• Clinical Research •

Comparison of binocular vision indices in Parkinson's disease patients *vs* age-sex-matched healthy controls

Reyhaneh Shariati–Moghaddam[1], Ali Shoeibi[2], Morad Amir Ahmad[3], Hadi Ostadimoghaddam[4], Hassan Hashemi[5], Akbar Derakhshan[6], Zahra Hemmatian[1], Abbasali Yekta[1], Mehdi Khabazkhoob[7]

[1]Department of Optometry, School of Paramedical Sciences, Mashhad University of Medical Sciences, Mashhad 1394491388, Iran
[2]Department of Neurology, School of Medicine, Ghaem Hospital, Mashhad University of Medical Sciences, Tehran 9919991766, Iran
[3]Department of Optometry & Physiotherapy, Erbil Technical & Medical Health Collage, Erbil Polytechnic University, Erbil, Kurdistan Region 44001, Iraq
[4]Refractive Errors Research Center, Mashhad University of Medical Sciences, Mashhad 1394491388, Iran
[5]Noor Ophthalmology Research Center, Noor Eye Hospital, Tehran 1983963113, Iran
[6]Department of Ophthalmology, School of Medicine, Eye Research Center, Khatam Al Anbiya Hospital, Mashhad University of Medical Sciences, Tehran 9195965919, Iran
[7]Department of Medical Surgical Nursing, School of Nursing and Midwifery, Shahid Beheshti University of Medical Sciences, Tehran 1983969411, Iran
Correspondence to: Abbasali Yekta. Department of Optometry, School of Paramedical Sciences, Mashhad University of Medical Sciences, Mashhad 1394491388, Iran. aa_yekta@yahoo.com
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Abstract

● **AIM:** To evaluate the differences in near point of convergence (NPC), fusional vergence, saccadic eye movements, versional eye movements, and heterophoria between patients diagnosed with Parkinson's disease (PD) and healthy subjects.

● **METHODS:** A cross-sectional comparative study was conducted, enrolling two cohorts: a PD group and a healthy control group. The PD group was recruited *via* non-random convenience sampling, while the control group was selected randomly from individuals without PD. All participants were screened according to predefined inclusion and exclusion criteria before undergoing a comprehensive optometric assessment, which included measurements of uncorrected visual acuity, corrected visual acuity, and objective and subjective refraction. Subsequently, binocular vision function evaluations were performed, covering NPC measurement, fusional vergence reserve assessment at both distance and near, saccadic eye movement testing, and versional eye movement and heterophoria assessment.

● **RESULTS:** A total of 42 PD patients and 41 healthy controls were included in the final analysis. The two groups were well-matched in terms of sex distribution [29 males (69.0%) in the PD group *vs* 29 males (70.7%) in the control group, P=0.867] and mean age (55.3±9.6y in the PD group *vs* 54.9±9.8y in the control group, P=0.866). The prevalence of abnormal versional eye movements was significantly higher in the PD group than in the control group (23.81%, 95%CI: 12.05%-39.45% *vs* 7.32%, 95%CI: 1.54%-19.92%; P=0.025). Near exophoria was more prevalent in PD patients (61.90%, 95%CI: 45.64%-76.43%) than in controls (17.07%, 95%CI: 7.15%-32.06%), with a significant difference [odds ratio (OR)=7.99; 95%CI: 2.83-21.99; P<0.001]. The mean NPC was significantly greater (more receded) in the PD group than in the control group (9.01±3.74 cm *vs* 7.20±2.15 cm; P=0.007). A statistically significant positive correlation was observed between PD severity and NPC values (Pearson's correlation coefficient=0.309; P=0.046). Except for distance base-out break and distance base-out recovery values, all other fusional vergence parameters were significantly lower in the PD group than in the control group (P<0.05). The mean saccadic test score was significantly lower in PD patients than in controls (3.29±0.57 *vs* 3.78±0.42; P<0.001). Among all fusional vergence indices, near base-in blur yielded the highest area under the curve (AUC=0.877), with a sensitivity of 69% and specificity of 90%, followed by distance base-out blur (AUC=0.824, sensitivity=97.6%, specificity=66.7%), near base-out blur (AUC=0.814, sensitivity=76.2%, specificity=72.7%), near base-out break (AUC=0.749, sensitivity=78.6%, specificity=67.6%), and near base-out recovery (AUC=0.749, sensitivity=95.2%, specificity=50%).

