Medical Journal of Bakırköy

Med J Bakirkoy 2026;22(2):147-155
DOI: 10.4274/BMJ.galenos.2026.2025.11-13

Research

Differentiating Progressive Supranuclear Palsy from Idiopathic Normal Pressure Hydrocephalus: A Comparative Study of MR Parkinsonism Indices and Midbrain Qualitative Features

Progresif Supranükleer Palsi ile İdiyopatik Normal Basınçlı Hidrosefalinin Ayırt Edilmesi: MR Parkinsonizm İndeksleri ve Mezensefalon Niteliksel Özelliklerinin Karşılaştırmalı Çalışması

Yunus Emre Şentürk[1], Enes Muhammed Cantürk[1], Ahmet Peker[1], Sezer Kula[1], Mert Bayramoğlu[1], Sabahattin Yüzkan[1], Eser Buluş[2]

[1]Koç University Hospital, Department of Radiology, İstanbul, Türkiye
[2]Koç University Hospital, Department of Neurology, İstanbul, Türkiye

ABSTRACT

Objective: Progressive supranuclear palsy (PSP) with ventricular dilatation and idiopathic normal pressure hydrocephalus (iNPH) may present with overlapping symptoms, particularly when gait disturbance predominates. This study compared midbrain qualitative signs and quantitative metrics to identify the most accurate marker for differentiating PSP from iNPH.

Methods: We retrospectively enrolled 32 patients with PSP, 33 with shunt-predictive iNPH, and 35 age-matched healthy controls, all of whom fulfilled established clinical criteria. High-resolution isotropic magnetization prepared rapid acquisition gradient echo (1.0 mm voxel size) was used to evaluate the hummingbird sign (HBS), morning glory sign, midbrain-to-pons area ratio (M/P), Magnetic Resonance Parkinsonism Index (MRPI), and its updated version, MRPI 2.0. Binary logistic regression analysis was performed to assess the predictive value of midbrain metrics and qualitative features.

Results: All imaging markers differed significantly among PSP, iNPH, and control subjects ($p<0.01$). The M/P ratio, MRPI, and MRPI 2.0 effectively distinguished all group pairs, with the M/P ratio demonstrating fair accuracy [area under the curve (AUC)=0.81; accuracy 74%]. Both MRPI versions achieved acceptable performance (AUC<0.78). The HBS demonstrated good discriminatory performance in differentiating PSP from iNPH (AUC=0.82; accuracy 81%) and emerged as the sole independent predictor in logistic regression [AUC=0.87; odds ratio (OR): 32; $p<0.01$]. The MRPI 2.0 outperformed all qualitative features (AUC=0.94; OR: 18; $p<0.01$) in distinguishing iNPH from healthy individuals.

Conclusion: Quantitative metrics for Parkinsonism showed stepwise differences across PSP, iNPH, and control groups. The HBS outperformed all quantitative measures in distinguishing PSP from iNPH when a predefined point-based system was applied.

Keywords: Hummingbird sign, progressive supranuclear palsy, idiopathic normal pressure hydrocephalus, Magnetic Resonance Parkinsonism Index, midbrain atrophy

ÖZ

Amaç: Ventriküler genişleme ile seyreden progresif supranüklear paralizi (PSP) ve idiyopatik normal basınçlı hidrosefali (iNPH), özellikle yürüme bozukluğunun belirgin olduğu klinik olarak örtüşen bulgulardır. Bu çalışma, PSP ile iNPH'yi ayırt etmede en doğru belirteci belirlemek için orta beyin ilişkili niteliksel bulgular ve niceliksel ölçümleri karşılaştırmıştır.

Gereç ve Yöntem: Tanımlanmış kriterleri karşılayan 32 PSP hastası, şant yanıtı öngörülebilen 33 iNPH hastası ve 35 yaş uyumlu sağlıklı kontrol grubu bu retrospektif çalışmaya dahil edildi. Yüksek çözünürlüklü izotropik *magnetization prepared rapid acquisition gradient echo* (1.0 mm voksel boyutu) kullanılarak hummingbird işareti (HBS), *morning glory* işareti, orta beyin-pons oranı (M/P), Manyetik Rezonans Parkinsonizm İndeksi (MRPI) ve güncellenmiş MRPI 2.0 değerlendirildi. Orta beyin ölçümlerinin ve niteliksel bulguların öngörü değerini belirlemek amacıyla lojistik regresyon analizi yapıldı.

Address for Correspondence: Yunus Emre Şentürk, MD, Koç University Hospital, Department of Radiology, İstanbul, Türkiye
E-mail: ysenturk@kuh.ku.edu.tr **ORCID ID:** orcid.org/0000-0002-0661-7867

Cite as: Şentürk YE, Cantürk EM, Peker A, Kula S, Bayramoğlu M, Yüzkan S, et al. Differentiating progressive supranuclear palsy from idiopathic normal pressure hydrocephalus: a comparative study of MR parkinsonism indices and midbrain qualitative features. Med J Bakirkoy. 2026;22(2):147-155

Received: 15.11.2025
Accepted: 04.02.2026
Publication Date: 08.06.2026

ÖZ

Bulgular: Tüm görüntüleme belirteçleri PSP, iNPH ve kontrol grupları arasında anlamlı farklılık gösterdi (p<0,01). M/P oranı orta derece [eğri altındaki alan (AUC)=0,81; doğruluk %74], MRPI ölçümleri ise kabul edilebilir performans gösterdi (AUC<0,78). HBS, PSP'yi iNPH'den ayırmada en iyi performansı gösterdi (AUC=0,82; doğruluk %81) ve regresyon analizinde tek bağımsız belirteç olarak öne çıktı [AUC=0,87; olasılık oranı (OR): 32; p<0,01]. MRPI 2.0 ise sağlıklı bireylerle karşılaştırıldığında iNPH lehine tüm niteliksel belirteçlerden üstün bulundu (AUC=0,94; OR: 18; p<0,01).

