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# Subthalamic deep brain stimulation improves vergence eye movements in Parkinson's disease

**Eva Muthig**
Universitätsklinikum Würzburg
**Saloni Jethwa**
University Hospital Ulm
**Anastasia Nosanova**
University Hospital Ulm
**Helen Friedrich**
Julius-Maximilians University Wuerzburg
**Nicolo Pozzi**
Universitätsklinikum Würzburg
**Tamina Settele**
University Hospital Ulm
**Torste Odorfer**
Universitätsklinikum Würzburg
**Stanislav Bardins**
Brandenburg University of Technology Cottbus – Senftenberg
**Erich Schneider**
Brandenburg University of Technology Cottbus – Senftenberg
**Martin Reich**
Universitätsklinikum Würzburg
**Daniel Zeller**
Universitätsklinikum Würzburg
**Maximilian U. Friedrich**
Maximilian.friedrich@uni-ulm.de

University Hospital Ulm

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## Abstract

# Background

Visuomotor manifestations are increasingly recognized as a clinical dimension of Parkinson's disease (PD). Among these, vergence dysfunction can cause double vision and impair everyday visual function, yet binocular control is rarely quantified objectively. Consequently, it remains unknown how vergence dysfunction relates to PD severity, and whether it is amenable to established PD treatments, including dopaminergic medication and subthalamic deep brain stimulation (STN-DBS).

# Methods

We used a high-resolution binocular video-oculography paradigm to quantify conjugate and vergence eye movements in 24 people with PD and bilateral STN-DBS across three controlled therapeutic states (medication/DBS off/off, on/off and off/on), alongside 36 age-matched controls. Motor severity was independently assessed based on standardized videography using blinded MDS-UPDRS-III ratings by three independent assessors.

# Results

Double vision was reported by 29% of participants with PD compared with 3% of controls ($p = .005$). In the OFF state, PD was associated with pronounced impairment of dynamic vergence, with convergence and divergence gains reduced by up to 65% and maximal convergence angles reduced by up to 42% compared with controls (all $p \leq .006$). Slow divergence latency was additionally prolonged ($p = .001$), whereas vergence stability did not differ significantly. Conjugate eye movements showed reduced vertical saccadic gain and fewer self-paced saccades, but largely preserved smooth pursuit. Vergence and vertical saccadic gain additionally scaled with MDS-UPDRS-III motor severity. STN-DBS improved slow vergence gain by up to 39%, maximal convergence angle by 20%, and increased vertical saccadic gain by 50%, whereas dopaminergic medication produced no significant improvement in these ocular motor parameters.

# Conclusion

These findings identify dynamic vergence dysfunction as a visuomotor feature of PD and demonstrate amenability to STN-DBS. The pronounced modulation of both conjugate and vergence eye movements by STN-DBS suggests that impaired binocular motor control in PD is associated with dysfunction of subthalamic circuits.

## Introduction

Parkinson's disease (PD) is the most common neurodegenerative movement disorder, canonically defined by a combination of bradykinesia with rigidity and/ or tremor[1]. Beyond these hallmark features, PD is increasingly recognized as a multisystem disorder encompassing a broad spectrum of non-canonical manifestations, including cognitive, balance, and sensory disturbances[2].

Among the latter, visual dysfunction in PD is still underrecognized, despite its negative impact on quality of life. While it can affect several stages of afferent visual processing[3], a range of eye movement disorders are commonly observed in people with PD (pwPD)[4]. For instance, hypometric saccades and reduced smooth pursuit gain are well-established abnormalities of conjugate gaze in pwPD, but their relationship to motor severity and therapeutic effects of dopaminergic medication or deep brain stimulation (DBS) remains somewhat controversial[4–6].

Vergence eye movements, which rotate the eyes in opposite directions to maintain binocular alignment and enable stereoscopic vision, have received comparatively less systematic attention, despite their direct relevance for everyday visual function[7–11]. More specifically, vergence dysfunction can lead to double vision, impairing fixation, reading, and spatial navigation, potentially compounding the fall risk already elevated in pwPD[9,10,12].

This gap is clinically consequential. Up to 38% of people with Parkinson's disease report double vision, frequently in the context of impaired vergence control[7–10,13,14]. Convergence insufficiency is particularly prevalent among people with double vision, often at a severity that interferes with daily activities[8,13] and quality of life[14]. Double vision has also been associated with visual hallucinations, suggesting that binocular dysfunction may interact with broader visuoperceptive disturbances in PD[15,16].

Despite this clinical relevance, vergence dysfunction in PD remains poorly characterized. Much of the literature has relied on self-reports, questionnaires or bedside measures of convergence and ocular alignment, which are clinically informative, but provide only coarse estimates of binocular motor function[7–9]. While these clinical studies suggest that dopaminergic medication may improve convergence ability and reduce double vision in some pwPD[9,13], it remains unknown to what extent vergence dysfunction in PD relates to reversible dopaminergic depletion, subthalamic network dysfunction, or a combination of both, and whether these influences differ across different components of vergence.

Infrared video-oculography (VOG) enables more granular and objective ocular motor assessments in the context of Parkinsonian and other neurological disorders, but is still primarily used for conjugate eye movement testing[17]. Yet, a small number of studies have applied VOG to measure vergence in pwPD. Hanuška et al. examined rapid, step-evoked vergence and reported prolonged latencies together with slowed and hypometric divergence[18], while Gupta et al. demonstrated preferential impairment of disparity-driven relative to blur-driven vergence in pwPD[19]. However, both studies assessed pwPD under

heterogeneous or uncontrolled medication conditions, precluding separation of disease-related impairment from medication effects that are thought to influence conjugate eye movements[4].

Evidence for neuromodulation is even more limited. While lesion mapping and brain stimulation studies show that subcortical brain circuits for binocular control are accessible to therapeutic or inadvertent neuromodulation[20–23], there is, at present, only abstract-level evidence indicating that STN-DBS can influence strabismus angle and vergence in pwPD, although again, medication status was not reported[6,24].

Taken together, existing studies underscore the relevance of vergence dysfunction in pwPD, but the effects of disease and established PD treatments on vergence remain unclear. This limits our ability to tailor pharmacological or brain stimulation therapies to improve ocular motor function as an underappreciated dimension of PD symptomatology.

To address this gap, we used a high-resolution video-oculography setup customized for vergence measurements to quantify the effects of PD severity, routine dopaminergic medication and bilateral STN-DBS on vergence eye movements. By quantifying conjugate and vergence eye movements across controlled therapeutic states within the same pwPD and in controls, we tested three principal hypotheses: first, that pwPD exhibit impaired dynamic vergence compared with age-matched controls; second, that vergence dysfunction is modulated by established PD treatments, and third, that the magnitude of ocular motor impairment scales with overall motor severity in pwPD. Together, these analyses aimed to characterize dynamic vergence dysfunction in PD and determine its relationship to disease severity and therapeutic modulation.

## Methods

## Ethics and Study Approval

The study was conducted in accordance with the principles of the Declaration of Helsinki and its later amendments. As part of a larger research project on video-based assessments in Parkinson's disease, the study was reviewed and approved by the Ethics Committee of Julius-Maximilians University Würzburg (#218/21-sc). All participants provided written informed consent prior to participation.

# Inclusion and Exclusion Criteria

Participants were included if they were ≥ 18 years of age and had no ophthalmological, neurological, or medical conditions known to affect binocular vision. For the PD group, diagnosis was based on the MDS clinical diagnostic criteria[1], and participants were required to have undergone bilateral deep brain stimulation (DBS) implantation to the subthalamic nucleus at least three months prior to study participation.

Exclusion criteria comprised a diagnosis of strabismus or binocular vision disorders impairing stereopsis, operationalized as stereopsis worse than 600 arcsec on the Lang stereo test[25]. Additional exclusion criteria were persistent diplopia due to cranial nerve dysfunction, visual field defects, visual hallucinations, a history of stroke, multiple sclerosis or other conditions associated with brain lesions, and severe cognitive impairment, defined as a Montreal Cognitive Assessment (MoCA) score < 18.

After video-oculography acquisition, datasets with insufficient signal due to pronounced artifacts, such as excessive blinking or impaired pupil tracking were discarded.

