

VENOUS ABNORMALITIES AND WHITE MATTER HYPERINTENSITIES IN IDIOPATHIC PARKINSON'S DISEASE PATIENTS

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Acknowledgements

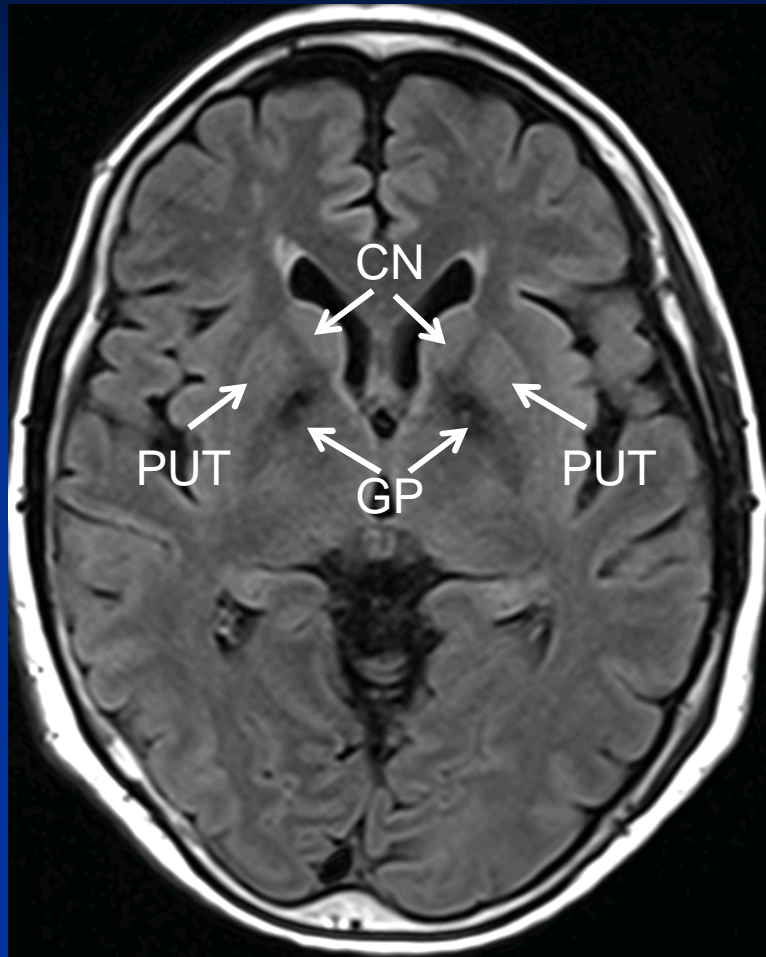
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Introduction

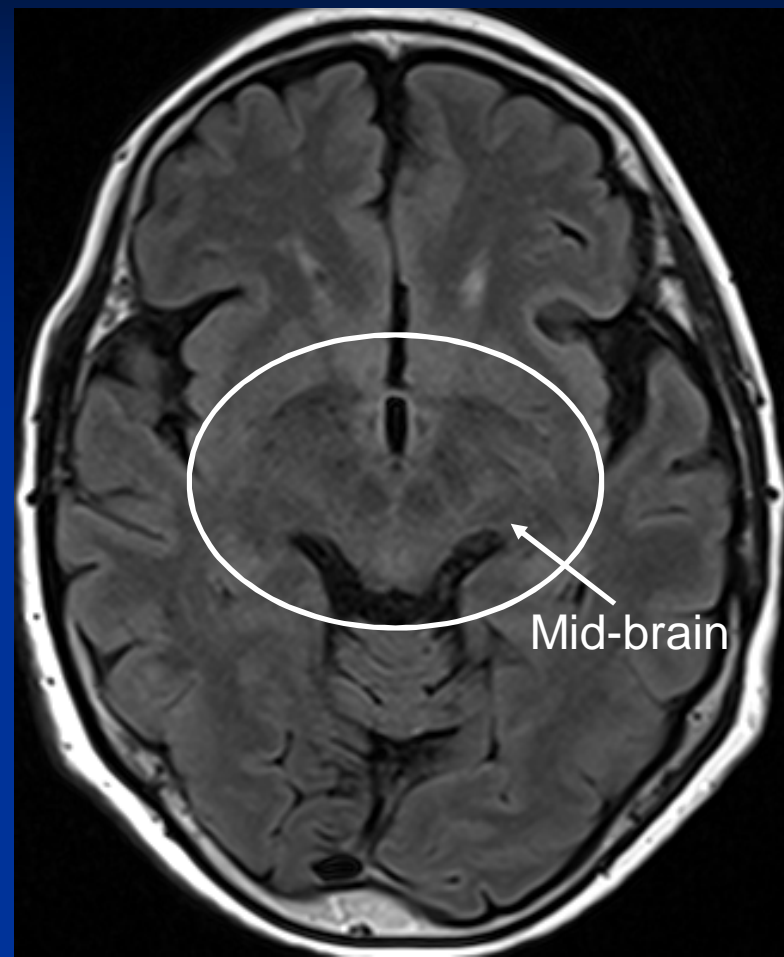
- Idiopathic Parkinson's disease (IPD) is the second most common neurodegenerative disease after Alzheimer's disease.
- It is estimated that 5 to 10 million people in the world are affected by IPD.
- The etiology of IPD remains unknown.
- Several studies have reported an increased presence of WMHs in IPD patients.
- There is a higher prevalence of radiological and clinical cerebrovascular disease in patients with IPD compared to controls.

