Title
Blood brain barrier: Selective regulation by sensory input

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Selective regulation of the blood–brain barrier by sensory input

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Little is known of the status of the blood–brain barrier in relation to physiological activity. Photic stimulation and convulsive agents have been shown to increase the uptake of radioactive sulfate from the blood into specific brain areas. We have previously found that as early as 1 h after monocular eyelid suturing in 1-day-old chicks, there are deficits in the rate of blood circulation through brain regions contralateral to the sutured eye.

This report indicates that changes in the permeability of the brain to specific circulating substances may occur in response to variations of sensory input.

The advantages of the avian visual system in such studies are: (1) The complete decussation of the avian optic tract in conjunction with the absence of major interhemispheric commissures reduces interactions between the two halves of the brain. (2) Metabolic deficits caused by monocular visual deprivation are largely confined to regions contralateral to the sutured eye. (3) The avian brain is symmetrical with no left or right dominance. (4) Regions of the brain that are primarily or secondarily innervated by the sutured eye can be compared to the corresponding unimpaired regions in the same animal. Thus, differences observed between paired experimental and control regions cannot be attributed to systemic hormonal variations (which should affect both regions equally) and must be directly caused by the experimental procedure. (5) As each animal serves as its own control, small differences between paired regions of a single animal can readily be distinguished.

The left eye of 1-day-old chicks was removed or sutured shut. Subsequently the penetrance into brain regions of [3,5-3H]tyrosine (57 Ci/m mole) (New England Nuclear Corp.), or methyl-[3H]choline chloride (2.34 Ci/m mole) relative to a freely diffusible compound, n-methyl-[14C]antipyrine (15.6 mCi/m mole), was determined by a method originally described by Oldendorf. Tyrosine and choline were chosen as they are both neurotransmitter precursors which can be actively taken up by cerebral tissue. 0.1 ml of a mixture, containing 15 µCi of either tritiated compound and 0.33 µCi of [14C]antipyrine, was injected into the heart. Ten seconds later, the chick was decapitated and optic lobes and cerebral hemispheres dissected out. At this short time interval no detectable amount of [3H]tyrosine was converted to volatile tritiated water. The rapid dissection of fresh tissue has been found to give more
reproducible results than the freezing and subsequent dissection of brain tissue. Individual lobes and hemispheres were dissolved by incubation at 60 °C for 5 h in 1 and 2 ml NCS tissue solubilizer (Amersham–Searle) respectively.

Eighteen milliliters standard toluene-based scintillation fluid was then added to each sample and the radioactivity in [3H] and [14C] determined. Quench corrections were made with an external standard and the correction of [3H] radioactivity for [14C] crossover was always less than 3% of the [3H]p counts. Efficiency of counting was 6–9% for [3H] and 35–41% for [14C]. The radioactivity due to antipyrine was between 900 and 2100 counts/min/100 mg wet tissue. As this varied from one bird to another, ratios were calculated for each individual bird before statistical analysis. The penetrance of the tritiated isotope relative to the [14C]antipyrine was calculated:

$$\frac{[3H]}{[14C]} \text{ in brain}$$

$$\frac{[3H]}{[14C]} \text{ of injected mixture}$$

Data were expressed as the ratio of penetrance in the right region (R) relative to the paired left region (L) of each bird. In order to avoid skewing data this ratio is presented as the natural logarithm (ln R/L).

One hour or 3 days after monocular suture, the relative penetrance of [3H] tyrosine into right brain region contralateral to the occluded eye, was increased (Table I). This increase was significant ($P < 0.05$) for both the optic lobe (receiving direct innervation from the treated eye) and cerebral hemisphere (secondarily associated with the treated eye). The increase was similar in magnitude to that found 1 h after major deafferentation of the optic lobe by eye removal (enucleation). The in-

### TABLE I

**Penetration of [3H]Tyrosine Relative to [14C]Antipyrine into Chick Brain Regions After Suturing or Removal of the Left Eye**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% Penetrance</th>
<th>ln R/L</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>1 h sutured (N = 13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optic lobes</td>
<td>23.3</td>
<td>24.8</td>
</tr>
<tr>
<td>Cerebral hemispheres</td>
<td>21.0</td>
<td>22.2</td>
</tr>
<tr>
<td>3 day sutured (N = 11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optic lobes</td>
<td>24.3</td>
<td>26.4</td>
</tr>
<tr>
<td>Cerebral hemispheres</td>
<td>19.7</td>
<td>20.9</td>
</tr>
<tr>
<td>1 h enucleated (N = 9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optic lobes</td>
<td>24.1</td>
<td>28.3</td>
</tr>
<tr>
<td>Cerebral hemispheres</td>
<td>24.3</td>
<td>25.2</td>
</tr>
<tr>
<td>3 day sutured, then unsutured for 1 h (N = 20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optic lobes</td>
<td>22.7</td>
<td>21.7</td>
</tr>
<tr>
<td>Cerebral hemispheres</td>
<td>19.4</td>
<td>19.2</td>
</tr>
</tbody>
</table>

* $P < 0.05$. 
creased penetrance of tyrosine into brain regions contralateral to the sutured eye is superimposed on a change in cerebral blood flow in the opposite direction\(^3\). Thus the net result of such increased penetrance is to maintain the amount of tyrosine entering the brain, in the face of reduced blood flow.

Three days after left eye closure, sutures were removed for 1 h and the penetrance of \([3^H]\)tyrosine again determined. The value for the right hemisphere returned to the level in the left hemisphere while the penetrance of tyrosine into the right optic lobe actually decreased to below that of the left lobe (Table I). Thus, changes in the blood–brain barrier caused by visual deprivation can be rapidly reversed after restoration of normal visual input.

No analogous changes in the permeability of \([3^H]\)choline were apparent either 1 h or 3 days after suture (Table II). This lack of a differential is probably not related to the greater penetrance of choline into brain tissue, as similar negative results have also been found for proline which has a lower penetrance (9–10\%) than either choline or tyrosine\(^5\). However, after monocular enucleation, the penetrance of choline was elevated in the contralateral optic lobe.

Changes in the uptake of chemicals in the blood by the brain are thus selective for certain components. The increased penetrance of tyrosine into brain areas receiving reduced sensory input is approximately as great as the reduction of the rate of cerebral blood flow in these areas\(^3\). This compensatory effect may ensure a constant supply of critical chemicals to the brain during variations in the velocity of cerebral blood flow.

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