## Assessment of motor, cognitive and visuomotor impairment

Participants completed a standardized questionnaire assessing history of strabismus, diplopia, visual impairment, visual correction including contact lens use, and demographic and clinical variables, including age, sex, education, and current medication. Motor severity was assessed through standardized videography of the MDS-UPDRS-III in each therapeutic state[26]. Recordings followed a predefined protocol ensuring consistent acquisition, complete coverage of all motor items and optimal conditions for computer vision-based analyses[27] (see Supplementary Section S1). Videos were randomized to be rated independently and in a blinded manner by two senior and one junior movement disorder specialists (T.O., M.U.F., T. S.) according to MDS-UPDRS criteria. Stereoscopic vision was assessed using the Lang stereo test, version 1 or 2, allowing documentation of the smallest detected disparity level. Interpupillary distance was measured manually for subsequent analysis of vergence eye movements. Global cognitive function was assessed using the Montreal Cognitive Assessment (MoCA, paper-based versions 8.1 and 8.2), administered and scored by a trained examiner (E.M.)[28].

## Videooculography (VOG)

Binocular eye movements were recorded using a high-resolution infrared camera-based goggle system (EyeSeeCam Sci 2, EyeSeeTec GmbH, Munich, Germany; https://eyeseetec.de/; software version 2.2.5), as described previously[29]. A five-point calibration procedure was used. Participants were instructed to follow a moving visual target, presented as a dot with a diameter of 1.3 cm, on either a vertical frontoparallel screen or a horizontal screen, depending on the task.

Both displays were LCD computer screens (AOC 27G 2/BK; 27-inch IPS panel; 1920 × 1080 pixels; 144 Hz refresh rate; 1 ms MPRT response time; brightness 250 cd/m²). All recordings were performed in a completely darkened room. The only light sources were the visual target and the computer used to operate and record the VOG system.

## Conjugate eye movement setup and tasks

For assessment of conjugate eye movements, participants were seated with their head stabilized in a chin rest at a viewing distance of 60 cm from a wall-mounted screen. Smooth pursuit was assessed using sinusoidal horizontal and vertical target motion. Horizontal pursuit covered a total range of 40° visual angle, corresponding to 43.7 cm on the screen, and vertical pursuit covered a total range of 30°, corresponding to 32.2 cm. Tasks were performed at frequencies of 0.1 Hz and 0.2 Hz.

Visually guided saccades were assessed by presenting the target at random positions along the horizontal or vertical center line of the monitor. Horizontal saccade amplitudes were 5°, 10°, 15°, 20°, and 40° to the left and right. Vertical saccade amplitudes were 5°, 10°, 15°, 20°, and 30° upward and downward. For self-paced saccades (N30), two targets separated by 20° visual angle, corresponding to 21.2 cm, were presented simultaneously. Participants were instructed to look back and forth between the two targets as quickly as possible for 30 seconds.

The following parameters were extracted for analysis: smooth pursuit gain at 0.1 Hz and 0.2 Hz, saccadic gain and latency, and the total number of self-paced saccades completed within 30 seconds (“N30 saccades”).

## Vergence setup and tasks

The standard VOG setup was extended by adding a horizontally mounted screen to enable assessment of depth-axis eye movements, i. e. vergence. The horizontal monitor was equipped with a custom-made contrast-enhancing film to compensate for visual distortions in narrow viewing angles. A custom-built mount was developed to ensure stable and reproducible positioning of the monitor and participant. The mount included a vertical support rod, a base plate with three independently adjustable threaded leveling feet for coarse planar alignment, and a tilt-adjustment mechanism between the monitor and support rod for fine angular alignment. A chin rest was rigidly attached to the monitor support structure and stabilized using the same leveling-foot system to minimize head movement and to support standardization of relative eye and screen positions.

Before vergence recordings, participants underwent a two-step positioning and calibration procedure. First, participants were seated centrally in front of the horizontal monitor, with the pupils positioned approximately 10 cm from the monitor and no more than 1.5 cm above the monitor edge, as illustrated in Supplementary Figure S1 (see Supplementary Section S2). The geometry and near point position was pragmatically chosen to match previously reported vergence ranges in pwPD and controls[9]. This standardized the starting geometry across participants, particularly for near convergence measurements, and minimized confounding effects of vertical gaze, which was inevitable with this screen-based setup.

Second, a five-point laser calibration was performed. The calibration laser was aligned centrally and orthogonally in both axes, with the central laser dot positioned 2.5 cm above the upper screen edge. Participants were then positioned on a chin rest approximately 4 m from a wall and sequentially fixated

the five projected laser points. This distance was chosen to approximate a vergence reference angle of 0°. The final binocular calibration was achieved through sequential monocular calibration.

After calibration, participants completed three vergence tasks. The analyzed fixation distances ranged from 11 cm to 69 cm from the pupils, corresponding to vergence angles of approximately 5° to 30°, depending on individual interpupillary distance.

The first two tasks assessed slow vergence at two target velocities. In the low-velocity condition, the target moved at 1.67°/s; in the high-velocity condition, it moved at 3.3°/s, velocities chosen to mirror those used in conjugate smooth pursuit tasks. In both conditions, the target moved smoothly from the farthest position toward the participant, paused for 5 seconds at the near position, returned to the far position, and paused again for 5 seconds. This sequence was repeated three times for each velocity.

The third task assessed fast vergence and was designed analogously to a visually guided saccade task. The target appeared at random positions along the center line of the horizontal screen, spanning approximately 5° to 30° of vergence demand, in line with previous work[18] .

Raw eye movement data were preprocessed using the EyeSeeCam Sci 2 software. Individual interpupillary distance was used to model the ocular axes and reconstruct vergence angle for subsequent analysis. A detailed description on vergence reconstruction is provided in the Supplementary Section S3.

For all vergence tasks, the following parameters were extracted: maximal convergence angle (MCA), vergence gain and latency, and the standard deviation of mean vergence angle at the extrema position as a surrogate measure of vergence stability, or holding. In addition, the subjective near point of convergence was documented as the position at which participants first perceived double images. This distance was measured from the screen edge to the reported onset position of diplopia.

# Study Design

pwPD underwent three VOG analyses alongside standardized videography of the MDS-UPDRS-III: (1) 60 minutes after intake of their clinically established dopaminergic medication and 45 minutes after DBS was turned off (“MED”); (2) in the morning after overnight withdrawal of their clinically established dopaminergic medication for at least 12 hours, with DBS on (“DBS”); and (3) with deactivated DBS following a 45-minute wash-out period (“OFF/OFF”). DBS and OFF/OFF assessments were always obtained consecutively in the morning after withdrawal of overnight medication, with the MED condition being assessed either on the same day after intake of regular dopaminergic medication, or during a separate afternoon session. In controls, VOG was assessed once.

## DBS electrode localization

Please refer to Supplementary Section S4 for a detailed description. In brief, deep brain stimulation electrodes were localized with Lead-DBS v3.2.1[30], with a modified PaCER interface. The postoperative CT was linearly coregistered (rigid followed by affine, with two exceptions described in Supplementary Section S4.2) to the preoperative T1-weighted MRI, and the T1-, T2- and T2*-weighted images were jointly normalized to Montreal Neurological Institute (MNI) ICBM 2009b nonlinear asymmetric space[31] with symmetric diffeomorphic registration (ANTs SyN)[32]. Lead trajectories were reconstructed with PaCER[33], and contacts were placed according to each patient's implanted lead model. The depth of every lead was verified against the distal end of the metal artifact on the CT and corrected where necessary (three patients; two further patients were re-reconstructed with their recorded lead models). Contact-position uncertainty was estimated from the agreement of independent coregistration (FLIRT[34], BRAINSFit[35]) and normalization methods (SynthMorph[36], SHOOT[37] using a three-cornered-hat decomposition; combined with the lead depth and axis errors, it was about 0.5 mm in native and 0.6 mm in MNI space, comparable to the inter-rater variability reported for Lead-DBS (0.52–0.75 mm)[38]. Active contacts were those that had the main stimulation program at the study visit, irrespective of polarity, with segments of directional leads counted individually. Contacts were assigned to the STN of the full DISTAL atlas[39] when the atlas value at the contact was at least 0.5, and within the STN to the sensorimotor, associative or limbic subdivision. As a sensitivity analysis, contacts were also evaluated against the atlas STN fitted to each patient's T2- and T2*-weighted MRI (T2 only in three patients). Imaging parameters, quality control and accuracy estimates are detailed in Supplementary Section S4.

