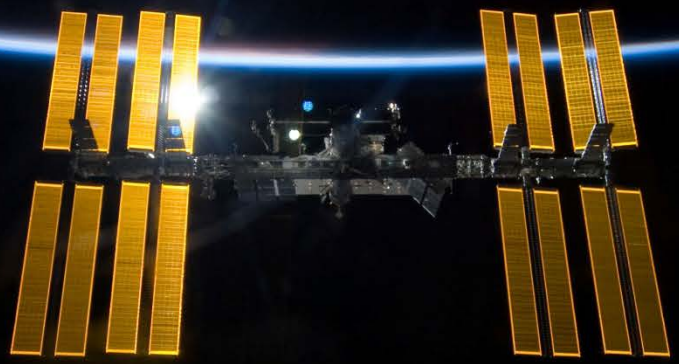
THE VISUAL IMPAIRMENT INTRACRANIAL PRESSURE SYNDROME IN LONG DURATION U.S. ASTRONAUTS: EPIDEMIOLOGY AND PATHOPHYSIOLOGY

Christian Otto, M.D., M.Sc.
Lead Scientist, NASA VIIP Risk

Universities Space Research Association, Houston, TX,

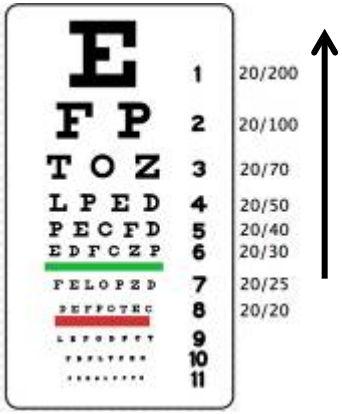


Sensorimotor Workshop
NSBRI, Houston, TX
Thursday August 29, 2013.

Visual Impairment Intracranial Pressure Syndrome Signs

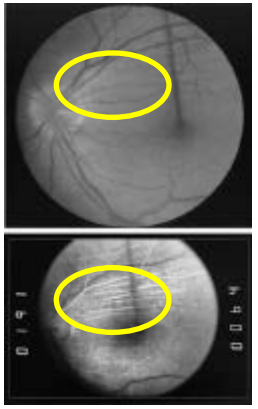
•Hyperopic Shifts

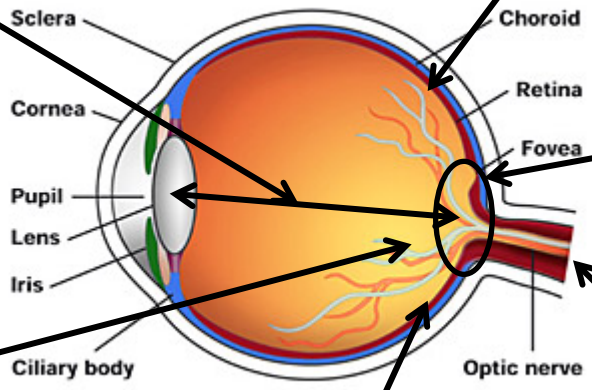
-Up to +1.75 diopters



•Choroidal Folds

- parallel grooves in the posterior pole





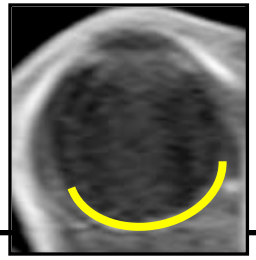
•Optic Disc Edema (swelling)

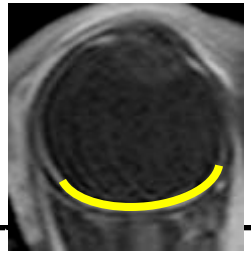
ICP

•Altered Blood flow

•"cotton wool" spots

•Globe Flattening



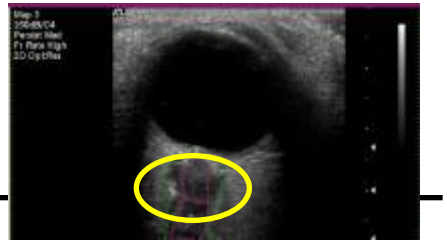


Normal Globe

Flatten Globe

MRI Orbital Image showing globe flattening

•Increased Optic Nerve Sheath Diameter



VIIP Clinical Findings

- To date 15 U.S. ISS long-duration spaceflight astronauts have developed some or all of the following findings:

Eye Findings

- Hyperopic shift
- Choroidal folds
- Cotton wool spots
- Optic Nerve Sheath Distention
- Globe flattening
- Edema of the Optic disc (papilledema)

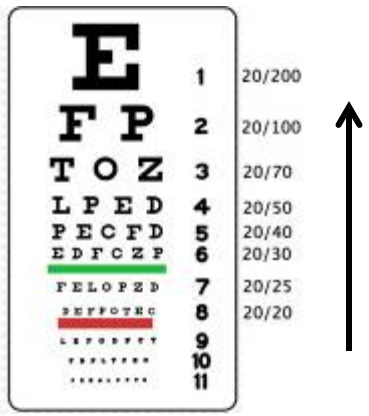
Signs of elevated intracranial pressure

- High postflight intracranial pressure in four crew members:
  - 15.4-21.3mmHg (Normal: 7-15mmHg) or,
    - 21-29 cmH2O, Normal: 9.5-20.4cmH2O

Initial Identification of the VIIP: Subjective Changes in Vision

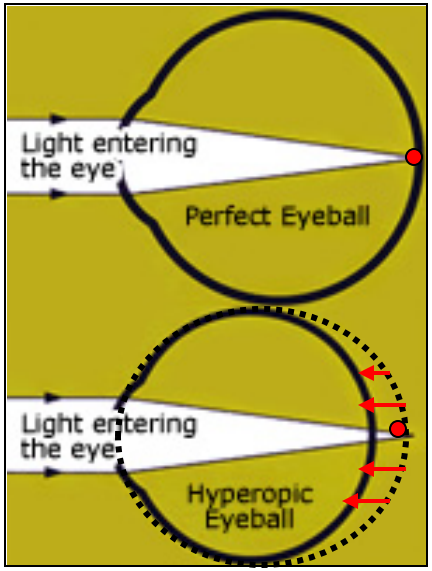
- 50% of long- duration (ISS) mission astronauts report a subjective degradation in vision, primarily increasing *farsightedness*
- ***Hyperopic shift***

Decreased near visual acuity, distant vision intact



(1 mm decrease in axial length is equivalent to a 3 diaper hyperopic shift)

Normal Eye



Hyperopic Eye

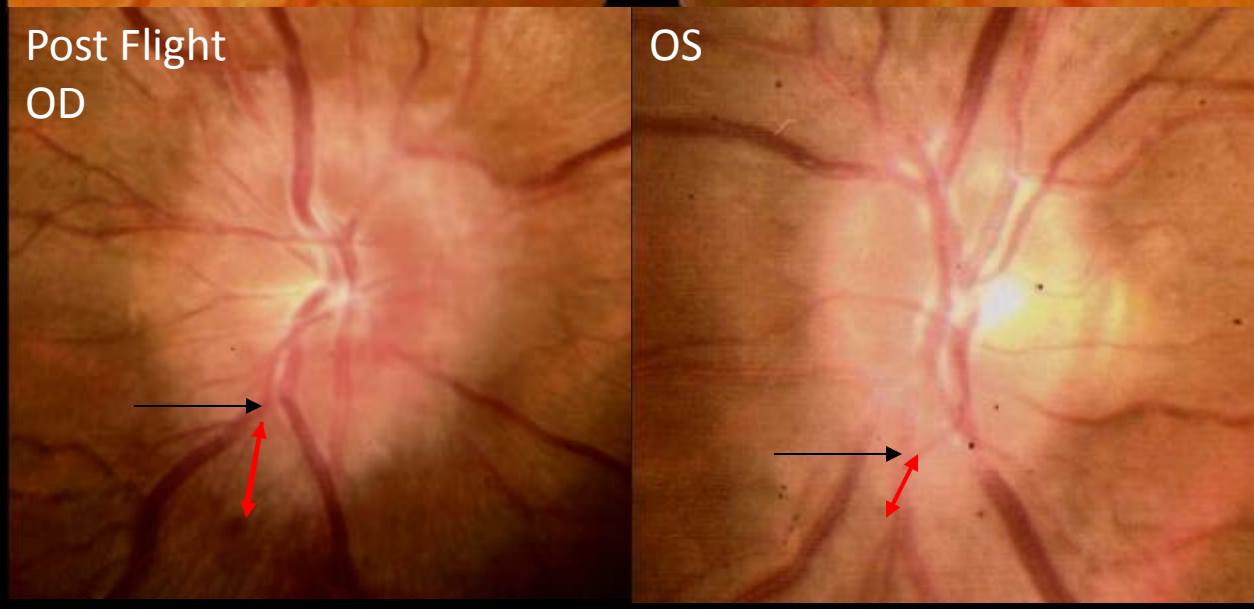
Pre to Post Flight Papilledema: A Clinical Sign of Raised Intracranial Pressure

Pre Flight

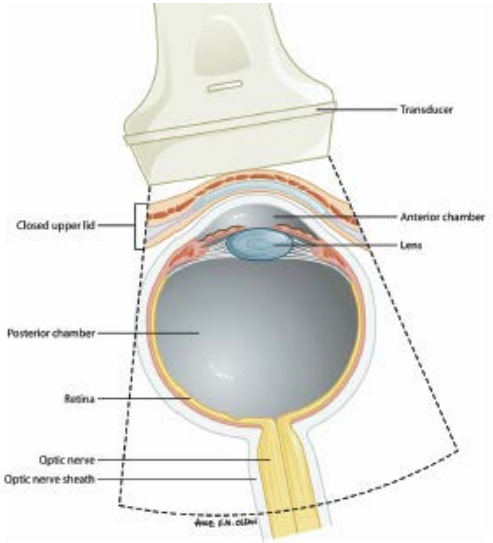
Fundoscopic images of the right and left optic disc.

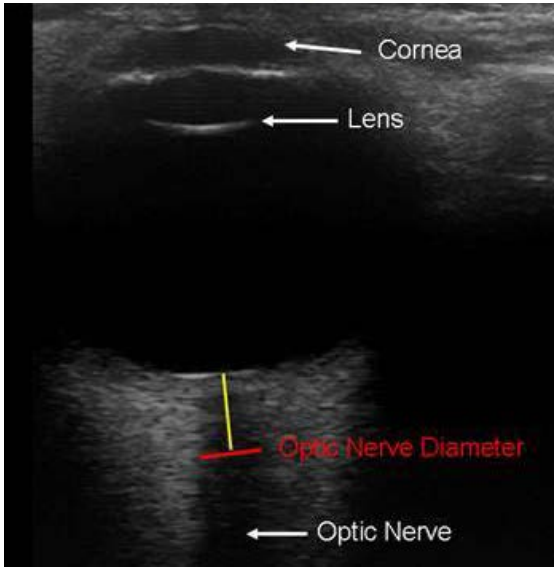
Post Flight

Fundoscopic images of the right and left optic disc showing **Grade 3 edema right** and **Grade 1 edema left** .



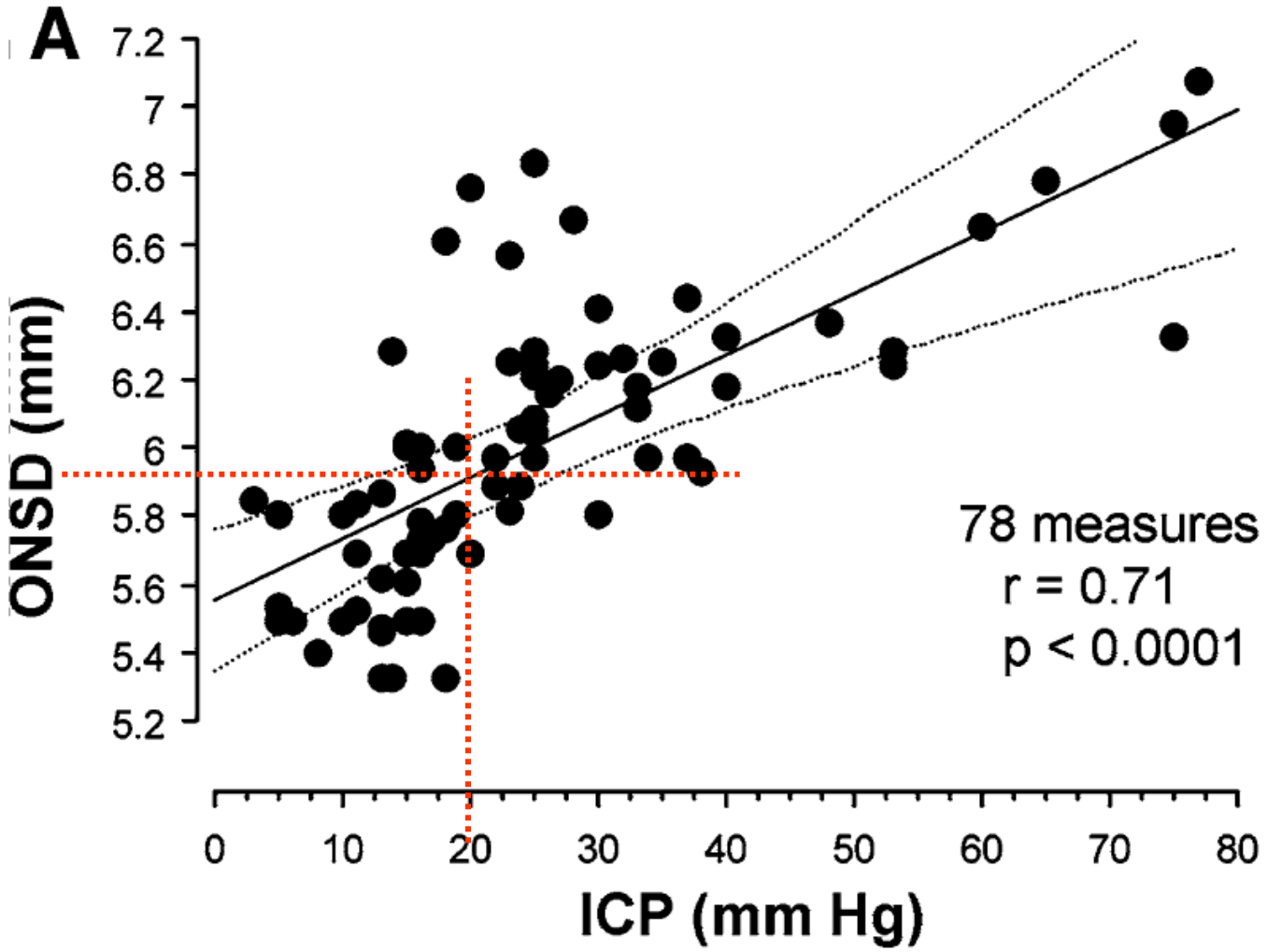
In Flight B-scan Ultrasound





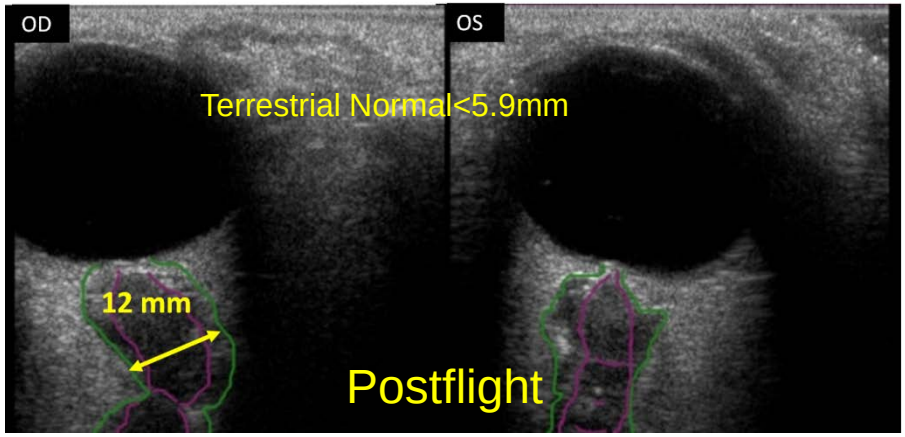
Mean ONSD Measurement & ICP

Because of a variable pressure-diameter relationship, the clinical relevance of this method relies on the demonstration of ongoing enlargement on serial US studies.

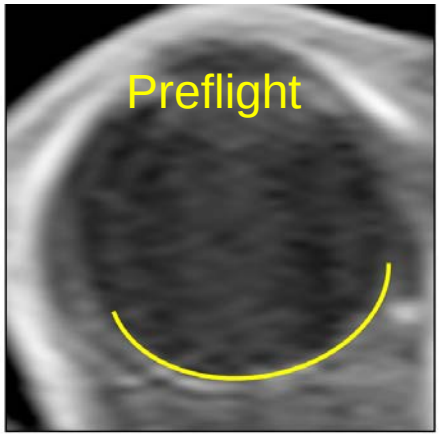


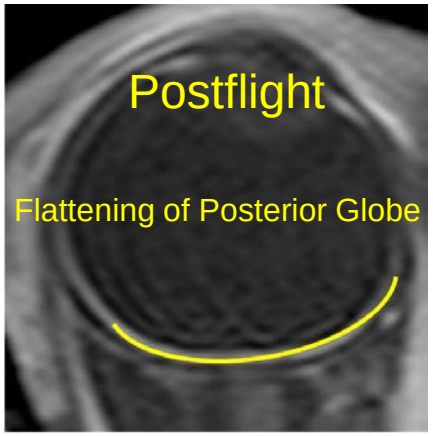
ISS Inflight Crew Ultrasound Imaging: Additional Signs of Raised Intracranial Pressure

1. Increased Optic Nerve Sheath Diameter

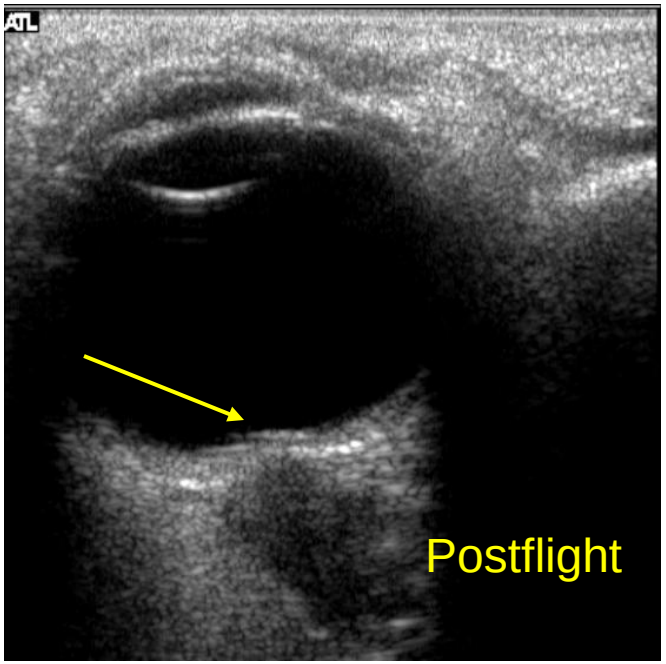


2. Posterior Globe Flattening

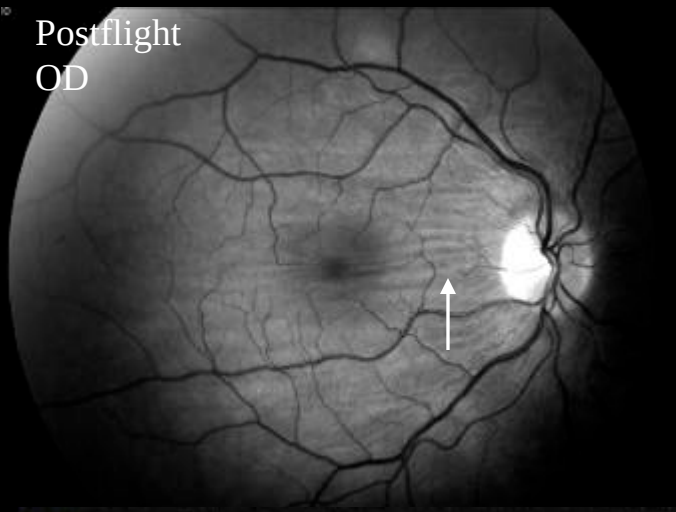


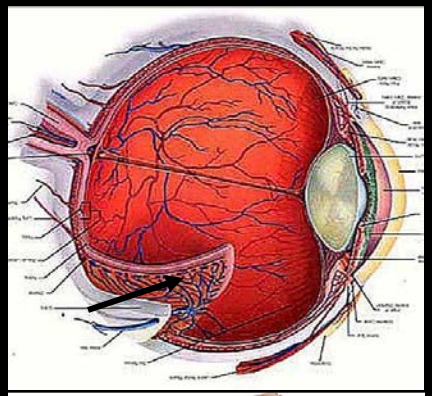


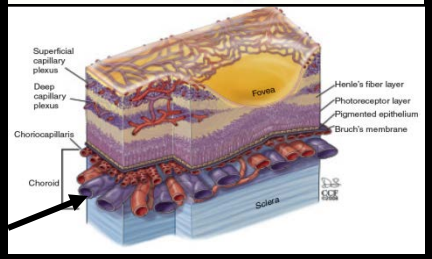
3. Raised Optic Disc

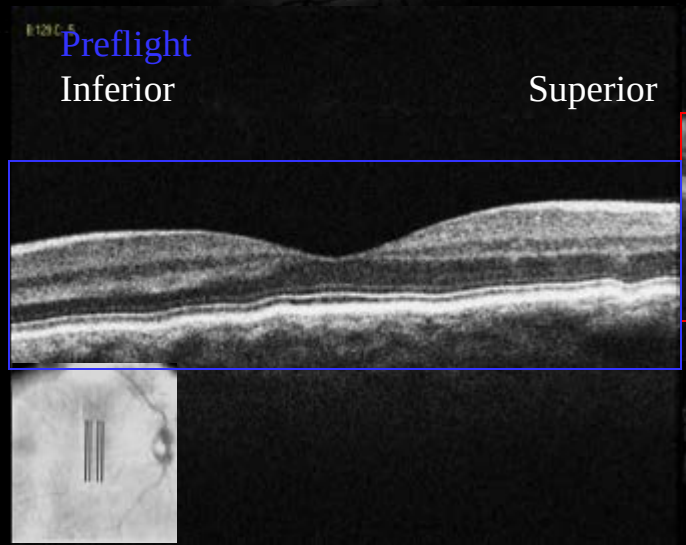


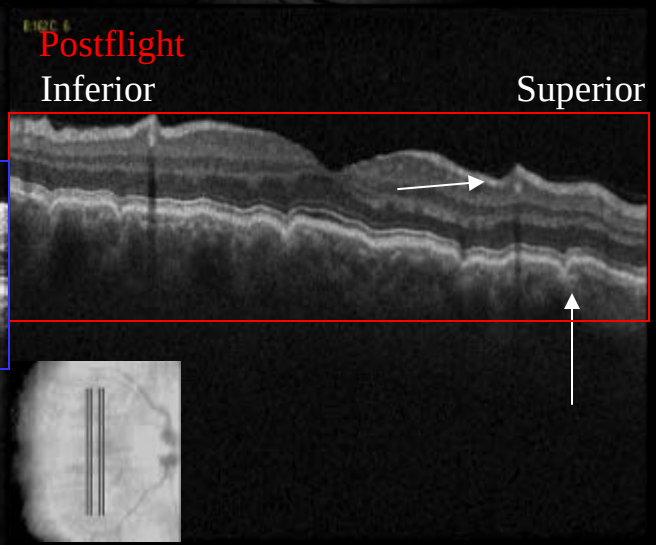
Choroidal Folds











Thickening of the choroid secondary to venous blood engorgement from uG fluid shift

VIIP Clinical Practice Guideline
Case Definition

Class 1 ≥ .50 diopter cycloplegic refractive change and/or cotton wool spot

Class 2 ≥ .50 diopter cycloplegic refractive changes or cotton wool spot

- Choroidal folds and/or optic nerve sheath distension and/or globe flattening and/or scotoma

Class 3 ≥ .50 diopter cycloplegic refractive changes and/or cotton wool spot

- Optic nerve sheath distension, and/or globe flattening and/or choroidal folds and/or scotoma
- Papilledema of Grade 0-2.

