

EARLY EFFECTS OF AGOMELATINE ON SELF-REFERENTIAL PROCESSING IN ACUTE DEPRESSED PATIENTS: A FMRI STUDY

P. Fossati¹, M. Jabourian², J. Laredo², N. Allailli¹, S. Lehericy³, P. Delaveau⁴

¹Psychiatry, CNRS USR 3246 & CR-ICM & AHP GH Pitié Salpêtrière, Paris, ²Neuroscience ISIS, Servier, Suresnes,

³Neuroradiology, CENIR & CR-ICM, ⁴Psychiatry, CNRS USR 3246 & CR-ICM, Paris, France

Increased Self-focus, the tendency to excessively appraise stimuli as strongly related to oneself, is a core feature of major depression. In major depressive disorder increased self-focus is associated with abnormal dorsal and ventral medial prefrontal activity as well as increased dorsolateral prefrontal activity.

Objective: Although Lemogne et al, 2010 suggested that Medial Prefrontal Activity does not change after reduction of depressive symptoms, sensitivity of brain regions involved in self-referential processing to antidepressant is unknown. The main goal here was to assess with fMRI early effects of agomelatine, on self-referential processing in depressed patients.

Methods: 25 acute depressed patients and 14 healthy controls were scanned before and after 7 days treatment, while performing self-referential processing task using emotional pictures. Patients were randomized to agomelatine 25mg/day (n=13) or placebo (n=12), healthy controls received placebo. Subjects were asked to evaluate pictures according to different conditions: *Self* (Does the picture relate to you?); *General* (Is the picture positive or negative?). Depression was assessed with Hamilton Scale.

Results: Depressed patients compared to controls at baseline showed hyperactivity in dorsolateral prefrontal cortex, dorsal anterior cingulate and ventrolateral prefrontal cortex (VLPFC). After 7 days treatment, Agomelatine, compared to placebo, normalized the hyperactivity of VLPFC to healthy volunteers' level.

Conclusion: Agomelatine targets specific brain structures, namely VLPFC, involved in automatic regulation of emotion during self-referential processing. These changes in brain activity at day 7 could contribute to the early clinical effects of agomelatine, suggesting an early set up of the brain for long term response and remission of depression.