Noradrenaline and Seizures

Tabakoff et al. (1) presented evidence on the role of brain noradrenaline (NA) in the development of tolerance to barbiturates: animals that suffered a 50 percent depletion of brain NA through intra-ventricular injection of 50 μg of 6-hydroxydopamine (6-OHDA) failed to develop tolerance to long-term barbiturate treatment, as measured by sleep time and hypothermia after a subsequent challenge dose of barbiturate, or by potentiation of seizures induced by pentyletetrazol (Metrazol). Tabakoff et al. (1) also compared the susceptibility of control and 6-OHDA-treated animals to Metrazol-induced seizures even in the absence of chronic barbiturate treatment and found no effect of the 6-OHDA.

We have recently obtained evidence that brain NA is indeed involved in Metrazol-induced seizures and that a marked alteration in these seizures occurs if NA is depleted (2). Animals that received 4 μg of 6-OHDA injected into the fibers of the dorsal noradrenergic bundle, a procedure that depleted forebrain NA to less than 5 percent of control values, showed a marked potentiation in the duration, number, and type of seizure elicited by subcutaneous administration of 70 mg of Metrazol per kilogram of body weight (Table 1). Thus, the seizures lasted longer, occurred more frequently, and were tonic rather than clonic. These data support our earlier report that depletion of both NA and dopamine (DA) in varying proportions also potentiates Metrazol-induced seizures (3). They also support data indicating that catecholamines are significantly involved in seizures induced by other means (4). An alteration in brain NA may therefore be important in the pathogenesis of human conditions such as epilepsy. We suggest that the failure of Tabakoff et al. (1) to observe a potentiation of Metrazol-induced seizures in rats treated with 6-OHDA reflects the modest (no more than 50 percent) depletion achieved by their manipulation. In other catecholaminergic systems, such a small loss would be without behavioral effect (5), and the effectiveness of this loss in altering the development of tolerance to barbiturates testifies to the pervasive role of brain NA in this phenomenon.

Mason and Corcoran have presented evidence that a profound depletion of brain norepinephrine (NE) results in a potentiation of pentyletetrazol-induced seizures. They suggest that the lack of such effects in our studies (1) was due to a less extensive destruction of brain NE neurons. We totally agree with their assessment and would like to reiterate certain points that appeared in (1) as well as in our previous publications on this subject (2, 3). Adrenergic receptor supersensitivity develops during the 2-week interval between injection of 6-hydroxydopamine (6-OHDA) and the testing of the animals in our studies and we have stated: "the development of recep-

Table 1. Seizure response to subcutaneous injection of Metrazol (70 mg/kg) in NA-depleted rats (4 μg of 6-OHDA was injected into the fibers of the dorsal NA bundle): N.S., not significant.

<table>
<thead>
<tr>
<th>Group</th>
<th>Duration of first seizure (sec)</th>
<th>Number of rats</th>
<th>Noradrenaline content of tissue*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With multiple seizures</td>
<td>With tonic seizures</td>
<td>Hippocampus-cortex</td>
</tr>
<tr>
<td>Control (N = 7)</td>
<td>32.9 ± 3.0</td>
<td>0/7</td>
<td>5/8</td>
</tr>
<tr>
<td>6-OHDA (N = 9)</td>
<td>113.2 ± 11.7</td>
<td>0/7</td>
<td>5/9</td>
</tr>
<tr>
<td>P</td>
<td>.01</td>
<td>.05</td>
<td>.001</td>
</tr>
</tbody>
</table>

*Percentages for the 6-OHDA-treated rats were, for NA: hippocampus-cortex, 2; hypothalamus, 26; cerebellum, 124; and spinal cord, 120; and for DA: 88.
tor hypersensitivity after destruction of certain noradrenergic terminals, and only partial depletion of NE in brain in our studies, may have combined to suppress differences in withdrawal symptoms between animals pretreated with 6-OHDA and those receiving control CSF [cerebrospinal fluid]" (2). Animals injected intraventricularly with 6-OHDA (50 μg) 48 hours before receiving pentylene
tetrazol did exhibit a greater incidence of seizures compared to the appropriate control mice (2). Referring to the statement by Mason and Corcoran that barbiturate tolerance was measured in our studies (1) by quantitating the pentylene
tetrazol-induced seizures, we point out that the pentylene
tetrazol-induced seizures were used as a measure of central nervous system excitability and the presence of physical dependence on barbiturates in the barbiturate-withdrawn mice. We have previously stressed that tolerance to and physical depen-
dence on sedative hypnotics are not identified phenomena (2, 3), and here again we speak against synonymous use of the terms "drug tolerance" and "dependence." **Boris Tabakoff**