● **CONCLUSION:** PD is associated with significant binocular vision function impairment, with receded NPC and reduced near fusional vergence reserves being the most prominent disorders. These findings highlight the potential value of binocular vision assessment as a non-invasive biomarker for the early detection and clinical monitoring of PD.

● **KEYWORDS:** Parkinson's disease; binocular vision; near point of convergence; fusional vergence; saccadic eye movement; heterophoria

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INTRODUCTION

Parkinson's disease is the second most prevalent neurodegenerative disorder globally, following Alzheimer's disease. Recent studies have shown a significant increase in its global prevalence, rising approximately 155% from 1990 to 2019[1]. This surge has led to an estimated incidence of 106.28 cases per 100 000 individuals, affecting over 8.5 million people worldwide[1].

Aging is the primary risk factor for Parkinson's disease, with the highest prevalence noted in individuals over 80 years old[2]. While motor symptoms are the most recognized signs of the disease[3-4], the visual system including both peripheral eye structures and central pathways may be among the first areas to experience neurodegeneration, representing an often-overlooked aspect of the condition[5]. Studies have shown that individuals with Parkinson's frequently encounter various visual disturbances, including blurred vision[6], diplopia[7], convergence insufficiency[8], reduced contrast sensitivity[9], and difficulties with accommodation and binocular vision[10]. Ocular motor abnormalities are also commonly observed in these individuals, including impaired saccadic and pursuit eye movements, head-leading eye movements, and restricted gaze in at least one direction[11-13]. Moreover, impairments in near vision tasks, gross convergence, and fusional vergence parameters are expected to occur due to these oculomotor deficits[14].

While previous studies have focused extensively on the visual aspects of Parkinson's disease[15-18], there has been limited attention paid to specific binocular vision indices such as vergence, near point of convergence (NPC), and saccadic movements. Furthermore, few studies have assessed the diagnostic value of these indices in determining the severity of Parkinson's disease. Given the increasing global aging population[19] and the strong correlation between age and the incidence of Parkinson's disease[2], it is crucial to evaluate binocular vision, especially near-vision-related indices, in this demographic. Therefore, the present study aimed to compare NPC, fusional vergence, saccadic test, versional eye movements and heterophoria between patients with Parkinson's disease and age- and sex-matched healthy individuals, and to assess their diagnostic utility.

PARTICIPANTS AND METHODS

Ethical Approval The Ethics Committee of Mashhad University of Medical Sciences approved the study protocol, which was conducted in accord with the tenets of the Helsinki Declaration. All participants signed a written informed consent. (ethical code: IR.MUMS.FHMPM.REC.1402.179).

This cross-sectional study comprised two groups: patients diagnosed with Parkinson's disease and healthy individuals. Both groups were selected from individuals referred to Qaem Hospital in Mashhad, Iran in 2025. Parkinson's patients were chosen through non-random convenience sampling, while the control group was randomly selected from individuals without Parkinson's disease. The inclusion criteria for the Parkinson's group were as follows: confirmation of diagnosis by a neurologist based on the Movement Disorder Society (MDS) diagnostic criteria; a minimum disease duration of two years; availability of medical records and medication history; and evaluation of all cardinal manifestations using the MDS-Unified Parkinson's Disease Rating Scale (UPDRS)[20]. After selection, individuals with a history of ocular pathology, best-corrected visual acuity worse than 20/32, traumatic brain injury or cerebellar lesions, supranuclear gaze palsy, ocular trauma or surgery, systemic chronic diseases, dementia, Alzheimer's disease, or any other neurological or neurodegenerative disorder were excluded from the study. In the control group, individuals were initially assessed by a neurologist to confirm the absence of Parkinson's disease. Following this confirmation, those with systemic illnesses, a history of stroke, or any neurological disease were excluded. Participants in two groups were matched for age and sex.

