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Distinguishing Parkinson Disease and atypical Parkinsonism: Comparison of QyScore®'s automated quantification with expert manual neuroimaging markers

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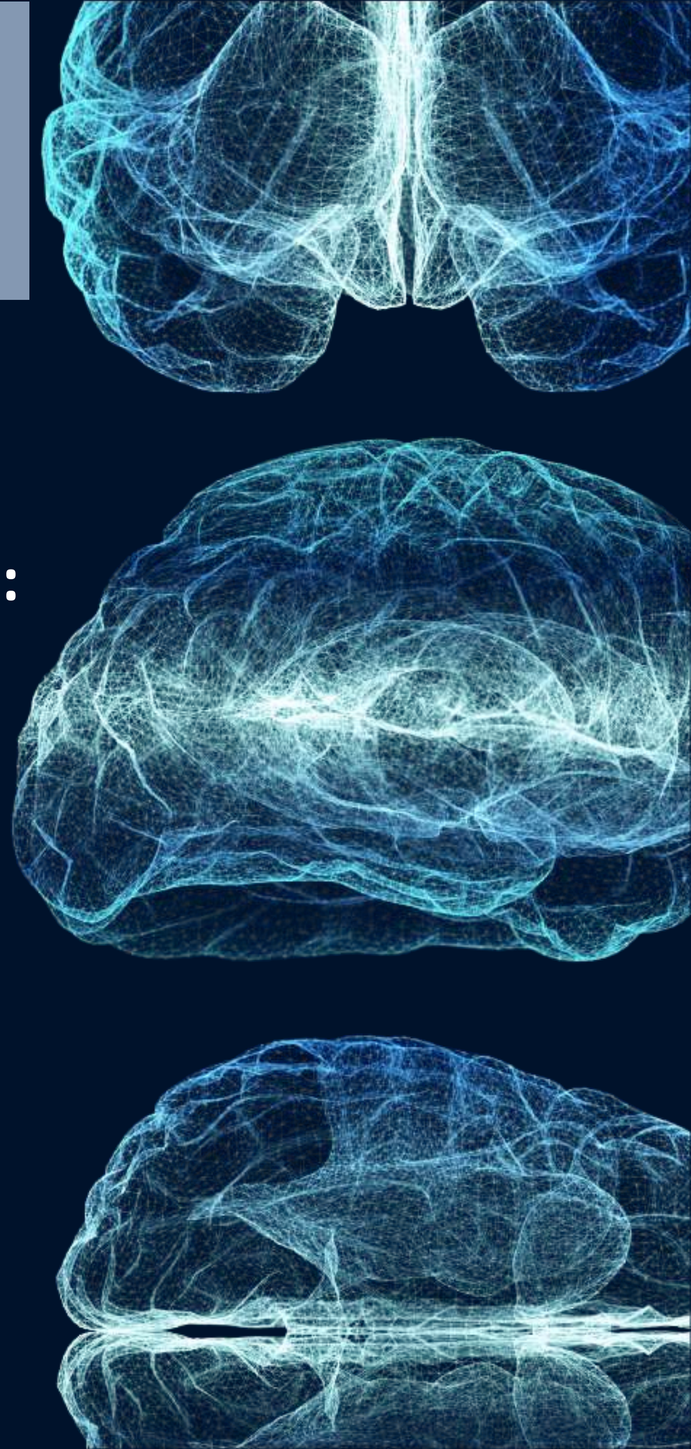

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Name	Disclosures	Company	Position
Francesca Mambrin	Nothing to declare		
Giovanni Mansueto	Nothing to declare		
Michele Tinazzi	Nothing to declare		
Francesca B. Pizzini	Nothing to declare		
Elizabeth Gordon	Employee	Qynapse	Scientific Director
Nicolas Guizard	Employee	Qynapse	R&D Director
Ayoub Gueddou	Employee	Qynapse	Engineer

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Introduction

Key Clinical Challenge:

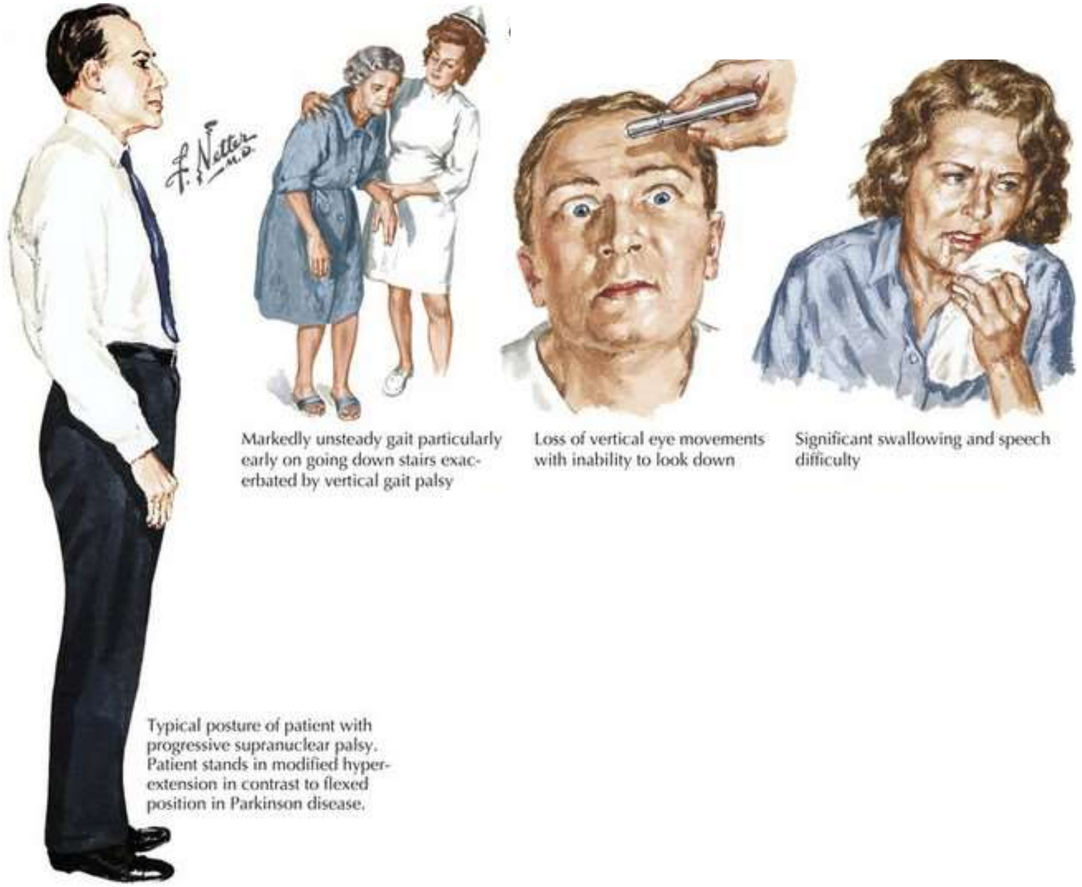
Differential diagnosis with Progressive Supranuclear Palsy (PSP)