# Statistical Analysis

Statistical analyses were performed using JASP version 0.98.1. Depending on data distributions and normality testing, the appropriate parametric test or non-parametric alternative was chosen. Prevalence of binocular symptoms across groups were assessed by comparing the frequency of self-reported diplopia using Fisher's exact test. To assess baseline differences in eye movement parameters, pwPD in the OFF medication/OFF stimulation condition (OFF/OFF) were compared with controls using Mann–Whitney U tests. To evaluate within-subject effects of dopaminergic medication and DBS in pwPD, eye movement parameters across therapeutic conditions were analyzed using Friedman tests. When Friedman tests indicated significant condition effects, Conover's post hoc tests were performed to identify the conditions between which significant differences occurred. For parameters showing significant DBS-related effects, pwPD in the DBS-ON (DBS) condition were additionally compared with controls using Mann–Whitney U tests to assess if parameters reapproached the level of controls under stimulation. Associations between eye movement parameters and clinical covariates were examined using Spearman's rank correlation coefficients. These analyses were performed at baseline, defined as the OFF/OFF condition in pwPD and the single available measurement condition in controls. Because several ocular motor parameters and MoCA scores were associated with age in the control group, age was considered a potential confounder. Age-adjusted non-parametric associations were therefore calculated by regressing the respective ocular motor parameter and MoCA score on age and correlating the resulting residuals using Spearman's rank correlation.

To investigate whether ocular motor abnormalities identified at the group level were related to motor disease severity, we performed a secondary two-stage analysis restricted to ocular motor features showing significant differences in the preceding between-group or within-subject analyses. First, univariate linear regression models were used to quantify the relationship between each candidate feature and motor severity, as measured by the MDS-UPDRS III. Candidate features were subsequently entered jointly into a multivariable linear regression model to determine whether individual ocular motor measures provided complementary information about motor severity after accounting for variance shared across features. Model fit was quantified using the coefficient of determination ($R^2$), and out-of-sample performance was assessed using grouped leave-one-subject-out cross-validation. As each participant contributed up to three observations, associations between individual ocular motor features and MDS-UPDRS-III scores across therapeutic states were estimated with linear mixed models including a random intercept per participant, and standard errors of the multivariable model were clustered by participant.

As this was an exploratory study aimed at characterizing vergence function and generating hypotheses regarding treatment-related modulation thereof, p-values were not by default corrected for multiple comparisons. Results should therefore be interpreted as exploratory. Tests were two-tailed, except for vergence parameters of pwPD with and without self-reported diplopia, which were compared using one-tailed Mann–Whitney U tests, based on the a priori hypothesis of reduced vergence function in participants with diplopia. The threshold for statistical significance was set at $p < .05$, denoted by * ($p < .01$ **, $p < .001$ ***).

## Results

# Subjects

A total of 30 pwPD were enrolled between November 2022 and August 2024. Three subjects withdrew from the study after written consent, and three datasets were excluded due to insufficient data quality. In total, data from 24 pwPD were included in the final analyses. In addition, a total of 61 controls were enrolled between November 2022 and April 2023. Four subjects withdrew from the study after written consent, two datasets were excluded due to a new diagnosis of multiple sclerosis and four due to insufficient data quality (11% in pwPD, 7% in controls, Fisher's exact test $p = .676$, OR = 1.66). Finally, data from 51 controls were included in the analyses. To account for age differences between the control cohort and the PD group, an age-matched control subsample was selected post-hoc and used for between-group comparisons. Demographic and clinical details of the cohort are reported in Table 1. Total MDS-UPDRS III scores were averaged across raters as inter-rater reliability was excellent (ICC(2,1) = 0.88). MDS-UPDRS-III scores in pwPD differed significantly across treatment conditions (Friedman test $\chi^2(2) = 27.20$, $p < .001$, Kendall's W = 0.618). Post hoc Conover tests showed significantly lower scores in the MED ($p = .021$, r = .407) and DBS ($p < .001$, r = 1) conditions compared to OFF/OFF.

# Verification of DBS lead placement

All 48 DBS leads from 24 pwPD were successfully reconstructed. Anatomical verification confirmed that 46/48 leads had at least one contact within the STN, with active contacts predominantly located within its sensorimotor and associative subdivisions (Supplementary Figures S3 and S4). Detailed electrode localization results and quality control analyses are provided in Supplementary Section S4.

Table 1
Demographic and Clinical Characteristics of Patients and Controls

| Variable | pwPD | Age-Matched Controls | All Controls |
|---|---|---|---|
| N | 24 | 36 | 51 |
| Age | 62.3 ± 7.1 years | 62.6 ± 6.1 years | 55.5 ± 15.2 years |
| Sex (f/m) | 4/20 (17% female) | 12/24 (33% female) | 16/35 (31% female) |
| Disease Duration | 12.5 ± 4.8 years | | |
| Hoehn & Yahr | 3 (2–4)* | | |
| MDS-UPDRS III (OFF) | 48.89 ± 12.93 | | |
| MDS-UPDRS III (MED) | 46.41 ± 15.77 | | |
| MDS-UPDRS III (DBS) | 32.86 ± 9.82 | | |
| LEDD (mg/d) | 367.5 (278.8–505.0)** | | |
| Diplopia (≥ 1 events) | 7 (29%) | 1 (3%) | 1 (2%) |
| MoCA | 26.0 ± 2.9 | 26.4 ± 3.1 | 26.8 ± 2.8 |
| *Note.* *Range, **IQR | | | |

# Conjugate Eye Movements

# Comparison of pwPD OFF/OFF and age-matched controls

Smooth pursuit gain did not differ significantly between pwPD OFF/OFF and controls (all $p > .060$; Fig. 1). However, descriptive patterns indicated larger group differences for horizontal than for vertical smooth pursuit.

In contrast, saccadic gain was significantly reduced in pwPD compared to controls for both horizontal and vertical movements (both $p < .001$; Fig. 1), with larger reduction observed for vertical (-52.7%, 0.38 ± 0.27 vs 0.81 ± 0.16) than horizontal saccades (-37.8%, 0.49 ± 0.24 vs 0.78 ± 0.20). Latency was not significantly influenced by PD (all $p > .393$).

Additionally, pwPD showed significantly lower number of self-paced saccades in 30 seconds (N30) compared to controls (42.33 ± 10.36 vs 52.72 ± 13.49; $p = .002$; Fig. 1).

Corresponding means and standard deviations are provided in Supplementary Table S1, while detailed statistical results are reported in Supplementary Table S2 (Supplementary Section S5).

# Effects of PD treatment on conjugate eye movement

For smooth pursuit, a significant treatment effect was observed for horizontal gain (0.1 Hz: $p$= .038; 0.2 Hz: $p$= .042), whereas vertical smooth pursuit remained unchanged (both $p$> .582; Fig. 1).

Post hoc analyses revealed no significant effect of dopaminergic medication but showed a modest improvement of horizontal smooth pursuit gain with DBS, increasing by 3.9% at 0.1 Hz and by 7.2% at 0.2 Hz (PD–DBS: $p$ = .010 and $p$ = .022, respectively; Fig. 1).

For saccades, a significant overall treatment effect was observed for vertical saccadic gain ($p$ = .005). Post hoc analyses indicated that this effect was driven by DBS, with vertical saccadic gain increasing by 49.7% ($p$ = .006; Fig. 1).

Saccadic latency remained unaffected by PD treatment in both directions (all $p$ > .330). Similarly, N30 saccades showed a numerical increase in response to medication or DBS, but this effect did not reach significance ($p$ = .146).

Across therapy states, vertical, but not horizontal saccadic gain was significantly associated with motor severity (linear mixed model; vertical: B = − 37.20, p < .001; horizontal: B = − 8.28, p = .254).

Corresponding descriptive statistics shown in Fig. 1 are summarized in Supplementary Table S1, while detailed statistical results can be found in Supplementary Tables S3-S5 (Supplementary Section S5).

