < 0.1$. The response to stroking was evident not only during the 1-min intervals after the first two applications but also during the 1-min intervals before the last three applications of stroking. These data are broadly consistent with previous studies that found an activational influence of tactile stimulation during the prenatal period (Angulo y Gonzalez, 1932; Narayanan et al., 1971).

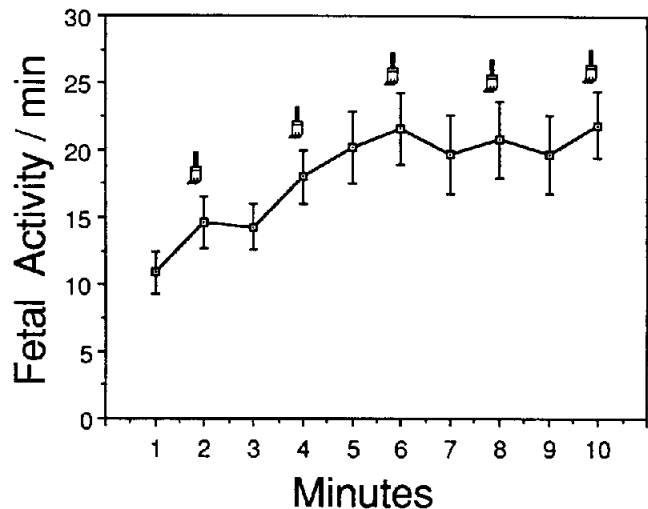


Figure 1. Activity of stroked rat fetuses over ten 1-min intervals during the observation in Experiment 1. (Tactile stimulation was applied immediately prior to the second, fourth, sixth, eighth, and tenth minutes [indicated by brush symbols]. Points represent mean number of fetal movements per 1 min; vertical lines indicate SE.)

Experiment 2: Response to Intraoral Infusions

Intraoral cannulation and infusion is a technique that has been widely used to deliver precise volumes of milk and other gustatory stimuli to rat pups during the postnatal period (Hall & Rosenblatt, 1977; Johanson & Hall, 1979; Kehoe & Blass, 1985). We have adapted this technique to the rat fetus and have found it useful as a means of presenting novel, familiar, and biologically relevant chemical cues as early as Day 17 of gestation (Smotherman & Robinson, 1987). In the experiments reported below, fetuses received repeated infusion consisting of a 20- μ l pulse, delivered over a 1–2-s period, of isotonic saline or a solution of lemon extract.

Experiment 2a: Behavior of Untreated, Implanted, and Saline-Infused Fetuses

Because the infusion technique has not previously been used in the study of fetal behavior, it is important to determine whether the presence of the cannula or the occurrence of an intraoral infusion per se influences spontaneous fetal activity. In addition to evaluating whether the cannulation or infusion procedures affect fetal behavior, these control groups provide important information about baseline fetal activity that is necessary in order to interpret data from all later experiments reported in this article.

Method

A total of 42 fetuses were observed on Day 19 of gestation, each from a different mother in one of three treatment conditions: observed in the bath without manipulation (untreated); implanted with an intraoral cannula but with no infusion (implanted); and implanted with a cannula and receiving five infusions of isotonic saline at 2-min intervals (saline). Overall activity of fetuses during the 10-min

observation period was broken into 1-min intervals and analyzed by a repeated measures ANOVA. In addition, responses to saline infusions were evaluated by comparing fetal activity during the 1-min intervals before and after each infusion of saline by a series of matched-pair *t* tests.

Results and Discussion

The ANOVA comparing untreated, implanted, and saline fetuses revealed a significant main effect of treatment, $F(2, 39) = 7.7, p < .01$. This effect was due to the greater activity of saline-infused fetuses relative to untreated and implanted controls (Figure 2). The latter two groups did not differ from each other. There was no indication that activity changed as a function of elapsed time during the observation or with repeated infusions of saline; the effect of time and the interaction were not significant. Although general activity was greater in the saline group, there was no indication that activity increased in the 1-min interval after each infusion of saline. None of the five *t* tests comparing intervals before and after each infusion revealed a significant change in fetal activity. Slightly more than half of the 75 saline infusions (52%) resulted in an increase in fetal activity.

The technique for cannula implantation is apparently benign, as evidenced by the lack of any difference between the untreated and implanted groups. Moreover, although saline-infused fetuses were more active overall, there was no indication for any of the three groups that fetal activity increased or decreased over the course of the observation. Nor was there evidence that saline-infused fetuses became more active after the moment of infusion. Therefore, in the experiments described below we interpret any change in fetal activity after infusion as evidence that fetuses are responsive to the substance infused.

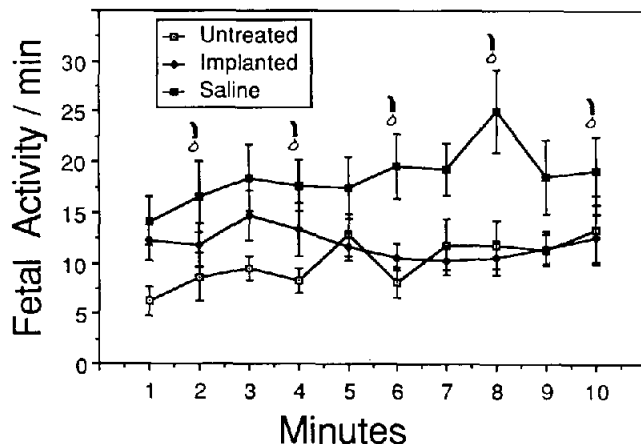


Figure 2. Activity of untreated, cannula-implanted, and saline-infused fetuses over ten 1-min intervals during the observation in Experiment 2. (Saline fetuses received an infusion of saline immediately prior to the second, fourth, sixth, eighth, and tenth minutes [indicated by infusion symbols]; untreated and implanted fetuses received no infusion. Points represent mean number of fetal movements per 1 min; vertical lines indicate SE.)