Class 4 ≥ .50 diopter cycloplegic refractive changes and/or cotton wool spot

- Optic nerve sheath distension, and/or globe flattening and/or choroidal folds and/or scotoma
- Papilledema Grade 2 or above.
- Presenting symptoms of new headache, pulsatile tinnitus and/or transient visual obscurations
- CSF opening pressure >25 cm H2O

Current U.S. ISS VIIP Incidence:

41 U.S. ISS astronauts flown to date as of Expedition 32:

- *Unclassified astronauts N=16 (No* MRI, OCT or ocular US)
- Non-cases N=6
- Confirmed cases: 19

Clinical Classification:

- Class One N=2
- Class Two N=11
- Class Three N=2
- Class Four N=4

68.4 % Class 1&2

31.6 % Class 3&4

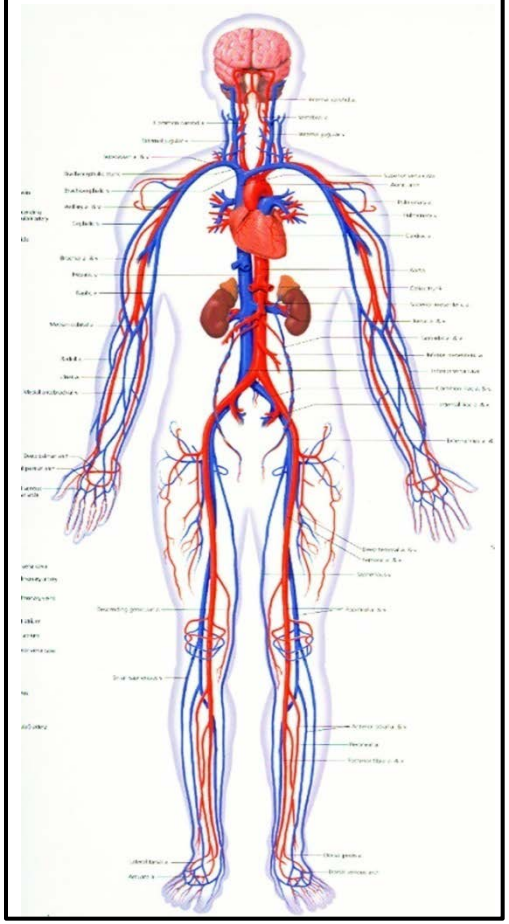
Increasing severity

Current VIIP Incidence as a % of U.S. ISS astronauts tested= 76.0%

Visual Impairment and Elevated Intracranial Pressure in Spaceflight

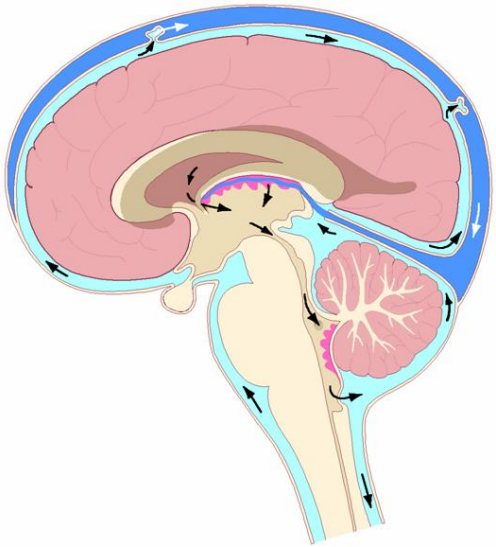
Primary Systems Involved

Cardiovascular



+

CNS



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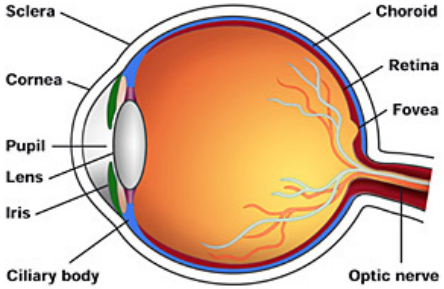
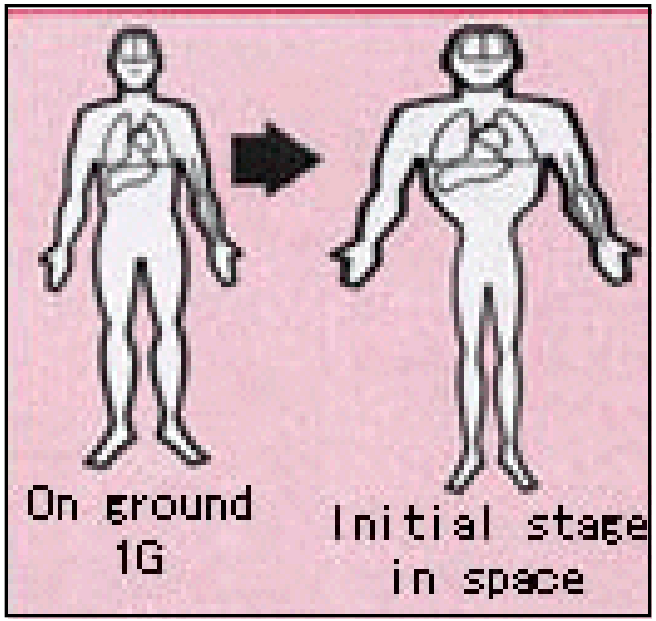
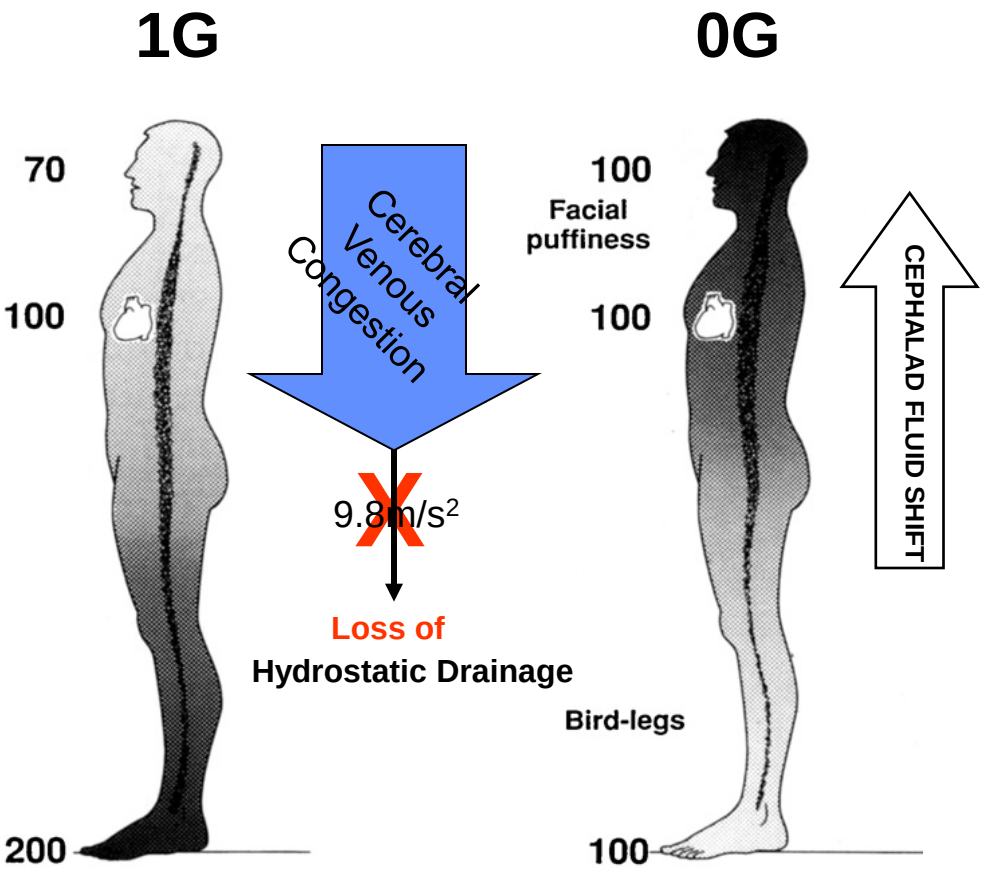
Ocular

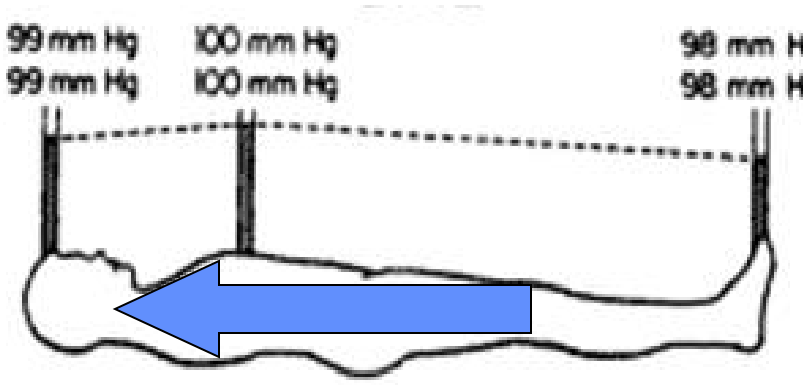


Cephalad Fluid Shift



Loss of Hydrostatic Drainage & Cerebral Venous Congestion

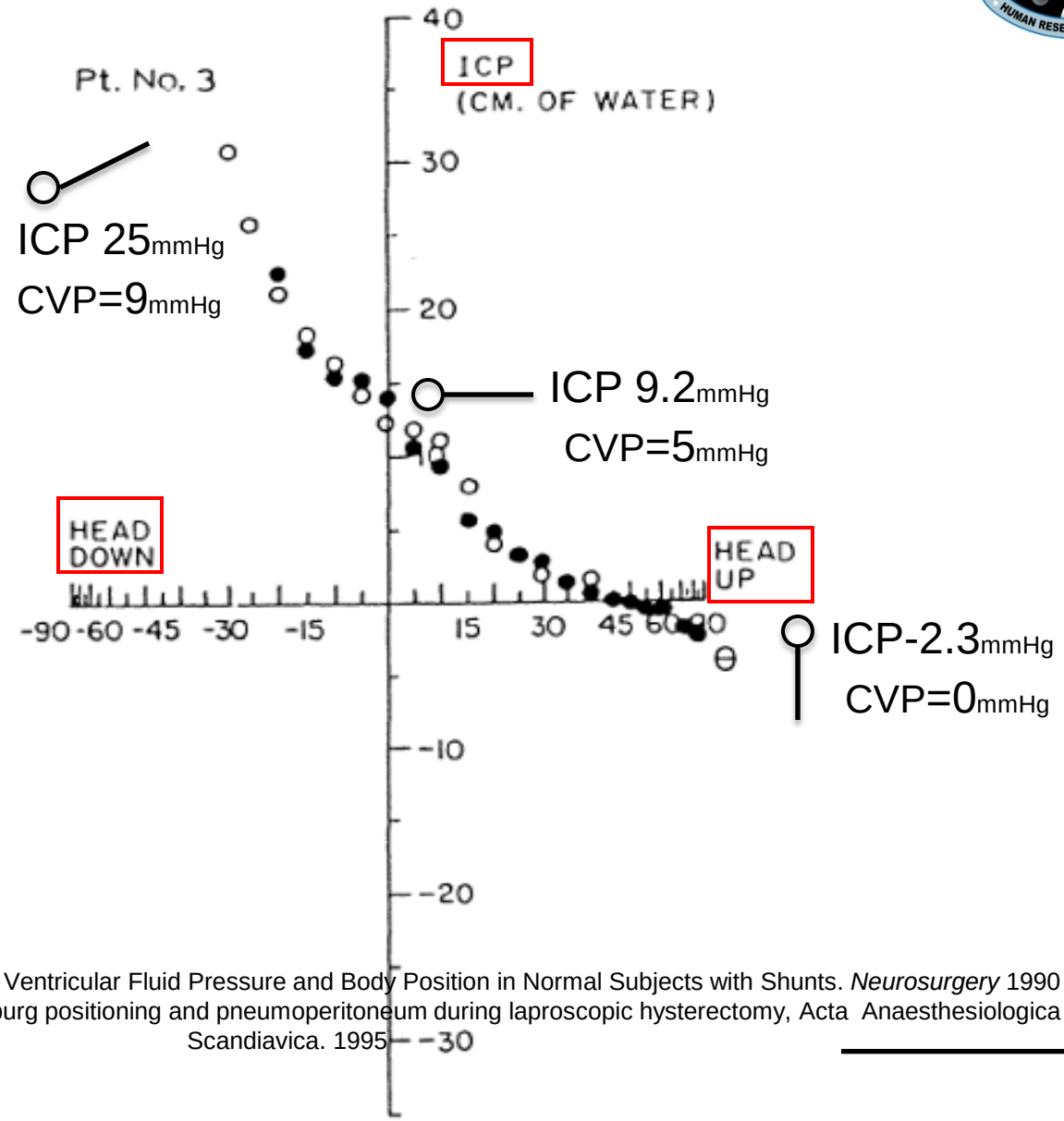




Adapted from Rowell, 1988

Adapted from Hargens & Richardson, Respiratory Physiology & Neurobiology. 2009

Tilt Angle vs ICP & CVP: Positional Fluid Shifts

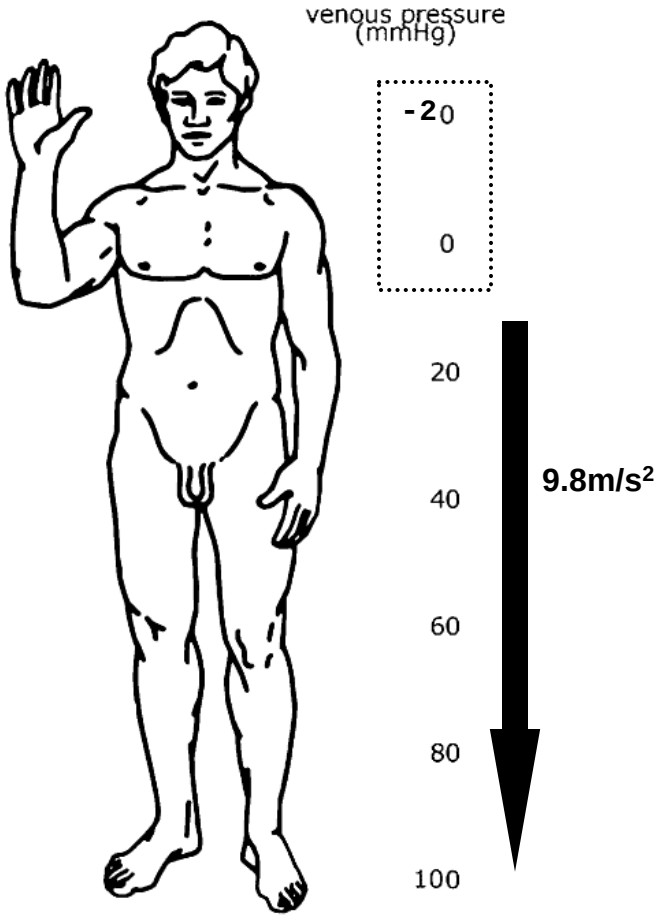


1. Chapman et al. The Relationship between Ventricular Fluid Pressure and Body Position in Normal Subjects with Shunts. *Neurosurgery* 1990
2. Hemodynamic changes due to Trendelenburg positioning and pneumoperitoneum during laproscopic hysterectomy, Acta Anaesthesiologica Scandiavica. 1995

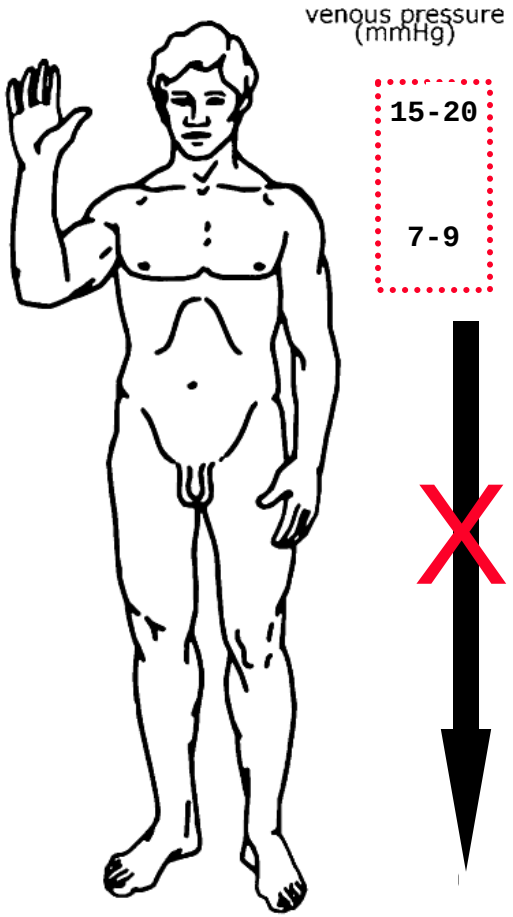
Redistribution of Venous Pressures From 1G to 0G

$$ICP = CSF_{out\ resistance} \times CSF_{formation} \uparrow SSS_{pressure}$$

Standing 1G



0G



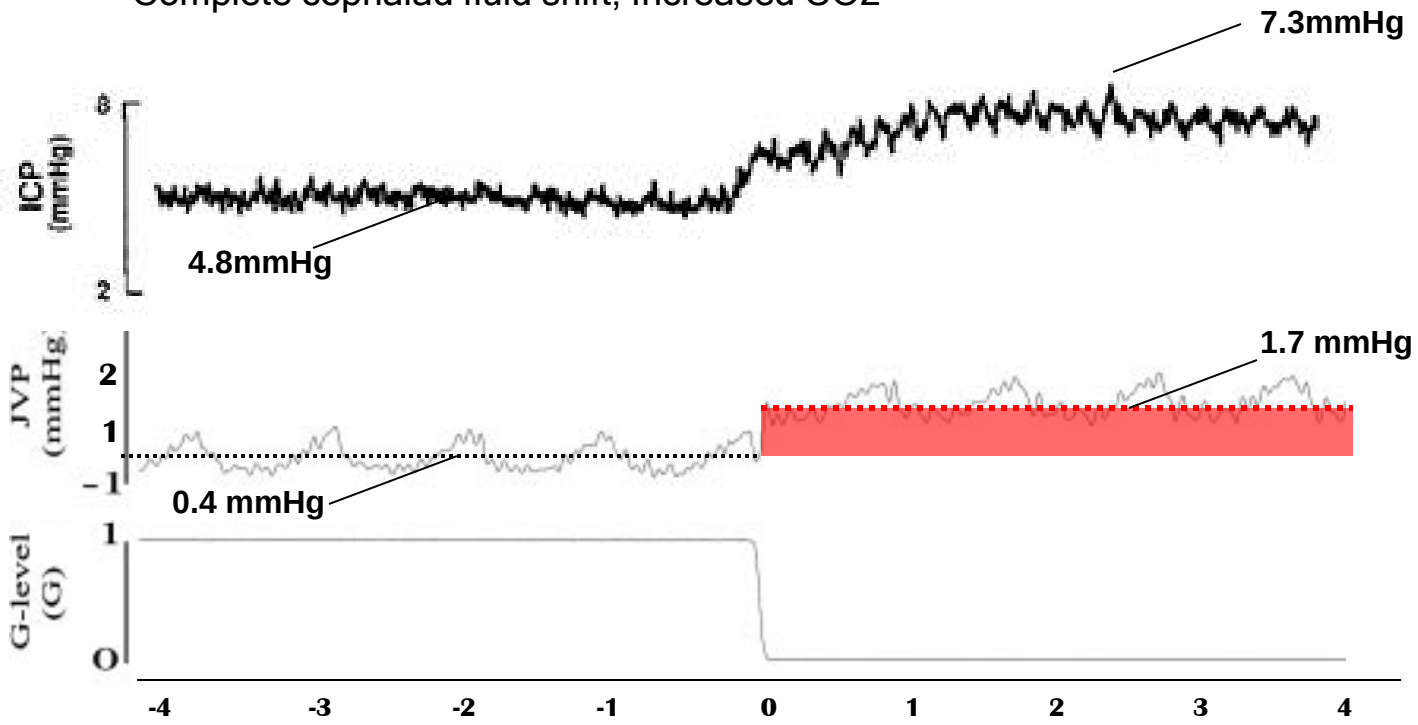
- Cranium is rigid
- Venous congestion
- Obligate arterial flow
- Transcapillary leak
- ++ICP~30-40

1. Hirvonen et al. Hemodynamic changes due to Trendelenburg positioning and pneumoperitoneum during laproscopic hysterectomy, Acta Anaesthesiologica Scandiavica. 1995
2. Hinghofer-Szalkay Gravity, the hydrorostatic indifference concept and the cardiovascular system. European Journal of Applied Physiology, 2010

3. Chapman et al. The Relationship between Ventricular Fluid Pressure and Body Position in Normal Subjects with Shunts. *Neurosurgery* 1990
4. Gisolf et al. Human cerebral outflow pathway depends on posture and central venous pressure. Journal of Physiology, 2004.

Jugular Vein Pressure & ICP Increases in Simulated Microgravity

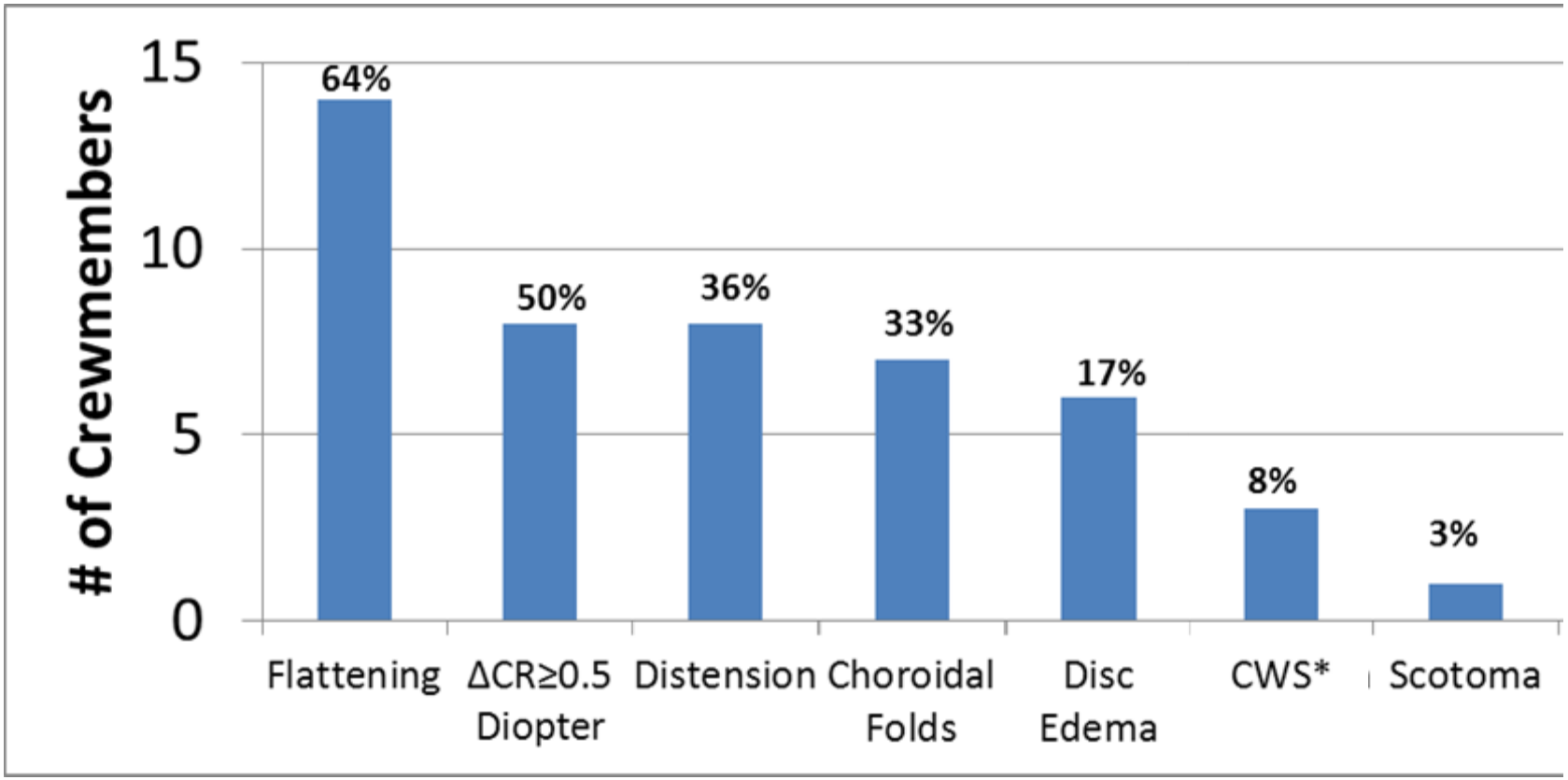
- Jugular bulb pressure approximates dural sinus pressure
- Jugular vein pressure measured in 7 animals during 4.5s free drop
- Loss of hydrostatic pressure gradient increased JV_P 1.3mmHg
  - i.e. loss of hydrostatic assisted venous drainage
- Similar study, ICP increased in 5 rats from 4.8 to 7.3 mmHg =52% increase in ICP
- Factors that may further raise ICP:
  - Complete cephalad fluid shift, Increased CO2



1. Gotoh et al. *Acute hemodynamic responses in the head during microgravity induced by free drop in anesthetized rats.* Am J Physiology-Regulatory Integrative & Comparative Physiology. 2004

2. GOTOH et al. Cerebral Circulation during Acute Microgravity Induced by Free Drop in Anesthetized Rats *Japanese Journal of Physiology*, **53**, 223–228, 2003

VIIP Ocular Findings in ISS Astronauts



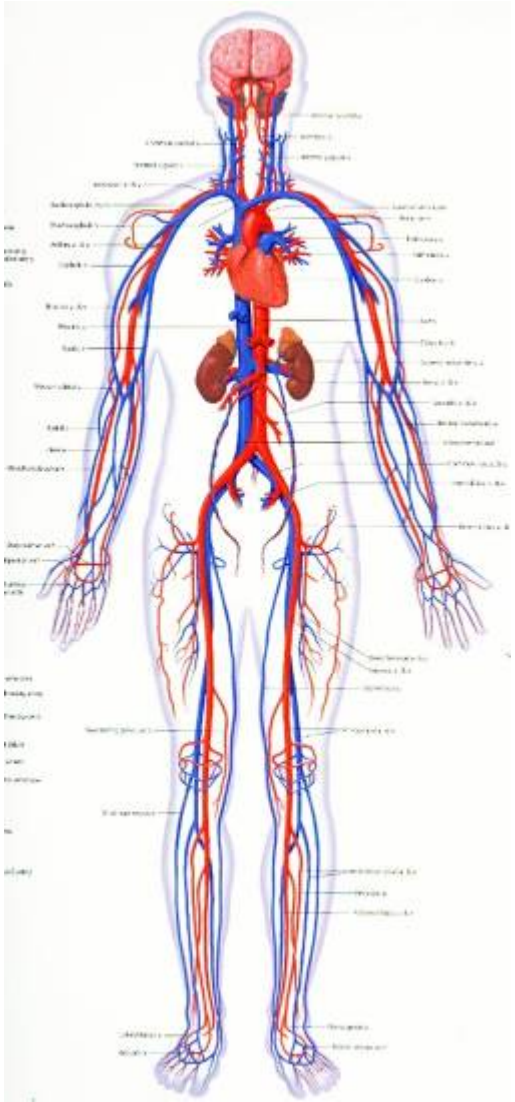
MRI in Idiopathic Intracranial Hypertension & VIIP: The Case for Elevated ICP

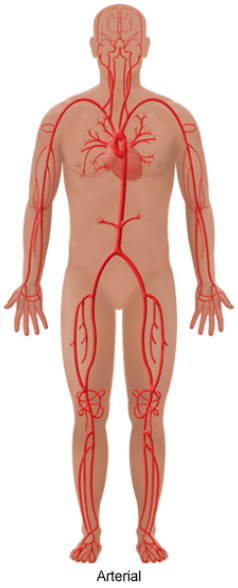
Kramer et al. ***Orbital and Intracranial Effects of Microgravity: Findings at 3-T MR Imaging.*** *Radiology*: Volume 263: Number 3—June 2012

Maralani et al. ***Accuracy of brain imaging in the diagnosis of idiopathic intracranial hypertension.*** Clinical Radiology. Dec. 2011.