Iron build up in the basal ganglia and midbrain



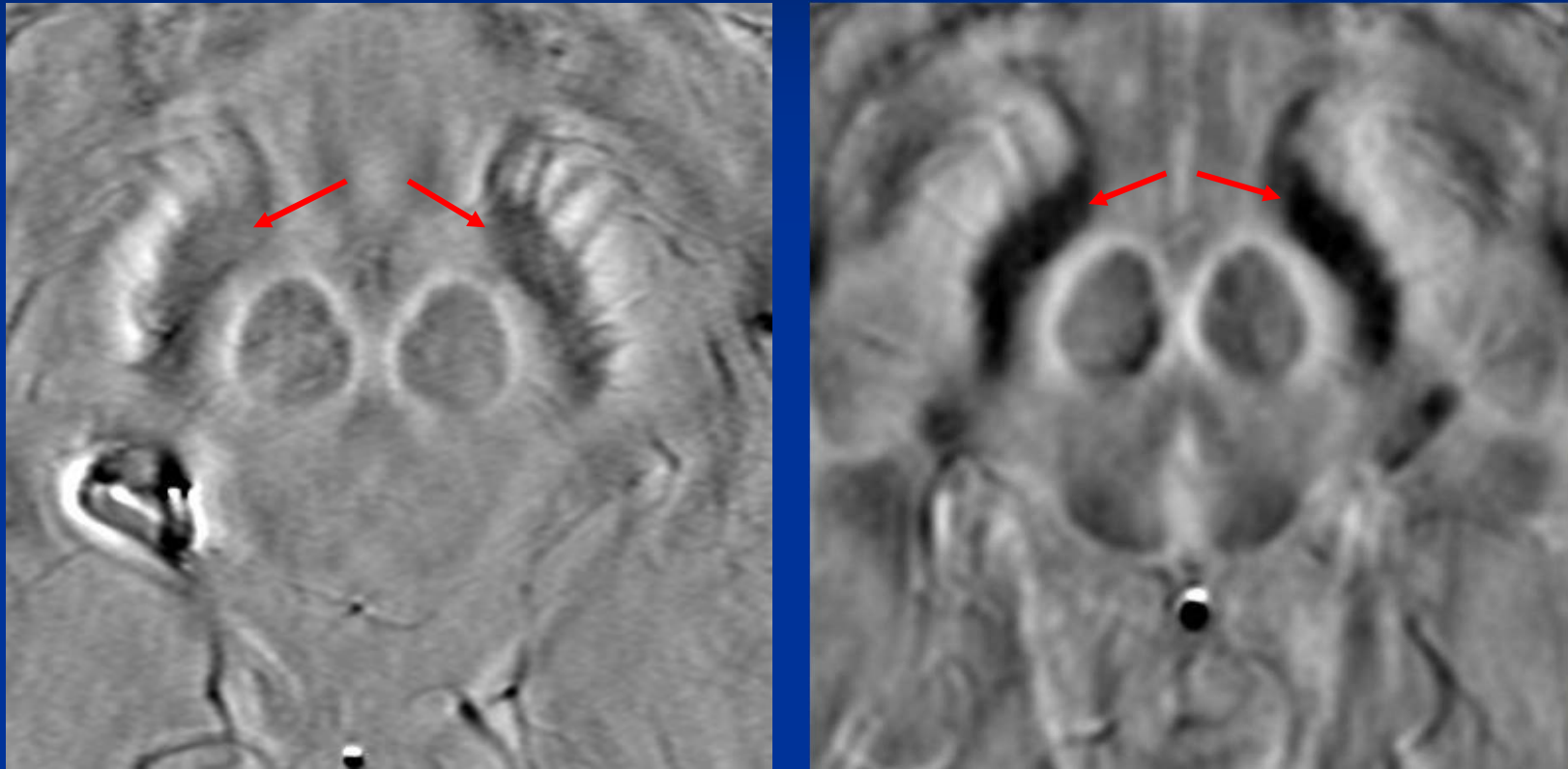
T2-FLAIR images of a IPD patient

CN: Caudate Nucleus
GP: Globus Pallidus
PUT: Putamen



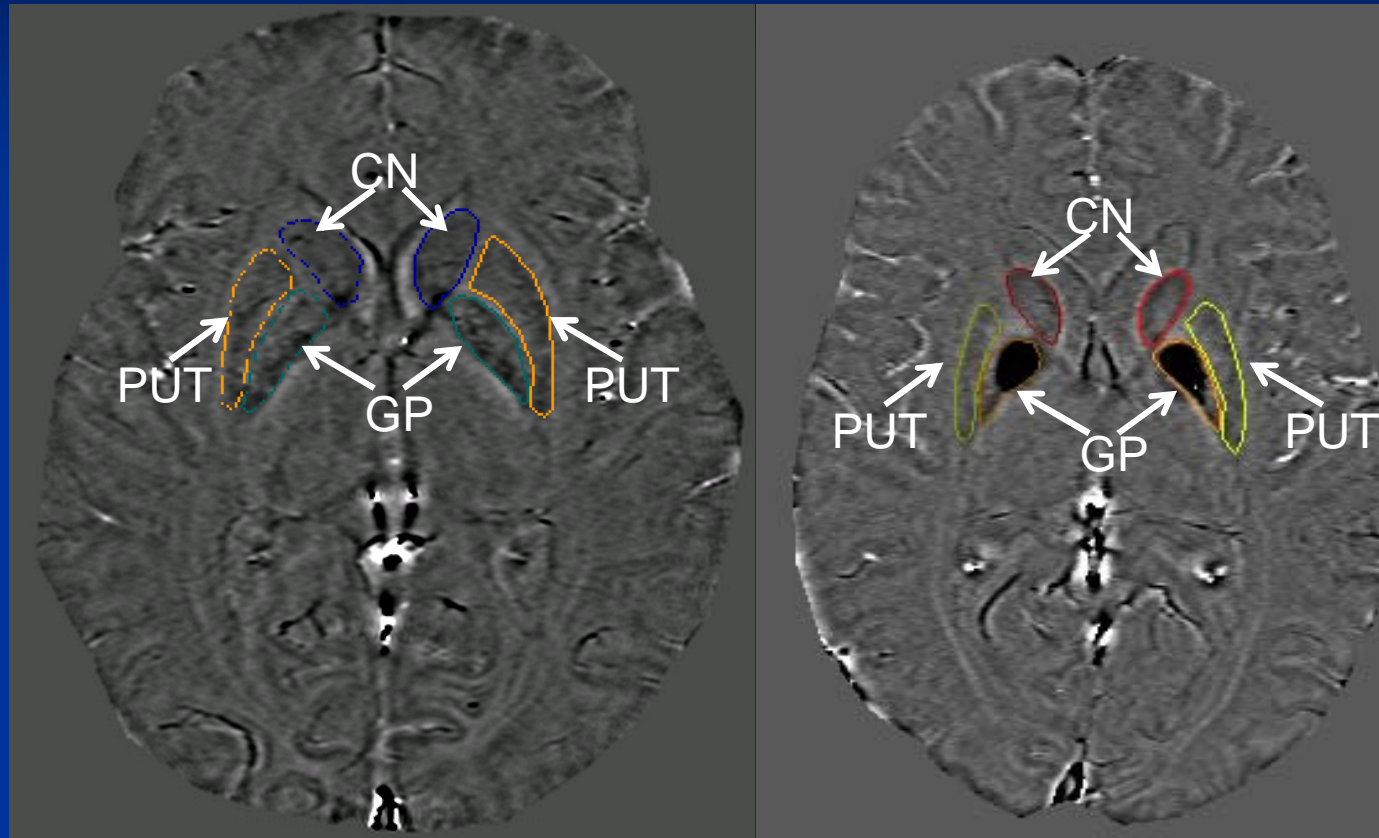
T2-FLAIR images of a IPD patient

Iron buildup in the midbrain



Age matched normal control (left) compared to an MS patient (right). Note the clear outline of the substantia nigra with dramatically increased iron content.

Iron build up in the globus pallidus for a patient with Parkinson's



SWI phase images filtered with a 96x96 high pass filter.

Age and gender matched normal control (left) and IPD patient (right). This is the same patient as shown in the FLAIR image in the previous slide. Note that the very dark signal represents high iron content.

Motivation for studying the extracranial vasculature of IPD patients

- In MS patients, iron deposition occurs in both the basal ganglia and midbrain similar to what is seen in IPD patients (Habib *et al.* 2012, AJNR) and MS patients also show a proclivity for extracranial abnormal venous vasculature (Feng *et al.* 2012, Neurological Research).
- Therefore, we were stimulated to determine if venous abnormalities were also present in the IPD population.
- The goal of this work is to address the question: “Is there a venous vascular component in IPD?”

VP = vascular Parkinson's

Multiple
Sclerosis

Both MS
and VVA

Venous vascular
abnormalities (VVA)

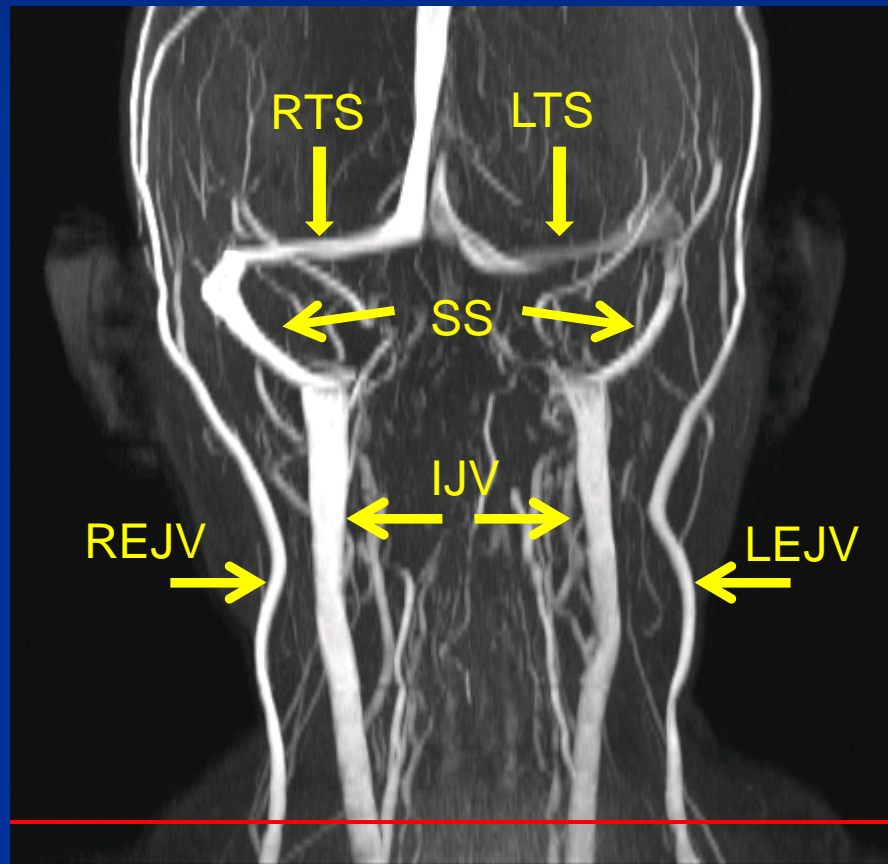
Diseases such as:
MS, intracranial
hypertension,
migraine and

