Using point process models to determine the impact of visual cues on basal ganglia activity and behavior of Parkinson's patients

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Using Point Process Models to Determine the Impact of Visual Cues on Basal Ganglia Activity and Behavior of Parkinson's Patients

Sridevi V. Sarma, Uri T. Eden, Ming L. Cheng, Ziv Williams, Emad Eskandar, Emery N. Brown

Abstract— **Deep brain stimulation is an effective therapy for Parkinson's disease (PD) that has enabled microelectrode recordings from single-unit cells in the sub-thalamic nucleus (STN) of the basal ganglia. This rare data is important to develop detailed characterizations of spiking activity to understand the pathophysiology of PD. Despite the point process nature of neuronal spiking activity, point process (PP) methods are not used to analyze these recordings. Therefore, we develop PP models using the generalized linear method to characterize spiking activity in 28 STN neurons in 7 PD patients executing a two-step motor task. In the first step of the task, patients could anticipate visual go cues and moved once prompted. In the second step of the task, go cues had a 50% chance of appearing. If cues failed to appear, movements were self-initiated. The point process models provide an accurate summary of pathological characteristics under different cued conditions such as bursting, 10-30Hz oscillations, and fluctuations in directional tuning. In particular, the models show that when cues can be anticipated or when patients self-initiate movements (in both cases an internal motor plan is formed prior to movement), pathological neural characteristics are suppressed. In contrast, when cues cannot be anticipated and later appear, there is no suppression of pathological neural characteristics. Consequently, movements deteriorate.**

I. INTRODUCTION

Deep brain stimulation (DBS) is a well established therapy for Parkinson's disease that has also given neurophysiologists the rare opportunity to record neural activity in awake humans ([2][24][25]). During surgery, microelectrode recordings are routinely performed in order to confirm the location of the target nuclei. The need to record neural activity in order to confirm proper positioning of the microelectrode in the STN allows the study of neural activity in Parkinson's patients during movement at no additional risk.

Despite the point process nature of neuronal spiking activity, general point process (PP) methods (non-Poisson) have not been used to analyze these recordings with the exception of two recent preliminary studies performed by

the investigators here ([16][30]). Current analyses typically involve computing several statistics from spike train data to uncover intrinsic and extrinsic factors associated with spiking propensity. For example, to analyze short-term history dependence within a spike train inter-spike interval histograms are typically generated ([19][31][29]). Long-term history dependence related to neural oscillations are often studied using frequency domain statistics such as the power spectra, which often entails transforming the spike train into a continuous-valued signal before computing its Fourier transform [19]. Furthermore, spectral analysis operates under the assumption that the window of spiking activity being transformed is stationary. Movement-related dependence such as directional tuning in a neuron is often inferred from a tuning curve which illustrates the vector sum of the average firing rates in each movement direction.

We develop point process models to characterize neural spiking activity in the STN across 7 Parkinson's patients executing different behavioral tasks described in the METHODS section below. The point process paradigm is a probabilistic framework that naturally takes into account the binary characteristics of spike train data [13].   We implement the point process model using generalized linear methods (GLM) [26] which allow us to capture the relative contribution of intrinsic factors (eg. short and long-term history effects) and extrinsic factors (eg. the impact of movement direction) on the probability that the neuron will spike at any given time-in one computation [33]. Therefore, we analyze modulations of bursting, oscillations and directional tuning simultaneously over time and study their relative importance in effecting spiking propensity for each subject group. The GLM framework also provides an efficient computational scheme, available in several software packages (eg. MATLAB, SAS), for model parameter estimation and a likelihood framework for conducting statistical inferences based on the estimated model [10].

Our point process (PP) models provide a summary of pathological characteristics such as bursting, 10-30Hz oscillations, and increased modulation in directional tuning while subjects execute three types of directed-hand movement tasks. In one task, the patients could anticipate that visual go cues would appear. In the other tasks, the go

cues had a 50% chance of appearing and hence patients could not anticipate whether a cue would appear. If it appeared, the movement was visually-guided else it was self-initiated. Our models showed that pathological activity such as 10-30Hz oscillations in STN was suppressed when patients could either anticipate cues or when they self-initiated movements, which facilitated movement. When patients could not anticipate cues which then later appeared, STN activity failed to significantly modulate and movement and reaction times increased. Despite the widely accepted theory that visual cues improve behavior in PD patients ([17],[23],[27] and many more), our analysis shows that it is not the cue itself but rather the ability to develop an internal motor plan (which can be facilitated by an anticipated cue) that suppresses abnormal neural activity and facilitates movements in PD patients.

