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BEHAVIORAL AND NEUROCHEMICAL EFFECTS OF PSYCHOTOMIMETIC DRUGS IN NEONATE CHICKS

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The effects of various psychoactive drugs on the behavior and brain neurochemistry of neonate chicks were examined. d-Amphetamine, l-amphetamine, p-hydroxyamphetamine, and l-dopa all elicited a similar behavioral excitement. Mescaline and 2,5-dimethoxy-4-methylamphetamine (DOM) caused opisthotonic postures. Cocaine and p-methoxyamphetamine induced some features of both groups and cocaine also elicited convulsions. Norepinephrine and dopamine produced sedation.

All agents inducing opisthotonos elevated brain norepinephrine. d-Amphetamine and l-dopa reduced serotonin while norepinephrine, dopamine and DOM all elevated serotonin. Dopa doubled the brain dopamine levels while norepinephrine reduced them.

Paradoxes in the data are discussed.

Amphetamines
2,5-Dimethoxy-4-methylamphetamine
Mescaline
Cocaine
Chick behavior
Neurochemistry

1. INTRODUCTION

Stereotyped behavior has been described in various mammalian species following the administration of certain central nervous system (CNS) stimulants (Randrup and Munkvad, 1967, 1968; Willner et al., 1970; Wallach and Gershon, 1971).

A close similarity exists among the drugs which elicit paranoid psychoses in man and stereotyped behavior in cats and dogs. The use of stereotyped behavior as a model for these paranoid psychoses has been suggested (Randrup and Munkvad, 1968; Wallach and Gershon, 1971; Wallach et al., 1971).

Pharmacological studies of stereotyped behavior in rats and dogs have suggested a dopaminergic mechanism (Randrup and Munkvad, 1968; Willner et al., 1970; Wallach et al., 1971). This mechanism should be sensitive to inhibitors of catecholamine metabolism. In order to further examine the mechanism of stereotyped behavior, an attempt was made to define a stereotyped behavior in the chick. A characteristic behavior of chicks following amphetamine administration has previously been reported (Selle, 1940; Clymer and Seifter, 1947; Dewhurst and Marley, 1965; Spooner and Winters, 1966; Marley and Morse, 1967; Rauzzino and Seifter, 1967). Since the neonate chick lacks an effective blood brain barrier, it would be an ideal model in which to study the induction of stereotyped behavior utilizing these agents. The responses of the chick to various CNS stimulants and other psychotomimetic and neurohumoral agents were examined. It was necessary to define a behavior which might be classified as stereotyped behavior; therefore, various parameters of the chick behavior were examined following administration of several compounds. The drugs were selected to include agents which produce stereotyped behavior in other animals and paranoid psychosis in man. Compounds

which induce perceptual distortions in man, and compounds which are related to or are proposed neurohumoral transmitters were included for comparison. An attempt was made to differentiate between the various agents or classes of agents based on changes in the behavior of the chick following the administration of these agents.

2. MATERIALS AND METHODS

2.1. *Behavioral observations*

Neonate, white leghorn unsexed chicks were placed in groups of 4 in plexiglass cages (28 cm X 16.5 cm) following i.p. injection of the drug to be tested. Observations were made every 10 min for 100 min. The posture and activities of the chick were observed and recorded at each observation. These were then summed for each parameter over the 10 observation periods and scores were compared to saline-treated controls utilizing the same age chick for comparison. Parameters observed included posture of the body, head, and wings, eyelid position, and activities including pecking and locomotion. Inasmuch as chick behavior tends to vary over age (see below), and since a tremendous quantity of data was generated by the studies, only a summary of the pertinent changes is presented for 1- and 3-day old chicks. The experiments represent a minimum of 2 cages of 4 animals each for 5 days, i.e., 10 cages of 4 animals or 40 chicks during the ages of 1 – 5 days for each dosage level of each drug.

Agents studied included d-amphetamine sulfate, l-amphetamine sulfate, p-hydroxyamphetamine hydrobromide, p-methoxyamphetamine hydrochloride, 2,5-dimethoxy-4-methylamphetamine (DOM), cocaine hydrochloride, mescaline sulfate, dopamine hydrochloride, l-dihydroxyphenylalanine (l-Dopa) and norepinephrine bitartrate. All the agents were dissolved in normal saline except l-dopa which was dissolved in hydrochloric acid and diluted with 1% ascorbic acid in NaOH solution to partially neutralize the excess acid. All doses are reported as the salts of the drug.

