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DETERMINATION OF DRUG CONCENTRATIONS IN SERUM AND DOPAMINE RECEPTOR OCCUPANCY IN BRAIN FOR OPTIMAL ANTIPSYCHOTIC DRUG THERAPY

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Evidence has been given that antipsychotic effects of dopamine receptor antagonists are associated with 60 and 80% striatal dopamine D2 and D3 receptor occupancy. Receptor occupancy correlates well with concentrations of the antipsychotic drugs in serum or plasma, much better than the dose. The latter is consistent with weak correlations between antipsychotic dose and serum concentrations and explained by the high interindividual variabilities in drug metabolism. Using positron emission tomography (PET) for in vivo determination of dopamine receptor occupancy in conjunction with drug concentration measurements “therapeutic windows” could be calculated for the atypical antipsychotic drugs amisulpride, risperidone and ziprasidone. On the other hand, analysis of drug concentrations in serum of schizophrenic patients who were treated with these drugs and who had responded to the medication confirmed the PET derived target levels and with some modifications also those of aripiprazole and clozapine. In vivo characterisation of dopamine receptor occupancy and measurement of blood levels should therefore be part of the clinical trials during the development of new antipsychotic drugs. They provide most relevant information for the later use of therapeutic drug monitoring to optimise the treatment of individual patients.

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