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References and Notes


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Carbon’s High-Temperature Behavior

Whittaker (1) presented evidence for the occurrence of stable “carbyme” forms of graphite—forms that contain a triple bond—at temperatures above 2600 K. He also suggested that the Swing’s bands of C₃ are not seen from carbon va-
por at these high temperatures because of the presence of excited states of C₃ at low energy. These excited states would have to be forbidden to transitions from the ground state and must be such as to deplete the population of the ground state and decrease the intensity of the Swing’s bands. A set of "² energetic states is sug-
gested as a possibility (2). Considerable controversy has surrounded the spectro-
scopic and thermodynamic properties of C₃ in the past (3, 4), and it is important to consider the possibility that previous ideas concerning C₃ may not be com-
plete.

Whittaker’s suggestion appears to be untenable. The Swing’s bands do not de-
crease in intensity as the temperature in-
creases. Painstaking experiments have shown that the Swing’s bands form a pseudocontinuum at high temperatures and that the intensity of the continuum increases with temperature as does the C₃ concentration (5). Spectral observa-
tions at still higher temperatures can be used to draw conclusions about the pop-
ulation of the ground state only if the in-
tensity of the continuum is taken into ac-
to. If new states of C₃ became popu-
lated at high temperatures, new features might be expected in the vibrational spectrum even though the new states were forbidden in the electronic spec-
trum. The infrared spectrum at about 3100 K has been examined, and it too is consistent with ground state C₃ (6).

The approximate energies of ex-
citation of the excited states of C₃ have been calculated (7). The "₂ energetic state was calculated to be at 3.03 eV, in excellent agreement with the energy of the Swing’s band. The "₂ energetic state was calcu-
lated to be at 3.04 eV, in agreement with weak bands found in the spectrum at 2.10 eV (8). These energies yield a popula-
tion of less than 0.2 percent for the triple-
let states at 3000 K and about 1 percent at 4000 K. This population is much too small to make the spectra due to the ground state disappear.

It is possible that the "₂ energetic state is popu-
lated by a nonequilibrium mechanism. However, at these temperatures the satu-
ratio vapor pressure of C₃ is substantial (≥ 10⁻⁴ atm at 3000 K and rapidly in-
creasing as a function of temperature (9)) and collisions will rapidly establish equi-
librium.

I conclude that the observations of the gas phase spectra cited by Whittaker provide no evidence for new forms of C₃.

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References and Notes


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The published spectrum by Phillips and Brewer (1) shows the 405.0-nm band of C₃ at ~ 3000 K, but the spectrum taken at 3200 K by Brewer and Engelske (2) does not show this band. None of our spectra taken over the temperature range of 3500 to 4200 K show the 405.0-nm band, and a similar result was reported by Null and Lozier (3) and Howe (4). The remarks I made about the dis-
appearance of C₃ emission were based on the behavior of the 405.0-nm band. A reexamination of our plates reveals a weak continuum starting at ~ 465.0 nm and extending to at least 360.0 nm, with a maximum at ~ 393.0 nm and a very weak band at 590.2 nm. These could corre-
spond to the pseudocontinuum and the "₂ "₃ transition of C₃. In this case, I must agree with Strauss that the behav-
ior of C₃ emission provides no evidence for new states of C₃.

 Apparently no new states are neces-
sary to account for the triple-bonded carbon forms. A recent theoretical study of C₃ molecules by Kertesz et al. (5) shows that models with alternating short and long bonds are energetically more stable than equidistant ones. This means that alternate bonds of all C₃ molecules have some triple-bond character regardless of whether n is odd or even. In view of this, the remarks I made in my report about C₃ molecules where n is even are not correct.

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