Experiment 2b: Fetal Behavior Following Lemon Infusion

The demonstration that intraoral cannulation is without effect on fetal behavior and is suitable for presenting test solutions to fetuses enabled further study of fetal responsiveness to chemical stimuli. Because it is known that prenatal exposure to lemonlike odors can influence the behavior of rat pups at the nipple (Pedersen & Blass, 1982), the effect of a solution prepared from lemon extract on fetal behavior was examined. The effectiveness of a lemon stimulus to elicit fetal responses was assessed by (a) comparing overall activity before and after each infusion and (b) characterizing temporal changes in fetal activity during the 1-min interval after infusion.

Method

A total of 19 subject fetuses were delivered into the bath, implanted with an intraoral cannula, and infused with lemon during a 10-min observation period. A series of matched-pair *t* tests ($df = 18$) was used to compare fetal activity during the 1-min interval before and after each of the five infusions, which were spaced at 2-min intervals. To compare responses to different forms of stimulation, we used a second analysis to examine fetal activity during the 1-min period following application of tactile stroking (Experiment 1), saline infusion (Experiment 2a), or lemon infusion. Activity during the twelve 5-s intervals following stimulus presentation was compared by a repeated measures ANOVA to assess the temporal distribution of fetal behavior after three forms of stimulation.

Results and Discussion

Fetuses responded vigorously to lemon infusion. Results of the five *t* tests confirmed that fetuses were much more active in the 1-min interval after each infusion (first: $t = 6.0$; second: $t = 4.1$; third: $t = 4.3$; fourth: $t = 6.4$; fifth: $t = 3.8$; all p values $< .01$). Not only was average activity greater, but lemon was highly consistent in eliciting fetal response; 85 of 95 infusions (90%) resulted in greater activity. This result stands in contrast to the occurrence of activation following stroking (64%) or saline infusion (52%), $\chi^2(2, N = 295) = 30.1, p < .01$. An analysis of temporal changes in activity after these three forms of stimulation indicated the significant main effects of mode of stimulation, $F(2, 51) = 15.3, p < .01$, and 5-s interval after presentation, $F(11, 561) = 9.6, p < .01$, and the interaction of these factors, $F(22, 561) = 8.6, p < .01$. Fetal activity peaked within 15 s after lemon infusion and declined thereafter. Such a close temporal relation between peak fetal activity and the moment of stimulation was absent among fetuses infused with saline or stroked (Figure 3), in which fetal activity remained at a constant level throughout the twelve 5-s intervals after stimulation.

These data demonstrate that intraoral infusion of lemon evokes both a quantitatively and a qualitatively different response from fetal rats than either tactile stroking (Experiment 1) or saline infusion (Experiment 2a). The response to lemon was robust but seemed to diminish with successive presentations. The first lemon infusion resulted in a 152%

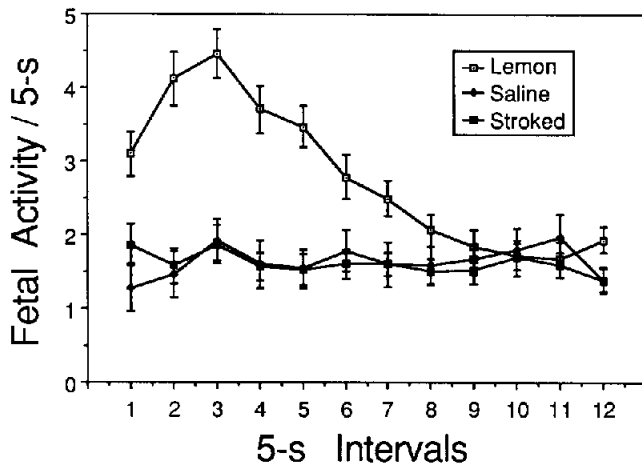


Figure 3. Activity of stroked, saline-infused, and lemon-infused fetuses over the twelve 5-s intervals after stimulation in Experiments 1, 2a, and 2b, respectively. (Points represent mean number of fetal movements per 5 s, [vertical lines indicate *SE*] calculated over all five stimulus applications.)

increase in fetal activity, the third infusion in a 108% increase, and the last infusion in a 64% increase, calculated relative to activity before infusion. The response to lemon also was both rapid and transient. Within the minute after stimulus presentation, lemon infusion resulted in 70% more fetal activity than saline infusion or stroking. Yet by the end of the minute following infusion, fetuses exposed to lemon, saline, or stroking exhibited equivalent levels of activity.

Experiment 2c: Repeated Lemon Infusions

The results of Experiment 1 indicated that tactile stroking resulted in a gradual increase in fetal activity over the course of the observation. Saline-infused fetuses (Experiment 2a), however, failed to show any systematic change in activity during the 10-min period. Further, lemon-infused fetuses (Experiment 2b) appeared to show less activation following the last infusion. Experiment 2c was designed to provide a more precise measure of changing responsiveness of rat fetuses to successive lemon infusions.

Method

Ten fetuses from different mothers were observed. After delivery into the bath and installation of the cannula, each fetus received 10 infusions of lemon at 1-min intervals (the first infusion occurring coincident with the beginning of the observation period). In order to evaluate changing responsiveness to successive infusions of lemon, fetal activity during each 1-min interval was compared in a repeated measures ANOVA. Five minutes after the conclusion of the initial 10-min observation, each fetus received an 11th infusion of lemon and was observed for 1 additional min. A matched-pairs *t* test ($df = 9$) was used to compare fetal activity following the 10th and 11th infusions.

Results and Discussion

The analysis demonstrated that the spike in fetal activity following infusion diminished over the course of 10 infusions, $F(9, 81) = 3.1, p < .01$. However, an additional infusion that occurred 5 min after the 10th infusion reinstated a strong fetal response to lemon. Fetal activity after the 10th and 11th infusions differed significantly, $t(9) = 3.5, p < .01$. In fact, the magnitude of activation following the delayed infusion was equivalent to fetal responses early in the observation. This pattern of decline and recovery in responsiveness is depicted in Figure 4, which shows activity during successive 15-s intervals during the observation.

