Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Allik J, McCrae RR. Toward a geography of personality traits: patterns of profiles across 36 cultures. J Cross Cult Psychol 2004;35(1): 13–28.
2. Baxter AJ, Scott KM, Vos T, Whiteford HA. Global prevalence of anxiety disorders: a systematic review and meta-regression. Psychol Med 2013;43(5):897–910.
3. Ferrari AJ, Somerville AJ, Baxter AJ, et al. Global variation in the prevalence and incidence of major depressive disorder: a systematic review of the epidemiological literature. Psychol Med 2013;43(3): 471–481.
4. Ben-Joseph A, Marshall CR, Lees AJ, Noyce AJ. Ethnic variation in the manifestation of Parkinson's disease: a narrative review. J Parkinsons Dis 2020;10(1):31–45.
5. Yu RL, Wu RM, Chan AY, et al. Cross-cultural differences of the non-motor symptoms studied by the traditional Chinese version of the International Parkinson and Movement Disorder Society-unified Parkinson's disease rating scale. Mov Disord Clin Pract 2017;4(1):68–77.
6. Rana AQ, Athar A, Owlia A, et al. Impact of ethnicity on non-motor symptoms of Parkinson's disease. J Parkinsons Dis 2012;2(4): 281–285.
7. Sauerbier A, Jitkritsadakul O, Titova N, et al. Non-motor symptoms assessed by non-motor symptoms questionnaire and non-motor symptoms scale in Parkinson's disease in selected Asian populations. Neuroepidemiology 2017;49(1–2):1–17.
8. Sauerbier A, Schrag A, Martinez-Martin P, et al. Dietary variations in a multiethnic Parkinson's disease cohort and possible influences on nonmotor aspects: a cross-sectional multicentre study. Parkinsons Dis 2018;2018:7274085.
9. Sauerbier A, Schrag A, Brown R, et al. Clinical non-motor phenotyping of black and Asian minority ethnic compared to white individuals with Parkinson's disease living in the United Kingdom. J Parkinsons Dis 2021;11(1):299–307.
10. Manson A, Stirpe P, Schrag A. Levodopa-induced-dyskinesias clinical features, incidence, risk factors, management and impact on quality of life. J Parkinsons Dis 2012;2(3):189–198.
11. Ahlskog JE, Muenter MD. Frequency of levodopa-related dyskinesias and motor fluctuations as estimated from the cumulative literature. Mov Disord 2001;16(3):448–458.
12. Investigators PSGCC. Long-term effect of initiating pramipexole vs levodopa in early Parkinson disease. Arch Neurol 2009;66(5): 563–570.
13. Chaudhuri KR, Jenner P, Antonini A. Should there be less emphasis on levodopa-induced dyskinesia in Parkinson's disease? Mov Disord 2019;34(6):816–819.
14. Cenci MA, Riggare S, Pahwa R, Eidelberg D, Hauser RA. Dyskinesia matters. Mov Disord 2020;35(3):392–396.
15. Lim SY, Tan AH, Ahmad-Annuar A, et al. Parkinson's disease in the Western Pacific region. Lancet Neurol 2019;18(9):865–879.
16. Politi C, Ciccacci C, Novelli G, Borgiani P. Genetics and treatment response in Parkinson's disease: an update on Pharmacogenetic studies. Neuromolecular Med 2018;20(1):1–17.
17. Goetz CG, Nutt JG, Stebbins GT. The unified dyskinesia rating scale: presentation and clinimetric profile. Mov Disord 2008;23(16): 2398–2403.
18. Goetz CG, Stebbins GT, Theeuwes A, et al. Temporal stability of the unified dyskinesia rating scale. Mov Disord 2011;26(14):2556–2559.
19. Hauser RA, Friedlander J, Zesiewicz TA, et al. A home diary to assess functional status in patients with Parkinson's disease with motor fluctuations and dyskinesia. Clin Neuropharmacol 2000; 23(2):75–81.
20. Rhode AK, Voyer BG, Gleibs IH. Does language matter? Exploring Chinese–Korean differences in holistic perception. Front Psychol 2016;7:1508.
21. Tajima Y, Duffield N. Linguistic versus cultural relativity: on Japanese–Chinese differences in picture description and recall. Cogn Linguist 2012;23(4):675–709.

