Short communication

Spatial memory deficits and thalamic serotonergic metabolite change in thiamine deficient rats

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The purposes of the present study were to verify the effects of a severe thiamine deficiency episode on spatial cognitive aspects and thalamic serotonergic parameters. The animals were submitted to a severe thiamine deficiency treatment that was interrupted after the onset of the last neurological signs. The results obtained confirm previous findings about TD deficiency effects on cognitive function and, further show that this vitamin increases the thalamic serotonine metabolite, 5-hidroxyindolacetic acid (5-HIAA), level. In addition, the present data shed light on the importance of this metabolite in spatial cognitive function.

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onset of the last neurological signs (i.e. seizures and impaired righting reflexes), by the administration of two i.p. doses of thiamine (100 mg/kg each) interspaced with an 8 h interval and returning to commercial chow. After a recovery period of thirty five days, in which the rats from both groups were treated with ad libitum standard diet and water, the animals were trained and tested in the MWM task as described elsewhere [2]. On the first day after the behavioral tests, all animals were killed, their brains separated and thalamus were quickly dissected out from both hemispheres. Serotonin (5-HT) and 5-hydroxyindolacetic acid (5-HIAA) contents were analyzed by high performance liquid chromatography (HPLC). 5-HT and 5-HIAA concentrations were calculated by interpolation of its respective standard curves. Obtained values are expressed as ng/g of tissue. The [5-HIAA]/[5-HT] ratio was used as an index of serotoninergic system activity as previously described [13]. Fig. 1A, shows thiamine deficient and control animals’ latencies obtained in the acquisition sessions of the spatial navigation task. Two-way ANOVA with repeated measures on the last element (2 × 5, factors: thiamine deficiency and sessions) showed significant main effects of thiamine deficiency (F1,30 = 6.00; p = 0.02) and time (F4,120 = 27.06; p = 0.00). There is a tendency of interaction between TD and time (F4,120 = 2.30; p = 0.06). Statistical analysis showed that the performance of animals from control group is significantly better compared to thiamine deficient animals in the third (t = 2.7, p = 0.01) and the fourth (t = 3.6, p = 0.001) sessions. However, thiamine deficient animals were able to learn the task, as in the fifth session there is no significant difference (t = 1.0, p = 0.33) between the performances of animals from the two groups.

Table 1 shows the thalamic biochemical data concerning 5-HT and 5-HIAA concentrations and the [5-HIAA]/[5-HT] ratio. When the 5-HIAA content or [5-HIAA]/[5-HT] ratio data of C and TD groups are compared, a significant increase was found in thiamine deficient subjects for both parameters (t = 2.37, p = 0.02 and t = 2.08, p = 0.05, respectively), while for the 5-HT level no significant difference between thiamine deficient and control rats was found. Using a different experimental design, in which the biochemical parameters assessments were done prior to the appearance of neurological signs, Mousseau et al. [9] also found alterations in thalamic 5-HIAA level and 5-HIAA/5-HT ratio in brain of thiamine-deficient rats.

The absence of thiamine deficiency effect (t = 1.5, p = 0.14) on thalamic 5-HT concentration, observed in the present study, is in accordance with Mousseau et al. [9] who also observed no change in this parameter, after fourteen days of thiamine deficiency without recovery period. Langlais et al. [8] have observed increase in hypothalamic and cortex 5-HT concentrations even 7 months after the thiamine deficiency was reverted. Thus, these data indicate that: (i) there is difference in brain area vulnerability to thiamine deficiency effects on serotoninergic system and/or (ii) the effect of thiamine deficiency depends on the length of the recovery period. The effect of thiamine deficiency on thalamic 5-HIAA level could be explained by the following factors: (i) decrease in active transport of the 5-HIAA out of the brain and/or (ii) decrease in levels of the cytoplasmatic serotonin binding protein (SBP) and/or dysfunction in the mechanism of 5-HT releasing from SBP, which could lead to increase access of 5-HT to the catalobic enzyme monoamine oxidase (MAO) and/or (iii) a increase MAO activity. It is known that thiamine deficiency does not induce any changes in MAO activity [9,12]. On the other hand, in recent study, Eliash et al. [5] have shown that selective MAO inhibitor, rasagiline, had a neuroprotective effect on TD animals, reducing the neuronal lesion in thalamus. Further studies are necessary to clarify this issue. The first hypothesis is in accordance with the evidence that thiamine deficiency decreases transport of injected [14C]-HIAA out of the brain [17].

Regarding the second hypothesis, Plaitakis et al. [16] have shown that thiamine deficient animals present a decrease on SBP expression. This protein is related to 5-HT storage or its transport and protection from MAO degradation [3]. If thiamine deficiency affects SBP, it could decrease cytoplasmatic 5-HT. A tendency for a decrease in the 5-HT level was observed in the present study and the absence of a significant effect may indicate activation of a feed-back mechanism regulating 5-HT biosynthesis. However, even considering the occurrence of this putative mechanism to adjust the level of the 5-HT to physiological range, in order to maintain neurotransmission effectiveness, a significant increase induced by thiamine deficiency in the thalamic 5-HIAA/5-HT ratio was found.

As can be seen in Fig. 1B, thalamic 5-HIAA concentration is significantly correlated to animals’ latencies on the third session of the spatial behavioral test (r = 0.34, p = 0.04). It suggests that this biochemical parameter could play a role in the initial phase of the learning process. The present work shows for the first time a correlation between a serotonergic thalamic parameter and the animal performance in a spatial task, indicating that the higher the thalamic 5-HIAA concentration the worse the animal’s performance in the beginning of the acquisition process.

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Table 1
Mean ± S.E.M. of serotonin and 5-HIAA contents and 5-HIAA/5-HT ratio for TD and C groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>[5-HT] (ng/g ± S.E.M.)</th>
<th>[5-HIAA] (ng/g ± S.E.M.)</th>
<th>[5-HIAA]/[5-HT]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>161.35 ± 18.87</td>
<td>855.34 ± 73.95</td>
<td>6.59 ± 1.02</td>
</tr>
<tr>
<td>Thiamine deficient</td>
<td>123.09 ± 17.01</td>
<td>1154.25 ± 102.44*</td>
<td>15.11 ± 3.97*</td>
</tr>
</tbody>
</table>

* P < 0.05 vs. control.
References


