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Pharmacological Manipulation of Milk-Induced Behaviors in Three-Day-Old Rat Pups

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CAZA, P A AND L P SPEAR *Pharmacological manipulation of milk-induced behaviors in three-day-old rat pups* PHARMAC BIOCHEM BEHAV **16**(3) 481–486, 1982 —The effects of a variety of pharmacological agents on the ingestive and behavioral activating responses to intraoral milk infusion were investigated in three-day-old Sprague-Dawley rat pups Results indicated that the ingestive component—typified by a mouthing response—was primarily influenced by serotonergic agents Mouthing behavior was increased following administration of the serotonergic agonist, quipazine, and decreased following the serotonergic antagonists, methysergide and methiothepin In contrast, the behavioral activating component was not found to be clearly influenced by drugs affecting any one neurotransmitter system, suggesting the tentative hypothesis that this activating response to milk infusion may in part be modulated by interactions between several neurotransmitter systems

Developmental psychopharmacology Sprague-Dawley rat pups Intraoral milk infusions Mouthing Behavioral activation Propranolol Phentolamine Quipazine Methysergide Methiothepin Scopolamine

INTRAORAL infusions of milk induce both ingestive and behavioral activating responses in neonatal rat pups maintained in a warm environment [7,8] The ingestive component is typified by a mouthing action, i e , movement of the mouth and jaws while the activating response is characterized by a variety of behaviors such as forelimb paddling, hindlimb treading, rolling, curling and forward locomotion These behaviors are observed when pups as young as one day postnatally receive milk infusions in a warm environment, although such responses are rarely observed in animals this young not given diet infusions (i e , [7]) Both the ingestive and activating behaviors induced by milk infusions are exaggerated following food and maternal deprivation For example, three-day-old pups exhibit greater responses following 24 hours of deprivation than after one or seven hours [8]

Neuroanatomical data suggest that the systems underlying milk-induced ingestive and activating responses may be separable Knife-cuts transecting diencephalic brain regions markedly reduce the ingestive component of the behavioral sequence following milk infusions while leaving the activating responses relatively undisturbed, more caudal mesencephalic transections disrupt the activating responses but not the ingestive mouthing response [13] Cellular dehydration has also been shown to differentially affect these two components, increasing mouthing but with no significant influence on the activation response [3] No additional physiological or pharmacological separation of these behaviors has been reported

The neurochemical mediation of another type of feeding-related response in the developing rat, suckling, has been investigated It appears that the suckling response may be, at least in part, under serotonergic control In rat pups beginning at 15 days postnatally methysergide, a serotonergic antagonist, induces suckling behavior, quipazine, a serotonergic agonist, has been shown to inhibit suckling in rat pups beginning at 10 days of age [17,27] In neonatal rat pups, the reverse pattern of pharmacologic modification has been observed Serotonergic antagonists, such as methiothepin, metergoline and methysergide, and the anticholinergic agent, scopolamine, have been shown to markedly reduce suckling in three-day-old rat pups [22] Thus it appears that both serotonergic and cholinergic influences on the suckling response exist

Although it has been suggested that the milk-induced ingestive response reflects a feeding system separable from suckling behavior [8,9], these two systems may share some commonalities as well For example, with milk-cannulation using Hall's posterior placement technique, deprivation has been shown to have little influence on intake in neonatal and infant rat pups [8], deprivation has likewise been shown to have little influence on suckling behavior in rat pups during the first week or two of life (see [2] for a review) Use of an anterior placement of the cannula for milk-induced ingestion

experiments, however, results in a deprivation-dependent effect on intake throughout the postnatal period [8]

Psychopharmacological approaches may provide a useful means for assessing the possible similarities and differences in the neurotransmitter system modulation of these two forms of ingestion While serotonergic and cholinergic antagonists have been shown to disrupt suckling in neonates, their effects on independent ingestion using the milk-cannulation technique have not been investigated It has been shown, however, in a non-ingestion experiment, that the serotonergic agonist, quipazine, induces an increase in mouthing behavior in neonatal rat pups that was dependent on the length of the deprivation period away from the mother [23]

In order to begin to assess the psychopharmacological characteristics of behaviors induced by the milk-cannulation technique, the present experiment investigated the possible roles of serotonergic and cholinergic systems in the modulation of milk-induced ingestive and behavioral activating responses in three-day-old rat pups In addition, α- and β-noradrenergic influences on these responses were also examined since the noradrenergic system appears to be functional in the early neonatal period [11], and has been implicated in behavioral arousal (e g , [12]) and deprivation alterations in locomotor activity [4,15] in adult animals