**IPD +
VVA?**

VP

IPD

Using MR venography to study the dural sinuses and extracranial veins



RTS: right transverse sinus

LTS: left transverse sinus

SS: sigmoid sinus

IJV: internal jugular vein

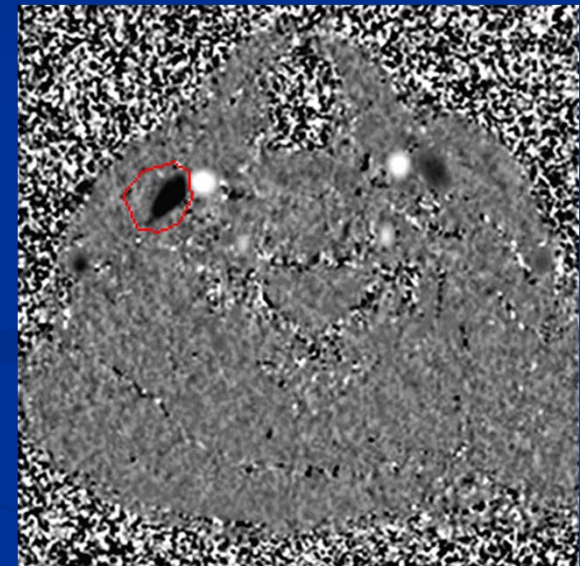
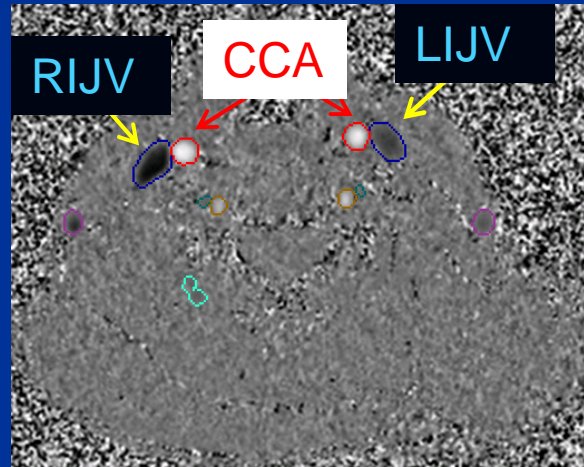
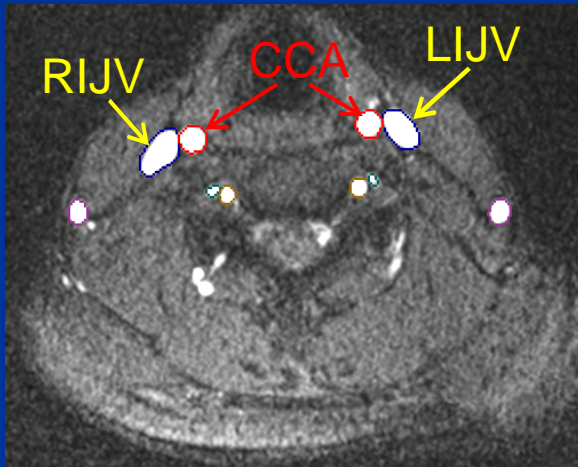
REJV: right external jugular vein

LEJV: left external jugular vein

2D time-of-flight (TOF) MRV
maximum intensity projection
(MIP) of the whole set in the
coronal view

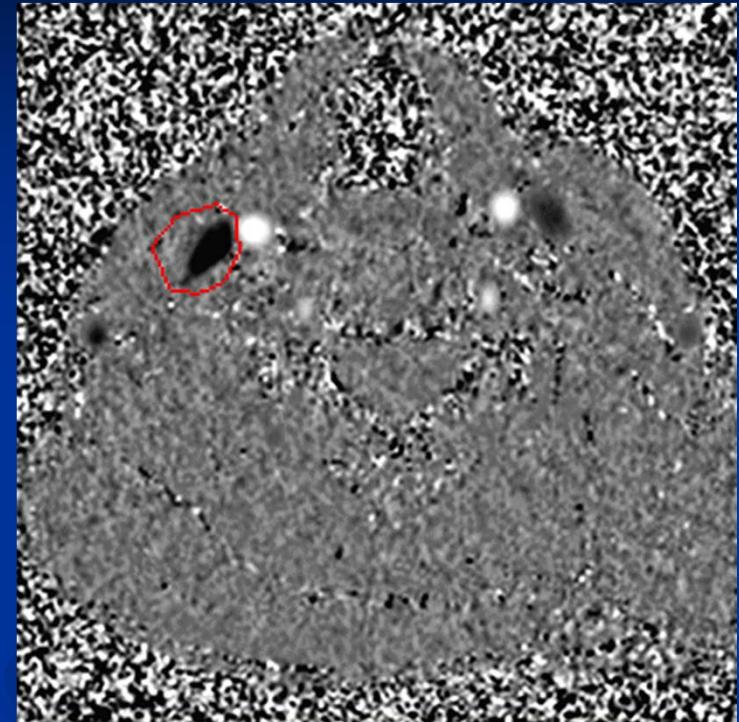
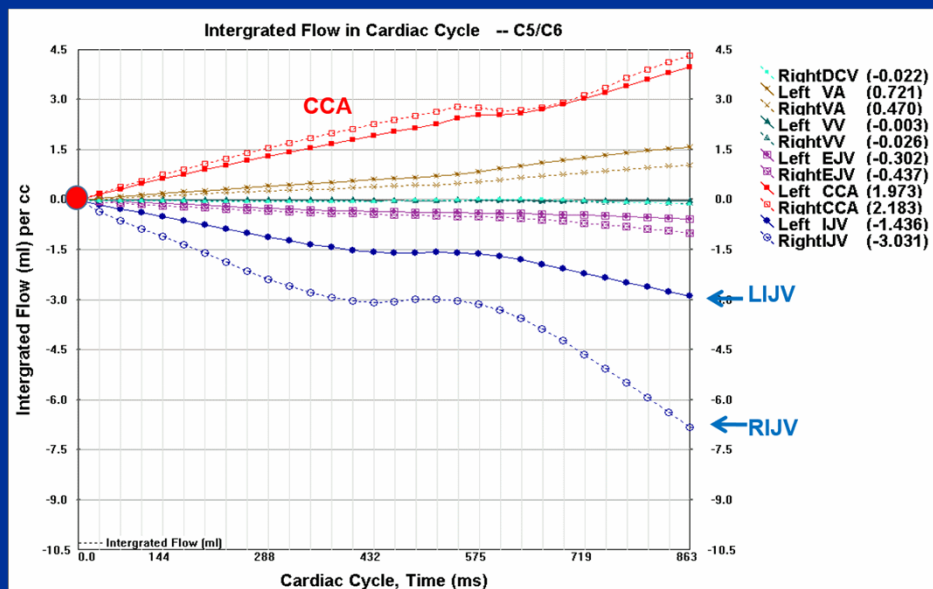
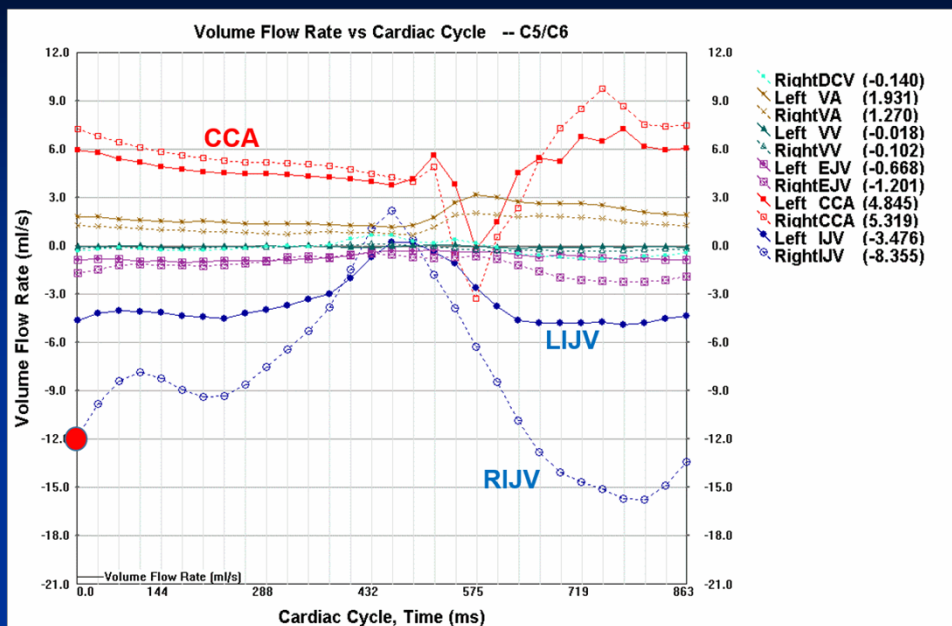
← C6/C7

Using 2D phase contrast flow quantification (PCFQ) to study the flow in each vessel.



