Hallmarks of psychiatric illness can reveal themselves remotely

Researchers discovered that healthy people and those with borderline personality disorder displayed different patterns of behavior while playing an online strategy game, so much so that when healthy players played people with borderline personality disorder, they gave up on trying to predict what their partners would do next.
Most people are so attuned to the nuances of social interaction that they can detect clues to mental illness while playing a strategy game with someone they have never met.

That was the finding of a team of scientists led by Read Montague, director of the Human Neuroimaging Laboratory at the Virginia Tech Carilion Research Institute. The researchers discovered that healthy people and those with borderline personality disorder displayed different patterns of behavior while playing an online strategy game, so much so that when healthy players played people with borderline personality disorder, they gave up on trying to predict what their partners would do next.

For their large neuroimaging study, the scientists used a multiround social interaction game, the investor-trustee game, to study the level of strategic thinking in 195 pairs of subjects. In each pair, one player played the investor and the other the trustee. The investor chose how much money to send the trustee, and the trustee in turn decided how much to return to the investor. Profit required the cooperation of both players.

"This classic tit-for-tat game allows us to probe people's responses to the social gestures of others," said Montague, who also directs the Computational Psychiatry Unit, an academic center that uses computational models to understand mental disease. "It further allows us to see how people form models of one another. These insights are important for understanding a range of mental illnesses, as the ability to infer other people's intentions is an essential component of healthy cognition."

The scientists classified the investors according to varying levels of strategic depth of thought. The healthy subjects fell into three categories: about half simply responded to the amount the other player sent; about
one-quarter built a model of their partner's behavior; and the remaining quarter considered not just their model of their partner, but also their partner's models of them.

Not surprisingly, the depth-of-thought style of play correlated with success, with the players who looked deeper into interactions making considerably more money than those who played at a shallow level.

When healthy subjects played people with borderline personality disorder, though, they were far less likely to exhibit depth of thought.

"People with borderline personality disorder are characterized by their unstable relationships, and when they play this game, they tend to break cooperation," said Montague. "The healthy subjects picked up on the erratic behavior, likely without even realizing it, and far fewer played strategically."

Notably, the functional magnetic resonance imaging of the subjects' brains revealed that each category of player showed distinct neural correlates of learning signals associated with differing depths of thought. The scientists used hyperscanning, a technique Montague invented that enables subjects in different brain scanners to interact in real time, regardless of geography. Hyperscanning allows scientists to eavesdrop on brain activity during social exchanges in scanners, whether across the hallway or across the world.

"We're always modeling other people, and our brains have a substantial amount of neural tissue devoted to pondering our interactions with other people," Montague said. "This study is a start to turning neural signals into numbers – not just theory-of-mind arguments, but actual numbers. And when we can do that across thousands of people, we should start to gain insights into psychopathologies – what circuits are involved, what brain regions are engaged, and how injuries, congenital disorders, and
genetic defects might play into psychiatric illness."

Montague believes the study represents a significant contribution to the field of computational psychiatry, which seeks to bring computational clout to efforts to understand mental dysfunction. "Traditional psychiatric categories are useful yet incomplete," said Montague, who delivered a TEDGlobal talk on the growing field of computational psychiatry last year. "Computational psychiatry enables us to redefine with a new lexicon – a mathematical one – the standard ways we think about mental illness."

Computationally based insights may one day help psychiatry achieve better precision in diagnosis and treatment, Montague said. But until scientists have the right instruments, they cannot even begin to make those connections.

"The exquisite sensitivity that most people have to social gestures gives us a valuable opening," Montague said. "We're hoping to invent a tool – almost a human inkblot test – for identifying and characterizing mental disorders in which social interactions go awry."

The study appeared in *PLoS Computational Biology* in the article "Computational Phenotyping of Two-Person Interactions Reveals Differential Neural Response to Depth-of-Thought."


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