In the present study, receptor antagonists were used to examine the role of these neurotransmitter systems in modulating milk-induced behaviors Receptor antagonists, when compared with receptor agonists or indirect-acting agonists and antagonists, may provide a particularly useful tool for the psychopharmacological assessment of the functional activity of a neurotransmitter system during ontogeny For example, responses elicited by a neurotransmitter receptor agonist, while indicative that functional receptors exist for that neurotransmitter, are not necessarily indicative of the presence of functional presynaptic components In addition, failure to obtain behavioral responses with an indirect-acting agonist or antagonist may indicate either (1) that although the neruotransmitter system may actually be functional, certain presynaptic components of the neurotransmitter system affected by the drug have not attained functional maturity or (2) that the neurotransmitter system itself is nonfunctional However, use of receptor antagonists should provide an index of the functional significance of the neurotransmitter system, since blocking the receptors of a nonfunctional neurotransmitter system presumably would be without observable effect Neurochemically, from the available data it appears that postsynaptic neurotransmitter receptors not only are capable of binding antagonists and agonists throughout the postnatal period, but that they retain their pharmacological specificity with age Neurotransmitter receptor binding experiments frequently use neurotransmitter antagonists or agonists as ligands and have shown that specific ligand binding to the receptors for the common putative neurotransmitter systems is evident in the early postnatal period (e g , [1, 10, 14, 16]) Moreover, it appears that increases in the amount of binding of ligands with these receptors with age are characterized by an increase in the number of receptors without an alteration in their affinity (e g , [1, 10, 14, 16]), or in the ability of other agonists and antagonists to competitively displace the ligands from the receptors (e g , [1]) Thus, in the present experiment, several receptor antagonists affecting different neurotransmitter systems were examined for their influences upon milk-induced mouthing and behavioral activation in this initial work beginning to assess the role of specific neurotransmitter systems in the modulation of these age-specific behavior patterns

METHOD

Subjects

Two hundred and sixty-one (261) three-day-old male and female Sprague-Dawley derived rat pups bred at SUNY-Binghamton were used for this investigation All pups were housed with their parents and conspecifics in standard maternity cages and maintained on a 16 hr light/8 hr dark illumination cycle (light onset at 0600 hrs) The day of parturition was designated as postnatal Day 0 Litters were culled to 10 pups within 24 hrs of birth Litters containing fewer than seven pups were not used On postnatal Day 2, all pups were removed from their parents and placed with conspecifics in a holding incubator maintained at 33±1°C Testing began 24 hrs after the initiation of the deprivation procedure

Apparatus

For testing, pups were individually placed in 500 ml glass beakers located inside a humidity-controlled incubator (Leahy Manufacturing Company), maintained at 33±1°C and illuminated for testing by a 25 W light bulb in a 24 cm diameter reflector that was placed inside the incubator Intraoral infusion tubing was attached to a 23 gauge needle fitted on a 1 ml syringe, and consisted of approximately 10 cm of PE 10 polyethylene tubing (Clay Adams) and approximately three feet of PE 20 tubing jointed together by a 25 gauge needle The tubing was passed through a small access aperture located in the front of the incubator door Milk was delivered intraorally through the tubing by an infusion pump (Sage Instruments, Model 341) situated outside the incubator A rectal probe (YSI series, 500, Model number 511) was used to measure the pup s internal temperature

Procedure

Testing procedures developed by Hall [8] were used in the experiment Approximately one hour prior to testing, all pups were weighed to the nearest 0 01 g, and implanted with oral cannulas (PE 20 polyethylene tubing) in the back of their mouths using the posterior placement procedure outlined by Hall [8] This placement essentially forces subjects to ingest any milk delivered, and was chosen for use so that differential effects of the drugs on mouthing and activation could be examined With the anterior placement, milk that is not actively ingested by mouthing will not be consumed, hence, drugs affecting mouthing would also affect milk consumption and thus might influence the magnitude of the activation response

