Genetic Testing for Psychiatric Disorders: Is It Ready for Primetime?

Dr. Secor:
Psychopharmacology, as in the study of genetic variations to pinpoint more effective personalized treatments for psychiatric disorders is making a rapid entrance into the mental healthcare scene. Clinicians, industry heads, insurance providers, and regulating agencies like the FDA are all weighing in on psychiatric pharmacogenomic testing. But they are by no means all on the same page. So is DNA testing in psychiatry actually ready for primetime? Let’s tackle this and other questions on today’s Clinician’s Roundtable. You’re listening to ReachMD, and I’m Dr. Mimi Secor, Nurse Practitioner. Joining me today is Dr. James Potash, Professor of Psychiatry and Behavioral Sciences, and Psychiatrist in Chief at the John Hopkins Department of Psychiatry. Dr. Potash’s ongoing research into the genetic and epigenetic basis of mood disorders has resulted in over 170 articles publications to date. Thanks for joining us today, Dr. Potash.

Dr. Potash:
It's a pleasure to be with you.

Dr. Secor:
So Dr. Potash, can you catch us up to speed on the current state of genetic testing for psychiatric
disorders? What kind of testing are being ushered into practices right now, and for what disorders?

Dr. Potash:
Well, the issue of looking at genetics in psychiatric illness has been around a long time. I’ve been involved in genetic research in psychiatry for almost 30 years now, and for many years, the focus was on figuring out which genes give rise to psychiatric illness, which variations in particular genes cause bipolar disorder, cause schizophrenia, cause depression. And part of the reason that that work has gone on is with the idea that that would provide a window into the brain, which would ultimately tell us about how the illness unfolds in the brain, which would lead to the design of new and better treatments; however, what’s become possible more recently is a very different tact, a different way of thinking about the impact of genetics in psychiatry, and that is through doing testing that would help us figure out, not how to design newer treatments and better treatments, but how to best make use of the existing treatments. So in recent years, there’s been a lot of interest in this idea that maybe we can figure out the person’s particular genetic profile, and with that information, figure out that they’ll respond better to one kind of antidepressant as opposed to another kind of antidepressant. And so there are now a number of tests on the market that are aiming to do that sort of thing.

Dr. Secor:
Let’s run through the latest psychiatric guidelines and where they’re currently sitting with genetic testing. What genes and associated tests are they supporting as clinically actionable, to put it their way?

Dr. Potash:
Well, that’s a good question. There have been a whole lot of tests that have come on the market. Most of the tests have come on to the market without there being clear evidence that those particular tests actually work to make a difference. I will tell you that one of the companies that markets tests contacted me, eight years ago now, and they wanted to come to my department; this is when I was Chairman of Psychiatry at the University of Iowa, but they wanted to come and they wanted to tell the department about their new test, and I said to them, ‘Does it work?’ And they said, ‘Yes.’ And I said, ‘How do you know.’ And they said, ‘Well, we did a study.’ And I said, ‘Well, what did the study show?’ They said, ‘Well, the study showed that if psychiatrists use these tests for their patients, that we found the psychiatrists feel more confident in making their prescribing recommendations to the patient.’ And I said, ‘Huh, okay. That’s very interesting.’ Of course, that has nothing to do with whether the test works, because what you actually want to know is whether the patients get better as a result of having the test than they would have done without it. Confidence in a psychiatrist has nothing to do with whether the patient actually has a good outcome. So that was striking to me because it was an example of marketing being out ahead of data. And unfortunately – that phenomenon has continued
ever since in this niche where the marketing continues to be out ahead of the data. And with all these tests that are out on the market, most of them have very little data supporting them, but some of them do have some data supporting them. And some of that data is encouraging certainly. And I will tell you that as someone who’s been focused on one hand on doing the research in genetics in psychiatry, and on the other hand as someone who regularly takes care of patients with depression and bipolar disorder, I would like nothing better than to have these genetic tests be a real value for patients. That’s certainly what all of us would love to see. But right now, the data so far is just pretty limited. It’s not conclusive yet that these tests actually help.

Dr. Secor:
So if we focus on the patient and provider voices around this technology, what kind of promise does psychiatric genetic testing hold for them? And have we already seen positive outcome changes since these tests have rolled out?

Dr. Potash:
I think there is promise. There’s reason to think that these tests can work. One study looked at how much of the variation in response to an antidepressant can be explained by genetics, and it’s suggested that 42% of the variation can be explained by genetics. That’s reason to think that genetic testing can work. There were studies going back to the 1960s that showed that the response to the two different major classes of antidepressants back then, the tricyclic antidepressants like imipramine, nortriptyline, and the MAO inhibitor antidepressants, and Parnate; that those responses tend to run in families. Again, that’s more reason to think that genetic tests should be able to tell us something about differential response to antidepressants. the largest and best-done study in this field came out in the past year, and that was a study based on the the GeneSight test. That had around a thousand people in it, so a big study. On the one hand, the optimistic view of that study is that on a number of measures, people who use the GeneSight test to guide prescribing. When the psychiatrist and patient made use of that test, decided which antidepressant the patient should go on. A number of different measures suggested those people who used the test did in fact have better outcomes who didn’t use the test. Unfortunately, the people who conducted the study had a lot of different measures, and they designated one primary measure before they started the study. And on that primary measure, there was not a statistically significant difference in outcome between people who used the test and people who didn’t. On a bunch of other secondary outcomes, there were differences. So in a technical sense, the study was negative; their primary outcome did not show a difference. But the silver lining is there’s reason to think that maybe there was something good going on there. The glass is sort of both half empty and half full.

Dr. Secor:
Good way to put it. You know, we know that insurance providers are pretty widely split on this, as well. Some coming down in favor, and reimbursing aggressively, and others withholding payments completely until more evidence is available. Where do you see things headed in this domain?