Christmas-Related Reduction in Beta Activity in Parkinson's Disease

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ABSTRACT: Background: Subthalamic nucleus (STN) beta (13 - 35 Hz) activity is a biomarker reflecting motor state in Parkinson's disease (PD). Adaptive deep brain stimulation (DBS) aims to use beta activity for therapeutic adjustments, but many aspects of beta activity in real-life situations are unknown.
Objective: The aim was to investigate Christmas-related influences on beta activity in PD.
Methods: Differences in Christmas Day to nonfestive daily averages in chronic biomarker recordings in 4 PD patients with a sensing-enabled STN DBS implant were retrospectively analyzed. Sweet-spot and whole-brain network connectomic analyses were performed.
Results: Beta activity was significantly reduced on Christmas Eve in all patients (4.00–9.00 p.m.: $-12.30 \pm 10.78\%$, $P = 0.015$). A sweet spot in the dorsolateral STN connected recording sites to motor, premotor, and supplementary motor cortices.
Conclusions: We demonstrate that festive events can reduce beta biomarker activity. We conclude that circadian and holiday-related changes should be considered when tailoring adaptive DBS algorithms to patient demands.

Key Words: adaptive deep brain stimulation; basal ganglia; movement disorders; neurophysiology; Parkinson's disease

Introduction

Festivities such as Christmas may have an influence on the dopaminergic system. They may also be exceptionally demanding for patients, for example, regarding physical activity, emotions, and stress.[1,2] Many Christmas activities may directly modulate our neural reward system, in which the neurotransmitter dopamine plays a central role,[3] leading to the question whether PD, as the neurological disorder most imminently associated with dopamine, is impacted by Christmas. With novel brain sensing–enabled implantable pulse generators for deep brain stimulation (DBS),[4] invasive brain signal recordings can now be performed chronically.[5-9] The recorded brain signals, mostly subthalamic nucleus (STN) beta activity that is associated with low levels of dopamine, can then be used to adapt stimulation to concurrent demand.[10-13] Most studies in this emerging field, however, were conducted in experimental settings. Therefore, the impact of life events and festivities on biomarker levels for adaptive DBS (aDBS) is unknown. In the present study, we made use of chronic brain signal recordings from DBS implants to describe the effect of Christmas festivities on PD biomarkers of the hypodopaminergic state.

Patients and Methods

Participants

Data from 4 PD patients with chronic brain signal recordings from STN DBS were included in the study. All participants provided written informed consent.[9] The study was approved by the local ethics committee of the Charité - Universitätsmedizin Berlin (EA2/256/60) and conducted in accordance with the ethical standards set by the Declaration of Helsinki. The inclusion criterion for the retrospective study was the availability of at least 22 days of chronic brain signal recordings starting from December 10 to January 1. For clinical details, see Table S1; for localization of the DBS electrodes, see Figure S1. Participants included 3 male and 1 female patients, with a mean age of 62.8 ± 7.19 years and a disease duration of 11 ± 2.69 years. Patients were informed about the potential relevance of life events and festivities for chronic brain activity recordings. Moreover, a telephone interview and a 7-point Likert self-report questionnaire were conducted regarding Christmas festivities and symptoms; 3 of 4 participants completed the questionnaire, and 1 participant was lost to follow-up.

Data Acquisition

Chronic sensing was set up as previously described.[9] In one case (sub-014) sensing was activated only in the right hemisphere. This has led to the availability of brain signal recordings from seven STNs in 4 patients, with a mean peak frequency of 18.8 ± 6 Hz. For more details on the recording setup, see Supplementary Methods.

