The purpose of this research was to study the activity of acetylcholinesterase in various regions of young and aged rat brain both before and after L-carnitine supplementation. Two groups of male albino rats were used for this study (4 and 24 months of age). L-carnitine was administered intraperitoneally 300 mg/kg/d for a period of 7, 14, and 21 days. The activity of acetylcholinesterase was measured in the cerebral cortex, the hippocampus, the hypothalamus, the striatum, and the cerebellum. Highly significant variation was observed in a duration-dependent manner in the hippocampus, the striatum, and the cortex of each aged rat after L-carnitine supplementation compared with the control group. Our results indicate that treatment of aged rats with L-carnitine restored the level of acetylcholinesterase.

MATERIALS AND METHODS

Male albino rats of the Wistar strain that belong to two different age groups aged 4 and 24 months (Group I and II, respectively) were used. Each age group was subdivided into four groups: one control group (Group Ia and Iia) and three experimental groups based on the duration of carnitine administration for 7 days (Groups Ib and Iib), 14 days (Group Ic and Iic), and 21 days (Group Id and IId). Experimental animals were administered L-carnitine (300 mg/kg body weight/d) intraperitoneally in 0.89% physiological saline. Control group animals received saline alone. After completion of duration-dependent treatment, all the animals were decapitated, the brains were quickly removed and dissected into the hypothalamus, the hippocampus, the cortex, the cerebellum, and the striatum according to Glowinski and Iversen's (9) method. Brain tissues were homogenized and used for the measurement of AChE.

RESULTS

The activity of AChE was high in young rats when compared with 24-month-old rats. Regional variation was observed in both groups. Maximum activity was observed in the striatum followed by the hippocampus, the cortex, and the hypothalamus. Aging produced significant alteration in certain regions such as the cortex, the hippocampus, the striatum (p < .001), the hypothalamus (p < .01), and the cerebellum (p < .05). L-carnitine was unable to produce profound changes in young rats, but it produced marked changes in aged rats. L-carnitine administration for 7 and 14 days produced slight differences, whereas treatment for 21 days produced significant changes in aged rats. L-carnitine was found to increase the activity of AChE in the hippocampus, the cortex, and the striatum (p < .001), but only a partial effect was observed in the hypothalamus (p < .01) and the cerebellum (p < .05). (See Table 1.)
we conclude from the present study that the administration ability of ACh after L-carnitine supplementation might be for the variation in ACh synthesis. An increase in the availability that could be indicative of different metabolic functions (17). The regional variability might be responsible for the variation in ACh synthesis. An increase in the availability of ACh after L-carnitine supplementation might be responsible for the increase in the activity of AChE. Finally, we conclude from the present study that the administration of L-carnitine ameliorates the age-related decrease of AChE activity.

**DISCUSSION**

Natural aging brings about a diffuse and multiple depletion of various biochemical markers in cholinergic neurons. A balance between the rate of synthesis, the rate of release, and the rate of utilization of neurotransmitters constitutes the main regulatory mechanism in neurotransmission. An age-related decrease in the activity of AChE observed in the present study in the hippocampus, the striatum, and the cortex is in agreement with previous reports (11,12). Loss of the postsynaptic enzyme activity of AChE may be responsible for defective AChE status. L-carnitine treatment preserved the activity of AChE significantly in the cortex, the hippocampus, and the striatum. It is known that the ACh content is highly related to the activity of AChE in these areas (13). Neurons require a high level of active acetate in the form of acetyl CoA for ACh synthesis. This process is stimulated by carnitine in a synergetic way in the brain (14).

The age-related decrease in AChE activity is thought to reflect the degeneration of cholinergic synapses (15). Acetyl CoA is synthesized within the mitochondria. Mechanisms for its transport into the cytoplasm have been considered as a possible regulating factor in ACh synthesis. Participation of carnitine in the passage of acetyl CoA through the mitochondrial membrane has been proposed by Tueck (16). Carnitine acetyl transferase (CarAT) is a mitochondrial enzyme found in the central nervous system and is located in the cholinergic nerve terminals. Intramitochondrial acetyl CoA is converted by CarAT to acetylcarnitine at the inner domain of the mitochondrial membrane. Acetylcarnitine may then diffuse to the outer mitochondrial surface and will be converted back to acetyl CoA, which is then available for ACh synthesis. Carnitine exhibits a differential regional distribution that could be indicative of different metabolic functions (17). The regional variability might be responsible for the variation in ACh synthesis. An increase in the availability of ACh after L-carnitine supplementation might be responsible for the increase in the activity of AChE. Finally, we conclude from the present study that the administration of L-carnitine ameliorates the age-related decrease of AChE activity.

**Table 1. Activity of Acetylcholinesterase in Various Regions of Young and Aged Rat Brain Before and After L-Carnitine Administration**

<table>
<thead>
<tr>
<th>Region</th>
<th>Young (Baseline)</th>
<th>Young (7 d)</th>
<th>Young (14 d)</th>
<th>Young (21 d)</th>
<th>Aged (Baseline)</th>
<th>Aged (7 d)</th>
<th>Aged (14 d)</th>
<th>Aged (21 d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortex</td>
<td>9.42 ± 0.52</td>
<td>9.50 ± 0.12</td>
<td>9.60 ± 0.22</td>
<td>9.74 ± 0.48</td>
<td>9.89 ± 0.48</td>
<td>10.46 ± 0.70</td>
<td>10.89 ± 0.45</td>
<td>11.34 ± 0.12</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>12.11 ± 0.43</td>
<td>12.28 ± 0.22</td>
<td>12.44 ± 0.52</td>
<td>12.59 ± 0.32</td>
<td>12.62 ± 0.42</td>
<td>12.89 ± 0.69</td>
<td>13.01 ± 0.55</td>
<td>13.11 ± 0.55</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>13.50 ± 0.48</td>
<td>13.61 ± 0.32</td>
<td>13.74 ± 0.59</td>
<td>13.86 ± 0.84</td>
<td>14.11 ± 0.38</td>
<td>4.33 ± 0.69</td>
<td>4.78 ± 0.84</td>
<td>4.89 ± 0.78</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>5.01 ± 0.67</td>
<td>5.12 ± 0.20</td>
<td>5.30 ± 0.34</td>
<td>5.49 ± 0.08</td>
<td>4.80 ± 0.42</td>
<td>12.62 ± 0.42</td>
<td>12.89 ± 0.69</td>
<td>13.01 ± 0.55</td>
</tr>
<tr>
<td>Striatum</td>
<td>42.38 ± 0.89</td>
<td>42.52 ± 0.32</td>
<td>42.71 ± 0.52</td>
<td>42.84 ± 0.42</td>
<td>40.84 ± 0.24</td>
<td>1.80 ± 0.52</td>
<td>41.32 ± 0.30</td>
<td>41.79 ± 0.67</td>
</tr>
</tbody>
</table>

Notes: This enzyme activity is measured as micromoles of substrate hydrolyzed/g/min. Values are expressed as mean ± SD for six animals in each group. On comparing groups Ib, Ic, and Id with group Ia and Groups Ib, Ic, and IId with Group Ia, *p < .05; **p < .01; ***p < .001. Comparison of Group Ila with Group Ia, *p < .01; ***p < .001. **p < .001. Comparison of Group IIa with Group Ia, *p < .05; **p < .01; ***p < .001. Comparison of Group IIa with Group Ia, *p < .01; ***p < .001.

**Acknowledgments**

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**References**


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