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EDITORIAL

Precision psychiatry

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Precision psychiatry is the dream of all clinicians. Among all medical specialties, psychiatry is probably the one which poses the most dilemmas at the time of drug prescription.

Which antidepressant/antipsychotic should I choose? Is this drug combination safe in this subject? Will the treatment be effective? And well tolerated? Is the patient a poor metabolizer? These are just a few of the many questions we all face every day when treating our patients. We have all seen subjects developing serious side effects such as tardive dyskinesia after a few years of treatment, or needing a large number of treatment changes before achieving stabilization of their psychopathological suffering.

All these issues would be solved by effective precision psychiatry. Precision psychiatry will allow us to know since the first consultation which treatments are the most beneficial and tolerable for each subject. With over 100 psychoactive compounds available, and their combinations, there are thousands of possibilities.

The topic of precision medicine gained much interest in the last decade,[1] and precision psychiatry followed this trend. The increase in biologic knowledge and the parallel development of electronic health records in many hospitals and health care centers made available an unprecedented amount of information to understand individual response to treatment. In a converging way, the need for cost savings in health care and the awareness of the huge societal costs of psychiatric disorders have also been drivers of precision psychiatry.

But, are we there yet? The short answer is yes and no. Yes because, at present, we have a much more detailed knowledge of the efficacy and tolerability profile of available psychoactive drugs from a purely clinical point of view. Moreover, genetic studies are advancing very rapidly, to the point that a number of commercial products – already available directly to consumers – deliver clear recommendations about which treatment is more or less fitting for each subject. However, concerns have been raised following the spread of these commercial initiatives. Indeed, all products available on the market at present are based on the analysis of few gene variants. Some of these variants correctly identify rapid or poor metabolizer status based on liver enzyme activity, which is of clear clinical utility, but other gene variants are related to genes expressed in the brain, whose effect, if any, is still unclear.[2]

Therefore, major scientific societies and guidelines still only support the use of genetic information on liver enzymes in routine clinical practice. Even this is not a trivial help, considering that up to 20% of the population is composed of either poor or rapid metabolizers, a status that, if unknown, greatly affects efficacy and tolerability of psychoactive drugs. However, genetic variants expressed in the brain are much more challenging. After the initial enthusiasm of the last decades, we have come to realize that single-gene variants have a very small clinical effect and, most importantly, with large variability across subjects, due to compensatory systems and complex gene expression mechanisms. A more promising approach is the use of the so-called polygenic risk scores, which take into account all the millions of variants present in the genome. While still under investigation, initial reports are very promising.[3,4]

In a not-so-distant future, we should therefore be able to identify the biological basis of precision psychiatry, also considering that genetics is not the only dimension at our disposal. Brain imaging and blood biomarkers are other very promising approaches. The ongoing recruitment of very large samples in many countries, such as the one million subjects of the ''All of Us'' precision medicine initiative underway in the United States, will provide an invaluable amount of data.

Another issue will then arise, with hundreds of clinical features collected through electronic health records plus hundreds of measured biological variables and thousands of genetic ones. Interpretation of this ''big data'' will be very challenging for the clinician.

As in other fields of medicine, the use of artificial intelligence will be necessary.[5] We may therefore hypothesize that, in future, electronic health records will include all the available information and, through a software analysis, allow us to obtain the best estimate in terms of treatment appropriateness. In any case, we must remain aware that our clinical expertise will always be preeminent. The information derived from analysis of a patient's individual features may certainly be useful

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and help prevent prescribing errors, in a step forward toward precision medicine, but the last word is always up to the treating clinician. A completely automated prescription system is unlikely to be possible in the near future – and, probably, never will.

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