Fifteen minutes prior to testing, the pups to be tested received a subcutaneous injection of one of five drugs utilized in each study, and were replaced into the holding incubator For Study A, the drug doses were 10 mg/kg and 20 mg/kg of the serotonergic antagonist, methysergide maleate (Sandoz, Inc), 8 mg/kg and 16 mg/kg of the β-adrenergic antagonist, propranolol hydrochloride (Sigma) and 0 9% physiological saline In Study B, 1 0 mg/kg and 2 5 mg/kg of the serotonergic agonist, quipazine maleate (Miles Laboratories), 3 0 mg/kg and 15 0 mg/kg of the α-adrenergic antagonist, phentolamine hydrochloride (CIBA) and saline were used Saline, 2 5 mg/kg and 10 mg/kg of the serotoner-

gic antagonist, methiothepin (Hoffman-LaRoche) and 2 0 mg/kg and 8 0 mg/kg of the cholinergic antagonist, scopolamine hydrobromide (Sigma) were tested in Study C All drugs were mixed on the day of administration and were injected in a volume of 5 cc/kg Following injection, pups were assigned to milk- or no milk-infusion conditions, thus in each study one pup from each litter was randomly placed in one of the 10 treatment conditions (2 Milk × 5 Drug Doses) At least eight animals were tested under each drug and infusion (milk or no-milk) condition in each of the three studies

Two pups (one no-milk and one milk-infusion) were tested simultaneously in adjacent testing chambers Immediately prior to testing, each subject's oral cannula was connected to the infusion tubing and the pup was placed in the testing chamber Subjects assigned to the milk-infusion condition received a 10 sec spurt of approximately 0 04 cc of milk (warm Half-n-Half dairy cream) every 60 sec Thus, the total volume of milk delivered to infused pups during the 10 min test period was approximately 0 4 cc Throughout the 10 min test, behavioral time-sampling data were collected at 20 sec intervals (see [21], for details of the time-sampling procedure) At each of the 30 sampling periods, the emitted behaviors of each of the two pups were observed and individually recorded Behavioral categories included roll, curl, hindlimb treading, forelimb paddling, grooming, mouthing, forward locomotion and lying still Internal body temperature was measured immediately after testing as any body temperature changes induced by the drugs could influence the vigor and/or the frequency of the behaviors examined All testing was conducted between 1100 and 1400 hrs

RESULTS

Internal body temperature, the total amount of mouthing and total activity were chosen as dependent measures for analysis Since preliminary examination of the data indicated that the various activity measures were highly correlated with each other, a composite total activity score was determined for each pup by summing the total number of paddling, treading, rolling and forward locomotion behaviors exhibited during the 10 min testing period The amount of stationary or lying still behavior was a mirror-image of the total activity displayed by a subject and therefore will not be discussed The other behaviors observed, grooming and curling, occurred so infrequently that statistical analyses could not be performed using these measures

Data from the saline-injected subjects were collapsed across the three studies to form a pooled control group Each of the six drugs assessed—propranolol, quipazine, methysergide, methiothepin, phentolamine and scopolamine—was compared separately with the saline control groups Thus, for each dependent measure, a 2 (Milk Condition) × 3 (Drug Dose) ANOVA was calculated for each of the six drugs Duncan's Multiple Comparison Tests were used for post-hoc comparisons Significance levels were established at an $\alpha=0\ 05$ To facilitate discussion of the drug actions, the three dependent measures, i e , mouthing, total activity and internal body temperature, will be discussed separately

Mouthing

It is evident from examination of Fig 1 that pups receiving infusions of milk exhibited significantly more mouthing behavior than those not receiving the infusions Moreover, mouthing behavior was influenced by drugs acting upon the

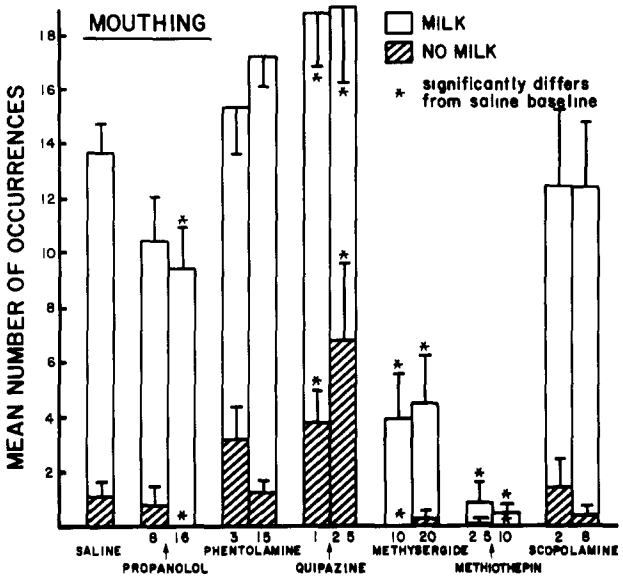

FIG 1 Mean number of occurrences of mouthing behavior in milk- and no milk-infused 5-day-old pups following various drug injections