Photography of chicks utilized individually housed chicks and a telephoto lens to enable the camera and the photographer to be a reasonable distance from the chick in order to minimize the disruptive influences. These chicks were not included in the behavioral tabulations.

2.2. *Neurochemistry*

3-day old chicks were sacrificed by decapitation at 20 or 30 min following drug administration. The brains were pooled for each sample and homogenized in cold 0.4 N $HClO_4$. The extract was utilized for the estimation of serotonin, norepinephrine and dopamine. The serotonin was extracted into n-butanol from one third of the perchloric acid extract and assayed according to the method of Snyder et al. (1965). The catecholamines in the remaining $HClO_4$ extract were adsorbed onto alumina at pH 8.6 and eluted with 0.2 N HCl. The norepinephrine and dopamine were estimated fluorometrically by the methods of Anton and Sayre (1962, 1964). Fluorescence was measured on an Aminco–Bowman Spectrophotofluorometer.

3. RESULTS

3.1. *Behavioral observations*

Certain changes in the behavior of the chick occurred with maturation. During this period the number of observations of standing decreased, while those of lying prone increased. Eyelids were closed more often and there was a decrease in aggressive pecking and locomotion (table 1, fig. 1: 1, 2).

Table 1
Summary of behavioral changes with maturation in chicks treated with saline.

	Chick age in days					
	1	2	3	4	5	p**
Standing	35*	31	30	25	19	< 0.001
Prone	0	0	2	10	14	< 0.001
Eyelid open	24	13	14	18	19	< 0.05
Pecking others	13	7	6	5	6	< 0.05
Walking	11	6	7	6	6	< 0.05

Crouching can be determined by subtracting the sum of standing and prone from 40.

* Maximum score is 40.

