Noradrenaline, adrenaline and tyrosine hydroxylase in adrenal medulla from Parkinsonian patients

Sir: Recent experimental\(^1\)\(^2\) and clinical\(^3\)\(^4\) studies have suggested that autografting of tissue from adrenal medulla into the striatum may improve symptoms resulting from nigro-striatal dopamine degeneration. Parkinson’s disease is associated with a severe dopaminergic and noradrenergic deficiency in the brain.\(^5\) Whether the disease affects central dopamine or noradrenaline levels, or peripheral levels as well, in particular those of the adrenal medulla, has not been reported and is of interest with regard to the usefulness of autografts in patients.\(^3\)^\(^4\)

Nine adrenal glands from subjects with no evidence of endocrinological, psychiatric or neurological disease (mean age: 75.3, SEM 1.9 years; post-mortem delay: 18.2, SEM 2.9 hours (range: 6.5–30)) and 12 adrenal glands from patients with Parkinson’s disease (mean age: 73.9, SEM 3 years; post-mortem delay: 20.6, SEM 1.7 hours (range 10–29)) were examined. The adrenal glands were stored at –70°C until adrenal medulla was dissected free from the cortex at –15°C, under a dissecting microscope. The whole tissue from each adrenal medulla was crushed into powder on dry ice, and biochemical assays were performed on an aliquot of the structure. Noradrenaline, adrenaline and dopamine were assayed by high performance liquid chromatography with electrochemical detection.\(^6\) The dopamine values are not mentioned as they were too low (in the order of 1 ng per mg tissue) and not reproducible. Tyrosine hydroxylase activity was assayed according to Pyunmirat et al.\(^7\)

The catecholamine content in adrenals from control subjects was in good agreement with studies in monkey\(^8\) (table). Adrenaline concentrations were four times higher than those of noradrenaline. In adrenal glands from patients with Parkinson’s disease, the levels of noradrenaline, adrenaline and tyrosine hydroxylase activity were slightly but not significantly decreased compared with control values (table). These observations contrast with the previously reported deficiency in tyrosine-hydroxylase,\(^6\) and suggest that the catecholaminergic systems in the adrenal medulla (unlike those in the brain)\(^6\) are not markedly affected in the disease. Thus the histopathological changes observed in adrenals in cases of Parkinson’s disease\(^10\) may not be associated with a massive catecholaminergic degeneration.

In monkey, the Parkinsonian syndrome induced by the administration of MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) is not associated with a catecholamine deficiency in adrenal gland catecholamines\(^3\)\(^8\). A difference from the central effects of the neurotoxin. Therefore, brain catecholaminergic neurons seem to have a specific vulnerability. The present data: (1) emphasise that adrenal autografts in the striatum of patients have the biochemical capacity to substitute a catecholaminergic activity; (2) suggest that the targets of the pathogenic process in Parkinson’s disease are mostly restricted to catecholaminergic neurons in the central nervous system; (3) are compatible with an efficiency of adrenal medulla autografts in patients with Parkinson’s disease. The mechanism by which these autografts provide a clinical improvement remains unknown: tyrosine hydroxylase might restore dopamine neurotransmission; implanted cells may reinnervate the host striatum; grafted cells might induce some recovery of dopamine neurons.\(^11\)

<table>
<thead>
<tr>
<th>Control (n = 9)</th>
<th>Parkinson (n = 12)</th>
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</thead>
<tbody>
<tr>
<td>Noradrenaline</td>
<td>194, 43</td>
</tr>
<tr>
<td>Adrenaline</td>
<td>866, 144</td>
</tr>
<tr>
<td>Tyrosine hydroxylase</td>
<td>71-3, 16-3</td>
</tr>
</tbody>
</table>

Values are expressed in ng/mg tissue for catecholamines and pg/h/mg tissue for tyrosine hydroxylase activity.

\(n = \) number of adrenal glands.

Data are the mean, SEM.

References


nerves are usually abnormal by the time spinal cord disease is apparent. However, Victor stated that the spinal cord initially is affected. A detailed neuropathological study of 41 patients with pernicious anaemia suggested that the peripheral nerves are rarely involved in early disease and that the earliest neuropathological evidence of Vitamin B12 deficiency is ballooning of large axons in the dorsal columns of the low cervical cord (spongiform change). At this stage a thin rim of myelin could be seen around the ballooned axons though there soon followed evidence of demyelination.

Neuropathological evidence, however, has shown that sub-clinical peripheral nerve involvement is common in patients with Vitamin B12 deficiency. Gilliatt et al. showed that antidromic lateral popliteal nerve action potentials were reduced at the knee in three out of four patients with pernicious anaemia and Cox-Klazinga and Endtz showed that distal conduction velocities to extensor digitorum brevis were reduced in 13 out of 20 such patients. Shorvon et al. stated that of 50 patients with pernicious anaemia, the eight who had signs or symptoms of spinal cord disease all had abnormal peripheral nerves on electrodiagnostic testing. Fine and Hallett reported the details of peripheral and central nerve conduction in two elderly (age range 73–77 years) and one younger schizophrenic patient with pernicious anaemia; all were seen within 4 months of the onset of their symptoms. The two elderly patients had absent sural nerve action potentials but they were relatively normal in the third. The somatosensory evoked potentials (SSEPs) were delayed in all three patients (N20 latencies, 22–23 ms) and despite poor sural nerve sensory action potentials, two of the cases had normal ERB’s point potentials (N9 latencies, 10–11 ms). They argued that the dorsal columns of the spinal cord were more sensitive to Vitamin B12 deficiency than the peripheral nerves. We present the case of a 72 year old spinsters with pernicious anaemia whose neurological symptoms came on rapidly. Electrodiagnostic testing showed normal peripheral nerve conduction but delayed SSEPs. Some improvement was seen after 9 months’ Vitamin B12 therapy.

Carmichael et al. (New Engl J Med, 1988, 254) have recently reported a significant decrease in noradrenaline, adrenaline and dopamine concentrations in adenal medullas of three patients with Parkinson’s disease compared with 15 controls. The discrepancies between their results and the present data may be due to differences in age and/or preterminal conditions between the subjects examined in the two investigations.

Delayed somatosensory evoked potentials in pernicious anaemia with intact peripheral nerves

Sir: Vitamin B12 deficiency is known to affect the spinal cord, brain, optic nerves and peripheral nerves. However, it is not clear which part of the neuraxis is most sensitive. Several authors state that the peripheral