II. METHODS

a. Subjects

Seven patients undergoing deep brain stimulator placement for the treatment of PD were included in the study. All patients had idiopathic PD with a Hoehn-Yahr score of 3 or higher and had a documented response to L-dopa replacement therapy. All patients received a thorough pre-operative neurological exam. Exclusion criteria for surgery included those patients with Parkinson "plus" syndromes, cognitive impairment, active psychiatric disorders, or anatomic abnormalities on magnetic resonance imaging (MRI) [1]. None of the patients had undergone prior surgery for the treatment of PD. Informed consent for the study was obtained in strict accordance with a protocol approved by the Institutional Review Board and the multidisciplinary movement disorders assessment committee at the Massachusetts General Hospital. The decision to offer surgery was based on clinical indications alone, and bore no relation to the patients' participation in this study. To ensure that the patients were comfortable with performing the behavioral joy-stick task, they practiced it prior to surgery. Subjects were able to remove their hand from the joystick or stop the task at any time. At all time points before and during surgery, the patients had the clear understanding that their participation was not related to the surgical outcome, and that they could withdraw from the study at any time.

b. Electrophysiology

Anti-Parkinsonian medications were withheld the night before surgery. No sedatives were given prior to or during performance of recordings. A local anesthetic was used prior to the incision and burr hole placement. The stereotactic localization using pre-operative MRI and computerized tomography, as well as general techniques of intraoperative microelectrode recordings have been described previously [1][20]. Single-unit recordings were made from the dorsal-lateral motor sub-territory of the STN based on stereotactic localization and reconstructions of the electrode trajectories. The STN has characteristic high firing rates in comparison to the surrounding structures and has clear dorsal and ventral borders that are evident when reconstructing neuronal activity along the electrode trajectories. Once within the STN, no attempt was made to explicitly select cells based on presence or absence of movement-related activity, or on whether the cells responded to passive and/or volitional movement. This was done specifically to limit the potential for a sampling bias.

We used an array of 3 tungsten microelectrodes, separated by 2 mm and placed in a parasagittal orientation. The electrodes were advanced simultaneously in 50-micron increments using a motorized micro-drive (Alpha Omega; Nazareth, Israel). The behavioral paradigm was controlled by a Macintosh G4 computer using custom-made software. Neuronal activity was band-pass filtered (300 Hz – 6 kHz) and sampled at 20 kHz. Spikes were sorted off-line using a standardized template-matching algorithm (Cambridge Electronics Design, Cambridge, England).

c. Behavioral Task

Once the microelectrodes were in the STN and stable single units were obtained, the subjects viewed a computer monitor and performed a behavioral task by moving a joystick with the contra-lateral hand. The joystick was mounted such that movements were in a horizontal orientation with the elbow flexed at approximately 45 degrees. Patients performed a two-step sequential motor task. Each task-set consisted of an anticipated-cued trial followed by an unanticipated trial. In the anticipated-cued trial, a central fixation spot was first displayed for 500 ms, after which, an array of four gray equally spaced circular targets would appear in the "up", "right", "down" and "left" directions. After a variable delay interval ranging 500 – 1000 ms, one of the gray targets would turn green. Following another variable delay interval ranging from 500 – 1000 ms, the central fixation spot would turn green indicating that the patients could move the joystick. Once within the target, patients were required to hold the cursor stationary for another 100 ms. The stimuli on the screen would then erase, and the patients would be allowed to return the spring-loaded joystick to its resting position. It is important to note that patients knew apriori that a go cue will appear during these trials.