serotonergic system Both doses of the serotonergic agonist, quipazine, elevating mouthing in infused as well as non-infused pups, $F(2,77)=7\ 69$, $p<0\ 001$ Conversely, the serotonergic antagonists, methiothepin and methysergide, depressed this behavior, $F(2,76)=39\ 44$, $p<0\ 001$ and $F(2,76)=15\ 62$, $p<0\ 001$, respectively However, this depression was greater for the subjects given milk infusions than for those receiving no milk (Milk × Drug Dose interactions $F(2,76)=5\ 15$, $p<0\ 01$ and $F(2,76)=10\ 87$, $p<0\ 001$ for each of the two drugs, respectively) These interactions are probably the result of a low baseline incidence of mouthing behavior in non-infused pups and may not reflect any differential selectivity of these antagonists on milk-induced mouthing The only other drug which influenced mouthing in these studies was the 16 mg/kg dose of the β-adrenergic antagonist, propranolol This dose decreased mouthing behavior for both infused and non-infused subjects, $F(2,78)=4\ 45$, $p<0\ 05$ A lower dose of this same drug, 8 mg/kg, had no effect on mouthing The other drugs administered the α-adrenergic antagonist, phentolamine, and the anticholinergic drug, scopolamine, did not significantly modify the mouthing behavior of either milk-infused or non-infused pups Thus, pharmacological modification of the ingestive mouthing response appears to be relatively confined to those agents affecting the serotonergic system

Total Activity

As can be seen in Fig 2, milk infusion induced a significant increase in the amount of total activity displayed by the pups After administration of the 16 mg/kg dose of propranolol, a significant increase in total activity was evident in both milk- and non-milk-infusion pups, $F(2,77)=4\ 93$, $p<0\ 01$ Pups receiving the lower (8 mg/kg) dose of this drug, although not significantly different from saline control animals, exhibited total activity scores intermediate to pups

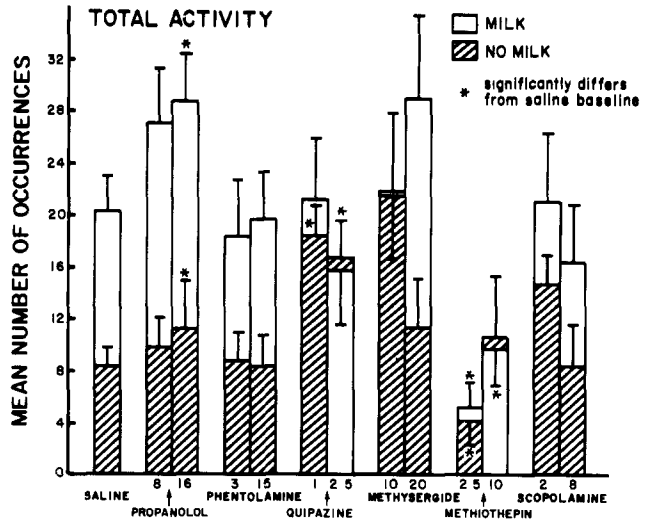

FIG 2 Mean number of occurrences of activity (sum of paddling, treading, forward locomotion, and rolling behaviors) in milk- and no milk-infused 3-day-old pups following various drug injections

TABLE 1

MEAN INTERNAL BODY TEMPERATURES (°C)
(MEANS/STANDARD ERROR OF MEAN)

