Introduction

Dopaminergic drugs exert their action through activation of dopamine D1 and D2 receptors [1]. Changes of dopamine receptor density or affinity following antiparkinsonian drug therapy is suggested to underlie the development of long-term treatment complications in patients with PD [2]. However, evidence for this has not been provided.

In order to assess whether dopaminergic treatment results in changes of dopamine D2 receptors, it appears necessary to investigate previously untreated parkinsonian patients before and after long-term treatment. Here, first results are presented in de-novo PD patients before and after three to four months of oral treatment with levodopa or lisuride, using positron emission tomography (PET) and the radioligand [11C]raclopride (RACLO) [3]. Lisuride is an ergot derivative which binds as an agonist directly to dopamine D2 receptors [4] and can be effective in the treatment of early PD patients [5]. We also studied two other previously untreated PD patients before and after 6-8 hours continuous i.v. L-dopa infusion. In addition, the results of one healthy Rhesus monkey before and after a single i.v. bolus injection of both drugs on successive occasions are given. The results summarised here have been reported in more detail elsewhere [6].

Methods

PATIENTS

Nine newly diagnosed never before treated PD patients (age range 41-72 years; mean 51±9 SD years) were studied before and after a period of 3-4 months of stable oral treatment with lisuride. The lisuride dose varied among 0.8 and 1.2 mg/day. The interval between last drug administration and beginning of the measurement was 3-4 hours in eight subjects and 7 hours in
one. In 2 patients, showing a good clinical response to therapy, a third raclopride scan was performed four days after lisuride withdrawal.

Seven newly diagnosed never before treated PD patients (age range 42-70 years; mean 58±11 SD years) were studied before and after a period of 3-4 months of stable L-dopa + carbidopa oral treatment. The L-dopa dosage was 300 mg/day. The time interval between the last drug administration and beginning of the PET measurement was 3 to 4 hours in all subjects.

Two further PD patients (age 44 and 67 years) were studied before and after 6-8 hours continuous i.v. L-dopa infusion. The infusion rate during the last four hours was in one patient 60 mg L-dopa/hour and in the other 80 mg L-dopa/hour. 50 mg benzeraside were administered orally every 4 hours starting one hour before the beginning of the infusion.

The data of 14 healthy volunteer subjects in the age range between 39 and 68 years (mean age: 53±10 SD years) were used for comparison.

ANIMAL SCANS

Three scans were performed in a healthy female Rhesus monkey weighing 5 kg: the first in an unmedicated condition, the second and the third scan after i.v. bolus administration of 25 μg lisuride and 300 mg L-dopa respectively. Lisuride was injected 10 minutes and L-dopa 30 minutes before application of the tracer. 20 mg of the peripheral dopa-decarboxylase inhibitor benzeraside were also injected i.v. 15 minutes before L-dopa administration. Lisuride and L-dopa plasma levels were assessed using an HPLC method.

SCANNING PROCEDURE

Details of the scanning and data analysis procedure are described elsewhere [6]. The scanner used (CTI type 933/04-16, four rings, Siemens) records 7 planes simultaneously (transaxial resolution after reconstruction 9.5 mm FWHM, plane width 8 mm FWHM). [11C]raclopride [7] was infused intravenously in a dose ranging from 2.7 to 7 mCi. [11C]raclopride is a selective dopamine D2 receptor antagonist (3). Specific [11C]raclopride binding in the striatum was calculated in each subject using the ratio index: (Target ROI activity - Cerebellum activity)/Cerebellum activity

Mean index values for mean of right and left putamen and caudate nucleus were calculated between 35 and 58 minutes after tracer administration. Cerebellum ROI values were expressed in becquerels per milliliter and normalised to body weight (in grams) and injected activity (in becquerels).

Since [11C]raclopride binding in cerebellum is low or negligible, uptake ratios measured after the establishment of a pseudo-equilibrium throughout the brain, reflect density of dopamine D2 binding sites in striatum [3].