Clearly, fetuses respond differently to repeated chemical stimulation than they do to tactile stroking. Stroking shows, if anything, a prolonged or cumulative effect on fetal activity, with fetal behavior increasing in frequency following the first two applications of stroking. Responses to lemon infusion, in contrast, are larger in magnitude and more closely linked to the time of stimulation, rising to a peak and dissipating rapidly. Responsiveness to lemon also diminishes when infusions are repeated in rapid succession (1–2-min intervals between infusions), unlike the pattern of increasing activity following successive applications of stroking.

Experiment 3: Effect of Prior Experience

The waning responsiveness of fetuses to lemon, demonstrated in the previous experiment, argues that the rat fetus is influenced by relatively short-term experiences. In studies of the learning abilities of rat fetuses, we have manipulated the experience of the fetus on Day 17 of gestation (by pairing an intra-amniotic mint stimulus with ip LiCl) and documented that this manipulation altered fetal responses to mint 2 days later (Smotherman & Robinson, 1985). Learning was demonstrated when conditioned fetuses showed an overall suppression in activity upon reexposure, within the amniotic sac, to a conditioned mint stimulus on Day 19. The existence of immediate (waning) and longer term (conditioning) experiential effects on fetal activity suggested the possibility that fetal responses to chemical infusions would differ as a function of prior experience with the stimulus. In Experiment 3 we investigated the responses of fetuses to infusions of the same stimulus employed in the conditioning experiments (mint) and assessed whether these responses could be modified by prior exposure to mint.

Experiment 3a: Fetal Behavior Following Mint Infusion

With the same procedures described in Experiment 2b, the responses of rat fetuses to five infusions of mint during a 10-min observation period were measured.

Method

Ten subject fetuses, each from a different mother, were placed in the water bath, implanted with a cannula, and infused with a mint

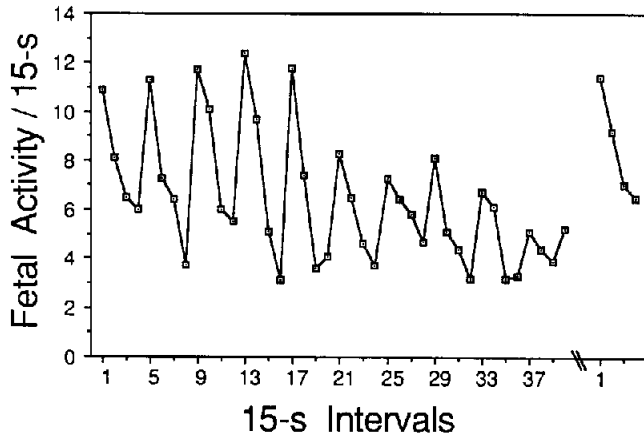


Figure 4. Activity of fetuses after repeated infusion of lemon over a 10-min observation period and one subsequent 1-min period in Experiment 2c. (Infusions were delivered at the beginning of each minute of observation. Points represent the mean number of fetal movements per 15 s. Data are plotted to depict the spike in activity following each infusion, the waning of response with successive infusion, and the recovery of response after a 5-min delay with no infusion).

solution during a 10-min observation session. Activity during the 1-min intervals before and after each of five infusions was compared by a series of matched-pair *t* tests ($df = 9$).

Results and Discussion

As with their response to lemon, rat fetuses showed greater activity following infusion to mint. On 41 of 50 occasions (82%), fetuses were more active during the 1-min interval following infusion of mint. This activational effect of mint was significant in four of the five successive infusions to each fetus: Activity increased 169% after the first infusion ($t = 4.0$, $p < .01$), 20% after the second ($t = 0.5$, $p > .05$), 74% after the third ($t = 4.0$, $p < .01$), 30% after the fourth ($t = 2.1$, $p < .01$), and 50% after the fifth ($t = 3.0$, $p < .01$). Inspection of the data for the 1-min interval after each infusion revealed that mint produced an activity pattern of peak-and-decline resembling that of lemon (Experiment 2b), although the magnitude of activity increase was not as pronounced as lemon and may have waned more rapidly. These data demonstrate that the mint stimulus employed in earlier learning experiments (Smotherman & Robinson, 1985), although qualitatively different from lemon, also activates fetal behavior when infused into the mouth of the Day 19 rat fetus.

Experiment 3b: Response to Novel or Familiar Mint

A single intra-amniotic injection of mint on Day 19 of gestation neither increases nor decreases the rate of fetal movement. Moreover, intra-amniotic mint remains neutral regardless of whether the fetus has experienced mint earlier in gestation. Only if prior exposure to mint by intra-amniotic injection is accompanied by an ip injection of LiCl does later

exposure to mint affect fetal behavior (Smotherman & Robinson, 1985). When directly infused into the mouth of the fetus, however, chemical stimuli such as lemon (Experiment 2b) or mint (Experiment 3a) activate fetal behavior. The purpose of Experiment 3b was to explore whether the immediate responsiveness of fetuses to intraoral infusions of mint is affected by prior exposure to mint.

Method

Twenty fetuses from different mothers were distributed equally between two treatment groups to assess the effect of prior experience with mint on the subsequent responsiveness to mint infusions. On Day 17 of gestation, 10 fetuses were exposed to saline and 10 fetuses to mint by intra-amniotic injection. Two days later, subjects from both groups were externalized from the uterus and prepared for observation in the water bath, implanted with an intraoral cannula, and either presented with mint by infusion for the first time (novel; saline on Day 17) or reexposed to mint (familiar; mint on Day 17). Five infusions of mint were delivered 2 min apart, occurring during the 12th 5-s interval of the first, third, fifth, seventh, and ninth minutes of observation.