Drug	Milk-Infused	No Milk-Infused
Saline	30 36/0 36	30 80/0 26
Propranolol 8 mg/kg	29 62/0 82	30 10/0 38
16 mg/kg	30 18/0 39	30 30/0 21
Phentolamine 3mg/kg	30 54/0 38	30 10/0 31
15 mg/kg	30 88/0 38	31 04/0 24
Quipazine 1 0 mg/kg	30 47/0 31	30 89/0 49
2 5 mg/kg	30 66/0 32	30 69/0 32
Methysergide 10 mg/kg	28 90/0 45	30 59/0 31
20 mg/kg	29 48/0 34	29 76/0 27
Methiothepin 2 5 mg/kg	30 96/0 36	31 57/0 49
10 mg/kg	30 71/0 71	31 60/0 46
Scopolamine 2 mg/kg	32 28/0 22	31 57/0 29
8 mg/kg	31 83/0 50	31 78/0 38

injected with the 16 mg/kg dose and those injected with saline Quipazine also elevated total activity, however, this elevation was only evident in non-infused subjects (Milk × Drug Dose interaction $F(2,76)=3\ 09$, $p<0\ 05$ Methiothepin depressed total activity and this effect was greater in infused relative to non-infused pups (Milk × Drug Dose interaction, $F(2,76)=3\ 81$, $p<0\ 05$) Given that the other serotonergic antagonist, methysergide, did not influence total activity and that quipazine and methiothepin have been shown to influence catecholaminergic systems as well as the serotonergic system (i e , [5,6]), it is difficult to interpret the influence of these particular drugs on total activity as indicative of a serotonergic modulation of this behavior The other drugs used, the α-noradrenergic agonist, phentolamine, and the anticholinergic agent, scopolamine, did not significantly effect total activity

Internal Body Temperature

Table 1 lists the mean internal body temperature of infused and non-infused pups following drug administration and testing Only two of the drugs affected this measure There was a significant effect of drug for scopolamine and methysergide with no significant Drug × Milk interaction in either case Scopolamine significantly elevated body temperature, $F(2,59)=4\ 40$, $p<0\ 05$, while body temperature was depressed after methysergide, $F(2,74)=9\ 08$, $p<0\ 001$ As neither of these drugs influenced activity, and no consistent relationship between drug-induced body temperature and mouthing changes is apparent, pharamcological modulation of milk-induced behavioral responses does not appear to be related to an alteration in body temperature

DISCUSSION

The results of the present study suggest that the ingestive and behavioral activating components of the milk-induced response can be separated pharmacologically, as well as neuroanatomically as was previously reported The ingestive component, mouthing, seems to be sensitive to serotonergic modulation The serotonergic receptor antagonists, methysergide and methiothepin, depressed mouthing, conversely the serotonergic agonist, quipazine, increased the occurrence of this behavior The behavioral activating responses induced by milk infusions were influenced by the β-adrenergic antagonist, propranolol, as well as by two drugs affecting the serotonergic system, quipazine and methiothepin

The pharmacological modification of the mouthing response in this experiment is similar to that reported for suckling behavior in three-day-old rats [23] In that investigation, it was reported that three different serotonergic antagonists, including both methysergide and methiothepin, markedly reduced the suckling behavior of three-day-old pups Thus, it appears that the serotonergic system may be involved in modulating both of these two feeding-related behaviors These two forms of ingestion have also been reported to be similar in terms of ingestive control Hall observed that deprivation had little influence on the intake of neonatal and infant rat pups in milk-cannulation experiments in which posterior cannula placements were used [8] A similar lack of influence of deprivation is also seen when examining suckling behavior in rat pups during the first week or two of life (e g , [2]) Thus, both psychopharmacological evidence and evidence with respect to intake control suggest that these two forms of feeding-related behaviors may share some similarities in terms of neural mediation

This suggestion, however, must be tempered by the lack of effect of the anticholinergic drug, scopolamine, on mouthing behavior in the present experiment In the Spear and Ristine [23] study, scopolamine was reported to be effective in reducing suckling of three-day-old rat pups The subjects in the Spear and Ristine [23] experiment, however, were not deprived at the time of testing whereas the subjects in the present investigation had been separated from their mother, and hence food, for 24 hrs prior to testing Spear and Ristine [23] have hypothesized that both a serotonergic and a cholinergic control of suckling exists and that these two systems are differentially affected by food deprivation The serotonergic system may exert a greater influence when the pup is food deprived since levels of this neurotransmitter

drastically increase in the deprived neonatal rat [25,26] Therefore, the observed discrepancy concerning the effect of scopolamine on modifying the mouthing response in the present experiment and the suckling response in the study of Spear and Ristine [23] could merely be related to differences in the deprivational state of the pup, rather than reflecting a differential cholinergic involvement in these two types of oral behavior