Clinical differentiators include:

- Axial rigidity
- Vertical gaze palsy
- Speech and swallowing difficulties
- Tremor is rare

MRI features play a significant role in supporting the clinical work up for differential diagnosis

Key clinical signs of Progressive Supranuclear Palsy



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Introduction

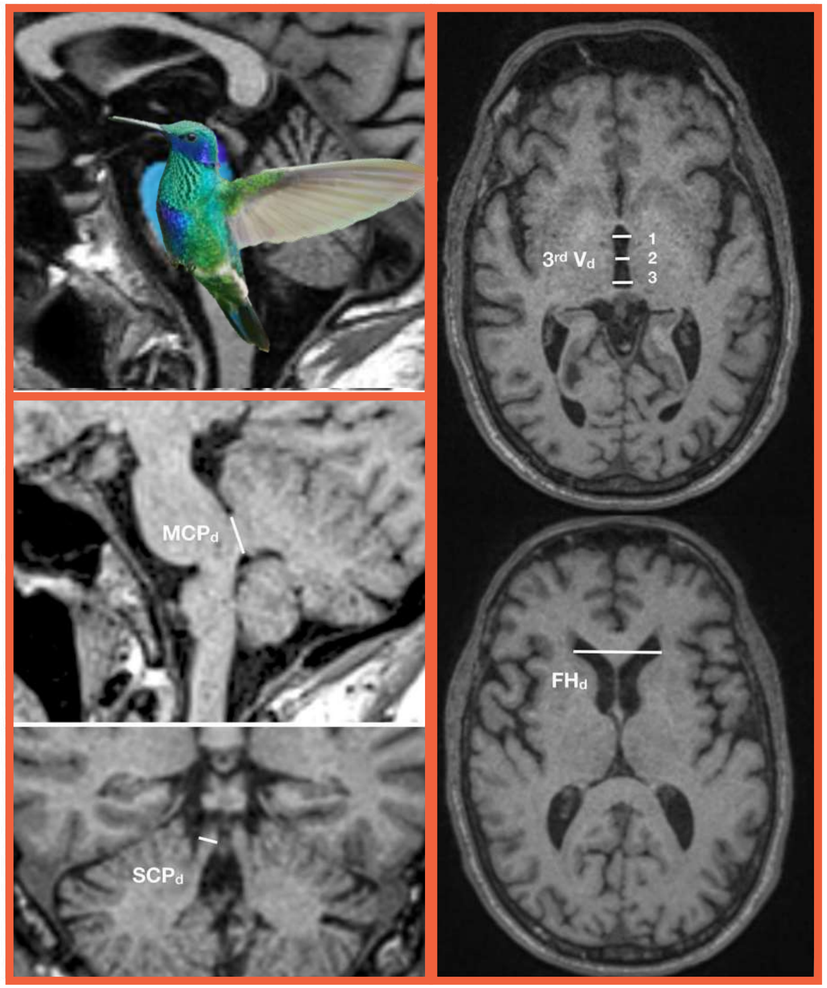
Most reliable indexes: M/P ratio, MRPI/MRPI 2.0

MRPI	MRPI 2.0
$MRPI = \frac{P\ x\ MCP}{M\ x\ SCP}$	$MRPI\ x\ \frac{3rdV}{FH}$

M: midbrain area
P: pons area
MCP: middle cerebellar peduncle width
SCP: superior cerebellar peduncle width
3rdV: 3rd ventricle width
FH: frontal horns of lateral ventricles width

Quattrone et al., (2018, 2022)

Magnetic Resonance Parkinsonism Index 2.0



Shoeibi et al., (2019)

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Study Motivation and Objective

Limitations:

- Manual tracing is time-consuming
- Impacted by clinician's expertise
- Subject to inter-observer variability

Increased interest in automated neuroimaging metrics for fast and reproducible analysis

The current study aimed:

To compare the accuracy of automated imaging markers quantified by QyScore®, an FDA-approved and CE-marked medical device used in clinical routine, with manual assessment performed by an expert trained neuroradiologist, in distinguishing Parkinson Disease from Progressive Supranuclear Palsy patients.

