Personalised psychiatry in action: pharmacogenetic tools for mood disorders

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Introduction

Personalised medicine (personalised psychiatry in a specific setting) is a new model towards individualized care, in which knowledge from genomics and other omic pillars (microbiome, epigenomes, proteome, and metabolome) will be combined with clinical data to guide efforts to new drug development and targeted prescription of the existing treatment options. About half of people who take antidepressants do not respond and many experience adverse effects. These detrimental outcomes are in part a result of the impact of an individual’s genetic profile on pharmacokinetics and pharmcodynamics. If known and made available to clinicians, this could improve decision-making and antidepressant therapy outcomes. This has spurred the development of numerous pharmacogenetic-based decision support tools.

Objectives

To provide a state-of-the-art review of the field of pharmacogenetics decision support tools for mood disorders via meta-analysis, primary papers, reviews, guidelines, and explore the Australasian ethnic and late-life contexts.

Methods

A narrative review of reports, white papers, primary papers and meta-analyses.

Findings

Meta-analysis results showed pharmacogenetic-guided prescribing has a positive effect on the likelihood of achieving symptom remission in MDD. It is important to understand ethnopsychopharmacology and pharmacogenetics in mood disorders in the Australasian context. The pharmacogenetic tools are likely to increase in availability, hence understanding their applicability to the ethnic context in multicultural countries if key.

Conclusions

With future advances in the omics technology and methodological developments for data integration, the goal of PPPM in psychiatry is promising.

References

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PRESENTER 1 – Up-to-date overview of personalized psychiatry and discovery pharmacogenetics: focus on mood disorders

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Introduction

Personalised medicine (personalised psychiatry in a specific setting) is a new model towards individualized care, in which knowledge from genomics and other omic pillars (microbiome, epigenomes, proteome, and metabolome) will be combined with clinical data to guide efforts to new drug development and targeted prescription of the existing treatment options.

Objectives

To provide an up-to-date introduction and overview of the field of personalized psychiatry drawing upon an authoritative review of the field.

To provide an introduction and overview of the field of discovery pharmacogenomics for mood disorders.

Findings

Personalised psychiatry combines neurobiology with basic science methodologies in genomics, epigenomics and transcriptomics demonstrates how statistical modeling of interacting biological and clinical information could transform the future of psychiatry. Personalised psychiatry addresses fundamental questions and requirements for personalized psychiatry from a basic research and translational perspective. The progress of uncovering single nucleotide polymorphisms (SNPs) underpinning treatment efficacy in mood disorders (e.g., SNPs associated with selective serotonin re-uptake inhibitors or lithium treatment response in patients with bipolar disorder and major depressive disorder) are encouraging, but not adequate. Genetic studies have pointed to a number of SNPs located at candidate genes across the genome that possibly influence response to antidepressants and mood stabilisers (lithium).

Conclusions

An integration of molecular science with that of traditional clinical practice is the way forward to drug discoveries and novel therapeutic approaches and to characterize psychiatric disorders leading to a better predictive, preventive, and personalized medicine (PPPM) in psychiatry. With future advances in the omics technology and methodological developments for data integration, the goal of PPPM in psychiatry is promising.

PRESENTER 2 – Introducing pharmacogenetic tools for mood disorders: focus on antidepressant guidance tools and a recent meta-analysis

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Introduction

About half of people who take antidepressants do not respond and many experience adverse effects. These detrimental outcomes are in part a result of the impact of an individual’s genetic profile on pharmacokinetics and pharmacodynamics. If known and made available to clinicians, this could improve decision-making and antidepressant therapy outcomes. This has spurred the development of numerous pharmacogenetic-based decision support tools.

Objectives

To provide a basic overview of pharmacogenetic decision support tools for guiding antidepressant medications.
To present the findings of the first systematic review and meta-analysis of prospective, randomized controlled trials (RCTs) that examined pharmacogenetic-guided decision support tools (DSTs) relevant to depressive symptom remission in major depressive disorder (MDD).

