

Rat Strain Differences in Brain Monoamine Metabolism Following Para-Chlorophenylalanine Treatment

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EMERY, D., J. ENGEL AND K. LARSSON. Rat strain differences in brain monoamines metabolism following para-chlorophenylalanine treatment. PHARMAC. BIOCHEM. BEHAV. 12(2) 311-312, 1980.—The effect of parachlorophenylalanine (PCPA) on 5-hydroxytryptamine (5-HT) was studied in sham-operated and castrated rats of two different rat strain. PCPA was more effective in depressing the brain 5-HT levels in Wistar (W) rats than in Sprague Dawley (SD) rats.

Strain differences Male rats Parachlorophenylalanine 5-Hydroxytryptamine Dopamine
Brain monoamines

WE [4] recently reported that the potentiation of masculine sexual behavior in castrated male rats following parachlorophenylalanine (PCPA) treatment varied with the particular strain used. Wistar (W) and Sprague Dawley (SD) males displayed a decline in behavioral responsiveness to PCPA treatment following castration, but the W rats retained their responsiveness longer than did the SD males. The present study was designed to test the hypothesis that W and SD rats differ also in the brain monoamine metabolism following castration and PCPA treatment.

METHOD

Animals

Male Wistar (W) and Sprague Dawley (SD) rats 70-75 days old (Møllegaard Breeding Laboratories, Ejby, Denmark) were used in all experiments. The rats were maintained with continuous access to food and water in air-conditioned temperature-controlled colony room in which lights were out between 11:00-23:00. The animals were maintained for 10 days after their arrival to the laboratory before they were included in the experiment.

Half of the animals were castrated and half of them sham-operated. Both operations were performed under ether anesthesia. On day 18 postcastration, half the animals within each strain started receiving 4 daily injections IP of parachlorophenylalanine methyl ester hydrochloride (PCPA) (H69/17 Hässle, Mölndal, Sweden). The other half of animals received 0.9% sodium chloride solutions.

Biochemical Methods

The rats were killed by decapitation 24 hr after the last

PCPA injection and the whole brain (olfactory lobe excluded) was taken out and placed in ice-cold perchloric acid. The brain was dissected into the following parts: (1) The DA-rich limbic areas (nuc olfactory tubercle, nuc accumbens, nuc interstitialis stria terminalis and the septal and amygdaloid nuclei), and (2) Diencephalon. The brains were homogenized in 10 ml 0.4 N perchloric acid containing 5 mg $\text{Na}_2\text{S}_2\text{O}_2$ and 20 mg EDTA. The extracts were purified and separated on a strong cation exchange column (Dowex 50) [5]. The following spectrofluorimetric analysis were performed: dopamine (DA) [1], noradrenaline (NA) [3] and 5-hydroxytryptamine (5-HT) [2].

RESULTS AND DISCUSSION

Strain differences were found in the endogeneous levels of monoamines, the SD males showing markedly higher levels of diencephalic NA than the W rats ($p < 0.004$, Mann-Whitney U-test). No strain differences were found in the effects of castration on the monoamine levels in the diencephalon. Strain differences were observed, however, in the limbic strain. Following castration, the W males showed a significant increase of 5-HT ($p < 0.05$), a slight, non-significant increase of DA, and a decrease of the NA levels ($p < 0.05$). On the other hand, the SD rats showed a decrease of the DA ($p < 0.004$) and NA levels ($p < 0.05$) in the limbic forebrain while the 5-HT levels did not show any significant changes. This suggest strain differences in the response to castration. Either castrated or sham-operated, the males showed a marked decrease of the 5-HT levels following PCPA treatment both in the limbic forebrain and the diencephalon. The drug treatment also affected the CA

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TABLE 1

MEAN \pm SEM BRAIN TISSUE LEVELS ($\mu\text{g/g}$) OF 5-HYDROXYTRYPTAMINE (5-HT), DOPAMINE (DA) AND NORADRENALINE (NA) OF CASTRATED AND SHAM-OPERATED WISTAR AND SPRAGUE DAWLEY RATS TREATED EITHER WITH PARACHLOROPHENYLALANINE (PCPA) OR SALINE

