THE CONCENTRATION OF DOPAMINE, 5-HYDROXYTRYPTAMINE, AND SOME OF THEIR ACID METABOLITES IN THE BRAIN OF GENETICALLY DIABETIC RATS

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This is a report of the concentrations of DA, DOPAC, HVA, 5-HT, and 5-HIAA in the brain of spontaneously diabetic male Wistar rats. These rats showed a marked increase in blood and urine glucose, polydipsia, polyuria, and weight loss that had an onset 11–23 days earlier. Controls were litter mates with no hyperglycemia, glucosuria or weight reduction. The spontaneously diabetic rats showed a significant reduction of DOPAC in the striatum, and DOPAC, HVA, and 5HIAA in the olfactory tubercles (to 69, 61, 62, and 65% of their respective controls). No changes were found in the concentrations of DA or 5-HT. Thus the spontaneously diabetic rats showed a marked reduction in striatal and mesolimbic DA and mesolimbic 5-HT metabolism. This reduction in metabolism could be the consequence of a reduction in the formation of DA and 5-HT.

INTRODUCTION

Experimentally-induced diabetic rats show a decreased behavioural response to d-amphetamine (1) and marked reduction in the rate of accu-

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mulation of striatal DOPA after decarboxylase inhibition (2). Binding of tritiated spiroperidol is increased in the striatum and mesolimbic system of diabetic rats (2, 3). These changes in DOPA accumulation and spiroperidol binding were reversed after insulin administration (2). Similarly, the marked suppression of the locomotor actions of apomorphine and haloperidol seen in the streptozotocin-induced diabetic rat are reversed by insulin treatment (4). We report the concentrations of DA, 5-HT and some of their acid metabolites in brain regions of spontaneously diabetic rats. These findings were presented to the Canadian Federation of Biological Societies (5).

EXPERIMENTAL PROCEDURE

Genetically diabetic male Wistar rats originating from the Biobreeding Laboratories Colony (Ottawa, Canada) were bred in the laboratory (BB rats). The onset of diabetes was spontaneous and varied between 73 and 134 days of age. The BB diabetic rats showed significant increases in blood and urine glucose; polydipsia, polyuria and weight loss. The duration of diabetes was between 11–23 days prior to killing the rats. The control group was formed by male litter mates with no hyperglycemia, glucosuria, or weight reduction. The rats were killed by decapitation and the brain removed quickly. Following dissection the tissues were frozen in dry ice and weighed. Samples of striatum consisted mainly of the head of the caudate nucleus (mean weight, 63 mg), the hypothalamus was the translucent tissue found below the thalamus between the anterior and posterior commissura (mean weight, 29 mg); the olfactory tubercles (mean weight, 35 mg) and hippocampus (mean weight, 117 mg) were dissected. Every determination was made from the tissues of one rat.

Brain regional concentrations of DA, DOPAC, HVA, 5-HT, and 5-HIAA were determined using high performance liquid chromatography with electrochemical detection (6) with some modification (B. A. Bailey, unpublished). The apparatus consisted of a solvent delivery system (Model M45, Waters Associates, Inc., Mississauga, Ontario, Canada) equipped with a 20 μl loop sample injector (Model 7125, Rheodyne Inc., Cotati, CA). Separations were achieved in a 250 mm long and 4.6 mm internal diameter, 5 μm particle size column (Altex Ultrasphere ODS) and a 170 mm long pre-column (Whatman Inc., Clifton, NJ). The amines and metabolites were detected on a carbon paste electrode (Model TL-3, Bioanalytical Systems, West Lafayette, IN) set at 0.75 V versus a Ag/AgCl reference electrode. Standard and test curves were displayed on a dual channel recorder (BD41, Kipp and Zonen, Holland). The mobile phase, consisting of 0.1 M NaH₂PO₄, 1 mM sodium octyl sulphate, 1 mM disodium EDTA and 12% acetonitrile adjusted to pH 3.3 with phosphoric acid was filtered through a Buchner funnel (fritted glass pore, diameter 10–15 μm) and degassed by vacuum. Tissues were homogenized in 0.1 M HClO₄ containing 0.67 mM EDTA and 100 ng/ml of isoproterenol as internal standard. Following centrifugation (Eppendorf centrifuge, Model 5412) the supernatant was injected directly into the system. The corresponding calibration curves were prepared daily and the correction factor for each of the measured compounds with respect to the internal standard (2 ng of isoproterenol) was determined. The minimum detectable amounts were 20 pg for DA, DOPAC, HVA, and isoproterenol and 100 pg for 5-HT and 5-HIAA, with a signal to noise ratio >3.

Plasma and urine glucose concentrations were determined spectrophotometrically by the glucose oxidase and peroxidase method (7).