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LETTER TO THE EDITOR

PENTYLENE TETRAZOL INDUCED MONOAMINE CHANGES IN RAT BRAIN

Sir,

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The convulsant activity of pentylenetetrazol (PTZ), is mainly due to its ability to selectively antagonize GABA mediated post synaptic inhibition in the mammalian brain though a direct excitatory effect on neuronal membranes cannot be ruled out as a contributory factor (1). Furthermore there are reports which indicate that 5-hydroxytryptamine (5-HT) and norepinephrine (NE) play a modulatory role in the genesis of PTZ induced seizures since, diminishing the influence of 5-HT and NE in the brain exacerbates PTZ induced seizures while increasing their influence affords protection against PTZ induced convulsions (2,3,4,5,6,7).

In the present study we have estimated in discrete regions of the rat brain the levels of catechol and indol amines at the onset of PTZ induced seizures to elucidate their involvement in PTZ induced seizures.

Adult male albino rats (150-200 g) of Wistar strain were used for this study. The animals were housed under standard laboratory conditions and fed with pellet feed and water ad libitum. All the experimental procedures were carried out at room temperature (28-30 degree Celsius) in the fore noon to avoid circadian rhythm influencing the brain biogenic amine levels. Animals were starved overnight prior to the experimentation. A standard dose of 80 mg/kg PTZ dissolved in saline and injected subcutaneously produced convulsions in 100% of our rats.

Control animals received equal volume of saline subcutaneously (sc). The test animals were sacrificed by quick decapitation at the onset of convulsion. The control animals were also sacrificed at the same time interval as that of the test animals. The brains were removed rapidly and dissected on ice cold glass plate into hypothalamus, striatum, hippocampus, midbrain, cerebellum, pons, medulla and cerebral cortex as previously described (8). Brain monoamines such as dopamine (DA), norepinephrine (NE), epinephrine (E), 5-hydroxy tryptamine (5-HT) and 5-hydroxy indole acetic acid (5HIAA) in these regions were estimated fluorimetrically (9) using Hitachi Model 650 1OM fluorescence spectrophotometer.

Chemicals: Standard DA, NE, E, 5 HT, & 5 HIAA were purchased from Sigma, USA and all other reagents were of analytical grade.

The results were analyzed for statistical significance by Student's t-test.

All the PTZ administered animals exhibited seizures at 8.5 ± 3.5 min. The changes in monoamine levels occurring in various regions at the onset of seizures is shown in Table I. DA level was significantly increased in midbrain only. NE level was decreased in all the regions except striatum. E level was significantly decreased in hypothalamus, striatum and cerebellum but was significantly increased in hippocampus and midbrain. 5-HT level was significantly decreased in all the regions except striatum whereas 5 HIAA level was significantly decreased in all the regions except hippocampus and pons medulla.

Seizure activity of PTZ is enhanced by measures which decrease the activity of central NE and 5-HT systems (7). Thus our finding, that at the onset of PTZ seizures NE and 5-HT levels were signifi-

TABLE I : Rat Brain monoamine levels at the onset of pentylenetetrazol (PTZ) induced seizures.

Amines/Areas			*Hypothalamus*	*Striatus*	*Hippocampus*	*Midbrain*	*Cerebellum*	*Pons medulla*	*cortex*
Dopamine	Control	(15)	676 ± 23	5073 ± 100	101 ± 6	252 ± 13	61 ± 4	175 ± 11	746 ± 18
	PTZ	(6)	594 ± 19	5129 ± 131	91 ± 11	345 ± 14***	56 ± 6	192 ± 16	726 ± 20
Norepinephrine	Control	(15)	1628 ± 27	426 ± 20	266 ± 12	550 ± 16	221 ± 16	597 ± 15	266 ± 14
	PTZ	(6)	863 ± 28***	390 ± 26	213 ± 18*	367 ± 14***	135 ± 9**	197 ± 20***	172 ± 15**
Epinephrine	Control	(15)	156 ± 7	165 ± 8	66 ± 4	308 ± 12	107 ± 7	212 ± 10	92 ± 6
	PTZ	(6)	69 ± 8***	109 ± 9***	99 ± 11**	385 ± 20**	64 ± 6**	224 ± 15	110 ± 10
5 HT	Control	(15)	960 ± 26	637 ± 22	487 ± 12	707 ± 24	108 ± 4	561 ± 20	357 ± 18
	PTZ	(6)	708 ± 34***	560 ± 24	406 ± 16**	548 ± 20**	75 ± 10**	408 ± 9***	223 ± 16***
5 HIAA	Control	(15)	850 ± 21	562 ± 15	329 ± 12	982 ± 31	279 ± 9	566 ± 20	534 ± 18
	PTZ	(6)	664 ± 18***	496 ± 17*	292 ± 16	783 ± 13***	223 ± 10**	562 ± 12	343 ± 17***

All the Values are expressed as ng/g(Mean ± SEM)
Number in parenthesis indicates the number of animals used.
*P< 0.05, ** P< 0.01, ***P<0.001

cantly decreased in all the brain regions studied except in striatum, supports the contention of other workers (2,3,4,5,6,7) that NE and 5-HT play a modulatory role in the genesis of PTZ induced seizures. Furthermore, since DA level was significantly increased in the midbrain region only, it sugggests that DA might not be involved in PTZ seizures. This suggestion of ours concurs with the report of Burly and Ferrendelli (7).

In conclusion, this study shows that PTZ alters the steady state level of monoamines in rat brain at the onset of convulsions. Further no single amine can be implicated solely as responsible for the seizures and it is probable that a set pattern of changes in the brain monoamines may be responsible for the final outcome.

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