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MAGNESIUM AND ZINC BLOOD LEVELS IN MICE SENSITIVE TO AUDIOGENIC SEIZURES

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Résumé

TAUX SANGUINS DE MAGNÉSIUM ET DE ZINC CHEZ LA SOURIS SENSIBLE À LA CRISE AUDIOGÈNE. - Les taux de magnésium et de zinc sanguins ont été déterminés chez des souris sensibles à la crise audiogène. Les valeurs du magnésium érythrocytaire sont nettement plus élevées chez ces animaux que chez les souris témoins. Aucune différence n’est constatée dans le cas du zinc. Les résultats sont discutés à la lumière de recherches faites chez l’homme, montrant l’existence de modifications des taux du magnésium et du zinc sanguins en rapport avec divers signes d’hyperexcitabilité cérébrale. Ils suggèrent également l’existence d’un contrôle génétique de la magnésémie.

Barbeau and Donaldson (1974) have observed a decrease in blood zinc level in cases of human essential epilepsy. On the other hand, there seems to be a relation between certain variations in magnesemia and the appearance of cerebral hyperexcitability as detected by electroencephalogram (Durlach et al., 1971 ; Durlach, et al., 1973 ; Durlach, 1976).

Thus, it seemed of interest to study the zinc and magnesium levels in the blood of a mutant mouse strain (Swiss Albino, Rb1) sensitive to audiogenic seizures.

Methods

Mice sensitive (Swiss Albino Rb1) and resistant (Swiss Albino Rb3) to audiogenic seizures were selected by the « Laboratoire d’Acoustique Animale de l’E.P.H.E. » (Busnel, 1959 and 1978). They were mated according to the rotation system of Falconer, and raised under identical conditions. The INRA standard diet used for feeding the animals contained 2 % of a mineral mixture composed of magnesium hydroxide (13.8 %), Ca diphosphate (70 %), Na Cl (15 %) and minute amounts of Fe, Zn, Mn, Co and Cu sulfates.

In all cases, the mice were four months old on the average, with maximal variations of plus or minus fifteen days.

Blood samplings were taken in the supraorbital vein without anesthesia, between 10 AM and 1 PM. In order to minimize the possible influence of circadian variations, mice of the two strains were treated alternately. Furthermore, within the time period of our experiment, no significant variation according to the
sampling hour was noticed. The blood was collected on Li heparine and immediately centrifuged. The levels of magnesium and zinc in erythrocytes and plasma were evaluated by atomic absorption spectrophotometry.

In March 1975, a first series of measurements was performed on twenty sensitive and twenty resistant mice, each group consisting of ten males and ten females. In a second series performed in May only males were used, of which thirty-eight were resistant and thirty-nine sensitive to audiogenic seizures. A third series was performed in October on twenty-one resistant and twenty-two sensitive females.

**Results**

Table 1 shows the overall results, with exception of the plasma zinc measurements, which were performed only on a small number of mice because of the difficulty in obtaining a sufficient amount of blood. As a matter of fact, the latter measurements did not show any appreciable variation which could be related to sex or strain. In resistant mice, the plasma zinc values were as follows: 0.87 ± 0.07 and 0.96 ± 0.19 mg/liter for five males and six females, respectively. In sensitive mice, the values were similar: 0.95 ± 0.08 and 0.91 ± 0.16 mg/liter for six males and seven females, respectively. Similarly, no significant differences could be found in the red blood cell zinc levels (table 1).

On the other hand, the red blood cell magnesium (RBC Mg) level was definitely higher in sensitive than in resistant mice. This difference was highly significant in the males, though statistically barely significant in the females. As for the plasma magnesium, a similar phenomenon could be observed, though less marked, and significant only in male mice.

### Table 1. — Red blood cell (RBC) Magnesium and Zinc and plasma (P) Magnesium levels in mg/l in two groups of mice: resistant and sensitive to audiogenic seizures.