# Vergence Eye Movements

# Comparison of PwPD OFF/OFF and age-matched controls

Table 2
Comparison of Age-Matched Controls and pwPD OFF/OFF on Vergence Eye Movement Parameters

| Parameter | Task | | *U* | *p* | *r* | 95% CI |
|---|---|---|---|---|---|---|
| Vergence gain | | | | | | |
| | slow vergence | CONV | 699 | **< .001*** | **− .618** | [-0.771, -0.398] |
| | | DIV | 650 | **< .001*** | **− .505** | [-0.694, -0.249] |
| | fast vergence | CONV | 526 | **.006*** | **− .429** | [-0.648, -0.146] |
| | | DIV | 565 | **.002*** | **− .471** | [-0.675, -0.201] |
| MCA | | | | | | |
| | slow vergence | | 681 | **< .001*** | **− .576** | [-0.743, -0.342] |
| | fast vergence | | 551 | **.005*** | **− .435** | [-0.649, -0.156] |
| Vergence stability | | | | | | |
| | slow vergence | | 388 | .514 | .102 | [-0.196, 0.382] |
| | fast vergence | | 556 | .062 | − .287 | [-0.534, 0.005] |
| Latency | | | | | | |
| | slow vergence | | 217 | **.001*** | **.498** | [0.241, 0.689] |
| | fast vergence | CONV | 270 | .096 | .266 | [-0.039, 0.526] |
| | | DIV | 265 | .050 | .310 | [0.012, 0.557] |

*Note.* Mann-Whitney U tests were conducted to assess differences in vergence eye movement parameters between age-matched controls and pwPD OFF/OFF. p-values are two-tailed. Abbreviations: CONV = convergence; DIV = divergence

At least one event of double vision was reported by 29% of PD patients (7/24) and 3% of controls (1/36, Fisher's exact test $p = .005$, OR = 14.41, 95% CI [1.64, 126.72]), in absence of any known ocular motor disorders.

Across all vergence tasks, pwPD in OFF/OFF state exhibited significantly reduced dynamic vergence parameters compared to controls. Convergence gain was reduced by 52% (slow: 0.32 ± 0.28 vs 0.66 ± 0.27, $p < .001$; fast: 0.17 ± 0.24 vs 0.35 ± 0.31, $p = .006$) and divergence gain by 54% (slow: 0.25 ± 0.28 vs 0.55 ± 0.34, $p < .001$) and 65% (fast: 0.12 ± 0.19 vs 0.33 ± 0.28, $p = .002$; Table 2; Fig. 2).

Likewise, maximal convergence angles (MCA) were significantly lower in pwPD (slow vergence: 12.7° ± 6.8° vs 20.9° ± 7.5°, $p < .001$; fast vergence: 9.9° ± 7.6° vs 17.0° ± 9.6°, $p = .005$; Table 2; Fig. 2). Vergence gain and MCA were strongly correlated across tasks (slow convergence: r = .923, $p < .001$, divergence: r = .891, $p < .001$; fast convergence: r = .903, $p < .001$, divergence: r = .779, $p < .001$). Within pwPD, those reporting double vision showed numerically lower MCA and vergence gains than those who did not, reaching significance for slow MCA and fast convergence gain (one-tailed; see Supplementary Figure S5, Supplementary Tables S6 and S7, Supplementary Section S6).

In contrast, vergence stability (as assessed by SD) showed no significant differences when compared to controls ($p > .062$). Given the markedly reduced maximal convergence angles in the pwPD cohort, we next tested whether participants had generated sufficient vergence to acquire the near target reliably. Using a pragmatic threshold of ≥ 90% of the vergence angle required to acquire the near target, none of the pwPD reached this criterion in either the slow or fast vergence task, irrespective of therapeutic state. The experimental geometry also resulted in a limited proportion of age-matched controls reaching this threshold (5/36 during slow and 2/36 during fast vergence).

Latency measures were generally increased in pwPD, reaching significance only for slow divergence ($p = .001$), while remaining non-significant for other conditions (fast convergence: $p = .096$, fast divergence: $p = .050$; Table 2). Group-wise means and standard deviations are provided in Supplementary Table S8 (Supplementary Section S7).

# Effects of oral dopaminergic medication and deep brain stimulation on vergence eye movements

Table 3
Changes Across Treatment Conditions in pwPD on Vergence Eye Movement

| Parameter | Task | | $\chi^2$ (Friedman) | df | *p* | Kendall's *W* |
|---|---|---|---|---|---|---|
| Vergence Gain | | | | | | |
| | slow vergence | CONV | 12.33 | 2 | **.002*** | .257 |
| | | DIV | 12.58 | 2 | **.002*** | .262 |
| | fast vergence | CONV | 5.30 | 2 | .070 | .115 |
| | | DIV | 4.08 | 2 | .130 | .085 |
| MCA | | | | | | |
| | slow vergence | | 10.58 | 2 | **.005*** | .220 |
| | fast vergence | | 2.08 | 2 | .353 | .043 |

*Note.* Friedman tests were performed to compare repeated measurements at PD OFF/OFF, MED and DBS. Effect sizes are reported as Kendall's W. p-values are two-tailed. Abbreviations: CONV = convergence; DIV = divergence

Table 4
Pairwise Comparisons of Treatment Conditions in pwPD on Vergence Eye Movement

| **Variable** | **Task** | **OFF/OFF vs MED** | | **OFF/OFF vs DBS** | |
|---|---|---|---|---|---|
| Vergence gain | | *p* | *r* | *p* | *r* |
| | slow vergence (CONV) | .745 | .013 | **.002*** | **− .667** |
| | slow vergence (DIV) | .514 | − .187 | **< .001*** | **− .693** |
| MCA | | | | | |
| | slow vergence | .874 | .020 | **.004*** | **− .580** |

*Note.* Conover post hoc tests were conducted for variables with significant Friedman results. p-values were not adjusted. Abbreviations: CONV = convergence; DIV = divergence

Table 5
Comparison between Age-Matched Controls and pwPD DBS

| **Parameter** | **Task** | | ***U*** | ***p*** | ***r*** | **95% CI** |
|---|---|---|---|---|---|---|
| Vergence gain | | | | | | |
| | **slow vergence** | **CONV** | **235** | **.003*** | **− .456** | **[-0.660, -0.189]** |
| | | **DIV** | **282** | **.023*** | **− .347** | **[-0.580, -0.062]** |
| | fast vergence | CONV | 281 | .090 | − .268 | [-0.525, 0.033] |
| | | **DIV** | **239** | **.016*** | **− .378** | **[-0.608, -0.089]** |
| MCA | | | | | | |
| | **slow vergence** | | **256** | **.007*** | **− .407** | **[-0.625, -0.131]** |
| | **fast vergence** | | **255** | **.033*** | **− .336** | **[-0.577, -0.041]** |

*Note.* Mann-Whitney U tests compared pwPD with active DBS and age-matched controls for MCA and vergence gain during slow and fast vergence. p-values are two-tailed. Abbreviations: CONV = convergence; DIV = divergence

Significant treatment effects were observed for dynamic vergence parameters during slow vergence, including convergence and divergence gain as well as MCA (all $p \leq .005$; Table 3; Fig. 2).

Post hoc testing revealed no effect of dopaminergic medication but showed a consistent improvement with DBS. MCA increased by 20.2% (12.7° to 15.2°, $p = .004$), while convergence gain improved by 38.8% ($p = .002$) and divergence gain by 33.5% ($p < .001$; Table 4).

A similar trend was seen for fast vergence, but this was not significant in the overall analysis (MCA 9.9° to 11.1°, all $p > .070$).

Vergence stability was not affected by PD treatment for slow or fast vergence ($p > .311$), and no latency parameter was found to be affected by treatment condition ($p > .214$).

Despite these improvements, both vergence gain and MCA remained significantly lower in pwPD with active DBS compared to controls (Table 5; Fig. 2).

Representative examples of VOG recordings consistent with the statistical results are shown in Fig. 3.

Across therapy states, both convergence and divergence gain were significantly associated with motor severity, whereas MCA showed a trend in the same direction (linear mixed model; convergence gain: B = − 15.50, p = .023; divergence gain: B = − 14.89, p = .029; MCA: B = − 0.51, p = .065).

