Predicting the chaos in Tourette syndrome tics

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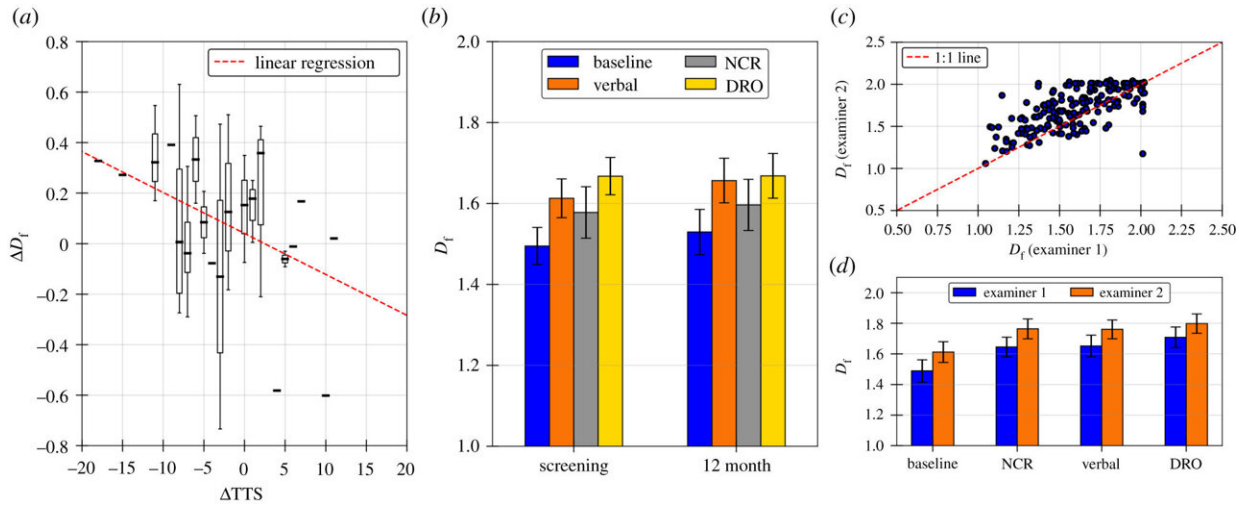

(a) Change in fractal dimension between screening and 12-month visit (ΔDf) as a function of change in YGTSS TTS (ΔTTS(b) Comparison of average Df for the patients under various suppression conditions during screening visits shows that DRO led to the most effective tic suppression (largest Df). Additionally, the fractal dimension of all suppression conditions increased at 12 months (when most patients met diagnostic criteria for TS). Error bars show 95% confidence intervals. (c,d) Rater-blind reproducibility of Df as an assessment tool. Comparison of Df for tic time series generated by two examiners, with examiner 2 being blind to visit and condition. Good agreement is observed between examiners, verifying inter-rater reliability of results. Error bars show 95% confidence intervals. Credit: Rajan Chakrabarty, Kevin Black

During the pandemic, news reports surfaced of a surge of young adults showing up at doctors' offices with unexplainable movement disorders that looked, perhaps to a non-specialist, a little bit like Tourette syndrome.

But when those patients were sent to see a specialist, "They'd say, 'that doesn't look at all like any of my first thousand patients,'" said Kevin Black, MD, a professor of psychiatry at the Washington University in St. Louis School of Medicine. People with experience knew that there were telltale properties of the tics associated with Tourette's, even though there is no one tool that allows a doctor to give a diagnosis on the spot.

However, research published today in the *Journal of the Royal Society Interface* by Black and Rajan Chakrabarty, the Harold D. Jolley Career Development Associate Professor of Energy, Environment and Chemistry in the university's McKelvey School of Engineering, may signal that a diagnostic tool is near.

They have replicated and expanded on previous work to show that tics associated with Tourette syndrome have a fractal pattern. They also discovered that a key characteristic of that pattern in any individual can predict how severe the disease will become.

