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**DORSOMEDIAL AND PRECUNEUS ACTIVATION DURING SELF REFERENTIAL PROCESSING PREDICT LONG TERM REMISSION TO AGOMELATINE IN MAJOR DEPRESSION**

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**Introduction:** Less than half of depressed patients achieve remission. Identification of biological markers may help clinicians to predict remission and improve patient's treatment.

**Objectives:** To identify brain regions whose activity during self-referential processing at baseline could predict long-term remission among patients with Major Depressive Disorder (MDD) and to investigate the brain effects of Agomelatine.

**Method:** Nineteen acutely depressed patients and fourteen healthy controls performed self-referential judgments on emotional pictures during two fMRI sessions: before treatment and after 6 to 7 weeks of Agomelatine in patients or one week of placebo in controls. Patients were treated during 6 months and remission was assessed (HAM-D<sub>≤7</sub>).

**Results:** Activation in dorsomedial prefrontal cortex (dmPFC) and precuneus, during self-referential processing at baseline, was lower in future remitters than in non-remitters and remained stable after 6/7 weeks of treatment in both groups of patients. Pre-treatment activation of dmPFC and precuneus predicted clinical remission at 6 months with a sensitivity of 100% and a specificity of 71.6%. After 6-7 weeks of Agomelatine, the brain activation of MDD patients during self-referential processing was normalized i.e. decrease in the excessive activation of the dorsolateral prefrontal cortex and increase in the ventral anterior cingulate cortex activation.

**Conclusions:** Pre-treatment activation of precuneus and dmPFC during self-referential processing appears to be a valid predictor of clinical remission. Such results are consistent with the idea that cortical midline structures activity may play a major role in treatment outcome of MDD and may help developing biomarkers-based treatment of MDD.