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Methods: Cohort

Forty-three participants were recruited through the Neurology Clinic of the University Hospital of Verona

- All underwent 3D-T1w MRI and full neuroradiological evaluation
- Repeat neuroradiological assessments were performed to investigate intra and inter-rater variability
  - (method based on Nigro at al. Eur Radiol (2017) 27:2665–2675)

	Number	Sex (M/F)	Age	Disease Duration (yrs)
Healthy Control (HC)	23	12/11	70.2 (7.1)	NA
PD	18	11/7	64.6 (6.9)	9.5 (1.2)
PSP	7	4/3	71.8 (5.8)	13.9 (4.0)

Neuroradiological evaluation		
M area	3rdV width	GcerbA
P area	FH width	BGA
M/P ratio	MRPI	GCA
MCP width	MRPI 2.0	MTA
SCP width		

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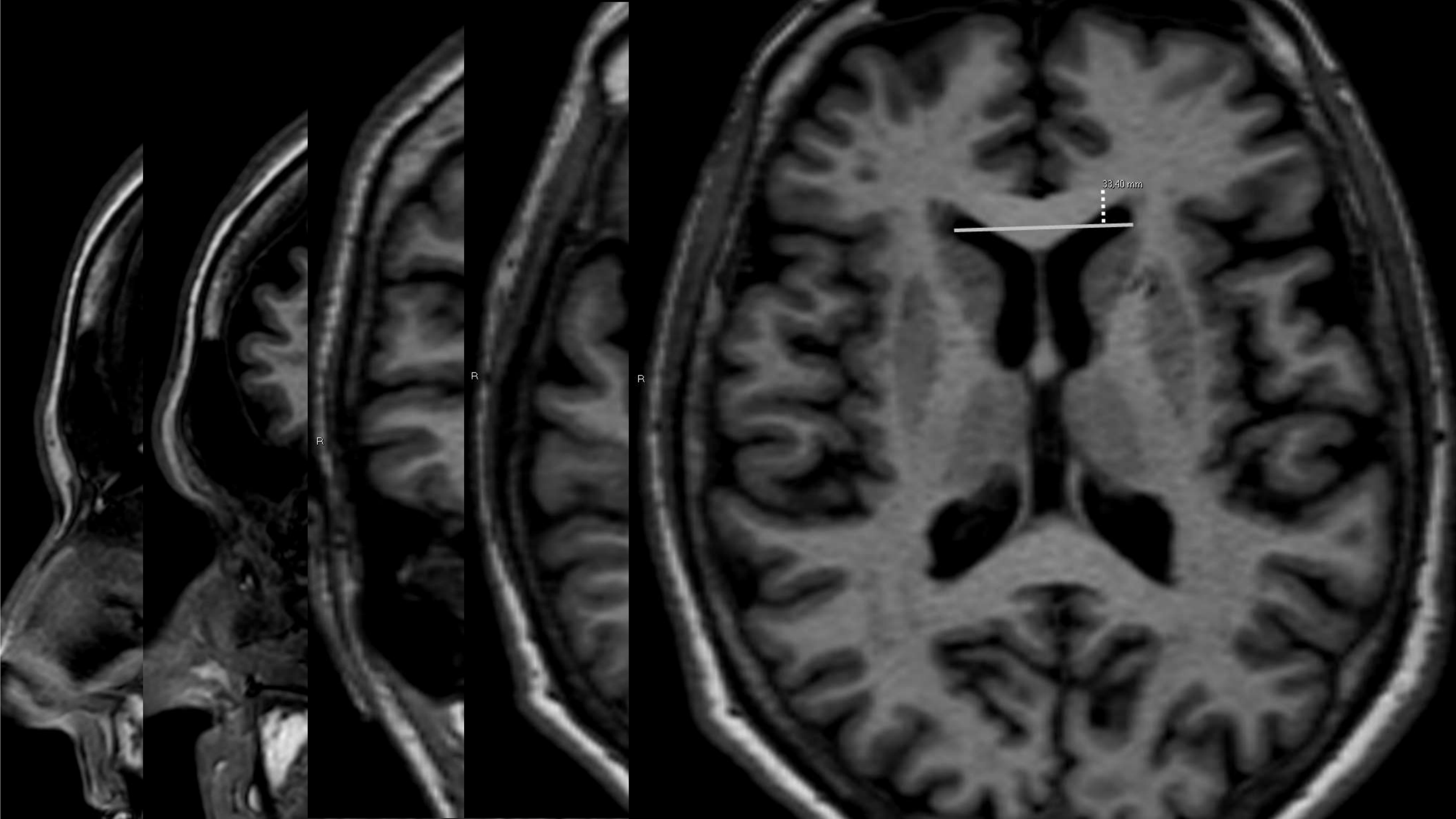
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33,40 mm

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Methods: Automated Image Analysis

3D-T1w image analysed using the QyScore® algorithm

Pre-processing (N3 intensity normalization)