** Results were analyzed by analysis of variance.

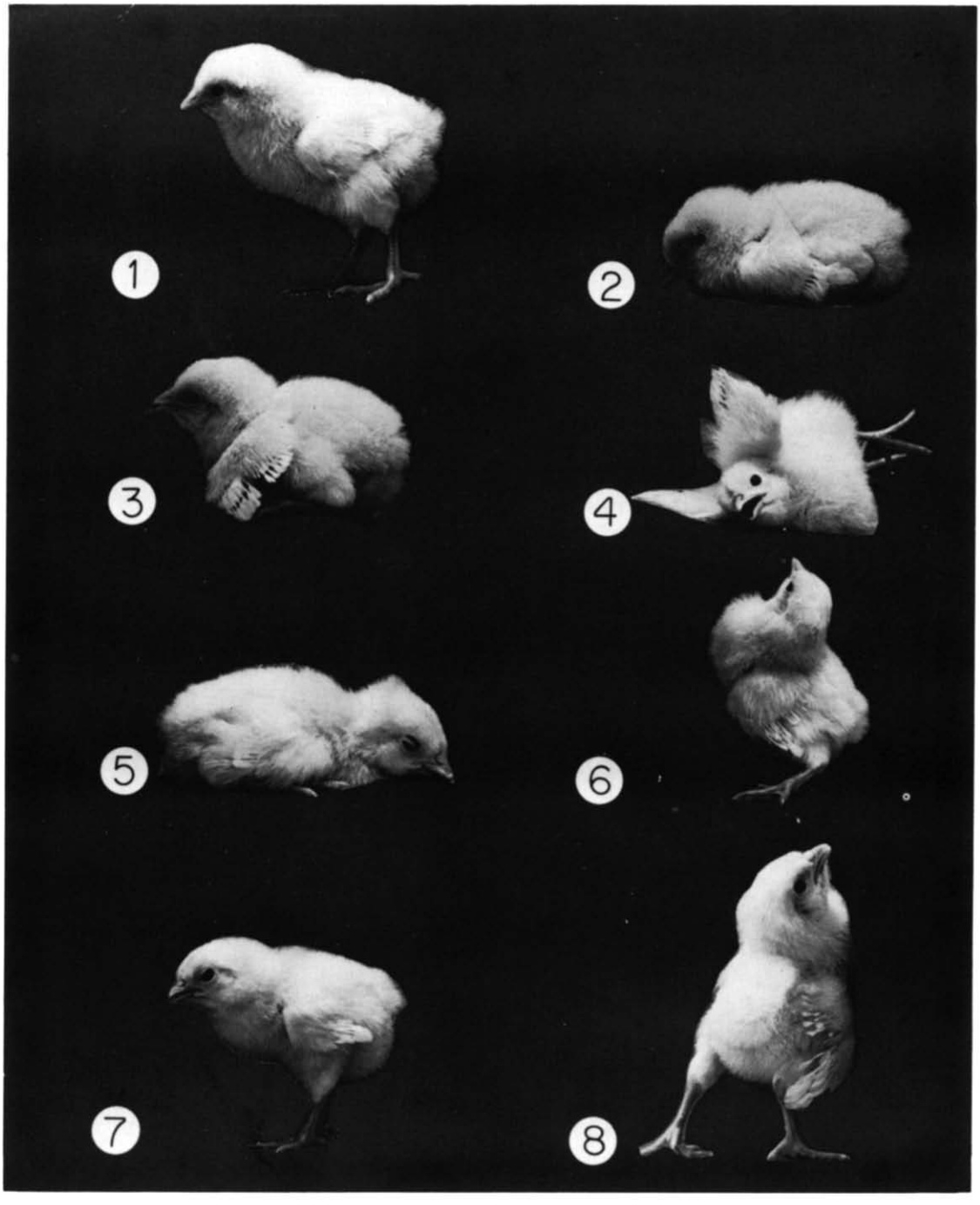

Fig. 1. Typical postures of chicks following drug administration. 1 and 2, saline; 3, d-amphetamine, 15 mg/kg; 4, cocaine, 32 mg/kg; 5, norepinephrine, 200 mg/kg; 6, mescaline, 100 mg/kg; 7, dopamine, 500 mg/kg; and 8, DOM, 20 mg/kg. See text for details.

Table 2
Summary of behavioral changes on 1-day old chicks following drug administration.

Drug	Dose	Posture		Wings		Opisthotonos	Eyes	Pecking		Locomotion
	(mg/kg)	Standing	Prone	Relaxed	Flapping		open	Cage	Others	
Saline	–	35	0	0	0	0	24	15	13	12
d-Amphetamine	4	31	1	3	1	0	33	4*	30*	22*
	8	18*	13*	27*	12*	0	39*	3*	22*	16*
	10	8*	21*	38*	12*	0	40*	4*	13	19*
	15	2*	34*	39*	22*	0	40*	3*	3*	26*
l-Amphetamine	4	39	0	0	0	0	38*	10	16	20*
	8	39	0	0	0	0	35*	23	20	30*
	16	39	0	1	0	0	40*	19	27*	29*
	32	24*	3*	26*	8*	0	40*	16	24*	22*
	64	4*	29*	39*	20*	0	34*	3*	3*	24*
p-Hydroxyamphetamine	32	32	1	14*	1	0	34*	12	8*	12
	64	26*	7*	33*	15*	0	40*	13	10	21*
p-Methoxyamphetamine	8	13*	11*	40*	8*	0	40*	4*	8	13
	16	0*	37*	40*	19*	0	40*	0*	4*	16
	32	0*	40*	40*	17*	0	38*	0*	2*	18
Cocaine	8	39	0	1	0	0	35*	21	20*	25*
	16	39	0	0	0	0	32*	17	13	16
	32	26	2**	14***	5	1	28	10	10	27*
	50	9*	6**	17***	6*	5	16	3*	2*	10
Mescaline	60	34	0	6	0	11*	22	13	8*	9
	80	20*	2	9*	0	17*	13*	4*	3*	9
	100	21*	4*	17*	0	27*	6*	2*	1*	8
l-Dopa	100	34	0	12***	3	1*	34*	13	6*	10
	200	28	3	23*	8***	2*	36*	11	6*	16
	500	24	6*	40*	18*	7*	28	8	4*	19*
Dopamine	50	36	0	0	0	0	22	15	9	7
	100	36	0	0	0	0	26	13	15	8
	150	38	0	0	0	0	20	9	9	7
	500	34	0	1	0	0	21	3*	1*	2*
Norepinephrine	10	21*	5*	6	0	0	10*	4*	2*	6
	50	4*	29*	13*	0	0	8*	1*	3*	5
	100	1*	26*	15*	0	0	7*	2*	3*	4*
	200	0*	37*	36*	0	0	2*	1*	0*	1*

Crouching can be determined by subtracting the sum of standing and prone from 40 (for all drugs except cocaine).

