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## EDITORIAL

### Pharmacogenetics in psychiatry: the need to prove its benefits<sup>☆</sup>

### Farmacogenética en psiquiatría: la necesidad de demostrar sus beneficios

María Jesús Arranz<sup>a,\*</sup>, Blanca Gutiérrez<sup>b</sup>

<sup>a</sup> Department of Psychosis Studies, Institute of Psychiatry, King's College, London, United Kingdom

<sup>b</sup> CIBERSAM, Instituto de Neurociencias, Universidad de Granada, Granada, Spain

Genetic advances in the field of psychiatry have been boosted by the development of high-throughput methodologies. New genotyping technologies, cheaper and faster, have facilitated the identification of a number of genes involved in pharmacokinetic and pharmacodynamic processes that contribute to the variability observed in response to pharmacotherapy.

Pharmacogenetic research in kinetic genes has identified several functional polymorphisms (relatively common mutations) in cytochrome-P450 (CYP) enzymes that render the enzyme protein either inactive, slow, or ultra-rapid. These variants directly influence drug plasma levels and, as demonstrated by numerous studies,<sup>1</sup> are implicated in the development of treatment associated side-effects. It has been estimated that the adjustment of doses according to the patients' genetically determined metabolic status will have a positive effect on both, drug efficacy (up to 15% improvement) and safety (10–20% decrease in adverse reactions).<sup>2</sup> In addition, pharmacogenetic research has identified several genes implicated in antipsychotic and antidepressant pathways that are associated with treatment response. Genetic variants in dopamine and serotonin receptors and transporters have been associated with the level of efficacy and drug-induced adverse reactions. Several tests for the genetic determination of the metabolic status of patients, prediction of the level of efficacy, and risk

of developing side-effects are already available in commercial and clinical laboratories. CYP functional polymorphisms aside, most of these tests are of limited predictive value, never reaching 100% certainty (and far from it). This is not surprising given that treatment response in psychiatric patients is determined not only by genetic factors, but environmental and clinical factors also play important roles<sup>3</sup> in treatment variability. Nevertheless, genetic information has the potential to improve treatment response by helping to select the most beneficial treatment at the right dose for patients according to their genetic propensities.

In spite of this, the use of pharmacogenetic information to assist drug selection in psychiatry is minimal. Lack of information and limited access to clinical or reference laboratories with capabilities for pharmacogenetic testing are partly to blame. However, the main reason that may hinder the use of pharmacogenetic tests is the lack of supporting research assessing the benefits. To date, no study has investigated if the adjustment of clinical doses according to the patient's CYP genetic variants results in a reduction of the incidence of side-effects, and in an improvement of response. Similarly, no prospective study has proved that the use of pharmacogenetic prediction tests for the selection of drug type positively influences the level of efficacy that is reflected in a reduction of hospitalization time, improvement of social functioning, etc. Thus, there is little supporting evidence encouraging the use of pharmacogenetic information in clinical settings. Without a prospective trial to prove the clinical and economical benefits of using genetic information to aid drug and dose selection, clinicians are right to doubt the benefits of a pharmacogenetic approach. The affluence of commercial tests offering a variety of genetic

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\* Corresponding author.

E-mail address: [maria.arranz@kcl.ac.uk](mailto:maria.arranz@kcl.ac.uk) (M.J. Arranz).

information, sometimes poorly translated into clinically useful information, reinforces the need for prospective validating studies.

In summary, pharmacogenetic research has provided evidence of the potential of using genetic information for the improvement of treatment outcomes in psychiatry. However, before pharmacogenetic tests are widely implemented in psychiatric clinics, an intermediate step including prospective trials is required to prove the clinical and economical benefits of pharmacogenetic testing. Once validated, further widespread use of pharmacogenetic testing can be achieved by introducing pharmacogenetics as part of clinicians' training, informing them of pharmacogenetics applications and benefits.

## Conflict of interest

The authors declare that they have no conflicts of interest.

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