Wallerian Degeneration of Peripheral Nerve

Age-dependent Loss of Nerve Lipids*

J. H. Hofteig 1, P. N. Vo, and A. J. Yates

Neuropathology Division, Pathology Department, The Ohio State University College of Medicine, 473 West 12th Avenue, Columbus, OH 43210, USA

Summary. The age-dependent loss of the major peripheral nerve lipids (cholesterol, phospholipid, and total galactolipid) was quantitated over a period of 9 weeks of Wallerian degeneration induced by surgical transection of rabbit sciatic nerves in animals of several ages. Proportionate losses of these lipids were determined by calculating the content of each lipid on a per nerve and on a per gram fresh weight basis remaining after a given period of Wallerian degeneration as a percent of original normal values at several times following surgery. The proportionate loss of each lipid from the distal stump was the most prompt and the most complete in nerves transected at 2 weeks of age, and the least in nerves transected at 20 weeks of age. The prompter clearance of these lipids from younger than older degenerating nerve gives convincing evidence that the suggestion from light-microscopic studies of faster clearance of neural debris in younger than in older animals is correct. A possible relationship between these biochemical findings and the phenomenon of greater functional recovery from peripheral nerve injury in younger than in older subjects is discussed.

Key words: Wallerian degeneration - Peripheral nerves - Lipids - Age dependence - Myelin

Material and Methods

Wallerian degeneration was initiated by surgical transection of the left sciatic nerve as previously described [21] in New Zealand white rabbits at several ages: 2, 8, 12, and 20 weeks of age. Animals 2-12 weeks of age were unsexed; adults were all females. Nerve transection in 20-week-old rabbits was performed aseptically under combined fentanyl and droperidol (Innovar-Vet) as previously described [21]. Younger animals were anesthetized with i.m. administered xylazine (Rompun), 5 mg/kg b.w., and ketamine (Vetalar), 40 mg/kg b.w. The distal nerve stump was reflected distally and inserted into a pocket of fascia to prevent spontaneous reanastomosis of proximal and distal nerve stumps. At the time of nerve excision there was no gross sign of reinnervation of the degenerated distal stump by new axonal sprouts from the proximal stump. The right sciatic nerves from these animals served as controls. Animals aged 2 weeks at the time of surgery were returned to nursing does until killing or until 5-6 weeks of age. Animals were operated upon in sufficient numbers to yield approximately 1 g of pooled normal or transected nerve at each of several time intervals following surgery. In addition, nerves from unoperated animals were pooled at 2, 8, 12, and 20 weeks of age. These latter pooled specimens provided data for the zero time point of each series. The number of nerves committed to
Table 1. Number of sciatic nerves pooled for each extraction of major nerve lipids

<table>
<thead>
<tr>
<th>Series*</th>
<th>Time interval since beginning of each series</th>
<th>0th days</th>
<th>3rd days</th>
<th>1st week</th>
<th>2nd weeks</th>
<th>3rd weeks</th>
<th>4th weeks</th>
<th>5th weeks</th>
<th>6th weeks</th>
<th>7th weeks</th>
<th>8th weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-week:</td>
<td></td>
<td>48</td>
<td>34</td>
<td>13</td>
<td>23</td>
<td>12</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8-week:</td>
<td></td>
<td>10</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-week:</td>
<td></td>
<td>5</td>
<td>6</td>
<td>6</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adult:</td>
<td></td>
<td>6</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
</tbody>
</table>

* Series name indicates the age at which surgery was performed. Adult animals were 20 weeks old at the time of surgery.  
* Total number of intact control nerves obtained from unoperated rabbits.  
* Identical number of intact contralateral control and transected nerves pooled separately with the exception of the data point 4 weeks post surgery in the adult series at which time five transected nerves were pooled and six contralateral control nerves were pooled.  
* With the exception of contralateral control nerves at 4 weeks post surgery, these adult nerves were previously excised, extracted, and assayed by Yates and Thompson [21].

Results

The absolute contents (μmol per nerve) and absolute concentrations (μmol/g fresh weight) of the major myelin lipids were evaluated at each of the data points indicated in Table 1. The results of these evaluations have been summarized in Table 2 and Figs. 1–3.

In Table 2 the net accretion or loss of each major nerve lipid is tabulated 7 weeks after the beginning of the 2-, 8-, and 12-week series and 6 weeks after the beginning of the adult series. Lipid accretion in the normal nerves expressed on the basis of μmol per nerve over this 6–7-week period was greater in the two youngest series than in the 12-week series. Changes in lipid concentration expressed on the basis of μmol/g fresh weight showed more variation, reflecting the effects of changes in these lipids and other constituents.