To provide a detailed analysis of fetal behavior at the moment of infusion, we examined fetal activity during the 5-s interval in which each infusion occurred and the three subsequent 5-s intervals. These activity measures were compared with the baseline rate of fetal activity during the 1 min preceding each of the five infusions in a series of matched-pair *t* tests ($df = 9$).

Results and Discussion

The baseline rate of fetal movement for the eleven 5-s intervals prior to infusion was virtually identical in both treatment groups; fetuses infused with novel mint performed 1.2 ± 0.2 movements/5 s and those with familiar mint 1.3 ± 0.2 movements/5 s. Inspection of the behavior of fetuses during the infusion indicated that the novelty or familiarity of the mint stimulus influenced the pattern of fetal response (Figure 5). Fetuses infused with novel mint showed an initial suppression in activity, a 62% reduction in movement relative to baseline, during the infusion interval ($t = 3.8$, $p < .01$). In contrast, fetuses infused with familiar mint exhibited no significant change in activity during the infusion ($t = 1.2$, $p > .05$). During postinfusion intervals, however, the findings from both novel and familiar mint replicated the overall activational effect (Experiment 3a). The change in fetal behavior over baseline was not significant during the first 5-s interval after infusion (novel: $t = 0.8$, $p > .05$; familiar: $t = 0.7$, $p > .05$) but did reflect increased activity during the second and third intervals (novel 2nd: $t = 3.7$, $p < .01$; novel 3rd: $t = 4.2$, $p < .01$; familiar 2nd: $t = 3.0$, $p < .05$; familiar 3rd: $t = 3.1$, $p < .05$).

In summary, prior experience with a mint stimulus modifies the response of rat fetuses to infusions of mint. When mint is presented for the first time, fetuses show a brief immediate response consisting of a sharp reduction in movement. This behavioral suppression is not apparent in fetuses exposed to mint made familiar through prior exposure. Regardless of experience, however, fetuses become more active

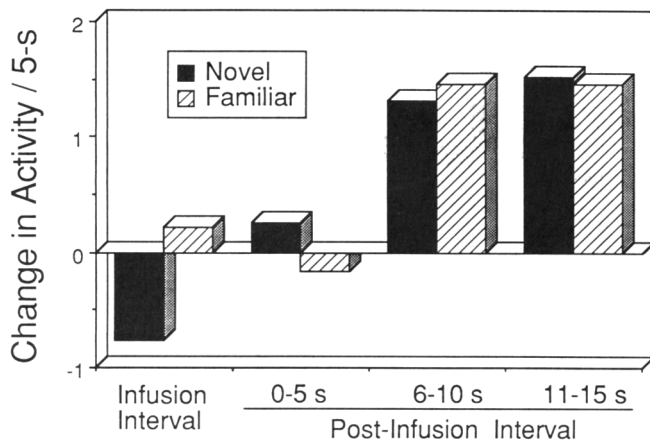


Figure 5. Differential response of rat fetuses to intraoral infusions of novel or familiar mint solutions. (Responses are plotted relative to baseline activity per 5 s, which is derived from the mean number of fetal movements during the 1-min period preceding each infusion. Response scores reflect the mean change from baseline in fetal activity during the 5-s interval in which the infusion was delivered and three 5-s intervals subsequent to infusion. Although both mint solutions have the net effect of activating behavior, novel mint suppresses activity at the moment of infusion.)

following a measurable delay after mint infusion. It is thus evident that rat fetuses are sensitive not only to the mode of stimulation and the specific nature of the stimulus (Experiments 1, 2a, 2b, and 3a) but also to prior experience with the stimulus.

Experiment 4: Influence of Context and Mode of Stimulation

It is clear from the preceding experiments that fetal responsiveness is complex; different stimuli presented within different modalities elicit qualitatively and quantitatively different patterns of fetal response. Fetuses are capable of responding to both tactile and chemical stimuli, becoming increasingly active with successive applications of the former and exhibiting a waning response to the latter. Further, fetal response to a given stimulus is modified by prior experience with the stimulus. In Experiment 4 the interaction of olfactory context before stimulation and mode of stimulation was investigated. On Day 17 the mint cue was presented to fetuses by intra-amniotic injection and paired with ip LiCl to effect conditioning (Smotherman & Robinson, 1985). On Day 19 the olfactory environment of the subject fetus was again manipulated by injecting mint or saline into the amniotic sac prior to observation in the water bath. Each fetus was then exposed to one of two modes of stimulation, tactile stroking (Experiment 4a) or lemon infusion (Experiment 4b), during the observation period.

Experiment 4a: Tactile Stroking

Method

A total of 40 subject fetuses were observed, 2 from each of 20 mothers. On Day 17 of gestation, all fetuses were treated with an

intra-amniotic injection of mint followed by an ip injection of LiCl. In order to manipulate olfactory context prior to testing on Day 19, each fetus, while still within the uterus, was pretreated by intra-amniotic injection. In one group of 10 mothers, both subject fetuses were pretreated with conditioned mint; in the other group of 10 mothers, both fetuses were pretreated with saline. Two minutes following pretreatment, each subject was delivered into the bath for behavioral observation.

Within each mother, one fetus received tactile stroking at 2-min intervals during the 10-min session, and the other was not stroked. Activity difference scores were calculated for each of the pretreatment conditions by subtracting the activity of the unstroked fetus from its stroked littermate. This measure of net responsiveness to stroking was calculated for the second, fourth, sixth, eighth, and tenth minutes (the 1-min intervals after the application of stroking). These data for saline- and mint-pretreated fetuses were compared with a series of Mann-Whitney *U* tests.

