

How can we improve the efficacy of antipsychotics in the era of personalized pharmacotherapy?

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The clinical context of the administration and dosage of antipsychotics may influence their efficacy, reported Philippe Vincent and Édouard Kouassi, from the Institut universitaire en santé mentale de Montréal and Université de Montréal. The efficacy of most antipsychotics depends on their pharmacokinetics, or their ability to get into the bloodstream after being absorbed. Vincent and Kouassi are responding in *The Lancet* to Stefan Leucht, who conducted a meta-analysis of over 200 articles on the efficacy and side effects of 15 antipsychotics. According to the data Leucht collected, five of the most recent second-generation antipsychotics (ziprasidone, aripiprazole, asenapine, iloperidone and lurasidone) were among the drugs with the lowest efficacy, despite having similar pharmacological properties compared to first-generation or to other second-generation antipsychotics. Leucht published his finding in *The Lancet* in September 2013; his article did not give any explanations for this surprising result.

Some [antipsychotics](#) require strict adherence on the part of patients. According to Vincent and Kouassi, specific conditions are required for some medications to be effectively absorbed. "For example, ziprasidone needs to be taken twice a day with a meal of 500 calories, whereas asenapine must absolutely melt under the tongue, and the patient must abstain from swallowing it, drinking, eating or smoking for 10 minutes afterward," Vincent said "This is a major challenge since more than one half of people with psychotic disorders do not take their medication as

prescribed."

Vincent and Kouassi also state that the titration of these antipsychotics is a challenge in clinical practice, as it is difficult to obtain the optimal therapeutic dosage on the first try. Doctors therefore have to use an empirical approach. "The major side effects show up well before the optimum therapeutic dose is determined, which can discourage patients from continuing their treatment," Kouassi said. "Doctors have to keep trying, as the pharmacokinetics of antipsychotic compounds differ for each patient. By adjusting the dose of a medication based on the degree of blood absorption, distribution, metabolism and elimination in a patient, doctors can personalize treatment, which becomes that much more effective. We maintain that all antipsychotics, with the exception of clozapine, can achieve the same efficacy if they reach comparable blood levels."

If the studies reported by Leucht had compared medications in terms of their blood concentrations, we would have more accurate conclusions about the efficacy of the medication. "This confirms that the future of psychiatric medicine will involve personalizing patient care," Vincent said.

More information: 1. Vincent P, Kouassi E. Efficacy of antipsychotic drugs for schizophrenia (Letter to Editors). *The Lancet* – 7 December 2013.

2. Leucht S, Cipriani A, Spineli L, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet* 2013;382:951-62.

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