Profile

Brenda Penninx: puzzling over depression

Brenda Penninx has spent the past 14 years poring over pieces of a puzzle. Since 2004 she has been principal investigator of the Netherlands Study of Depression and Anxiety (NESDA), trying to build a clearer picture of depressive disorders. "We've got over 2000 patients in whom we collected genetic, imaging, and biomarker data and information about psychological and environmental factors", says the professor of Psychiatric Epidemiology at VU University in Amsterdam, the Netherlands. "We need all these pieces and we need to collect them at this big scale if we're going to understand something like depression, which is heterogeneous in both symptoms and aetiology." The same goes for trying to make sense of the complex interactions at a molecular level with genetics or biomarkers. "It's a complicated problem so, for me, you can tackle it only at a big scale."

Already, the study has identified two main groups of people with depression, each with a unique genetic and biomarker profile. The first group is what she describes as having typical depression: they have insomnia, a decreased appetite, and weight loss. Then there's what she calls the atypical group who have symptoms such as an increased appetite and hypersomnia. Those with typical depression, she says, seem to have more HPA axis dysregulation and more often are exposed to stress-related risk factors such as childhood trauma and negative life events. Those with atypical depression have a different genetic and biomarker profile with more inflammation and leptin dysregulations. "It has led us to believe that these two types of patients might need different approaches in terms of treatment", she says. "So we are taking observational data and turning them into interventions."

People with atypical depression, for instance, might benefit most from interventions that target the risk profiles that most affect them—obesity and metabolic dysregulation such as high glucose, high blood pressure, high waist circumference, and an unfavourable lipid profile. Penninx and her colleagues are doing trials of two interventions that they think might help: one is on nutrition and the other is of running therapy. For people with atypical depression, she wants to test the idea that drugs could target the inflammatory underpinnings of the disease. Naturally for an epidemiologist, Penninx wants to test the idea at scale, but finding money to fund such studies is not easy. "There have been some small-scale studies showing a beneficial impact of anti-inflammatory agents in depression", she says. "I don't think any of the studies have been large-scale enough to convincingly conclude that it's a feasible standard clinical practice at the moment. We're trying to get grants to prove that one way or another."

Before becoming principal investigator of NESDA, Penninx had a couple of stints working in America—first as a visiting fellow at the National Institute on Aging in Bethesda, MD, and then as an Associate Professor at the Department of Internal Medicine at Wake Forest University Health Sciences in Winston-Salem, NC. Pinned to the notice board above her desk is the front cover of a local US medical journal, showing a picture of her and her colleagues at the National Institute of Aging. Next to it is a photograph of her, her husband, and their two children straddling the equator in Uganda with a foot in each hemisphere. "I love that picture", she says. "We turned it into a New Year's card for our friends." On first glance the photograph—with all members of the family standing in front of each other with their arms and legs stretched out—looks like Leonardo da Vinci's Vitruvian Man. The sketch was based on a Roman architect's descriptions of the human body's proportions, among them that the body is eight times the length of the head. Beyond mere proportions, the relationship between head and body is important to Penninx.

"In the last 20 years lots of psychiatric research has connected brain function to somatic conditions, and it is clear that depression is not merely a brain condition, it truly is an entire body condition", she says. "There are improvements, but we still have some steps to take to translate this into treatments." One of those steps is the intervention she is testing, running therapy for patients with atypical depression. Motivating a depressed patient to run is inherently tricky, she says, but made more complicated if a doctor has not bought into it as real treatment. "It's not enough to tell a patient to go get some exercise", she says. "It requires attention, guidance, and support—it's obviously much easier for an overstretched GP to prescribe a pill." That running therapy isn't supported by various health insurance plans, either, is another potential barrier.

Still, it's the complexity of this problem that Penninx loves. "The puzzle in psychiatry, and also in old age which I started off in, is quite large and that attracts me", she says. "The multidisciplinary nature of the condition like depression is huge, not only the brain but interactions between brain, genes, physiology, environment, and a person's personality are at play. I really like to bridge disciplines and connect people into finding better ways of solving the depression puzzle. The more people involved, the more pieces we have, the clearer the picture we'll get—and then we can have more confidence in how to make people better."

Dara Mohammadi

Brenda Penninx