IIH MRI Signs vs VIIP		
Imaging Assessment	**Present in IIH (Specificity)**	**Seen in VIIP**
Venous Stenosis Score	100%	?
Flattening of Posterior Globes	100%	Yes
Optic Nerve Protrusion	100%	Yes
Partially Empty Sella	95.3%	Yes
Optic Nerve Sheath Distension	88.4%	Yes
Optic Nerve Tortuosity	86%	Yes

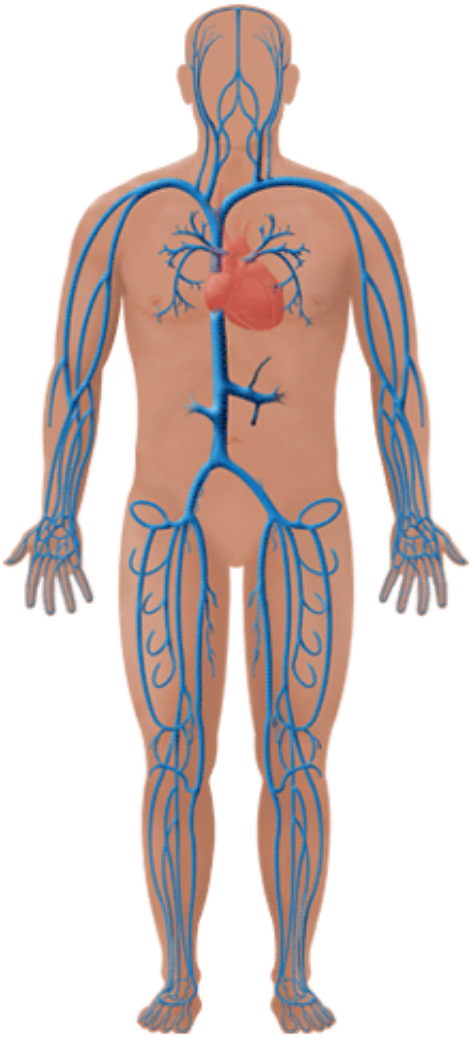
Vascular Capacitance: Venous & Arterial





Arterial

20%=1L

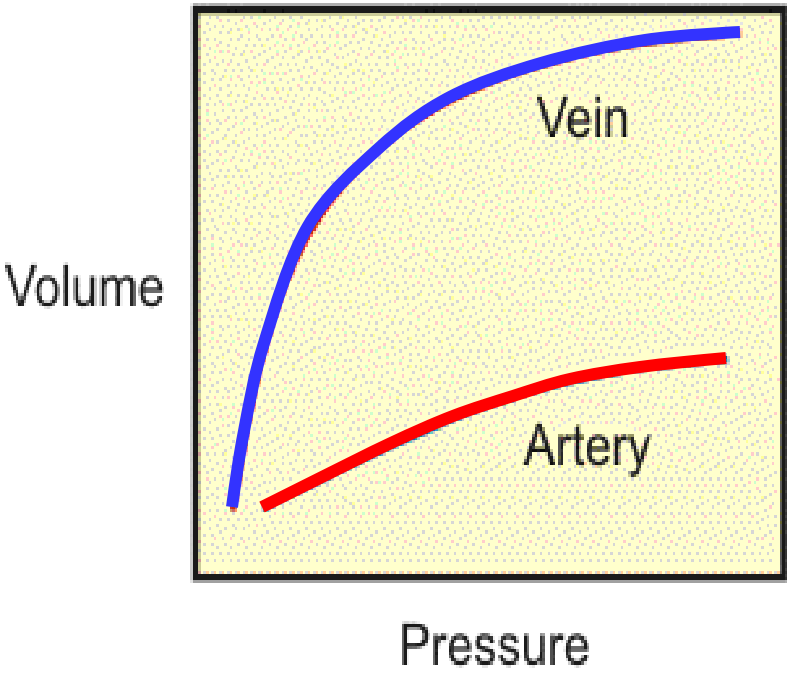


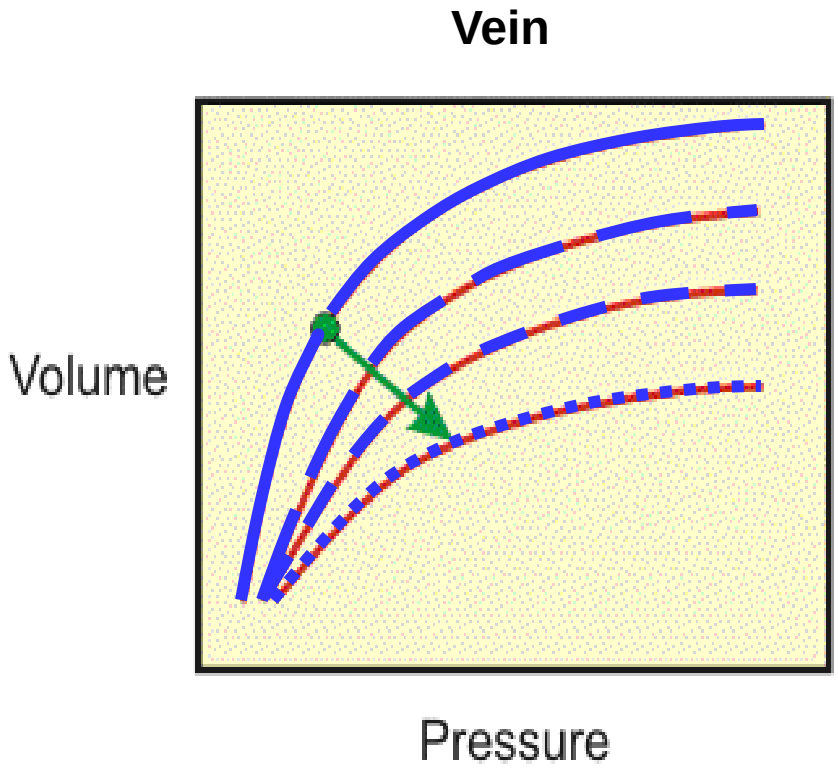
Venous

70-80%=4L

Venous Compliance

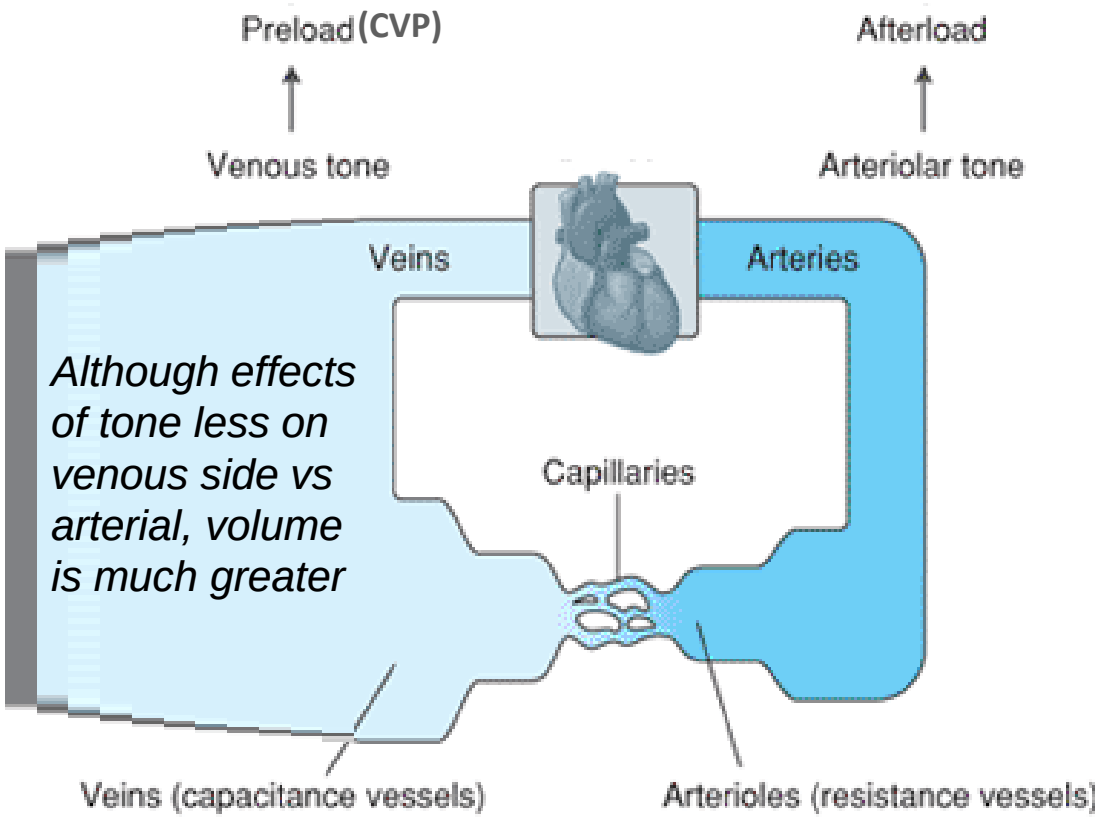
$$C = \frac{\Delta V}{\Delta P}$$



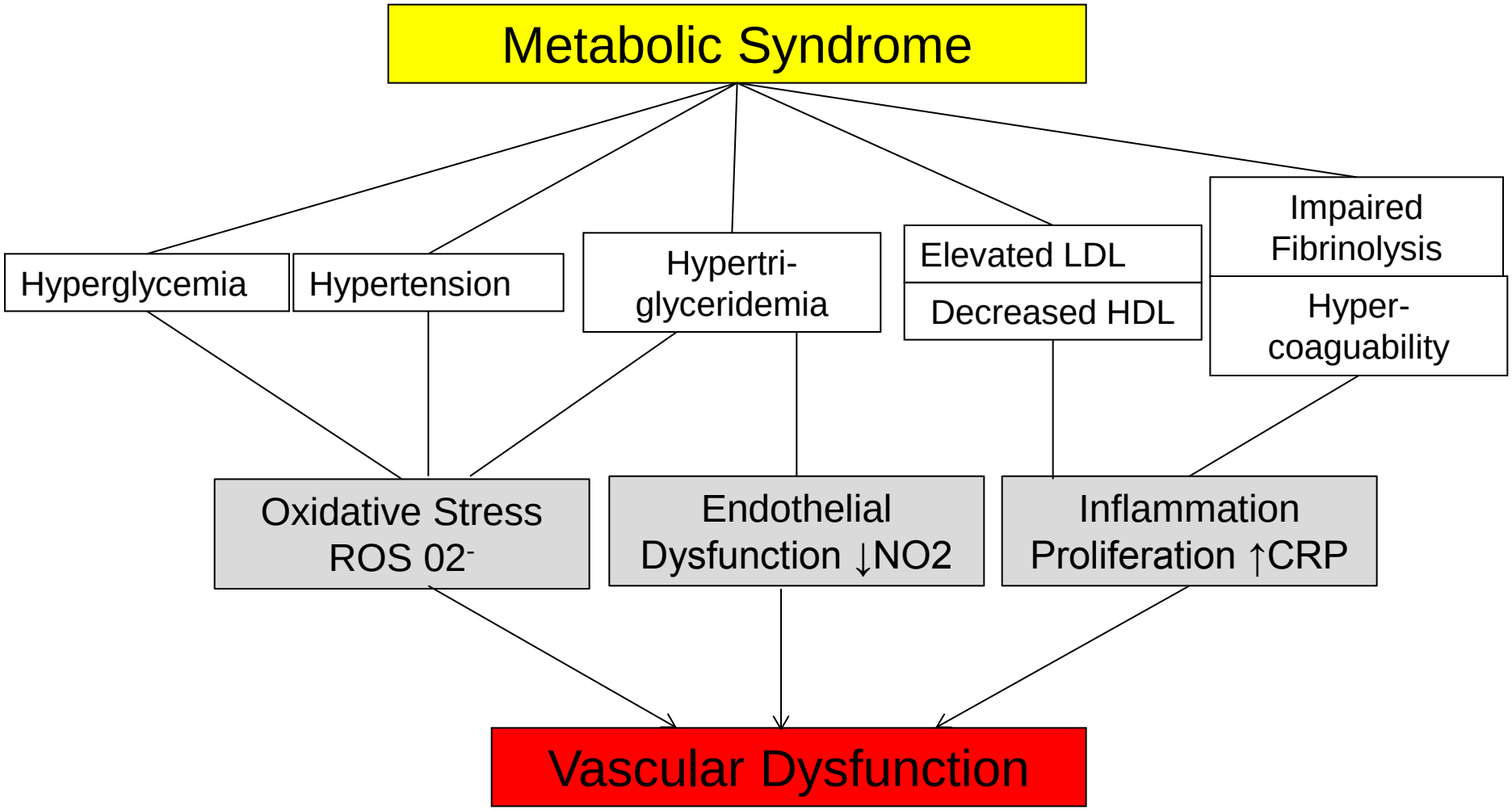


Factors Increasing Venous Tone will Increase Cerebral Venous Outflow Resistance

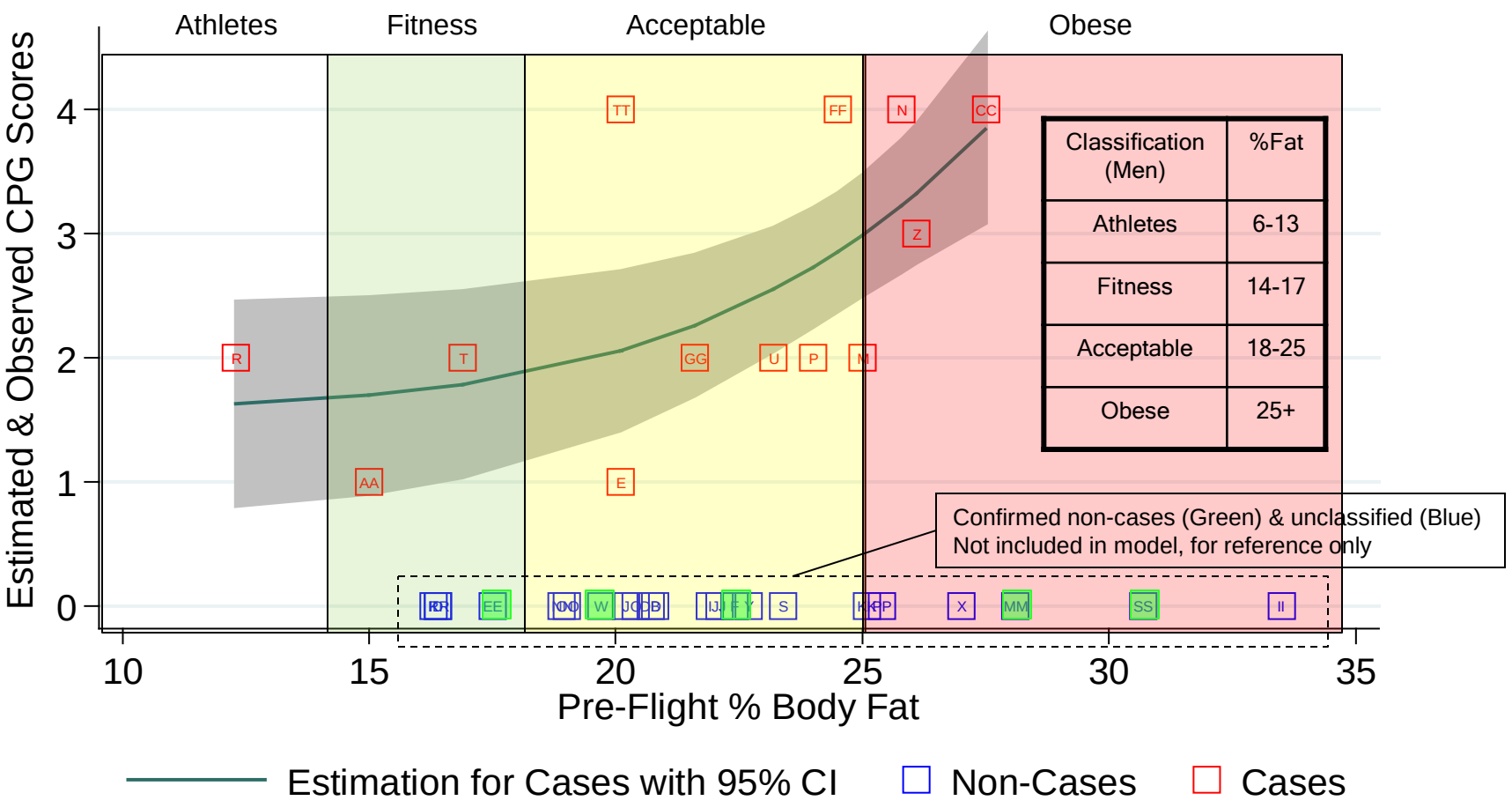
- **Resting Tone of Venous Vessels Influenced by:**
  - SNS tone↑
    - ✓ Resting Blood Pressure
  - Endothelin↑
  - Nitric oxide↓
  - Inflammatory cytokines ↑



Metabolic Syndrome-Vascular Relationship



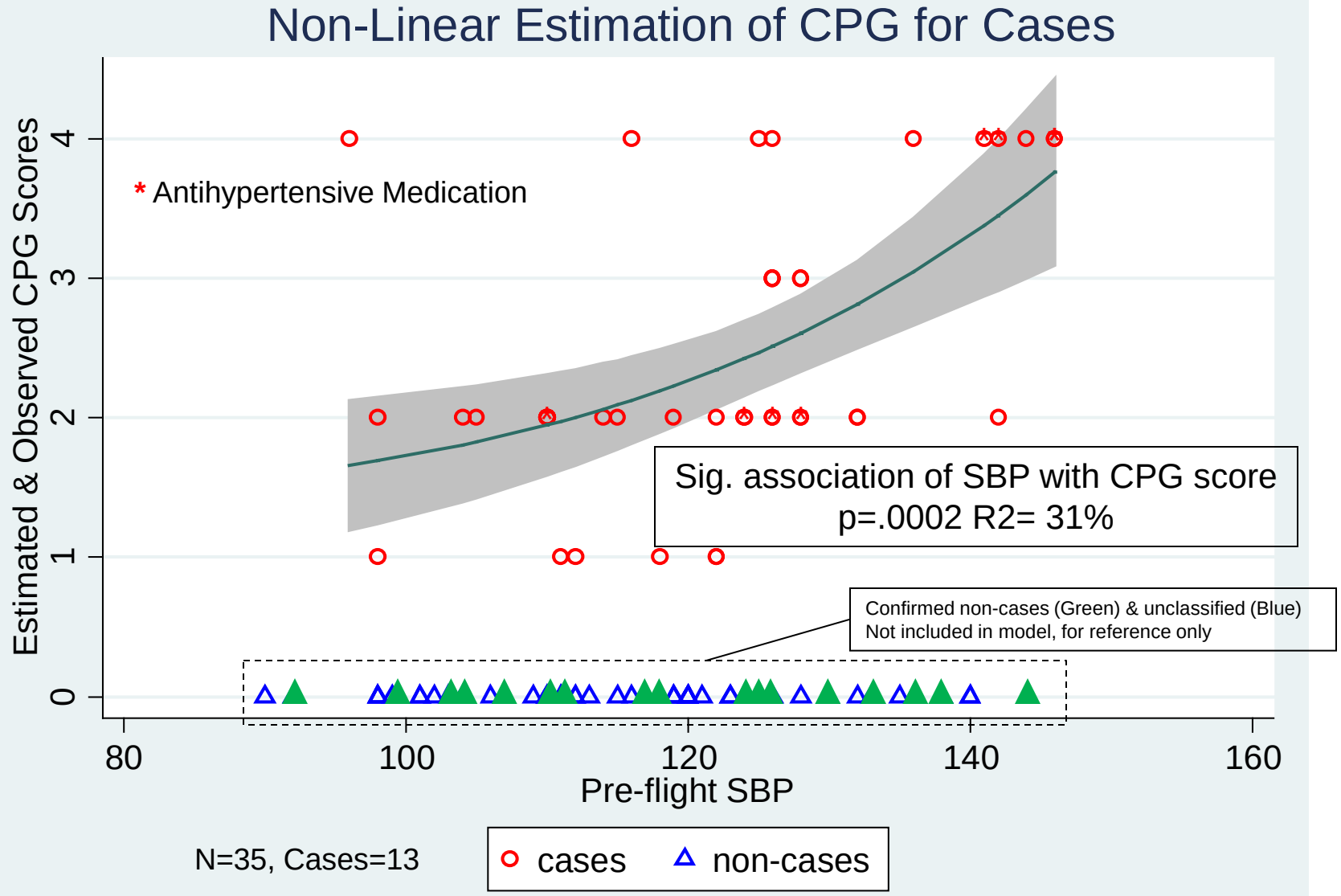
Occupational Surveillance Data Mining: Percentage Body Fat