* $p < 0.005$.
** Clonic opisthotonic convulsions also occurred.
*** Not significant due to high variability.

Table 3
Summary of behavioral changes on 3-day old chicks following drug administration.

Drug	Dose	Posture		Wings		Opisthotonos	Eyes	Pecking		Locomotion
	(mg/kg)	Standing	Prone	Relaxed	Flapping		open	Cage	Others	
Saline	–	30	2	0	0	0	14	9	6	7
d-Amphetamine	4	36	0	7	0	0	35*	11	19*	20*
	8	25	5	23*	0	0	39*	7	11*	14
	10	26	8	28*	4*	0	36*	7	6	18*
	15	2*	29*	40*	12*	0	39*	1*	1*	19*
l-Amphetamine	4	37	1	0	0	0	34*	11	6	12
	8	35	0	0	0	0	36*	20*	13*	23*
	16	32	0	0	0	0	39*	18	16*	23*
	32	34	0	17*	6*	0	40*	18	19*	25*
	64	20	18**	38*	8*	0	30*	3*	4	13
p-Hydroxyamphetamine	16	37	0	8	0	0	24	7	6	3
	32	32	0	9*	0	0	14	4*	4	4
	64	30	1	31*	3	0	33*	10	10	22*
p-Methoxyamphetamine	8	8*	20*	36*	7*	0	34*	5	6	13
	16	9*	18*	40*	7*	0	38*	4*	3	11
	32	1*	39*	40*	10*	0	35*	2*	1*	13
Cocaine	8	40	0	0	0	0	38*	25*	25*	35*
	16	40	0	0	1	0	36*	21*	16*	23*
	32	34	1**	9	0	0	20	11	7	25*
	50	19	1**	20*	2	10*	26	9	4	17*
Mescaline	60	27	2	2	0	23*	13	8	2*	5
	80	26	1	5	0	23*	13	3*	3*	4
	100	17*	3	20*	0	32*	11	1*	0	2
l-Dopa	100	33	0	0	1	2	35	14*	3*	9
	200	29	0	22*	8*	3	36	9	3***	16*
	500	29	3	34*	18*	1	29	9	3*	30*
Dopamine	50	33	3	0	0	0	15	7	4	7
	100	28	5	0	0	0	15	6	5	6
	150	22	4	0	0	0	15	2*	5	2
	500	30	2	0	0	0	13	4*	1*	1*
Norepinephrine	10	20	3	0	0	0	12	2*	3	3
	40	4*	33*	25*	0	0	1*	1*	1*	1*
	100	0*	37*	36*	0	0	1*	0*	0*	0*
	200	0*	36*	34*	0	0	1*	0*	0*	2

Crouching can be determined by subtracting the sum of standing and prone from 40 (for all drugs exept cocaine).

* $p < 0.05$.
** Clonic opisthotonic convulsions also occurred.
*** Not significant due to high variability.

Table 4
Summary of behavioral changes on 1- and 3-day old chicks following DOM.*

Drug	Dose (mg/kg)	Posture		Wings		Opistho-tonos	Eyes Open	Pecking		Loco-motion
		Standing	Prone	Relaxed	Flapping			Cage	Others	
1-Day old chicks										
Saline	–	39	0	0	0	0	34	3	2	10
DOM	5	25**	0	1	0	13**	38	0	1	1
	10	16**	6**	8**	2**	9**	33	0	0	6
	20	13**	11**	15**	8**	12**	31	0	0	11
3-Day old chicks										
Saline	–	37	0	0	0	0	31	0	1	6
DOM	5	29	1	0	0	10**	35	0	0	2
	10	24**	4	8**	0	14**	34	0	0	0
	20	14**	11**	12**	0	14**	27	0	0	1

Crouching can be determined by subtracting the sum of standing and prone from 40.

* These chicks were rated by a different rater and consequently were compared to this rater's saline observations.
** $p < 0.05$.

