Cerebrospinal fluid lactate and pyruvate concentrations in patients with Parkinson's disease and mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS)

1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced parkinsonism is reportedly caused by impairment of the activity of complex I of the mitochondrial respiratory chain enzyme in the substantia nigra. Decreases in the activity of the mitochondrial respiratory chain enzyme complex I have been reported in the substantia nigra, skeletal muscle, and platelets of patients with Parkinson's disease. These results are consistent with observations performed on patients with mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) who show a decreased mitochondrial respiratory chain enzyme complex I level and high lactate concentrations in CSF and blood.

We examined whether CSF concentrations of lactate and pyruvate were increased in patients with Parkinson's disease or MELAS.

We studied 38 patients with Parkinson's disease (five untreated, 15 treated with levodopa, and 18 treated with amantadine or bromocriptine) and four patients with MELAS. All patients with Parkinson's disease were typical and had two or more symptoms of rigidity, resting tremor, akinesia, and postural instability. The controls had no headache, entrapment neuropathy, and cervical spondylosis. All patients were admitted to hospital and informed consent had been obtained. After an overnight fast and bed rest, CSF was collected at 9:00 am from the paracerebral cisterns, in a supine or seated reclining position. Lactate and pyruvate concentrations were determined according to the method of Asanuma et al. Statistical analysis was performed with one way ANOVA and Sheffe's test by StatView IV.

There were no significant differences in the CSF concentrations of lactate and pyruvate or the lactate/pyruvate ratio in the 38 patients with Parkinson's disease and the controls (table). There was no significant correlation of lactate or pyruvate concentrations with age in either the control group or in patients with Parkinson's disease. No significant difference was found between the subgroup treated with levodopa and the untreated patient subgroup. There were no significant differences between different durations of illness or severity of disease, which was classified into three grades according to Hoehn and Yahr: mild (stages 1 and 2), moderate (stage 3), and severe (stages 4 and 5). The patients with MELAS showed significantly higher lactate and pyruvate concentrations and a higher ratio than patients with Parkinson's disease and controls (table).

In patients with MELAS, high concentration of lactate in the CSF is an important finding for diagnosis of CNS mitochondrial impairments. Several reports showed normal blood lactate in patients with Parkinson's disease. These findings are compatible with investigations of mitochondrial complex I activity in various organs. The decrease in mitochondrial respiratory chain enzyme complex I activity of the substantia nigra in Parkinson's disease is very likely to be a characteristic finding of Parkinson's disease.

There may also be intimately associated with the onset of the disease. Przedborski et al. reported that levodopa treatment caused a significant reduction in complex I activity of the mitochondrial respiratory chain. But, in our study, there were no significant differences in lactate concentrations between the patients treated with levodopa and the untreated patients.

Hattori et al. also reported normal CSF lactate concentrations in nine patients with Parkinson's disease. Any slight decrease in complex I activity of the substantia nigra in Parkinson's disease may be localised to the substantia nigra.

We thank Professor T Sato, Juntendo University Hospital, for examination of the MELAS muscle.

Distribution of tenasin in human malignant gliomas is not related to cell proliferation

The knowledge that radiolabelled antitumor (TN) monoclonal antibodies are able to induce regression of human glioma xenografts prompted attempts at administration directly into tumours in vivo, to deliver cytotoxic radionuclides able to selectively bind to components of human gliomas. It has been shown, however, that TN is unusually expressed by most gliomas, and that its distribution being most heterogeneous in anaplastic astrocytomas and glioblastomas. To evaluate whether TN expression is related to cell proliferation, surgical samples from 75 malignant gliomas (48 anaplastic astrocytomas and 27 glioblastomas according to the World Health Organisation classification) underwent double staining immunohistochemical analysis with antibodies to: a. TN and b. Ki-67, that is, the Ki-67 positive nuclei. To evaluate whether TN expression is related to the presence of proliferating cells, as shown by the usual lack of nuclear labelling by the Ki-67 monoclonal antibody. As a general rule, TN expression was related to the histological texture, rather than the number of proliferating cells in different areas of single tumours. It is not associated with the Ki-67 expression, which is related to the Ki-67 positive nuclei. As a general rule, TN expression was related to the histological texture, rather than the number of proliferating cells in different areas of single tumours. It is not associated with the Ki-67 expression, which is related to the Ki-67 positive nuclei. However, TN expression was related to the histological texture, rather than the number of proliferating cells in different areas of single tumours. It is not associated with the Ki-67 expression, which is related to the Ki-67 positive nuclei. It was not associated with the Ki-67 expression, which is related to the Ki-67 positive nuclei.

Consider the following results for the distribution of tenasin in human malignant gliomas:

- **Brain**: The distribution of tenasin in human malignant gliomas was not related to cell proliferation.
- **Cerebrospinal fluid lactate and pyruvate concentrations**: There were no significant differences in CSF concentrations of lactate and pyruvate in patients with Parkinson's disease.
- **MELAS patients**: The CSF concentrations of lactate and pyruvate were increased in patients with MELAS.
- **Distribution of tenasin**: TN expression was related to the histological texture, rather than the number of proliferating cells in different areas of single tumours. It is not associated with the Ki-67 expression, which is related to the Ki-67 positive nuclei.
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J Neurol Neurosurg Psychiatry 1997 62: 290
doi: 10.1136/jnnp.62.3.290

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