Results and Discussion

Fetal responsiveness to stroking was influenced by the olfactory context provided just prior to observation. Pretreatment with conditioned mint modified the subsequent pattern of fetal responsiveness to successive applications of stroking (Figure 6). The Mann-Whitney *U* tests comparing saline and mint pretreated fetuses showed them to differ in net responsiveness during the eighth and tenth minutes of the observation ($ps < .05$). It appeared that saline-pretreated fetuses became more active in response to stroking as the observation progressed, a finding that replicated the overall change in fetal activity reported in Experiment 1. In contrast, mint-pretreated fetuses became less active and actually showed suppressed activity with successive applications of stroking. These findings demonstrate how manipulation of the olfactory context by presentation of the conditioned mint stimulus alters the responsiveness of Day 19 rat fetuses to tactile stimulation.

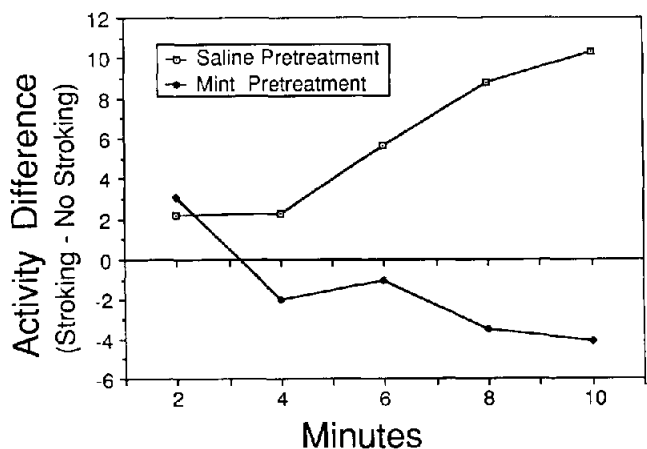


Figure 6. Differential response of rat fetuses to stroking following pretreatment with saline or conditioned mint. (Each point represents the mean activity difference between stroked and unstroked fetuses. Tactile stroking was administered immediately prior to the second, fourth, sixth, eighth, and tenth minutes of each observation session. Activity scores are the number of fetal movements during the 1-min interval after stroking.)

Unlike the findings of Experiment 3b, in which fetuses were shown to distinguish a mint infusion as a function of prior experience, there appears to be nothing about the mint stimulus per se that produces this altered response to stroking. Without prior conditioning, presentation of mint does not alter fetal responses to stroking. This was demonstrated in an experiment in which fetuses were exposed to mint without associated LiCl on Day 17, then pretreated with either mint or saline prior to observation on Day 19. Fetuses pretreated with mint were as active after stroking as fetuses pretreated with saline. Both mint- and saline-pretreated fetuses showed the characteristic increase in responsiveness following repeated application of stroking (Figure 6). Thus the reduction of fetal activity after stroking, documented in Experiment 3b, is contingent on pretreatment with a conditioned mint stimulus. Only when mint was paired with LiCl on Day 17 was it found effective as a contextual cue, altering fetal responsiveness to tactile stimulation.

Experiment 4b: Chemical Infusion

Method

As in Experiment 4a, 20 mothers each provided 2 subject fetuses for study. All fetuses were exposed to mint and ip LiCl on Day 17. In order to manipulate olfactory context prior to testing on Day 19, fetuses from 10 mothers were pretreated with mint, and the others were pretreated with saline. Two minutes after pretreatment, after delivery into the bath, each subject fetus was implanted with an intraoral cannula. Within each mother, one fetus received infusions of lemon at 2-min intervals during the 10-min session, and the other received infusions of saline. Activity difference scores were calculated for each of the pretreatment conditions by subtracting the activity of the saline-infused fetus from that of its lemon-infused littermate. This measure of net responsiveness to lemon infusion was calculated for the 1-min intervals after each infusion. Data for saline- and mint-pretreated fetuses were compared with a series of Mann-Whitney *U* tests.

Results and Discussion

Fetal responsiveness to lemon infusion, like responses to stroking, was influenced by olfactory context (Figure 7). All fetuses were activated by lemon infusion (i.e., net response to lemon infusion was positive for both pretreatments across all five infusions). Pretreatment with saline resulted in the typical waning response to repeated lemon infusion reported in Experiments 2b and 2c. However, pretreatment with the conditioned mint stimulus resulted in an altered pattern of responsiveness, with fetuses exhibiting less response to lemon after the first infusion ($p < .05$) and more response after the fourth infusion ($p < .05$). Thus it appeared that the response of mint-pretreated fetuses to lemon did not wane over the course of the observation. The lack of a waning response may help interpret the pattern of fetal activity described in Experiment 2c. Specifically, it may be taken as evidence that diminished activation in response to lemon infusion is not due to receptor fatigue (which should occur regardless of pretreatment) but is likely due to some other process, such as selective attention or habituation. Whatever this process may

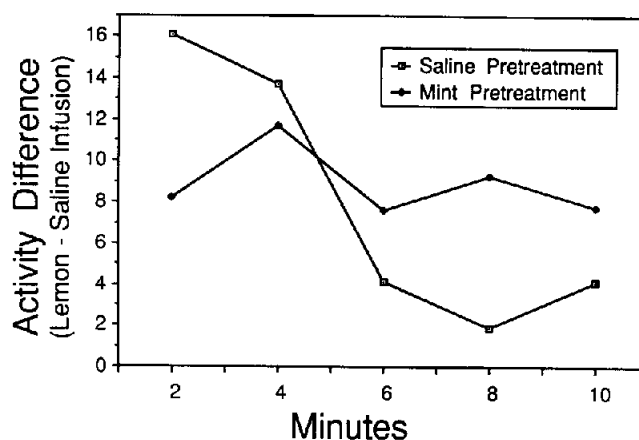


Figure 7. Differential response of rat fetuses to intraoral infusions of lemon following pretreatment with saline or conditioned mint. (Each point represents the mean activity difference between lemon-infused and saline-infused fetuses. Infusions were delivered immediately prior to the second, fourth, sixth, eighth, and tenth minutes of each observation session. Activity scores are the number of fetal movements during the 1-min interval after infusion.)

be, it is influenced by the olfactory context present immediately before testing.