Although mouthing behavior was predominantly influenced by serotonergic manipulation, it was also reduced by the 16 mg/kg dose of the β-adrenergic antagonist, propranolol Conversely, at this dose, total activity was elevated The lower dose of this drug (8 mg/kg) had no significant effect on mouthing or on total activity Spear and Ristine [23] also reported a similar dose-dependent effect on propranolol on suckling behavior, although 16 mg/kg of propranolol significantly reduced suckling, higher and lower doses were without effect

Pharmacological modulation of the milk-induced behavioral activation is difficult to interpret Although α-noradrenergic agonists such as clonidine induce hyperactivity in rat pups younger than 20 days of age [18, 20, 21], blocking the α-noradrenergic system with phentolamine in the present experiment had no effect on the milk-induced behavioral activation Indeed, the only neurotransmitter antagonist that was observed to decrease milk-induced behavioral activation was methiothepin This finding is consistent with previous observations that methiothepin produces behavioral depression in rat pups [23] Since this sedating effect of methiothepin has not been observed after administration of other serotonergic antagonists to neonates (see [23], also the present study), it seems improbable that this effect of methiothepin is serotonergically mediated Methiothepin, however, has been reported to block dopaminergic and noradrenergic receptors to some extent as well as serotonergic receptors [5] Thus, it is possible that the sedating effects of methiothepin are a result of general monoaminergic blockade Perhaps more than one neurotransmitter system is involved in modulating behavioral activation in the neonate According to this hypothesis, pharmacological manipulation of a single neurotransmitter system may be ineffective in reducing behavioral activation because of substrate redundancy in the neurotransmitter systems mediating this response Such substrate redundancy might be expected if the activation response is critical to the survival of the neonate Indeed, a recent finding by Pederson and associates [19] illustrates the potential importance of activation to the neonatal pup They demonstrated that young pups can learn to attach to the mother's nipple when a nonbiologic odor is painted on the nipple, if and only if the pup was previously behaviorally activated (by stroking or amphetamine injection) in the presence of this odor This suggestion of redundant neurochemical controls of behavioral activation in neonates is most conjectural and needs to be substantiated by further experimentation

Two of the drugs used in this experiment, propranolol and quipazine, were observed to increase total activity The serotonergic agonist, quipazine, increased baseline, but not milk-induced, behavioral activation responses, whereas the β-adrenergic antagonist, propranolol, increased these responses in both milk-infused and non-infused pups Quipazine has previously been shown to induce behavioral activation and mouthing in neonates [22] Since the latter response, but not the former is affected by maternal deprivation, these two quipazine induced responses may be mediated by drug-induced interactions with different neurotransmitter systems Quipazine, although primarily a serotonergic agonist, has also been reported to interact with the noradrenergic system as well [6] Perhaps quipazine-induced mouthing is mediated by interaction with serotonergic systems while quipazine-induced activation is a function of the drug's interaction with noradrenergic systems In the present experiment, the β-noradrenergic antagonist, propranolol, at a dose of 16 mg/kg, elevated total activity The β-adrenergic system has been proposed to be primarily inhibitory in nature in adult animals [24] These results suggest that the β-adrenergic system may be functioning in an adult-typical inhibitory fashion very early in postnatal life Indeed the noradrenergic systems previously have been suggested to be functional even in neonatal rat pups [11]

The results of the present experiment suggest that the two components of the pup's response to milk infusions may be modulated by separable neurotransmitter systems As a preliminary hypothesis, we propose that the ingestive mouthing response may be primarily serotonergically-mediated while the milk-induced behavioral activating response may in part be modulated by interactions between several neurotransmitter systems, including the noradrenergic system Clearly, more work is needed to characterize neurotransmitter systems or subsystems that are involved in influencing these age-specific behaviors of neonates Different drugs as well as ontogenetic characterizations of drug-induced responses need to be examined The induction of behaviors by milk-infusion appears to be one useful model system for such investigations

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REFERENCES

1 Ben-Barak, J and Y Dudai Cholinergic binding sites in rat hippocampal formation Properties and ontogenesis *Brain Res* **166** 245–247, 1979

2 Blass, E M , W G Hall and M Teichner The ontogeny of suckling and ingestive behaviors In *Progress in Psychobiology and Physiological Psychology* vol 8, edited by J M Sprague and A N Epstein New York Academic Press, 1979

3 Bruno, J P The ontogeny of thirst systems in rats Unpublished doctoral dissertation, the Johns Hopkins University, Baltimore, MD, 1979