Supplementary Tables S9 and S10 summarize the detailed statistical results, while Supplementary Figure S6 illustrates DBS-related changes at the individual level (Supplementary Section S7).

# Correlation of Conjugate and Vergence Eye Movements

For pwPD in the OFF/OFF state and controls, no significant correlations were detected between slow vergence gain and smooth pursuit gain or fast vergence gain and saccadic gain (all $p > .156$). No significant associations were observed between MoCA scores and ocular motor measures (see Supplementary Section S8).

# Predictive value of eye movements for motor severity

To determine whether disease-related ocular motor abnormalities provided complementary information about motor severity, features showing significant effects in the preceding group-level analyses were subsequently examined using linear regression models. In single-predictor models, vertical saccadic gain explained the largest proportion of variance in MDS-UPDRS-III scores ($R^2 = 0.25$, Fig. 4), consistent with its strong univariate association with motor severity. The remaining individual features showed substantially lower explanatory power. When these features were considered jointly, the multivariable model explained a moderate proportion of the variance in MDS-UPDRS-III scores (in-sample $R^2 = 0.43$, LOOCV-$R^2 = 0.23$). Notably, vertical and horizontal saccadic gain emerged as the principal independent contributors to the model, with coefficients of opposite direction (vertical gain: B = -39.20, p < .001; horizontal gain: B = 28.95, p = .001), whereas the remaining ocular motor features did not contribute significantly (Supplementary Figure S7, Supplementary Section S9).

## Discussion

Vergence dysfunction is an underrecognized, yet clinically relevant dimension of Parkinson's disease that can profoundly compromise reading, spatial navigation, and other activities requiring fine binocular

coordination. Despite a considerable prevalence of double vision in pwPD and emerging evidence for its interaction with broader visuoperceptive disturbances such as hallucinations[15,16], objective characterization of vergence dynamics and their response to established treatments has remained sparse.

Here, we used high-resolution binocular video-oculography across three controlled therapeutic states in order to disentangle disease-, medication-, and stimulation-related contributions to ocular motor function in pwPD treated with bilateral STN-DBS. Three principal findings emerged: first, 29% of pwPD reported double vision, corresponding to a more than 10-fold elevation in odds relative to age-matched controls, in the absence of preexisting visuomotor disorders. Second, pwPD exhibited pronounced deficits across dynamic vergence parameters, with gains reduced by up to 65% relative to controls in the OFF state, while scaling with motor severity. Third, and most strikingly, bilateral STN-DBS significantly improved dynamic vergence by up to 39%, revealing that binocular control is amenable to DBS (see Fig. 5 for an illustrative overview).

Parkinson's disease has long been associated with a spectrum of subtle ocular motor abnormalities that are most sensitively detected using instrumented eye tracking. Despite considerable heterogeneity across studies, the most reproducible conjugate gaze abnormalities involve saccadic hypometria and impairments of internally generated saccades more than purely visual reflexive ones. Our findings closely reproduced this established phenotype: in comparison to controls, pwPD showed predominantly vertical saccadic hypometria and reduced frequency of self-paced saccades, while smooth pursuit was largely preserved. This pattern is commonly attributed to dysfunction within basal ganglia–ocular motor circuits, in particular excessive inhibitory drive from the substantia nigra pars reticulata (SNr) onto superior colliculus neurons that preferably discharge with non-visually guided saccades[40,41].

With regard to vergence eye movements, we found pervasive disease-related abnormalities affecting both slow, pursuit-like and fast, saccade-like vergence, most prominently involving reduced gain and maximal convergence angle, alongside prolonged latency in slow divergence, extending previous reports of impaired fast vergence in PD[18]. These findings also complement clinical studies based on static measures such as the near point of convergence by demonstrating a marked impairment of the dynamic generation and scaling of vergence responses in pwPD[8,42]. Moreover, pwPD experiencing double vision showed greater vergence impairment, suggesting a potential link between VOG-based vergence assessment and the clinical manifestation of double vision. This association underscores the potential clinical relevance of the observed vergence deficits beyond their characterization as objective ocular motor abnormalities.

By contrast, we found no significant disease-related difference in vergence stability, used here as a proxy for vergence maintenance. This finding should be interpreted cautiously, particularly in the light of previous reports of impaired vergence maintenance in PD[43]. Matching convergence ranges in prior clinical reports[9], our near target of convergence was positioned approximately 10 cm from the eyes, requiring an estimated convergence of about 15° per eye for an average interpupillary distance of 6.1 cm,

compared to approximately 9.5° per eye in the study by Gupta et al.[43] Still, we found that only a minority of our participants could reliably acquire this near target. Consequently, the absence of group differences in vergence stability should not be interpreted as evidence of preserved vergence maintenance in pwPD, as its stability can only be meaningfully assessed once sufficient convergence had been generated. Nonetheless, these insights critically inform future investigations of vergence holding mechanisms.

From a neuroanatomical perspective, vergence eye movements engage circuits that span midbrain, pontine and cerebellar nuclei[23,44,45]. A key premotor hub lies in the rostral superior colliculus (SC)[23,46–48] and connects vergence-related pontocerebellar structures with the basal ganglia motor network, including the STN and the SNr[49]. In the parkinsonian state, excessive inhibitory drive along the STN–SNr–SC pathway is thought to interfere with conjugate saccade generation[50]. In line with this notion and extending prior reports, we observed a marked restoration of vertical saccade gain (up to 50%) by STN-DBS[4,5,40,51]. Notably, vergence gain improved to a similar extent (up to 39%), which implicates partly overlapping midbrain substrates that interface with basal ganglia motor loops and jointly coordinate eye movements in three-dimensional space[23,46]. A complementary, or alternative mechanism may involve indirect modulation of cerebellar vergence circuitry through a disynaptic STN–pontine–cerebellar pathway that projects onto midbrain premotor vergence hubs[52–54].

In contrast to the effects of DBS, we did not observe significant effects of dopaminergic medication on eye movements. This observation appears to differ from clinical reports of levodopa-related improvements in convergence ability[9]. However, Almer et al. assessed clinical measures of static convergence capacity, including base-out fusional amplitudes, whereas our paradigm quantified the gain, latency, and amplitude of visually guided dynamic vergence responses. Importantly, the MED condition reflected participants' regular morning dopaminergic regimen rather than a standardized levodopa challenge using an increased dose. Together with the modest improvement in MDS-UPDRS-III scores, this suggests that some participants may not have achieved a robust dopaminergic ON state. The absence of an ocular motor medication effect should therefore not be interpreted as evidence that dynamic vergence is intrinsically unresponsive to dopaminergic therapy. This may also contribute to the heterogeneous effects of dopaminergic treatment on ocular motor function reported across studies, which likely depend on the task and outcome examined, disease stage, and pharmacodynamic factors. Whether the apparent difference between medication and DBS observed here reflects differences in treatment efficacy or genuinely distinct modulation of ocular motor circuitry will require confirmation using standardized levodopa challenge paradigms. Nevertheless, under the therapeutic conditions tested here, dynamic vergence was robustly modulated by STN-DBS, but not by regular dopaminergic medication, underscoring the importance of explicitly accounting for therapeutic state when characterizing ocular motor dysfunction in PD.

Notably, ocular motor abnormalities scaled with motor severity. Earlier studies found a relationship between single saccadic gain measures and motor severity in the OFF state[55], while more recent work

has linked saccadic variability to greater motor impairment in PD[56]. We extend this to vergence, showing that convergence and divergence gain inversely relate to motor severity with moderate effect size. Notably, while in multivariable analyses vergence measures did not explain independent variance in motor severity beyond saccadic gain measures, the model indicated that the relative dissociation between vertical and horizontal saccadic gain carries additional information about motor severity compared with vertical saccadic gain in isolation.