			Limbic forebrain			Diencephalon			
			5-HT	DA	NA	5-HT	DA	NA	
Wistar	Castr.	NaCl	0.66 \pm 0.022	2.47 \pm 0.083	0.64 \pm 0.027	0.53 \pm 0.017	0.20 \pm 0.019	0.89 \pm 0.059	
	"	PCPA	0.05 \pm 0.006*	1.64 \pm 0.073*	0.55 \pm 0.045	0.04 \pm 0.006*	0.15 \pm 0.030	0.72 \pm 0.029*	
	"	Sham	NaCl	0.59 \pm 0.023	2.11 \pm 0.205	0.73 \pm 0.024	0.49 \pm 0.031	0.21 \pm 0.020	0.85 \pm 0.022
	"	"	PCPA	0.08 \pm 0.010*	1.85 \pm 0.088	0.60 \pm 0.046*	0.07 \pm 0.007*	0.19 \pm 0.015	0.80 \pm 0.032
Sprague-D.	Castr.	NaCl	0.53 \pm 0.033	1.88 \pm 0.081	0.62 \pm 0.044	0.52 \pm 0.021	0.23 \pm 0.010	1.06 \pm 0.017	
	"	PCPA	0.09 \pm 0.008*	1.73 \pm 0.060	0.57 \pm 0.029	0.09 \pm 0.010*	0.19 \pm 0.016	0.92 \pm 0.026*	
	"	Sham	NaCl	0.56 \pm 0.038	2.37 \pm 0.057	0.77 \pm 0.030	0.57 \pm 0.024	0.27 \pm 0.038	1.11 \pm 0.051
	"	"	PCPA	0.13 \pm 0.004*	2.10 \pm 0.301	0.61 \pm 0.034*	0.10 \pm 0.009*	0.22 \pm 0.014	0.96 \pm 0.054*

Groups compared	Limbic forebrain			Diencephalon		
	5-HT	DA	NA	5-HT	DA	NA
W sham saline — SD sham saline	NS	NS	NS	NS	NS	<0.004
W sham PCPA — SD sham PCPA	<0.004	NS	NS	<0.02	NS	<0.02
W cast PCPA — SD cast PCPA	<0.008	NS	NS	<0.008	NS	<0.004

Each value represents 3–5 experiments, each experiment including 2 pooled brain parts. For the various group comparisons, the Mann-Whitney U-test was used.

*In the upper part of the table denotes $p < 0.05$ in comparisons with respective NaCl groups. NS in the lower part of the table denotes $p > 0.05$.

levels which were slightly decreased in both brain regions analyzed, these changes however, reaching statistical significance only in some few cases (see Table 1).

Focussing our attention upon the central problem of this study, significant strain differences were found in the response to the PCPA treatment. PCPA was more effective in depressing the 5-HT levels in the W rats than in the SD males for both sham-operated and castrated males (see Table 1). No strain differences were found in the DA and NA levels in the limbic forebrain following PCPA treatment. In the diencephalon, the SD rats showed higher NA levels than the W rats. Since the endogeneous levels of NA were significantly higher in the SD rats, the effects of PCPA treatment were estimated on the basis of procentual changes rather than absolute values. Group comparison did not reveal any statistically significant differences under this condition.

In a previous experiment we have found that castration of W rats causes an increase in the 5-HT synthesis (measured as accumulation of 5-HT after inhibition of aromatic amino

acid decarboxylase by NSD-1050) in the limbic forebrain and the diencephalon. Also the accumulation of DOPA was found to be increased in the limbic forebrain after castration. None of these effects were observed until at least 20 days after castration. Assuming that the masculine sexual behavior of the rat is under inhibitory influence of 5-HT neuronal mechanisms [6] it is reasonable to expect that rats which are particularly sensitive to PCPA biochemically also show an increased behavioral responsiveness to this treatment. Evidence that this indeed is the case has been found [4].

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