CCA: common carotid artery
RIJV: right internal jugular vein
LIJV: left internal jugular vein

Flow quantification as a function of the cardiac cycle



Flow rate and integrated flow for the right internal jugular vein (RIJV). The red circle follows the darkening of the signal in the phase image above.

The use of MRV and flow quantification to study IPD is a novel concept.

For more details see www.ms-mri.com

Materials and Methods

- MRI sequences:
 - 2D TOF MRV of the head and neck
 - Phase Contrast Flow Quantification at C6/C7
 - T2-FLAIR
- 21 IPD patients: 62.6 ± 8.0 years old
- 10 age and gender matched normal controls: 57.6 ± 7.2 years old
- 12 of the IPD patients have Unified Parkinson Diagnostic Rating Score (UPDRS) available for analysis.

Vascular abnormalities in IPD

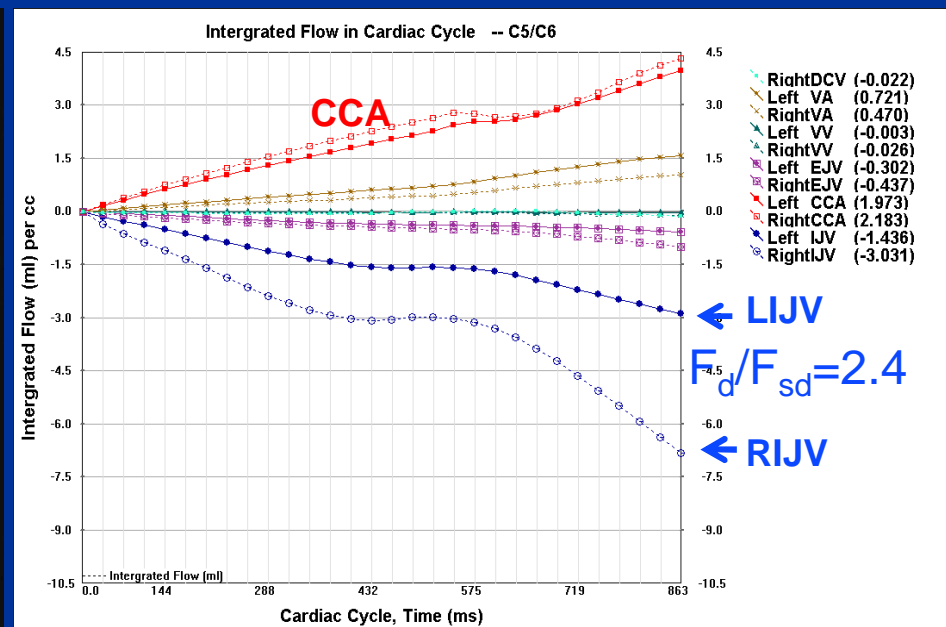
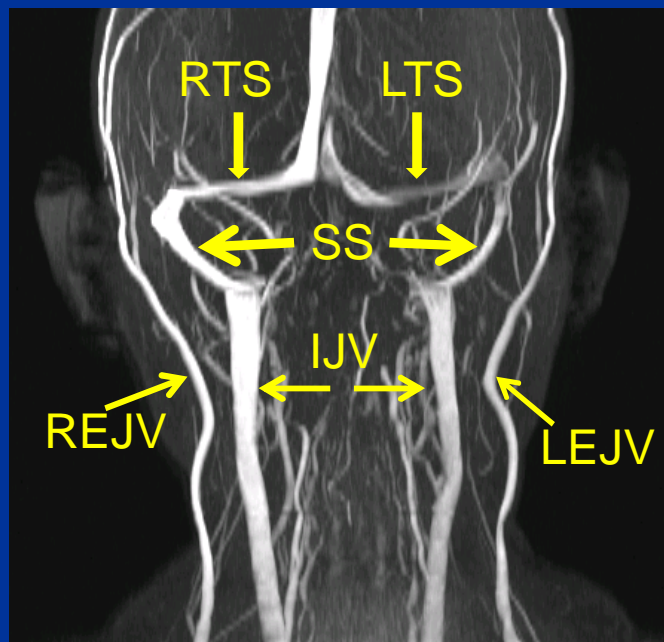
In retrospectively reviewing the 21 IPD cases and 10 volunteers we observed significant venous vascular structural and flow abnormalities. We broke these variations up into the following 4 categories:

Category	Venous Structural	Quantitative Flow in LIJV	No. IPD	No. NC
1	Lack of TS, SS and IJVs	Low flow	4	1
2	Lack of TS, stenotic LIJV	Low flow	3	0
3	Normal	low flow	8	1
4	Normal	Normal	6	8
Total			21	10

- The threshold of normalized sub-dominant IJV flow (F_{sd}/tA) was calculated from the mean minus the standard deviation of the normal population to be 14%.
- The threshold of the dominant-subdominant IJV flow ratio (F_d/F_{sd}) was determined from a receiver operating characteristic (ROC) curve to be 3.4.

Category 4: Normal venous structures and normal flow

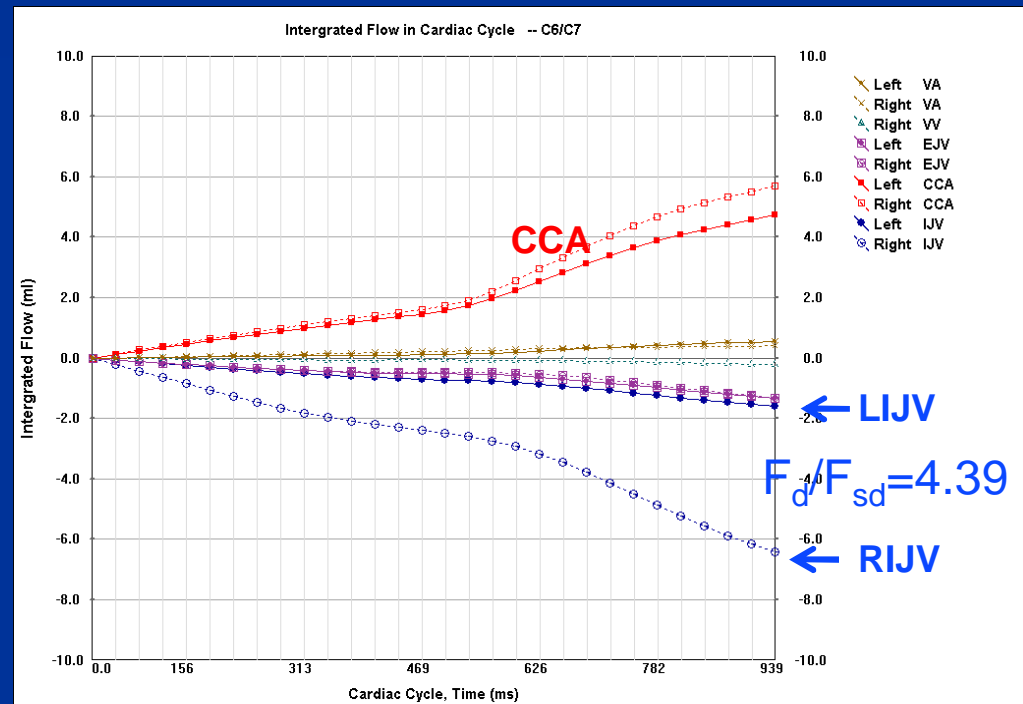
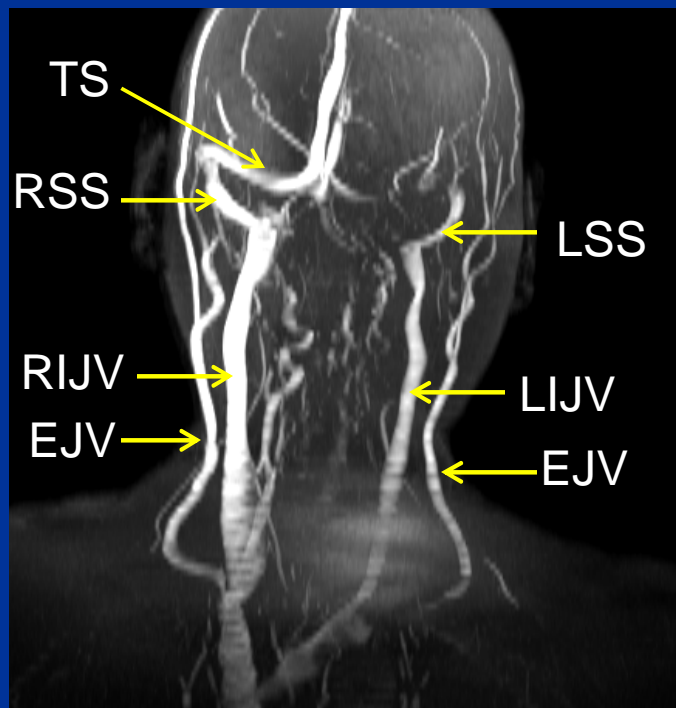
- 1) the transverse/sigmoid sinuses are visible in 2D TOF
- 2) neither IJV is stenotic
- 3) F_d/F_{sd} (IJV) at C6/C7 is less than 3.4