Clinically, these findings highlight vergence dysfunction as an important, yet insufficiently recognized dimension of PD. Vergence deficits are not routinely screened for and not captured in conventional rating scales, yet the present findings suggest that they are associated with motor severity, while symptoms such as double vision are frequently overlooked unless actively elicited. Importantly, pwPD reporting diplopia also exhibited greater objectively measured vergence impairment, suggesting a potential link between the physiological abnormalities captured by VOG and a binocular visual symptom experienced by patients. Although this exploratory subgroup analysis was limited by the small number of participants reporting diplopia, it supports the clinical relevance of the quantitative vergence abnormalities identified here. Quantitative video-based assessment of vergence may therefore complement routine neurological assessment by identifying ocular motor abnormalities that remain invisible to standard bedside examination. Whether the observed DBS-related improvements in vergence gain and maximal convergence angle translate into better reading performance, reduced diplopia, improved mobility, or enhanced vision-related quality of life, however, remains to be established. Nevertheless, the present data suggest that vergence function - as a potentially relevant domain for daily functioning - may also benefit from neuromodulation.

Several limitations should be considered. First, although the association with self-reported diplopia provides initial evidence for the clinical relevance of the observed vergence abnormalities, eye-tracking measures were not systematically linked to functional outcomes such as reading performance or vision-related quality of life. Future studies should systematically determine how quantitative vergence metrics relate to visual symptoms and functional outcomes in everyday life. Second, while we selected the near point to match the reported range in clinical studies[9], our experimental setup may still have reduced the statistical power of the vergence stability analysis. Future studies should aim at harmonizing and standardizing VOG-based vergence measurements in pwPD and beyond. Third, although this is, to our knowledge, the first study to systematically characterize disease-, routine medication-, and deep brain stimulation-related effects on vergence within a single group of pwPD, the sample size was moderate. Importantly, the medication condition reflected participants' regular morning dopaminergic regimen rather than a standardized levodopa challenge using an increased dose, limiting conclusions regarding the intrinsic dopaminergic responsiveness of ocular motor dysfunction. In addition, treatment conditions were assessed in a fixed order, such that order and residual carry-over effects cannot be fully excluded despite the predefined washout periods. Notably, the DBS condition preceded the OFF/OFF condition within the same morning session, so that fatigue or prolonged medication withdrawal may have disadvantaged OFF/OFF performance and thereby inflated the apparent DBS effect. These limitations

partly reflect the challenges of studying people with advanced PD and bilateral STN-DBS across multiple treatment states, so that confirmation in larger independent cohorts using standardized levodopa challenge paradigms is warranted. Fourth, individual vergence responses to DBS showed considerable heterogeneity, raising the possibility that differences in electrode location may contribute to variability in vergence improvement. While electrode locations were reconstructed and anatomically verified, more sophisticated DBS mapping analyses are underway to characterize the neural substrates associated with stimulation-related changes in vergence.

In summary, Parkinson's disease can profoundly impair dynamic vergence eye movements. Their amenability to STN-DBS highlights binocular motor dysfunction as a distinct and potentially modifiable aspect of PD that extends beyond canonical skeletomotor manifestations. Given its relevance for everyday visual function and frequent underrecognition in clinical practice, our findings support greater consideration of vergence dysfunction in the clinical assessment of PD, particularly in patients undergoing DBS.

# Declarations

### Author contributions

Conceptualization and study design: M.U.F.

Methodology: M.U.F., H. F., S. B., E. S.

Investigation: E. M., H. F., N. P., A. N., S. J., M.U.F.

Data curation and analysis: E. M., M.U.F., A. N., S. J., T. S., S. B.

Visualization: E.M., A. N., S. J., M. U. F.

Writing – original draft: E.M., M. U. F., D. Z.

Writing – review & editing: All authors.

Supervision: M.U.F, D. Z., M. R.

Funding acquisition: M.U.F.

All authors critically revised the manuscript for important intellectual content and approved the final version.

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**Disclosures**

M.U.F. reports consulting fees from CereGate GmbH and Tovly LLC, outside of the submitted work, and serves as an associate editor at npj Parkinson's disease. E.S. is the general manager and a shareholder of EyeSeeTec GmbH.

**Data and code availability**

Anonymized data (e. g. VOG traces) and code supporting the main results will be shared upon request to the corresponding author.

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# Figures

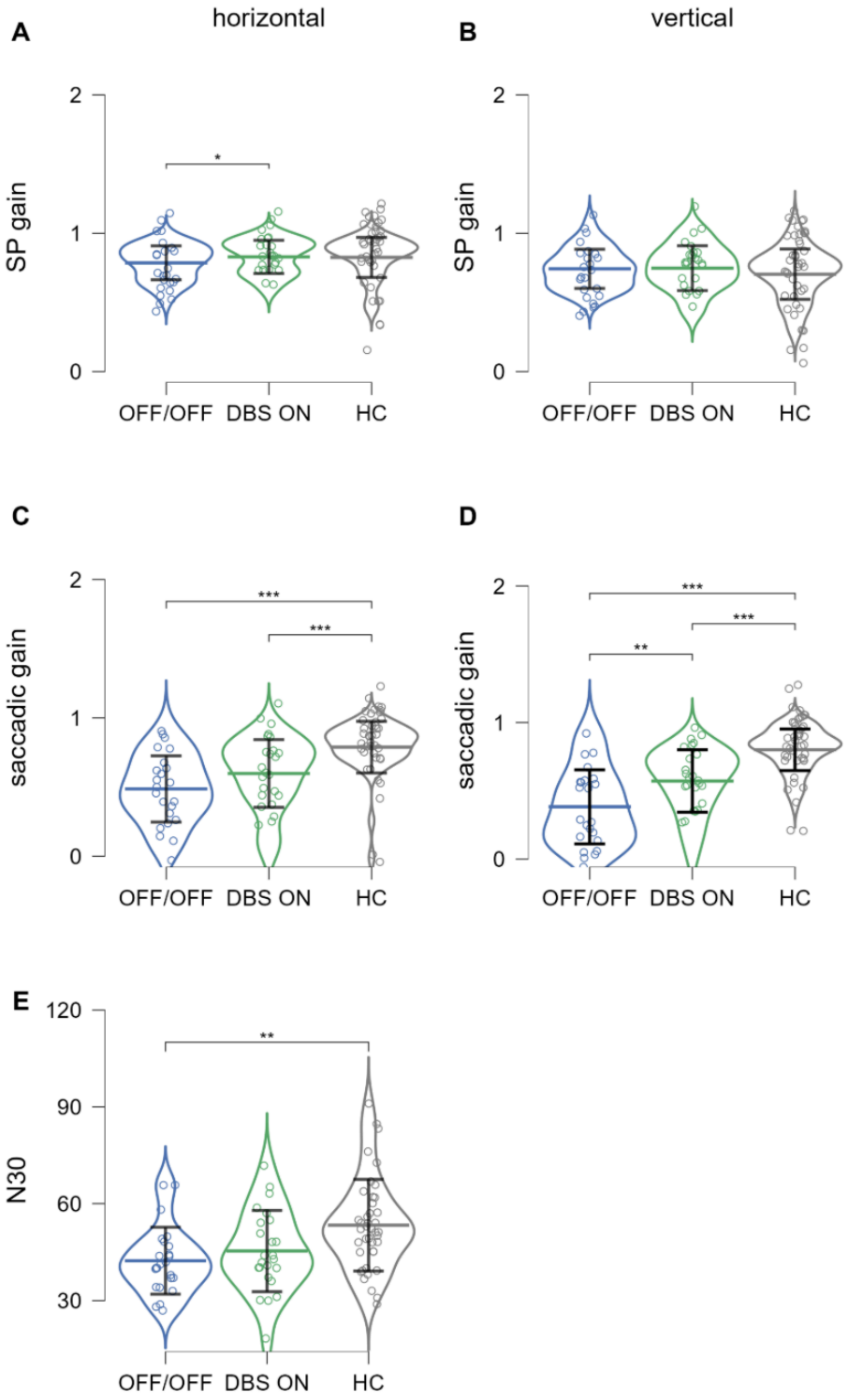
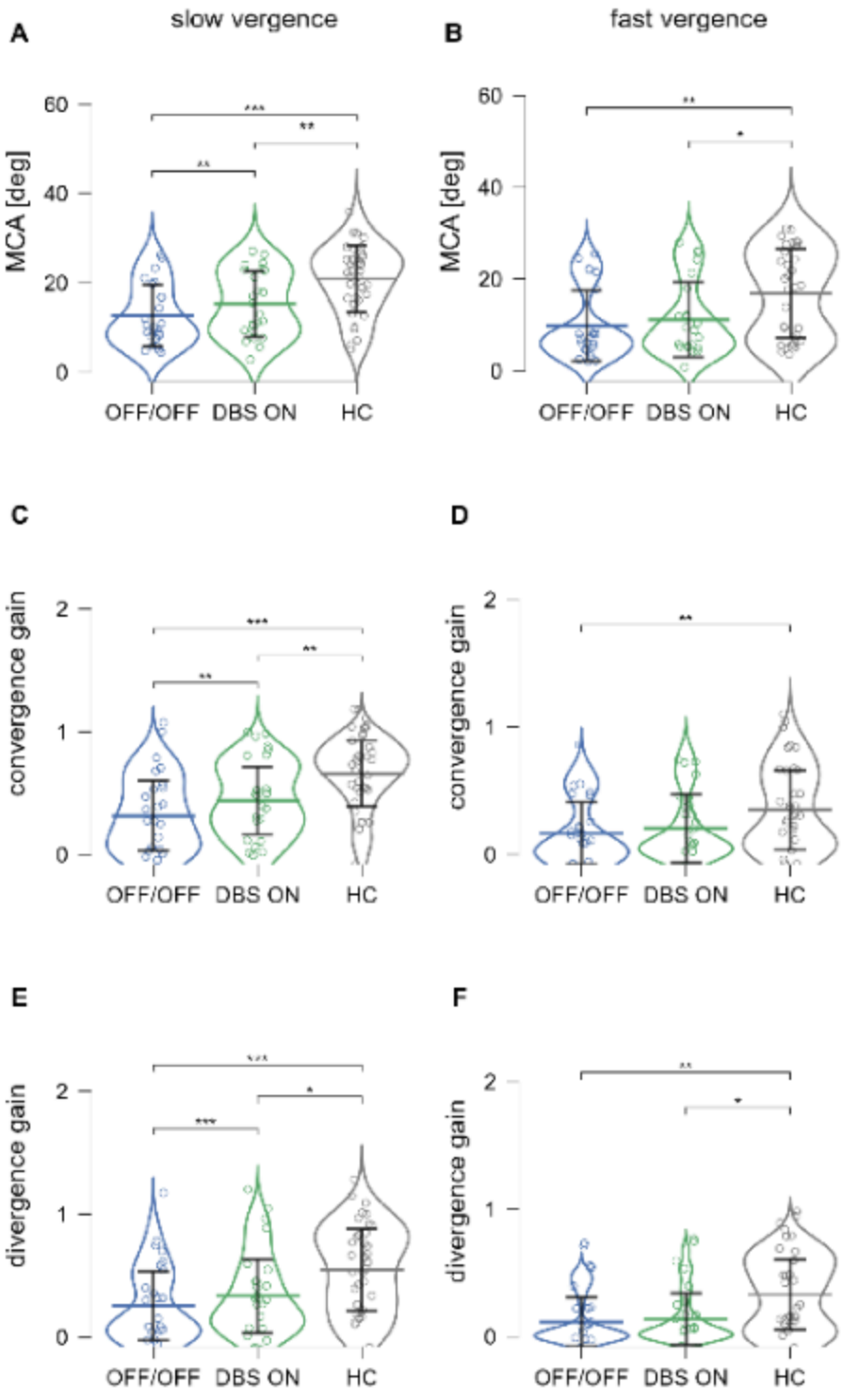