Data and Statistical Analysis

Data analysis was performed using custom-written toolboxes and scripts in MATLAB (Mathworks, Natick, MA, USA) and open source software including the Perceive toolbox (https://github.com/neuromodulation/perceive/), the CircaDiem Toolbox (https://github.com/joramvanrheede/circa_diem), SPM12 (https://github.com/spm/spm12), and Lead-DBS v2.6 (https://github.com/netstim/leaddbs).[14] All recordings were performed in Germany from German patients following the German tradition to celebrate Christmas on Christmas Eve (December 24). Therefore, recordings from 12.00 p.m. December 24 through 12.00 p.m. December 25 were designated as Christmas data. Recordings outside this time window from December 10 to January 1 were designated as non-Christmas data. To normalize data and ensure comparability across the

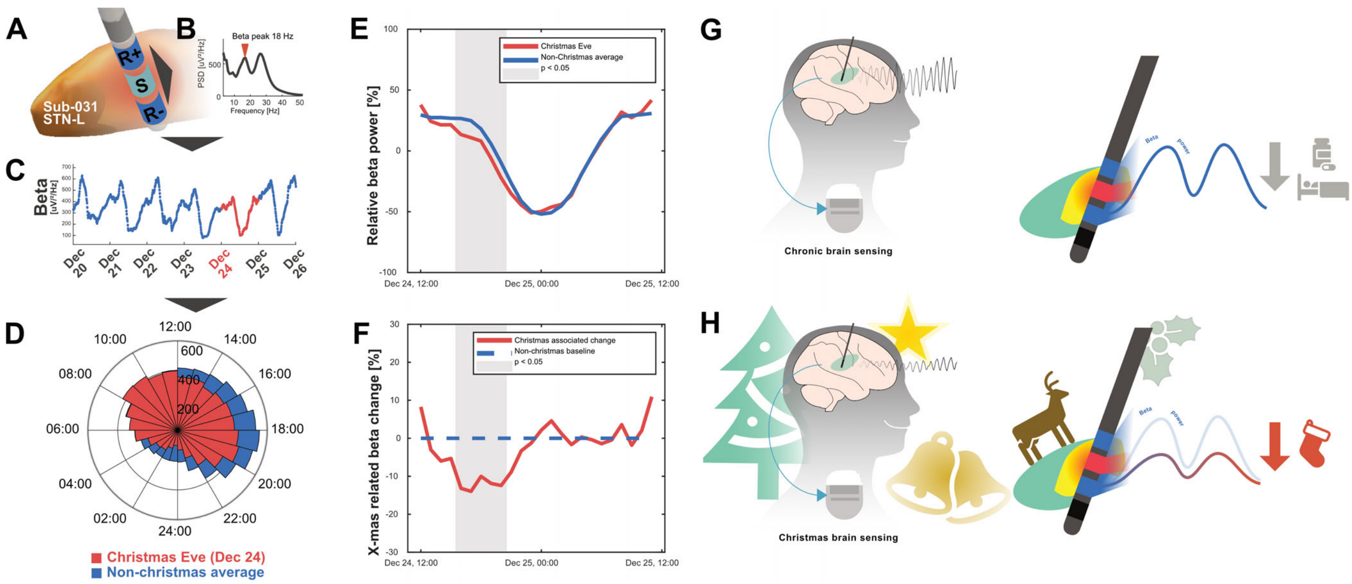

FIG. 1. Beta band activity is suppressed during Christmas. Representative example from a single patient (sub-031) shown in panels A-D. (**A**) The active stimulation contact is marked green (S), and recording contacts are marked blue (R– and R+). (**B**) The power spectrum had peaks in the low- and high-beta frequencies, from which a peak at 18 Hz was chosen for chronic sensing. (**C**) Although the overall circadian periodic pattern is maintained, even on visual inspection, during Christmas Eve (red) a decrease in the peak daytime activity is visible. (**D**) The rose plot representation shows the comparison of hourly biomarker averages obtained at Christmas Eve (red), compared to the non-Christmas average from this recording (blue). Across seven subthalamic nuclei included in the final analysis, (**E**) there was a sustained and consistent suppression of beta biomarker levels during Christmas Eve (red line) and the non-Christmas average (blue line) that can be best appreciated in the (**F**) Christmas-related percentage change to the non-Christmas baseline. The gray shaded area represents the period of significant difference after correction for multiple comparisons, which lies between 4.00 and 9.00 p.m. on Christmas Eve. (**G**) Schematic representation of chronic brain sensing during non-Christmas conditions. Subthalamic biomarker recordings (beta-filtered signal, black) is recorded from DBS electrodes implanted in the subthalamic nucleus (green) and connected with an implantable pulse generator; beta power, recorded in a bipolar configuration (blue contacts) adjacent to the stimulation contact (red) from the DBS electrodes in the subthalamic nucleus, may be influenced by medication and activity levels. During Christmas, we suggest several (**H**) Christmas-induced changes. Christmas mood and increased dopamine release may result in biomarker suppression, with various potential contributing factors such as Christmas magic, reward, increased food, alcohol consumption, and reduced physical activity. [Color figure can be viewed at wileyonlinelibrary.com]

