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Payton Beeler  
*Washington University in St. Louis*

Nicholas O Jensen  
*Washington University in St. Louis*

Soyoung Kim  
*Washington University School of Medicine in St. Louis*

Amy Robichaux-Viehoever  
*Washington University School of Medicine in St. Louis*

Bradley L Schlaggar  
*Washington University School of Medicine in St. Louis*

See next page for additional authors

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Authors
Payton Beeler, Nicholas O Jensen, Soyoung Kim, Amy Robichaux-Viehoever, Bradley L Schlaggar, Deanna J Greene, Kevin J Black, and Rajan K Chakrabarty

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Fractality of tics as a quantitative assessment tool for Tourette syndrome

Payton Beeler¹, Nicholas O. Jensen³, Soyoung Kim⁴, Amy Robichaux-Viehoever⁵, Bradley L. Schlaggar⁸,⁹, Deanna J. Greene¹⁰, Kevin J. Black⁴,⁵,⁶,⁷ and Rajan K. Chakrabarty¹,²

¹Center for Aerosol Science and Engineering, Department of Energy, Environmental and Chemical Engineering, ²Institute for Public Health, and ³Computational and Systems Biology Program, Division of Biology and Biomedical Sciences, Washington University in St Louis, St Louis, MO 63110, USA
⁴Department of Psychiatry, ⁵Department of Neurology, ⁶Department of Radiology, and ⁷Department of Neuroscience, Washington University School of Medicine, St Louis, MO 63130, USA
⁸Kennedy Krieger Institute, Baltimore, MD 21205, USA
⁹Departments of Neurology and Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA
¹⁰Department of Cognitive Science, University of California San Diego, La Jolla, CA 92033, USA

PB, 0000-0003-4759-1461; KJB, 0000-0002-6921-9567; RKC, 0000-0001-5753-9937

Abstract

Tics manifest as brief, purposeless and unintentional movements or noises that, for many individuals, can be suppressed temporarily with effort. Previous work has hypothesized that the chaotic temporal nature of tics could possess an inherent fractality, that is, have neighbour-to-neighbour correlation at all levels of timescale. However, demonstrating this phenomenon has eluded researchers for more than two decades, primarily because of the challenges associated with estimating the scale-invariant, power law exponent—called the fractal dimension Df—from fractional Brownian noise. Here, we confirm this hypothesis and establish the fractality of tics by examining two tic time series datasets collected 6–12 months apart in children with tics, using random walk models and directional statistics. We find that Df is correlated with tic severity as measured by the YGTTS total tic score, and that Df is a sensitive parameter in examining the effect of several tic suppression conditions on the tic time series. Our findings pave the way for using the fractal nature of tics as a robust quantitative tool for estimating tic severity and treatment effectiveness, as well as a possible marker for differentiating typical from functional tics.

1. Introduction

Tics are brief, purposeless, unintentional behaviours appearing as repeated movements of skeletal or vocal musculature, affecting more than 20% of all children [1,2]. Approximately 0.5% of children have Tourette syndrome (TS), which is diagnosed when both motor and vocal tics occur over a period of a year or longer [3]. Tic disorders, including TS, are moderately heritable, but despite decades of active scientific research, no consensus has been reached on their pathophysiological foundations [4,5]. The COVID-19 pandemic has resulted in increased symptoms in children diagnosed with tic disorders, as well as an influx of patients with sudden onset of severe tics and tic-like attacks, the latter of which are commonly believed to be functional tic-like movements [6,7]. The similarity of tics and functional tic-like movements, and the variability of symptoms over time in tic disorders make diagnosis of functional tic-like movements a historically challenging task. Current best practice requires extensive expertise with tic disorders, thorough elicitation of historical information from the patient and family, and careful observation of the patient.