⬇

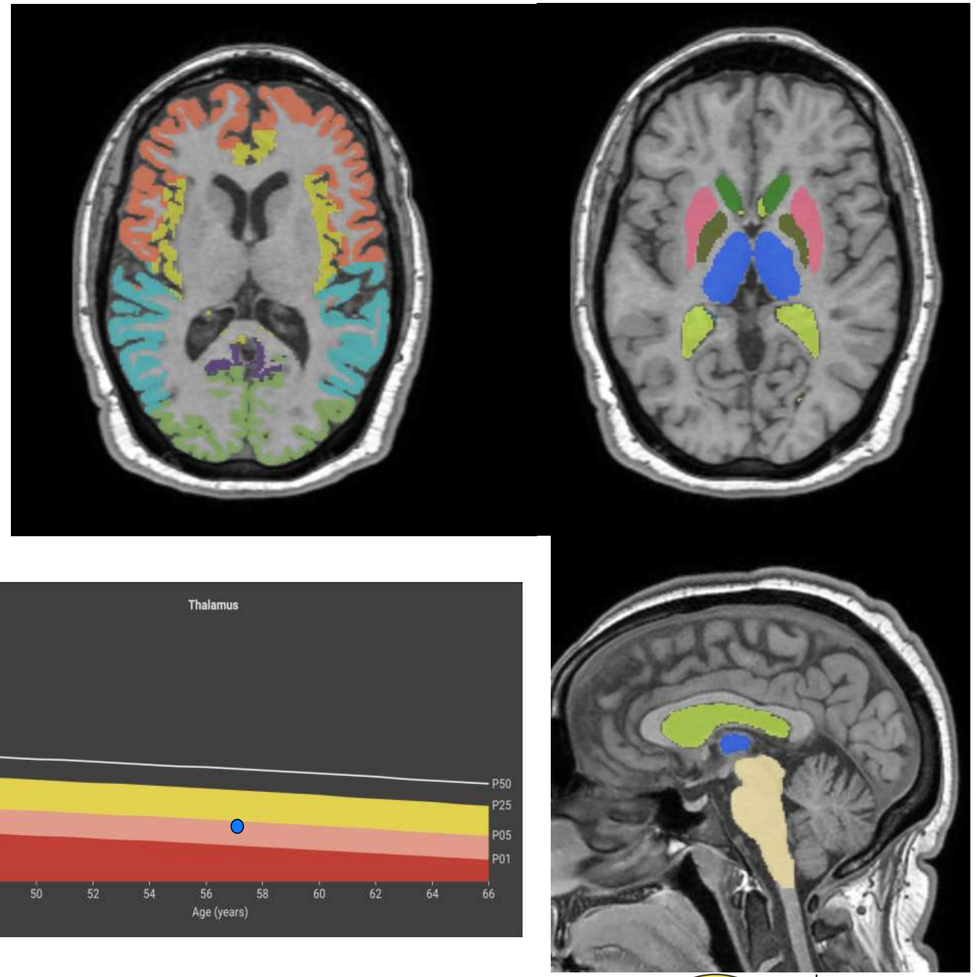
Tissue class classification
GM, WM, CSF, Cortical Lobar GM volumes

⬇

The basal ganglia, thalamus, brainstem, ventricles and cerebellum segmented using a 3D convolutional neural network (UNet) approach

⬇

Volumes derived from these segmentations were then compared with age and sex-matched healthy controls, to produce population-normed z-scores



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Methods: Automated MRPI

3D-T1 images registered into MNI space

⬇

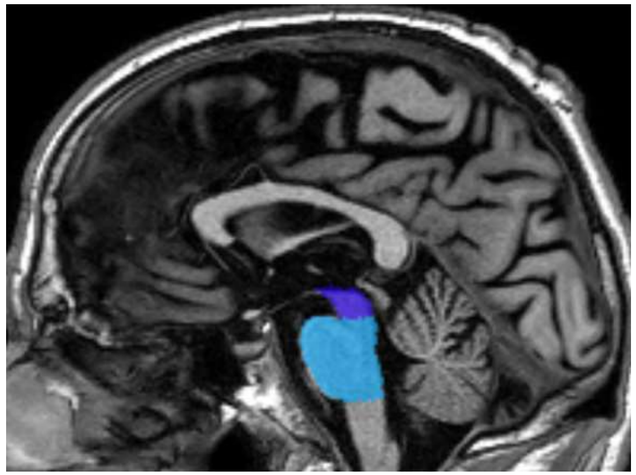
QyScore brainstem segmentation automatically subdivided into **pons** and **midbrain** based on the width and position in the mid-sagittal plane

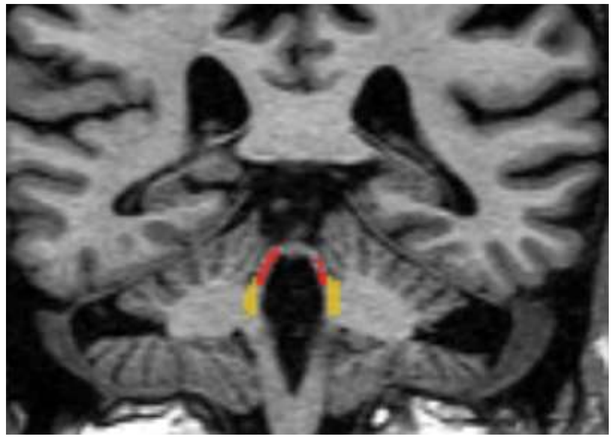
⬇

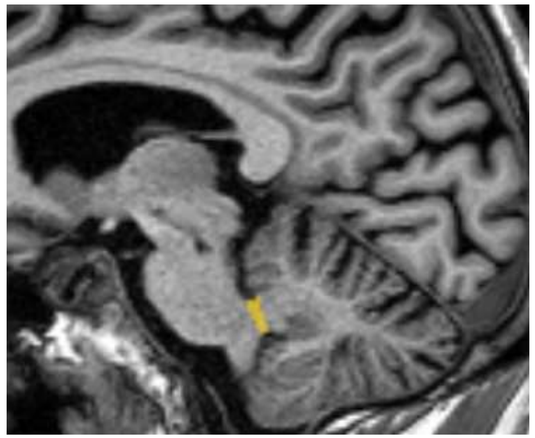
Inhouse manual atlas of the full 3D volumetric segmentation of the **SCP** and **MCP** registered onto the patient MNI image

⬇

Diameter computed from the 3D structure modelling multiple measurement inputs and accounting for possible registration errors







Methods: Statistical Analysis

Kruskal-Wallis H Test and **Mann Whitney U Test** (with false discovery rate (FDR) correction for multiple comparisons) were used to determine differences in neuroimaging markers and indices across the groups.

