A New Way to Slice Up the Brain—and the Mind

By Grace Huckins

To cure and treat diseases, scientists and physicians seek out their physical causes. Epilepsy can be treated by electrically modulating—or, in extreme cases, removing—the part of the brain in which seizures originate. Parkinson's Disease is caused by cell death in a region in the middle of the brain called the substantia nigra; stimulating nearby regions, or administering drugs that mimic the effect of the dead cells, can alleviate symptoms. And devices like cochlear implants and artificial retinas might help when someone's sensory equipment isn't working properly.

But things get much fuzzier when it comes to mental illness. Scientists still have very little idea which parts of the brain contribute to different psychiatric conditions—and, given how difficult it can be to treat mental illness, some psychiatrists and neuroscientists worry that terms like "depression" and "schizophrenia" may capture whole suites of different brain problems, each of which might have its own optimal treatment. Scientists at the National Institute of Mental Health have tried to combat these concerns by designing a new framework for understanding mental illnesses, the Research Domain Criteria (RDoC), which analyzes psychiatric conditions according to various domains of mental functioning (like "negative valence" and "cognitive systems"). But these domains, too, weren't necessarily informed by what we know about the brain. The terms used in RDoC, and the terms used throughout human neuroscience—memory, emotion, motor control—are largely inherited from psychology, says Ellie Beam, a MD/PhD candidate at Stanford.

"What we were doing was taking what had been defined in psychology and trying to identify neural correlates of it," Beam says. "Especially in psychiatric neuroimaging, we just weren't

finding a one-to-one correspondence between our diagnostic labels and our neuroimaging results."

So Beam wanted to see if the wealth of human neuroscience research conducted over the past couple of decades could suggest a new, neuroscientifically informed way of talking about what the brain does—and, potentially, of understanding mental illness. The idea, at a high level, was this: If two capacities that we typically think of as separate (say, memory and emotion) seem to use exactly the same brain regions, maybe we should consider them to be the same thing. Conversely, if emotion makes use of two completely separable brain circuits, perhaps it needs to be divided up into more specific subtypes, like positive and negative emotion.

Paper trail

To elucidate the links between psychological concepts and brain regions, Beam, who worked in the laboratories of Stanford professors Amit Etkin and Russ Poldrack, analyzed almost 20,000 articles from the human neuroscience literature. Most of these articles used functional magnetic resonance imaging (fMRI), a tool that allows researchers to examine brain activity while humans do a particular task. Beam used natural language processing techniques to extract from each of these papers a list of terms describing what the authors were studying and the locations in the brain that were identified as significant. In this way, she obtained a lengthy list of pairs of brain regions and psychological terms.

In principle, Beam might have then identified the list of terms associated with each individual brain region and called every one of those lists a separate psychological construct. But brain regions work together in circuits to accomplish particular goals, and hundreds of different constructs would have been nearly impossible for scientists to work with. So Beam divided the brain up into circuits using those lists of terms; the more similar the terms associated with any one region, the more likely they were to end up in the same circuit. The approach Beam and her colleagues used allowed them to define any number of circuits they wanted; they ended up finding that six circuits worked well. Using machine learning to name the circuits based on the list of shared terms, they came up with the following six brain-based psychological constructs: memory, reward, cognition, vision, (motor) manipulation, and language. The results were published last year in the journal *Nature Neuroscience*.

All of these terms are familiar to psychology. Some details about the constructs, however, surprised Beam. Emotion, for example, did not appear on her list of six constructs; instead, emotion-related terms seemed divided between the "memory" and "cognition" domains. But when she considered the issue further, however, Beam says, the result began to make sense.

"There's no reason really why these would need to be separate processes," Beam says. "If anything, having emotion as part of decision making, it's how we got to be able to do it so quick." In psychiatry, too, emotion and cognition seem strongly linked; for example, depression, which is typically thought of as a primarily emotional condition, is associated with a number of cognitive symptoms like poor focus. When it comes to analyzing the brain, it might be inaccurate to view emotion as separate from cognition—and that inaccuracy could hamper scientific progress.

Measuring up

Beam and her colleagues used a few criteria to quantify just how much better their new framework was: reproducibility (how well the framework predicted psychological terms from brain structures, and vice versa), modularity (how well the circuits partitioned psychological terms and brain structures from each other), and generalizability (how well the general framework captured the results of individual studies). They compared their six domains with the RDoC framework, which proposes six alternative domains—including two separate emotion domains—and the traditional Diagnostic and Statistical Manual (DSM) classification of psychiatric conditions. Though both RDoC and the DSM did well by some metrics—the DSM categories were fairly modular, and the RDoC categories fairly generalizable—only the biologically informed framework determined by Beam proved successful across the board.

Beam cautions that these results don't necessarily mean that brain functions absolutely should be divided up into the six categories she discovered. "Let's take this as a hypothesis," she says. With any luck, though, this new framework, or another neuroscientifically informed framework, may potentially push forward the study of the mind and of mental illness.

"Ultimately, [I] hope that we can use our understanding of the brain to come up with a new language for understanding our own minds," Beam says.

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