In 1998, Peterson & Leckman [8] noted that tics tend to arise in clusters (bouts of several tic occurrences within a few seconds, separated by longer tic-free intervals), but also that at longer timescales, bouts of tics lasting several
Figure 1. (a) Fractal pattern in the occurrence of tics. Tics tend to arise in bouts of several tic occurrences within a few seconds, separated by longer tic-free intervals, and at longer timescales, bouts of tics lasting several seconds similarly recur in grouped episodes over the course of hours. Figure adapted from [9]. (b) Trajectory of a tic-modulated random walk (black) is compared with that of Brownian diffusive motion (blue) and non-Brownian ballistic motion (red). The position of each walker at time $t$ is normalized by the maximum displacement of the walker, rendering the trajectories in one-dimensional space as a function of time. (c) Estimation of $D_f$ for a walker undergoing diffusive motion (blue), non-Brownian ballistic motion (red) and tic-modulated motion (black).

seconds similarly recur in grouped episodes over the course of hours [8,9]. Such recursive behaviour in turn extends to longer time spans (days, weeks and months), maintaining self-similarity (figure 1a). Their observation suggests that the chaotic temporal nature of tics could possess an inherent fractality, that is, have neighbour-to-neighbour correlation at all levels of timescale. However, confirming this phenomenon has eluded researchers for more than two decades, primarily because of the challenges associated with estimating the scale-invariant, power law exponent—called the fractal dimension $D_f$—from fractional Brownian noise.

Here, we uncover the fractal pattern associated with the occurrence of tics from time series datasets collected 6–12 months apart in children. We demonstrate that at timescales ranging from seconds to minutes, the occurrences exhibit neighbour-to-neighbour correlation, and have an associated $D_f$. The robustness and replicability of $D_f$ as a quantitative measure lends itself as a simple yet accurate tool for quantifying tic fractality and severity. We are unaware of any previous attempts at estimating $D_f$ of tics, which would not only provide quantitative insights into the chaotic nature of tic disorders, but also facilitate new ways for assessing tic disorders quantitatively. We also hypothesize that $D_f$ may be a sensitive parameter in differentiating tics associated with TS from functional tic-like movements.

2. Methods

2.1. Measuring the time series of tics

The clinical methods appear in detail elsewhere [10]. Briefly, we first recorded the timing of tics in patients during 5 min video sessions corresponding to one of four conditions: free to tic (baseline); verbal request not to tic (verbal); immediate token rewards for 10 s tic-free periods (differential reinforcement of other, 'DRO'); and tokens given at the same timing as in a previous DRO session regardless of current tic appearance (non-contingent reinforcement, 'NCR'). Author K.J.B. recorded the timing of tics as they occurred, and rewards were delivered using a custom computer program connected to a token dispenser [11]. In some participants, the NCR condition was omitted, so that most participants had 30–40 min of video at each visit. Video sessions were conducted within the first 6 months after onset of tics (screening visit), when provisional tic disorder (PTD) can be diagnosed, and again at the 12-month anniversary of the first tic (12-month visits), when a chronic tic disorder can be diagnosed. At the 12-month visit, all children still had tics, and most met diagnostic criteria for TS [12]. Data from 78 children were used to generate 535 tic time series during screening visits (164 baseline, 84 NCR, 144 verbal, 143 DRO) and 358 tic time series during 12-month visits (97 baseline, 72 NCR, 94 verbal, 95 DRO). Reproducibility and repeatability of conclusions were confirmed by co-author A.R.V., who independently recorded tic timing from the video recordings blind to visit or video condition [13]. Analysis was then performed on both sets of tic time series.

2.2. Modelling tic-modulated motion

Next, we used a random walk model in which the velocity of walkers is reversed with each tic exhibited by the patient, generating what is hereafter referred to as a ‘tic-modulated random walk’. The random walkers are first placed at position $x=0$, and given an initial velocity of one position unit (arbitrary) per second. Time is then incremented by 0.1 s, and the walker will either reverse velocity or continue with the same velocity as the previous time step, according to a certain probability function ($p_{\text{rand}}(t)$).

Walkers undergoing tic-modulated motion have $p_{\text{rand}}(t)$, which is determined by the tic time series. If a tic is not detected at time $t$, then $p_{\text{rand}}(t)$ is equal to zero, and the walker continues moving with the same velocity as the previous time step. If a tic is detected at time $t$, then $p_{\text{rand}}(t)$ is equal to unity, and the velocity of the walker is reversed. This is summarized by

$$p_{\text{rand}}(t) = \begin{cases} 0, & \text{no tic detected at } t, \\ 1, & \text{tic detected at } t. \end{cases} \quad (2.1)$$