Sonuç: Parkinsonizmle ilişkili niceliksel ölçümler PSP, iNPH ve kontrol grupları arasında kademeli farklılık gösterdi. Literatürde tanımlanmış puanlama sistemi uygulandığında tek başına hummingbird işareti olası PSP'ni, iNPH'den ayırmada niceliksel ölçümlerden daha başarılıdır.

Anahtar Kelimeler: Hummingbird işareti, progresif supranükleer palsi, idiyopatik normal basınçlı hidrosefali, Manyetik Rezonans Parkinsonizm İndeksi, orta beyin atrofisi

INTRODUCTION

Progressive supranuclear palsy (PSP) is a primary tauopathy characterized by abnormal tau deposition leading to progressive neurodegeneration (1). Clinically, PSP presents with postural instability, gait disturbance, cognitive impairment, urinary symptoms, and frontal executive dysfunction; vertical supranuclear gaze palsy is a hallmark feature (2). However, early gaze palsy may be subtle, resulting in low sensitivity of the National Institute of Neurological Disorders and Stroke-Society for PSP (NINDS-SPSP) diagnostic criteria despite high specificity (3). This diagnostic challenge is particularly evident in Parkinsonism-predominant PSP from other parkinsonian disorders (4). Consequently, magnetic resonance imaging (MRI) plays an important role in early diagnosis, with qualitative imaging signs, such as the hummingbird sign (HBS) and the morning glory sign (MGS), proposed as suggestive markers of the PSP spectrum (5).

Idiopathic normal pressure hydrocephalus (iNPH), which has an estimated annual incidence of 5.5 per 100,000 and is considerably more common than PSP, is thought to result from impaired cerebrospinal fluid (CSF) absorption and altered brain compliance (6,7). Clinically, iNPH is characterized by gait instability, urinary incontinence, and frontal executive dysfunction (8). MRI features such as disproportionately enlarged subarachnoid space hydrocephalus (DESH), narrowed callosal angle, ventricular enlargement, and periventricular hyperintensities support the diagnosis (9). iNPH may be misdiagnosed as PSP due to overlapping clinical features, particularly parkinsonism and gait disturbance. Early differentiation often requires prolonged clinical surveillance or invasive CSF testing, and coexistence of PSP pathology and iNPH-related CSF disturbance has been reported (10). An accurate distinction is essential because treatment strategies differ substantially between the two conditions (11,12).

MRI assessment of PSP traditionally relies on qualitative midbrain atrophy features, including mesencephalic beaking and loss of lateral tegmental convexity (13). However, these signs may be subtle or absent in early or Parkinsonism-predominant cases, limiting the sensitivity of qualitative assessments. Consequently, several midbrain morphometric indices were proposed, including the MR Parkinsonism Index (MRPI), the midbrain-to-pons area ratio (M/P), and the more recent MRPI 2.0. Although initial reports suggested improved performance of MRPI 2.0 in distinguishing PSP from idiopathic Parkinsonism, subsequent studies have questioned its superiority in differentiating Parkinsonism-predominant PSP from other Parkinsonian disorders (14,15). Notably, the application of quantitative midbrain indices, including MRPI 2.0, for differentiating PSP from iNPH has received relatively limited attention in the literature. Therefore, the objective of this study was to investigate the diagnostic value of midbrain morphometric indices, including MRPI 2.0, when combined with classical qualitative MRI features, in differentiating the PSP spectrum from iNPH.

METHODS

Study Group Selection

This retrospective study was carried out at a single center between January 2018 and December 2024. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Non-Interventional Clinical Research Ethics Committee of Koç University under reference (approval no: 2025.318.IRB2.145, date: 11.07.2025). Patient data were reviewed using the institution's digital medical record system. Inclusion criteria for the PSP group were the fulfillment of the clinical diagnostic criteria for probable PSP spectrum, according to the neuropathologic guidelines of the NINDS-SPSP, and the availability of isotropic T1-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE) imaging at diagnosis (3). All clinical diagnoses of PSP were confirmed by a neurologist specializing in movement disorders (Eser Buluş). Initially, 41 patients with probable PSP were identified; however, only 32 (14 females, 18 males) had corresponding MRI available at the time of diagnosis and were included in the study. Similarly, 46 patients presenting with the full

clinical triad suggestive of iNPH—gait disturbance, urinary incontinence, and cognitive impairment—were identified in the digital medical records. However, 13 of these did not demonstrate the supportive imaging features required for a diagnosis of shunt-predictive probable iNPH, as outlined in the criteria endorsed by the Japanese Society of Normal Pressure Hydrocephalus (16). Those imaging requisites include disproportionately enlarged subarachnoid spaces, an Evans index >0.3, and a steeply narrowed callosal angle [non-compartmental analysis (NCA) <90°]. The remaining 33 patients (14 females, 19 males) fulfilled the complete clinical triad and all required imaging features for shunt-predictive probable iNPH. Among these, 15 patients underwent ventriculoperitoneal shunt surgery. All included iNPH patients had pre-intervention MRI available, including isotropic T1-weighted MPRAGE sequences. Exclusion criteria for both groups included the absence of MRI at the time of diagnosis, the presence of space-occupying lesions or large areas of encephalomalacia, indicative of prior major trauma, large-vessel occlusion, or hemorrhage. However, no participants from either group met these exclusion criteria. For the control group, 35 age-matched healthy subjects (15 females, 20 males) were selected from individuals who attended the neurology outpatient clinics during the same period and presented with symptoms indicative of a non-neurodegenerative condition, including tension-type headache and migraine-type headache, or who attended for routine check-up. Control subjects were included only if their brain MRI examinations were normal, with no evidence of localized or diffuse abnormalities. Figure 1 illustrates the participant selection process with a flow diagram.