Best Fit (curvilinear) for Cases; R^2=.38, p<.01

N=35, 13 Cases, total observations=35

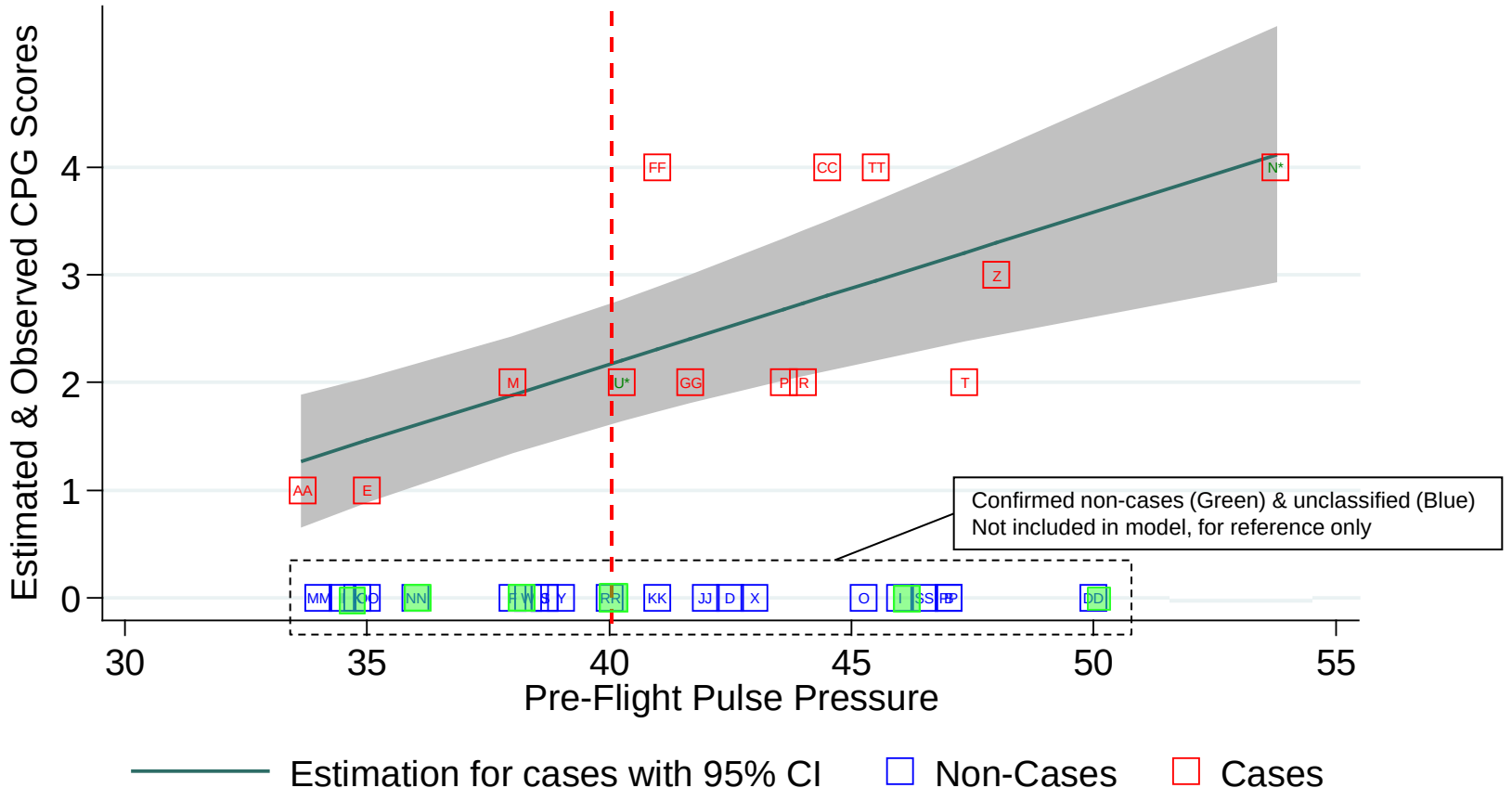
Preflight Systolic Blood Pressure Non-Cases vs Cases per CPG



Occupational Surveillance Data Mining: Resting Pulse Pressure (Sitting)

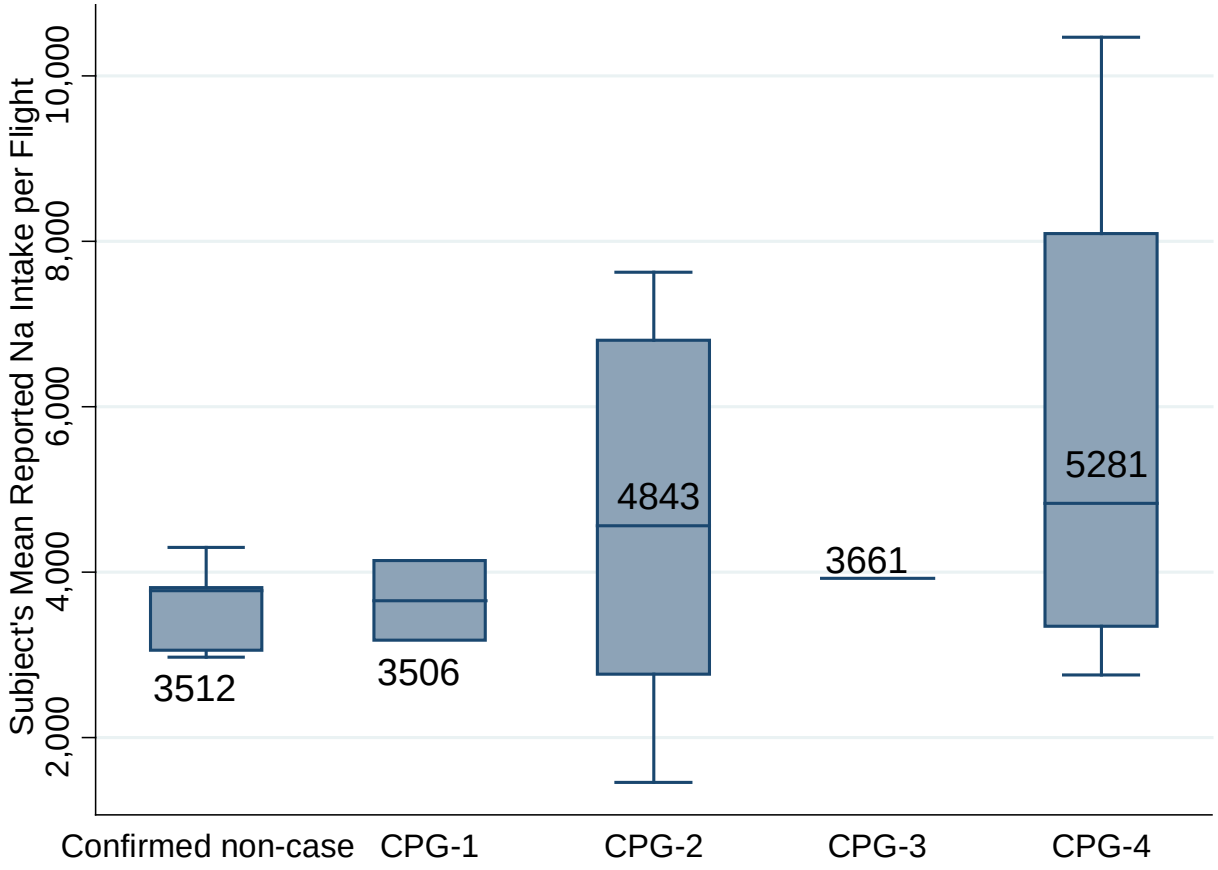
Cases per CPG vs Pulse Pressure

(Annual Preflight Exam 4-Year Mean)



Best Fit (curvilinear) for Cases; R^2=.45 (including BP meds predictor), p<.01

Self Reported ISS Inflight Daily Sodium Intake



- Current recommended daily sodium limit = **2300mg/day**
- If 51y or high BP, recommended limit=1500mg/day
- Applies to majority of U.S. adults

Sodiummgday	Jackknife Coef.	Std. Err.	z	P>|z|	[95% Conf. Interval]	
cpg_revised	.2186174	.1105193	1.98	**0.048**	.0020036	.4352312…yes … positive, but weak
Total	**5**	**2**	**9**	**1**	**4**	21

Number of Astronauts per category in this Sodium analysis.

Occupational Data Mining in ISS Astronauts: Cardiovascular Variables Correlating with CPG

Cardiovascular Variable	Significant Correlation Across CPG Classification	R^2	P value
Biochemistry:			
LDL	√	0.43	P<0.02
HDL	-	0.22	P<0.09
Triglycerides	-	-	
Hemoglobin A1c	√	-	P<0.01
Fasting serum glucose	√	0.125	P<0.008
Homocysteine	√	-	P<0.01
Oral sodium intake	√	0.22	P<0.05
Body Composition:			
Body Mass Index	√	0.41	P<0.01
Percentage Body Fat	√	0.38	P<0.01
Cardiac:			
Resting systolic blood pressure (pre-in-post flight)	√	0.31	P<0.0002
Pulse Pressure (pre-in-post flight)	√	0.45	P<0.01
CT Coronary Calcium Score	-	-	-
Aerobic Capacity:			
Decreased Maximal Oxygen Uptake	√	-	P<0.04

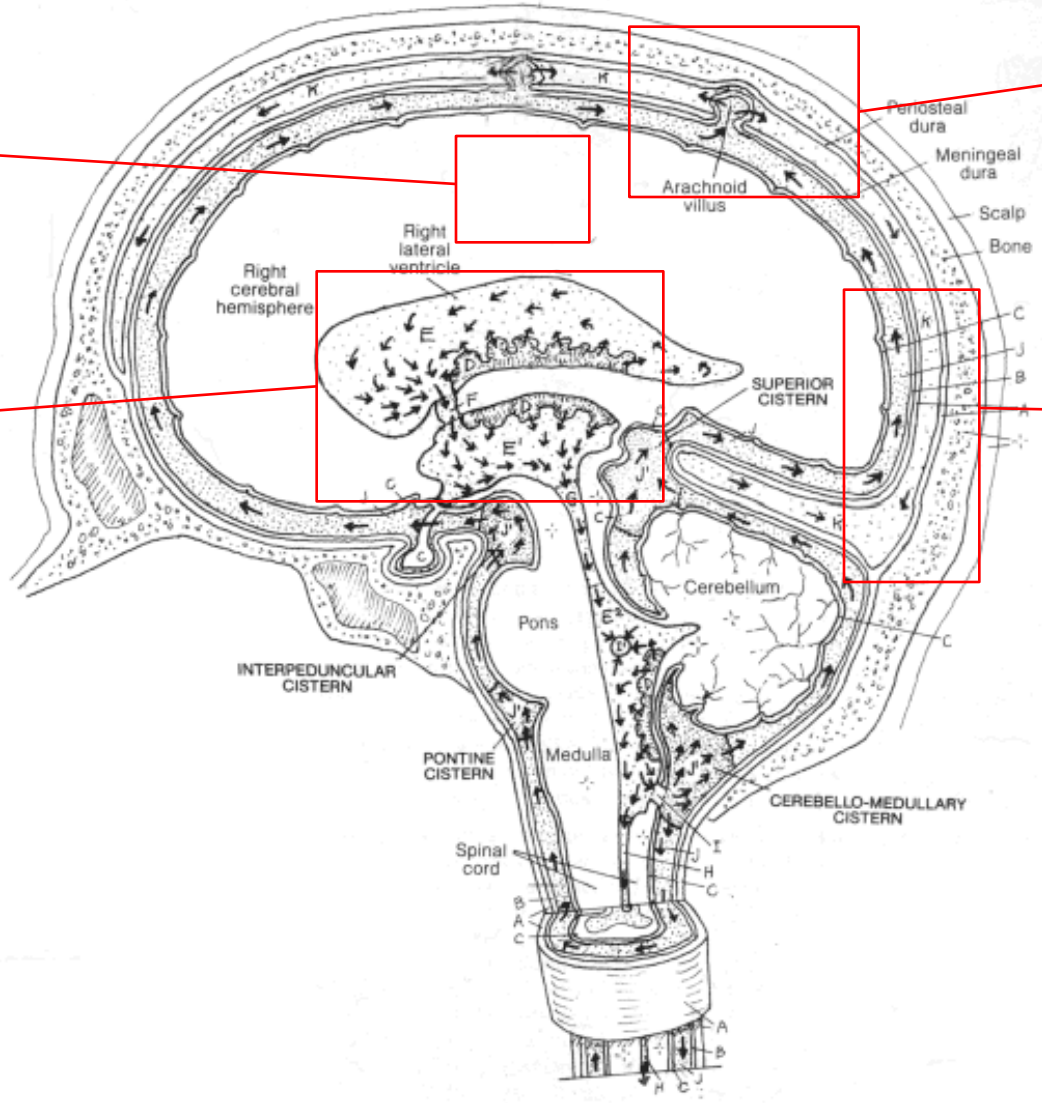
Key Brain Areas Affected by Fluid Shift

Interstitial fluid

CSF Production

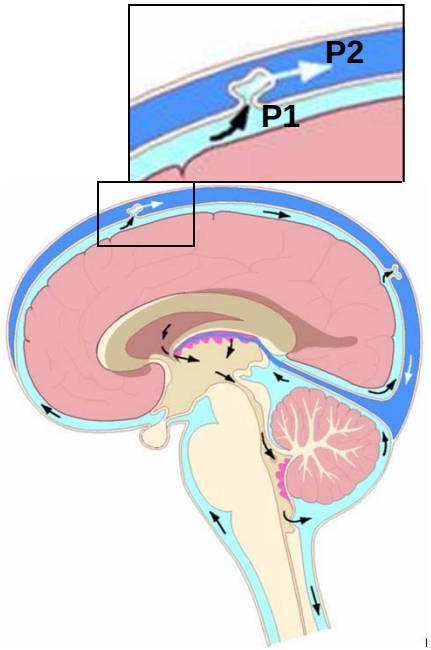
CSF Resorbtion
(AG-Venous/Lymphatic)

Venous Congestion

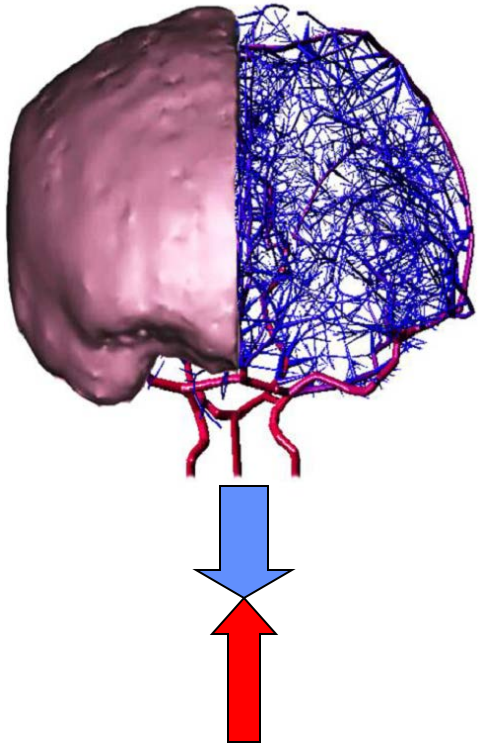


Pressure and Compliance Changes in the Craniospinal Axis

CSF & Venous

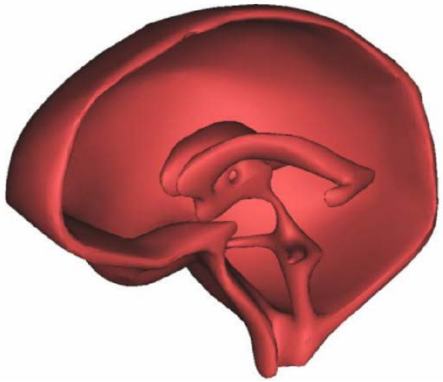


Venous (↑ P2)

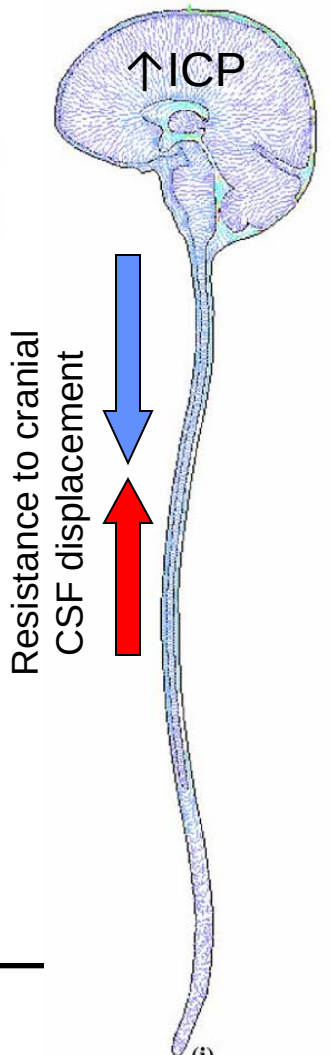


Resistance to cerebral venous drainage

CSF(↑ P1)



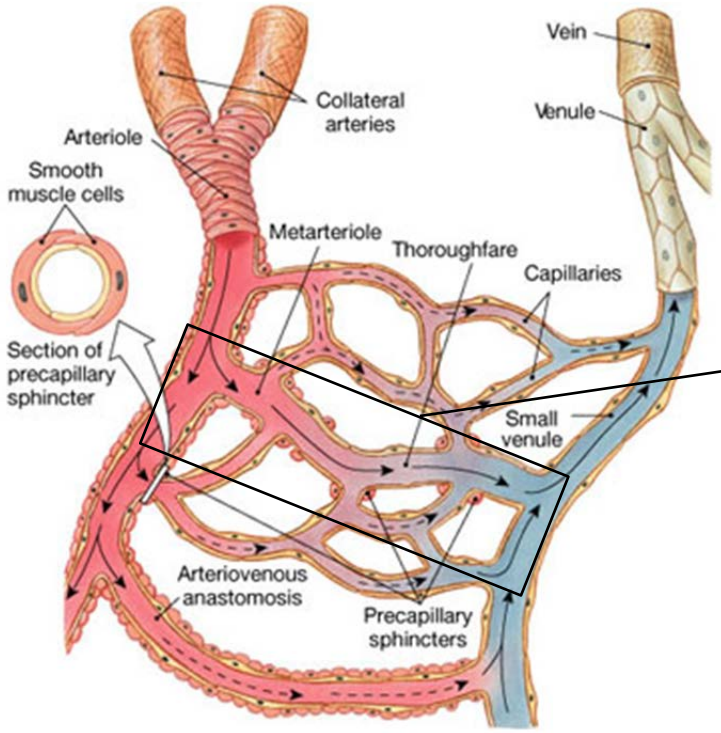
Craniospinal Axis

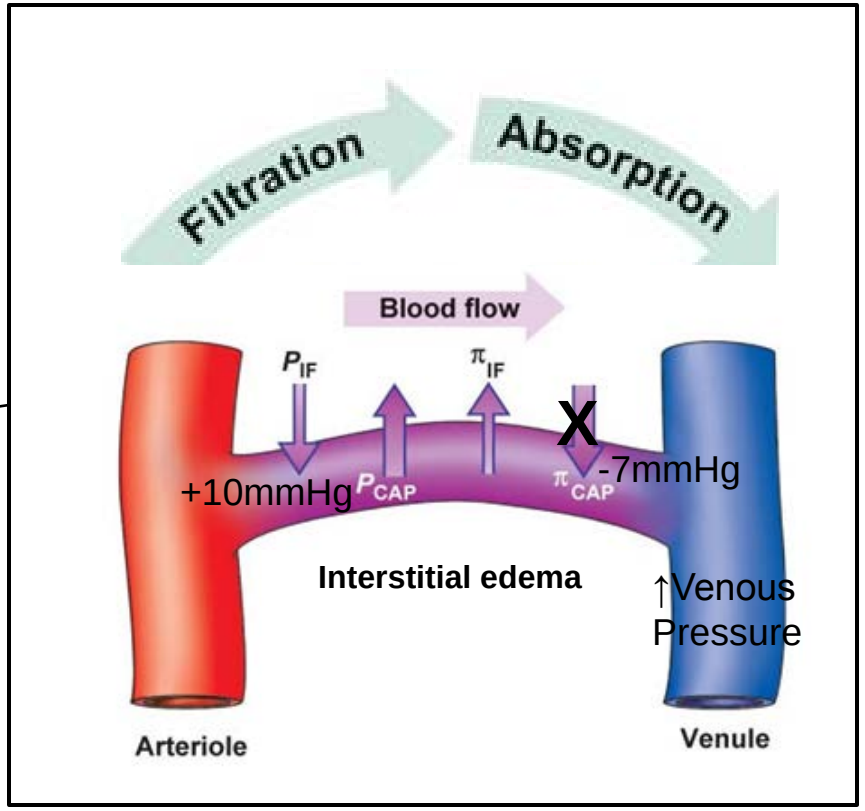


$$ICP = CSF_{out\ resistance} \times CSF_{formation} + SSS_{pressure}$$

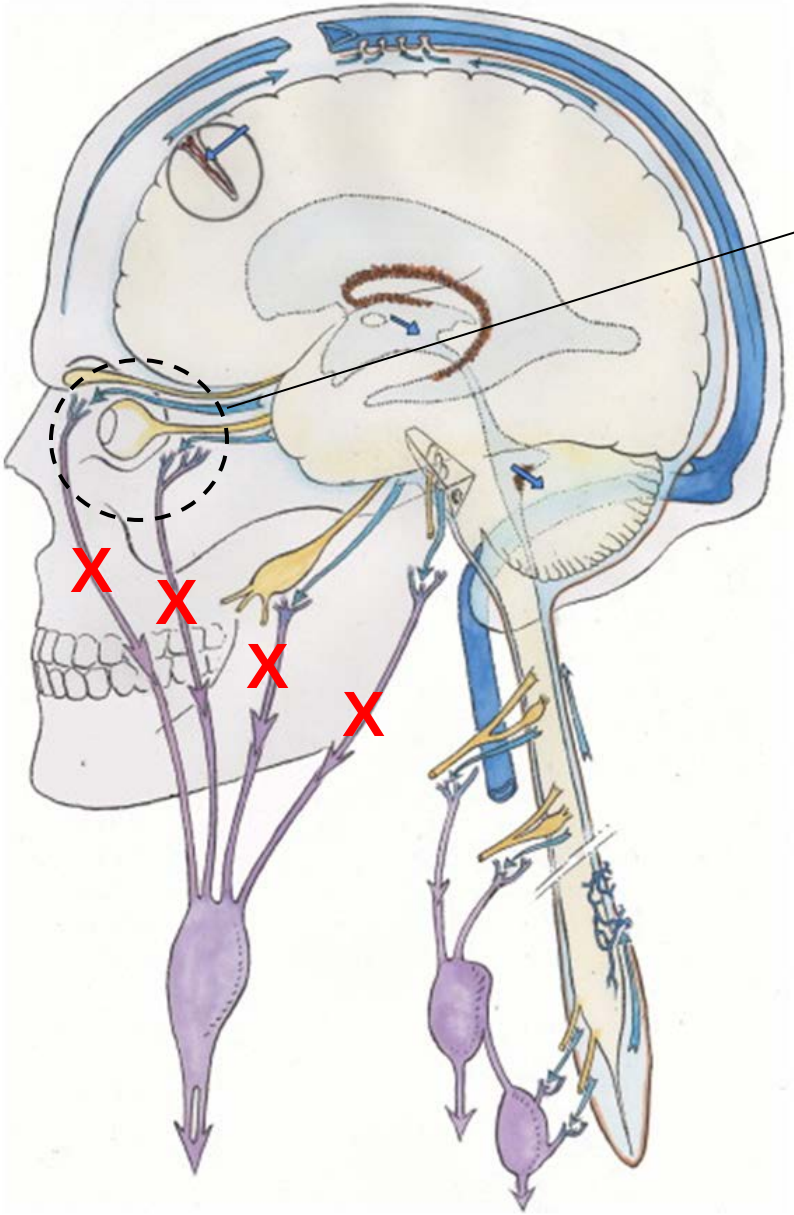
CVR=CPP/CBF CPP=MAP-ICP

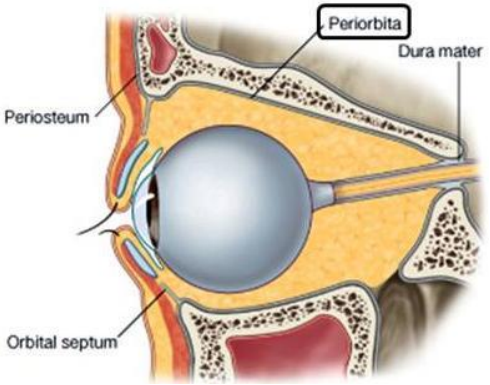
Venous Congestion May Cause Increased Transcapillary Pressure & Decreased Absorbtion