Overall diagnostic accuracy was investigated using **Area Under the receiver operator Curve (AUC)** analysis for each marker.

- Randomised permutation testing (each 10,000 permutations) was used to compare the AUCs

Inter and intra-rater variability was calculated using an **Interclass Correlation Coefficient (ICC)** analysis

- Two-way mixed, absolute agreement, using single measures

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Results: Interclass Correlation Coefficient

ICC analysis highlighted generally good but variable reliability of expert manual measurements across the markers

- SCP diameter and hence derived MRPI particularly affected

Comparison	M area	P area	M/P	MCP diameter	SCP diameter	MRPI	3rdV	FH	MRPI2.0
Intra-rater	0.83	0.83	0.68	0.67	0.38	0.57	0.94	0.95	0.81
Inter-rater	0.75	0.86	0.63	0.53	0.14	0.48	0.91	0.66	0.56

SCP may be disproportionately impacted because:

- Is the smallest measurement taken (3 – 4 mm)
- Taken from a subjectively chosen single coronal slice

PACS upgrade between the initial and repeat reviews

- Kodak to a Fuji PACS system, which is less flexible in the MPR (Multiplanar Reconstruction/ Reformation) of the volumetric acquisition

Highlighting the value of an automated solution

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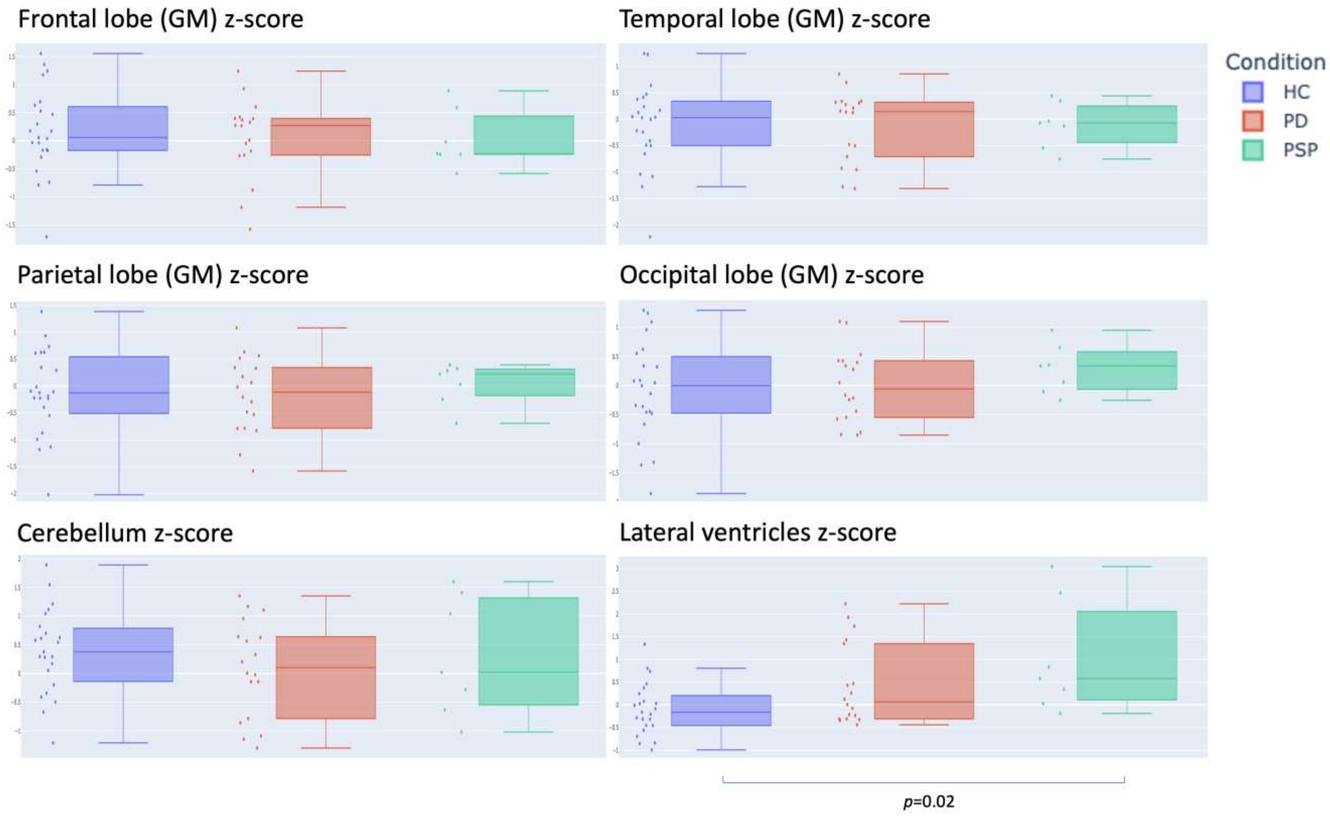
Results: Global QyScore® markers

Kruskal Wallis H test revealed no significant differences in any of the cortical grey matter (whole-brain or lobar) or cerebellum volumes