The principal finding of Experiments 4a and 4b is that fetal responsiveness to stimulation is modified by olfactory context. When the fetus is briefly reexposed to a conditioned chemical stimulus (mint), its subsequent responsiveness to other forms of stimulation, whether tactile stroking or lemon infusion, is modified. The effects of pretreatment with a conditioned stimulus are robust: They are manifest in spontaneous activity (Smotherman & Robinson, 1985) and in evoked activity involving different stimulus modalities, mechanical and chemical, and persist for at least as long as our testing procedure can detect (10–15 min).

General Discussion

The experiments reported in this study provide definitive evidence that rat fetuses are sensitive to external stimulation before birth. The findings of Experiment 1 confirm earlier reports in which fetuses were found to respond to tactile stimulation (see Smotherman & Robinson, in press, for a review). The data from Experiment 2 extend the general conclusion of fetal responsiveness to include at least one other mode of stimulation: chemical infusion. Fetal responses to chemical stimuli change with repeated infusions, both within the span of a single observation session and after a delay of 2 days. Short-term effects of experience are evident in the waning fetal response to repeated infusion of lemon over a 10-min period (Experiment 2c). More lasting experiential effects are evident following manipulation on Day 17 of gestation and testing 2 days later. On Day 19 fetal responses to novel and familiar mint differ. Mint infusion increases fetal activity, but fetuses exposed to mint for the first time exhibit a brief suppression in movement before becoming more active

(Experiment 3). Reexposing a fetus to a chemical stimulus experienced earlier in gestation alters its responsiveness to tactile and other chemical stimulation. The effect of repeated applications of stroking is reversed, suppressing fetal activity, whereas the typical waning response to repeated infusions of lemon is eliminated (Experiment 4).

Fetal sensory responsiveness is complex, exhibiting stimulus specificity and little or no cross-modal generality in the pattern of response. Fetal responses to the tactile and chemical stimuli employed in this study, for example, are qualitatively different. Infusion of lemon or mint is a more potent behavioral activator than stroking, consistently eliciting very high rates of fetal movement. There is also a close temporal association of fetal response with the moment of chemical infusion, consisting of a rapid rise and fall in activity, a pattern that is absent with tactile stroking. Over a series of applications, the activational effects of stroking appear to summate; after fetuses are stroked for the second time, their activity remains elevated during both pre- and poststroking intervals. In contrast, fetal activity returns to near baseline levels after each infusion of lemon or mint, and the magnitude of successive activity peaks diminishes with repeated presentation. The lack of correspondence between fetal responses to stroking and infusion is suggestive that fetuses process information from the tactile/kinesthetic modality differently than from olfactory or gustatory receptors. Comparison of a greater variety of tactile and chemical stimuli is necessary to clearly evaluate this possibility.

The chemical stimuli employed in this study (lemon and mint) are complex, containing both odor and taste components. Therefore, these experiments do not specifically exclude olfactory or gustatory mechanisms in the transduction of chemical stimuli. For several reasons, however, we anticipate that olfaction is important in fetal chemical responsiveness. Indirect evidence obtained from 2-deoxyglucose autoradiographic neural mapping suggests that the accessory olfactory bulb (AOB) is functional in near-term rat fetuses whereas the main olfactory bulb is probably not (Pedersen et al., 1983). The AOB is responsible for processing information from the vomeronasal organ, which can be entered and directly stimulated by chemical cues presented in a liquid medium (Takagi, 1981). Involvement of the vomeronasal system, or perhaps the main olfactory system, thus appears the most likely mechanism of fetal chemoreception. The primacy of olfaction in fetal chemical responsiveness is consistent with unpublished experiments we have conducted (Smotherman, 1986). Infusions of solutions lacking clear olfactory components (sucrose and quinine hydrochloride) do not activate fetal behavior, but a solution lacking clear gustatory components (lemonlike citral) is sufficient to elicit a spiked pattern of fetal response nearly identical to that elicited by lemon. We are currently exploring the role of fetal olfaction through experiments employing transection of olfactory pathways in the brain.

Regardless of how chemical information is obtained by the rat fetus, it is subjected to central processing before its translation into behavior response. At the most basic level, fetal responses change with repeated presentation of the same stimulus. The waning responsiveness of fetuses exposed to a

series of lemon infusions is consistent with the potentially toxic effects of lemon, peripheral fatigue of receptors, or a central attentional process such as habituation. The recovery of response after a 5-min delay argues that lemon is not toxic and does not impair the fetus's ability to move. Moreover, the hypothesis of receptor fatigue is incompatible with the lack of waning responsiveness to repeated lemon infusion after pretreatment with conditioned mint. Therefore, the waning response to lemon is probably due to a short-term experiential process, such as habituation (Jeffrey & Cohen, 1971; Thompson & Spencer, 1966). This interpretation is consistent with evidence for habituationlike effects in human fetuses (Leader, Baillie, Martin, & Vermeulen, 1982).

The ability of rat fetuses to discriminate between novel and familiar chemical cues is further evidence that fetuses are sensitive to changes in their intrauterine environment and can modify their behavior as a result of prior experience in utero (Smotherman, 1982b; Smotherman & Robinson, 1985; Stickrod, Kimble, & Smotherman, 1982a, 1982b). The behavioral suppression seen during novel mint infusion also bears on the associative abilities of the rat fetus. In adult animals, hesitation or delayed response is just one of a collection of responses to the appearance of novel stimuli, the orientation reflex (OR), which includes reorientation of head and sensory organs toward the source of stimulation, adjustment of posture, heart rate deceleration, peripheral vasoconstriction, increased skin conductance, and changes in the electroencephalogram (Rohrbaugh, 1984; Sokolov, 1960). The characteristic reduction in movement by rat fetuses after novel stimulation suggests that some features of the OR may be expressed before birth.