After completion of the anticipated-cued trial, the screen remained blank for 1000 ms. This would be followed by one of two possible unanticipated trials. As before, a fixation spot and gray circular array would appear, but would be followed by a go cue with 50% chance. In these

trials, the patients were required to move the joystick in the same direction as in the preceding anticipated-cued trial. If the patient moved and a go cue appeared afterwards or if the patient waited too long before moving (>= 4 seconds after fixation), he/she would not receive a reward. Therefore, patients had an incentive to wait for a possible go cue and if no go cue appeared within a short time period, self-initiated movements were made. The trials were pseudo-randomly interleaved in blocks such that each direction and trial type was presented once within each block, rendering a 50% chance of a go cue appearing on any given unanticipated trial. All directions and trial types were counterbalanced such that an equal number of directions and trials types were tested for each cell. Furthermore, variable delays for cue presentation on anticipated-cued trials and unanticipated trials were each timed separately. If patients strayed beyond the confines of a 60-wide invisible corridor, moved the cursor to an incorrect target, failed to return the joystick to its resting position or failed to reach the target within 4 seconds from fixation, the trial would abort and repeat again. The patients were instructed to maintain their gaze on the central of the screen at all time-points during the trial. See **Figure 1** for a schematic of two-step sequential motor task which renders three trial types.
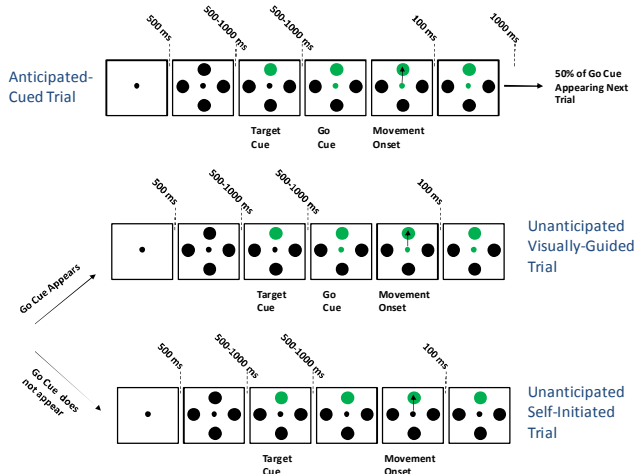

Figure 1: Schematic of two-step sequential motor task. Anticipated-cued trial (Top), Unanticipated Visually-Guided trial (middle), Unanticipated Self-Initated trial (bottom).

Table 1: Distribution of trials and recorded neurons per patient

d. A Point Process Model of STN Dynamics

The point process framework has proven in practice to be a powerful and flexible framework that is capable of modeling spike train activity from a diverse range of neuronal types and neural circuits, such as: place cells from the rat hippocampus [4,18]; retinal ganglion cells of the salamander, rabbit, and cat [23]; and neurons from the supplementary eye field of the macaque monkey [22].

Inspired by a preliminary studies of co-authors here [16][30] , we formulate a point process model to relate the spiking propensity of each STN neuron to factors associated with movement direction and features of the neuron's spiking history. We analyze oscillations, bursting and directional tuning modulations across trials for three different trial types.

A point process is a binary stochastic process defined in continuous time (eg. number of neuronal spikes in a given time interval) and is characterized entirely by the conditional intensity function, which is defined below [31]. Consider the time interval $(0,T]$ as the continuum, and events as neuronal spike times. Let $t_1,...,t_n$ denote the times of each neural spike such that $0 < t_1 < t_2 ... < t_n \leq T$. Then, if $N(T)$ is the sample path of the associated counting process ($N(T)$ is the number of spikes in the interval $(0,T]$), the conditional intensity function is the following

$$\lambda(t \mid H_t) = \lim_{\Delta t \to 0} \frac{P(N(t+\Delta t) - N(t) = 1 \mid H_t)}{\Delta t} . \quad (1)$$

H_t is the history of the sample path and that of any covariates up to time t , and $t_{N(t)}$ is the time of the last spike prior to t . Consequently,

$$\lambda(t \mid H_t)\Delta \approx \mathrm{Pr}\,ob(spike\ in\ (t,t+\Delta]\mid H_t) . \quad (2)$$

When Δ is small, equation (2) is roughly the spiking propensity at any time The well-known homogeneous Poisson process is a special point process in which all events are independent and the CIF does not dependent on history. Because the CIF characterizes a point process in its entirety, defining a model for a CIF defines a model for the spike train.

We use Generalized linear models (GLM) [26][33] to characterize the CIF for each neuron. In a GLM, the log of the CIF is a modeled as a linear function of parameters that multiply the covariates which describe the neural activity dependencies The GLM is an extension of the multiple linear regression model in which the variable being predicted, in this case spike times, need not be Gaussian. GLM also provides an efficient computational scheme for model parameter estimation and a likelihood framework for conducting statistical inferences based on the estimated model [10].

