Pharmacogenetic testing improves mental health care

Dr. Julio Monterrey explains the benefits of genetic screening for psychiatric care

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Introduction

Dr. Julio Monterrey is a Stanford-trained, board-certified psychiatrist and neuroscientist who specializes in diagnosing and treating complex cases. Dr. Monterrey is a keen observer of medical technology who has adopted pharmacogenetic (PGx) testing as a regular part of patient history taking. Through his experience, Dr. Monterrey has seen substantial benefits from PGx testing for his patients and his practice. He is now an advocate for wider adoption of PGx screening to guide and improve patient care. We spoke with Dr. Monterrey to hear what he has learned working with PGx testing in his psychiatry practice.

Q: Can you describe your current practice?

Julio Monterrey (JM): I'm a board-certified psychiatrist and I treat children and adults. My research background has focused on transcranial magnetic stimulation (TMS) and neuroimaging, specifically neuroimaging in kids with autism. Right now, my work is mostly clinical. I have a virtual group private practice specializing in treating children and adolescents with eating disorders and a virtual individual private practice where I provide consultation on complex psychiatric cases. I do see some patients in person whenever that is needed, but it's mostly virtual at this point and that was really kicked off with COVID-19.

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Q: Can you describe the traditional diagnostic procedure for someone before genetic testing?

JM: When a patient walks into the office, I don't have a preconceived notion of what I'm looking for. The first thing I always ask the person is why they are here and what are they looking to get help with. I start by putting together the events that led up to their chief complaint. From there, I will do a general screening of various mood disorders, current symptoms, past symptoms, and then collect additional history, including substance use, sleep issues, past medical conditions, medications, family history, and history of mental illness. I also want to know broader things like their social history, their living situation, what they do for work, any legal issues that are going on for them. The history taking is especially important in psychiatry because, traditionally, we haven't had biological markers that we can use to diagnose someone. The diagnoses are clinical and they are symptom based. We cluster the symptoms into syndromes and then we say you meet the diagnostic criteria for this syndrome, which we call a disorder. Any laboratory exams have generally been more for ruling out a medical condition.

Q: What kinds of conditions can be ruled out by lab tests?

JM: As an example, for depression, you would want to rule out hypothyroidism. You would want to check the person's thyroid stimulating hormone (TSH) level. If the person is very anxious, you also want to rule out hyperthyroidism and you would do the same TSH exam. Also, with depression, you can see some fatigue so you would want to do a complete blood count and check for anemia.

Q: How did you start using PGx testing?

JM: When I was in training, we understood what benefits PGx could deliver, but medical doctors are taught very early in medical school that you never just follow a lab result, you have a person in front of you. The most important information you can gather to make the right diagnosis is the clinical history and presentation. So, if someone's clinical history and presentation meet the diagnostic criteria for depression, there are guidelines for first-line treatments and this is what we're going to go with. Collectively, we knew that there was a benefit to PGx, but it's very difficult to convince a doctor that a lab test should dictate their prescribing practice because we're taught to prioritize the clinical history and presentation. So, there was this unspoken resistance about PGx.

I came to PGx because patients were hearing about it from their friends who had gotten it done and for whom it was making a huge difference. People were saying "I found the right medication. I feel

so much better," or "I felt like less of a guinea pig," or, "hey, my friend really benefited from this genetic test, can I get this?". That's how I started incorporating PGx testing into my practice. And that's when I really saw the benefit of it.

I would also like to share a story. One of the first cases that led me to ordering PGx testing was a 16-year-old girl I was treating for depression and suicidal ideation, so we needed to get her feeling better as quickly as possible. We chose Mirtazapine because it has a quicker onset of efficacy compared to selective serotonin reuptake inhibitors (SSRIs) and Mirtazapine typically helps with sleep symptoms, which she was also having. We started at a lower dose and titrated up, as tolerated, for about two months. She didn't get better so we added Wellbutrin because she had some ADHD symptoms and maybe her lack of focus and attention was affecting her academic performance, leading to her depression, but that didn't really help either.

Again, this is a 16-year-old girl who is suicidal for two months at this point—no improvement in her symptoms. She is starting to feel hopeless, which is making her condition worse and her mom is even more concerned at this point because it has been so long without a relief in her symptoms. So, I said let's get PGx testing. What resulted was that she was a rapid metabolizer of Mirtazapine and was not likely to respond at lower doses. Unfortunately, this 16-year-old girl had suffered for two months but, thankfully, she did not act on her suicidal ideation. It was at that point that I decided that PGx is really important. In mental health, cases can be high risk and you want the treatment to be quick and effective. I tell families how PGx has been helpful in other cases. That's the thing that got me really into being an advocate for PGx.