Methods
Random-effects meta-analysis was performed on RCTs that examined the effect of DSTs on remission rates in MDD. RCT quality was assessed using the Cochrane Collaboration Criteria.

Findings
A total of 1737 eligible subjects from five RCTs were examined. Individuals receiving pharmacogenetic-guided DST therapy (n = 887) were 1.71 (95% CI = 1.17 – 2.48, p = 0.005) times more likely to achieve symptom remission relative to individuals who received treatment as usual (n = 850). Notable risks of bias and a high degree of between-study heterogeneity were present in all five RCTs included. Non-industry sponsored trials have yet to be conducted and as such the magnitude of this particular bias is unknown.

Conclusions
Meta-analysis results showed pharmacogenetic-guided prescribing has a positive effect on the likelihood of achieving symptom remission in MDD.

PRESENTER 3 – Ethno-psychopharmacology and pharmacogenetics for mood disorders: an Australasian context
Chee NG

Introduction
Ethno-psychopharmacology, the psychiatric medicine subspecialty that addresses “cultural variations and differences … influencing the effectiveness of prescription medicines used in the treatment of mental disorders,” has made significant progress in the past two decades and now presents intriguing new opportunities on the horizon.

Objectives
To provide an expert review of the field of ethnopsychopharmacology and pharmacogenetics for mood disorders as it relates to the Asian context.

Methods
Presentation of various reviews and primary papers from the author, collaborators and international experts.

Findings
There are many examples of the clinical value of ethnopsychopharmacology and pharmacogenetics in mood disorders. For example, cytochrome enzymes CYP2D6, CYP3A4, CYP1A2, and CYP2C19 metabolize most psychotropics. Their clinical relevance is dramatically illustrated by genetic differences controlling these enzymes and resulting in marked variations among patient populations. A notable and clinically most relevant example is CYP2D6, with 50 mutations that directly affect the psychotropics’ metabolism and are illuminatingly ethnic-specific. Examples of such clinically relevant and ethnically specific markers are CYP2D6*17, found in Africans, and CYP2D6*10, found in Asians. Both result in slower metabolism of CYP2D6 substrates (such as risperidone and paroxetine), thus developing higher plasma concentrations and requiring lower doses for therapeutic effect in this group of slow/poor metabolizers.

Conclusions
It is important to understand ethnopsychopharmacology and pharmacogenetics in mood disorders in the Australasian context. The pharmacogenetic tools are likely to increase in availability, hence understanding their applicability to the ethnic context in multicultural countries if key.
PRESENTER 4 – Critical appraisal of the clinical and health policy value of antidepressant pharmacogenetic tools

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Introduction
The field of pharmacogenetic tools for mood disorders is growing in use and interest from consumers. There are fierce debates in the academic journals on an almost weekly basis, arguing for and against the use of these tools. One must have an appreciation for the processes for reviewing the scientific and clinical value of these tools.

Objectives
To provide an authoritative review of the most recent position statements, guidelines, meta-analyses, debates in the field of pharmacogenetic tools for guiding mood disorder medications.

Methods
A narrative review of reports, white papers, primary papers and meta-analyses.

Findings
There are two recent position statements reviewing antidepressant pharmacogenetic decision support tools – one from the American Psychiatric Association’s Biomarkers Task Force, the other from the International Society for Psychiatric Genetics Pharmacogenetics Taskforce. These were fiercely debated in the literature.

A recent meta-analysis conducted by Bousman et al. provides a useful quantitative overview of this field and the associated strengths of weaknesses of clinical trials, and sources of bias.

Clinicians must consider the role of these tools in guiding the choice and dose of medications with genetics, however they must also consider the role of shared decision making in this process. Clinicians should consider the role of the Oxford Evidence Based Medicine system for reviewing the value of these tools and consider there are around 60 companies offering such tools in the world with wild variability in the science and validity of the offerings.

There is significant interest from policy makers to see more research into the value of these tools and to develop new tools, particularly in the Australian context.

Conclusions
Clinicians need to be aware of the growth of this field given consumer demand and emerging evidence from clinical trials. Clinicians should be aware of the various debates occurring in the literature.