- Lateral ventricles were larger in PSP vs HC

QyScore Marker (z-score)	H	FDR corrected
Whole Brain	1.86	*p*=0.55
Cortical Grey Matter (GM)	0.08	*p*=0.98
Cerebellum	1.08	*p*=0.72
Cerebellum Grey Matter	5.06	*p*=0.14
Frontal Lobe (GM)	0.59	*p*=0.85
Insular Lobe (GM)	0.95	*p*=0.74
Limbic Lobe (GM)	0.22	*p*=0.96
Occipital Lobe (GM)	1.58	*p*=0.60
Parietal Lobe (GM)	0.38	*p*=0.92
Temporal Lobe (GM)	0.05	*p*=0.98
Lateral Ventricles	**8.05**	***p*=0.04**

Median and interquartile range of z-scores for the QyScore markers



HC did not significantly differ from PD in any of the key subcortical markers or indices *p*>0.05
Mann Whitney U Test applied to investigate the comparison of interest in these markers: PD vs PSP

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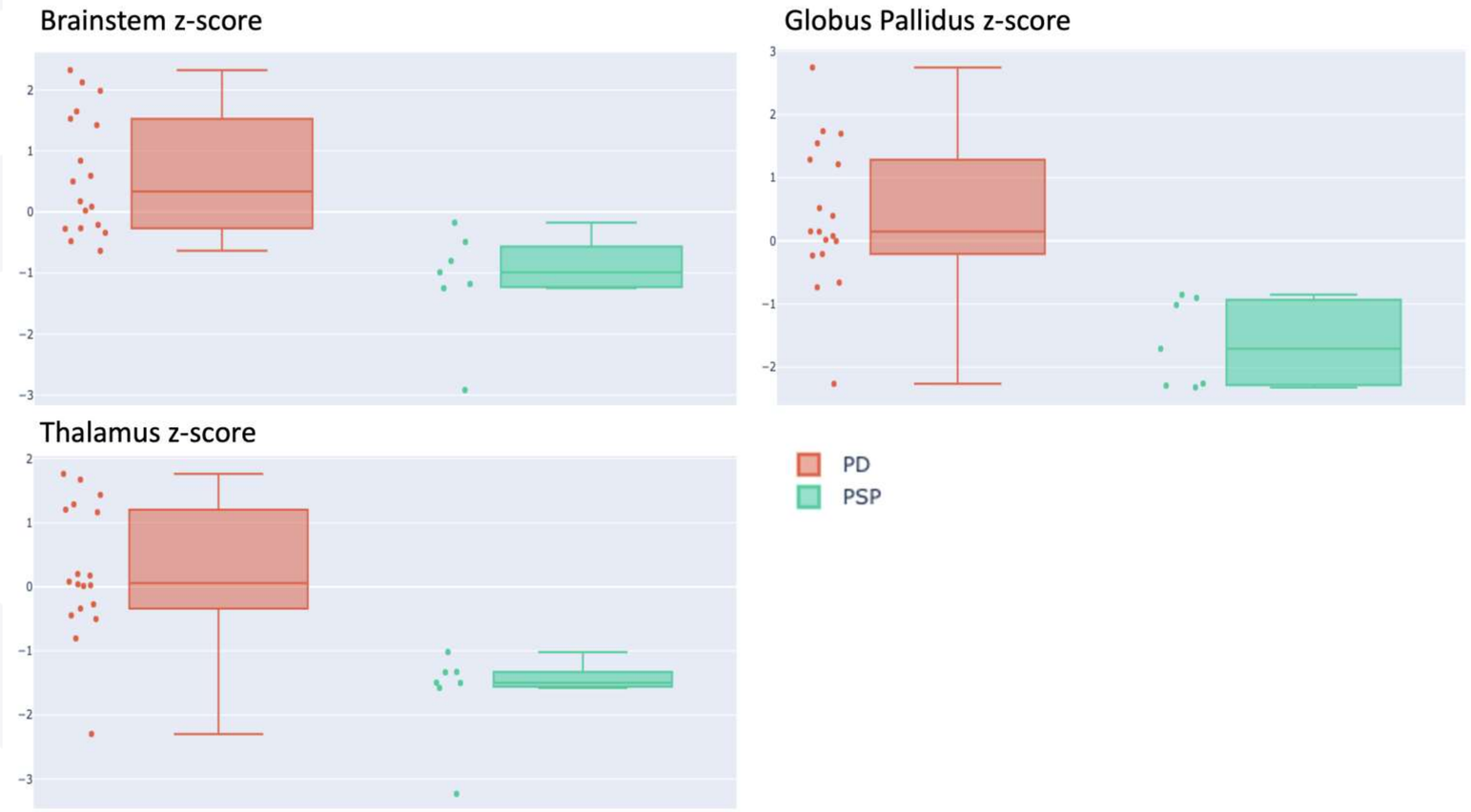
Results: QyScore® structural volumes



Metric	PD	PSP	U	FDR corrected
Brainstem z-score	0.6 (0.9)	-1.1 (0.8)	7.0	***p*=0.006**
Globus Pallidus z-score	0.4 (1.1)	-1.6 (0.7)	5.0	***p*=0.005**
Thalamus z-score	0.2 (1.0)	-1.1 (0.8)	6.0	***p*=0.005**