seven recording locations, chronic brain activity estimates were smoothed with Gaussian smoothing kernel of 30 samples' length, normalized to the percentage average amplitude of all non-Christmas days defined as $100 \times$ (Christmas data − mean[non-Christmas data])/mean(non-Christmas data) and binned into 1-hour-long biomarker averages (see Fig. 1C,D).[9]

Binned hourly Christmas biomarker data were statistically compared to non-Christmas averages using nonparametric Wilcoxon signed-rank tests across recording locations. Multiple comparisons were corrected using the cluster permutation approach described by Maris and Oostenveld.[15] For correlation analyses, a single average Christmas-related percentage change value was obtained by averaging Christmas and non-Christmas recordings across all significant bins and subtracting non-Christmas data from Christmas data (see Fig. 1). Electrode localizations were performed using the advanced reconstruction pipeline implemented in Lead-DBS, version 2.6, with default settings as previously described.[16] To identify a spatial Christmas sweet spot in the STN, averaged Christmas-related biomarker changes were projected to the contact location and interpolated in three dimension (see Fig. 2A). Average Christmas-related changes in beta biomarker levels with distance to the sweet spot were correlated. To characterize brain networks associated with Christmas-related brain activity changes, we used the Lead-DBS fiberfiltering tool and connectome mapper pipeline to estimate structural and functional connectivity, respectively (for more information, see Supplementary Methods). All statistical hypothesis tests were performed using nonparametric Wilcoxon signed-rank tests. Correlations were performed using Spearman's and Pearson's correlations while stating the results of a Lilliefors test on data normality.

Results

All patients reported that they celebrated Christmas (see Table S2 for details). They had spent Christmas Eve with their family (3 of 4) or friends (1 of 4), enjoying a festive meal (all four patients). None of the patients reported to have taken additional dopaminergic medication. When comparing self-reported Likert scales (pre-Christmas/Christmas Day/post-Christmas), only mild modulation was reported for motor signs ($2.7 \pm 0.9/3.3 \pm 1.9/2.7 \pm 0.5$;