RTS: right transverse sinus; LTS: left transverse sinus;
SS: sigmoid sinus; IJV: internal jugular vein;
REJV: right external jugular vein; LEJV: left external jugular vein

Category 3: Normal venous structures and abnormal flow

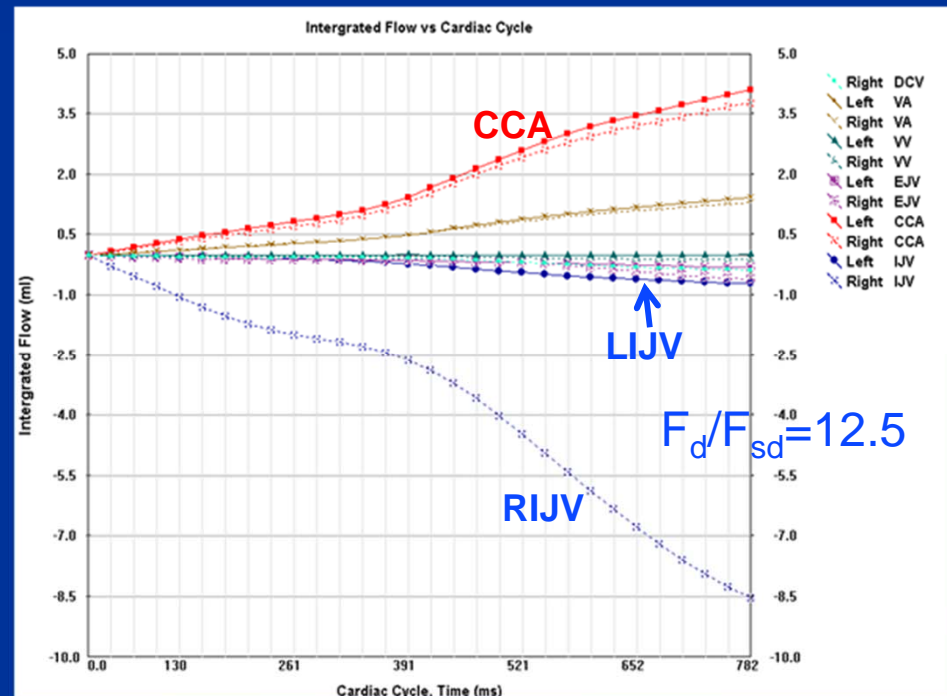
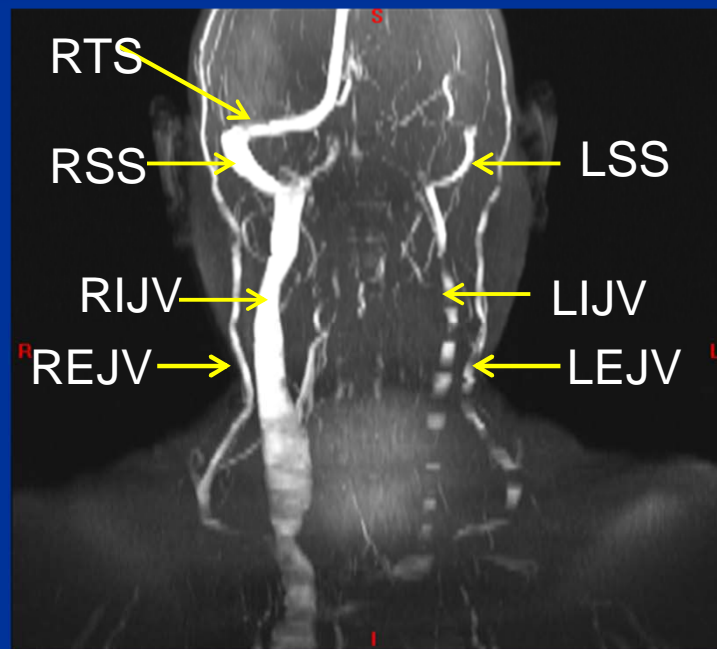
- 1) transverse sinuses may or may not show on TOF.
- 2) sigmoid sinuses are visible
- 3) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow is seen in one or both of the IJVs
- 4) $F_{sd}/tA < 14.1\%$ at C6/C7



RTS: right transverse sinus;
 RSS: right sigmoid sinus; LSS: left sigmoid sinus;
 RIJV: right internal jugular vein; LIJV: left internal jugular vein;
 REJV: right external jugular vein; LEJV: left external jugular vein

Category 2: Abnormal venous structures and abnormal flow

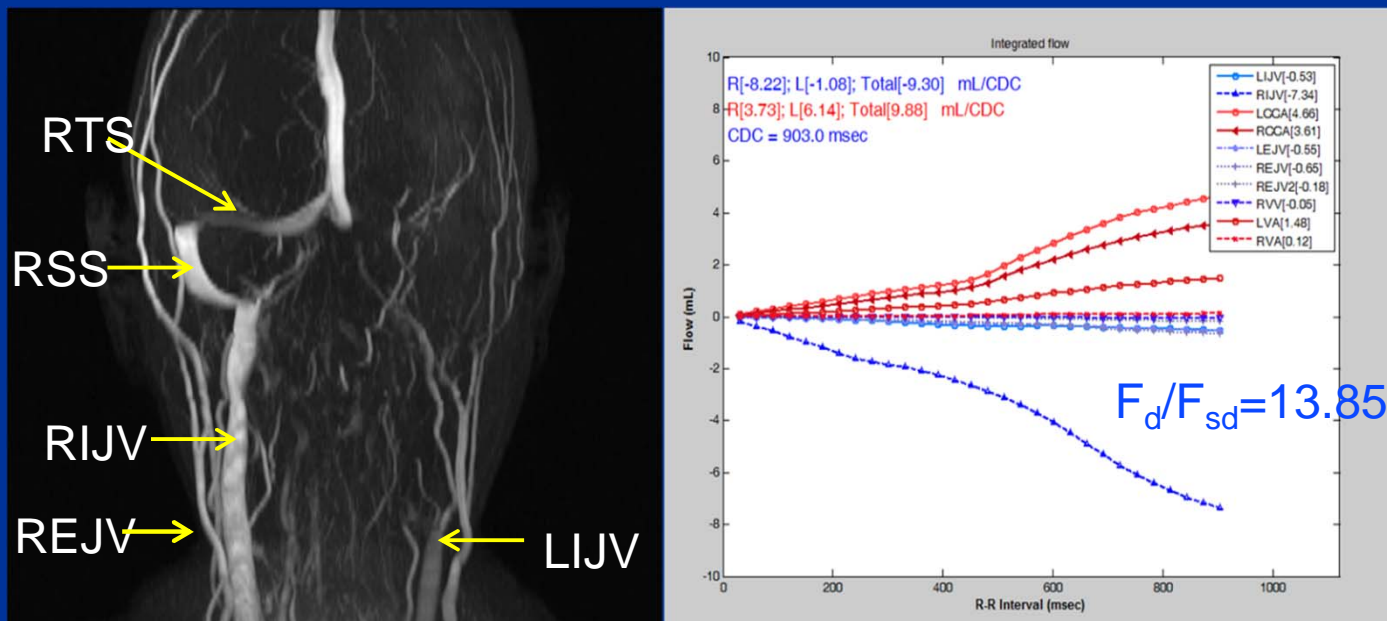
- 1) missing one or both transverse sinuses
- 2) sigmoid sinuses are visible
- 3) presence of banding and/or stenosis along the IJVs
- 4) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
- 5) $F_{sd}/tA < 14.1\%$ at C6/C7