Although rat fetuses exhibit distinct responses to stroking and chemical infusion, at some level there is evident integration of sensory information obtained through different modalities. A contextual stimulus (conditioned mint) presented prior to observation alters subsequent responses of fetuses to repeated stroking or lemon infusion. Variation in responsiveness of fetal rats to the same stimulus also has been anecdotally noted in an earlier study of tactile stimulation (Narayanan et al., 1971). Contingent responses of this sort resemble some of the defining characteristics of behavioral states in the fetus (Nijhuis, Precht, Martin, & Bots, 1982). The alteration in response is persistent (lasting at least 10 min) and expressed simultaneously in more than one behavioral variable (response to stroking and lemon). It is plausible, therefore, that reexposure to a conditioned mint stimulus induces a change of behavioral state in the rat fetus. The existence of statelike phenomena in fetal rats argues that sensory responsiveness and fetal behavior is the consequence of central coordination of selective attention and sensorimotor control. These findings support the emerging view that rat fetuses are responsive to environmental conditions within the uterus and exhibit considerable behavioral and sensory competence during the prenatal period (Smotherman & Robinson, 1987, in press).

Although extrapolation of the chemical abilities of the rat fetus to humans may seem premature, recent discoveries about the olfactory competence of the human neonate suggest that chemosensation may be well developed in the human fetus as well (Cernoch & Porter, 1985; Macfarlane, 1975).

Anatomical evidence indicates that functional chemoreceptors may be present as early as 7–9 wk gestational age, and behavioral evidence from preterm infants has documented taste discrimination at 6–7 mo gestational age (Mistretta & Bradley, 1986). The behavior of the human fetus, like that of other mammalian species, shows diversity early in gestation and near term becomes temporally organized as the fetus exhibits short-period and circadian rhythmicity (Nijhuis et al., 1983; Robertson, 1985; Robertson, Dierker, Sorokin, & Rosen, 1982; Serman & Hoppenbrouwers, 1971). Humans exhibit movement at a relatively early point in gestation (as early as 8 wk) and are capable of interacting with their intrauterine environment for a long period of prenatal development (deVries et al., 1982). Because it is important for the fetus to perceive and interact with its intrauterine environment (Smotherman & Robinson, 1987, in press), the ability of the fetus to utilize information gained through experience, as this study suggests, may show comparable levels of development and sophistication in the period before birth.

References

- Angulo y Gonzalez, A. W. (1932). The prenatal development of behavior in the albino rat. *Journal of Comparative Neurology*, 55, 395–442.
- Barcroft, J., & Barron, D. H. (1939). The development of behavior in foetal sheep. *Journal of Comparative Neurology*, 70, 477–502.
- Bekoff, A., & Lau, B. (1980). Interlimb coordination in 20-day-old rat fetuses. *Journal of Experimental Zoology*, 214, 173–175.
- Blass, E. M., & Pedersen, P. E. (1980). Surgical manipulation of the uterine environment of rat fetuses. *Physiology and Behavior*, 25, 993–995.
- Carmichael, L. (1934). An experimental study in the prenatal guinea pig of the origin and development of reflexes and patterns of behavior in relation to the stimulation of specific receptor areas during the period of active fetal life. *Genetic Psychology Monographs*, 16, 337–491.
- Cernoch, J. M., & Porter, R. H. (1985). Recognition of maternal axillary odors by infants. *Child Development*, 56, 1593–1598.
- Coghill, G. E. (1929). *Anatomy and the problem of behavior*. New York: Cambridge University Press.
- deVries, J. I. P., Visser, G. H. A., & Prechtel, H. F. R. (1982). The emergence of fetal behavior: I. Qualitative aspects. *Early Human Development*, 7, 301–322.
- Garcia, J., Lasiter, P. A., Bermudez-Ratoni, F., & Deems, D. A. (1985). A general theory of aversion learning. In N. S. Braveman & P. Bronstein (Eds.), *Experimental assessments and clinical applications of conditioned food aversions* (Annals of the New York Academy of Sciences, Vol. 443, pp. 8–21). New York: New York Academy of Sciences.
- Hall, W. G., & Rosenblatt, J. S. (1977). Suckling behavior and intake control in the developing rat pup. *Journal of Comparative and Physiological Psychology*, 91, 1232–1247.
- Hamburger, V. (1963). Some aspects of the embryology of behavior. *Quarterly Review of Biology*, 38, 342–365.
- Jeffrey, W. E., & Cohen, L. B. (1971). Habituation in the human infant. In H. W. Reese (Ed.), *Advances in child development and behavior* (Vol. 6, pp. 63–97). New York: Academic Press.
- Johanson, I. B., & Hall, W. G. (1979). Appetitive learning in 1-day-old rat pups. *Science*, 205, 419–421.
- Kehoe, P., & Blass, E. M. (1985). Gustatory determinants of suckling in albino rats 5–20 days of age. *Developmental Psychobiology*, 18, 67–82.
- Leader, L. R., Baillie, P., Martin, B., & Vermeulen, E. (1982). The assessment and significance of habituation to a repeated stimulus by the human fetus. *Early Human Development*, 7, 211–219.
- Macfarlane, A. (1975). Olfaction in the development of social preferences in the human neonate. In *Parent-infant interaction* (Ciba Foundation Symposium, Vol. 33, pp. 103–113). New York: Elsevier.
- Mistretta, C. M., & Bradley, R. M. (1986). Development of the sense of taste. In E. M. Blass (Ed.), *Handbook of behavioral neurobiology: Vol. 8. Developmental psychobiology and developmental neurobiology* (pp. 205–236). New York: Plenum Press.
- Narayanan, C. H., Fox, M. W., & Hamburger, V. (1971). Prenatal development of spontaneous and evoked activity in the rat. *Behaviour*, 40, 100–134.
- Nijhuis, J. G., Martin, C. B., Jr., Gommers, S., Bouws, P., Bots, R. S. G. M., & Jongsma, H. W. (1983). The rhythmicity of fetal breathing varies with behavioural state in the human fetus. *Early Human Development*, 9, 1–7.
- Nijhuis, J. G., Prechtel, H. F. R., Martin, C. B., Jr., & Bots, R. S. G. M. (1982). Are there behavioural states in the human fetus? *Early Human Development*, 6, 177–195.
- Pedersen, P. E., & Blass, E. M. (1981). Olfactory control over suckling in albino rats. In R. N. Aslin, J. R. Alberts, & M. R. Peterson (Eds.), *The development of perception: Psychobiological processes* (pp. 359–381). Hillsdale, NJ: Erlbaum.
- Pedersen, P. E., & Blass, E. M. (1982). Prenatal and postnatal determinants of the 1st suckling episode in albino rats. *Developmental Psychobiology*, 15, 349–355.
- Pedersen, P. E., Stewart, W. B., Greer, C. A., & Shepherd, G. M. (1983). Evidence for olfactory function in utero. *Science*, 221, 478–480.
- Robertson, S. S. (1985). Cyclic motor activity in the human fetus after midgestation. *Developmental Psychobiology*, 18, 411–419.
- Robertson, S. S., Dierker, L. J., Sorokin, Y., & Rosen, M. G. (1982). Human fetal movement: Spontaneous oscillations near one cycle per minute. *Science*, 218, 1327–1330.
- Robinson, S. R., & Smotherman, W. P. (1987). Environmental determinants of behaviour in the rat fetus: II. The emergence of synchronous movement. *Animal Behaviour*, 35, 1652–1662.
- Rohrbaugh, J. W. (1984). The orienting reflex: Performance and central nervous system manifestations. In R. Pavauramam & D. R. Davies (Eds.), *Varieties of attention* (pp. 323–373). New York: Academic Press.
- Smotherman, W. P. (1982a). In utero chemosensory experience alters taste preferences and corticosterone responsiveness. *Behavioral and Neural Biology*, 36, 61–68.
- Smotherman, W. P. (1982b). Odor aversion learning by the rat fetus. *Physiology and Behavior*, 29, 769–771.
- Smotherman, W. P. (1986). [Fetal responsiveness to olfactory stimuli]. Unpublished raw data.
- Smotherman, W. P., Richards, L. S., & Robinson, S. R. (1984). Techniques for observing fetal behavior in utero: A comparison of chemomyelotomy and spinal transection. *Developmental Psychobiology*, 17, 661–674.
- Smotherman, W. P., & Robinson, S. R. (1985). The rat fetus in its environment: Behavioral adjustments to novel, familiar, aversive and conditioned stimuli presented in utero. *Behavioral Neuroscience*, 99, 521–530.
- Smotherman, W. P., & Robinson, S. R. (1986). Environmental determinants of behaviour in the rat fetus. *Animal Behaviour*, 37, 1859–1873.
- Smotherman, W. P., & Robinson, S. R. (1987). Psychobiology of fetal experience in the rat. In N. A. Krasnegor, E. M. Blass, M. A. Hofer, & W. P. Smotherman (Eds.), *Perinatal development: A*

