ONCOLOGY

THE SIGNIFICANCE OF HIGHER NERVOUS ACTIVITY IN THE APPEARANCE AND DEVELOPMENT OF TUMORS OF THE BREAST IN MICE

L. L. Maliugina, A. I. Mironova, V. K. Fedorov, and L. M. Shabad

The Laboratory of Experimental Genetics of Higher Nervous Activity (Head—V. K. Krasuskii) of the I. P. Pavlov Institute of Physiology (Head—Academician K. M. Bykov) of the Academy of Sciences of the USSR and the Laboratory of Experimental Oncology (Head—Corresponding Member Acad. Med. Sci. USSR, L. M. Shabad) of the Institute of Oncology (Head—Corresponding Member Acad. Med. Sci. USSR, A. I. Serebrov) of the Academy of Medical Sciences, USSR, Leningrad

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There are several reports in the literature of studies of the relationship between growth of tumors in various animals and aspects of higher nervous activity.

These studies may be divided into 2 groups: the first group consists of investigations of the appearance of tumors in animals after trauma to the nervous system [3, 5, 6, 10]; the second group is made up of investigations in which tumor growth was studied in animals with normal higher nervous activity [4, 8].

In earlier investigations on mice of the Cm-black strain, injected subcutaneously with a carcinogenic compound, we showed that in animals with mobile nervous processes, induced tumors appeared less often than in animals with inert nervous processes. On the basis of these findings we suggested that there is an essential relationship between the degree of mobility of its nervous processes and the resistance of an animal to carcinogenic agents.

The present investigation, a continuation of these earlier studies, was carried out on female mice belonging to the high-cancer strain C3HA, a considerable proportion of which develop "spontaneous" tumors of the breast [7], i.e., tumors due to estrogenic stimulation and to the so-called milk factor with a definite hereditary susceptibility.

EXPERIMENTAL METHOD

In the experiment 112 females of the C3HA strain were used, in 50 of which (47.7%), aged between 7 and 12 months, tumors of the breast had developed, while 62 mice were without tumors. Of these 112 mice, 96 (aged from 7 to 12 months) were investigated by the alimentary conditioned reflex method [1, 2, 9]. Before investigation all the animals received a diet in excess of normal requirements. During the investigation (2-4 months) they were put on a normal diet (25 calories per mouse per day with protein accounting for 18% of the calorific value), while at the end of the investigation they were formed into groups of 4-6 animals and again put on the ordinary diet.

The physiological investigation of the mice consisted of production of 2 conditioned reflexes (positive—to a bell, and inhibitory—to a light) and the bilateral modification of these reflexes. The mobility of the nervous processes was measured by the rate of modification of the reflexes in these mice, the criteria for the assessment of this property of the nervous system being: 1) the onset of modification, i.e., that state of conditioned reflex activity of the animals in which for the first time the reflex in response to a reinforced stimulus was greater in magnitude than the reflex to the stimulus when not reinforced by food, 2) the end of modification, characterized
by prolonged (not less than 5 successive experiments) dominance of the positive over the inhibitory reflex, and
3) total modification, in which the magnitude of the positive and inhibitory conditioned reflexes regained its
initial value as it was before modification.

After 5 months all the experimental animals were subjected to regular inspection — observations were made
of the time of appearance of tumors of the breast, the situation and number of tumor nodules. After death, all
the animals were examined and the tumors and the lungs, containing metastases, examined microscopically. Of
the 50 mice which developed tumors, multiple nodules were observed in 23 (46%) and metastases of the tumor
in the lungs were found in 14 mice (28%).

The majority of the tumors of the breast were adenocarcinomas and small-cell intraacinous carcinomas,
or tumors of mixed structure. Solid carcinomas, cystadenocarcinomas and adeno-acanthomas were observed in
isolated cases.

Some of the mice (numbering 49) from the age of one month and before the beginning of the investigation
(7-12 months) were kept in individual cages measuring 10 x 10 x 20 cm, and the remaining 63 mice in groups
of 8-26 mice in large cages. These two groups differed sharply in the degree of mobility of their nervous pro-
cesses: in the animals kept separately the mobility of the nervous processes was found to be on the average twice
as high as that of the mice living in groups (12 experiments were required to modify the reflexes in the "individual"
mice and 20 experiments for the "group" mice). As regards the proportion which formed tumors, these groups
showed no difference from each other: in the first group tumors appeared in 40.5% of cases and in the second
group in 40%.

**EXPERIMENTAL RESULTS**

The difference in the keeping of the animals, and in particular the difference in the average degree of
mobility of the nervous processes, makes it essential to make a separate analysis of the results obtained from the
2 groups of mice mentioned.

**TABLE 1**

Statistical Treatment of the Results of Mobility of Nervous Processes in Healthy and Tumor-
Bearing Mice

<table>
<thead>
<tr>
<th>Modification of conditioned reflexes</th>
<th>Mice without tumors</th>
<th>Mice with tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>no. of specimens</td>
<td>M₁+m₁</td>
</tr>
<tr>
<td>Onset of modification</td>
<td>25</td>
<td>4.56±0.42</td>
</tr>
<tr>
<td>End of modification</td>
<td>24</td>
<td>11.04±1.00</td>
</tr>
<tr>
<td>Total modification</td>
<td>24</td>
<td>14.45±1.40</td>
</tr>
<tr>
<td>Mice kept separately</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onset of modification</td>
<td>32</td>
<td>4.19±0.47</td>
</tr>
<tr>
<td>End of modification</td>
<td>31</td>
<td>17.39±1.7</td>
</tr>
<tr>
<td>Total modification</td>
<td>31</td>
<td>22.7±2.2</td>
</tr>
</tbody>
</table>

In Table 1 are shown the results, treated statistically, of experiments on mice kept separately. It is clear
from these results that by all criteria the mobility of the nervous processes among unaffected animals is higher
than in the group of animals with tumors. This difference is slight, however, not statistically significant, and
may only be detected as a tendency towards higher mobility of nervous processes in unaffected mice. Here also
are indicated the results of experiments on mice kept together. As can be seen, in the mice with tumors the
mobility of the nervous processes is considerably less than in the group of animals without tumors. These differ-
ences are more marked than in the animals kept separately, nevertheless they are not statistically significant.