All participants underwent an interview, which was followed by thorough optometric examinations. For those diagnosed with Parkinson's disease, staging of the condition was performed using the UPDRS, recognized as the leading and most widely accepted method for diagnosing parkinsonism and evaluating the stage and progression of the disease over time. The first measurement taken was uncorrected distance visual acuity. This was followed by objective refraction using an auto-refractometer, which was then fine-tuned through retinoscopy. Corrected visual acuity was assessed, and subjective refraction was documented. The evaluation of binocular vision included the unilateral cover test to identify heterotropia. An alternate

cover test, using prism neutralization with accommodative targets, was performed at both distance and near to measure heterophoria or heterotropia. The comitance of the deviations was evaluated by measuring the angles of deviation across nine gaze positions. Deviations of less than 20 prism diopters ($^{\Delta}$) with a variation of less than 2^{Δ} across gazes, or greater than 20^{Δ} with a variation of less than 5^{Δ}, were classified as comitant. Positive and negative fusional vergence reserves (including blur, break, and recovery) were evaluated through the use of horizontal prism bars and accommodative targets at both far and near fixation distances. NPC was measured in centimeters utilizing the push-up technique with a Royal Air Force Rule (RAF). NPC abnormality was defined as an NPC of ≥10 cm. The Broad H test was conducted to evaluate ocular motility, focusing on the functionality of extraocular muscles and any restrictions in ocular movement. Instances of non-conjugate eye movements or diplopia in various gaze positions were recorded. The presence of diplopia or suppression was assessed using the Worth 4-Dot test. Additionally, saccadic eye movements were evaluated with the Southern California College of Optometry (SCCO) saccadic test.

Statistical Analysis Quantitative variables were expressed as mean±standard deviation (SD) and were compared across groups using the independent samples *t*-test. Categorical variables were analyzed using the Chi-square test. Logistic regression was employed to investigate the relationship between categorical variables and Parkinson's disease, with odds ratios (OR) reported alongside 95% confidence intervals (CI). Pearson correlation coefficients were calculated to evaluate the relationship between binocular vision metrics and the severity of Parkinson's disease as measured by UPDRS scores. To assess the diagnostic efficacy of binocular vision indices in Parkinson's disease, receiver operating characteristic (ROC) curves were constructed, and the area under the curve (AUC) was reported. In addition to AUC and 95%CIs, optimal cut-off points were established using Youden's Index, and sensitivity, specificity, positive likelihood ratio, and negative likelihood ratio were documented for NPC and vergence indices. $P<0.05$ was considered statistically significant.

RESULTS

The present study encompassed 42 individuals diagnosed with Parkinson's disease and 41 healthy participants. Among these, 29 (69%) of the Parkinson's patients and 29 (70.7%) of the controls were male (P=0.867). The average age was 55.3±9.6y for the Parkinson's group and 54.9±9.8y for the control group (P=0.866). The mean UPDRS score among Parkinson's patients was 23.0±12.52, with a range of 6 to 52. The mean duration of Parkinson's disease among patients was 5.7±3.1y (range: 3-14y). In the Parkinson's disease group, oculomotor assessments were performed at a mean interval of 145.7±99.1min (range: 5-420min) following the most recent administration of levodopa or a dopamine agonist.

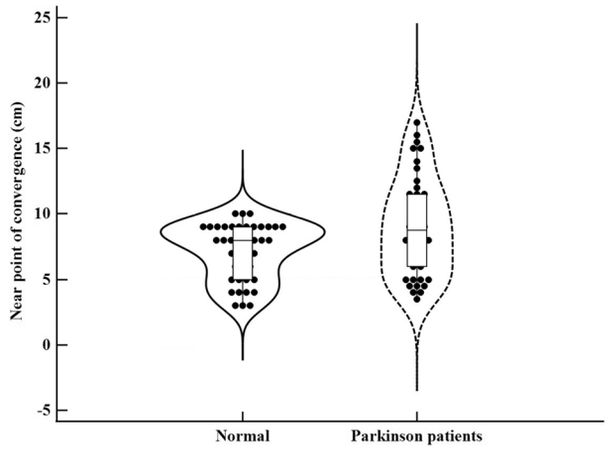

Figure 1 The distribution of near point of convergence in Parkinson's disease patient and healthy controls.