The results of the behavioral studies on 1- and 3-day old chicks, representative of the entire 5 day period, are presented in tables 2–4. Three classes of compounds were identified. One group was characterized by the amphetamines; this group included d- and l-amphetamine, p-hydroxyamphetamine, l-dopa, to some extent, cocaine, and p-methoxyamphetamine.

Following low doses of these agents, there was an increase in alertness, observed as an increase in the number of observations of open eyelids, locomotion, and a more erect posture. There was also an increase in the amount of pecking following d- and l-amphetamine and cocaine. At higher doses, a change in posture, from standing to prone, was associated with a relaxing or dropping of the wings and occasional periods of wing-flapping and ataxic locomotion (fig. 1: 3). Cocaine, 32–50 mg/kg, induced a convulsant state characterized by clonicity and opisthotonos which often caused chicks to lie on their sides (fig. 1: 4). Although the chicks ultimately survived, these doses were already in the toxic range.

The primary differences between the behavioral responses of 1- and 3-day old chicks to the CNS stimulants are reflections of maturational changes. The number of observations of standing, aggressive pecking, and locomotion decreased in saline treated chicks (table 1), thereby making drug effects less evident. The sensitivity of the chicks to some of the drug effects also decreased with maturity. For example, prone posture following d-amphetamine appeared at about 8 mg/kg in 1-day old chicks and at 15 mg/kg in 3-day old chicks. The postural effects of p-hydroxyamphetamine are almost eliminated by day 3.

A second class of compounds was characterized by mescaline and DOM. Mescaline and DOM produced a decrease in the number of observations of standing, an increase in the occurrences of crouching, relaxation of the wings and opisthotonos (fig. 1: 6 and 8). In addition, mescaline caused increased eyelid closure and DOM elicited chirping.

Very few differences were observed with this group between 1- and 3-day old chicks. The older chicks tended to close their eyes less frequently following mescaline, and there were no observations of wing flapping in older chicks after DOM. p-Methoxyamphetamine exhibited some characteristics of this group also. No increase in locomotion was observed, and pecking was decreased; however, opisthotonos was not observed.

Dopamine in high dosage elicited decreases in pecking and locomotion. These chicks appeared to be slightly sedated (fig. 1: 7). Norepinephrine at doses of

Table 5
Relative changes in brain serotonin (5-HT), norepinephrine (NE) and dopamine (DM) levels following drug administration.

Drug	Dose (mg/kg)	Time (min)	Percent of control ± S.E.M.		
			5-HT	NE	DM
Saline	–	20	100.0 ± 7.3	100.0 ± 18.4	100.0 ± 27.5
d-Amphetamine	15	20	81.6 ± 4.1**	155.1 ± 23.0	63.1 ± 18.7
p-Methoxyamphetamine	32	20	86.9 ± 5.5	70.5 ± 4.3	90.3 ± 21.6
p-Hydroxyamphetamine	64	20	95.6 ± 5.6	72.2 ± 7.7	81.7 ± 12.9

* Each value represents 7 determinations. Saline treated chick brain amine levels were: 5-HT: 0.21 μg/g; NE: 0.28 μg/g; DM: 0.28 μg/g.
** $p < 0.05$ from saline group.

Table 6
Relative changes in brain amine levels following l-dopa.

Drug	Dose (mg/kg)	Time (min)	Percent of control ± S.E.M.*		
			5-HT	NE	DM
Ascorbic acid	10	30	100.0 ± 3.4	100.0 ± 11.9	100.0 ± 11.7
l-Dopa in ascorbic acid	200				
	10	30	76.7 ± 0.4**	81.4 ± 16.8	192.7 ± 10.9**

* Each group represents 8 determinations. Ascorbic acid-treated chick brain amine levels were: 5-HT: 0.20 μg/g; NE: 0.30 μg/g; DM: 0.32 μg/g.
** $p < 0.005$ from ascorbic acid control group.

Table 7
Relative changes in brain amine levels following catecholamine administration.