Dr. Potash:
I guess my feeling is that certainly in the absence of conclusive evidence right now, it seems a little hard to make the argument that every insurance company ought to be paying for everybody who comes in for treatment of depression to get tested. I will add, by the way, that review of this issue was published in the American Journal of Psychiatry about a year ago; a review that very systemically looked at all of the data that existed for every one of the genetic tests for antidepressants in particular, and that’s where most of the activity has been. And that review concluded that we can’t be sure at this point that these tests actually work. So it’s hard to argue that everybody coming in for depression should have these tests paid for by insurance. Now, where you get into a grayer area I think is this question of, well if you set aside the idea that everybody should get it when they first show up for treatment, if you instead say, well let’s look at the people who’ve failed several different attempts at treatment; the so-called treatment resistant patients. Those are the people who haven’t done well, they typically are people who are suffering terribly, and you know, they’re desperate for answers often. Is it possible that using these tests could give you some useful information that maybe would help you find a better direction for them? You know, the answer to that is, probably. It adds some information that could be of help. So I’m part of the Leadership of the International Society for Psychiatric Genetics, and our society has a work group focused on genetic testing. And the guidelines that our work group has put out, which is the result of dozens of people within the society coming together to sort of decide what makes the most sense given what we know at the moment. The guidelines from the society suggest that, in people who have failed a number of drug trials, that it may make sense to do.

Dr. Secor:
So for those just tuning in, this is the Clinician’s Roundtable on ReachMD. I’m Dr. Mimi Secor, and I’m speaking with Dr. James Potash from Johns Hopkins Department of Psychiatry about genetic testing in psychiatry. So, Dr. Potash, let’s focus on another source of controversy. There have been some ongoing disputes between genetic testing industry, mental health advocacy groups, and regulating agencies in terms of whether this kind of testing should even be regulated. And if so, by whom? What is the current situation?

Dr. Potash:
The regulation that has existed in this area has tended to be regulation that’s very narrow. That is, the regulation is around the question of if you do the test, does the result that you get about someone’s genetic profile accurately reflect their genetic profile? That’s a very narrow question. It’s not really, but
it’s certainly something that you do want to know. Does the test give the genetic result that it reports to
give, that’s something that you want to know. But the bigger question you want to know is: Does the
result guide treatment in a way that leads to better outcomes? That is the treatment of depression; are
people less depressed as a result of having gotten the test than they would have been otherwise? That
part has not been regulated. With regard to insurance, I know there have been issues around whether
unnecessary testing gets done because if insurance is willing to pay, in a sense it’s a way of generating
income for somebody. I was interviewed about a case in Atlanta where the allegation was made that a
psychiatrist was ordering tests on everybody and patient’s were receiving large bills when they hadn’t
even realized that this testing was happening, and that those expenses were going to come back to
them. These tests are not cheap. They’re often in the vicinity of $2,000. And on the one hand, that’s a
substantial cost to the health system. On the other hand, when insurance doesn’t cover it, it’s a very
substantial out-of-pocket cost to people. So you certainly only want to do it if you know there’s going to
be a lot of benefit there.

Dr. Secor:
Let’s consider one of the strongest objections to genetic testing, and that’s coming from the FDA
directly, which argues that changing drug treatments based on testing results can be a big mistake, and
even lead to serious health consequences. What’s your view on the risk-to-benefit ratio of this testing
at this point?

Dr. Potash:
You know, I think that what these tests actually get at is the issue of how rapidly people metabolize our
drugs. And to the extent that there is benefit from these tests, it hinges on this idea that you will learn
that some people need higher doses of medicine than average; whereas, other people may need lower
doses than average. Now, typically, psychiatrists have always known that there’s variation in how
much of a dose people need in order to get well. And so the standard practice has typically been you
start at a low-ish dose and you gradually build up the dose, and you keep going up until the person
gets well. So, you know, a major criticism of the test has been, well how much more information do you
really get from the test. And maybe the answer is you may know to go up to a higher dose more
quickly for someone than you might have otherwise. You know, I don’t think at a clinical level there’s a
lot of downside to doing the test. I think the big downside is that the level of resource expenditure, you
know, both for an individual and for our health system as a whole.

Dr. Secor:
Yeah, which is really important. So before we wrap up our discussion today, Dr. Potash, let’s come
back to the broader question I floated a little bit earlier, which is whether psychiatric genetic testing is
actually ready for primetime. What are your thoughts on this? And now at the end of our conversation,
is there anything our audience should keep in mind as we look at the role for genetic testing in the months and years to come?

Dr. Potash:
Yeah, at the level of primary care, I think to my mind, is the tests are not ready for primetime, because I don’t think that when a person comes into primary care depressed, that they should be getting genetic testing. I think our standard approach of using one of our well-established medicines, which are relatively effective and have relatively few side effects, as a first try makes sense. I think that to the extent that genetic testing makes sense right this minute, it would be in people who’ve gone through a couple of tries with medications and haven’t done well. And those would typically be people that are going to be referred to psychiatrists.

Dr. Secor:
Yeah, good point. So, on that note, I’d like to thank my guest, Dr. James Potash, for joining me on the topic of genetic testing in psychiatry. Dr. Potash, it was great having you on the program today, and it was very informative. I appreciate it so much. I know the listeners will, as well. So, thank you.

Dr. Potash:
It was really, really nice to be with you. Thank you, Mimi.

Dr. Secor:
I’m Dr. Mimi Secor, and you’ve been listening to Clinician’s Roundtable on ReachMD. To access this episode and others in our series, visit ReachMD.com/cliniciansroundtable, where you can be part of the learning. Thanks for listening.