The Magnetic Resonance Parkinsonism Indices

All planimetric measurements were ultimately performed using isotropic T1-weighted MPRAGE images acquired in the sagittal orientation, with an isotropic voxel size of 1.0 mm, bandwidth of 180 Hz/pixel, repetition time/echo time of 2400/3.7 ms, field of view of 250×250×160 mm, matrix size of 205×256×256, and a flip angle of 8°. The isotropic MPRAGE datasets were subsequently reformatted into coronal-oblique, sagittal, and axial planes to enable measurement of midbrain area (M), pons area (P), lengths of the superior cerebellar peduncle (SCP) and middle cerebellar peduncle (MCP), third ventricular width (V3), and the left-to-right width of the frontal horns of the lateral ventricles (FH). The MRPI was calculated using the formula: MRPI=(P/M)×(MCP/SCP). The MRPI 2.0 was derived by incorporating ventricular dimensions into that formula: MRPI 2.0=MRPI×(V3/FH). All measurements were performed manually by a fellowship-trained neuroradiologist with 7 years of experience in the field. Figure 2 illustrates the planimetric measurements used to calculate MRPI and MRPI 2.0 in patients with PSP, patients with iNPH, and control subjects. The M/P, a conventionally recommended metric for differentiating PSP from other atypical Parkinsonian syndromes, was also calculated (17). All planimetric measurements were repeated after 4 weeks to assess the intra-rater agreement.

Qualitative Parameters

The HBS was independently evaluated by two experienced neuroradiologists, Yunus Emre Şentürk (6 years of neuroimaging experience) and Ahmet Peker (5 years of neuroimaging experience), according to the ordinal scoring system described by Kim et al. (18). This system evaluates four features: the shape of the third ventricle, the contour of the beak, the configuration of the midbrain, and the overall sagittal appearance of the midbrain-to-pons interface. Each feature was scored on a scale from 0 to 2. A total composite score >5 was considered indicative of a positive HBS, as this threshold yielded the best performance compared with other thresholds when accounting for the Kim et al. (18) series. Similarly, the MGS was independently evaluated by two raters (Yunus Emre Şentürk and Ahmet Peker) on axially reformatted MR images, in accordance with the method outlined by Adachi et al. (19). An imaginary horizontal line was drawn posterior to the cerebral aqueduct. A second line was then extended from the lateral margin of the cerebral peduncle to the point where the first line intersected the tegmentum. The MGS was considered positive when the lateral tegmental border of the midbrain was located medial to this second line. The HBS and MGS statuses of all cases were re-evaluated by the central rater after a minimum interval of four weeks to assess intra-rater agreement.

Statistical Analysis

All statistical analyses were performed using SPSS version 28 (IBM Corp., Armonk, NY, USA). The Shapiro-Wilk test was used to assess the normality of all continuous variables. Parameters following a normal distribution, such as the M/P, MRPI, and MRPI 2.0, were compared across groups using one-way analysis of variance, with post-hoc pairwise comparisons using Tukey's honestly significant difference test. The Cohen's kappa analysis was performed for all patients with PSP spectrum and iNPH to assess the inter- and intrarater reliability of HBS and MGS between the outcomes of the central (Yunus Emre Şentürk) and the co-rater (Ahmet Peker). Intrarater reliability was assessed using a two-way mixed-effects intraclass correlation coefficient for absolute agreement. Variables that demonstrated significant differences were subsequently included in a backward stepwise logistic regression (BSLR) model to evaluate the discriminatory power of individual planimetric