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Q: How has PGx testing changed your practice?

JM: I actually conceptualize PGx as part of the history taking—not in the lab section of our whole patient encounter. Of course, it is a lab but it is also genetic history for the patient. That conceptualization of PGx, I think, will address a lot of the concerns that physicians have. PGx is unlike other lab tests. If you're checking TSH level, sodium level, kidney function, these are dynamic numbers that you follow and trend over time. What specific genetic allele you have is not changing, so you're really looking at the person's history.

The other thing I haven't spoken about is when you get labs done or when you do an intervention, you have to be able to justify it because most interventions will have some sort of risk that you and the patient have to weigh against the possible benefits. The risks of

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PGx that have been voiced to me have been concerns for privacy and what we do with the genetic data. That concern is a big barrier for more widespread adoption. The question is, can I really justify it?

PGx captures a patient's genetic history. I just talked about how important getting the history is, so why wouldn't you want to complete that by getting the genetic history? Once that clicked, it was just something I thought I should be getting for everybody. Of course, we've got to talk about the risk—benefit but, in my experience, the benefits far outweigh any kind of security or privacy risks.

Q: How has PGx testing affected patient care?

JM: My patients have really had an incredible experience with PGx. They feel that their experience, their symptoms, and their reactions to previous medication are validated, which can be very therapeutic for someone. A lot of my patients that are requesting PGx have bounced around from different providers, have had incomplete relief of their symptoms, and, from their perspective, providers have sometimes given up on them.

With PGx testing, we can maybe see why someone is feeling a certain way, or why they haven't responded to treatment in the way we wanted them to respond. Just to be able to move on to the next intervention with guidance from something like PGx can be very healing because, when a patient has had such a struggle, they've lost a little bit of faith in the medical community. They've lost faith in our ability to assess and treat because they have only experienced a partial response, or no response, to treatment. The validation and subsequent emotional reset have been huge. It helps to remove that friction and barrier between patient and provider. Patients can say "okay, now I feel like I'm better understood, and I can move forward. What are some next steps I can take?"

Q: What psychiatric conditions benefit the most from PGx testing?

JM: I'll answer this on two levels. One is at the medication management level for specific conditions. For example, looking at specific genes like *SLC6A4*, the gene that encodes the receptor that SSRIs bind to, is relevant to any condition that I might treat using an SSRI—anxiety, depression, obsessive-compulsive disorder. These results offer a specific benefit to the management of the condition by assessing the medication risk for side effects and/or nonefficacy.

Then you can see benefits on the symptom characterization level. I would say PGx is helpful for conditions with complex symptoms like borderline personality disorder, where patients have a lot of socioemotional sensitivity that may be difficult to explain. However, sometimes an *MTHFR* polymorphism or an allelic variant of *COMT* is such that maybe the patient is not recycling their neurotransmitters at a typical speed, then we can validate their experience. From this, I can begin to understand how a patient may stay in a depressed state for a little bit longer than the average person or may stay in an elevated happy state for longer than the average person. And, if they have reduced activity of *MTHFR*, for example, they may benefit from activated folic acid supplementation. That's specifically for borderline, where I have anecdotally found the PGx testing very useful.

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Q: How do you select PGx assays and interpret results for your practice?

JM: Personally, I try to look for the most comprehensive panel to recommend to the patient. If a company has a pretty comprehensive panel, I would probably go with them. But I also tell my patients that I'm happy to work with whatever assay is out there that they prefer. Oftentimes, people will want to go with what their friends have have benefited from, so I'll go with that.

In terms of interpreting the results, I have done a lot of my own reading and most of that comes from my background in research. A lot of these companies offer a service where they go step by step with the clinician to explain what the results mean. I personally haven't felt a need to do that yet, but I might do it just to see what they say.

I think that interpretation is key. Not all providers have the interest in doing all the literature reading that I have, or maybe they don't have the time. I schedule time in my weekly calendar to be able to read and keep up with things. That's something that I prioritize, and I know that not everyone has the luxury to do that. Companies providing interpretation services are really important to get clinicians to feel comfortable ordering PGx tests and describing the results. That is also a barrier. Generally, we don't get formal training in any of this stuff, either in med school or in my specialty training in residency. I know how to order a basic metabolic panel and I know how to interpret that, so I have no problems ordering that. But, to order a test that I have no idea how I'm going to read, if that was the situation, I'm less likely to order it because I don't know how it's going to help, and I don't know what I'm going to tell the patient.

