### Abnormal neural filtering of irrelevant visual information in depression

Martin Desseilles, MD <sup>1,2,4,5</sup>; Evelyne Balteau, PhD <sup>1</sup>; Virginie Sterpenich, PhD <sup>1</sup>;

Thien Thanh Dang-Vu, MD, PhD <sup>1,3</sup>; Annabelle Darsaud, PhD <sup>1</sup>; Gilles Vandewalle,

PhD<sup>1</sup>; Geneviève Albouy, PhD<sup>1</sup>; Eric Salmon, MD, PhD<sup>1,3</sup>; Fréderic Peters, PhD<sup>1</sup>;

Christina Schmidt, MPsych<sup>1</sup>; Manuel Schabus, PhD<sup>1</sup>; Stephen Gais, PhD<sup>1</sup>; Christian

Degueldre, MSc<sup>1</sup>; Christophe Phillips, PhD<sup>1</sup>; Andre Luxen, PhD<sup>1</sup>; Marc Ansseau,

MD, PhD<sup>2</sup>; Pierre Maquet, MD, PhD<sup>1,3</sup>; Sophie Schwartz, PhD<sup>4,5</sup>

1 Cyclotron Research Centre, University of Liège, Belgium

2 Department of Psychiatry, University of Liège, Belgium

3 Department of Neurology, University of Liège, Belgium

4 Department of Neurosciences, University of Geneva, Switzerland

5 Geneva Neuroscience Center, University of Geneva, Switzerland

#### Introduction

The pathophysiology of major depressive disorder (MDD) includes both affective and cognitive dysfunctions. We aimed to clarify how regions regulating affective processing interact with those involved in attention, and how such interaction impacts on perceptual processing within sensory cortices. Based on previous work showing that top-down influences from attention can determine the processing of external inputs within early sensory cortices, we tested with functional MRI (fMRI) whether MDD alters attentional ('top-down') effects on the neural filtering of irrelevant, non-emotional visual stimuli.

#### Methods

The present 3 Tesla fMRI study was conducted in 14 non-medicated patients with a first episode of unipolar MDD and 14 matched controls. During scanning, subjects performed two tasks imposing two different levels of attentional load at fixation (easy or difficult), while irrelevant colored stimuli were presented in the periphery. The low load task required a key-press for any red target irrespective of its orientation. The high load task (difficult, conjunction) required a key-press for any upright yellow target or upside-down blue target. Only the task instructions distinguished the high load and low load conditions for the central task. The peripheral colored stimuli were always irrelevant to the central task, and participants were instructed to ignore them.

## Results

For High versus Low attentional load contrast we found that both populations strongly engaged inferior frontal and superior parietal regions during increased attentional load at fixation, consistent with the recruitment of a distributed attentional network subtending top-down influence under higher-load condition in all participants.

For Low versus High attentional load contrast we found that controls compared to MDD patients increased response in visual cortices corresponding to the color-responsive area V4 (Figure A). The latter activation was specifically driven by enhanced response to peripheral colored stimuli during low load compared to high load condition in the controls (Figure B). For the same contrast (Low > High load), MDD patients showed a significant attenuation of BOLD response in bilateral ventral medial prefrontal frontal (vmPFC) region during high attentional load, encompassing the medial OFC and rostral/subgenual cingulate cortex (SgAcc; Figure C). This modulation of brain response in the patients was driven by the attentional task, independently of the presence or absence of peripheral stimuli (Figure D).

We found that functional connectivity was increased between the right IPS and V4, as well as between the right frontal cortex and V4 (p < 0.001), selectively in the context of low attentional load in controls but not in patients.

# Conclusion

Analyses of fMRI data revealed that MDD patients show (i) an abnormal filtering of irrelevant information in visual cortex, (ii) an altered functional connectivity between fronto-parietal networks and visual cortices, and (iii) a hyperactivity in subgenual cingulate/medial orbitofrontal cortex that was modulated by attentional load.

These results demonstrate that biological abnormalities contribute to the cognitive deficits seen in major depression, and clarify how neural networks implicated in mood regulation influence executive control and perceptual processes.

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## Figure