Abnormalities in versional eye movements were observed in 10 patients with Parkinson's disease (23.81%; 95%CI: 12.05%-39.45%), compared to 3 healthy controls (7.32%; 95%CI: 1.54%-19.92%; P=0.025). All three control participants exhibited isolated limitation of upgaze. In the Parkinson's disease group, 8 patients (19.05%; 95%CI: 8.60%-34.12%) showed upgaze palsy, while 2 patients (4.76%; 95%CI: 0.58%-16.16%) demonstrated combined limitations in upgaze and right-gaze.

The prevalence of exophoria at far was 4.88% (95%CI: 0.60%-16.53)% in healthy controls and 14.29% (95%CI: 5.43%-28.54%) in patients with Parkinson's disease; at near, exophoria was observed in 17.07% (95%CI: 7.15%-32.06%) of controls and 61.90% (95%CI: 45.64%-76.43%) of Parkinson's patients (OR=7.99; 95%CI: 2.83-21.99, P<0.001). Although no cases of esophoria were observed at either far or near in the Parkinson's group, one control participant (2.44%, 95%CI: 0.06%-12.86%) exhibited esophoria at near.

The mean NPC was significantly more receded in the Parkinson's group (9.01±3.74 cm) compared to the control group (7.20±2.15 cm; P=0.007; Figure 1) and exhibited a statistically significant positive correlation with UPDRS scores (Pearson correlation=0.309, P=0.046).

Based on our findings, the prevalence of abnormal NPC was 7.32% (95%CI: 1.54%-19.92%) in healthy controls and 38.1% (95%CI: 23.57%-54.36%) in patients with Parkinson's disease indicating a significantly higher odds of NPC abnormality in the latter group (OR=7.79; 95%CI: 2.06-29.48, P<0.001). The ROC analysis for NPC yielded an AUC of 0.637 (P=0.028). When applying a cut-off of >10 cm, NPC showed a sensitivity of 38.1% and a specificity of 100% for the detection of Parkinson's disease.

Table 1 Fusional vergence indices (mean±SD, effect size) in Parkinson's disease *vs* controls, and unified Parkinson's disease rating scale correlations

Parameters	Parkinson's disease	Controls	*P*	Effect size (95%CI)	r^a	P^b
Distance						
Base in break	7.76±2.94	11.51±4.96	<0.001	-0.923 (-1.374 to -0.468)	-0.227	0.149
Base in recovery	4.07±2.44	7.1±4.91	<0.001	-0.783 (-1.228 to -0.334)	-0.316	0.042
Base out blur	6.95±2.26	11.78±4.29	<0.001	-1.787 (-2.581 to -0.977)	-0.339	0.028
Base out break	11.6±3.33	12.56±7.17	0.440	-0.176 (-0.622 to 0.27)	-0.309	0.046
Base out recovery	7.71±3.17	8.09±5.34	0.720	-0.087 (-0.54 to 0.365)	-0.400	0.009
Near						
Base in blur	7.38±2.70	12.80±4.34	<0.001	-1.768 (-2.533 to -0.99)	-0.413	0.007
Base in break	11.48±2.97	14.59±4.38	<0.001	-0.833 (-1.28 to -0.382)	-0.474	0.002
Base in recovery	7.69±3.27	10.15±4.33	0.005	-0.641 (-1.081 to -0.198)	-0.470	0.002
Base out blur	9.38±2.81	13.64±3.78	<0.001	-1.407 (-2.119 to -0.684)	-0.355	0.021
Base out break	14.52±3.77	20.76±8.69	<0.001	-0.952 (-1.416 to -0.483)	-0.517	<0.001
Base out recovery	9.62±3.81	13.82±4.80	<0.001	-0.983 (-1.459 to -0.501)	-0.514	<0.001

[a]Pearson correlation coefficient; [b]*P*-value for Pearson correlation coefficient. CI: Confident interval.