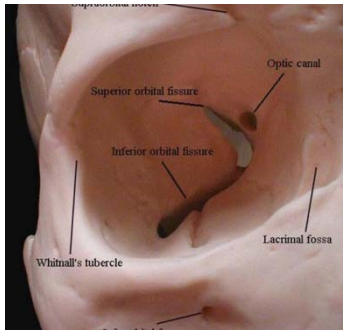


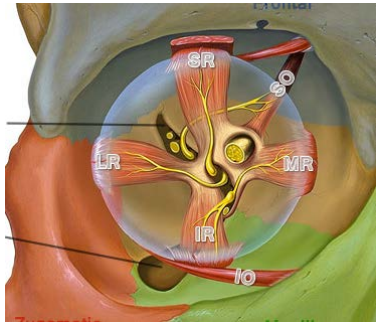


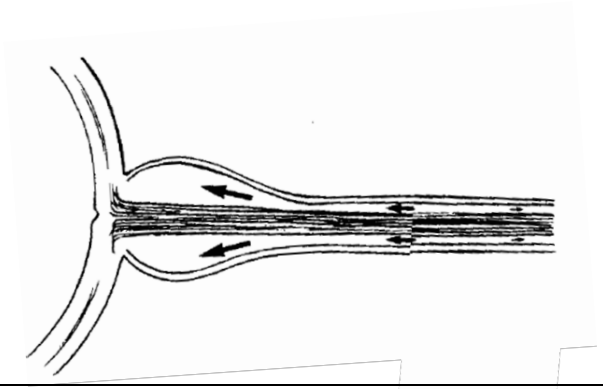
Venous Congestion & Interstitial Edema Inhibit Lymphatic CSF Drainage-Impacts on Optic Nerve





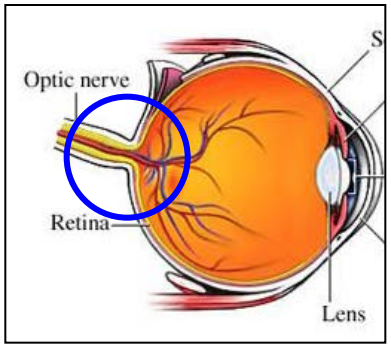




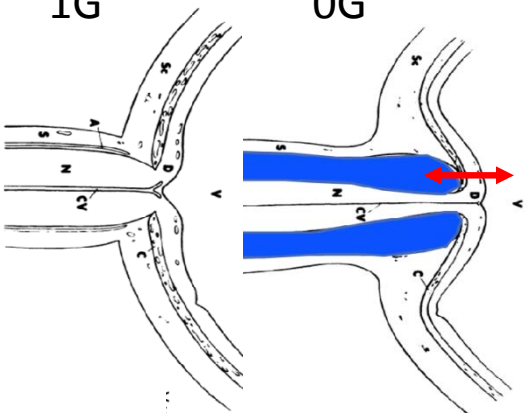


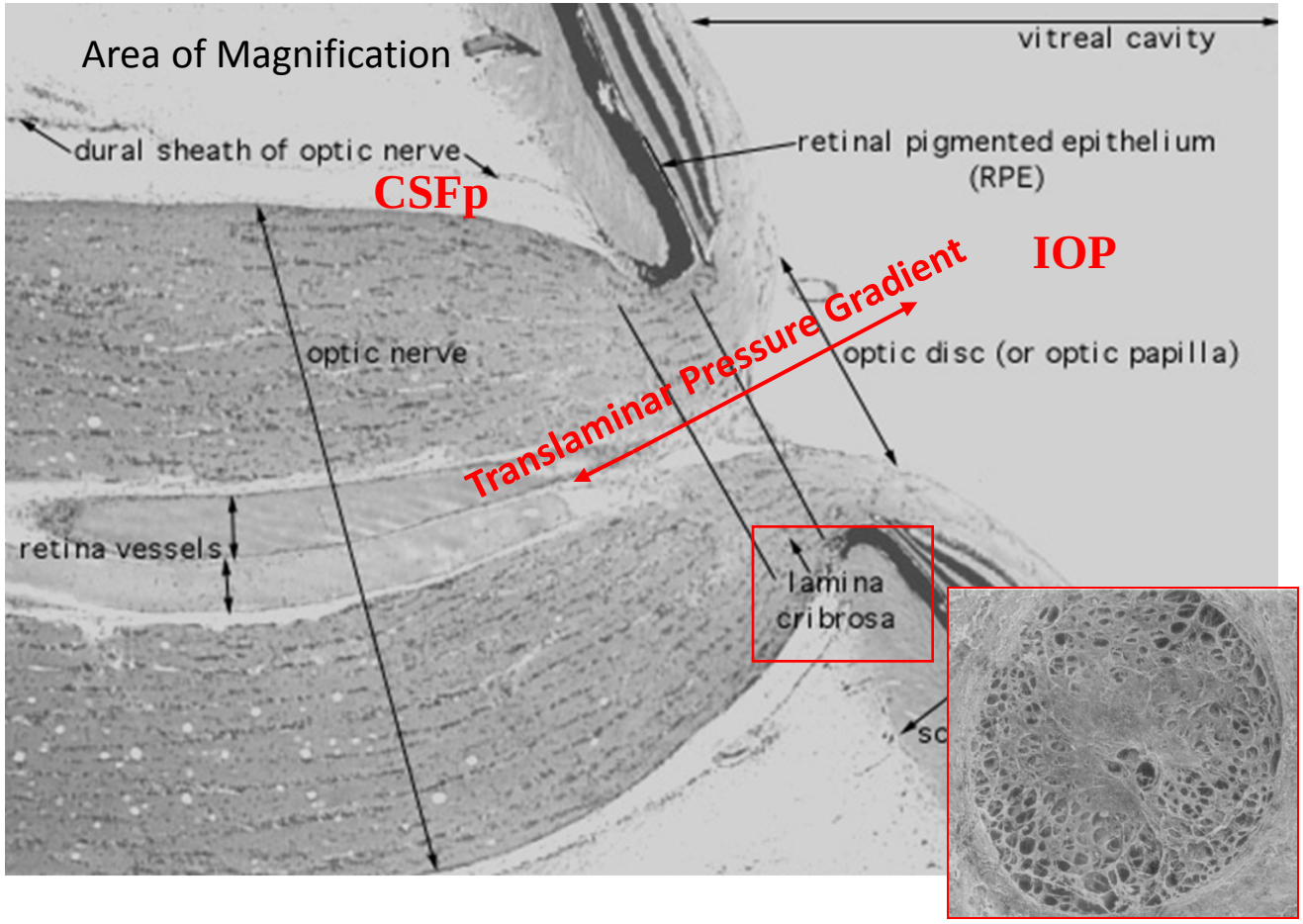
The Translaminar Pressure Gradient: A Mechanism for Papilledema

Area of Interest:

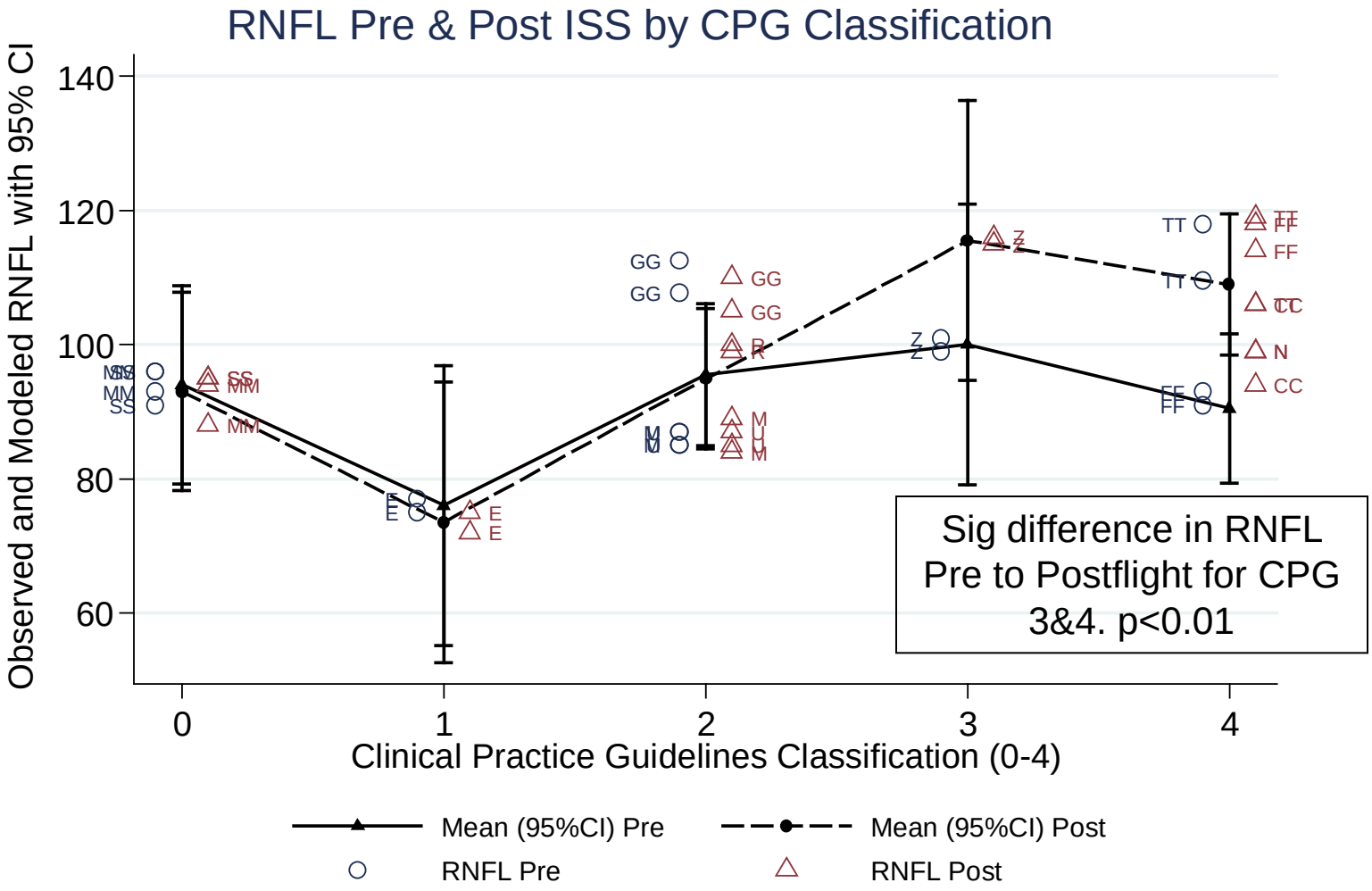


Translaminar Pressure Gradients:



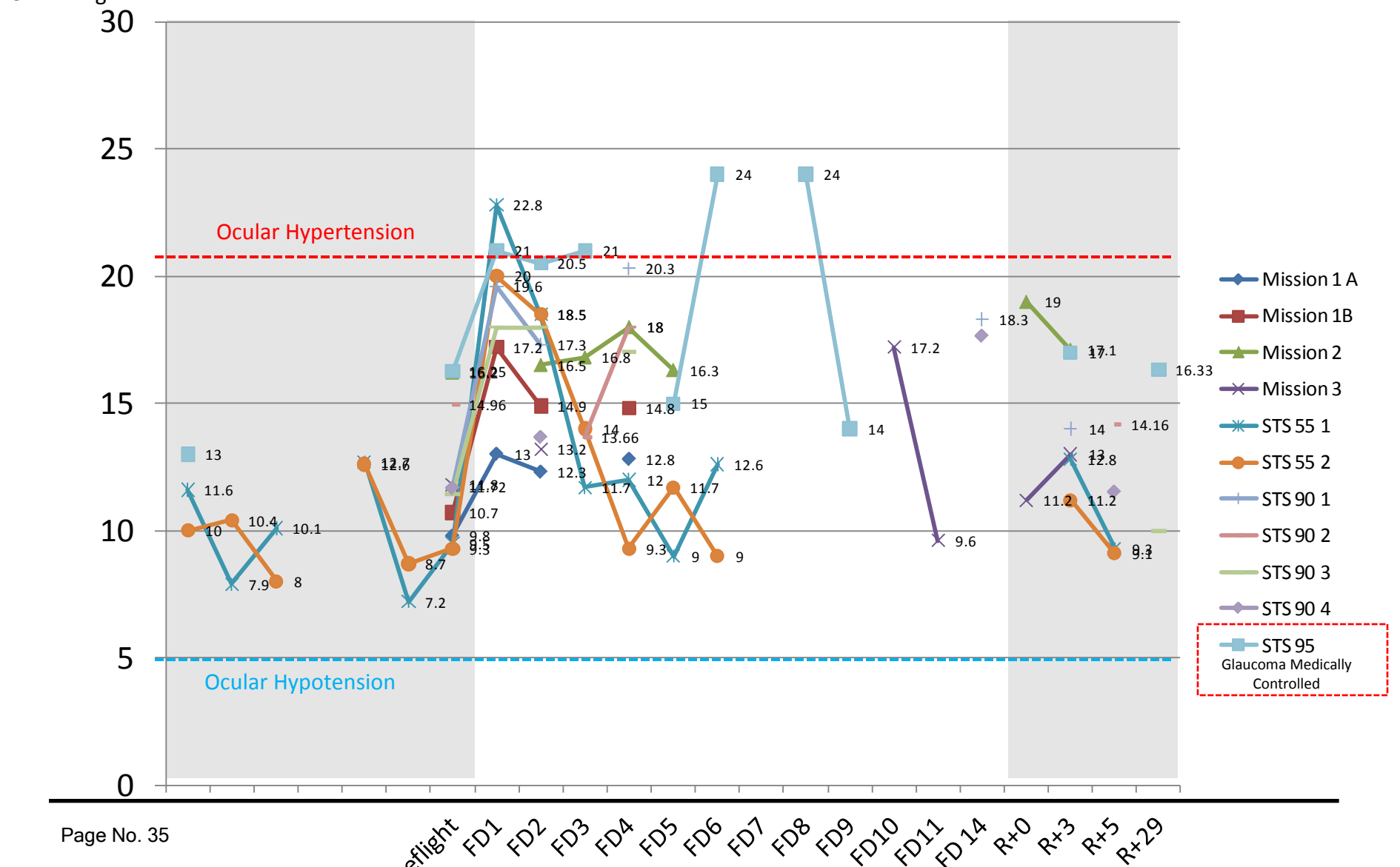


OCT: Average RNFL Change in VIIP Cases Pre to Postflight

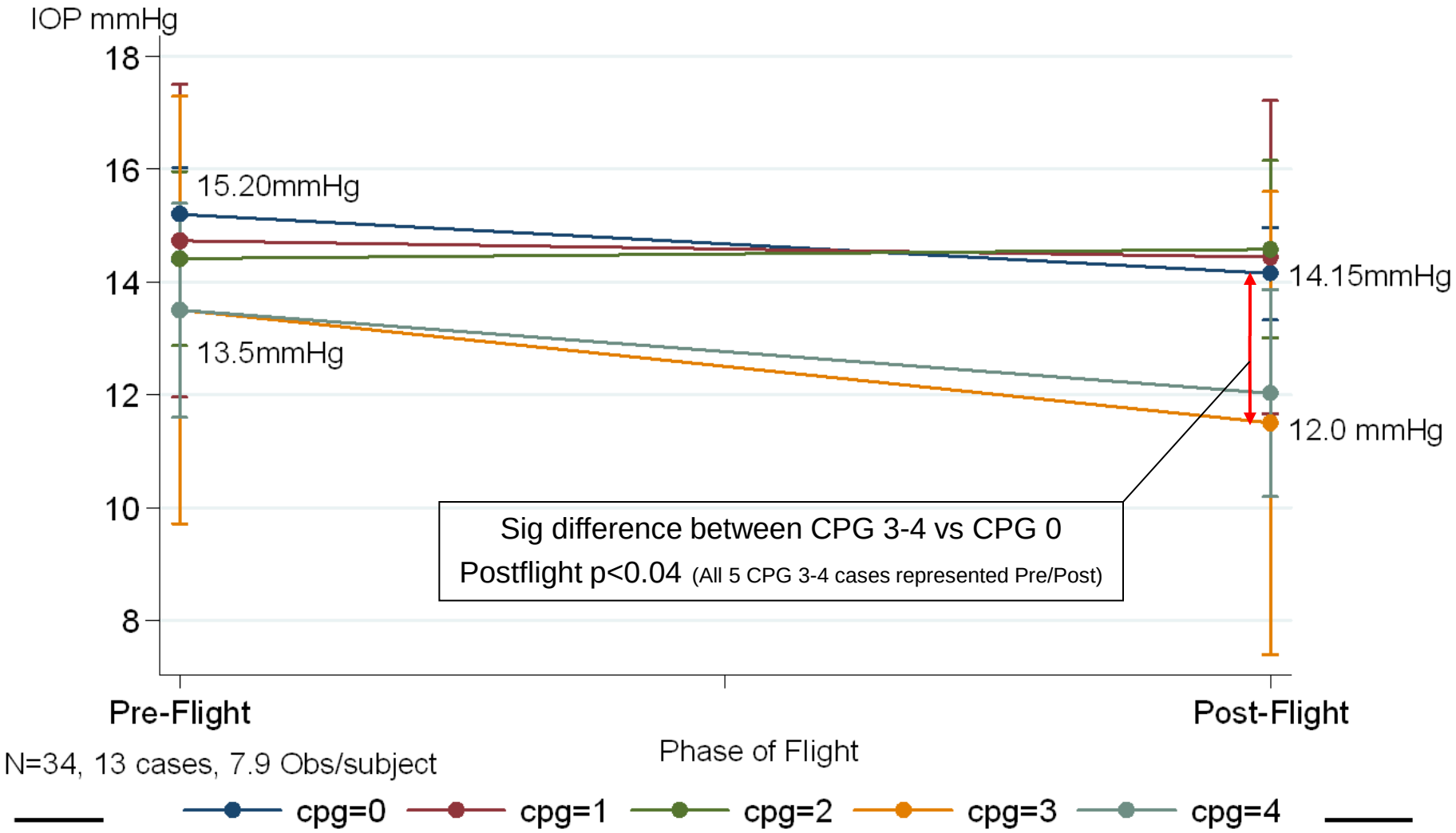


IOP for Six Shuttle Missions (12 Subjects)

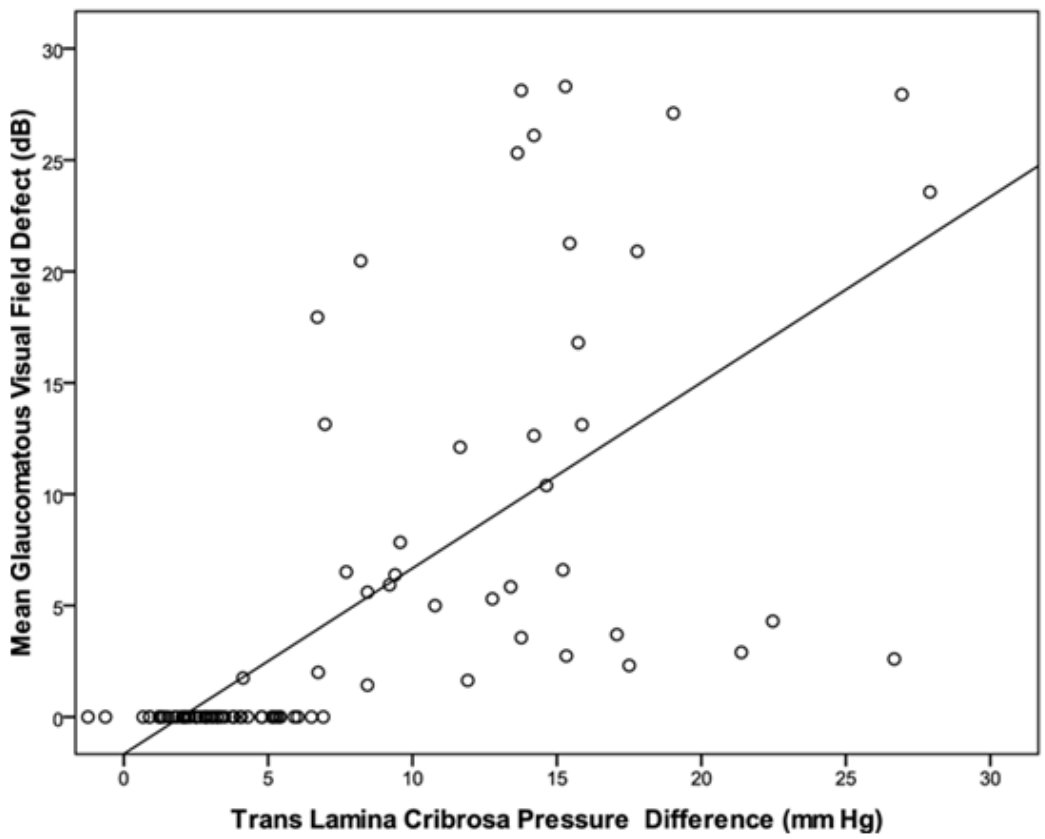
Pre-flight, In-flight-Post-flight



Mean IOP Pre & Postflight in ISS Crew per VIIP CPG: Does Low IOP Predispose to Papilledema Formation?