RTS: right transverse sinus;
 RSS: right sigmoid sinus; LSS: left sigmoid sinus;
 RIJV: right internal jugular vein; LIJV: left internal jugular vein;
 REJV: right external jugular vein; LEJV: left external jugular vein

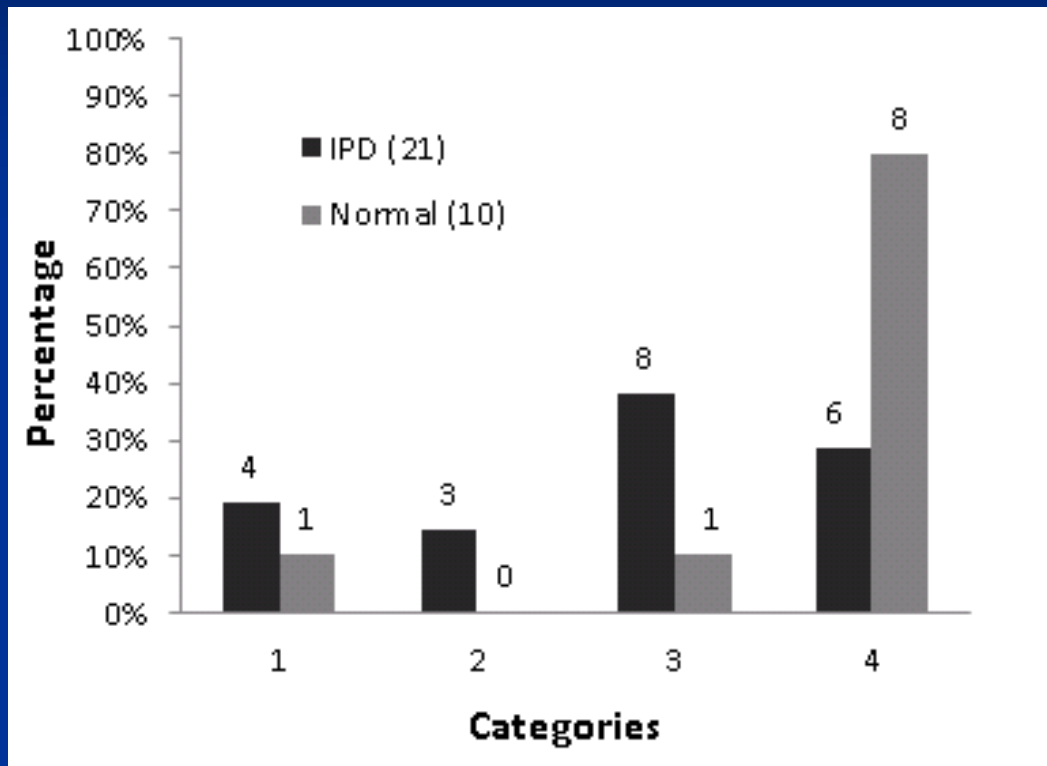
Category 1: Severely abnormal venous structures and abnormal flow

- 1) missing one or both transverse sinuses
- 2) missing one or both sigmoid sinuses
- 3) absence or local absence of IJVs on the TOF
- 4) F_d/F_{sd} at C6/C7 is greater than 3.4 or circulatory flow in one or both of the IJVs
- 5) $F_{sd}/tA < 14.1\%$ at C6/C7



RTS: right transverse sinus;
RSS: right sigmoid sinus;
RIJV: right internal jugular vein; LIJV: left internal jugular vein;
REJV: right external jugular vein

Distribution of IPD patients and normal controls according to the defined categories

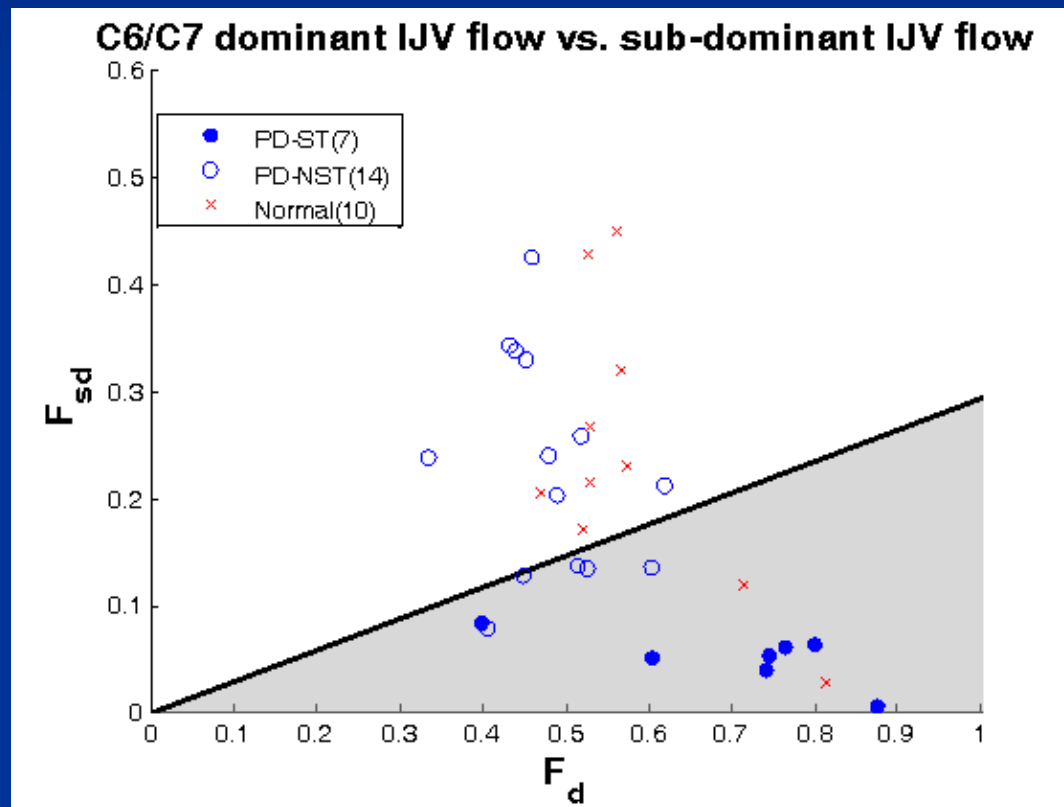


Category 1-3 IPD 15/21 71%
NC 2/10 20%

Category 4 IPD 6/21 29%
NC 8/10 80%

The distribution of the two populations had significant difference ($\chi^2=7.58$, $p=0.05$).