Specialists had long suspected there was some kind of pattern to tics associated with Tourette's, and in the late 1990s, a seminal paper by Bradley Peterson and James Leckman was able to uncover that pattern—but only over a period of seconds to minutes.

Black, a neuropsychiatrist who specializes in movement disorders, has been heading a research study on tics for years. As part of the New Tics Study, he'd collected an impressive amount of data about tics in children as they were going through the year-long diagnosis process.

He had all that data—nearly 1,000 minutes of footage documenting the timing of tics in 78 kids taken in two sessions, a year apart—but he needed machine learning to sort it out. He reached out to Chakrabarty. "My initial thought was, 'Let's just see if we can replicate Peterson's finding,'" Black said.

Chakrabarty is an aerosol scientist and an expert on the chaotic ways in which particles affected by everything from wind to humidity to sunlight move through the air.

"Tics are chaotic," Chakrabarty said. "Tics are a kind of chaos in human biology, in our neural networks." His lab turned to the tools he uses to find the patterns in the chaos of the atmosphere.

Chaos is in fact not entirely random. Instead, it presents itself in degrees. Something can be very chaotic, or just a little chaotic, and that chaos can have a pattern. One way to quantify a particular kind of chaos is using a parameter called fractal diffusion. A straight line has zero fractal diffusion. If a system has some measure of chaos, then the fractal dimension is between one and two. If it's closer to two, it's less chaotic; closer to one is more chaotic.

Payton Beeler, a Ph.D. student in Chakrabarty's lab, used Black's data to figure out two things. First, is the timing of Tourette's tics really fractal in nature? Second, does the fractal dimension say anything about how severe the tics are, or will become?

Black shared his data with the Chakrabarty lab. It consisted of data points from two visits. When a person with tics came in for an initial screening visit they were observed under several different situations. Each time they had a tic, the observer noted the time. The person came back a year later and repeated the screening process.

Notably, for a Tourette's diagnosis, a person must have had tics for a year or more.

Beeler compared Black's data to two scenarios, a non-chaotic system and a completely chaotic system that was fractal in nature. Visually, the tic data looks more like that of the chaotic system but does not match point-for-point. The amount that the tic data strays from the chaotic system gave her the fractal dimension value.

Next, Beeler validated her findings against clinical ratings of tic severity. "What we found is exactly what we expected. If the clinical 'tic score' goes up, we see a drop in the fractal dimension, and vice versa. Our finding is very correlated with classical clinical measures," she said.

Because the fractal dimension is the same across time and in different conditions, Black said, "It means that the fractal character relates somewhat to the actual tics and your behavioral state."

Identifying syndrome at earliest stage

In practice, this is what the finding means: a doctor could analyze the timing of tics in a patient's first hour-long visit and diagnose a person with Tourette syndrome if the tic pattern was indeed fractal in nature. The doctor could get a measurement of fractal dimension and, if they analyzed the timing of that person's tics over a month- or year-long period, they would get the same fractal dimension value.

"It may boil down the year-long diagnosis process into one number," Beeler said. A number that a doctor can determine in one day as opposed to over one year.

The ability to determine whether or not someone has Tourette syndrome when they first present with tics can save time, money, frustration and

worry—and can even help those without Tourette's get the help they need.

"Almost all of the research that's been on Tourette syndrome has been on people who have had tics for a long time," Black said. "Any brain changes we find thereafter could be causal. But they could be related to having had tics for a long time." This data will help researchers identify people with Tourette syndrome at the earliest stages of the disease and learn more about how it affects the brain.

And then there are other kinds of tics—like the ones that seemed to increase during the pandemic. Known as "functional tics or functional tic-like movements," these conditions require treatment entirely different from Tourette syndrome.

Understanding how these functional disorders differ from Tourette's is Black's next step. He suspects functional movements may have fractal patterns more like those of non-tic movements. He'd like to see how well the fractal dimension can discriminate between different types of disorders.

More information: Payton Beeler et al, Fractality of tics as a quantitative assessment tool for Tourette syndrome, *Journal of The Royal Society Interface* (2022). DOI: 10.1098/rsif.2021.0742

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