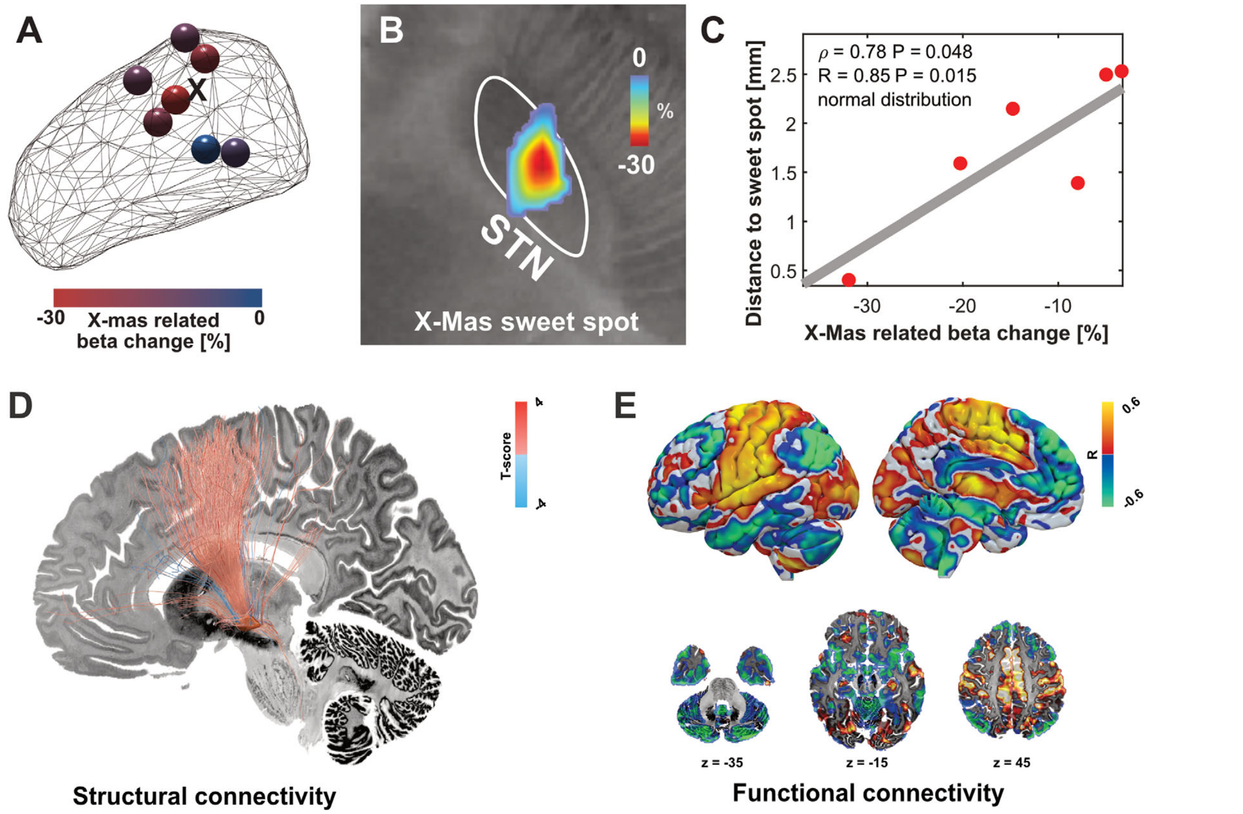

FIG. 2. Sweet spots and connectivity of Christmas. Christmas-related beta change was strongest in recording configurations close to the dorsolateral portion of the subthalamic nucleus (**A**+**B**). Contacts were reconstructed in MNI (Montreal Neurological Institute) space and color coded according to Christmas-related beta biomarker suppression (**A**) from low (blue) to high suppression (red). The optimal stimulation target, as previously described,[18] is marked with a black X and lies within 0.9 mm of the Christmas sweet spot (**B**, MNI coordinates: $X = -12.96$, $Y = -12.84$, and $Z = -6.52$). There was a significant correlation (**C**) of distance to the Christmas sweet spot and Christmas-related beta biomarker reduction. Connectivity reveals brain networks connected to recording sites with strong reduction in beta biomarker levels. Fiber streamlines associated with beta biomarker reduction (**D**, red) depicting relevant structural connectivity as part of the hyperdirect pathway and connecting the motor, premotor, and supplementary motor cortices to the subthalamic recording sites. The subthalamic nucleus is shown as an orange structure to give an anatomical reference to streamlines passing in the vicinity of the recording sites. Whole-brain functional connectivity to cortical and subcortical regions remotely distributed from recording sites and featuring polysynaptic connectivity (**E**). Of note, connectivity to sensorimotor, premotor, and supplementary motor cortices are also highlighted as positively (red-yellow) correlated with beta reduction and in agreement with the structural connectivity patterns. The BigBrain template warped to MNI space was used as a backdrop for volumetric representation.[34] [Color figure can be viewed at wileyonlinelibrary.com]