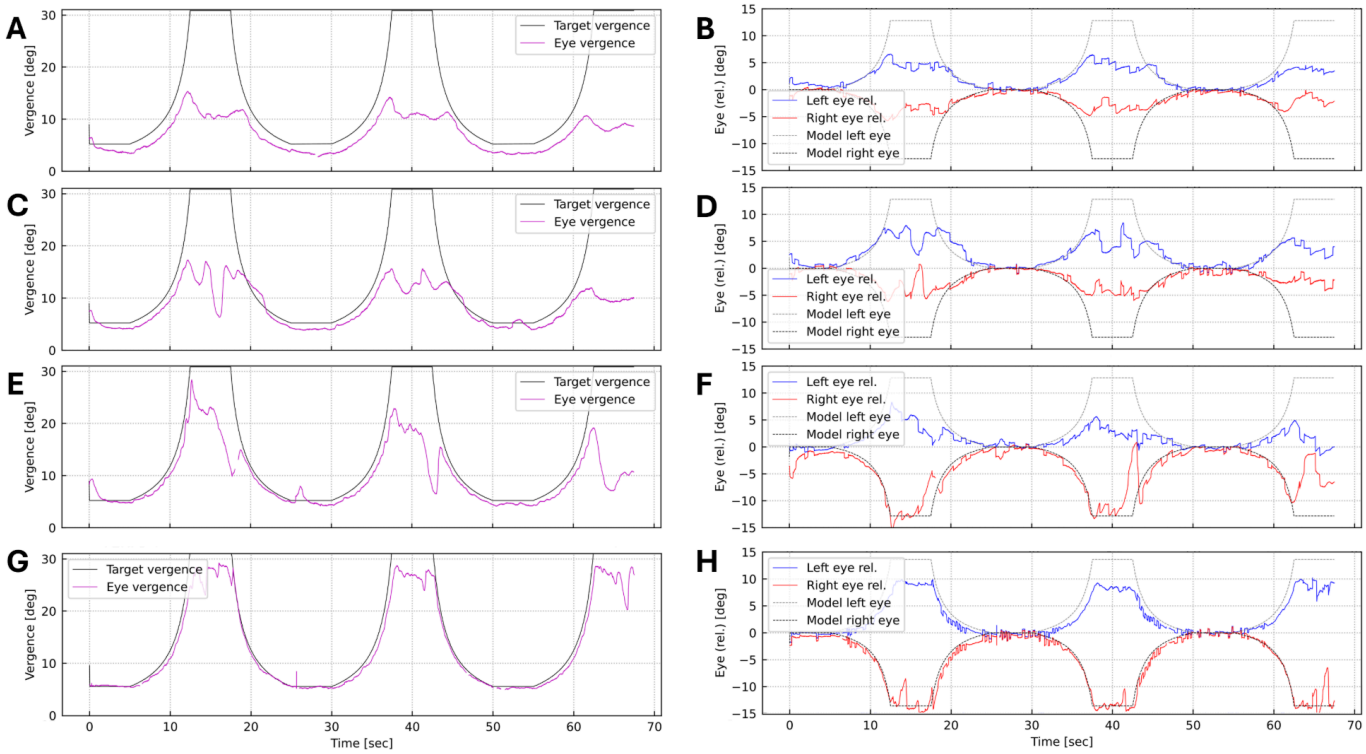

**Figure 1**

**Conjugate eye movement measures in pwPD in OFF/OFF and DBS condition, and age-matched controls (HC)**. (A) Horizontal smooth pursuit (SP) gain and (B) vertical smooth pursuit gain. (C) Horizontal saccadic gain, (D) vertical saccadic gain, (E) N30 saccades. Violin plots illustrate the distribution of the data with overlaid individual data points. Significant group differences are indicated.




## Figure 2

**Vergence eye movement measures in pwPD in OFF/OFF and DBS condition, and age-matched controls (HC)**. (A) Maximal convergence angle in degree (MCA) in slow vergence and (B) MCA in fast vergence task. (C) Convergence gain for slow, and (D) for fast vergence, (E) divergence gain for slow and (F) for fast vergence. Violin plots illustrate the distribution of the data with overlaid individual data points. Significant group differences are indicated.




## Figure 3

**Representative vergence recordings during a slow vergence task.** In the left panels, target position is shown in black and vergence angle in magenta. In the right panels, eye position is shown for the right eye (red) and left eye (blue) separately; positive values indicate deflection to the right and negative values indicate deflection to the left. (A-B) show recordings from a pwPD in the OFF/OFF condition, highlighting a successive break down of vergence capability throughout the three experimental repetitions. (C-D) show recordings from the same patient in the MED ON condition, while (E-F) show recordings in the DBS ON condition, suggesting increased vergence capability across the three repetitions with DBS, but not medication. (G) and (H) show recordings from an age-matched control participant, showing greater vergence capability across repetitions.