- psychobiological perspective* (pp. 39–60). New York: Academic Press.
- Smotherman, W. P., & Robinson, S. R. (in press). The uterus as environment: The ecology of fetal behavior. In E. M. Blass (Ed.), *Handbook of behavioral neurobiology: Vol. 9. Developmental psychobiology and behavioral ecology*. New York: Plenum Press.
- Sokolov, E. N. (1960). Neuronal models and the orienting reflex. In M. A. B. Brazier (Ed.), *The central nervous system and behavior* (pp. 187–276). New York: Macy Foundation.
- Sterman, M. B., & Hoppenbrouwers, T. (1971). The development of sleep-waking and rest-activity patterns from fetus to adult in man. In D. J. McGinty & A. M. Adinolfi (Eds.), *Brain development and behavior* (pp. 203–227). New York: Academic Press.
- Stickrod, G. (1981). In utero injection of rat fetuses. *Physiology and Behavior*, 27, 557–558.
- Stickrod, G., Kimble, D. P., & Smotherman, W. P. (1982a). In utero taste/odor aversion conditioning in the rat. *Physiology and Behavior*, 28, 5–7.
- Stickrod, G., Kimble, D. P., & Smotherman, W. P. (1982b). Met-5-enkephalin effects on associations formed in-utero. *Peptides*, 3, 881–883.
- Takagi, S. F. (1981). Multiple olfactory pathways in mammals: A review. *Chemical Senses*, 6, 329–333.
- Thompson, R. F., & Spencer, W. A. (1966). Habituation: A model phenomenon for the study of neuronal substrates of behavior. *Psychological Review*, 73, 16–43.
- Windle, W. F., & Griffin, A. M. (1931). Observations on embryonic and fetal movements of the cat. *Journal of Comparative Neurology*, 52, 149–188.

Received July 28, 1986

Revision received November 6, 1986

Accepted November 21, 1986 ■

Call for Nominations for the Editor of *JEP: General*

The Publications and Communications Board has opened nominations for the editorship of the *Journal of Experimental Psychology: General* for the years 1990–1995. Sam Glucksberg is the incumbent editor. Candidates must be members of APA and should be available to start receiving manuscripts in early 1989 to prepare for issues published in 1990. Please note that the P&C Board encourages more participation by women and ethnic minority men and women in the publication process, and would particularly welcome such nominees. To nominate candidates, prepare a statement of one page or less in support of each candidate. Submit nominations no later than February 15 1988 to

Donald J. Foss
 Department of Psychology
 University of Texas
 Austin, Texas 78712

Other members of the search committee are James J. Jenkins, Jean Mandler, J.E.R. Staddon, and Saul Sternberg.