Specifically, we define the CIF for each neuron to be a function of movement direction which corresponds to {Up, Right, Left and Down} and the neuron's spiking history in the preceding 150 msec. Rather than estimating the CIF continuously throughout the entire trial, we estimate it in

time windows around key epochs and at discrete time intervals each 1 msec in duration. We first estimate the CIF during the fixation period of 500msec (FX). Fixation is when the subject is at rest and is thus used as a baseline. We then estimate the CIF over 500msec windows centered at the target cue (TC), go cue (GC), and movement (MV) onsets. **Figure 2** below highlights all of the time periods for which we estimate the CIF.
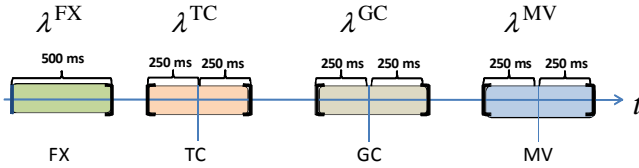

Figure 2: Time periods over which the CIF denoted by equation (3), is estimated are shaded.

Going forward, we omit the superscripts denoting the epoch for a simpler read and express the rate function as

$$\lambda(t \mid H_t, \theta) = \lambda^S(t \mid \theta) \cdot \lambda^H(t \mid H_t, \theta) , \quad (3)$$

where the component $\lambda^S(t \mid H_t, \theta)$ describes the effect of the behavioral stimulus (movement direction) on the neural response and the component $\lambda^H(t \mid H_t, \theta)$ describes the effect of spiking history on the neural response. The units of $\lambda(t \mid H_t, \theta)$ and $\lambda^S(t \mid \theta)$ are in spikes per second and is dimensionless. The idea to express the CIF as a product of a stimulus component and a temporal or spike history is appealing as it allows one to assess how much each component contributes to the spiking propensity of the neuron. If spiking history is not a factor associated with neural response, then will be very close to 1 for all times and (3) reduces to an inhomogeneous Poisson process.

The model of the stimulus effect is

$$\log \lambda^S(t \mid \alpha) = \sum_{d=1}^{4} \alpha_d I_d(t) \quad (4)$$

where

$$I_d(t) = \begin{cases} 1 & \text{for all t if movement is in direction } d \\ 0 & \text{otherwise} \end{cases} .$$

The $\{\alpha_d\}_{d=1}^{4}$ parameters measure the effects of movement direction on the spiking probability. For example, if e^{α_1} is significantly larger than e^{α_2}, e^{α_3}, and e^{α_4} during movement, then the probability that a neuron will spike is greater when the patient moves in the UP direction, indicating that the neuron may be tuned in the UP direction.

Our model of spike history effect is

$$\log \lambda^H(t \mid H_t, \beta, \gamma) = \sum_{j=1}^{10} \beta_j \, n(t-(j):t-(j+1))$$
$$+ \sum_{k=1}^{14} \gamma_k \, n(t-(10k+9):t-10k) \quad (5)$$

where $n(a:b)$ is the number of spikes observed in the time interval $_{[a,b)}$ during the epoch.

The $\{\beta_j\}_{j=1}^{10}$ parameters measure the effects of spiking history in the previous 10 msec and therefore can capture refractoriness and/or bursting on the spiking probability in the given epoch. For example, if e^{β_1} is close to zero for any given epoch, then for any given time t, if the neuron had a spike in the previous millisecond then the probability that it will spike again is also close to zero (due to refractory period). Or if e^{β_5} is significantly larger than 1, then during fixation and for any time t, if the neuron had a spike 5 milliseconds ago then the probability that it will spike again is modulated up, indicating burstiness.

The $\{\gamma_k\}_{k=1}^{14}$ parameters measure the effects of the spiking history in the previous 10 to 150 msec on the spiking probability, which may be associated with not only the neuron's individual spiking activity but also that of its local neural network. For example, if e^{γ_4} is significantly larger than 1, then for any time t during fixation if the neuron had one or more spikes between 40-50 milliseconds ago then the probability that it will spike again is modulated up, indicating 20-25 Hz oscillations.