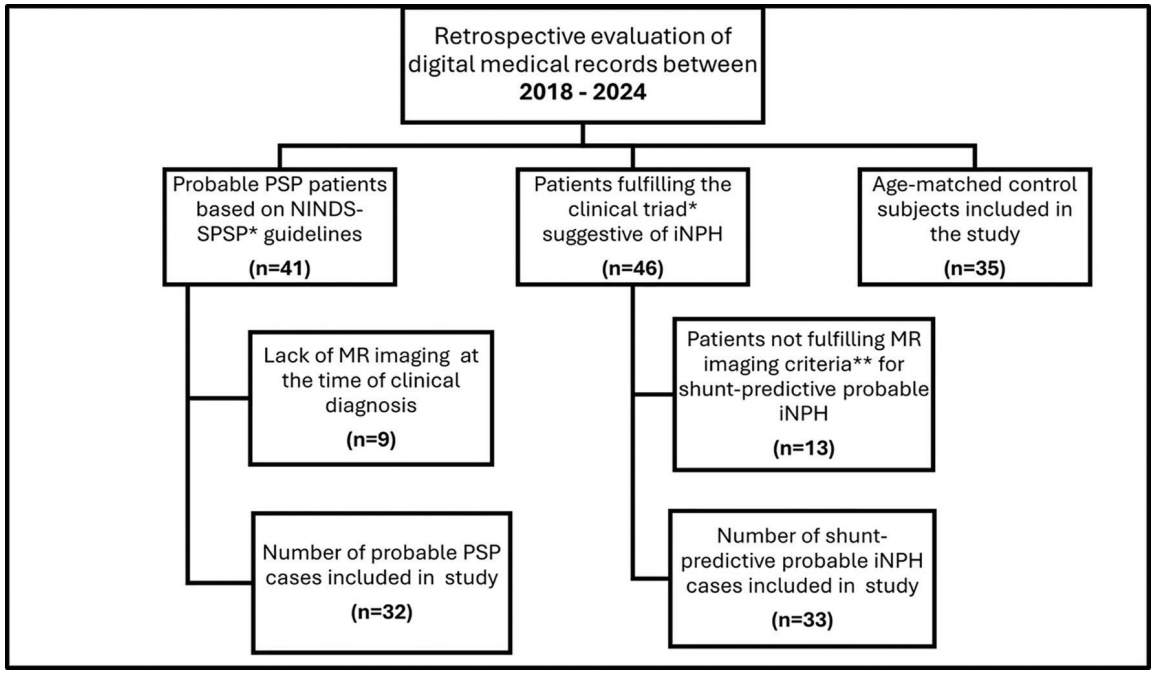

Figure 1. Flow chart of the study group selection process

*: NINDS-SPSP guidelines for the probable PSP diagnosis (see the reference number 3), **: Guidelines for management of idiopathic normal pressure hydrocephalus (third edition): endorsed by the Japanese Society of Normal Pressure Hydrocephalus (see the reference number 16)

NINDS-SPSS: National Institute of Neurological Disorders and Stroke-Society for progressive supranuclear palsy, PSP: Progressive supranuclear palsy, iNPH: Idiopathic normal pressure hydrocephalus, MR: Magnetic resonance

features for differentiating PSP from iNPH, and iNPH from control subjects. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographics

Baseline characteristics and symptoms on admission are presented in Table 1. Each group's mean age resembled that of the others, while the patients with PSP had a wider age range, with a mean age of 73±10 years. The gender distribution was similar across groups, as shown in Table 1.

The Quantitative Parkinsonism Features

The Evans index exceeded 0.3 in all iNPH patients and in 48% of those with PSP. The M/P ratio, MRPI, and MRPI 2.0 differed among groups based on analysis of variance statistics ($p<0.001$, for each analysis). Table 2 summarizes the distribution of means for each midbrain metric parameter. Post-hoc pairwise comparisons revealed notable mean differences in all three midbrain metrics between PSP and iNPH, and between iNPH and control subjects ($p<0.001$). Figure 3 presents box plots of the distribution of each midbrain metric across groups. These findings indicate a clear stepwise separation of the three groups, with iNPH values consistently falling between those of PSP and control subjects. All quantitative parkinsonism parameters demonstrated excellent intra-rater reliability, with kappa (κ) values of 0.94 for the M/P ratio, 0.92 for MRPI, and 0.91 for MRPI 2.0 (all $p<0.001$).

The Qualitative Assessment of the Midbrain

The presence of the HBS in each group was evaluated using the visual scoring system proposed by Kim et al. (18), in which a composite score of ≥5, agreed upon by both raters, was considered HBS-positive. HBS was identified in 29 patients with PSP (90.6%) and 9 patients with iNPH (27.3%); none of the control subjects exhibited this sign ($p<0.001$). In contrast, the MGS was less frequently observed, with 15 PSP patients (47.0%) and 4 iNPH patients (12.1%) classified as MGS-positive ($p=0.003$). None of the control subjects had a positive MGS.

The central rater identified HBS positivity in 39 (60%) cases, while the co-rater identified 36 (55%) cases. Interrater reliability for HBS was almost perfect ($\kappa=0.85$; $p<0.001$), with almost perfect intrarater agreement ($\kappa=0.89$; $p<0.001$). For the MGS, the central rater and co-raters identified 19 (29%) and 16 (24%) positive cases, respectively. Interrater agreement was substantial ($\kappa=0.77$; $p<0.001$), and intrarater agreement was almost perfect ($\kappa=0.85$; $p<0.001$).

