Decreased Dopamine in the Retinas of Patients With Parkinson's Disease

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Dopamine and its metabolites dihydroxyphenylacetic acid and homovanillic acid were measured in the retinas of eight patients with Parkinson's disease who died. They were divided into two groups according to their last dose of levodopa therapy. One group of three patients had not received levodopa therapy for at least 5 days before death, and the other group of five patients had received therapy 2–15 hours before death. Each patient was matched with controls for delay between death and freezing. In the three patients without levodopa therapy, the retinal dopamine content was lower than normal. In the five patients who received levodopa therapy before death, the retinal dopamine content was similar to that in the controls. This study is the first direct evidence to the authors' knowledge that retinal dopamine concentration is decreased in Parkinson's disease, as it is in the nigrostriatal pathway. Invest Ophthalmol Vis Sci 31:2473–2475, 1990

Dopamine (DA) is a neurotransmitter in the retina. There are two pathologic disorders of the dopaminergic system: Parkinson's disease and diabetes. The former is characterized by a loss of dopaminergic neurons in the nigrostriatal pathway and a marked impairment in the motor system. In addition, there are clinical reports of alterations in the visual system of patients with parkinsonism. Increased latency of the visual-evoked potentials,4 5 abnormalities may be related to retinal DA depletion. However, more recent studies describe abnormal electroretinograms in these patients, either after flash stimulation or pattern stimulation.6 7 These results suggest that the visual system abnormalities may be related to retinal DA depletion. Dopaminergic neurons have been identified in the retinas of different animal species, including humans.8–11 A recent study identified retinal dopaminergic neurons in patients with parkinsonism by their tyrosine hydroxylase immunoreactivity; reduced DA...
innervation was observed in the central retina although the cell density was not changed. However, there are no published data to our knowledge on retinal DA content in these patients. Such data could help to elucidate the possible dopaminergic origin of abnormal visual responses in these patients.

Materials and Methods. We analyzed retinas from human eyes obtained post mortem from the Banque d’Yeux Nationale, located at the Laval University Medical Center. After postmortem enucleation, the eyes were kept at 4°C and frozen at −80°C. The retinas were dissected from the frozen eyes. We assessed DA and its metabolites, dihydroxyphenylacetic acid (DOPAC), and homovanillic acid (HVA), by high-performance liquid chromatography with electrochemical detection in duplicate. The observations on paired eyes were positively correlated and not independent (P < 0.0005). We therefore averaged the four observations for each subject.

Results. This study included retinas from eight patients with parkinsonism, divided into two groups according to their last dose of levodopa therapy (Table 1). Three patients had not received levodopa therapy before death. The other five patients received therapy 2–15 hr before death. Control subjects were chosen from our bank of 60 subjects who did not receive drugs that could influence the amounts of DA and its metabolites in the retina. The criteria for matching patients and controls was the delay between death and freezing; this has been shown to influence retinal DA content. We chose an interval of time corresponding to a change in retinal DA content of ±0.1 ng/mg of protein, which is equal to ±1.7 hr. In patients without levodopa therapy, two had a similar delay between death and freezing of the eyes (#51 and #43). Nine control subjects were matched, and a statistical analysis (t-test, one-tailed) showed a significant difference (P < 0.05) in the retinal DA content, but not in the metabolites DOPAC and HVA, between patients and controls. The retinal DA content in the patients was only 40% of the mean control value. For the third patient (#150), no statistical analysis was possible. Nevertheless, the retinal DA concentration was only 60% of that of matched control value (Table 1). These results suggest that retinal DA content is lower in patients with parkinsonism than in controls.

In the patients who received levodopa therapy, no statistical comparison with control values was done, since the total delays were different for each of these patients (Table 1). Nevertheless, a comparison with matched controls showed values similar to normal. These results suggest that levodopa therapy induced the synthesis of DA in these retinas.

Discussion. There is much evidence which attests to the decrease in the DA content in the nigrostriatal pathway in Parkinson’s disease, but the DA content in the retinas of patients with parkinsonism has not been measured previously to our knowledge. We report the first direct evidence that retinal DA content is decreased in Parkinson’s disease.

Evaluation of neurotransmitter levels in postmortem human tissue is difficult because alterations occur after death, and there are other potential differences among patients. In three patients with parkinsonism, retinal DA content was decreased. In the other patients, this was not the case. Drugs received before death may explain this apparent discrepancy. Treatment with the DA precursor levodopa leads to storage of DA into the central nervous system, which

Table 1. Concentration of DA and its metabolites DOPAC and HVA in the retina of parkinsonians and matched controls (mean ± SEM)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Parkinsonian patients</th>
<th>Controls</th>
<th>Parkinsonian patients</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DA</td>
<td>DOPAC</td>
<td>HVA</td>
<td>DA</td>
</tr>
<tr>
<td></td>
<td>ng/mg of protein</td>
<td>ng/mg of protein</td>
<td>ng/mg of protein</td>
<td>ng/mg of protein</td>
</tr>
<tr>
<td></td>
<td>T_e (km)</td>
<td>T_e + T_f (km)</td>
<td>L-Dopa (last dose)</td>
<td>T_e (km ± SD)</td>
</tr>
<tr>
<td>51/M/82</td>
<td>1.30</td>
<td>13.00</td>
<td>nil</td>
<td>0.57</td>
</tr>
<tr>
<td>43/F/82</td>
<td>4.30</td>
<td>13.45</td>
<td>29 days</td>
<td>0.44</td>
</tr>
<tr>
<td>150/F/77</td>
<td>7.45</td>
<td>18.45</td>
<td>9 days</td>
<td>0.54</td>
</tr>
</tbody>
</table>

T_e = delay between death and enucleation; T_f = delay between enucleation and freezing; ND = nondetectable.
may last a few days; there is almost complete depletion after 7 days or more. Therefore, patients who received their last dose of levodopa at least 5 days before death were considered to be free of exogenous levodopa.

In the striatum of these patients with parkinsonism, DA metabolites may vary in relation to the extent of the disease. Decreased retinal concentrations of metabolites may be the result of retinal DA neuronal degeneration, and an increase may be caused by increased DA turnover in the remaining retinal dopaminergic neurons. This may explain the variability observed in the retinal content of DOPAC and HVA.

In conclusion, this study gives the first direct evidence of decreased DA in the retinas of patients with Parkinson's disease. This may explain, at least in part, the abnormal visual responses of these patients, and the normalization seen after dopaminergic therapy.

**Key words:** retina, Parkinson's disease, dopamine, human

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**References**