By combining equations (4) and (5), we see that the CIF may be written as

$$\lambda(t \mid H_t, \theta) = \exp\left\{ \sum_{d=1}^{4} \alpha_d^{ep} I_d(t) \right\} \cdot$$
$$\exp\left\{ \sum_{j=1}^{10} \beta_j^{ep} \, n(t-(j):t-(j+1)) + \sum_{k=1}^{14} \gamma_k^{ep} \, n(t-(10k+9):t-10k) \right\} \quad (6)$$

The model parameter vector $\theta = \{\alpha_d, \beta_j, \gamma_k\}$ contains 28 unknown parameters (for each epoch and time window modeled). We compute maximum-likelihood estimates for θ and 95% confidence intervals of for each neuron using glmfit.m in MATLAB.

The Kolmogorov-Smirov (KS) statistic, based on the time-rescaling theorem, was used to assess model goodness-of-fit. The time-rescaling theorem is a well known result in probability theory which states that any point process with an integrable conditional intensity function may be transformed into a Poisson process with unit rate [9]. A KS plot, which plots the empirical cumulative distribution function of the transformed spike times versus the

cumulative distribution function of a unit rate exponential, is used to visualize the goodness-of-fit for each model. The model is better if its corresponding KS plot lies on the 45 degree line. We computed 95% confidence bounds for the degree of agreement using the distribution of the KS statistic.

III. RESULTS

As mentioned above, we built point process models for 37 STN neurons in 7 Parkinson's patients which captured spiking dynamics for three trial types. At most 28 neurons passed our goodness-of-fit criterion which required the KS statistic of each model to be less than 0.05. Once the 28 models were selected for analysis, we determined for each neuron and for each epoch within the trial, whether the neuron exhibited refractoriness, bursting, HFOs, and directional tuning. The neuron's model parameters and their 95% confidence bounds were used to make these determinations as described next.

First, we note that the product of the rate function for a given neuron and a small time interval, $\lambda(t|H_t)\Delta$, is approximately the probability that the neuron will fire in time interval Δ given history of extrinsic and intrinsic dynamics up to time t, which is captured in H_t. Then by virtue of equation (6), we allow the probability that each STN neuron will fire at some time t within an epoch to be modulated by movement direction (captured in α parameters), short-term history spiking dynamics (captured in β parameters) and long-term history spiking dynamics (captured in γ parameters).

Figure 3 shows an example of a single neuron's optimal model parameters and their 95% confidence intervals during the peri-movement epoch. We highlight in **Figure 3** and discuss below how certain parameter value ranges indicate refractoriness, bursting, HFOs, and directional tuning.

1. **Refractoriness:** As illustrated in the second row of Figure 3, both the PD and primate STN neurons exhibit refractory periods before and after onset of movement as indicated by down modulation by a factor of 10 or more due to a spike occurring 1 msec prior to a given time t. That is, if a spike occurs 1 msec prior to time t, then it is very unlikely that another spike will occur at time t ($e^{\beta_i} \leq 0.1$ for all e^{β_i} within its 95% confidence band, i=1,2,or 3). This is expected since after an action potential (a spike) occurs, some time (refractory period) must elapse before the neuron can again produce another action potential in response to a stimulus [7].

2. **Bursting:** As illustrated in the second row of **Figure 3**, the PD STN neuron fires in rapid succession before and after movement onset as indicated by up modulation by a factor of 2 or more due to prevalent spiking activity occurring 2-10 msec prior to some time t. That is, if a spike occurs 2-10 msec prior to time t, then it is very likely that another spike will occur at time t. Formally, a neuron bursts if its model parameters satisfy the following: for at least one $i = 2,3,...,10$, $LB_i > 1$ and $UB_i \geq 1.5$ where $LB_i \leq e^{\beta_i} \leq UB_i$.

3. **10-30 Hz Oscillations:** As illustrated in the third row first two columns of **Figure 3**, the PD STN neuron exhibits10-30 Hz oscillatory firing before and after movement. That is, the probability that the PD STN neuron will fire at a given time t is up modulated by a factor of 2 or more if a spike occurs 30-100 msec prior to t. Formally, a neuron has 10-30 Hz oscillations if its model parameters satisfy the following: for at least one $i = 2,3,...,10$, $LB_i > 1$ and $UB_i \geq 1.5$ where $LB_i \leq e^{\beta_i} \leq UB_i$.