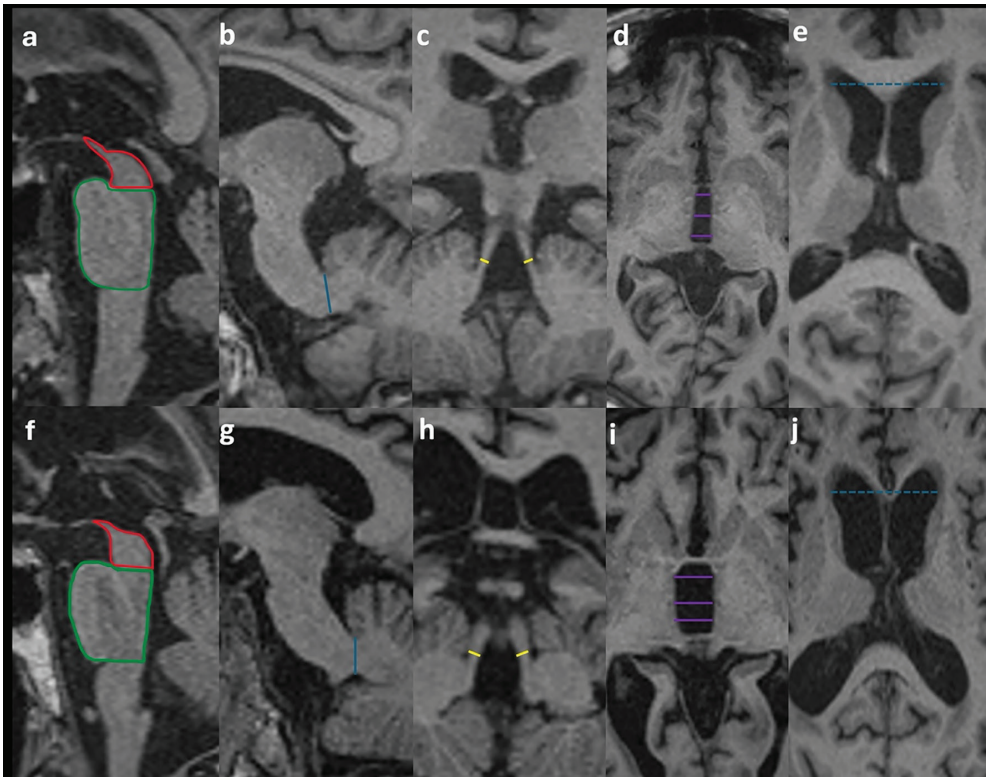

Figure 2. Representative isotropic T1-weighted MPRAGE series from a 65-year-old male with definite progressive supranuclear palsy (PSP) **(a-e)** and a 72-year-old male with definite idiopathic normal pressure hydrocephalus (iNPH) **(f-j)**. In the patient with PSP, the midbrain-to-pons area ratio (M/P) was 0.16; **a)**, the middle cerebellar peduncle (MCP) thickness was 9.4 mm; **b)**, the mean superior cerebellar peduncle (SCP) thickness was 2.5 mm; **c)**, the mean third ventricle width was 9 mm; **d)**, and the lateral ventricular bifrontal (FH) width was 33.0 mm; **e)**. the calculated MRPI [(P/M)×(MCP/SCP)] was 24.0, and MRPI 2.0 (MRPI×third ventricle size/FH) was 6.5. In the iNPH patient, the M/P ratio was 0.19; **f)**, the MCP thickness was 10 mm; **g)**, the mean SCP thickness was 3.2 mm; **h)**, the mean third ventricle width was 10 mm; **i)**, and the FH width was 56 mm; **j)**. the calculated MRPI was 16.1, and the MRPI 2.0 was 3.1. Both patients underwent standardized MRI measurement protocols to assess the diagnostic performance of midbrain metrics

MPRAGE: Magnetization-prepared rapid acquisition gradient echo, MRI: Magnetic resonance imaging, MRPI: Magnetic resonance parkinsonism index

Performances of Qualitative and Quantitative Parameters

The receiver operating characteristic analysis for both quantitative parameters is summarized in Table 3 and Figure 3. The M/P demonstrated good discriminatory performance between the PSP and iNPH groups, with an area under the curve (AUC) of 0.81 and an accuracy of 0.74. Although slightly lower than the M/P, MRPI and MRPI 2.0 also demonstrated fairly good performance, with AUCs of 0.77 and 0.74, and accuracies of 0.77 and 0.72, respectively. Overall, the midbrain morphometrics demonstrated superior performance in differentiating iNPH from control subjects. Among these, the MRPI and MRPI 2.0 demonstrated excellent discriminatory power, with AUCs of 0.93 and 0.92 and accuracies of 0.88 and 0.87, respectively. The M/P also performed well, though slightly below the threshold for excellence, achieving an AUC of 0.90 and an accuracy of 0.82. In the qualitative assessment of midbrain shape, the HBS demonstrated good diagnostic utility for distinguishing PSP from iNPH (AUC HBS: 0.82; AUC MGS: 0.67). In addition, HBS and MGS demonstrated poor efficacy in distinguishing iNPH from control subjects (AUC HBS: 0.62; AUC MGS: 0.55).

Logistic Regression Analysis

To evaluate the combined predictive value of quantitative midbrain metrics and qualitative imaging signs in distinguishing iNPH from PSP, a BSLR was performed. Collinearity was identified among the morphometric parameters because MRPI values are derived from the M/P. MRPI 2.0 was therefore retained due to its inclusion of ventricular dimensions. The final model combining MRPI 2.0, HBS, and MGS showed strong performance (Nagelkerke R^2=0.41; AUC=0.87; accuracy=81%). HBS was the strongest independent predictor of PSP [odds ratio (OR): 32; p<0.001), followed by MGS (OR: 9; p=0.021). The MRPI 2.0 was not an independent predictor (p=0.97).

A second BSLR model differentiating iNPH from controls similarly excluded the M/P and MRPI due to collinearity.

Table 1. Demographics and clinical characteristics

Study groups	PSP, n=32	iNPH, n=33	Control subjects, n=35
Age, year, (mean±SD)	73±10	75±6	74±5
Gender (female/male),	14/18	14/19	15/20
Lower extremity dyscoordination, n (%)	24, (75)	26, (79)	0
Cognitive impairment, n (%)	25, (78)	26, (79)	0
Urinary incontinence, n (%)	4, (13)	12, (36)	0
Gaze palsy, n (%)	10, (31)	1, (3)	0

iNPH: Idiopathic normal pressure hydrocephalus, SD: Standard deviation, PSP: Progressive supranuclear palsy

Table 2. Midbrain metric means and standard deviations across study groups*

Group	M/P ratio (mean±SD)	MRPI (mean±SD)	MRPI 2.0 (mean±SD)
Control subjects, n=35	0.286±0.041	10.71±1.69	2.18±0.68
iNPH, n=33	0.220±0.032	15.67±3.36	4.10±1.32
PSP, n=32	0.180±0.032	21.60±7.70	6.02±2.47

*: Statistically significant differences were observed across all groups for each midbrain metric, as determined by analysis of variance with F-statistics ($p<0.001$ for all comparisons), iNPH: Idiopathic normal pressure hydrocephalus, M/P: Midbrain-to-pons area ratio, MRPI: Magnetic Resonance Parkinsonism Index, PSP: Progressive supranuclear palsy, SD: Standard deviation