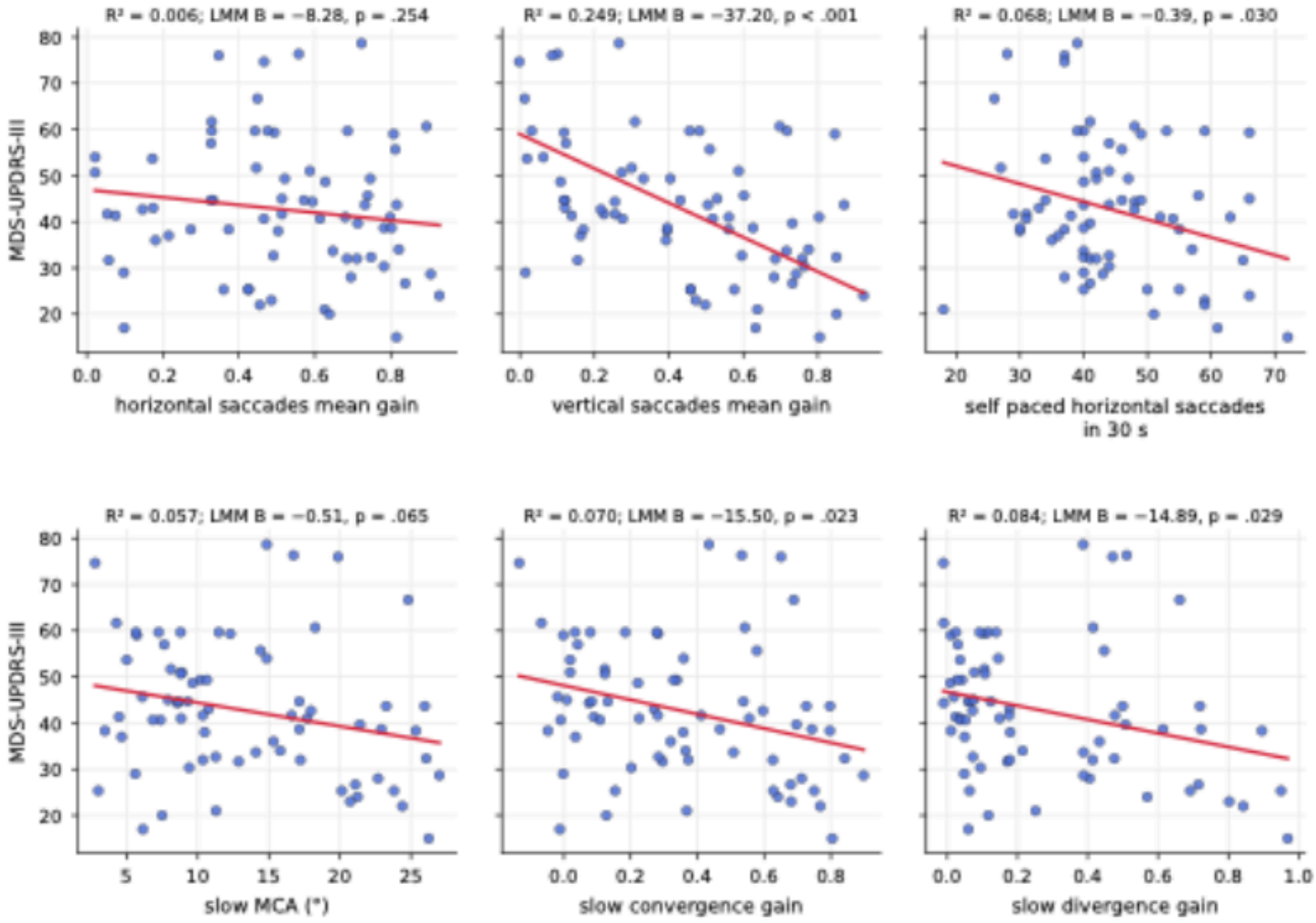



**Figure 4**

**Single-feature associations between ocular motor parameters and MDS-UPDRS-III scores across therapeutic states.** Each panel shows the data distribution and the relationship between one ocular motor parameter and total MDS-UPDRS-III scores (OFF/OFF, MED, and DBS conditions pooled). Red lines indicate fixed-effect fits of linear mixed models with a random intercept per participant. Panel titles report the $R^2$ of the single-predictor regression used in the prediction analysis and the mixed-model estimate (B) with its p-value. Vertical saccadic gain showed the strongest association with motor severity, followed by vergence gain measures.

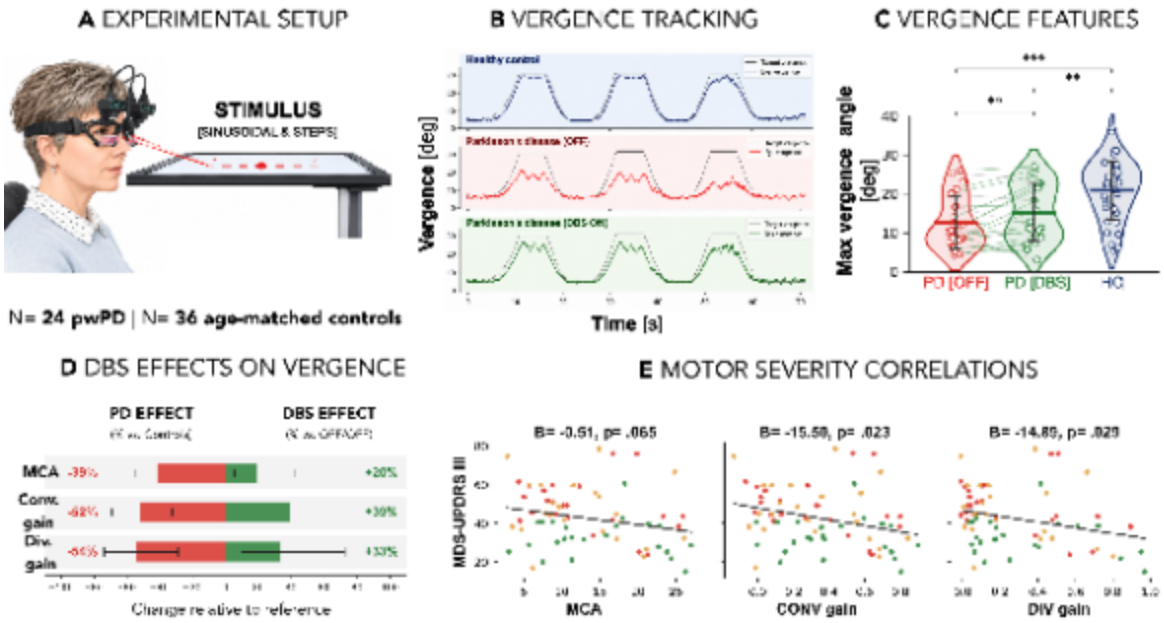



**Figure 5**

**Synopsis of the experimental paradigm and principal findings.** (A) Experimental setup for binocular video-oculographic (VOG) assessment of dynamic vergence in 24 people with Parkinson's disease (pwPD) and 36 age-matched healthy controls (HC). Visual targets moved along the midline of a horizontally mounted monitor to elicit convergence and divergence eye movements. (B) Illustrative vergence traces showing near-normal target tracking in HC, impaired vergence responses in pwPD in the medication OFF/DBS OFF condition (OFF/OFF), and partial improvement with STN-DBS. (C) Maximal convergence angles during slow vergence in pwPD OFF/ OFF and DBS ON and in HC. Individual observations and group distributions are shown, with paired observations connected for pwPD. (D) Relative reductions in maximal convergence angle (MCA), convergence gain, and divergence gain in pwPD compared with HC, alongside improvements induced by STN-DBS relative to OFF/OFF. Percentages refer to slow vergence and are calculated relative to the respective reference condition. (E) Associations between MCA, convergence gain, divergence gain, and motor symptom severity, assessed using the MDS-UPDRS part III. Lines indicate fixed-effect fits of linear mixed models with a random intercept per participant; annotations report the fixed-effect estimate (B) and p-value. $p < .05$ *, $p < .01$ **, $p < .001$ ***. The experimental setup illustration was refined using OpenAI's GPT-Image based on the authors' drawings and setup photos. Quantitative plots were generated strictly based on original study data.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- VergencePDSI.docx