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Use of the Catheterized Rat in Studies on Social Interactions and Plasma Catecholamines

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PASHKO, S., K. H. DeTURCK AND W. H. VOGEL. *Use of the catheterized rat in studies on social interactions and plasma catecholamines*. PHARMAC. BIOCHEM. BEHAV. 13(3) 471–473, 1980.—Catheterized rats were subjected to various social conditions and amphetamine treatment and plasma norepinephrine and epinephrine levels were measured. Normal interactions involving another male or female rat did not alter plasma catecholamine levels. Social interactions with a mouse or an amphetamine treated, hyperactive male rat had no effect on plasma epinephrine but increased norepinephrine levels significantly. A low dose of amphetamine given to the catheterized rat increased only plasma norepinephrine levels. The catheterized rat was found to be a very useful animal model for the study of social interactions and their effects on physiological processes as reflected in changes in certain blood chemicals.

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THE effects of social interactions on the behavior of animals have been extensively studied. In contrast, little attention has been paid to chemical changes caused by such social influences, as crowding, isolation, or aggression, although plasma and/or brain catecholamine levels can be markedly altered in response to changes in the social environment of animals [1–4, 7, 9].

The paucity of data can be partly explained by a lack of available methodology. Experimental procedures required the removal of the animal from the social situation and decapitation to excise tissues or restraint to obtain blood. In the first case the animal can be used only once, whereas the animal can be reused in the second case. However, the continuity of the study is then disturbed, and restraint stress influences the plasma levels of both NE and E [6]. An animal model has recently become available which allows for phlebotomy through a catheter and which is used in studies on stress and drug blood levels [5, 6, 8]. We have modified the existing model and have applied this model successfully in studies on the social interaction among rats.

Preparation of the rat has been described in detail [5,8]. Briefly, catheterization was done under pentobarbital anesthesia (42 mg/kg) using the jugular vein and a catheter of silastic tubing which was protected by a steel spring. The steel spring-catheter was supported by a swivel pulley allowing free movement of the animals in the experimental chamber (12×12 inches). Blood samplings and twice daily patency checks could thus be made.

Previous experiments in this laboratory had determined that catecholamine levels were "normal" one day after implantation of the catheter, but all experiments reported herein were performed at least two days after surgery. Drawing 5 samples totaling 1.5 ml of blood from the animals over a period of one hour was without significant effect on plasma catecholamine levels and blood hematocrit.

Animals were male Wistar rats weighing approximately 300 g and each animal was used in only one experiment. Animals were placed in the experimental chamber after surgery and received water and food ad lib. Experiments were started just before 1:00 p.m. by obtaining a blood sample of 0.25 ml from the catheterized rat (zero time). At 1:00 a second animal previously housed in a group of 4–5 and fed ad lib was placed in the experimental chamber until 1:30 p.m. Blood was obtained from the catheterized animal at 1:01, 1:05, 1:15, 1:30 and 2:00 p.m.

Plasma catecholamines, norepinephrine and epinephrine, were determined radioenzymatically (Cat-a-kit; Upjohn Co., Kalamazoo, MI). Statistical analysis of the plasma levels was performed using the paired *t*-test.

A second animal placed into the experimental chamber with the catheterized animal revealed that these animals paid no special attention to the catheter; they did not seem to be affected or disturbed and did not try to bite or gnaw at the steel spring.

Placement of a male (300 g) or female (250 g, diestrous) Wistar rat into the chamber produced no obvious behavioral changes in the catheterized rat. Social interactions appeared minimal and many of the catheterized animals kept resting and eating, or participated in mutual grooming and soon huddled together. As can be seen in Table 1, no changes in plasma norepinephrine or epinephrine were apparent.