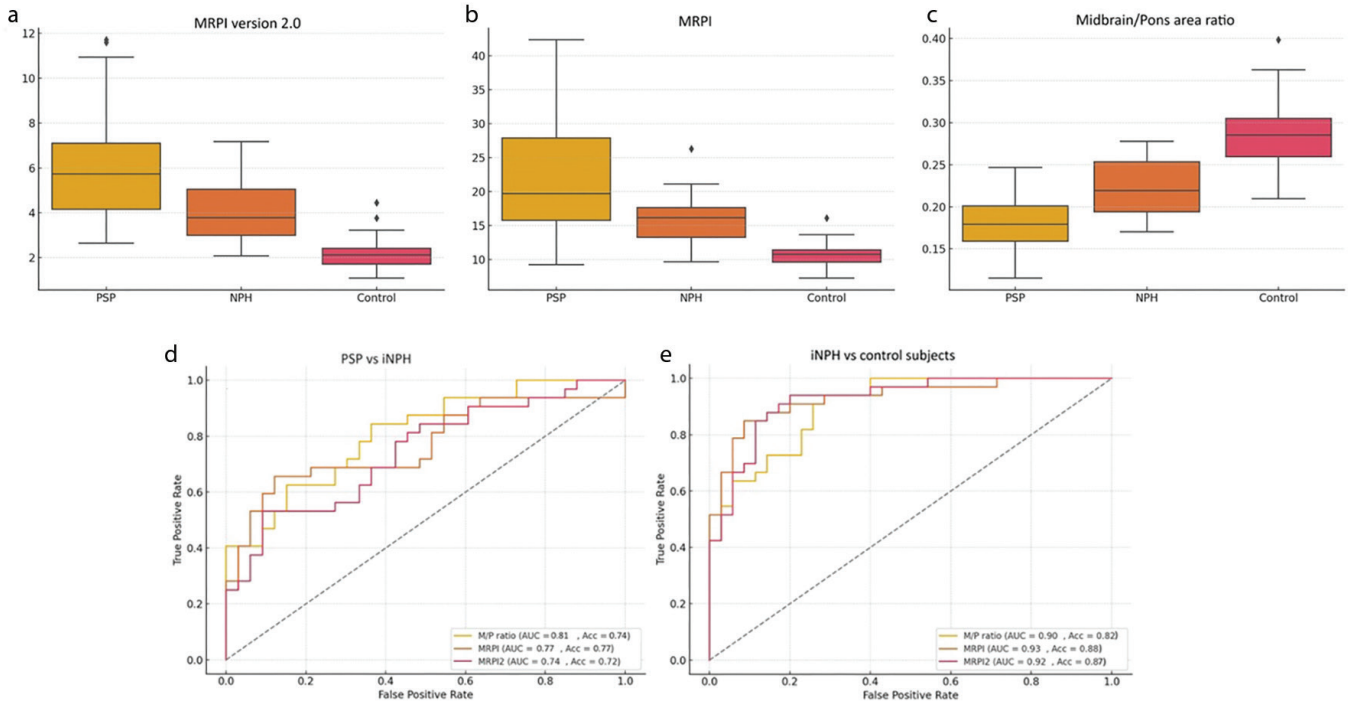

Figure 3. Box plot illustration of the Parkinsonism indices in progressive supranuclear palsy (PSP), idiopathic normal pressure hydrocephalus (iNPH), and age-matched control subjects. The indices include the midbrain-to-pons area ratio (M/P); **a)** Magnetic Resonance Parkinsonism Index (MRPI); **b)** and MRPI 2.0; **c)** One-way ANOVA analysis demonstrated significant differences among the three groups for each parameter ($p<0.01$). Subsequent Tukey HSD post-hoc analysis confirmed significant pairwise differences between the PSP, iNPH, and control groups for the M/P, MRPI, and MRPI 2.0 indices ($p<0.01$ for each pairwise comparison). **d)** ROC curve for differentiating PSP from iNPH. The M/P ratio shows good discriminatory performance and outperforms both MRPI and MRPI 2.0. **e)** ROC curve for differentiating iNPH from control subjects. All quantitative midbrain metrics demonstrate excellent discriminative performance favoring iNPH

ANOVA: Analysis of variance, HSD: Honestly significant difference, ROC: Receiver operating characteristic

Table 3. Performance of midbrain-based imaging metrics in the discrimination of PSP, iNPH, and control groups

Parameters	Group-wise comparison	AUC	Accuracy	Sensitivity, (%)	Specificity, (%)	Best cut-off
M/P ratio	PSP vs. iNPH	0.81	0.74	84	64	0.20
	PSP vs. control	0.98	0.96	94	97	0.22
	iNPH vs. control	0.90	0.82	94	71	0.27
MRPI	PSP vs. iNPH	0.77	0.77	66	88	18.9
	PSP vs. control	0.94	0.96	94	97	13.9
	iNPH vs. control	0.93	0.88	85	91	12.7
MRPI 2.0	PSP vs. iNPH	0.74	0.72	53	91	5.7
	PSP vs. control	0.98	0.93	97	89	2.8
	iNPH vs. control	0.93	0.87	94	80	2.5

iNPH: Idiopathic normal pressure hydrocephalus, M/P: Midbrain-to-pons area ratio, MRPI: Magnetic resonance parkinsonism index, PSP: Progressive supranuclear palsy, AUC: Area under the curve

MRPI 2.0 emerged as the only significant predictor (OR: 18.4), favoring an iNPH diagnosis over controls (Nagelkerke R^2=0.52; AUC=0.93; accuracy=87%).

DISCUSSION

The current study demonstrates that midbrain morphometric measurements are useful for differentiating the PSP spectrum from iNPH. Among quantitative indices, the M/P showed the highest overall accuracy in favoring PSP, whereas both MRPI and MRPI 2.0 demonstrated favorable but limited performance. Specifically, an M/P <0.2 yielded high sensitivity (84%) but poor specificity, whereas MRPI and MRPI 2.0 exhibited nearly 90% specificity at the expense of low sensitivity. These complementary performance patterns suggest that combining quantitative parameters may be more informative than relying on a single metric.

