EDITORIAL

Brain Structural and Functional Effects of Psychopharmacological Treatment in the Major PsychosesAntonio Vita^{1,*} and Paolo Brambilla^{2,3,*}

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The relationship between pharmacological treatment and structural and functional brain characteristics in the major psychoses is a matter of lively debate.

On one hand, a better knowledge of the morpho-functional effects of psychotropic drugs may help to refine the pathophysiological hypotheses of major psychoses, individuating the cerebral structures and circuitries that are involved in the diseases. On the other hand, it may be of help to guide the administration of the best antipsychotic, antidepressant or mood stabilizing medication at a personalized level in subjects with schizophrenic or affective psychoses.

Furthermore, in the case of schizophrenia, a better definition of the role played by antipsychotic treatment on the progressive trajectory of brain abnormalities is crucial to understand the nature of such abnormalities and whether they could be moderated or prevented. In this respect, contrasting data have emerged on the role of First Generation vs Second Generation Antipsychotics.

Conversely, more consistent evidence of a normalizing effect of functional and structural brain changes in depressive and bipolar disorder has been reported for mood stabilizing compounds.

From a clinical viewpoint, some evidence exists on the relationship between brain structural and functional changes and clinical response to psychotropic medication. This may help to identify *a priori* patients who will benefit from a given treatment, a possibility especially useful for costly treatments or treatment with complex management or serious side effect profiles. A thorough understanding of the *pros* and *cons* of currently available pharmacological treatments is critical to better define the clinical features of treatment-refractory patients and guide the development of new treatment strategies.

Given the high number of papers that have appeared on brain structural and functional effects of psychopharmacological treatment in the major psychoses, often reporting contrasting results, a systematic and critical review of the available literature on this topic seemed timely and useful. This has been completed for this thematic issue of *Current Neuropharmacology* by some of the most recognized and respected experts in the field.

In the issue, R. Roiz-Santianez *et al.*, review existing neuroimaging studies addressing the impact of antipsychotic drug treatment on brain changes in schizophrenia. Longitudinal Magnetic Resonance Imaging (MRI) studies do not reveal a consistent pattern of antipsychotic treatment effects on brain structure in schizophrenia, and most of the studies do not find a linear relationship between the degree of exposure to antipsychotic medication and progressive brain changes.

P. De Rossi *et al.*, review brain functional changes induced by antipsychotic drugs as assessed by modern functional neuroimaging techniques (i.e. functional MRI, Positron Emission Tomography (PET), Single Photon Emission Tomography (SPECT) and MR spectroscopy (MRS)). Based on this review, the authors suggest that a network-based perspective and a functional connectivity approach are needed to fill the currently existing gap of knowledge in the field of the mechanisms of action of psychotropic drugs beyond the effects on single neurotransmitter systems.

C. McDonald analyzes MRI and Diffusion Tensor Imaging (DTI) studies of cerebral structural effects of psychotropic drugs used for the treatment of bipolar disorder. The studies which report positive findings tend to form a relatively consistent picture suggesting that lithium and antiepileptic mood stabilizer use is associated with increased gray matter volume, especially in limbic structures, consistent with the neuroprotective characteristics of these medications identified by preclinical studies. There is less support for an effect of antipsychotic or antidepressant medication on brain structure.

N. Dusi *et al.*, focus their attention on brain structures which are found to be altered in depressive disorder, particularly those located in the prefrontal and orbitofrontal cortex and the medial temporal areas. These volumetric alterations may also represent biological predictors of response to pharmacological treatment, a finding with great clinical relevance.

M. Wessa and G. Lois review brain functional alterations in major depression, especially located in the limbic and prefrontal neural networks, which are mainly linked to the altered emotional processing observed in major depressive patients. Results from pharmacological fMRI studies in depressed patients show a reduction of limbic activation in response to emotional stimuli during treatment.

We believe that the findings of the studies reviewed in this special issue of *Current Neuropharmacology* will be of great interest, both for the clinician and the researcher and may stimulate new focused research in this fascinating clinical and translational neuroscientific area.

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