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Do Antipsychotic Medications Affect Cortical Thinning?

Answers from a new analysis in Biological Psychiatry

Philadelphia, PA, September 3, 2015 – People diagnosed with schizophrenia critically rely upon treatment with antipsychotic medications to manage their symptoms and help them function at home and in the workplace.

But despite their benefits, antipsychotic medications might also have some negative effects on brain structure or function when taken for long periods of time.

In fact, “the role played by antipsychotic treatment on the pathophysiologic trajectory of brain abnormalities in schizophrenia is currently a matter of lively debate,” explains Dr. Antonio Vita, Professor of Psychiatry at the University of Brescia, Director of the Psychiatric Unit at Spedali Civili Hospital, and first author on a study addressing this topic in the current issue of *Biological Psychiatry*.

It is clear from cross-sectional and longitudinal magnetic resonance imaging studies that patients with schizophrenia show progressive structural brain abnormalities. The findings indicate that lower gray matter volume or greater gray matter loss over time are associated with the duration of antipsychotic treatment or cumulative antipsychotic intake.

However, most of this prior literature did not take into account the potential impact of whether a patient was prescribed first-generation or second-generation antipsychotics. These two classes of drugs are equally effective treatments, but have different pharmacological properties and therefore, work differently in the body.

Vita and his colleagues compiled data from eighteen imaging studies, resulting in a total of 1155 patients with schizophrenia and 911 healthy control subjects, in order to evaluate the influence of antipsychotic type on gray matter changes over time.

As expected, their analysis confirmed that patients with schizophrenia show progressive cortical gray matter loss relative to healthy controls, which is related to cumulative antipsychotic intake during the interval between imaging scans.

Interestingly, greater gray matter loss was correlated with higher mean daily dose in studies including patients treated with first-generation antipsychotics, whereas the opposite effect, i.e., less progressive loss, was observed in studies including only patients treated with second-generation antipsychotics.

This is consistent with the results of several studies in animals and some clinical studies with patients indicating that second-generation antipsychotics may have a neuroprotective effect on the brain.

“The possibility that antipsychotic medications might have long-term effects on brain structure or function that might be beneficial or detrimental is an important issue deserving further study as many people treated with these medications will remain on them for several decades,” said Dr. John Krystal, Editor of *Biological Psychiatry*.

“Although this is a clinically meaningful result, many issues remain to be clarified: for instance, we still do not know whether the effects on the brain of antipsychotics vary as a function of age and stage of illness, or whether they may occur only when a certain threshold of exposure (daily dose or cumulative dose) is reached,” added Vita.

“Clarification of these issues will have crucial importance in the clinical management of schizophrenia and will allow a better understanding of the mechanisms underlying the progression of structural brain abnormalities in the disease.”

The article is “The Effect of Antipsychotic Treatment on Cortical Gray Matter Changes in Schizophrenia: Does the Class Matter? A Meta-analysis and Meta-regression of Longitudinal Magnetic Resonance Imaging Studies” by Antonio Vita, Luca De Peri, Giacomo Deste, Stefano Barlati, and Emilio Sacchetti (doi: 10.1016/j.biopsych.2015.02.008). The article appears in *Biological Psychiatry*, Volume 78, Issue 6 (September 15, 2015), published by Elsevier.

Notes for editors

Full text of the article is available to credentialed journalists upon request; contact Rhiannon Bugno at +1 214 648 0880 or Biol.Psych@utsouthwestern.edu. Journalists wishing to interview the authors may contact Antonio Vita, M.D., Ph.D., at +39 030 2184856 or vita@med.unibs.it.

The authors' affiliations, and disclosures of financial and conflicts of interests are available in the article.

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The journal publishes novel results of original research which represent an important new lead or significant impact on the field, particularly those addressing genetic and environmental risk factors, neural circuitry and neurochemistry, and important new therapeutic approaches. Reviews and commentaries that focus on topics of current research and interest are also encouraged.

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