Selective Sparing of Human Nucleus Accumbens in Aging and Anoxia

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ABSTRACT: Objective: To investigate the effects of aging and anoxia on the nucleus accumbens. Methods: The number of neurons in nucleus accumbens and caudate nucleus in 35 patients over 65 and 35 under 65 years, all without neurological or psychiatric diseases were counted. Results: There was no statistically significant difference between the number of neurons in the accumbens in the two groups, but there was a decrease in the number of neurons in the elderly group. There was no reduction in volume of the neuronal nucleoli of the accumbens measured in 12 elderly patients compared to controls. These data suggest a sparing of the accumbens from changes associated with aging. There was relative preservation of the nucleus accumbens in 3 patients with anoxic encephalopathy. Conclusions: These results show that accumbens was resistant to both aging and anoxia, the mechanism of which is discussed.


Anoxia Group
There were 3 cases: the first was a man of 55 years suffering from cardiac arrest for 5 minutes; afterwards, he suffered from repeated pulmonary infections resulting in decortication and died 7 months after onset. The second, a man of 75 also suffering from repeated pulmonary infections with severe cerebral anoxia leading to vegetative existence, died 7 months after onset. The third was a woman of 63, suffering from uremia and acidosis leading to bradypnea with respiratory arrest who died after one month.

Histopathological Methods
Specimens were coronal sections, taken from the middle region of Ace (Figure 1) according to standard level suggested by von Brockhaus19 and Walsh et al.20 It was characterized by scarcity of perforating fibers, clustering of neurons and Islands of Calleja.21-22 These specimens were embedded in paraffin, cut at a thickness of 8 μm and stained with Luxol-fast-blue hematoxylin and eosin (LH&E) and Nissl stain.

Quantitative Assessment
A) Cell Counting
The cell population of the Ace and that of the head of caudate nucleus (CN) of subject group 1 were counted according to the method of Vonsattel et al.23 using a Nikon microscope giving a magnification of 400X. Each field covered a surface of 0.0087 mm² of the slide, which was defined by means of an eyepiece grid. The first 1 mm² from ependymal surface was skipped, and all “dead” areas (e.g., vessels or bundles of fibers) larger than 0.0015 mm² on the slides were deleted. For each case, the average number of neurons was counted in 15 fields of Ace as well as CN was taken.

B) Measurement of the nucleolar volume
This was done according to Mann’s view24 which regards nucleolar volume as an accurate reflection of the levels of protein synthesis in nerve cells. Neuronal nucleoli of Ace were measured by using an Image Analysis System (IBAS 2000). Twelve cases were randomly selected from the elderly group and 12 from the control group. For each case, 35 neuronal nucleoli were measured.

Table 1: Comparison of the Number of Neurons (cells/field) of Ace and CN in 2 Groups (X ± Sx).

<table>
<thead>
<tr>
<th>Age 20 to 65</th>
<th>Age greater than 65</th>
<th>Percentage difference (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ace 25.57 ± 0.53 (N = 35)</td>
<td>CN 18.88 ± 0.38 (N = 35)</td>
<td>1.6</td>
<td>0.2</td>
</tr>
</tbody>
</table>

| Ace 25.15 ± 0.51 | CN 16.53 ± 0.205 | 12.4 | 0.001 |

Table 2: Comparison of Mean Volume of the Nucleoli of Ace in 2 Groups (X ± Sx).

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>mean volume (μm)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>control</td>
<td>14</td>
<td>8.61 ± 0.41</td>
<td>&gt; 0.5</td>
</tr>
<tr>
<td>elderly</td>
<td>12</td>
<td>8.57 ± 0.41</td>
<td></td>
</tr>
</tbody>
</table>

Neuropathological Observation
For the anoxic group, both macroscopic and microscopic features of the Acc, CN and putamen were observed.

RESULTS
Quantitative Study
A) Cell Counting: There was no significant difference in the number of neurons in Ace of elderly subjects and that of control subjects (P > 0.2), while there was a definite decrease in the number of neurons in CN of the elderly group compared to controls (P < 0.001) (Table 1).

B) The volume of the nucleoli of Ace. There was again no difference between the elderly and control groups (Table 2).

Figure 1: A sketch of the coronal section from the middle region of nucleus accumbens.
Figure 2: A section from an anoxic encephalopathic brain showing relative preservation of the nucleus accumbens (arrows) with severe bilateral damage to the caudate nucleus.

Neuropathological Observation

Anoxic Group There were 2 cases of anoxic change at late stage where the Acc was relatively preserved bilaterally, while the caudatoputamen was severely damaged on both sides (Figure 2). Light microscopy revealed an absence of neurons with gliosis of CN, while there was partial preservation of neurons and only slight gliosis of Acc, (Figure 3). Another subject died in acute stage; the caudatoputamen showed complete necrosis, while Acc was completely spared (Figure 4). Light microscopy confirmed the macroscopic findings.

DISCUSSION

The fact that the number of neurons and the volume of the nucleoli of neurons of Acc of the elderly patients showed no reduction implies that aging has no deteriorating effect on that nucleus, while it has a definite effect on CN. There is a decreased number of neurons in elderly amygdala and in elderly hippocampus, the two structures have close connections with Acc, all three belonging to limbic system; this again supports the sparing of Acc in aging.

The symmetrical sparing of Acc in 3 cases of anoxic encephalopathy speaks eloquently for the sparing of this nucleus during anoxia. This cannot be explained by vascular factors, because the nucleus accumbens is supplied by the recurrent artery of Heubner, which also supplies the rest of the striatum (Perlmutter et al., Dunker et al., and Earpenter et al.). Furthermore, in anoxic encephalopathy, the selective vulnerability of the Purkinje cells of cerebellum, CA1, CA3 and endfolium of hippocampus and sparing of CA2 and the motor nuclei of the brain stem and anterior horn cells of the spinal cord cannot be due to impairment of blood supply and has been already explained by pathoclisis; this is also the mechanism in our three cases.

According to the report of Herkenham et al. and Myers et al. the Acc was completely intact, at the early stage of Huntington’s disease, while CN suffered degenerative change; at later stages, the Acc revealed only slight change, while the CN was almost completely destroyed. These data also point to the fact that Acc is resistant to degenerative processes.

Uemura et al. showed in their experiment on gerbils that NADPH-diaphorase positive neurons were strikingly preserved in the ischemic dorsolateral portion of the striatum, in which there was severe neuronal loss. Beal et al. did experimental research on rats with quinolinic acid and found that concentrations of both somatostatin and neuropeptide Y as well as the density of NADPH-diaphorase neurons and terminals are 2-3-fold higher in Acc than in the remainder of striatum. Ferrente et al. did research on six cases of Huntington’s disease and found the sparing of NADPH-diaphorase neurons of CN in a honeycomb pattern along a 50 μm-wide track in the middle of the CN, excluding the Acc. It may be concluded that the mechanism of the sparing of nucleus accumbens in aging, anoxia and Huntington’s disease is due to the presence of large amount of NADPH-diaphorase neurones in that nucleus.

Figure 3: A) Photomicrograph showing preserved neurons in nucleus accumbens of the brain shown in Figure 2. B) Complete loss of neurons with gliosis of the caudate nucleus in the brain shown in Figure 2. Magnification 400x.


