

## Editorial

# Antidepressants Again

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## Editorial

The recent months have brought some interesting publications, which contribute to the long-term and unresolved debate concerning the role of antidepressant treatment in depression. It is an important area as not all patients treated for Major Depressive Disorder (MDD) respond to currently available pharmacological therapies.

Firstly, there is a large-scale, three-centre study by Hollon et al [1] on the effects of Cognitive Therapy (CT) in combination with Antidepressant Medications (ADM) as compared with antidepressants alone on both remission and recovery in 452 patients with chronic or recurrent MDD. The sample derived from a total of 2097 patients screened for the study; they met the inclusion criteria of DSM-IV MDD and a score of 14 or more on the 17-point Hamilton Rating Scale for Depression (HRSD). The latter and the Longitudinal Interval Follow-up Evaluation (LIFE) were used for the evaluations of recovery within up to 42 months. ADM was personalised with up to four classes of ADM used, including serotonin reuptake inhibitors, serotonin-noradrenalin reuptake inhibitors, tricyclic antidepressants and monoamine oxidase inhibitors. Cognitive therapy (Beck model) entailed 50-minute sessions delivered twice weekly for the first fortnight and then weekly and monthly, being adjusted to the individual patient's needs. Remission rates were 63.6% for ADM+CT vs. 60.3% for ADM at 12 months, and 80.1% for ADM+CT vs. 77.2% for ADM at 18 months of treatment (both  $P > 0.05$ ). The rate of recovery was improved by ADM+CT when compared with ADM alone (72.6% vs. 62.5%;  $P = 0.01$ ) but this effect showed significant interactions with severity and chronicity, and as a result, statistically significant beneficial effects of combined treatment (ADM+CT) were limited to patients with severe nonchronic MDD ( $P = 0.001$ ). In addition, fewer ADM+CT patients had side effects when compared with ADM alone (49 vs. 71,  $P < 0.05$ ). The study has an acknowledged limitation as there is no CT alone group to provide some insight into the benefits of cognitive monotherapy vs. ADM alone. The authors draw measured conclusions pointing out that the combined treatment (ADM-CT) has positive effects in a subgroup of patients with severe nonchronic forms of depression. They also reflect that ADM and CT work through different mechanisms.

Here, it might be tempting to comment on the still existing schism between the biological psychiatry of depression and the psychotherapy school, with the latter being concerned with 'the

medicalisation misery' [2]. Instead, I draw your attention to the paper by McRae, Rekshan, Williams, Cooper and Gross [3] in which the authors find some adaptive changes in emotion regulation caused by ADM treatment (without psychotherapy).

The above study was conducted in a short term of eight weeks in a large group of 1008 adult patients with MDD. The participants were treated with either selective serotonin reuptake inhibitors or serotonin-noradrenaline reuptake inhibitors at doses adjusted according to clinical routine. The treatment excluded psychotherapy over the eight weeks of study reported. HRSD and Emotion Regulation Questionnaire by Gross and John were used to assess treatment outcomes. The authors report improvements in emotion regulation, and in particular they demonstrate significant decreases in emotion suppression and increases in reappraisal as compared with the baseline before the ADM treatment. Emotion suppression is a form of negative maladaptive emotion regulation which associates with depressive disorders, while reappraisal is adaptive and positive. This work demonstrates that ADM alone can result in a change from maladaptive to adaptive emotion regulation in patients with depression as observed in this large-sample short term study. Although the duration of the observation is an acknowledged limitation of this research which deserves a long-term follow up, it is most interesting to know that antidepressant treatment alone and without psychotherapy can positively influence emotion regulation in MDD.

This links rather neatly with another recent paper, a systematic meta-analysis by Ma [4] who reviewed some sixty fMRI studies conducted on 1569 participants (both patients with depression and healthy volunteers) in order to assess the effects of antidepressants on brain regional activity in the context of emotion regulation. The author concludes that the anterior cingulate cortex, amygdala and thalamus increased their respective activities in response to positive emotions but reduced activity in response to negative emotions following ADM. In particular, ADM increased the activity of the dorso-lateral prefrontal cortex (essential in mediating emotion regulation) during both negative and positive emotions in patients, which is interpreted as an ADM-dependent increase in the engagement of the regulatory mechanism that controls emotions.

The above scientific evidence of antidepressant effects on emotional processing is a major step forward in our understanding of the brain processes involved in the response to pharmacological treatment of depression. It adds an important extra layer of knowledge to what neurobiologists have known for quite a while that antidepressants improve neuroplasticity, an intrinsic feature of the brain that is impaired by depression [5].

Linking the established neurobiology opinions on the cellular and molecular mechanisms of antidepressants with the most recent findings about ADM influence on emotion regulation, and the effects of combined antidepressant and cognitive therapy, contributes to the debate concerning optimisation of MDD treatment. It is an important

debate as over 350 million people suffer from depression world-wide (WHO, October 2012).

## References

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