4. **Directional Tuning:** As illustrated in the first row of **Figure 3**, the PD STN neuron appears to exhibit more directional tuning before and after movement onset than the primate neuron. That is, the PD STN neuron seems more likely to fire in some directions than in others unlike the primate neuron. To quantify directional tuning, we performed the following test for each neuron and each time relative to onset (ℓ):

1. For each direction $d^* = \{U, R, D, L\}$, compute
$p_{d^*,d} = \text{Prob}(e^{\alpha_{d^*,l}} > e^{\alpha_{d,l}}) = \text{Prob}(\alpha_{d^*,l} > \alpha_{d,l})$ for $d \neq d^*$. Define $p_{d^*,d^*} = 0$. Use the Gaussian approximation for $\alpha_{d,l}$, which is one of the asymptotic properties of ML estimates to compute $p_{d^*,d}$ (Brown et al., 2003).

2. If $\max_{d^*=1,2,3,4} p_{d^*,d} \geq 0.975$ then neuron exhibits directional tuning.

Figure 4 illustrates a population summary of modulations in bursting, beta oscillations, and directional tuning for each trial type. When the fractional change from baseline (defined to be the first 500 msec of each trial-fixation or FX) is statistically significant in a less pathological direction (i.e., decreased bursting, decreased HFOs, increased directional tuning), we denote it with a '+' symbol. As shown in **Figure 4**, during anticipated +cue trials (top row), there is an increase in directional tuning and a decrease in beta oscillations early on during the trial immediately after target cue onset. After movement initiation, this suppression of pathological activity becomes more pronounced, which has been previously reported in studies where patients could anticipate go cues ([1] ,[34]). During self-initiated –cue trials (bottom row), we also see an increase in directional tuning and a decrease in beta

oscillations later on during the trial. The average reaction time for anticipated +cue trials is 0.69 seconds and average movement times for anticipated +cue trials and self-initiated –cue trials are 0.38 and 0.34 seconds, respectively.

Interestingly, during unanticipated +cue trials (middle row), we did not observe significant suppression of beta oscillations or significant increase in directional tuning at any time during the trial even though cues were presented. Although bursting decreased right after fixation and during movement, motor performance deteriorated. The average movement and reaction times are 0.43 and 1.55 seconds, respectively.
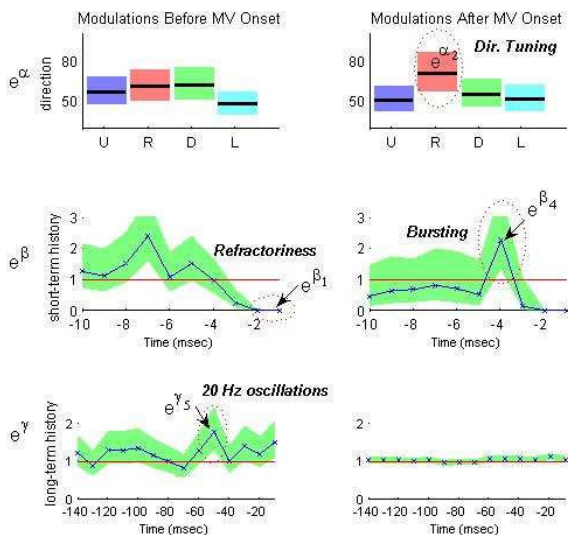

Figure 3: Optimal model parameters for an STN neuron during MV- and MV+ periods of a PD patient executing anticipated-cued trials before movement (left) and after movement (right). Top row (movement direction modulation): optimal extrinsic factors e^{α_d} for d=1,2,3,4 (U,R,D,L) are plotted in black lines from left to right and corresponding 95% confidence intervals are shaded around each black line in a unique color for each direction. Middle row (short-term history modulation): optimal short-term history factors e^{β_i} for i=1,2,…,10 are plotted in blue from right to left and the corresponding 95% confidence intervals are shaded in green. Bottom row (long-term history modulation) optimal long-term history factors e^{γ_j} for j=1,2,…,14 are plotted in blue from right to left and corresponding 95% confidence intervals are shaded in green. Note the change in time scale for bottom row.