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Q: How has your experience been with insurance companies and reimbursement for PGx testing?

JM: In my experience, reimbursement has been very company-specific. I have worked with PGx testing companies where they promise their clients that they will not be charged over a certain amount, usually around $400 for the test. This means that the testing company will bill insurance and, whatever amount they get reimbursed, the patient will pay no more than $400. There are other companies that say 99% of people will get their testing covered by their insurance, you don't have to worry. So, we go through the whole thing. We get the test results. Everything is fine and insurance then comes back to the patient and says they are not going to cover it. Then, the patient ends up with a bill for the full cost of the test, around $5500. I've had cases like that.

What I usually end up saying to the patient is let's pick a testing company and call your insurance company and tell them "my psychiatrist wants to order this test and I've already tried a number of medications"—because the criteria for many insurance companies is having failed at least one medication. I have them explain that this test would substantially inform the next steps in their treatment. After having done that process, it's been a much smoother experience for my patients, and for myself, and I haven't had anymore of those $5500 cases.

Q: What do you think are some of the main barriers to broader adoption of PGx testing?

JM: One of the community clinics I work at, with a primarily underserved Latino population, sees about 30,000 visits per month. I was discussing with the clinic the advantages of PGx as part of the psychiatry services for these patients in this low socioeconomic area. The concern from the leadership was what was going to happen with the genetic data. This is a population that is largely minority, underserved, and already marginalized. There is concern that someone will get ahold of this genetic data and use it against them or have some sort of prejudice because of the genetic information in there. This was a big concern from some of these community clinics where it kind of stalled the conversation.

Q: Do you end up educating your colleagues on PGx and advocating for adoption?

JM: Absolutely. What I'm seeing right now is an exponential growth in adoption. It's coming from our network of colleagues where we're all sharing our experiences, and, at the end of the day, how happy our patients are with saying, "this is my genetics, and now

I understand better" or "I can give this to my doctor, and they can better dose any medication." It's not just psychiatric medications, it can be antibiotics, or any other medication, because PGx gives you pharmacokinetic information about how the patient is going to metabolize their medication. Patients have had such a positive experience, why wouldn't you want to offer this service to your patient? There's been a lot of adoption for providers, especially when we get to talking as colleagues and really smooth over some of the concerns they have. At the end of the day, you're still using your clinical judgment to treat. Now you just have more data to inform your treatment decision.

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Q: Are psychiatrists getting onboard with genetic testing?

JM: Right now, I would say the great majority are not onboard and it's from a lack of understanding of what PGx testing is. The top three concerns would be what's my liability—I'm signing up to manage the results of this test. Then there is this idea that "a test is not going to tell me what to do." And, finally, how do I read it and describe the results to my patients? Those three things I think are still very true for most psychiatrists.

Q: What do you see as the biggest potential impact for PGx testing on health care?

JM: It depends on the test, but if we're talking about a broader PGx test than what I typically use, then you can likely use PGx results to really take preventive medicine to the next level. We may be able to reach out and say you are at increased risk for a particular disease and we want to make sure that you know what to do to stay healthy. To me, having preventive medicine take off like that is one of the biggest, most exciting parts of PGx that is possible for the future.

For the more specific assays, it will be having more genes that will help us fine tune the probability of medication response and reduce the risks of side effects. I think building on that genetic library will be very important to help patients feel like less of a guinea pig and help guide clinicians better in terms of the best options for the patient.

Q: Do you have any thoughts on how that would affect the economics of health care?

JM: There are multiple ways to quantify this. On a direct level, if you can get to an effective treatment faster, and get the patient to remit in terms of their symptoms and condition, then that's going to save

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costs for office visits, failed medication trials, and lab tests. It's really kind of an investment to decrease costs in the future.

Then there's another higher level. With untreated depression, untreated anxiety, untreated severe mental illness, how we define these disorders is by a problem in the global functioning of the person. You can be sad, and that's not depression until the sadness is so severe that you are not able to really function at an adequate level in your personal life or occupation. So, untreated psychiatric conditions have an effect on family life and have an effect on the local and broader economy, because people are not productive. Maybe kids are having their schooling affected because their parent is not able to be there to support them in school. These are broader economic effects that occur when you have untreated psychiatric conditions, which certainly have an economic impact.

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M-GL-00384 v1.0