mean ± standard deviation), joy (3 ± 1.6/4.3 ± 0.9/2.7 ± 1.2), and stress (5.7 ± 0.9/5 ± 1.6/3.7 ± 2.4) (see Fig. S3). One patient reported relevant motor sign improvement on Christmas Day. Peak beta amplitude significantly decreased during the afternoon on Christmas Eve in comparison with the non-Christmas average. An individual example is presented in Figure 1A–D. A continuous cluster of sustained beta suppression ($-12.30 \pm 10.78\%$, $P = 0.015$) was identified between 4.00. and 9.00 p.m. on December 24 (see Fig. 1E,F). Christmas Eve–related suppression of beta activity was consistently present in all recordings and patients (range: -2.8% to 31.9%) and most pronounced at 5.00 p.m., a time when typically presents are being unwrapped. Recording sites in five of seven STN were located within the motor part of the STN, and two of seven in the associative STN according to their minimum Euclidian distance to the respective centers of gravity (see Fig. S2).

The strongest Christmas-related beta suppression could be localized to a sweet spot in the dorsolateral STN (see Fig. 2A) only 0.9 mm from a previously reported optimal stimulation target location,[17,18] with higher Christmas-related modulation in comparison to recording locations in relative distance to this sweet spot (Pearson's $R = 0.85$, $P = 0.015$; Spearman's rho $= 0.78$, $P = 0.048$).

Normative connectome analyses revealed a positively correlated structural connectivity pattern represented by fiber streamlines connecting mainly motor (M1, premotor and supplementary) cortices to the subthalamic recording sites (Fig. 2D). Similarly, the whole-brain functional connectivity pattern (Fig. 2E) showed a positive connectedness to these regions, whereas the cerebellum and parietal cortex showed negative associations.

Discussion

This retrospective analysis demonstrates that invasive brain signal recordings can reveal significant modulations of beta activity, potentially beyond motor sign severity. We found a consistent subthalamic beta suppression in PD patients during the afternoon of Christmas Eve, when compared to other days. Moreover, we could define a Christmas sweet spot in the dorsolateral STN in direct proximity to the optimal target location for clinical response.

Given the previously demonstrated relationship between dopaminergic medication and beta activity,[5,19-23] as well as the direct anticorrelation of beta and dopamine in nonhuman primates,[24] our findings could directly signal higher dopamine levels in patients during the festivities. Multiple studies have suggested that social behavior,[25,26] music,[27] food intake,[28] alcohol consumption,[29] and reward expectation and experience[30,31] can influence dopamine release—all very important components of a Christmas celebration. Besides this potentially joyful message, our results indicate that life events, such as festivities during the holiday season, will have a direct impact on electrophysiological biomarkers for aDBS. Considering this critically, lower biomarker activity reflecting special occasions may coincide with time points of high therapeutic demand, a factor that could lead to undesirably low therapeutic delivery. A potential bias on the observed biomarker levels may be contamination with motion artifacts, possibly influencing circadian periodicity[9]—an aspect that may, during Christmas, reflect low-activity festive programs with extensive meals resulting in weight gain.[32] Moreover, fluctuations in medication adapted to fit the festive schedule may have a modulatory effect on beta activity, even though patients did not report changes in their medication routine for Christmas. Further limitations result from the retrospective data analysis on a small sample size of patients without prospective and objective symptom and medication assessments. Future studies should include objective (non-) motor symptom measures, wearables, and ecological self-reports for more detailed characterizations. Importantly, Christmas is a relatively exclusive festival, giving our findings unclear transcultural applicability to other festivities. The change in beta band activity during other religious and nonreligious holidays in a similar season such as Hanukkah, Kwaanza, or Chinese New Year should be investigated. In addition, seasonal aspects in festivities in different seasons such as Easter or Pesach, as well as festivities that temporally move in the calendar like Eid Mubarak, should be investigated, as well as electrophysiological signatures of not purely joyful celebrations such as Yom Kippur. Finally, whether the sweet-spot and connectomic analyses really differentiate from the optimal target that is known to have a high beta activity cannot be determined by our study. The majority of recording sites resided within the motor and not limbic STN. Nevertheless, our connectivity analysis showed an overlap with a previously described functional magnetic resonance imaging (fMRI)–Christmas network in healthy adults.[33]

