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PREDICTION OF STEADY-STATE OCCUPANCY OF THE SEROTONIN TRANSPORTER BASED ON SINGLE-DOSE OCCUPANCY: A [^{11}C]DASB PET STUDY

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Introduction: Clinical studies point toward a potential role of the serotonin transporter (SERT) binding as a predictor of clinical outcome in the treatment of depression. After long-term treatment with clinical doses of SSRIs the expected SERT occupancy is about 80%. Here, we were interested to investigate the relationship of SERT occupancy values between short- and longterm treatment.

Objectives: To test if the SERT occupancy at steady-state can be predicted based on the single dose occupancy by escitalopram (S-citalopram) or citalopram (racemate of S-citalopram and R-citalopram).

Methods: 18 patients with major depressive disorder received either escitalpram (10mg/d) or citalopram (20mg/d) in a double-blind, randomized, longitudinal study. They underwent three PET scans using the radioligand [^{11}C]DASB: PET1 baseline, PET2 6 hours after first drug intake and PET3 after three weeks of daily oral treatment. Occupancy of SERT was quantified in six subcortical regions: thalamus, N.caudatus, putamen, mibrain, dorsal raphe and median raphe nuclei. Data was analyzed by means of multiple linear regression models corrected for baseline SERT availability values using SPSS 15.0.

Results: Single dose occupancy of the SERT significantly predicted steady-state occupancy after three weeks in three regions: thalamus (r^2=0.45, p=0.009), N.caudatus (r^2= 0.4, p=0.006) and putamen (r^2=0.43, p=0.005). Other regions did not show significant relationships.

Conclusions: In this study we demonstrated that single-dose occupancy in SERT rich regions such as thalamus, N.caudatus and the putamen could serve as reliable predictors for steady-state occupancy. However, a linear model failed to explain the relationship in regions known for serotonergic cell origin.

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