Drug	Dose (mg/kg)	Time (min)	Percent of control ± S.E.M.*		
			5-HT	NE	DM
Saline	–	30	100.0 ± 10.0	100.0 ± 9.3	100.0 ± 7.8
Dopamine	500	30	158.9 ± 9.2**	86.2 ± 10.7	88.1 ± 7.4
Norepinephrine	200	30	167.7 ± 9.9***	88.4 ± 7.5	74.9 ± 3.7

* Each group represents 7 determinations. Saline treated chick brain amine levels were: 5-HT: 0.22 μg/g; NE: 0.34 μg/g; DM: 0.39 μg/g.
** $p < 0.02$ from saline group.
*** $p < 0.005$ from saline group.

10 mg/kg or higher induced sedation associated with a typical sleep posture including crouching or a prone position, wing drop, eyelid closure and decrease in locomotion and pecking (fig. 1: 5). The younger chicks were more sensitive to the effects of norepinephrine than were the older chicks.

3.2. *Neurochemistry*

The neurochemical data were obtained from 3-day old chick brains and are presented in tables 5–8. Each table represents a separate experiment with its own control.

A significant decrease in serotonin levels was pro-

Table 8
Relative changes in brain amine levels following drug administration.

Drug	Dose (mg/kg)	Time (min)	Percent of control ± S.E.M.*		
			5-HT	NE	DM
Saline	–	30	100.0 ± 4.6	100.0 ± 21.1	100.0 ± 19.4
DOM	20	30	113.2 ± 3.3**	498.1 ± 7.1****	90.7 ± 8.7
Mescaline	100	30	104.4 ± 5.2	241.4 ± 15.0***	72.4 ± 9.0
Cocaine	32	30	102.2 ± 6.1	206.0 ± 6.2***	81.8 ± 13.1

* Each group represents 7 determinations. Saline treated chick brain amine levels were: 5-HT: 0.34 μg/g; NE: 0.34 μg/g; DM: 0.32 μg/g.
** $p < 0.05$ from saline group.
*** $p < 0.005$ from saline group.
**** $p < 0.001$ from saline group.

duced by both d-amphetamine, 15 mg/kg, and l-dopa, 200 mg/kg (tables 5 and 6). A similar change was not produced by p-hydroxyamphetamine, 64 mg/kg, and p-methoxyamphetamine, 32 mg/kg. l-Dopa also elicited a significant increase of brain dopamine but not of brain norepinephrine.

Administration of dopamine, 500 mg/kg, and norepinephrine, 200 mg/kg, elicited an increased level of serotonin without altering norepinephrine levels. Norepinephrine also decreased dopamine levels (table 7).

4. DISCUSSION

Several groups of drugs were differentiated from the behavioral observations described. The CNS excitants, d- and l-amphetamine, p-hydroxyamphetamine, p-methoxyamphetamine and l-dopa produced a characteristic excitement associated with an increase in alertness as exemplified by a more erect posture and of open eyelids followed by a prone position, wing dropping and flapping. Mescaline and DOM produced opisthotonos, wing dropping and decreased pecking. Norepinephrine, and to a slight extent, dopamine, produced sedation.

This classification agrees with the previous observations of Wallach and Gershon (1971). The amphetamines, l-dopa and cocaine produced a paranoid psychosis in man and stereotypy with a desynchronization of the electro-encephalogram in cats (Wallach and Gershon, 1971). Mescaline and LSD primarily produced a perceptual distortion in man and a hypersynchronous electro-encephalogram in cats (Winters et al., 1969). DOM, an amphetamine derivative, elicited a hypersynchronous electro-encephalogram and behavioral changes which would classify it in the same group of psychotomimetic agents as LSD and mescaline (Wallach et al., in preparation). In the current study, cocaine was not clearly classified. Cocaine elicited behavioral changes in posture, wing position, aggression, and locomotion similar to d- and l-amphetamine; however, at high dose, cocaine also elicited opisthotonos, wing drop, and decreased pecking, characteristics of the DOM and mescaline group. p-Methoxyamphetamine failed to increase locomotion or cause opisthotonos, but decreased pecking and postural changes are weakly suggestive of the mescaline and DOM group. Norepinephrine and dopamine both produced effects which would differentiate them from the other two classes of structurally related compounds.

