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The Area Method and the Table-Look-Up Method for [123I] Epidepride SPECT Studies of Dopamine D2 Receptors

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Receptor tracers with very high affinity are necessary for studying neuroreceptors in areas with low receptor concentrations. The slow kinetics, however, induces serious problems. [123I]Epidepride, a high affinity dopamine D2 tracer, here studied by the the area method1 and the table look-up method2, illustrates these problems.

Eight volunteers were studied using a Tomomatic 232. Scanning and blood sampling was performed intermittently up till 24 or 36 hours after [123I]Epidepride bolus injection. Blood sampling was in six volunteers performed as venous sampling, and in two also as arterial sampling. All samples were octanol extracted. Reproducible HPLC could only be performed on samples drawn up to 260 min after injection. ROI-set at the OM+1 and OM+5 levels were transposed on all time frames. Mean activity was scaled to the blood samples. The octanol-extracted plasma activity and HPLC metabolite corrected activity per ml were calculated. The areas below the brain and plasma curves were calculated by integration to 1500 minutes and to infinity using exponential extrapolation. Distribution volumes (Vd1500 and Vd) with and without metabolite correction were calculated for all regions. The two compartment table look up method of Iida et al.2 was also employed by a multiexponential fit of the arterial curve and calculating the ratio of a set of early and late time frames (selecting "early" = 25 min or 2h; "late" = 10h or 21h). Regional Vdtable was calculated by transposition of the ROI-set.

In striatum and cortex Vd1500 and Vd were significant larger than in the reference region, cerebellum. Metabolite correction increased Vd1500 and Vd by 30%. Vd1500 was 20% lower in striatum and 6-7% lower in cortical regions than Vd. Vd, calculated by the table look up method showed also an underestimation of Vd, relative to Vd, with all chosen pairs of frames.

We conclude 1' that the table look up method requiring prolonged arterial sampling and yielding low Vd values cannot be recommended, 2' that extrastriatal Vd can be accurately determined both to infinity, at 1500 min and even at shorter times (6 to 8 h). 3' Striatal Vd is massively influenced by the extrapolation and by the metabolite correction rendering accurate quantitation of doubtful value.
