ROLE OF THE STRIATUM IN THE MECHANISM
OF SEROTONINERGIC EFFECTS ON THE COURSE
OF METRAZOL CONVULSIONS IN RATS

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The effect of 5-hydroxytryptophan (5-HT) and parachlorophenylalanine (PCPA) on behavioral and
electroencephalographic manifestations of metrazol convulsions during electrical stimulation and
destruction of the striatum was studied in freely moving rats. The effect of the compounds on
the seizures, the myoclonic spasms, and the spike-and-wave activity evoked by metrazol did not
depend significantly on the functional state of the corpus striatum. Meanwhile the ability of 5-HT
to ameliorate, and of PCPA to aggravate the course of the generalized convolution and the post-
convulsive state was potentiated by stimulation and abolished by destruction of the striatum. It
is suggested that activation of the serotoninergic mechanisms may be responsible for the aboli-
tion of the convulsions that is observed in the case of excitation of the corpus striatum.

KEY WORDS: metrazol convulsions; serotoninergic substances; striatum.

Serotoninergic agents are known to affect the course of metrazol convulsions: the serotonin precursor 5-
hydroxytryptophan (5-HT) blocks, whereas the inhibitor of serotonin synthesis parachlorophenylalanine (PCPA),
on the other hand, intensifies convulsions of this sort [4-6]. As the writer showed previously [1-3], a change in
the functional activity of the striatum, which has a high concentration not only of dopamine and acetylcholine,
but also of serotonin, has a distinct influence on the character of metrazol convulsions.

It was therefore decided to study the effect of electrical stimulation and blocking of the striatum on the
ability of 5-HT and PCPA to modify the various indices of convulsions evoked by metrazol.

EXPERIMENTAL METHOD

Experiments were carried out on 65 albino rats of both sexes weighing 180-300 g. The pharmacological
agents 5-HT (100 mg/kg) and PCPA (300 mg/kg twice at an interval of 24 h) were injected intraperitoneally 0.5
and 48 h respectively before provocation of the convulsions. In the experiments of series I the effect of sero-
tonergic drugs on behavioral (30 rats) and electroencephalographic manifestations (four rats) of metrazol con-
vulsions were studied in intact animals; in series II the action of the drugs was assessed on the anticonvulsive
TABLE I. Effect of Serotoninergic Drugs on Some Indices of Metrazol Convulsions Before (I) and After (II) Destruction of Striatum (M ± m)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Control</th>
<th>5-hydroxytryptophan</th>
<th>Parachlorophenylalanine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Threshold dose (in mg/kg) of metrazol to obtain myoclonic spasms</td>
<td>Duration of convulsion (in sec)</td>
<td>Status epileptiformis (in %)</td>
</tr>
<tr>
<td></td>
<td>I</td>
<td>II</td>
<td>I</td>
</tr>
<tr>
<td>Control</td>
<td>25.5±2.4</td>
<td>43.8±4.5</td>
<td>38.0±5.9</td>
</tr>
<tr>
<td>5-hydroxytryptophan</td>
<td>34.4±5.5</td>
<td>57.6±6.3</td>
<td>60.2±7.8</td>
</tr>
<tr>
<td>Parachlorophenylalanine</td>
<td>13.0±2.4</td>
<td>26.3±4.5</td>
<td>26.8±3.2</td>
</tr>
</tbody>
</table>

Fig. 1. Effect of 5-HT and PCPA on cortical responses evoked by single stimulation of striatum after subconvulsant doses of metrazol. I) Character of spontaneous changes (A) and changes evoked (B) by caudate stimuli on EEG in sensomotor cortex of same rat under normal conditions (1) and after administration of 5-HT (2) and PCPA (3); II) combined changes in duration of cortical responses on EEG to striatal stimulation (40 μA, 0.1 msec) in a rat before (a) and after administration of increasing doses of metrazol (10, 20, and 30 mg/kg in b, c, and d, respectively); unshaded column — control, columns with cross-hatching and oblique shading — after 5-HT and PCPA, respectively. Ordinate, time (in sec).

Effect of electrical stimulation of the striatum. The methods of obtaining convulsions and of stimulating the brain were described in detail previously [1, 2]. In series III the effect of 5-HT and PCPA was studied on the course of the convulsions in 23 striatectomized rats. For this purpose, 2 weeks before the experiments bilateral electrolytic destruction of the striatum was carried out (silver electrodes, dc of 2 mA, duration 20–30 sec). After the end of the experiments the location and volume of the lesions in the corpus striatum were determined in every case.

EXPERIMENTAL RESULTS

Interference with the activity of the serotoninergic systems of the brain clearly modified the course of the preconvulsive period, the generalized fit, and the postconvulsive state evoked by metrazol (Fig. 1).