Table 2 Area under the curve, Youden index, sensitivity (%), specificity (%), cut-off point, and likelihood ratios of fusional vergence for differentiating Parkinson's disease from healthy controls

Indices	AUC (95%CI); *P*	Youden index J	Sensitivity	Specificity	Cut of point	+LR	-LR
Distance							
Base in break	0.749 (0.643 -0.855); <0.001	0.4210	73.8	68.3	≤8	2.33	0.38
Base in recovery	0.699 (0.588 -0.811); <0.001	0.2956	88.1	41.5	≤6	1.50	0.29
Base out blur	0.824 (0.63 -1.018); <0.001	0.6429	97.6	66.7	≤10	2.93	0.036
Base out break	0.486 (0.351 -0.622); 0.845	0.1786	7.1	75.0	>14	0.29	1.24
Base out recovery	0.483 (0.345 -0.621); 0.811	0.2045	11.9	67.6	>10	0.37	1.30
Near							
Base in blur	0.877 (0.768 -0.987); <0.001	0.5905	69.0	90.0	≤8	6.90	0.34
Base in break	0.696 (0.582 -0.81); <0.001	0.3682	90.5	46.3	≤14	1.69	0.21
Base in recovery	0.652 (0.534 -0.769); 0.011	0.2346	38.1	85.4	≤6	2.60	0.73
Base out blur	0.814 (0.67 -0.958); <0.001	0.4892	76.2	72.7	≤10	2.79	0.33
Base out break	0.749 (0.634 -0.863); <0.001	0.4614	78.6	67.6	≤16	2.42	0.32
Base out recovery	0.749 (0.634 -0.864); <0.001	0.4524	95.2	50.0	≤14	1.90	0.095

AUC: Area under the curve; CI: Confident interval; LR: Likehood ratios.

As shown in Table 1, all fusional vergence indices, except for the distance base-out break and distance base-out recovery, were significantly lower in the Parkinson's group. The most notable effect sizes were observed for distance base-out blur, near base-in blur, and near base-out blur. Additionally, all vergence indices, with the exception of distance base-in break, demonstrated statistically significant negative correlations with UPDRS scores. The strongest correlation was found for near base-out break (Pearson correlation=-0.517, *P*<0.001) and near base-out recovery (Pearson correlation=-0.514, *P*<0.001).

Table 2 presents the diagnostic metrics obtained from the ROC analysis. All vergence indices, except for the two-distance base-out measures, showed statistically significant AUC values. The most notable diagnostic performances were observed for the following indices: near base-in blur (AUC: 0.877, sensitivity: 69%, specificity: 90%), distance base-out blur (AUC: 0.824, sensitivity: 97.6%, specificity: 66.7%), near base-out blur (AUC: 0.814, sensitivity: 76.2%, specificity: 72.7%), near base-out break (AUC: 0.749, sensitivity: 78.6%, specificity: 67.6%), and near base-out recovery (AUC: 0.749, sensitivity: 95.2%, specificity: 50%). Figure 2 displays the ROC curves for the fusional vergence indices with AUC>0.70 in discriminating Parkinson's disease from healthy controls.

Saccadic performance in patients with Parkinson's disease was significantly lower (mean=3.29±0.57) compared to the control group (mean=3.78±0.42; *P*<0.001). Based on our findings, among healthy controls, 78% and 22% achieved Grade 3 and Grade 4, respectively, on the saccade test scoring system; in contrast, among patients with Parkinson's disease, 56.6%, 39.8%, and 3.6% scored Grades 4, 3, and 2, respectively (*P*<0.001).