IV. DISCUSSION

Two of the trial types performed, anticipated (+cue) and unanticipated visually-guided (+cue), were identical in terms of visuospatial timing and presentation (top and middle, **Figure 1**). The only difference between these two task conditions was the subject's ability to anticipate the "go cue" that was present in both. This anticipatory difference, however, resulted in suppression of pathological oscillations and improvement in reaction time and movement time in the former compared to the latter. In contrast, in both the anticipated (+cue) and unanticipated self-initiated (-cue) conditions, we obtained similar suppression of pathological oscillations and improvement in behavioral measures despite the presence of the "go cue" (GC) in the former and the lack of the GC in the latter.

To cue or not to cue. These results explicitly demonstrate that external cues are neither necessary nor sufficient for motor facilitation in PD. This is consistent with the findings previously described by [21]. In the unanticipated self-initiated (-cue) condition, our subjects were compelled to move by an impending deadline. There is a 50% chance the external GC will appear at the start of each trial. If the subject does not move by the end of the GC epoch, which is defined whether the GC is presented or not, the subject fails the trial and no award is received. Thus, at some point during the GC epoch, the subject decides to self-initiate movement in the absence of an external GC. We will term this internal impetus to move an "internallygenerated" cue. In the unanticipated self-initiated trials, this "internally generated" cue is as effective in suppressing pathological oscillations and facilitating movement time as the anticipated external cue in the anticipated condition. It is therefore likely that the internal impetus to move triggers the same downstream effects that dampen pathological activity and facilitate movement, without requiring the presentation of the external cue.

We believe, like the external GC in the anticipated condition, the internally generated cue in the unanticipated self-initiated condition activates prefrontal cortical activity that leads to diminished pathological STN and basal ganglia coherence through well-described circuitry. The activation of prefrontal cortical activity during self-initiated movements was demonstrated in [21] as well. Although there is no way to determine when the internal cue was generated by the subject, the internal cue should be generated on average after the external cue would usually have appeared, when the subject realizes that the external "go cue" is not coming and an "internal cue" is necessary. This leads to the prediction that, if both the internal and the external cues result in physiological modulation via the same mechanism, this modulation would occur earlier in anticipated trials vs. unanticipated self-initiated trials. Indeed, we find the neurophysiological changes seen in HFOs and DTs with self-initiation occur on average 500 milliseconds after those seen in anticipated trials, as we would have predicted.

What may be critical for motor facilitation in PD is a clear trigger that activates a pre-existing motor plan already formulated in prefrontal cortex. This clear trigger can be an internal cue to move, and exists in the presence or absence of an external "go cue". Therefore, we hypothesize that it is the activation of a specific motor plan, not the presentation of a cue, that is the critical event that provides the cortical

drive that modulates the abnormal physiology of the basal ganglia, leading to motor facilitation.
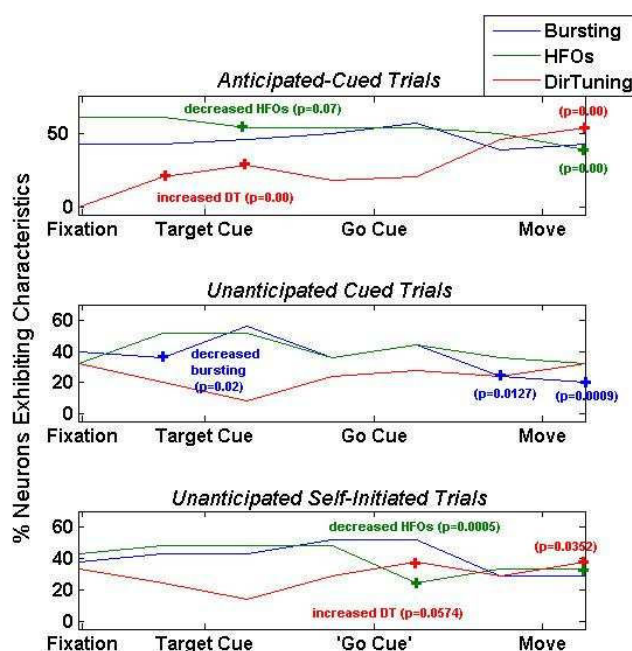

Figure 4: Modulations of each characteristic for each trial type. Anticipated-Cued Trials (top); Unanticipated Cued Trials (middle); Unanticipated Self-Initiated Trials (bottom). When the factional change from baseline is statistically significant in a less pathological direction (decreased bursting, decreased HFOs, increased directional tuning), then we denote that with a '+' symbol and in interesting cases note the p-value.

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