Scatter plot of dominant IJV flow vs. sub-dominant IJV flow at C6/C7 level in IPD patients and normal controls

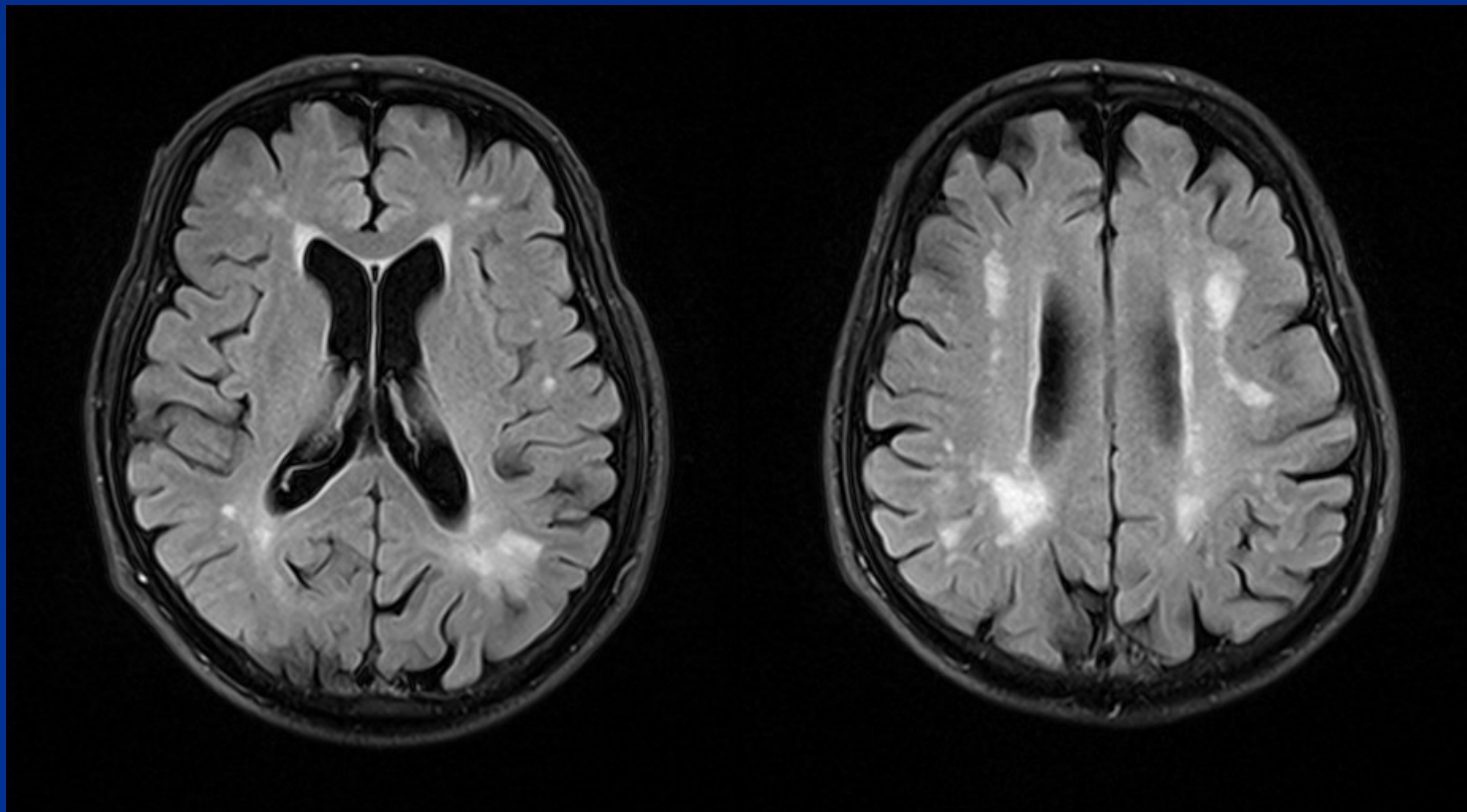


20% of NC fall
below 3.4:1

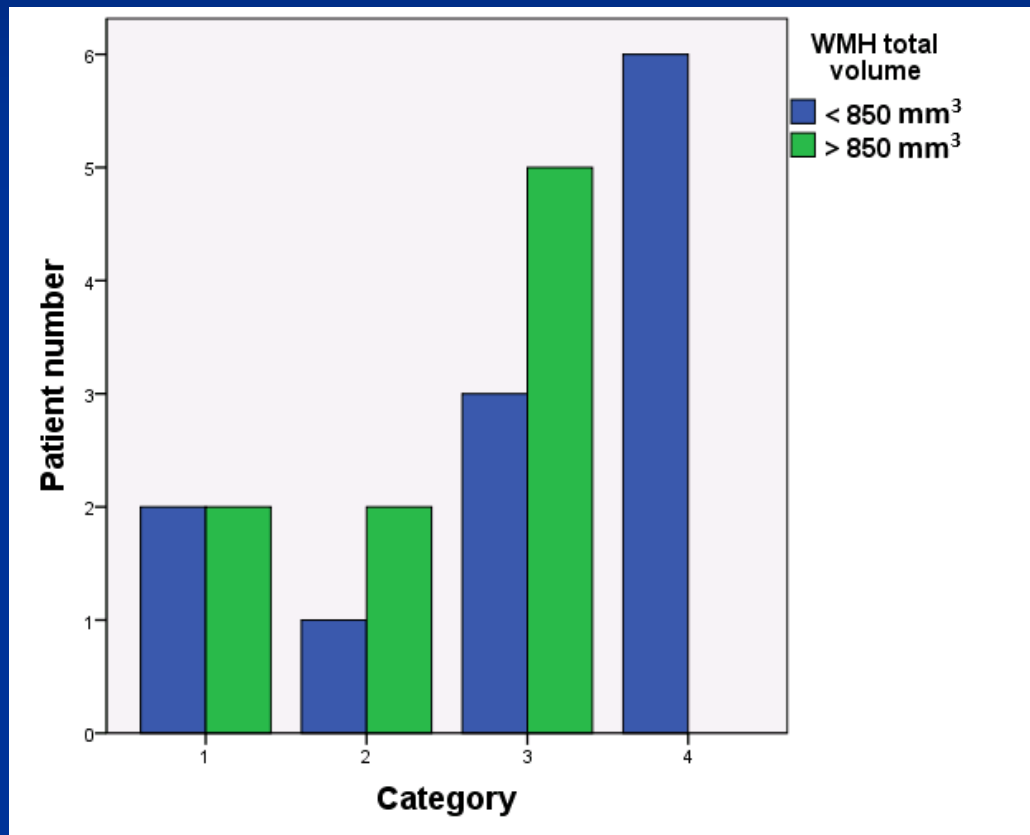
while

57% of IPD fall
below 3.4:1

Parkinson's patients show white matter hyper-intensities in FLAIR



The distribution of IPD patients with high and low WMHs volume in different categories