Among the qualitative parameters, only the HBS achieved good performance. When all quantitative and qualitative factors were combined, diagnostic performance improved, and the HBS emerged as a hallmark predictor distinguishing the PSP spectrum from iNPH. A challenge in interpreting HBS is the lack of a universally accepted verification method for equivocal cases. In this study, the systematic approach of Kim et al. (18) was applied, resulting in three clinically overt PSP cases being classified as HBS-negative. This stricter definition, favoring definite midbrain atrophy, likely contributed to the enhanced diagnostic performance of HBS in the combined regression model. Consistent with prior work by Kim et al. (18), who reported AUC values of 0.72-0.76 for HBS in PSP versus idiopathic parkinsonism, our cohort demonstrated an even higher AUC of 0.82 for distinguishing PSP from iNPH. Therefore, the diagnostic performance of HBS appears superior to the midbrain metric markers when either an informative scoring system is used or a scoring system is applied systematically.

Among quantitative parameters, the simpler M/P slightly outperformed the more complex MRPI and MRPI 2.0, despite MRPI 2.0 incorporating ventricular measurements to enhance discrimination. In our cohort, MRPI 2.0 showed poor sensitivity, which was likely influenced by ventricular enlargement observed in 48% of PSP cases, in which the Evans index exceeded 0.3. This ventriculomegaly may reduce the discriminatory advantage of the ventricular component of MRPI 2.0. Consistent with our results, Constantinides et al. (20) reported that the M/P outperformed MRPI, with both parameters showing comparable moderate-to-good diagnostic performance. As in their study, the combined use of M/P and MRPI failed to produce high specificity (>80%), likely due to collinearity between variables. Another series also questioned the performance of the MRPI, reporting a cutoff >13 with high specificity (84%) but low sensitivity (29%) (10). In contrast, our higher cut-off of 18.9 improved sensitivity but remained insufficient for standalone clinical decision-making compared to previous reports. A small study of 19 PSP and 17 iNPH cases reported considerable overlap between PSP and iNPH using MRPI 2.0 without providing diagnostic performance measurements (21). In contrast, the clearer stepwise differences observed across all quantitative metrics among the PSP, iNPH, and control groups are likely attributable to the larger sample size of our study.

Although MRPI 2.0 was designed to improve differentiation by incorporating ventricular dimensions, our findings indicate performance comparable to the original MRPI in distinguishing PSP from iNPH. Ventricular enlargement resembling iNPH has been reported in up to 38.2% of PSP cases, particularly in the Parkinsonism-predominant subtype. iNPH has been identified as one of the most frequent mimics of PSP (22,23). This overlap likely limits the added value of MRPI 2.0 in this context. Nonetheless, MRPI 2.0

has demonstrated excellent performance in distinguishing PSP from Parkinson's disease in larger series (24). MRPI 2.0 values were significantly higher in iNPH patients than in controls and outperformed HBS in distinguishing the two groups in our cohort. While classical markers such as NCA, DESH, and periventricular hyperintensities remain sufficient for diagnosing probable iNPH, MRPI 2.0 also achieved a sensitivity of 94% and specificity of 80% at a cutoff of 2.5, suggesting its potential utility as a supportive imaging marker in diagnosing probable iNPH.

Study Limitations

Our cohort has several limitations. First, the study design was retrospective and performed at a single center. Second, although all cases met established diagnostic criteria, complete exclusion of overlapping PSP and iNPH pathology is not possible because shunt-responsive PSP has been reported in the current literature (25). Third, the low sample size limited the performance of multivariable regression models; however, overfitting was minimized by restricting the number of variables included. Finally, PSP subtypes were not analyzed separately, although prior studies indicate no significant differences in MRPI among those PSP subtypes (15).

CONCLUSION

Quantitative midbrain indices, including MRPI 2.0 and previous morphometric parameters, showed a stepwise distribution among PSP, iNPH, and healthy control subjects. MRPI 2.0 did not outperform the original MRPI, and the simpler M/P ratio showed slightly better discriminatory power for distinguishing PSP from iNPH. Of all imaging features, the HBS remained the most reliable marker and an independent predictor of PSP versus iNPH.

ETHICS

Ethical Committee Approval: This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Non-Interventional Clinical Research Ethics Committee of Koç University under reference (approval no: 2025.318.IRB2.145, date: 11.07.2025).

Informed Consent: Retrospective study.

Acknowledgment

The results of the current study were presented during a scientific session at the 48th European Society of Neuroradiology Annual Congress in September 2025.

FOOTNOTES

Author Contributions

Surgical and Medical Practices: E.B., Concept: Y.E.Ş., A.P., S.Y., Design: Y.E.Ş., Data Collection or Processing: Y.E.Ş., E.M.C., Analysis or Interpretation: Y.E.Ş., E.M.C., S.K., E.B., Literature Search: Y.E.Ş., A.P., M.B., Writing: Y.E.Ş., S.Y.

Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: The authors declare that this study received no financial support.