4 Campbell, B A and H C Fibiger Potentiation of amphetamine-induced arousal by starvation *Nature* **233** 424–425, 1971

5 Fuller, R W Pharmacology of central serotonin neurons *A Rev Pharmac Toxicol* **20** 111–127, 1980

6 Francès, H , Y Lecrubier, A J Puech and P Simon Evidence for the role of noradrenaline in some effects of quipazine *Psychopharmacology* **67** 307–310, 1980
7 Hall, W G Feeding and behavioral activation in infant rats *Science* **205** 206–209, 1979
8 Hall, W G The ontogeny of feeding in rats I Ingestive and behavioral responses to oral infusions *J comp physiol Psychol* **93** 977–1000, 1979
9 Hall, W G and T E Bryan The ontogeny of feeding in rats II Independent ingestive behavior *J comp physiol Psychol* **94** 746–756 1980
10 Harden, T K , B B Wolfe, J R Sporn, J P Perkins and P B Molinoff Ontogeny of β-adrenergic receptors in rat cerebral cortex *Brain Res* **125** 99–108, 1977
11 Kellogg, C and P Lundborg Ontogenetic variation in responses to L-DOPA and monoamine receptor stimulating agents *Psychopharmacology* **23** 187–200, 1972
12 Kety, S S The biogenic amines in the central nervous system Their possible roles in arousal, emotion, and learning In *The Neurosciences Second Study Program* edited by F O Schmitt New York Rockefeller University Press, 1970
13 Kornblith, C L and W G Hall Brain transections selectively alter ingestion and behavioral activation in neonatal rats *J comp physiol Psychol* **93** 1109–1117, 1979
14 Morris, M J , J P Dausse, M -R Devynck and P Meyer Ontogeny of α_1- and a_2-adrenoceptors in rat brain In *Biogenic Amines in Development,* edited by H Parvez and S Parvez Amsterdam Elsevier/North Holland Biomedical Press, 1980
15 Murphy, J M and Z M Nagy FLA-63 blocks food deprivation-induced behavioral arousal in the mouse *Physiol Psychol* **7** 407–411, 1979
16 Nelson, D L , A Herbet, J Adrien, J Bochaert and M Hamon Serotonin-sensitive adenylate cyclase and [^{3}H] serotonin binding sites in the CNS of the rat—II Respective regional and subcellular distributions and ontogenetic developments *Biochem Pharmac* **29** 2455–2463, 1980
17 Nock, B , C L Williams and W G Hall Suckling behavior of the infant rat Modulation by a developing neurotransmitter system *Pharmac Biochem Behav* **8** 277–280, 1978
18 Nomura, Y The locomotor effect of clonidine and its interaction with α-flupenthixol or haloperidol in the developing rat *Naunyn-Schmiedeberg s Arch Pharmac* **313** 33–37, 1980
19 Pederson, P E , P J Kinsley and C L Williams Activation produced by various forms of stimulation contributes to olfactory learning in young pups Paper presented at annual meeting of Eastern Psychological Association, New York, 1981
20 Reinstein, D K and R L Isaacson Clonidine sensitivity in the developing rat *Brain Res* **135** 378–383, 1977
21 Spear, L P and J Brick Cocaine-induced behavior in the developing rat *Behav Neural Biol* **26** 401–415, 1979
22 Spear, L P and L A Ristine Quipazine-induced behavior in neonatal rat pups *Pharmac Biochem Behav* **14** 831–834 1981
23 Spear, L P and L A Ristine Suckling behavior in neonatal rats Psychopharmacological investigations *J comp physiol Psychol* in press, 1982
24 Szabadi, E Adrenoreceptors on central nervous system neurons Microelectrophoretic studies *Neuropharmacology* **18** 831–843, 1979
25 Tissari, A H Pharmacological and ultrastructural maturation of serotonergic synapses during ontogeny *Med Biol* **53** 1–14 1975
26 Tissari, A H and I T Tikkanen Maturation of the responses of brain 5-hydroxytryptamine turnover, plasma nonesterified fatty acids and corticosterone to stress during ontogeny In *Maturation of Neurotransmission* (satellite symposium 6th meeting of the International Society of Neurochemistry Sainte-Vincent) Basel Karger, 1978
27 Williams, C L , J S Rosenblatt and W G Hall Inhibition of suckling in weaning-age rats A possible serotonergic mechanism *J comp physiol Psychol* **93** 414–429 1979