

MODIFICATION OF EFFECTS OF REPETITIVE RESTRAINT STRESS ON BRAIN BIOGENIC AMINES BY L-TYROSINE*

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ABSTRACT Repetitive immobilization of rats for 28 sessions of 4 h each on an unpredictable schedule over 84 calendar days increased brain levels of DA, NE and 5HT. A similar effect, though less in magnitude, was seen by ig L-tyrosine 0.5 mg/kg on the same schedule. Combining the stress and L-tyrosine produced brain amine levels that were similar to those of L-tyrosine alone.

KEY WORDS physical restraint; L-tyrosine; brain; dopamine; norepinephrine; serotonin

Exposure of rats to acute stress causes an increase of brain noradrenergic activity⁽¹⁾. Chronic stress increases both metabolism and release of brain norepinephrine (NE), even beyond the ability of neurons to synthesize NE, resulting in a depletion of brain stores of NE⁽²⁾. Elevated dopamine (DA) levels in hypothalamic nuclei after stress⁽³⁾ and increased utilization of DA in rat brain stem after 15 min of foot shocks⁽⁴⁾ have been reported. Acute applications of restraint stress to rats decreased the serotonin (5HT) content of the hypothalamus⁽⁵⁾ and increased the turnover rate of 5HT in cerebral cortex⁽⁶⁾. Prolonged or repeated exposure to stressful stimuli evoked an activation of brain 5HT neurons⁽⁷⁾.

The present paper describes the effects of repeated sessions of restraint stress, applied on an irregular/unpredictable schedule with small doses of L-tyrosine on the levels of DA, NE, and 5HT in rat brain.

METHODS

Adult ♂ Sprague-Dawley derived rats weighing 280 ± 5 g were housed 3-4/cage with free access to Purina Laboratory Chow and tap water. Group A was not subject to any restraint stress, but each rat was handled and weighed daily, and, on those days on which stress was applied to groups B and D, each rat in group A received intragastrically (ig) distilled water 1 ml/kg at 8 AM. Group B was treated in the same manner as group A except that these rats were subjected to 4 h of restraint stress (1-5 PM) according to a randomized/irregular schedule⁽⁸⁾. Group C was treated similarly to group A except that these rats received ig L-tyrosine (0.5 mg/kg) in water. Group D received both the L-tyrosine and the stressful stimulus.

Restraint stress consisted of a total of 28 sessions, of 4 h each, randomly distributed within 84 d⁽⁸⁾. Rats were physically restrained in individual metal boxes with fixed walls and floor and an adjustable lid permitting pressure-controlled restraint. This immobilization produced no physical damage but was a severe psychological stress to the rats.

Following the last day of dosage and/or restraint, all rats remained 2 d undisturbed in

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Tab 1. Effects of stress and L-tyrosine on rat brain biogenic amines (ng/g). $\bar{x} \pm SD$

Group	Restraint	Dosage	Rats	Dopamine	Norepinephrine	Serotonin
A	-	Water	15	767 ± 108	309 ± 46	851 ± 112
B	+	Water	14	1064 ± 197	397 ± 56	1113 ± 108
C	-	L-tyr	11	959 ± 227	352 ± 41	970 ± 117
D	+	L-tyr	12	908 ± 130	350 ± 23	1053 ± 73
		A vs B		p < .01	p < .02	p < .01
		A vs C		p < .02	p < .05	p < .02
		B vs D		p < .02	p < .05	NS
		C vs D		NS	NS	NS

their home cages, then were decapitated between 1 and 3 PM on the 2nd day. The brains were rapidly transected at the fovea interior just forward of the superior peduncles, washed in cold 0.9% saline, blotted dry, and stored at 60°C until assay. DA, NE and 5HT were determined in whole brain⁽⁹⁾; L-tyrosine was determined fluorimetrically⁽¹⁰⁾. Statistical comparisons were made by ANOVA with Dunnett's *post hoc* test.

RESULTS

As shown in Table 1, the repetitive stress by itself evoked significant elevations in brain levels of all 3 biogenic amines (A vs B). A significant elevation in levels of all 3 amines was also noted in the rats given the treatment regimen of L-tyrosine though not exposed to the stressful stimuli (A vs C). The rats given L-tyrosine and exposed to restraint stress had levels of DA and NE, but not of 5HT, that were less than those obtained with restraint stress alone (B vs D). These rats had brain biogenic amine levels that did not differ significantly from those given L-tyrosine but not exposed to the restraint stress (C vs D). In this regard, it should be noted that brain levels of L-tyrosine were not significantly different from control levels at either 5 h or 48 after L-tyrosine 0.5 mg/kg.

DISCUSSION

The fact that a regimen of small doses of L-tyrosine influenced brain levels of DA and

NE when given over an 84-d period should not be surprising in view of a recent review⁽¹¹⁾. Such a dosage regimen would not be expected to result in feedback changes in an enzyme such as tyrosine hydroxylase since it was not a loading type of dose. The effects of the dosage regimen on brain 5HT levels may reflect a catecholamine-indoleamine interaction; an additional complexity may lie in the non-specificity of conversion of amino acid precursors to amines. For example, L-tyrosine can be converted to DA and NE only in neurons that contain tyrosine hydroxylase.

Nevertheless, the alterations of restraint stress-induced elevations of all 3 brain biogenic amines by L-tyrosine suggests that dietary factors may be capable of acting as modulating factors in the organism. The small dosages used, given at a time of day when the rats would have ceased eating 2-3 h previously, lend support to the possibility that massive, loading-type doses are not required to alter brain biogenic amine levels⁽¹¹⁾. These effects of L-tyrosine plus stress may be similar to the interactions of L-tryptophan and stress previously reported⁽¹²⁾.

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L-酪氨酸改变反复束缚应激对脑内生物胺的作用

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提要 大鼠在 84 d 内随机给予 28 次反复束缚限制活动处理, 每次 4 人, 能升高脑内 DA, NE 和 5 HT 水平。同样程序下仅 ig L-酪氨酸 0.5 mg/kg 也可产生上述类似效应。应激加 L-酪氨酸的升高脑内生物胺水平作用,

类似于单独给 L-酪氨酸。

关键词 身体的约束; L-酪氨酸; 脑; 多巴胺; 去甲肾上腺素; 血清素