Placement of a male mouse (28 g) in the chamber

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TABLE 1

PLASMA LEVELS OF NOREPINEPHRINE AND EPINEPHRINE IN CATHETERIZED RATS IN RESPONSE TO SOCIAL INTERACTIONS AND AMPHETAMINE

	Time (minutes)					
	0	1	5	15	30	60
Epinephrine						
1. Catheterized rat, alone (N=3)	198 ± 77	197 ± 42	197 ± 38	174 ± 68	190 ± 62	189 ± 58
2. Plus male rat (N=8)	217 ± 79	251 ± 74	261 ± 99	222 ± 56	242 ± 86	199 ± 66
3. Plus female rat (N=4)	138 ± 28	187 ± 18	278 ± 47	251 ± 45	243 ± 22	248 ± 48
4. Plus mouse (N=4)	187 ± 10	190 ± 13	177 ± 25	183 ± 23	201 ± 30	218 ± 26
5. Amphetamine (N=4)	205 ± 44	389 ± 91	452 ± 113	492 ± 166	366 ± 43	260 ± 63
6. Plus amphetamine-treated rat (N=5)	165 ± 23	226 ± 31	189 ± 26	194 ± 45	157 ± 24	173 ± 34
Norepinephrine						
1. Catheterized rat, alone (N=3)	250 ± 55	286 ± 37	275 ± 62	240 ± 54	209 ± 57	260 ± 108
2. Plus male rat (N=8)	320 ± 75	518 ± 38	463 ± 196	381 ± 69	399 ± 101	312 ± 80
3. Plus female rat (N=4)	237 ± 67	290 ± 42	345 ± 68	408 ± 56	302 ± 9	347 ± 27
4. Plus mouse (N=4)	218 ± 30	325 ± 41*	295 ± 43	371 ± 30*	357 ± 57	301 ± 51
5. Amphetamine (N=4)	254 ± 26	362 ± 81	642 ± 110*	481 ± 89*	416 ± 51	586 ± 156
6. Plus amphetamine-treated rat (N=5)	194 ± 43	543 ± 142†	523 ± 122*	429 ± 99*	425 ± 65*	418 ± 89

Plasma epinephrine and norepinephrine levels are given as averages ± SEM in pg/g of plasma.

Blood was drawn from the catheterized rat at the indicated times. Social interaction occurred between one and thirty minutes. Amphetamine was given to the catheterized rat (0.7 mg/kg IV) after the 0 minute drawing.

*Indicates a significant difference from 0 minute at $p<0.05$ and † indicates a significant difference from 0 minute at $p<0.01$ as measured using the paired t-test.

provoked some significant behavioral changes in the catheterized rat. In most cases, the rat permitted the mouse only a small amount of space before it would forcefully push it into a corner. At times, the animals would nip at each other. Epinephrine levels did not change significantly, but norepinephrine levels increased significantly ($p<0.05$) at 1 and 15 min, and correlated well with any increase in aggressive behavior observed during the confrontation.

The intravenous injection (through the catheter) of a small dose of amphetamine (0.7 mg/kg) into the catheterized rat produced some minor increase in locomotive activity shortly after injection. Increases in norepinephrine levels showed large variations and, thus, were not significant statistically. Increases in epinephrine were larger in this case, and approached statistical significance in spite of large variations. Placement of an amphetamine-treated, hyperactive rat (1 mg/kg, IP, 15 min before the experiment) with the untreated, catheterized rat, produced markedly increased motor activity in the latter, but no signs of overt aggression or territorial behavior. No significant increase in epinephrine levels was observed, although norepinephrine levels increased significantly ($p<0.05$) at 1, 5, 15 and 30 min despite large individual variations. For the most part, elevated NE levels corresponded to an overall increase in the motor activity of the catheterized animal.

In our hands, the catheterized rat proved to be an excellent model for the study of social interactions. The catheter allowed for the continuous sampling of blood during the entire experiment without interruption of social interactions and observations. A good correlation between behavioral excitement and norepinephrine levels was obtained. A male or female rat provoked no obvious behavioral changes in the catheterized rat and no marked changes in plasma norepinephrine and epinephrine levels were observed. Behavioral changes were produced by the presence of a mouse or an amphetamine-treated rat and norepinephrine levels increased significantly. Since plasma norepinephrine is mainly derived from the peripheral sympathetic nervous system and epinephrine from the adrenal medulla, the significant increases in norepinephrine, but not epinephrine, seem to indicate that the social interactions studied affected mostly the sympathetic nervous system. The observation that a rat responded differently to a "normal" and an amphetamine treated rat is rather interesting as it seems to indicate that a rat can distinguish between "normal" and drug-induced behavior of another animal.

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