In conclusion, this study provides first evidence that Christmas has an influence on the hypodopaminergic parkinsonian state, reflected in electrophysiological biomarker dynamics (see Fig. 1G,H). Explanations may remain speculative and range from increased dopamine related to joyful spirit to reduced activity and lower signal contamination during feasting. Studies that use such biomarker dynamics for therapeutic adjustment should try to account for such changes, to ensure that the optimal treatment is delivered for the individual situation the patients are facing. Given the robust association between biomarker suppression and motor sign alleviation, we conclude that participating in joyful festivities can be generally recommended to patients with Parkinson's disease.

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Data Availability Statement

All Matlab code and data for figure generation from aggregated group results is available through GitHub (https://github.com/neuromodulation/XMas). Individual patient data fall under the health data category of the European General Data Privacy Regulation (GDPR) and require the lawful definition of data sharing agreements from all data controllers. Data sharing agreements can be set in place upon reasonable request to the corresponding author.

References

1. Folyovich A, Matis R, Al-Muhanna N, et al. Christmas, acute ischemic stroke and stroke-related mortality in Hungary. Brain Behav 2021;11(5):e02104.
2. Olsson A, Thoren I, Mohammad MA, et al. Christmas holiday triggers of myocardial infarction. Scand Cardiovasc J 2021;55(6):340–344.
3. Baik JH. Dopamine signaling in reward-related behaviors. Front Neural Circuits 2013;7:152.
4. Schuepbach WM, Rau J, Knudsen K, et al. Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med 2013;368(7):610–622.
5. Feldmann LK, Lofredi R, Neumann WJ, et al. Toward therapeutic electrophysiology: beta-band suppression as a biomarker in chronic local field potential recordings. npj Parkinson's Dis 2022;8(1):44.
6. Gilron R, Little S, Perrone R, et al. Long-term wireless streaming of neural recordings for circuit discovery and adaptive stimulation in individuals with Parkinson's disease. Nat Biotechnol 2021;39(9):1078–1085.
7. Kehnemouyi YM, Wilkins KB, Anidi CM, Anderson RW, Afzal MF, Bronte-Stewart HM. Modulation of beta bursts in subthalamic sensorimotor circuits predicts improvement in bradykinesia. Brain 2021;144(2):473–486. doi:10.1093/brain/awaa394
8. Neumann WJ, Staub F, Horn A, et al. Deep brain recordings using an implanted pulse generator in Parkinson's disease. Neuromodulation 2016;19(1):20–24.

9. van Rheede JJ, Feldmann LK, Busch JL, et al. Diurnal modulation of subthalamic beta oscillatory power in Parkinson's disease patients during deep brain stimulation. npj Parkinson's Dis 2022;8(1):88.

10. Adaptive DBS Algorithm for Personalized Therapy in Parkinson's Disease (ADAPT-PD). https://clinicaltrials.gov/ct2/show/NCT0454771221.04.2021.

11. Arlotti M, Marceglia S, Foffani G, et al. Eight-hours adaptive deep brain stimulation in patients with Parkinson disease. Neurology 2018;90(11):e971–e976.

12. Little S, Pogosyan A, Neal S, et al. Adaptive deep brain stimulation in advanced Parkinson disease. Ann Neurol 2013;74(3):449–457.

13. Velisar A, Syrkin-Nikolau J, Blumenfeld Z, et al. Dual threshold neural closed loop deep brain stimulation in Parkinson disease patients. Brain Stimul 2019;12(4):868–876.

14. Neumann WJ, Memarian Sorkhabi M, Benjaber M, et al. The sensitivity of ECG contamination to surgical implantation site in brain computer interfaces. Brain Stimul 2021;14(5):1301–1306.

15. Maris E, Oostenveld R. Nonparametric statistical testing of EEG- and MEG-data. J Neurosci Methods 2007;164(1):177–190.

