Sonic Genetics
Quality is in our DNA

Sonic PGx
Making medicines personal

Pharmacogenomics in mental health

Information for Doctors

There are many different medications available to treat psychiatric disorders and the choice can sometimes be overwhelming. Finding the most appropriate medication and dose for each patient can be difficult – one patient's clinical response to a particular medication can be quite different to another patient treated with the same medication at the same dose.

The Sonic PGx Panel is a pharmacogenomic test that provides personalised guidance on medications and dose according to your patient's genetic variation.

Approximately 50% of patients with depression respond well to their initial antidepressant. For the remainder, a period of prolonged trial and error is often needed to assess responses to each medication at each dose. Indeed, less than 50% of patients with depression achieve remission of their illness within 12 months of starting antidepressant medication.

Differences in treatment outcomes for patients with psychiatric disorders may be caused by variations in the genes that influence how well patients metabolise medications. Accordingly, this determines how much medication reaches the central nervous system (CNS) where it can work. The genes that control the metabolising enzymes CYP2C19 and CYP2D6 are particularly important.

Several randomised controlled trials have shown that testing these genes helps doctors select the most appropriate medication and dose for patients with depression. The relative rate of symptom remission in patients who have pharmacogenomic-guided antidepressant prescription has been estimated as 1.71 times higher than those who have antidepressants prescribed without pharmacogenomic guidance.

Improvement in care (clinical utility) arising from pharmacogenomic testing has also been documented. For instance, patients with CYP2C19 and CYP2D6 genes that cause very fast or very slow metabolism have two-thirds more medical visits and four times more disability claims than patients with normal metaboliser pharmacogenomic test results, unless prescribing is adapted to account for the differences in metabolism.

One in 6 people have variations in CYP2D6 that slow drug metabolism[1]

One in 3 people have variations in CYP2C19 that accelerate drug metabolism[1]

Patient case study

Jane, 53-year-old

- Experiencing depression and self-esteem issues
- She has heard there are side-effects of taking antidepressants, such as weight gain
- Patient may be worried that finding a medication that will be of clinical benefit to her will take a long time

What can pharmacogenomics uncover?

- Healthcare provider requests the Sonic PGx Panel
- Result identifies that Jane is a CYP2D6 poor metaboliser and is not a good candidate for tricyclic antidepressants
- Identifies CYP2C19 status is a normal metaboliser
- Citalopram is metabolised through CYP2C19, not CYP2D6, and potentially a better starting point for this patient

Knowing more about how Jane's genetic profile could influence her response to medication can guide treatment decisions. A healthcare provider can address her fears by minimising the risk of side-effects and start with a medication that has better potential for success.

Evidence of utility

The authors of a recent meta-analysis[2] identified five randomised control trials which assessed the utility of pharmacogenomics in the management of major depressive disorder. The trials were identified through a systematic search of published literature. They had been performed in Australia, the US and Spain, with variations in selection criteria, numbers of gene tested, types of clinicians involved and prescribing practices.

All of the trials involved the management of patients in the community, that is, not hospitalised. In each trial, all subjects had a pharmacogenomic test performed at enrolment. All trials included assessment of the CYP2D6 and CYP2C19 genes, with varying degrees of overlap for other genes. The subjects were randomised to the test report being provided immediately or after a delay of 8–12 weeks. There were no constraints on what clinicians could prescribe.

The primary goal of each trial was to assess the impact of pharmacogenomic-informed prescribing versus treatment-as-usual on the severity of the subjects' clinical state as measured using the Hamilton Depression Rating Scale 17. A total of 1,737 subjects were included in the meta-analysis.

As would be expected given the diversity of the trials, there was significant heterogeneity. Nonetheless, pharmacogenomic-informed prescribing was associated with a 1.7-fold improvement in the rate of remission compared with treatment as usual (95% confidence interval 1.17-2.48; p=0.005).

Conclusion

Pharmacogenomic-informed prescribing can improve outcomes for patients with major depressive disorder being managed in the community.

Medications with PGx guidance based on selected genes*

Antidepressants

Amitriptyline	CYP2D6, CYP2C19
Citalopram	CYP2C19
Clomipramine	CYP2D6, CYP2C19
Desvenlafaxine	CYP2D6
Doxepin	CYP2D6, CYP2C19
Duloxetine	CYP2D6
Escitalopram	CYP2C19
Fluoxetine	CYP2D6
Fluvoxamine	CYP2D6
Imipramine	CYP2D6, CYP2C19
Mirtazapine	CYP2D6
Nortriptyline	CYP2D6
Paroxetine	CYP2D6
Sertraline	CYP2C19
Venlafaxine	CYP2D6
Vortioxetine	CYP2D6

Anti-psychotics

Aripiprazole	CYP2D6
Brexpiprazole	CYP2D6
Chlorpromazine	CYP2D6
Haloperidol	CYP2D6
Olanzapine	CYP2D6, CYP1A2
Paliperidone	CYP2D6
Risperidone	CYP2D6

Anti-addictives

Naltrexone	OPRM1

Anti-ADHD

Atomoxetine	CYP2D6
Clonidine	CYP2D6
Dextroamphetamine	CYP2D6
Lisdexamfetamine	CYP2D6

Benzodiazepines

Clobazam	CYP2C19
Diazepam	CYP2C19

Therapeutic drug monitoring for a wide range of psychotropic medications, including clozapine, is also available through your local Sonic Healthcare pathology laboratory. Please contact Sonic Genetics for details.

*Correct at time of printing

1. Gaedigk A, Sangkuhl K, Whirl-Carrillo M, et al. Prediction of CYP2D6 phenotype from genotype across world populations. *Genet Med*. 2017; 19(1):69-76
2. Bousman C, Aranadjelovic K, Mancuso S, et al. Pharmacogenetic tests and depressive symptom remission: A meta-analysis of randomized controlled trials. *Pharmacogenomics*. 2019: 20(1):37-47

For further information, please refer to our website, www.sonicgenetics.com.au or call us on 1800 010 447

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