<table>
<thead>
<tr>
<th>Variables</th>
<th>resistant to audiogenic seizures</th>
<th>sensitive to audiogenic seizures</th>
<th>Significance Level</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sex n m σ</td>
<td>n m σ</td>
<td>P</td>
</tr>
<tr>
<td><strong>RBC Mg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>10 47.28 1.66</td>
<td>10 50.88 2.20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>male</td>
<td>38 47.92 2.34</td>
<td>39 51.59 2.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>female</td>
<td>10 48.61 2.15</td>
<td>10 51.49 3.95</td>
<td>0.06</td>
</tr>
<tr>
<td>female</td>
<td>21 52.91 4.19</td>
<td>22 54.33 5.45</td>
<td>(N.S.)</td>
</tr>
<tr>
<td><strong>P Mg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>10 17.92 1.52</td>
<td>10 18.97 0.71</td>
<td>(N.S.)</td>
</tr>
<tr>
<td>male</td>
<td>38 18.99 1.74</td>
<td>39 20.69 2.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>female</td>
<td>10 18.32 1.30</td>
<td>9 19.00 1.81</td>
<td>(N.S.)</td>
</tr>
<tr>
<td>female</td>
<td>21 19.57 1.61</td>
<td>22 19.80 1.43</td>
<td>(N.S.)</td>
</tr>
<tr>
<td><strong>RBC Zn</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>10 9.82 0.75</td>
<td>10 9.62 0.22</td>
<td>(N.S.)</td>
</tr>
<tr>
<td>male</td>
<td>38 8.76 1.01</td>
<td>39 9.08 0.87</td>
<td>(N.S.)</td>
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<td>10 9.65 0.30</td>
<td>(N.S.)</td>
</tr>
<tr>
<td>female</td>
<td>21 9.34 0.52</td>
<td>22 9.10 0.73</td>
<td>(N.S.)</td>
</tr>
</tbody>
</table>

n : number of animals tested.
m : mean.
σ : standard deviation.
P : significance levels of the differences between means.
No significant variation could be related to sex. Experiments done in May and October gave somewhat higher values than those performed in March.

Discussion

The present investigation does not reveal a decrease in blood zinc, such as was found by Barbeau and Donaldson (1974) in cases of human essential epilepsy. This disagreement is not, however, surprising, since audiogenic seizures of mice are quite different from human epilepsy.

On the other hand, the existence of a higher RBC Mg level in sensitive male mice can be considered in the light of the following observations:

1. On the one hand, a deficit in magnesium leads, in mice and normal rats, to spontaneous seizures. This phenomenon appears to be in contradiction with the observations reported above. Similarly, in man, a lower plasma Mg level, even moderate, usually leads to various disturbances of the nervous excitability, among which are minor perturbations of the electroencephalogram (sharp alpha waves, presence of theta). The literature on the subject has been reviewed elsewhere (Durlach, 1976; Chutkow, 1980) and will not be discussed here.

2. On the other hand, certain observations made in man cast a light on another phenomenon: a high RBC Mg level is regularly found in patients showing, during the hyperpnea test, a frequency decrease in the electroencephalogram. This finding seems to indicate an association between high RBC Mg concentration and a certain degree of cerebral hyperexcitability detected by the decrease in frequency during the hyperpnea test (Durlach et al., 1973).

The present work suggests two conclusions:
1. Some degree of increase in RBC Mg level is found in two different populations, both showing some changes in cerebral excitability: on the one hand, mice sensitive to audiogenic seizures and on the other hand, human beings showing mild signs of cerebral hyperexcitability. Of course, a great deal more research is necessary to determine the exact relationship between the observed cerebral hyperexcitability and the RBC Mg level.
2. The strain-dependent differences in RBC Mg levels suggest that, in mice, genetic factors may affect the regulation of magnesium. This observation may be correlated with earlier studies made in human populations. We shall briefly recall that the latter studies showed that there exist important and stable variations in RBC Mg concentration among different human groups (Henrotte, 1973a; Henrotte, 1973b; Henrotte, 1973c; Henrotte et al., 1974) and that, in contrast with the very low individual variability, there was a very high variability between individuals (Henrotte et al., 1973; Darlu and Henrotte, 1976; Henrotte et al., 1976), which is compatible with a control of RBC Mg by genetic factors. Studies on twins and families also confirm the importance of genetic factors on the regulation of RBC Mg in man (Darlu and Moreau, 1978; Henrotte et al., 1978; Darlu and Henrotte, 1980).

Acknowledgements

We wish to thank the « Laboratoire d'Acoustique Animale de l'E.P.H.E. » for supplying the strains of mice used in this study.

Summary

Blood magnesium and zinc levels were determined in mice sensitive to audiogenic seizures. Red blood cell Mg concentrations were found higher in these animals than in normal control. No variations were observed for blood zinc levels. These results are discussed in the light of physiological studies relating to hyperexcitability and Mg or Zn metabolism in man. They also suggest the occurrence of genetic factors in red blood cell Mg regulation.
References