Translaminar Pressure Difference & Visual Field Defect



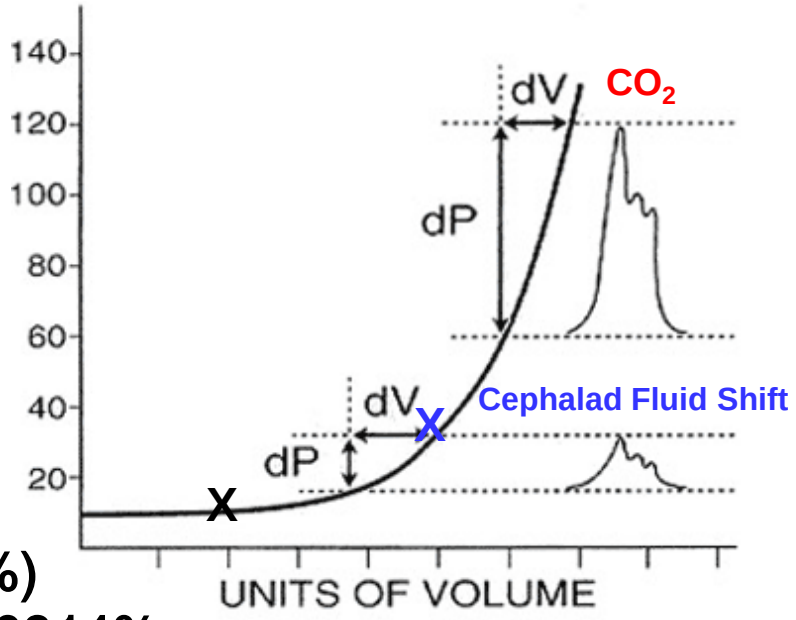
Examples:

ICP	IOP	TLP	Delta
10	15	-5	5
25	17	+8	13
35	17	+18	23

- Amount of glaucomatous visual field defect correlated positively with the TLP pressure difference (P _ 0.005) r=0.69

CO_2 Levels on ISS

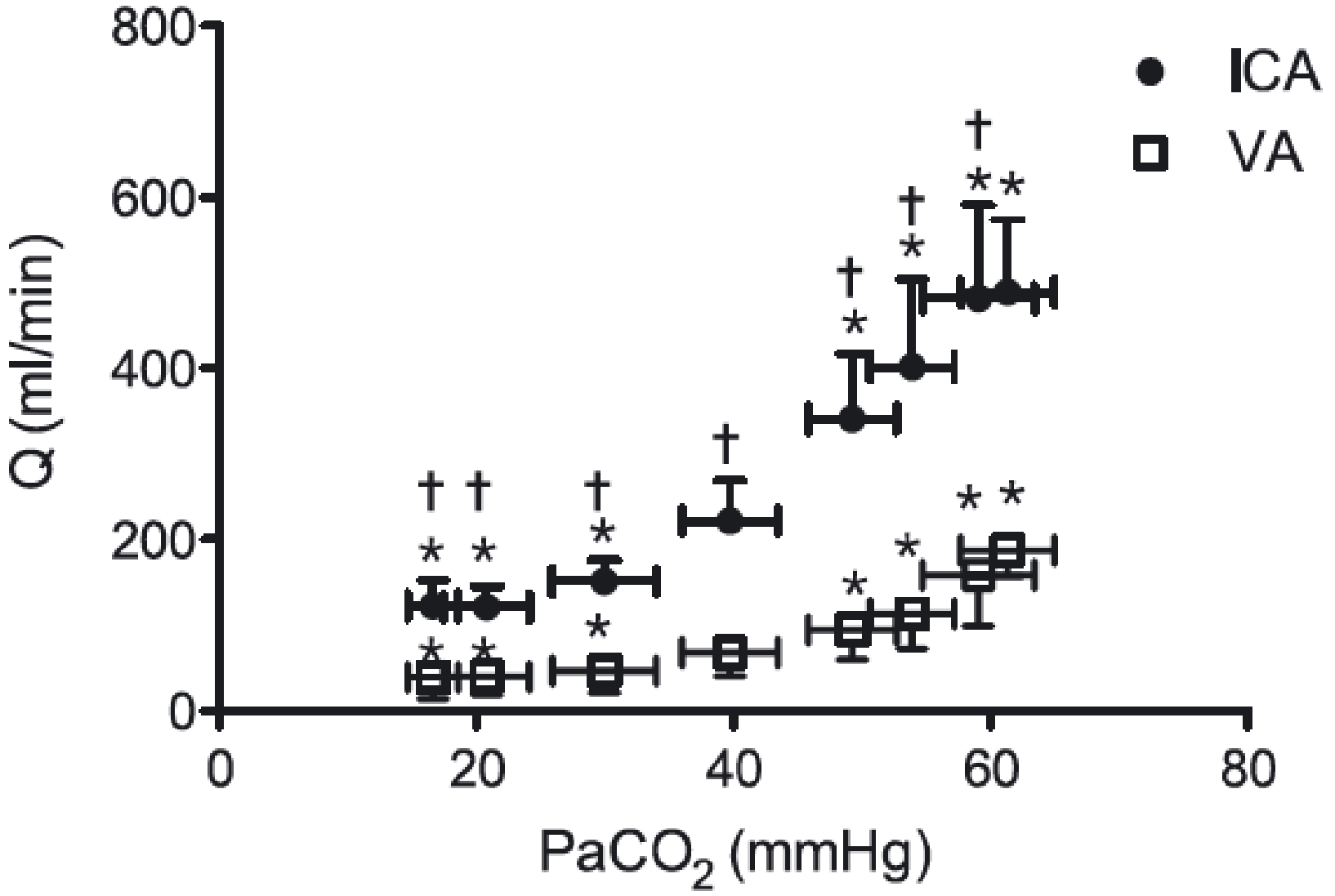
Adapted from Alperin et al. Radiology, 2000

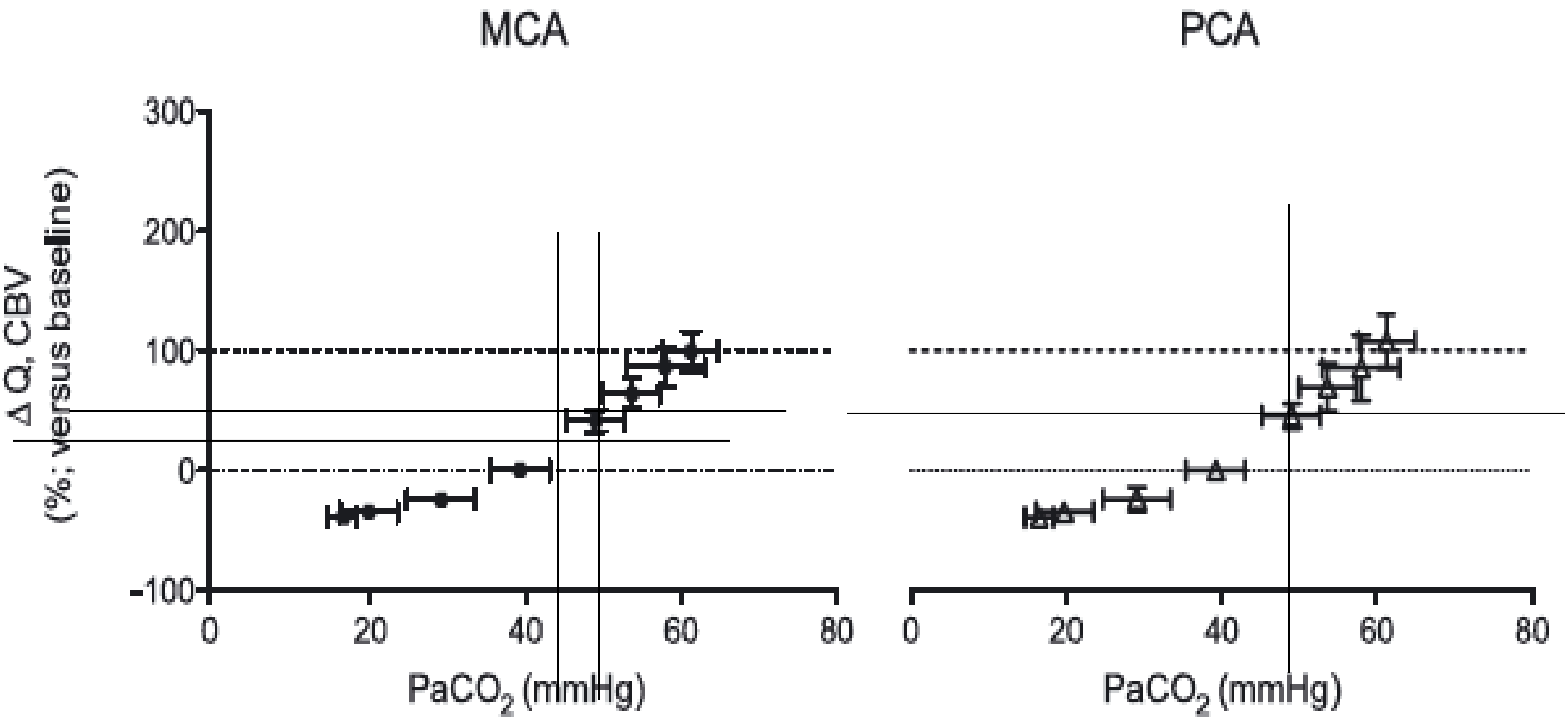


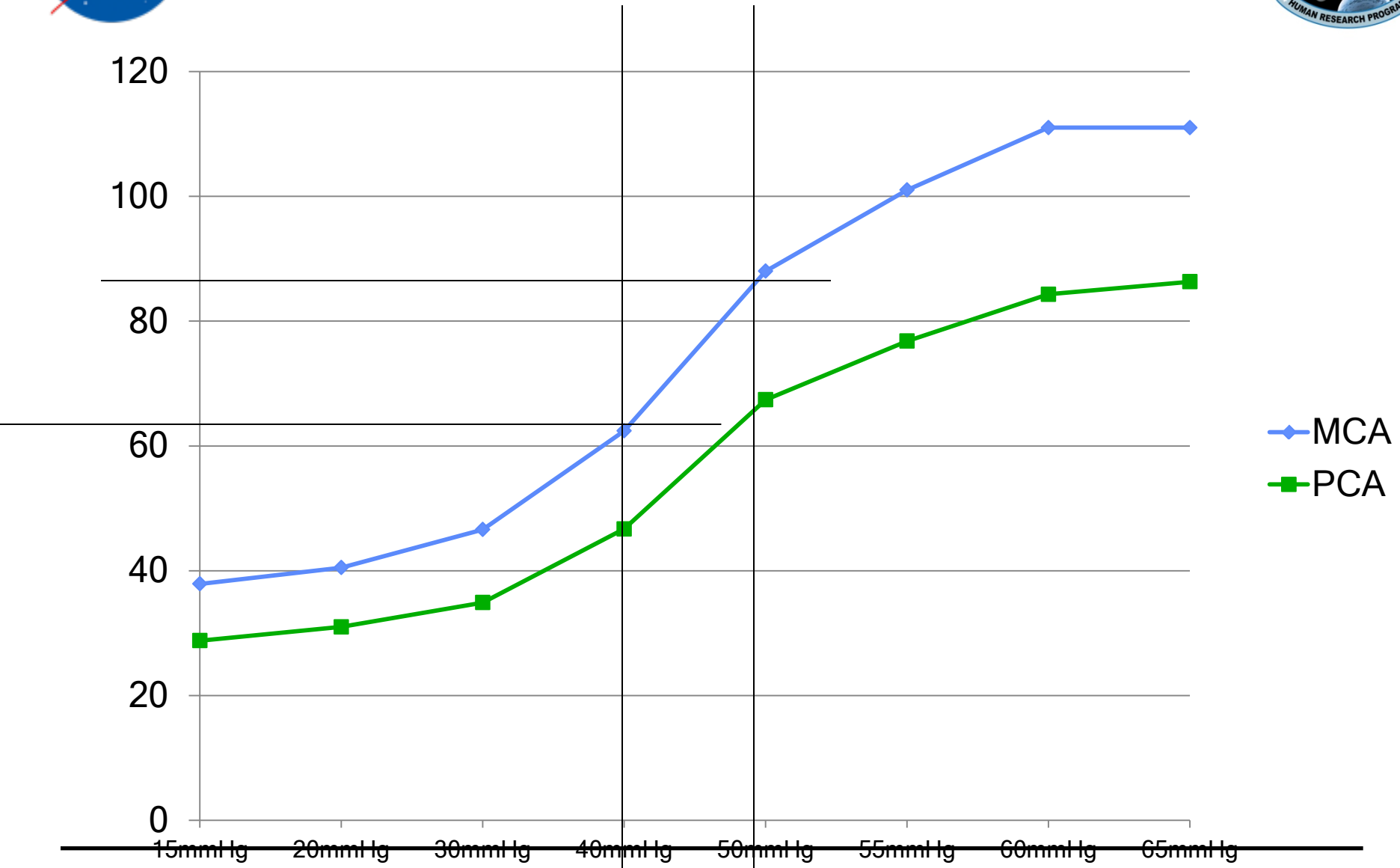
- **CO_2 is an extremely potent vasodilator**
  - Every 1mmHg increase $PaCO_2$=4% increase in dilation

- CO_2 mission average=3.56mmHg **(0.33%)**
  - 10x normal sea level atmospheric: **0.0314%**
  - Average Peak CO_2=8.32mmHg **(0.7%)** (20x)

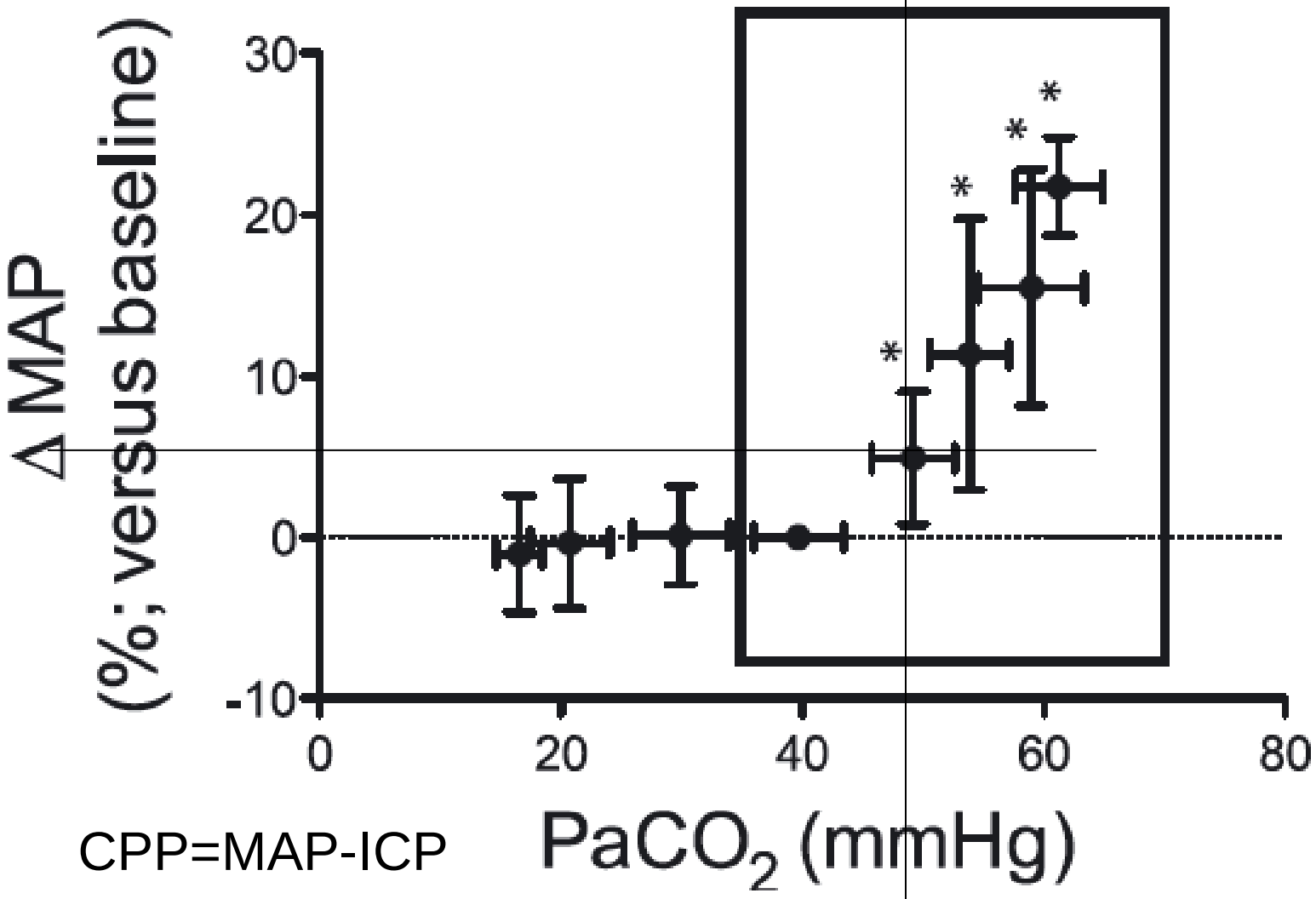
- ***CO_2 may cause increased CSF production due to increased flux of $HCO3^-$ across choroid plexus & accompanying H2O***


800
600
400
200
0
Q (ml/min)
0
20
40
60
80
PaCO2 (mmHg)
ICA
VA


MCA
PCA
300
200
100
0
-100
Δ Q, CBV
(%; versus baseline)
0
20
40
60
80
PaCO2 (mmHg)
0
20
40
60
80
PaCO2 (mmHg)

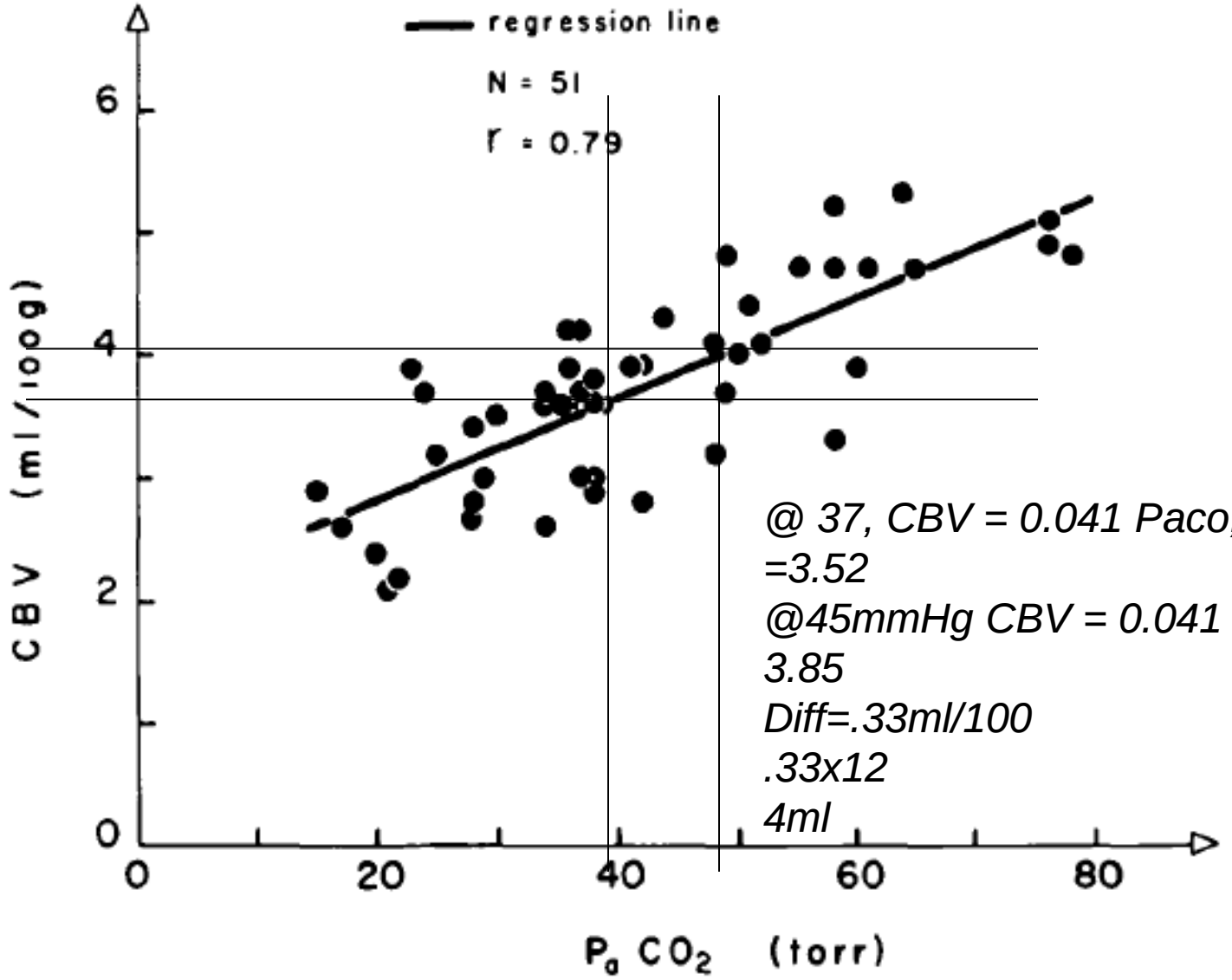

120
100
80
60
40
20
0
15mmHg
20mmHg
30mmHg
40mmHg
50mmHg
55mmHg
60mmHg
65mmHg
MCA
PCA

Increased BP with Elevated CO2 Causing Decreased Compliance



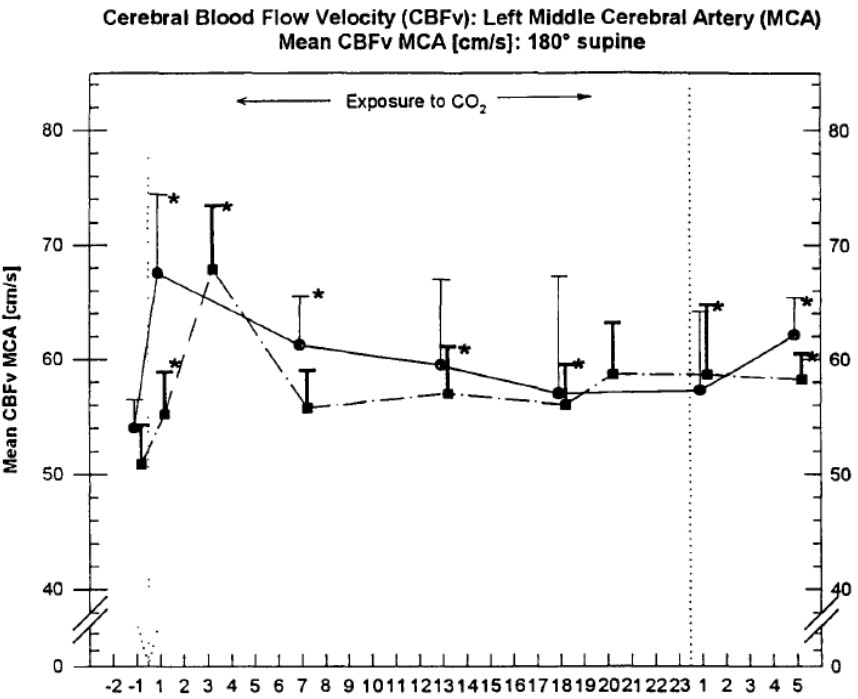
CPP=MAP-ICP

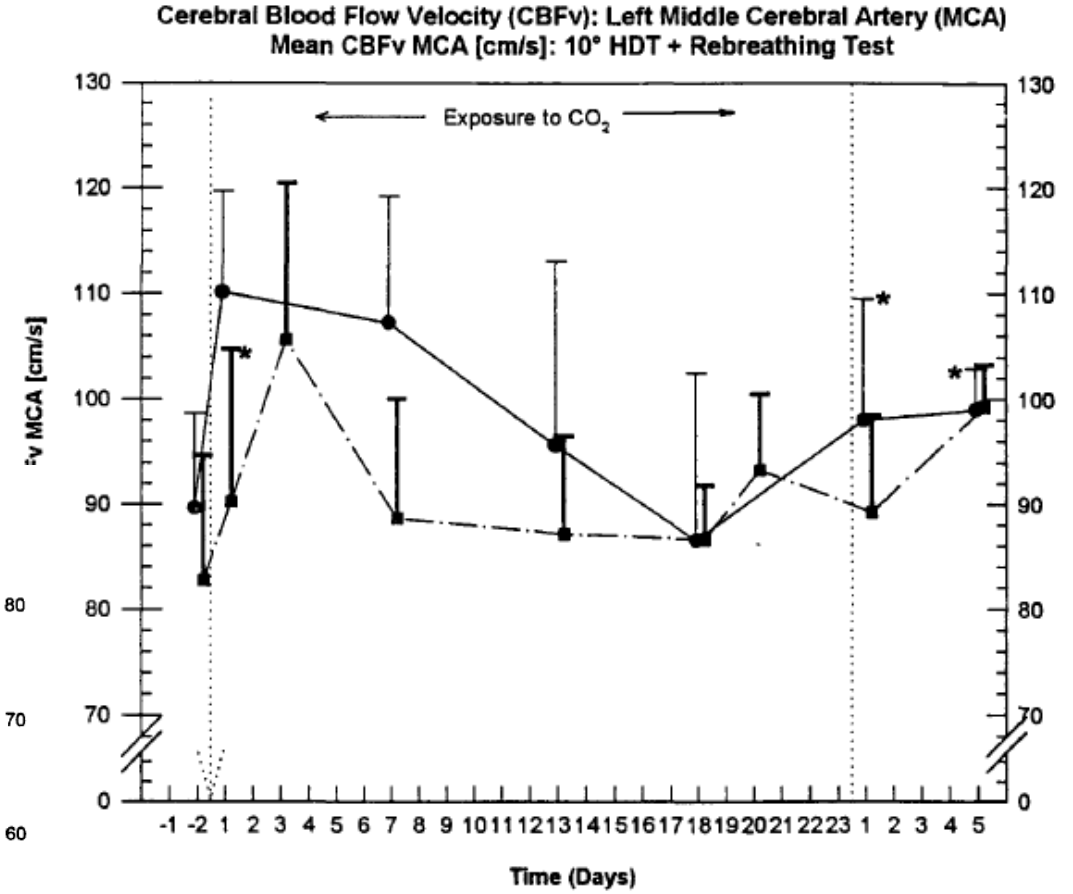
Cerebral Blood Volume Change with Changing PaCO2