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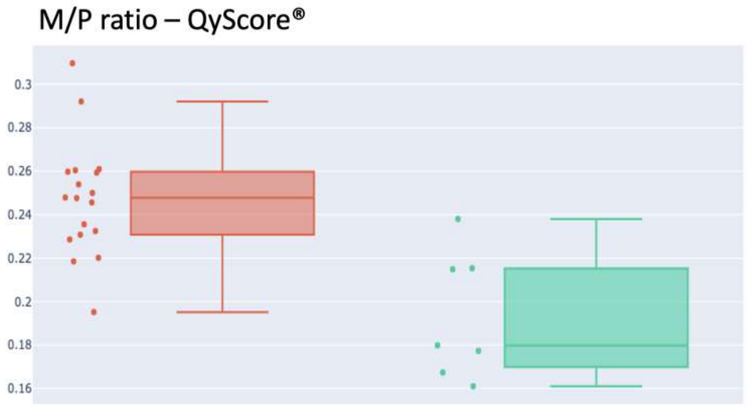
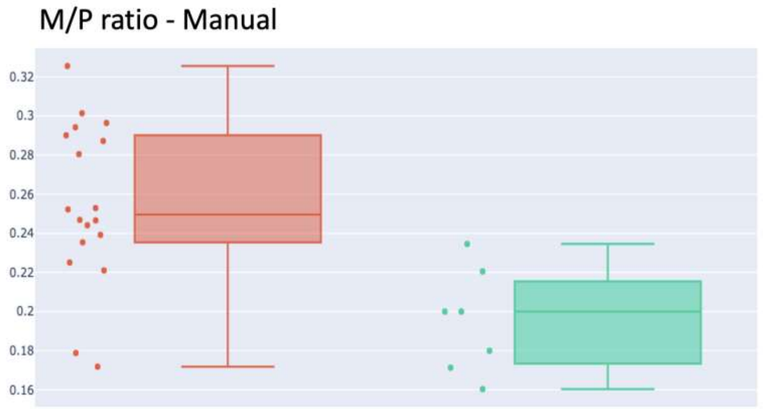
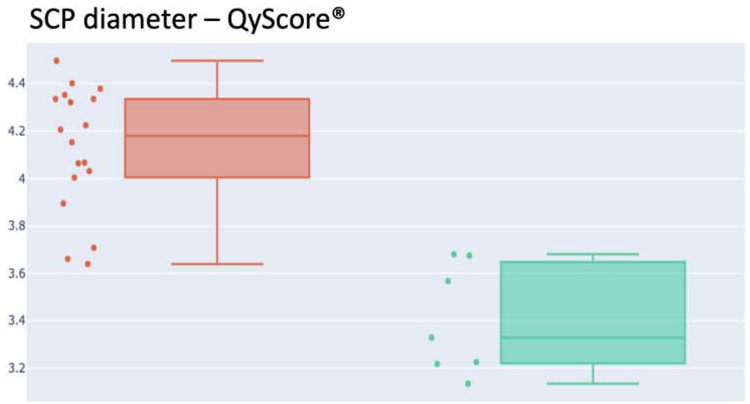
Results: M/P ratios and SCP diameter







PD
PSP

Metric	PD	PSP	U	FDR corrected
M/P ratio QyScore	0.3 (0.1)	0.2 (0.1)	9.0	***p*=0.006**
M/P ratio Manual	0.3 (0.1)	0.2 (0.1)	12.0	***p*=0.007**
SCP diameter (mm) QyScore	4.1 (0.3)	3.4 (0.2)	4.0	***p*=0.005**

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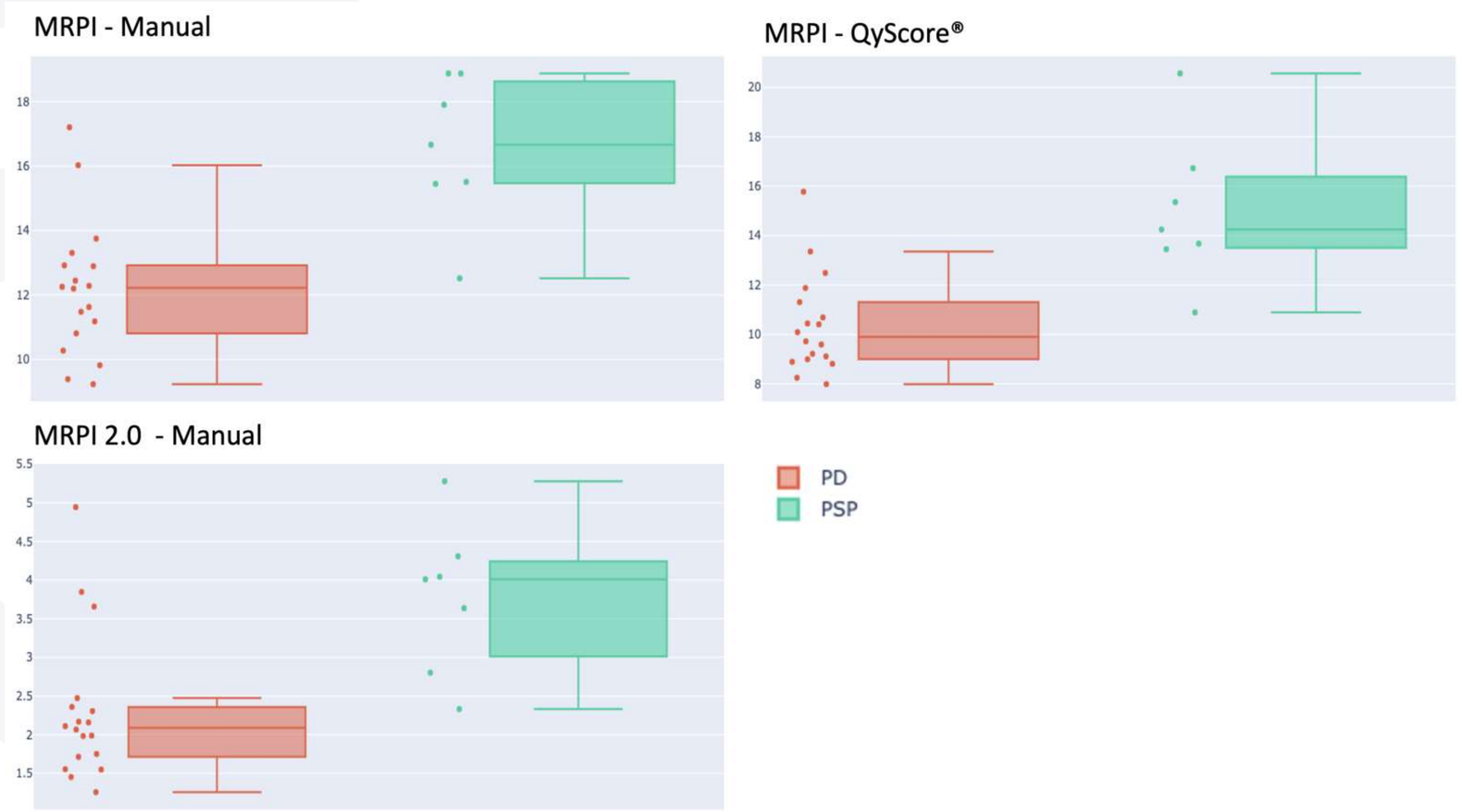
Results: MPRI and MPRI 2.0