Figure 1b shows the trajectory of a tic-modulated random walker with data obtained from one child with TS (black line). The trajectory of the tic-modulated random walker is compared with two cases that represent the two extremes of a tic time series. The first case is the most chaotic case for a tic time series, Brownian diffusive motion. Under this regime, $p_{\text{rand}}(t)$ is a constant value of 0.5. A tic-modulated time series that closely resembles Brownian diffusive motion indicates that the patient is equally likely to tic or not tic at any given time. The second case is the most ordered case for a tic time series, non-Brownian ballistic motion. Under this regime, $p_{\text{rand}}(t)$ is a constant value of zero (i.e. the patient has a 0% chance of exhibiting a tic at any given time). When compared to the trajectory of a walker undergoing Brownian diffusive motion, some
excursive episodes of the walker (i.e. longer periods without a tic) can be observed in the tic-modulated trajectories. Qualitatively speaking, the mobility of the tic-driven walker is stronger than that of Brownian diffusive motion but weaker than that of non-Brownian ballistic motion.

### 3. Results

Figure 2a shows that for individual patients, the change in \( D_f \) of the tic time series is correlated with change in tic severity, as measured by the Yale Global Tic Severity Scale total tic score (TTS) between screening and 12-month visits (\( r = -0.33, p = 0.03 \)). Patients with decreased TTS between screening and 12-month visits (greater improvement in tics) also had increased \( D_f \) of the tic time series. These findings are consistent with previous results, which show that \( D_f \) is a local property that is independent of the Hurst coefficient [16].

### 4. Discussion

In the present study, we validate the hypothesis of fractal timing of tics in TS first reported over 20 years ago [8] and extend that observation for the first time to tics shortly after they appear (PTD). We first show that \( D_f \) of the tic time
series is correlated with a standard clinical measure of tic severity (TTS), suggesting that $D_t$ of the tic time series can be used as an objective measure of tic severity. Additionally, we measure for the first time the effect of tic suppression on the temporal dynamics of tic occurrence by quantification of $D_t$. Using this analytical framework, we further demonstrate that various tic suppression techniques have an effect on this relationship, with increased effectiveness reflected by increased $D_t$. Overall, DRO and verbal instruction were effective tic suppression conditions during screening and 12-month visits, with DRO being the most effective. In addition, all conditions showed increased $D_t$ at 12-month visits compared to screening visits, which may be attributed to the passage of time, with continuing cognitive development and additional practice with environmental tic suppression resulting in improved tic inhibition in the social environment. Finally, we demonstrate the robustness of this parameter via the congruence with our results by a blinded rater. Additionally, we also use a stochastic random walk model to observe $D_t$, which does not require complex mathematical treatment in order to obtain $D_t$. Future work should be directed to extend the scaling analysis to longer time spans, since qualitatively the temporal dynamics of tics have been observed to maintain self-similarity over months and even years. This method for analysing the timing of tic occurrence shows promise for documenting and understanding tic suppression-based behaviour therapies for TS [18]. We also speculate that tic timing patterns in patients with functional tics may be different than those seen in TS, potentially providing an objective tool to help with diagnosis [6]. Future work will include examination of the behaviour of tics outside of a laboratory setting, and the effects of environmental stressors on tic suppression.

**Data accessibility.** All relevant datasets used for this study, including time series of tics and calculated fractal dimensions, can be found in the electronic supplementary material, datasets S1 and S2. The data are provided in the electronic supplementary material [19]. Code is available at https://doi.org/10.5281/zenodo.5940339.

**Authors’ contributions.** P.B.: data curation, formal analysis, investigation, methodology, software, validation, visualization and writing—original draft; N.O.J.: data curation and writing—review and editing; S.K.: data curation and writing—review and editing; A.R.-V.: methodology, project administration, supervision and writing—review and editing; B.L.S.: project administration and writing; D.H.G.: methodology, project administration and writing—review and editing; K.J.B.: formal analysis, funding acquisition, project administration, resources, supervision and writing—review and editing; R.K.C.: conceptualization, formal analysis, funding acquisition, project administration, supervision, writing—original draft and writing—review and editing. All authors gave final approval for publication and agreed to be held accountable for the work performed therein.

**Competing interests.** The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. This study was approved by the Washington University Human Research Protection Office (IRB), protocol nos. 20119157 and 201707059. Each child assented and a parent (guardian) gave informed consent.

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