REFERENCES

1. Hauw JJ, Daniel SE, Dickson D, Horoupian DS, Jellinger K, Lantos PL, et al. Preliminary NINDS neuropathologic criteria for Steele-Richardson-Olszewski syndrome (progressive supranuclear palsy). Neurology. 1994;44:2015-9.
2. Williams DR, Lees AJ. Progressive supranuclear palsy: clinicopathological concepts and diagnostic challenges. Lancet Neurol. 2009;8:270-9.
3. Litvan I, Agid Y, Calne D, Campbell G, Dubois B, Duvoisin RC, et al. Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome): report of the NINDS-SPSP international workshop. Neurology. 1996;47:1-9.
4. Shin HW, Hong SW, Youn YC. Clinical aspects of the differential diagnosis of Parkinson's disease and parkinsonism. J Clin Neurol. 2022;18:259-70.
5. Kato N, Arai K, Hattori T. Study of the rostral midbrain atrophy in progressive supranuclear palsy. J Neurol Sci. 2003;210:57-60.
6. Lemcke J, Stengel D, Stockhammer F, Güthoff C, Rohde V, Meier U. Nationwide incidence of normal pressure hydrocephalus (NPH) assessed by insurance claim data in Germany. Open Neurol J. 2016;10:15-24.
7. Ishida T, Murayama T, Kobayashi S. Current research of idiopathic normal pressure hydrocephalus: pathogenesis, diagnosis and treatment. World J Clin Cases. 2023;11:3706-13.
8. Relkin N, Marmarou A, Klinge P, Bergsneider M, Black PM. Diagnosing idiopathic normal-pressure hydrocephalus. Neurosurgery. 2005;57(3 Suppl):S4-16; discussion ii-v.
9. Hashimoto M, Ishikawa M, Mori E, Kuwana N; Study of INPH on neurological improvement (SINPHONI). Diagnosis of idiopathic normal pressure hydrocephalus is supported by MRI-based scheme: a prospective cohort study. Cerebrospinal Fluid Res. 2010;7:18.
10. Georgiopoulos C, Papadimitriou S, Nyholm D, Kilander L, Löwenmark M, Fällmar D, et al. Quantitative brain stem assessment in discriminating neurodegenerative disorders from normal pressure hydrocephalus. J Neuroimaging. 2024;34:612-8.
11. Clerici I, Ferrazzoli D, Maestri R, Bossio F, Zivi I, Canesi M, et al. Rehabilitation in progressive supranuclear palsy: effectiveness of two multidisciplinary treatments. PLoS One. 2017;12:e0170927.
12. Nikaido Y, Urakami H, Okada Y, Akisue T, Kawami Y, Ishida N, et al. Rehabilitation effects in idiopathic normal pressure hydrocephalus: a randomized controlled trial. J Neurol. 2023;270:357-68.

13. Mueller C, Hussl A, Krismer F, Heim B, Mahlknecht P, Nocker M, et al. The diagnostic accuracy of the hummingbird and morning glory sign in patients with neurodegenerative parkinsonism. Parkinsonism Relat Disord. 2018;54:90-4.
14. Quattrone A, Morelli M, Nigro S, Quattrone A, Vescio B, Arabia G, et al. A new MR imaging index for differentiation of progressive supranuclear palsy-parkinsonism from Parkinson's disease. Parkinsonism Relat Disord. 2018;54:3-8.
15. Madetko N, Alster P, Kutyłowski M, Migda B, Nieciecki M, Koziorowski D, et al. Is MRPI 2.0 more useful than MRPI and M/P ratio in differential diagnosis of PSP-P with other atypical parkinsonisms? J Clin Med. 2022;11:2701.
16. Nakajima M, Yamada S, Miyajima M, Ishii K, Kuriyama N, Kazui H, et al.; The research committee of idiopathic normal pressure hydrocephalus. Guidelines for management of idiopathic normal pressure hydrocephalus (third edition): endorsed by the Japanese society of normal pressure hydrocephalus. Neurol Med Chir (Tokyo). 2021;61:63-97.
17. Massey LA, Jäger HR, Paviour DC, O'Sullivan SS, Ling H, Williams DR, et al. The midbrain to pons ratio: a simple and specific MRI sign of progressive supranuclear palsy. Neurology. 2013;80:1856-61.
18. Kim YE, Kang SY, Ma HI, Ju YS, Kim YJ. A visual rating scale for the hummingbird sign with adjustable diagnostic validity. J Parkinsons Dis. 2015;5:605-12.
19. Adachi M, Kawanami T, Ohshima H, Sugai Y, Hosoya T. Morning glory sign: a particular MR finding in progressive supranuclear palsy. Magn Reson Med Sci. 2004;3:125-32.
20. Constantinides VC, Paraskevas GP, Velonakis G, Toulas P, Stefanis L, Kapaki E. Midbrain morphology in idiopathic normal pressure hydrocephalus: a progressive supranuclear palsy mimic. Acta Neurol Scand. 2020;141:328-34.
21. Önder H, Kocer B, Turan A, Kertmen H, Comoglu S. The overlap in neuroimaging findings between idiopathic normal pressure hydrocephalus and progressive supranuclear palsy. Ann Indian Acad Neurol. 2022;25:1087-91.
22. Fu MH, Huang CC, Wu KLH, Chen YF, Kung YC, Lee CC, et al. Higher prevalence of idiopathic normal pressure hydrocephalus-like MRI features in progressive supranuclear palsy: an imaging reminder of atypical parkinsonism. Brain Behav. 2023;13:e2884.
23. Onder H, Kocer B, Comoglu S. Idiopathic normal pressure hydrocephalus-like MRI features in patients with progressive supranuclear palsy: a comparative case-control study. Neurol Res. 2022;44:807-13.
24. Quattrone A, Sarica A, La Torre D, Morelli M, Mechelli A, Arcuri PP, et al. Progressive supranuclear palsy with marked ventricular dilatation mimicking normal pressure hydrocephalus. Neurol Sci. 2022;43:1783-90.
25. Schott JM, Williams DR, Butterworth RJ, Janssen JC, Larner AJ, Holton JL, et al. Shunt responsive progressive supranuclear palsy? Mov Disord. 2007;22:902-3.