Metric	PD	PSP	U	FDR corrected
MRPI manual	12.2 (2.1)	16.5 (2.3)	11.0	***p*=0.006**
MRPI 2.0 manual	2.3 (0.9)	3.8 (1.0)	14.0	***p*=0.005**
MRPI QyScore	10.4 (2.0)	15.0 (3.0)	9.0	***p*=0.005**

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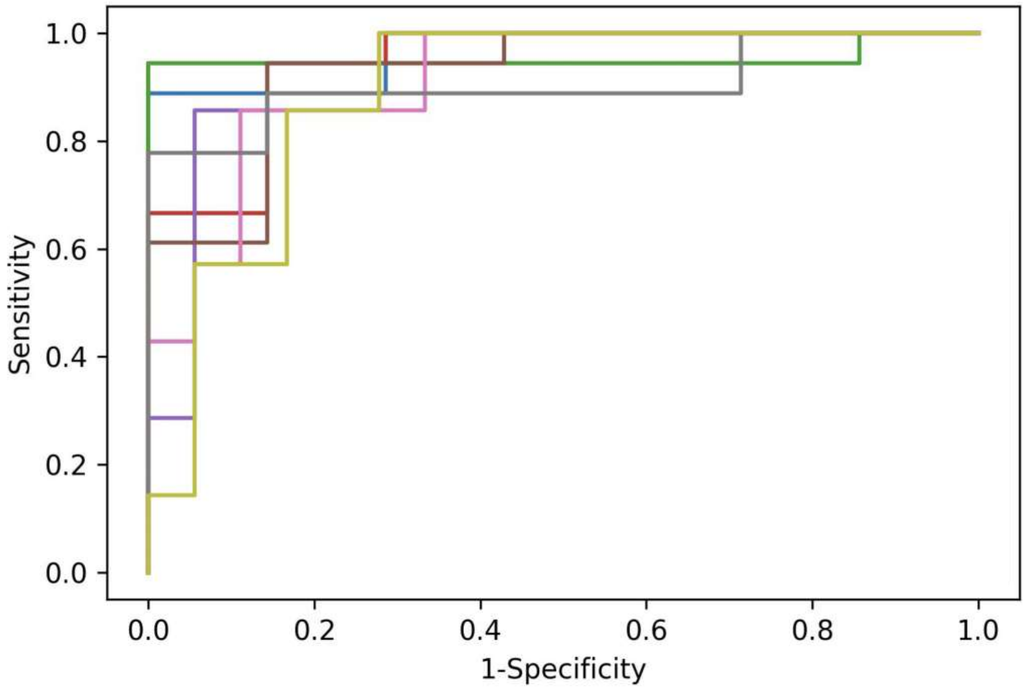
Results: Area Under the receiver operator Curve



- SCP diameter – QyScore **(AUC=0.968)**
- Globus Pallidus z-score – QyScore **(AUC=0.960)**
- Thalamus z-score – QyScore **(AUC=0.952)**
- Brainstem z-score – QyScore **(AUC=0.944)**
- MRPI – QyScore **(AUC=0.929)**
- M/P ratio – QyScore **(AUC=0.928)**
- MRPI – Manual **(AUC=0.913)**
- M/P ratio – Manual **(AUC=0.905)**
- MRPI 2.0 – Manual **(AUC=0.889)**

SCP diameter and MRPI 2.0: ***p* = 0.36**

Figure 1: Area under the curve (AUC) for the best QyScore® and expert manual visual indices in discriminating PD and PSP patients

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Limitations and Next Steps

Caveats

- Small sample size for PSP cohort (n=7)
- Late stage of disease

Next Steps

- Final development and testing of the QyScore MRPI 2.0
- Application on a larger and earlier cohort
- Additional ML classification algorithms using a fuller set of image features

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Conclusions

- Automated neuroimaging markers and MRPI index quantified using QyScore® performed as well as expert neuroradiologists in distinguishing PD and PSP patients.
- Employing automated neuroimaging solutions avoids the time-consuming nature and operator-dependant variability of manual reads and is reliable irrespective of the PACS system employed in any given clinical centre.
- AI and machine learning solutions show promise in providing precise and reproducible measures within the clinical setting

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THANK YOU FOR YOUR ATTENTION!

FOR MORE INFORMATION:

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