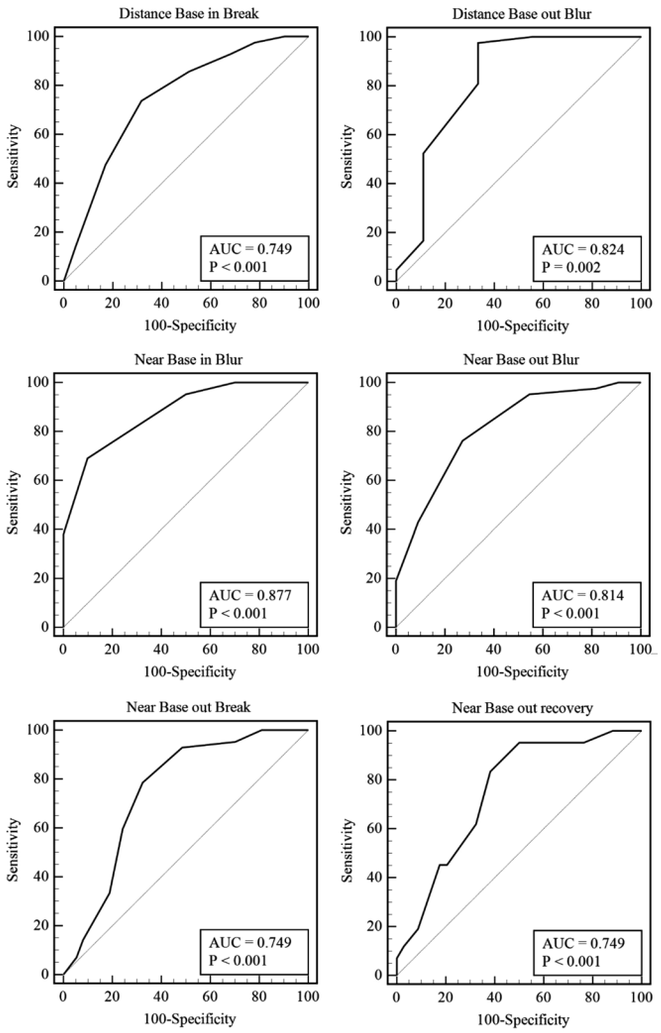

Figure 2 Receiver operating characteristic (ROC) curves for fusional vergence indices with area under the curve (AUC) >0.70 in discriminating Parkinson's disease from healthy controls.

DISCUSSION

The present study examined certain binocular vision characteristics in patients with Parkinson's disease compared to age and sex matched healthy individuals. Our thorough analysis uncovered significant differences in the distribution of these indices across the two groups and highlighted the diagnostic significance of various vergence metrics *via* ROC analysis. An important consideration is that the majority of our patients were assessed in the "on" state (*i.e.*, during the therapeutic window following levodopa or dopamine agonist intake), which may have influenced the observed results.

Our findings indicated that NPC was significantly more remote in patients with Parkinson's disease and exhibited a positive correlation with the severity of the disease as assessed by the UPDRS. In alignment with our results, several studies have reported a recession in NPC among those with Parkinson's disease, which worsens as the disease severity escalates[21-22]. A remote NPC is a key indicator of convergence insufficiency[23-24], and numerous studies have highlighted a higher incidence of this condition within this population[9,25]. Nevertheless, it has been shown that after vergence training in Parkinson's patients, NPC decreased and convergence insufficiency improved[26].

For example, Herrero-Gracia *et al*[9] found that the prevalence of convergence insufficiency rises significantly with the progression of Parkinson's disease. Additionally, Archibald *et al*[27] conducted a longitudinal study indicating that NPC deteriorated from 6.9 cm in the first year to 9.8 cm in the second year among 45 patients with Parkinson's disease. Moreover, changes in NPC were directly correlated with variations in UPDRS scores[27].

Deterioration of NPC indicates a disruption in convergence, which may be associated with the weakness of the oculomotor muscles or damage to the neural pathways that govern eye movements in individuals with Parkinson's disease[28]. This dysfunction is likely a consequence of the underlying pathophysiology of Parkinson's, which primarily involves the degeneration of dopaminergic neurons in the substantia nigra and the disruption of ocular motor neural circuits[29]. A deficiency of dopamine in the basal ganglia, particularly in structures like the globus pallidus, significantly impairs convergence control[30-31]. Furthermore, dopamine plays a crucial role in modulating the activity of the frontal eye fields and the superior colliculus; its reduction in Parkinson's disease results in a decrease in sensorimotor processing for near visual targets, as well as impairments in the timing and accuracy of vergence movements[32]. Neurodegenerative changes in Parkinson's also impact the oculomotor nuclei (for instance, the Edinger-Westphal nucleus and the rostral interstitial nucleus of the medial longitudinal fasciculus) and the visual cortex, leading to a reduction in convergence amplitude and an increase in exophoria[31]. Additionally, cognitive factors, environmental influences, and the state of medication further affect NPC[33]. Almer *et al*[21] documented an NPC of 13.1 cm during the "on state" compared to 18.1 cm in the "off state, highlighting its variable nature. Therefore, NPC may function as a non-invasive clinical measure for monitoring the progression of Parkinson's disease.