These data suggest several paradoxes. Firstly, why did l-dopa elicit an amphetamine-like response while dopamine, the reputed active metabolite of l-dopa, did not produce this response? The ineffectiveness of dopamine in eliciting a clear behavioral change has also been observed by Marley and Stephenson (1970) with intrahypothalamic administration and Grunden and Marley (1970) with intraventricular administration; however, Key and Marley (1962) reported that dopamine was sedative to young chicks and Spooner and Winters (1965) observed a biphasic change from wakefulness to sleep. Hanig (1968) also observed this

paradoxical situation. Intravenously, l-dopa induced arousal followed by catatonia while dopamine elicited only catatonia. This paradox might be explained by (1) l-dopa acting directly and not through its metabolite dopamine; (2) l-dopa acting through some unknown metabolite of dopa as suggested by Sourkes (1971) and Sandler et al. (1971); (3) l-dopa may increase brain dopamine while dopamine, administered i.p., may not reach the brain in sufficient quantity to alter behavior. The neurochemical data lend credence to this hypothesis; (4) serotonin may be released by l-dopa as the brain levels of serotonin are reduced. Reduction in the levels of brain serotonin by l-dopa has been shown in chicks (Hanig and Seifter, 1971), in mice (Everett and Borcherding, 1970), and in rats (Butcher and Engel, 1969; Friedman and Gershon, in preparation).

A decrease in serotonin following d-amphetamine has previously been observed by Hanig (1968). This, coupled with the recent study by Schrold and Squires (1971) suggesting that p-chlorophenylalanine could block part of the amphetamine syndrome lends credence to this hypothesis. The failure of p-methoxyamphetamine and p-hydroxyamphetamine to elicit a similar change in the level of serotonin while producing similar behavioral changes, however, leaves this possible mechanism of action open to question.

Another unexpected result was that hydroxyamphetamine had a CNS stimulant action in chicks, whereas it is devoid of this action in mammals. Hydroxyamphetamine is reputedly devoid of the CNS stimulating effects of amphetamine in mammals (Innes and Nickerson, 1970). Recently, Lewander (1971) demonstrated that only a small fraction of a dose of hydroxyamphetamine enters the brain of rats. The absence of an effective blood–brain barrier in the neonate chick may allow this compound to produce an amphetamine-like response. Thus, it would appear that the reason p-hydroxyamphetamine lacks CNS stimulating effects is due to its relative inability to cross the mammalian blood brain barrier.

Cocaine, which in man and other mammals had an effect similar to that of amphetamine (Willner et al., 1970; Wallach and Gershon, 1971), appeared to be more toxic to the chick than would be expected from its relative potency as compared to amphetamine in other species. This compound produced a higher rate of deaths at the dose required for behavioral excitement than did the amphetamines. The deaths appeared to involve a central excitation characterized by the loss of the righting reflex, and an opisthotonic convulsion followed either by recovery or death.

Smythies et al. (1967) and Shulgin et al. (1969) have postulated that p-methoxyamphetamine is a hallucinogenic compound. This study presented evidence that p-methoxyamphetamine, at least in the chick, may belong to both the mescaline–DOM group and the amphetamine class of compounds. At present there is a paucity of data in other species and the studies in man are insufficient to resolve this question.

The ability of DOM, mescaline and cocaine to increase the levels of brain norepinephrine, without norepinephrine or l-dopa administration inducing the same opisthotonic response, suggest that if norepinephrine was involved, then DOM, mescaline and cocaine blocked its release. No evidence is available to support this hypothesis. The increase in the 5-HT level in chick brain following DOM has also been observed in rat brain (Freedman et al., 1970) and in cat brain (Wallach et al., in preparation).

In summary, amphetamines, p-methoxyamphetamine, p-hydroxyamphetamine and l-dopa elicited behavioral changes in the neonate chick which were characterized by opening of the eyelids, erect posture followed by a change to a prone posture, dropping of the wings, occasional periods of wing flapping, ataxic locomotion, and excitement. At lower doses, some of the drugs produce an increase in aggressive pecking. This group of behavioral symptoms might be a model similar to the stereotyped behavior observed in various mammalian species. The inability of cocaine to produce similar behavioral changes without opisthotonic convulsions would tend to reduce the effectiveness of this chick model. The characteristic opisthotonos of the chicks following DOM and mescaline might be a comparable model for the class of agents which induces perceptual distortions in man; however, cocaine also induced opisthotonos. Although definite differences could be determined between some of the compounds from each group, the overlap of the groups on pecking, locomotion and wing drop suggest that the chick is a poor model for differentiating these compounds.

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