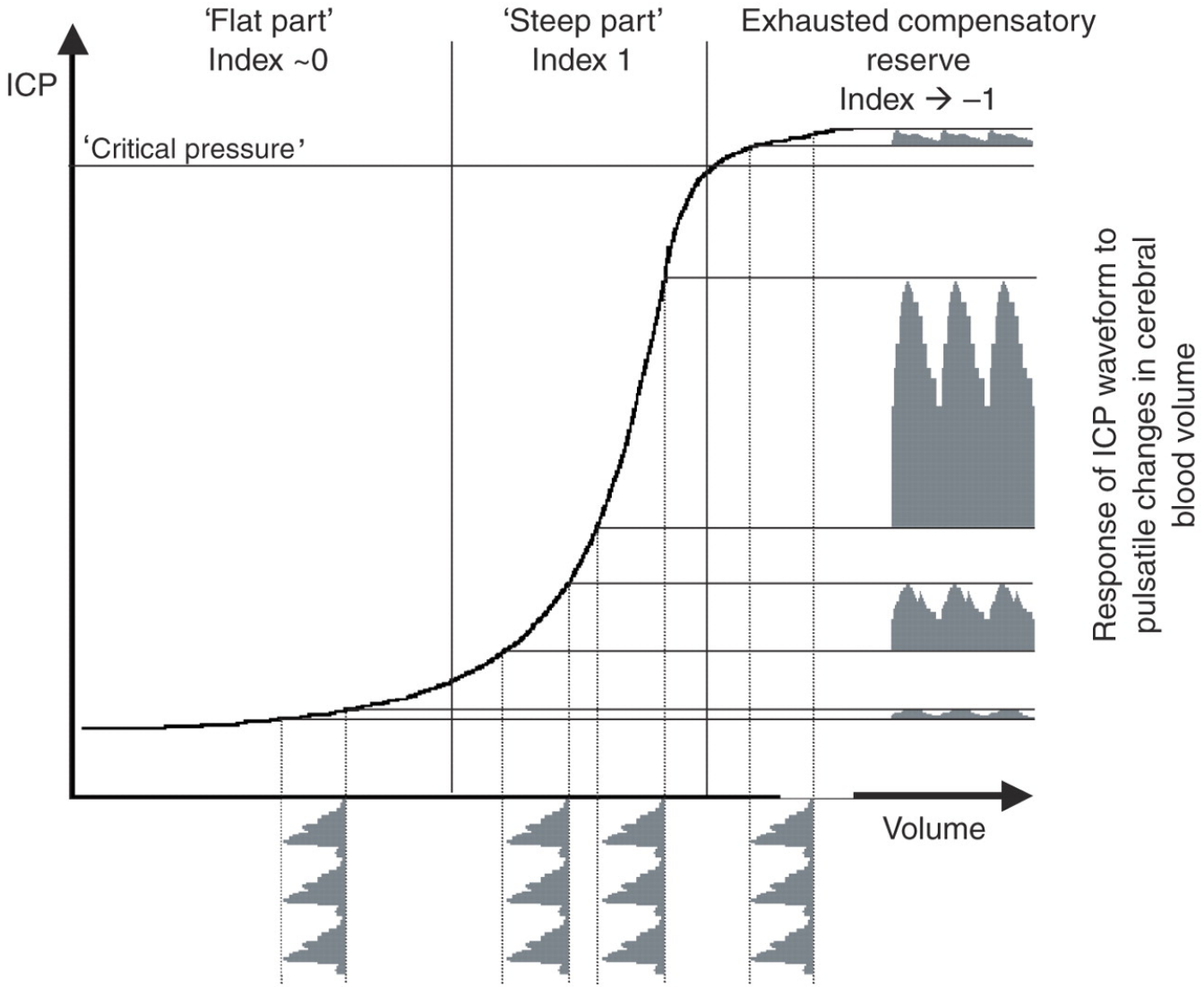


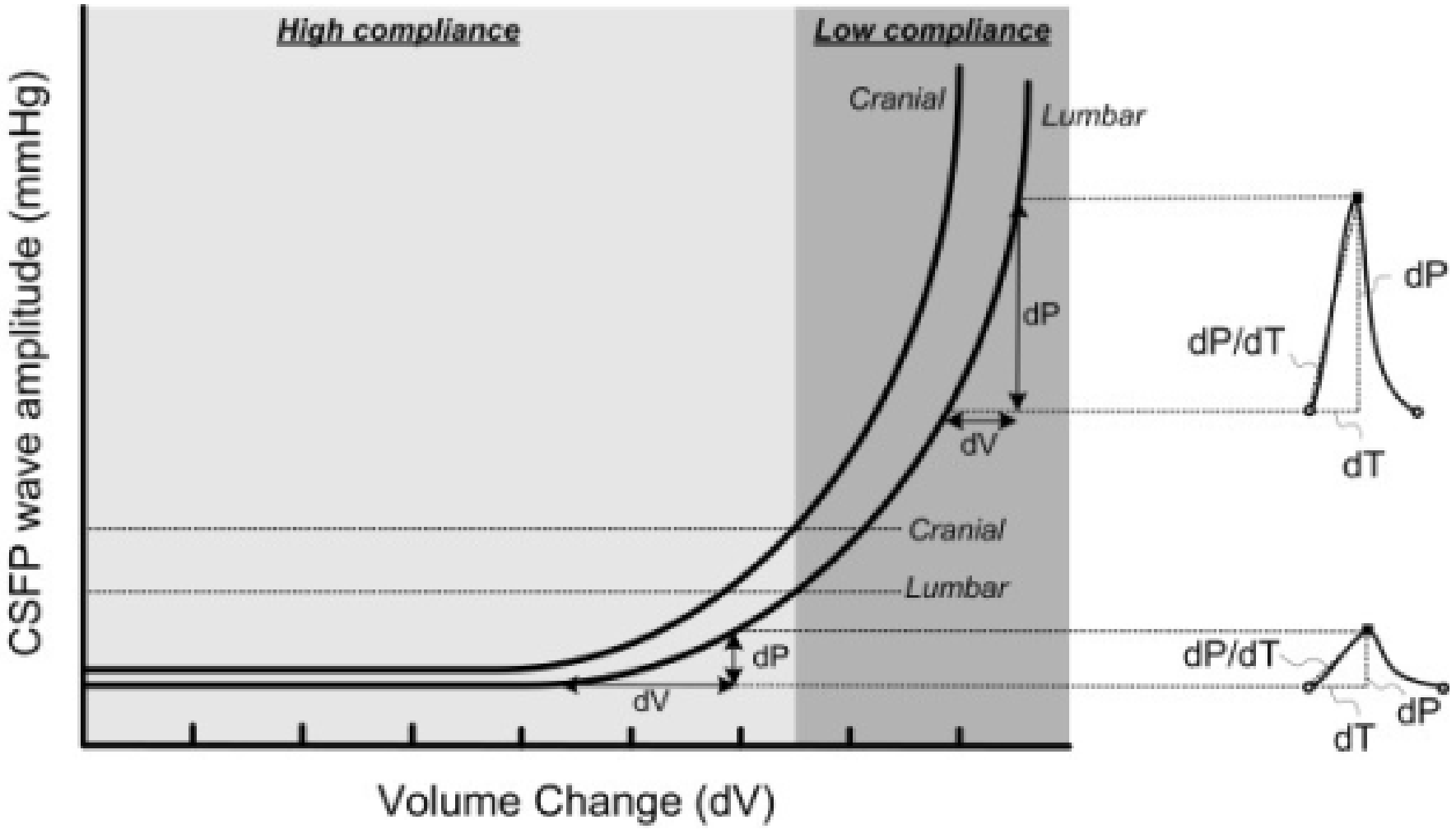
@ 37, CBV = 0.041 Paco,+ 2 =3.52
@45mmHg CBV = 0.041 Paco,+ 2 3.85
Diff=.33ml/100
.33x12
4ml

Cerebral Blood Flow Velocity During Hypercapnia &10° HDT + Hypercapnia






'Flat part'
Index ~0
'Steep part'
Index 1
Exhausted compensatory reserve
Index → –1
ICP
'Critical pressure'
Volume
Response of ICP waveform to pulsatile changes in cerebral blood volume
Pulsating changes in cerebral blood volume


High compliance
Low compliance
Cranial
Lumbar
dP
dV
dP/dT
dP
dT
Cranial
Lumbar
dP
dV
dP/dT
dP
dT
CSFP wave amplitude (mmHg)
Volume Change (dV)

Data mining – Contributions of CO_2 to the VIIP syndrome

- **PI:** TBD
- **Aims:** This retrospective data mining effort will evaluate the in-flight CO_2 levels during flight with the time course of identified visual changes experienced by crew members to determine if increase CO_2 levels could be a contributing factor to the VIIP syndrome.

- Zwart et al. 2012 found a difference in CO2 concentrations between cases and non-cases:
  - In-flight cabin CO2 concentrations were higher ($P < 0.05$) for OC+ (N=5) than OC- astronauts (N=15).

	FD15	FD30	FD60	FD120	FD180
Cabin CO_2, *mm Hg*					
OC-	2.6 ± 1.4	2.9 ± 1.3	2.9 ± 0.9	2.6 ± 1.2	2.9 ± 0.6
OC+ *	3.6 ± 0.7	3.7 ± 0.5	3.8 ± 0.5	3.3 ± 0.8	3.1 ± 1.1

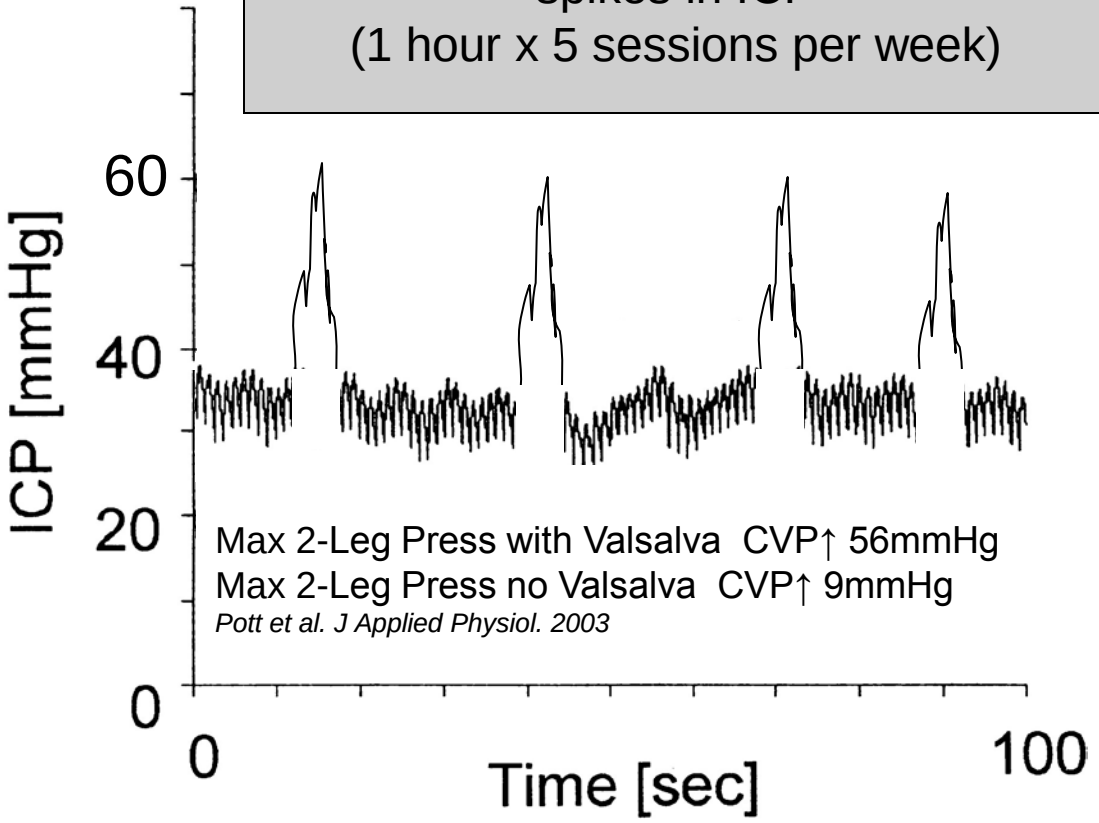
* $P < 0.05$

Zwart et al. Journal of Nutrition. Feb 2012.

Limit Resistive Training:

Resistive Exercise
Does in-flight resistance training cause additional transient elevations in ICP?

Resistive Exercise Repetitions causing spikes in ICP
(1 hour x 5 sessions per week)



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- N=27 Astronauts, mean time to MR imaging was 606 days +/- 822
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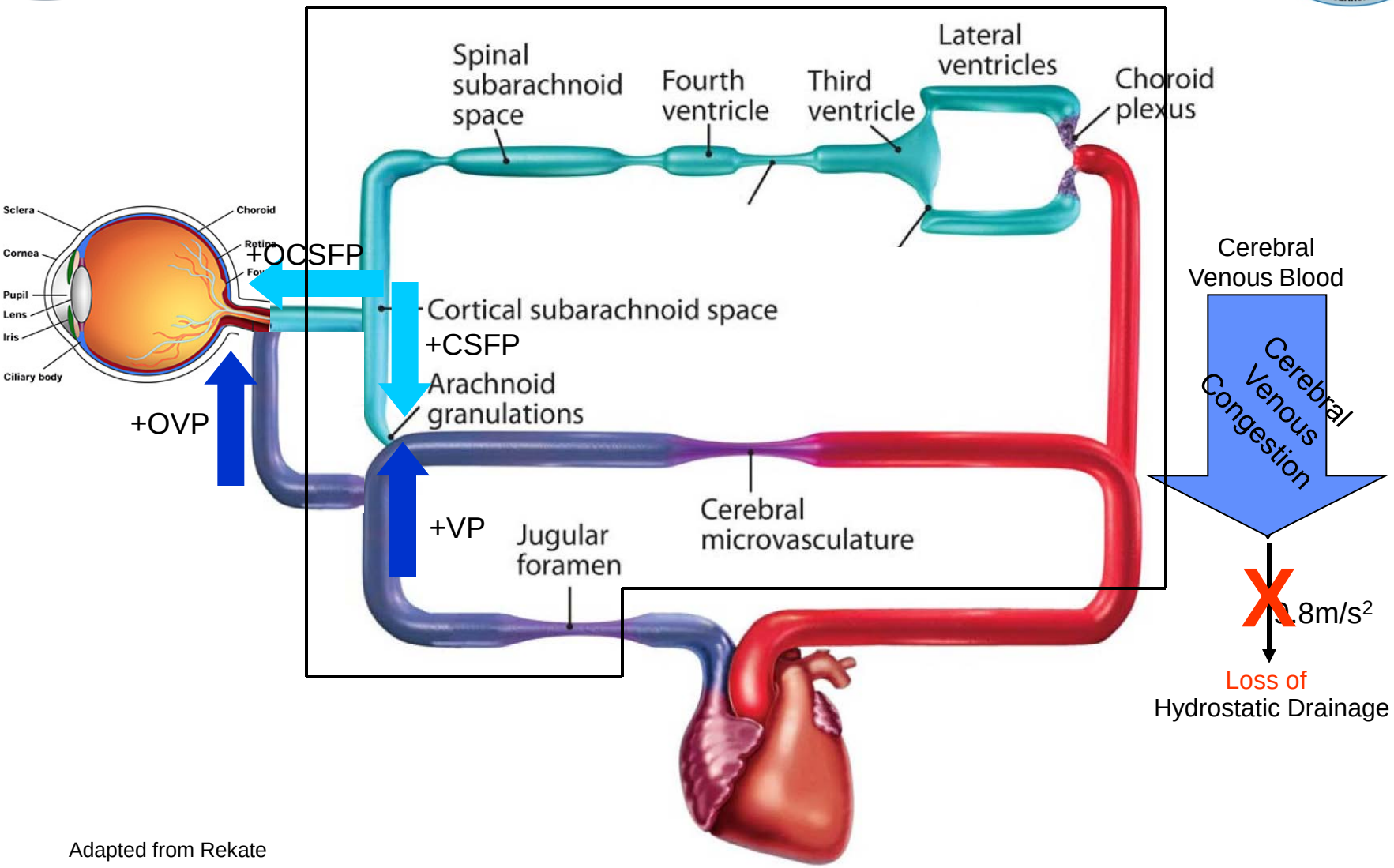
Cumulative Lifetime Exposure to Microgravity Relative to Imaging Findings

Time in UG	No. Subjects	Globe Flattening	Optic Nerve Sheath Kinking	ONSD>5.9 mm	Optic Disc Protrusion	Moderate or Greater Pituitary Concavity
<30d (Short)	12	1	1	5	0	0
>30d (Long)	15	6	3	9	4	3

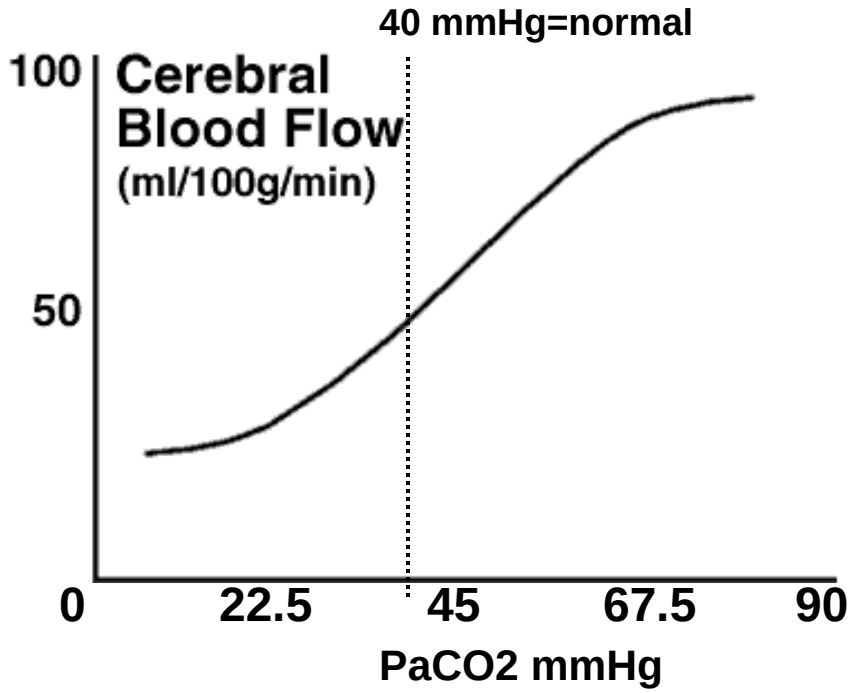
A Working Model: Potential Interaction of the CNS, Vascular, & Ocular System in the VIIP



Adapted from Rekate

Supplemental O2 as a Treatment Option

- As the arterial tension of CO2 rises, CBF increases, when it is reduced vasoconstriction is induced.
- Hyperventilation can lead to a mean reduction in intracranial pressure of about 50% within 2-30 minutes.



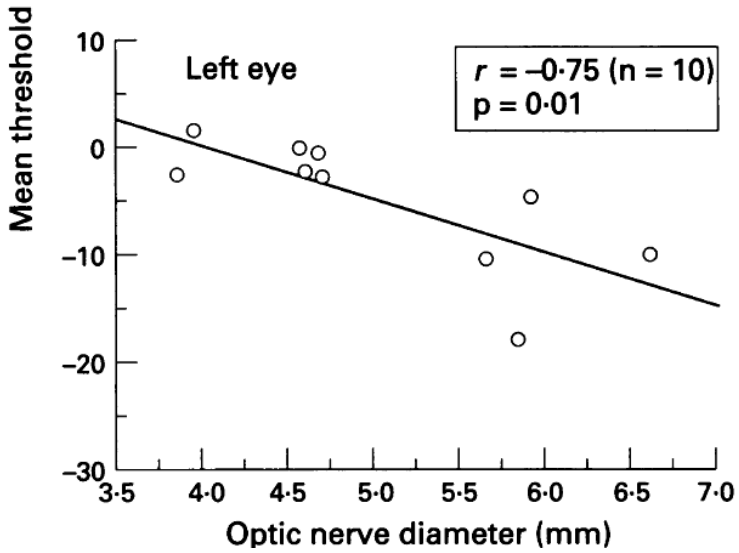
Supplemental O2 to drive down PaCO2 & venous congestion/ICP

Ruben B H. "Intracranial hypertension" in *Advances in Anaesthesia.* Edit. Gallagher T J. p.1, London Year Book Medical Publishers Inc. 1984.

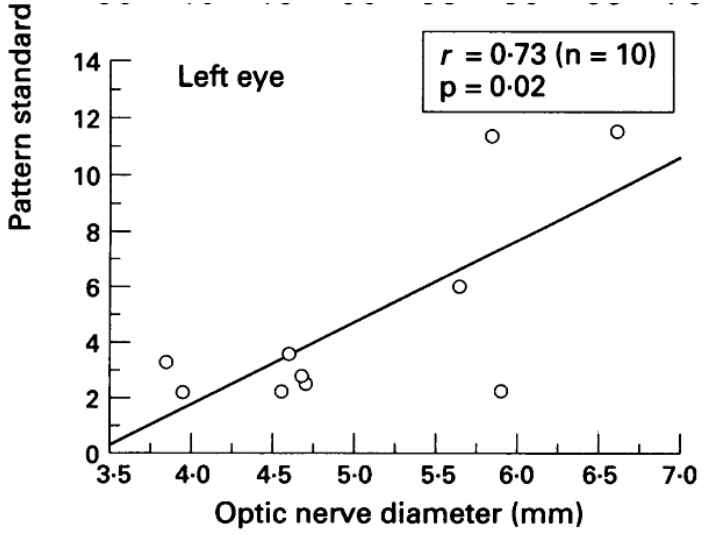
Correlation of ONSD & Visual Field Deficit

- T. Salgarello et al. *Optic nerve diameters and perimetric thresholds in idiopathic intracranial hypertension.* British Journal of Ophthalmology 1996;80:509-514
- 20 patients with IIH (mean age=47) papilledema grade 1.1(range 0-4), 20 controls
- CSF pressure=260-320mmH2O, Mean duration disease=7.65 years
- Perimetric defects in 70% of eyes (28/40)
- Deficit associated with papilledema grade

MD: Average deviation from age matched controls

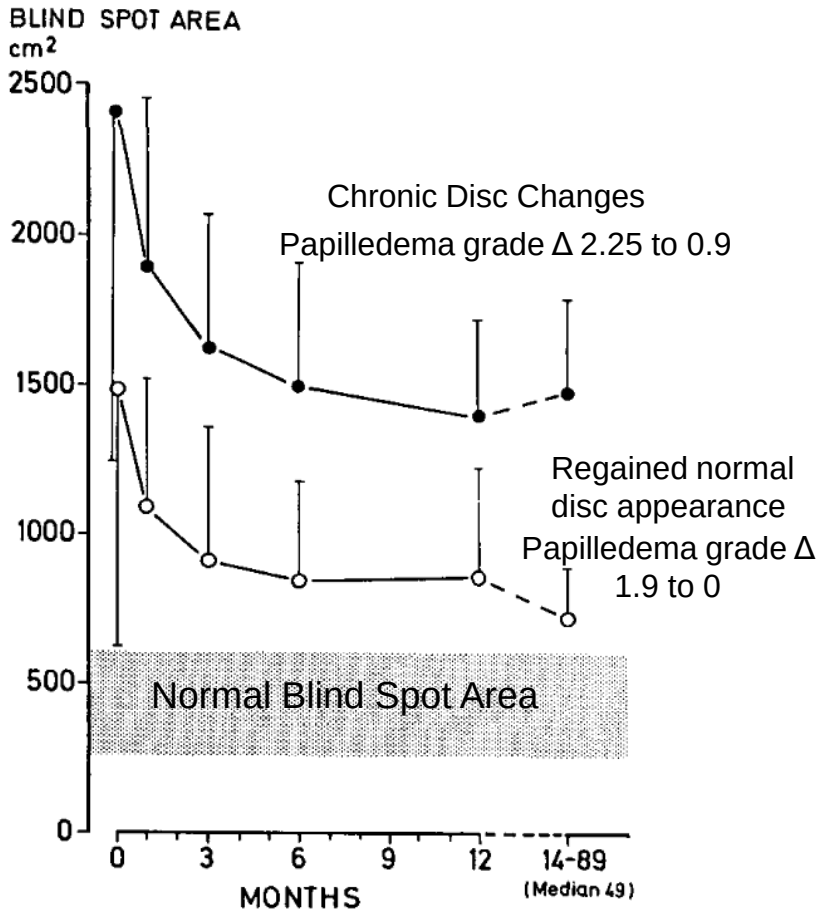


PSD: Measure of visual field irregularities



Blind Spot Enlargement Following Papilledema

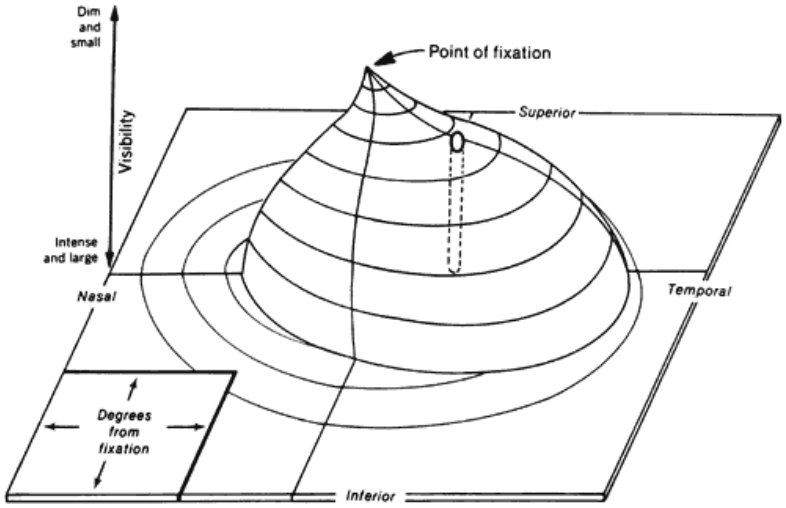
- Sorenson et al. **Clinical course and prognosis of pseudotumor cerebri. A prospective study of 24 patients.** Acto Neurol Scand., 1988:77:164-172
- 24 IIH patients, symptoms present 1-30 months
- Median CSFp=25mm Hg (range 8-45), all had papiledema initially
- Followed for 49 months, treated with Diamox and diuretics 6-18 months
- Patients who regained normal disc (50%) had shorter duration of disease (median=4 months) vs those who developed chronic changes (median=12months)
- Visual field testing not conducted



