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THE INFLUENCE OF TREATMENT-RESISTANCE ON THE SEROTONIN_{2A} RECEPTOR IN UNIPOLAR MELANCHOLIC DEPRESSION

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Introduction: Major depression is one of the most common mental diseases, and quite a number of patients are resistant to several psychopharmacological interventions, even when applying current treatment guidelines. To date, it remains unclear as to how the serotonergic system is implicated in treatment-resistance found in melancholically depressed patients.

Objectives & aims: In this study, we examined the involvement of post-synaptic 5-HT_{2A} receptors in the pathophysiology of treatment resistance in major depression with ¹²³I-5-I-R91150 SPECT, focusing on the frontal cortex and hippocampus.

Method: 15 unipolar antidepressant naïve (ADN) patients and 15 treatment-resistant depressed (TRD) patients, all of the melancholic subtype, matched for age and gender were studied. All subjects were antidepressant free when they underwent a static ¹²³I-5-I-R91150 SPECT scan.

Results: Compared to ADN patients, TRD patients displayed significantly less 5-HT_{2A} receptor binding index (BI) in the dorsal regions of the prefrontal cortex and in the anterior cingulate cortex. No hippocampal 5-HT_{2A} receptor BI differences were observed.

Conclusions: Our results suggest that when confronted with treatment resistance in melancholic depression the 5-HT_{2A} receptors in the DPFCA-ACC axis are significantly more down-regulated when compared to depressed ADN patients. This might to some extent explain the observed continued cognitive problems and might reflect the long-term serotonin depletion with reduced neurogenesis in treatment resistant patients.