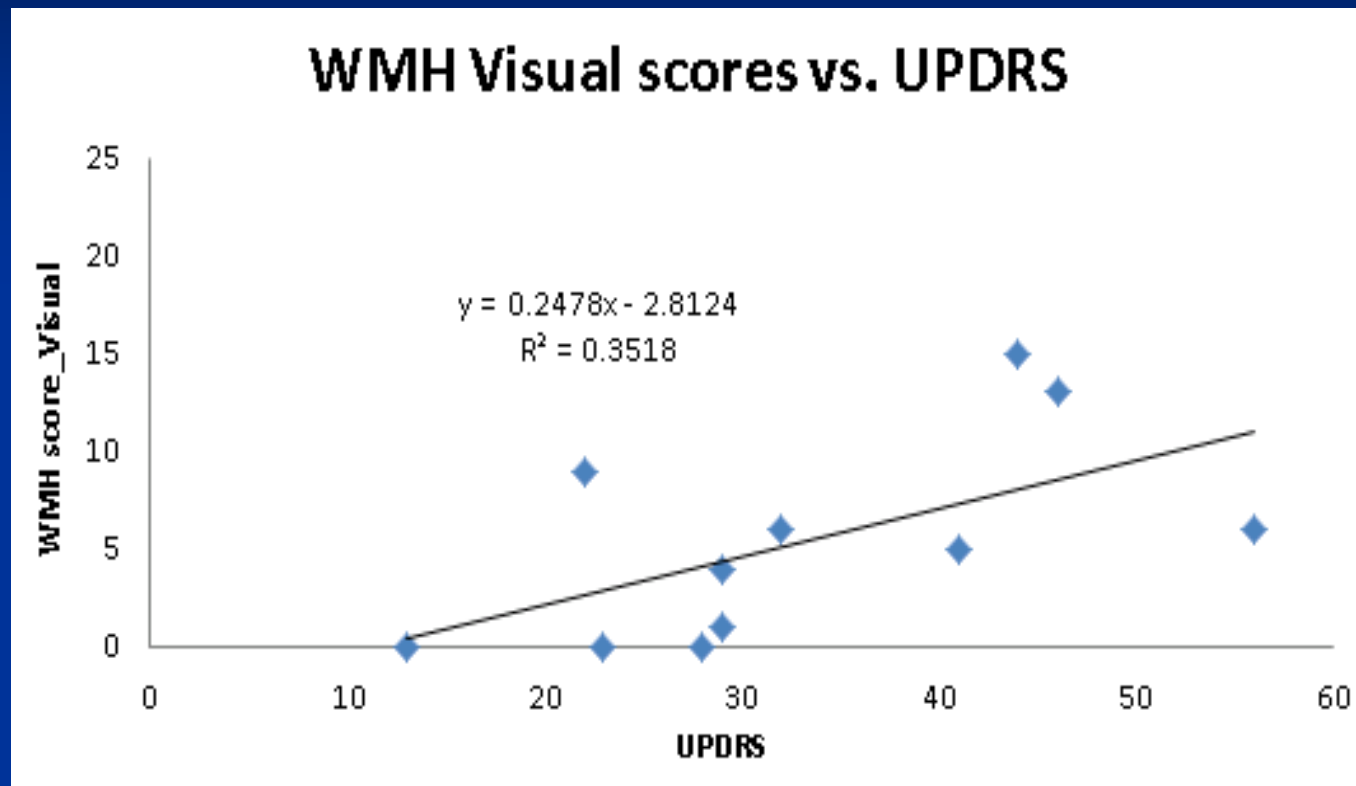
IPD patients with high WMH volume

Category 1-3 9/15 60%

Category 4 0/6 None

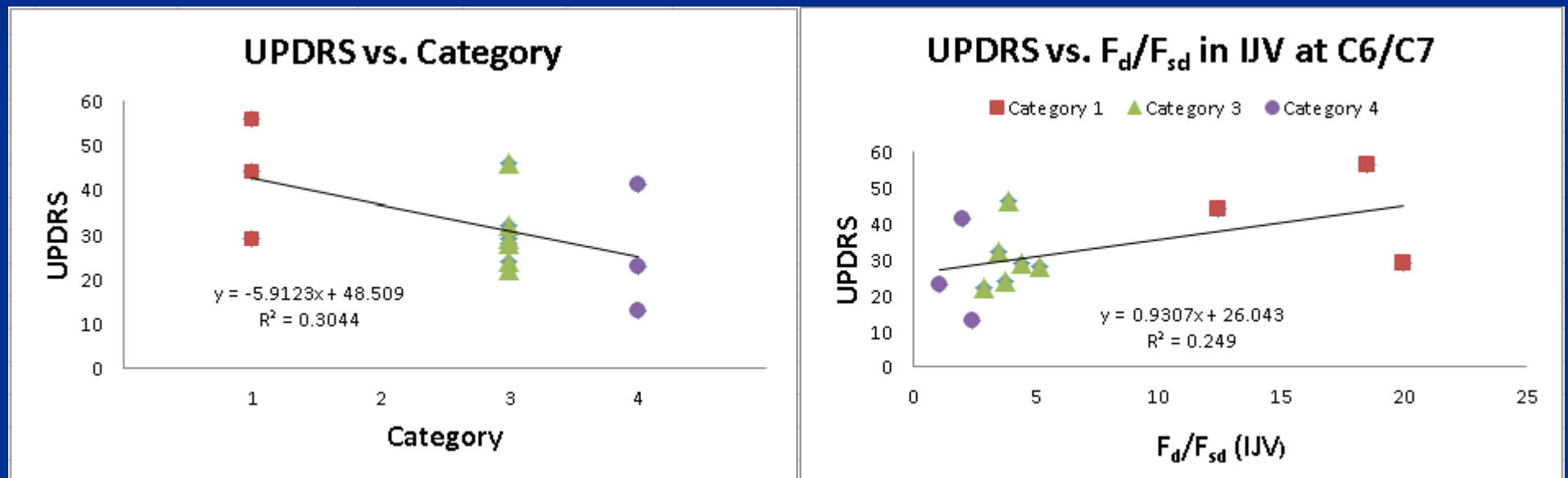
WMHs total volume threshold (850mm³) was decided by the mean plus the standard deviation of the normal population (340+508).

Scatter plot of WMH visual score vs UPDRS



The MRI visual rating scale proposed by Scheltens *et. al.* was also used in our study for evaluating the WMH level.

Scatter plots of UPDRS vs. Category and UPDRS vs. F_d/F_{sd} at C6/C7



LIMITATIONS

- The small patient sample size

We would be interested in sharing our protocol and collaborating with sites to increase this number and create a database of IPD cases using this MRI protocol

www.mrinnovations.com

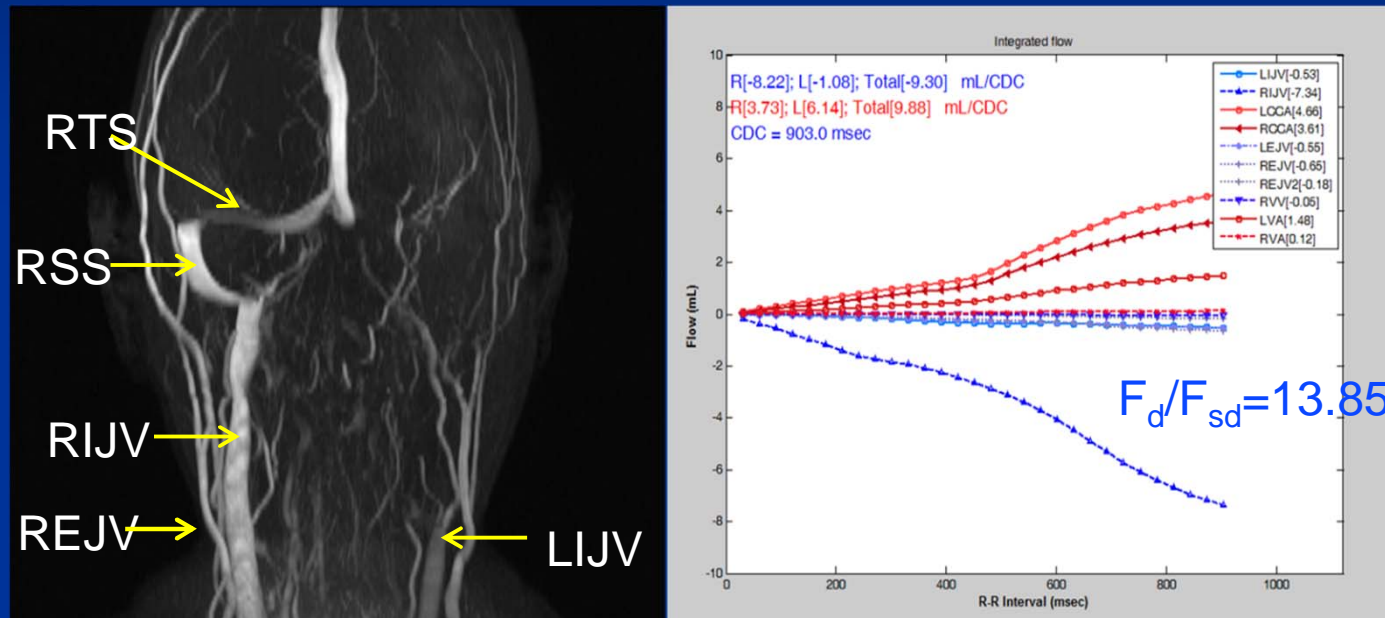
- The lack of 3D time-resolved contrast-enhanced angiography (3D CE MRAV) scans

Using CE-MRAV would make it possible to visualize all dural sinuses even in the presence of slow flow.

CONCLUSIONS

- There are a variety of venous vascular abnormalities in patients with IPD.
- Higher prevalence of WMHs in IPD patients with venous abnormalities.
- IPD patients with high volume of WMHs and abnormal venous structures tend to have more severe Parkinson's symptoms.
- The structural and/or venous flow abnormalities in the transverse sinus, sigmoid sinus and IJVs may lead to an important imaging sub-classification of IPD that will enhance our understanding of the etiology of IPD.

THANK YOU!



Category 1 for IPD venous vascular abnormalities

To participate in a collaborative project contact
Rachel Martis-Laze at rdmlaze@gmail.com
Prof. Haacke at nmrimaging@aol.com