Short Communication

Relatively High Levels of Dopamine in Nucleus accumbens of Levodopa Treated Patients with Parkinson's Disease

M. Goldstein 1, A. Lieberman 2, and J. Pearson 3

Departments of Psychiatry 1, Neurology 2 and Pathology 3, New York University Medical Center, New York, N.Y., U.S.A.

With 1 Figure

Received November 20, 1981

Summary

The dopamine levels were found to be low in the putamen and relatively high in the nucleus accumbens in two Parkinson disease patients treated with levodopa up to the time of their deaths. Tyrosine hydroxylase immunocytochemistry revealed a severe degeneration of the nigro-striatal dopamine neuronal system in both postmortem brains. The relatively high dopamine levels in the nucleus accumbens may be responsible for the occurrence of dyskinesias.

Introduction

Degeneration of nigro-striatal dopaminergic neurons is well established as the basis of Parkinson's disease (PD). Surviving neurons are capable of converting L-Dopa to dopamine (DA), thereby replenishing the missing DA in the basal ganglia. Dopamine in the nucleus accumbens and nucleus caudatus of some PD patients was found to be reduced to a smaller extent than in the putamen (Price et al., 1978). These findings suggest that in some patients, the putamenal DA is less well preserved compared to DA in the other regions of the striatum. In L-Dopa treated PD patients, the accumulation of DA in...
the various striatal regions will depend on the extent of DA neuronal survival. We have, therefore, analyzed the DA levels in specific regions of brains obtained from 2 PD patients who were treated with levodopa up to the time of their deaths. We have also analyzed the morphological changes in these postmortem brains immunocytochemically, by labelling DA neurons with specific antibodies to tyrosine hydroxylase (TH) (Markey et al., 1975).

Methods

The postmortem brains were obtained between 7–13 hours after the deaths of 2 PD patients. Age matched control brains were similarly obtained from 2 male patients who died of non-neurological diseases. Brains were dissected and samples taken for biochemical analysis were immediately frozen.

Five millimeter cerebral slices were made from postmortem brain and required tissues removed. The nucleus accumbens was defined as that region of the junction of the caudate nucleus and putamen inferior to the internal capsule and anterior to the anterior commissure. The putamen was sampled superlaterally between 2 and 7 millimeters deep to the external capsule at the level of the anterior commissure. The substantia nigra was sampled in a slice of mesencephalon cut coronal to the long axis of the brain stem which included the rostral part of the decussation of the superior cerebellar peduncle and caudal half of the red nucleus; the sample included reticulata and compacta, but did not encompass the paranigral region. The remainder of the dissected brain samples were fixed in a 10% buffered formalin. The catecholamine containing neurons were localized with the peroxidase-immunoperoxidase technique using specific antibodies to TH (Markey et al., 1979; Pearson et al., 1979). The catecholamines were assayed using high pressure liquid chromatography procedure with electrochemical detection (Hallman et al., 1978).

Patient 1 was a 64 year old man with a 14 year history of PD. The patient had been treated with levodopa for 12 years. He was on 750 mg/day of levodopa combined with 75 mg of carbidopa. The patient had a good initial response to levodopa, but within 3 years he developed diurnal oscillations in performance (“on-off” phenomena) associated with marked involuntary choreoathetoid movements. Over the next 9 years, despite medication, his condition worsened and he become bedbound. The involuntary movements persisted and he developed a moderate dementia. The patient died suddenly of a pulmonary embolus.

Patient 2 was a 72 year old man with a 10 year history of PD. The patient had been treated with levodopa for 10 years. He was on 1000 mg/day of levodopa combined with 100 mg of carbidopa. The patient had an excellent initial response to levodopa. He began to show a decreased response to levodopa after 5 years, at which time he developed involuntary choreoathetoid movements. After 9 years of treatment with levodopa, he developed diurnal