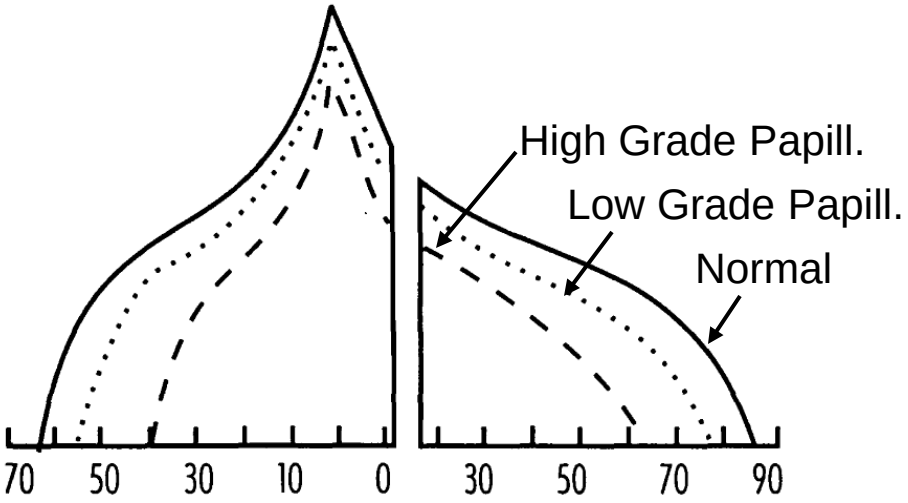
Visual Loss Associated with Papilledema Grade

- *M.Wall.* **Asymmetric Papilledema in Idiopathic Intracranial Hypertension: Prospective Interocular Comparison of Sensory Visual Function.** IOVS, Jan.1998, Vol. 39, No. 1
- 9 IIH patients (mean age=31.8) with asymmetric papilledema 2+ grade diff.
  - High grade=3 (2-5) vs Low grade=1 (0-2)
- Mean CSFp=347.2 mm H2O
- Visual loss most prominent in eye with higher grade papilledema
- High grade papilledema should be regarded as a risk factor for visual loss

The Visual Island



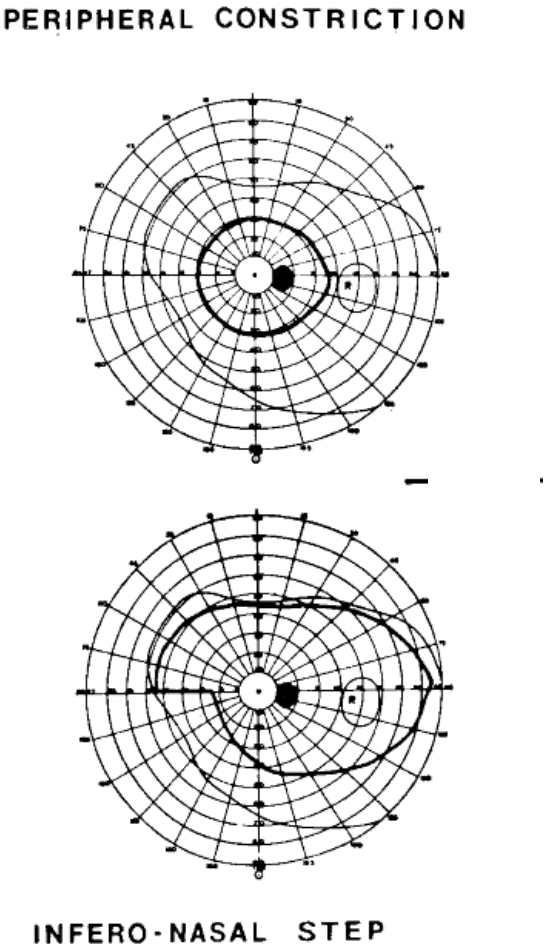
Depression of the visual island with increasing papilledema grade



Profile Perimetry

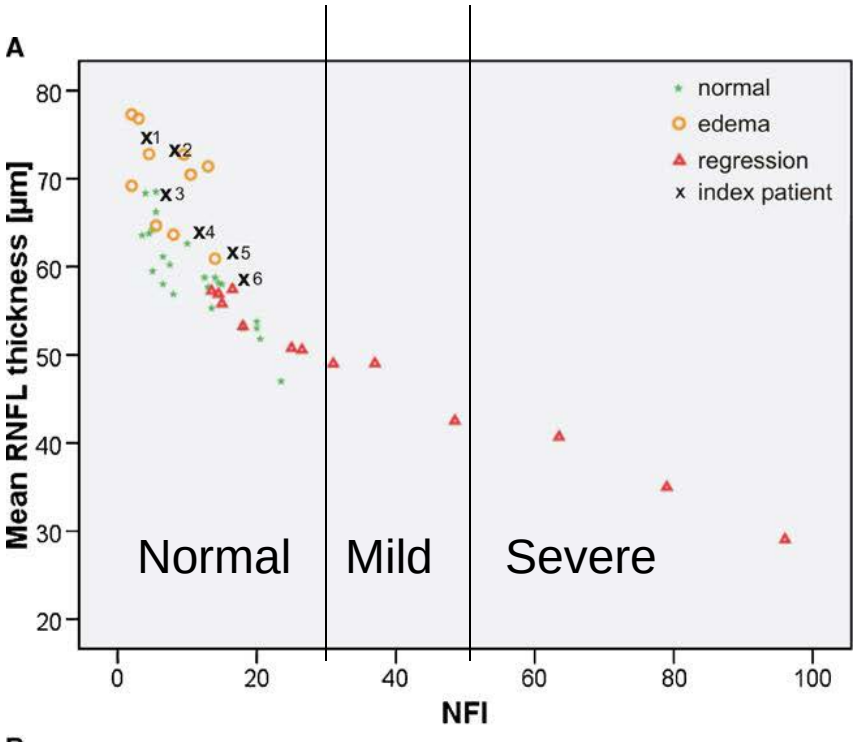
Mild Papilledema and Visual Field Loss

- *G. Rebolleda* et al. ***Follow-up of Mild Papilledema in Idiopathic Intracranial Hypertension with Optical Coherence Tomography.*** IOVS. 2009 Vol 50, No 11
- N=22, mean age=40, recent diagnosis of IIH
- Mild papilledema, mean= Frisen 2 (range 1-3)
- Mean CSFp=35cmH2O (range 25.5-45)
- 1 Year follow-up:
  - Perimetry: 66% normal VF, 18% enlargement blind spot, 16% irreversible field loss
  - OCT: 10 RNFL thinner than normal (3 visual field constriction, 3 inferonasal defects, 1 had a scotoma)
- RNFL swelling and attrition may occur simultaneously
- Perimetry needed with OCT, since OCT cannot distinguish between decreased swelling vs axonal loss
- *Both OCT and perimetry required for F/U*



Visual Field Damage Following Regression of Papilledema

- R. Laemmer. ***Detection of nerve fiber atrophy in apparently effectively treated papilledema in idiopathic intracranial hypertension.*** Graefes Arch Clin Exp Ophthalmol (2010) 248:1787-1793
- 23 IIH patients, mean age 33.8, 23 controls
- Mean follow-up in patients with regression of papilledema=27 months
- 8/13 (63%) regressive papilledema group had mild-moderate concentric visual field damage-superior and inferior regions
- Patients with papilledema, only 1/10 detectable visual field loss
- Data show significant reduction RNFL as a sign of axon loss in patients with apparently treated papilledema
- Minor loss of axons will be masked by structure of retina, with overlapping receptive fields. Thus, 40% of RNFL may be lost before occurrence of visual field damage



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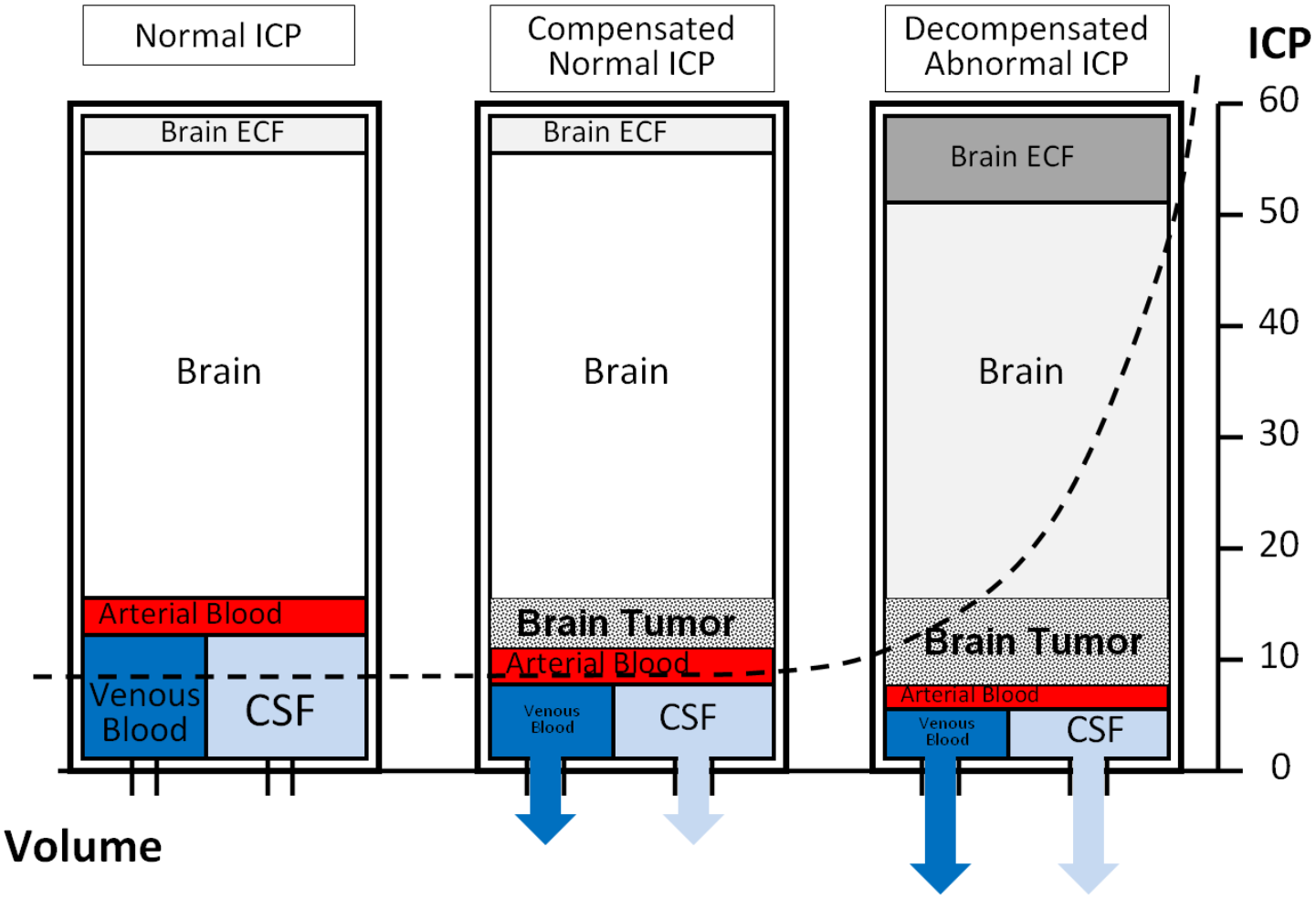
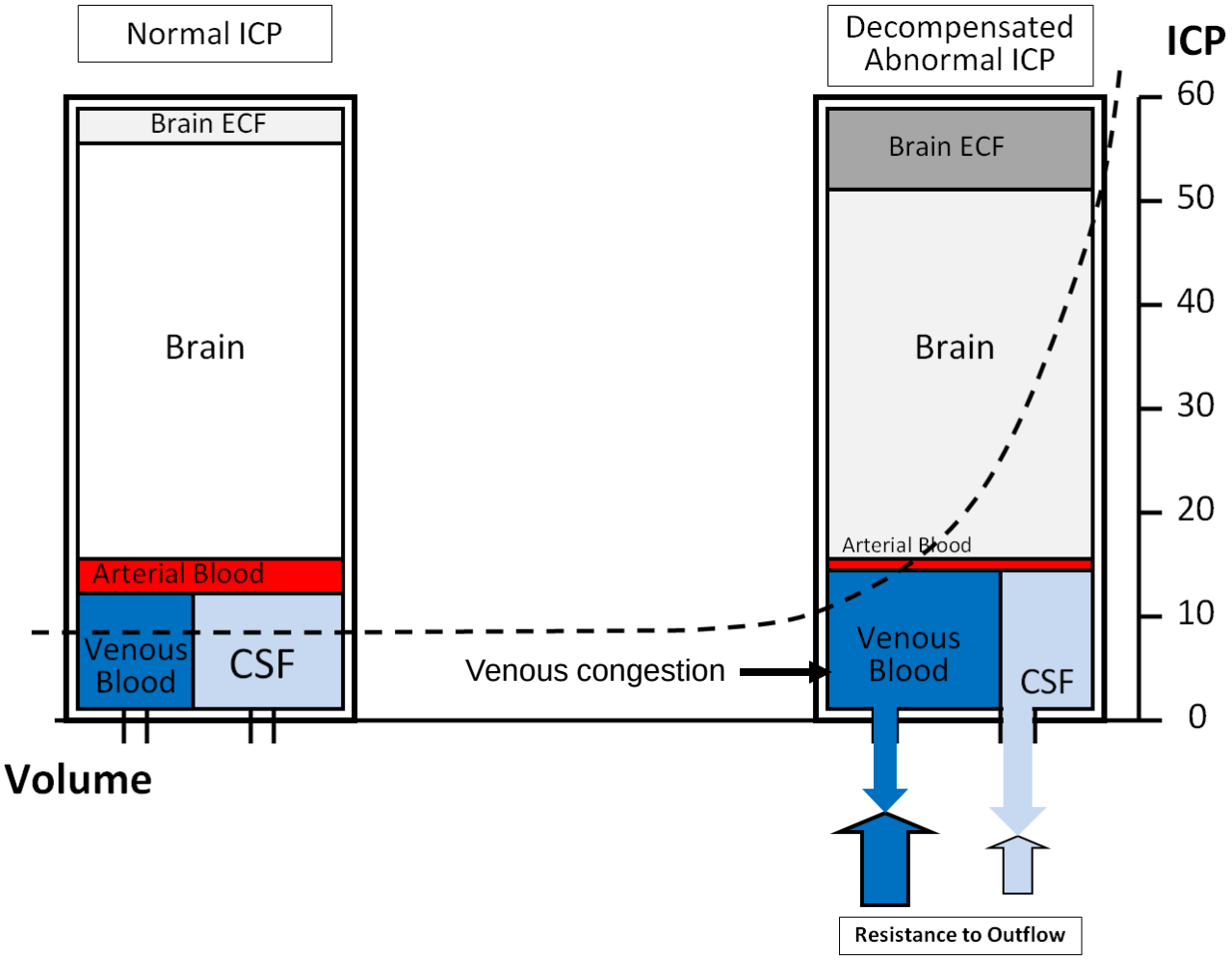
Monroe Kelly Principle & ICP

Accommodation of up to 120ml volume change while maintaining normal ICP



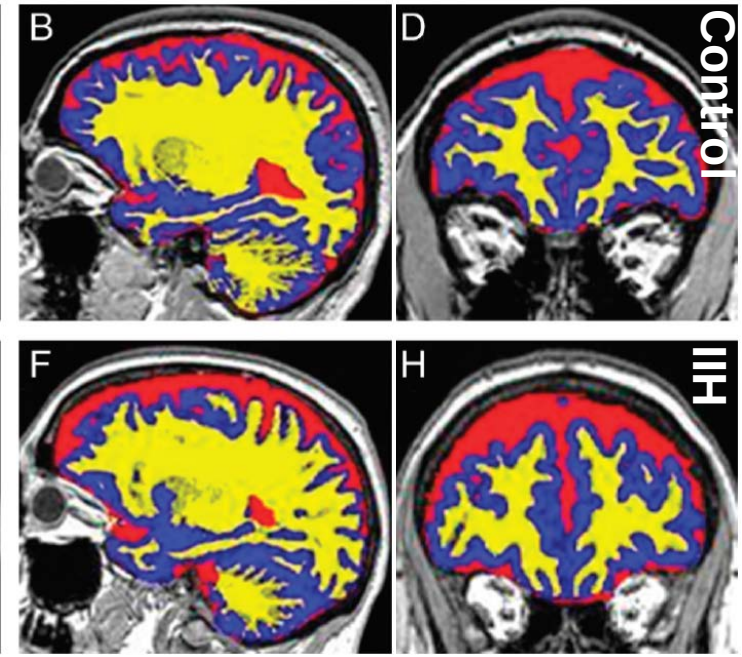
Fluid Shift & Inadequate Cerebral Venous & CSF Accommodation May Increase ICP in 0G



0G Cephalad fluid shift causes venous blood & CSF outflow resistance

Increased CSF Vol., Venous Congestion, & Increased interstitial Vol.

- Alperin et. al. *MRI Evidence of Impaired CSF Homeostasis in Obesity-Associated Idiopathic Intracranial Hypertension.* AJNR. July, 2012
  - 3D volumetric MR imaging
  - N=11 IIH newly diagnosed non-treated women vs N=11 overweight healthy women



Grey Matter=Blue
White matter=Yellow
CSF=Red

Cranial Volumetric Measurements

	ICCSF (mL)	EVCSF (mL)	GM (mL)	ICV (mL)	Nor VCSF (%)	Nor EVCSF (%)
Control (n = 11)	238 ± 25	220 ± 24	557 ± 31	1332 ± 81	1.4 ± 0.5	16 ± 1
IIH (n = 11)	309 ± 56	290 ± 52	602 ± 57	1438 ± 124	1.3 ± 0.4	20 ± 2
P value	0.002	0.0011	0.038	0.029	0.511	0.0007

ICCSF:Intracranial CSF, EVCSF: Extraventricular CSF, GM: Grey Matter, ICV: Intracranial Vol, Nor VCSF: Normalized Ventricular CSF, Nor EVCSF: Normalized Extraventricular CSF

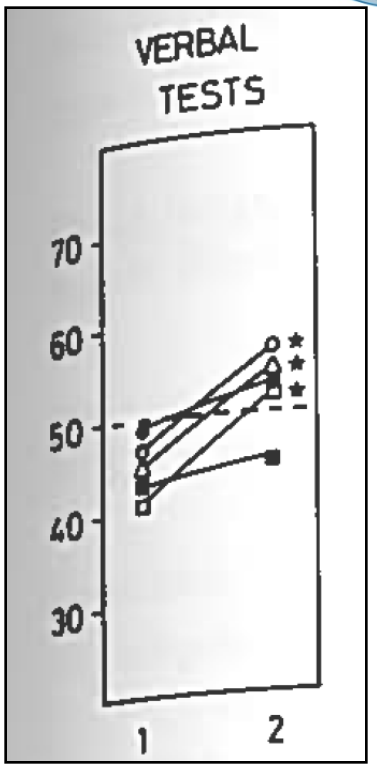
Arterial & Venous Volumetric Flow Rate Measurements

Subjects	TCBF (mL/min)	Total IJV (mL/min)	Nor IJV (%)
Control (n = 11)	789 ± 116	628 ± 72	81 ± 10
IIH (n = 11)	823 ± 68	532 ± 87	65 ± 7
P value	0.414	0.011	0.001

- Less venous volume draining via the IJV
- Likely increased drainage via secondary vessels
- Implying an increased resistance to venous outflow

Prolonged Elevations in ICP and Impaired Cognition

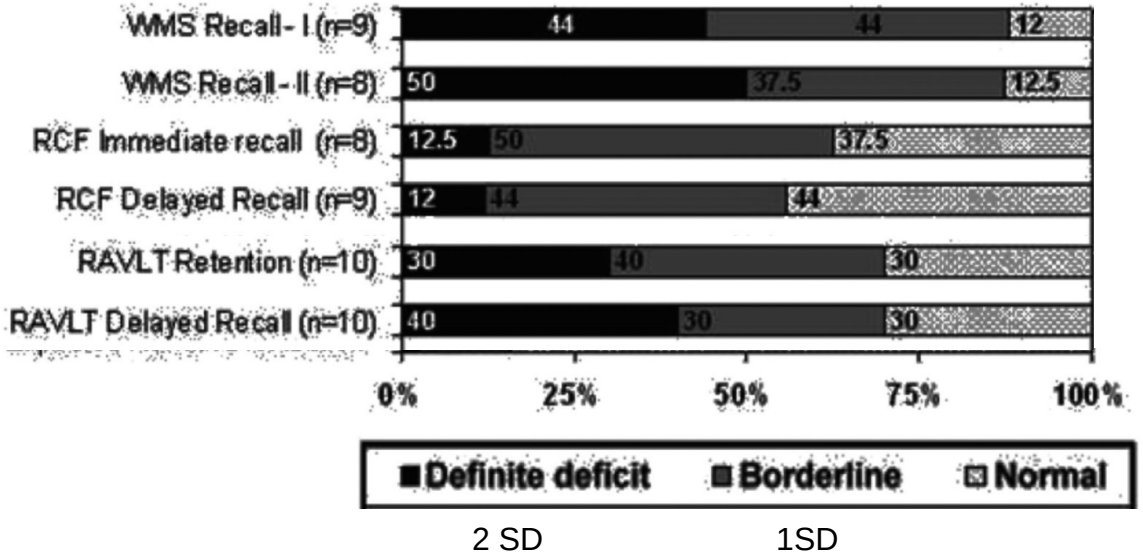
- Sorenson et al. *Persistent disturbances of cognitive functions in patients with pseudotumor cerebri.* Acta Neurol Scand. 1986
  - Prospective
  - N=5, mean papilledema 2, mean ICP 25.6 mmHg.
  - Difficulties in learning and memory for 6-30 months.
  - Testing showed a slight impairment in verbal tests.
  - At 12 month follow-up, after intensive medical or surgical treatment in 4/5 subjects the intellectual impairment reversed, and papilledema had resolved in 4 patients



- Walton, D. *Language deficits in patients with IIH.* Thesis.1999
  - Prospective
  - N=9, All subjects experienced mild deficits in short term memory and auditory processing of linguistic information.
  - Particular difficulty in following complex directions containing prepositional information and in immediate recall of words or numbers.

Prolonged Elevations in ICP and Impaired Cognition- Cont'd

- Kharkar et al. *Cognitive impairment in patients with pseudotumor cerebri syndrome.* Behavioural Neurology, 2011.
  - ✓ Retrospective N=10. Cognitively tested at presentation
  - ✓ 8

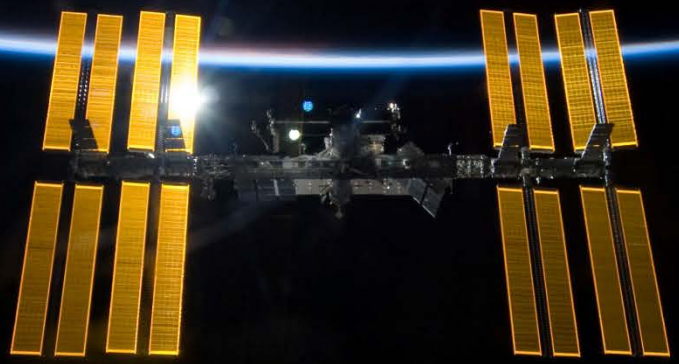


- Concept of cognitive reserve in mild Cognitive Impairment

THE VISUAL IMPAIRMENT INTRACRANIAL PRESSURE SYNDROME IN LONG DURATION U.S. ASTRONAUTS: EPIDEMIOLOGY AND PATHOPHYSIOLOGY

Christian Otto, M.D., M.Sc.
Lead Scientist, NASA VIIP Risk

Universities Space Research Association, Houston, TX,



Sensorimotor Workshop
NSBRI, Houston, TX
Thursday August 29, 2013.