The present represents the first comprehensive report on fusional vergence indices in patients with Parkinson's disease. With the exception of the distance base-out break and distance base-out recovery, all other fusional vergence parameters showed significant declines in individuals with Parkinson's. The most notable differences between the Parkinson's group and the control group were found in the near base-out break (20.76 *vs* 14.52) and near base-in blur (12.80 *vs* 7.38). Given that these indices are critical components of convergence insufficiency, and prior studies consistently demonstrate an increased prevalence of convergence

insufficiency in Parkinson's, the noted decrease in fusional vergence is expected. The reduced vergence performance in individuals with Parkinson's disease is linked to the degeneration of nigrostriatal dopaminergic pathways and the considerable disruption of subcortical networks that regulate eye movements[30-31]. The loss of dopamine in the caudate and putamen negatively impacts motor planning and cognitive flexibility, thus interfering with the neural signals required for sustaining binocular stability[30,34]. This leads to a reduction in both the amplitude and speed of vergence responses, diminished blur thresholds, and particularly severe deficits during the break and recovery phases. Since recovery demands active, sustained control by central nervous system pathways, its increased vulnerability compared to blur highlights the dysfunction of executive-motor circuits resulting from dopaminergic degeneration.

In the present study, patients with Parkinson's disease exhibited significantly poorer horizontal saccadic performance compared to control subjects. Although Buhmann *et al*[35] found no significant correlation between saccadic parameters and the severity of Parkinson's disease, it appears that saccadic dysfunction, like other aspects of binocular vision, is influenced by a deficiency in dopaminergic activity. The reduction of dopamine in the nigrostriatal pathway results in an excessive inhibitory output from the substantia nigra pars reticulata to the superior colliculus. This disruption affects not only self-initiated saccades but, in the later stages of the disease, even reflexive saccadic processing. Hence, our findings suggest that saccadic dysfunction in Parkinson's disease represents a progressive impairment that initially affects horizontal movements and eventually impacts more basic and reflexive pathways, despite contrasting with the results reported by Buhmann *et al*[35].

According to the results, the near vergence indices showed significant diagnostic accuracy in distinguishing Parkinson's patients from healthy subjects. Specifically, near base-in blur had a sensitivity of 69%, specificity of 90%, and an AUC of 0.877. Similarly, near base-out blur demonstrated a sensitivity of 76.2%, specificity of 72.7%, and an AUC of 0.814. In contrast, the distance vergence metrics were notably less effective; for example, distance base-out break had a sensitivity of only 7.1% and an AUC of 0.486, while distance base-out recovery exhibited a sensitivity of 11.9% and an AUC of 0.483. This difference in diagnostic performance may be attributed to the fact that distance divergence is primarily controlled by posterior and brainstem systems, which are less dependent on the dopaminergic pathways of the basal ganglia.

However, distance base-in recovery demonstrated a high sensitivity of 88.1% but a low specificity of 41.5%, with an AUC of 0.699. This suggests that while it can effectively identify a significant number of true cases, it also results in a considerable number of false positives among healthy individuals. Ultimately, the notable diagnostic potential of near vergence indices, particularly near base-in blur and near base-out blur, indicates that they may serve as cost-effective, non-invasive screening tools, especially during the early stages of disease when clinical diagnosis proves to be difficult. Nevertheless, given that no single index attains high diagnostic accuracy independently, we recommend the utilization of a composite panel. This panel could include near base-in blur combined with distance base-out blur and NPC as a diagnostic approach.

In conclusion, this study demonstrates that Parkinson's disease is associated with significant impairment in binocular vision. The predominant binocular abnormalities identified in our cohort included increased NPC and diminished near fusional vergence measurements. These findings highlight the potential utility of binocular vision assessment as a non-invasive biomarker for early detection and monitoring of Parkinson's disease.

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