16. Horn A, Kuhn AA. Lead-DBS: a toolbox for deep brain stimulation electrode localizations and visualizations. Neuroimage 2015;107: 127–135.

17. Horn A, Kuhn AA, Merkl A, Shih L, Alterman R, Fox M. Probabilistic conversion of neurosurgical DBS electrode coordinates into MNI space. Neuroimage 2017;150:395–404.

18. Caire F, Ouchchane L, Coste J, et al. Subthalamic nucleus location: relationships between stereotactic AC-PC-based diagrams and MRI anatomy-based contours. Stereotact Funct Neurosurg 2009;87(6): 337–347.

19. Brown P, Oliviero A, Mazzone P, Insola A, Tonali P, Di Lazzaro V. Dopamine dependency of oscillations between subthalamic nucleus and pallidum in Parkinson's disease. J Neurosci 2001;21(3):1033–1038.

20. Kuhn AA, Kempf F, Brucke C, et al. High-frequency stimulation of the subthalamic nucleus suppresses oscillatory beta activity in patients with Parkinson's disease in parallel with improvement in motor performance. J Neurosci 2008;28(24):6165–6173.

21. Lofredi R, Tan H, Neumann WJ, et al. Beta bursts during continuous movements accompany the velocity decrement in Parkinson's disease patients. Neurobiol Dis 2019;127:462–471.

22. Steiner LA, Neumann WJ, Staub-Bartelt F, et al. Subthalamic beta dynamics mirror Parkinsonian bradykinesia months after neurostimulator implantation. Mov Disord 2017;32(8):1183–1190.

23. Tinkhauser G, Pogosyan A, Tan H, Herz DM, Kuhn AA, Brown P. Beta burst dynamics in Parkinson's disease OFF and ON dopaminergic medication. Brain 2017;140(11):2968–2981.

24. Schwerdt HN, Amemori K, Gibson DJ, et al. Dopamine and beta-band oscillations differentially link to striatal value and motor control. Sci Adv 2020;6(39):eabb9226. doi:10.1126/sciadv.abb9226

25. Saez I, Zhu L, Set E, Kayser A, Hsu M. Dopamine modulates egalitarian behavior in humans. Curr Biol 2015;25(7):912–919.

26. Robinson DL, Zitzman DL, Williams SK. Mesolimbic dopamine transients in motivated behaviors: focus on maternal behavior. Front Psychiatry 2011;2:23.

27. Salimpoor VN, Benovoy M, Larcher K, Dagher A, Zatorre RJ. Anatomically distinct dopamine release during anticipation and experience of peak emotion to music. Nat Neurosci 2011;14(2):257–262.

28. Volkow ND, Wise RA, Baler R. The dopamine motive system: implications for drug and food addiction. Nat Rev Neurosci 2017; 18(12):741–752.

29. Di Chiara G. Alcohol and dopamine. Alcohol Health Res World 1997;21(2):108–114.

30. Pasquereau B, Tremblay L, Turner RS. Local field potentials reflect dopaminergic and non-dopaminergic activities within the primate midbrain. Neuroscience 2019;399:167–183.

31. Rowe JB, Hughes L, Ghosh BC, et al. Parkinson's disease and dopaminergic therapy--differential effects on movement, reward and cognition. Brain 2008;131(Pt 8):2094–2105.

32. Yanovski JA, Yanovski SZ, Sovik KN, Nguyen TT, O'Neil PM, Sebring NG. A prospective study of holiday weight gain. N Engl J Med 2000;342(12):861–867.

33. Hougaard A, Lindberg U, Arngrim N, et al. Evidence of a Christmas spirit network in the brain: functional MRI study. BMJ 2015; 351:h6266.

34. Amunts K, Lepage C, Borgeat L, et al. BigBrain: an ultrahigh-resolution 3D human brain model. Science 2013;340(6139): 1472–1475.

Supporting Data

Additional Supporting Information may be found in the online version of this article at the publisher's web-site.

In Vivo Investigation of Glucose Metabolism in Idiopathic and *PRKN*-Related Parkinson's Disease

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