DESH vs. Tap Test:

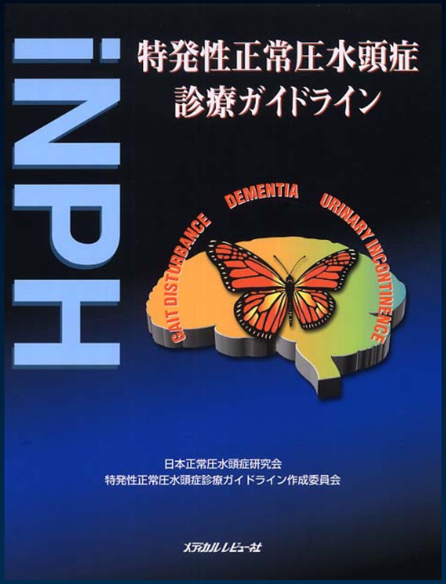
The impacts of DESH on clinical practice of NPH

Etsuro Mori, M.D., PhD
Dept. of Behavioral Neurology and Cognitive Neuroscience
Tohoku University Graduate School of Medicine

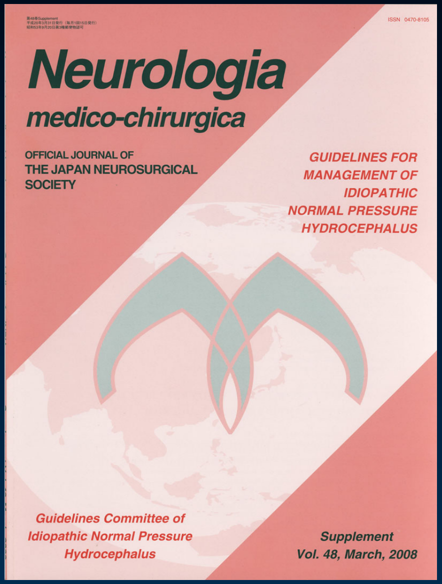
Introduction

- Adoption of DESH in the guidelines have changed clinical practice in Japan
  - The majority of iNPH is DESH
  - DESH differentiates iNPH from atrophy
  - Tap test or any other specific tests are not mandatory for the diagnosis
  - If a condition mimicking iNPH is not DESH, secondary NPH or non-communicating hydrocephalus is suspected

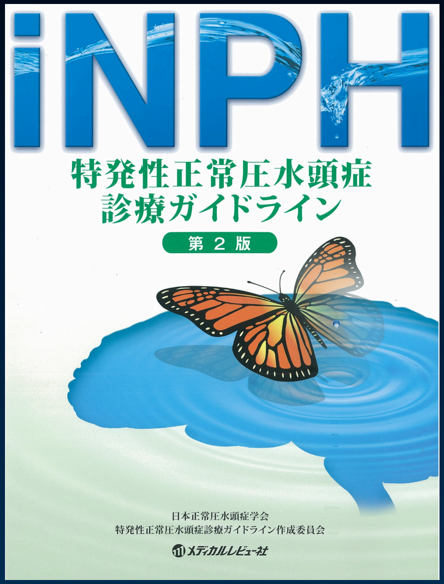
Clinical guidelines for iNPH



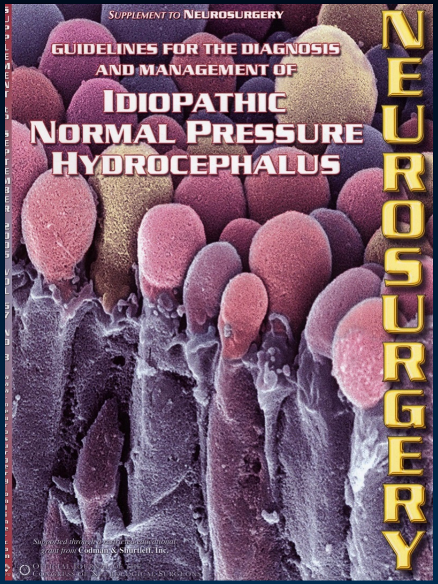
2004



2008



2011



2005

The first edition of the Japanese guidelines for management of iNPH was published in 2004, and its English version in 2008.

Clinical guidelines for iNPH

Neurologia medico-chirurgica
The Japan Neurosurgical Society

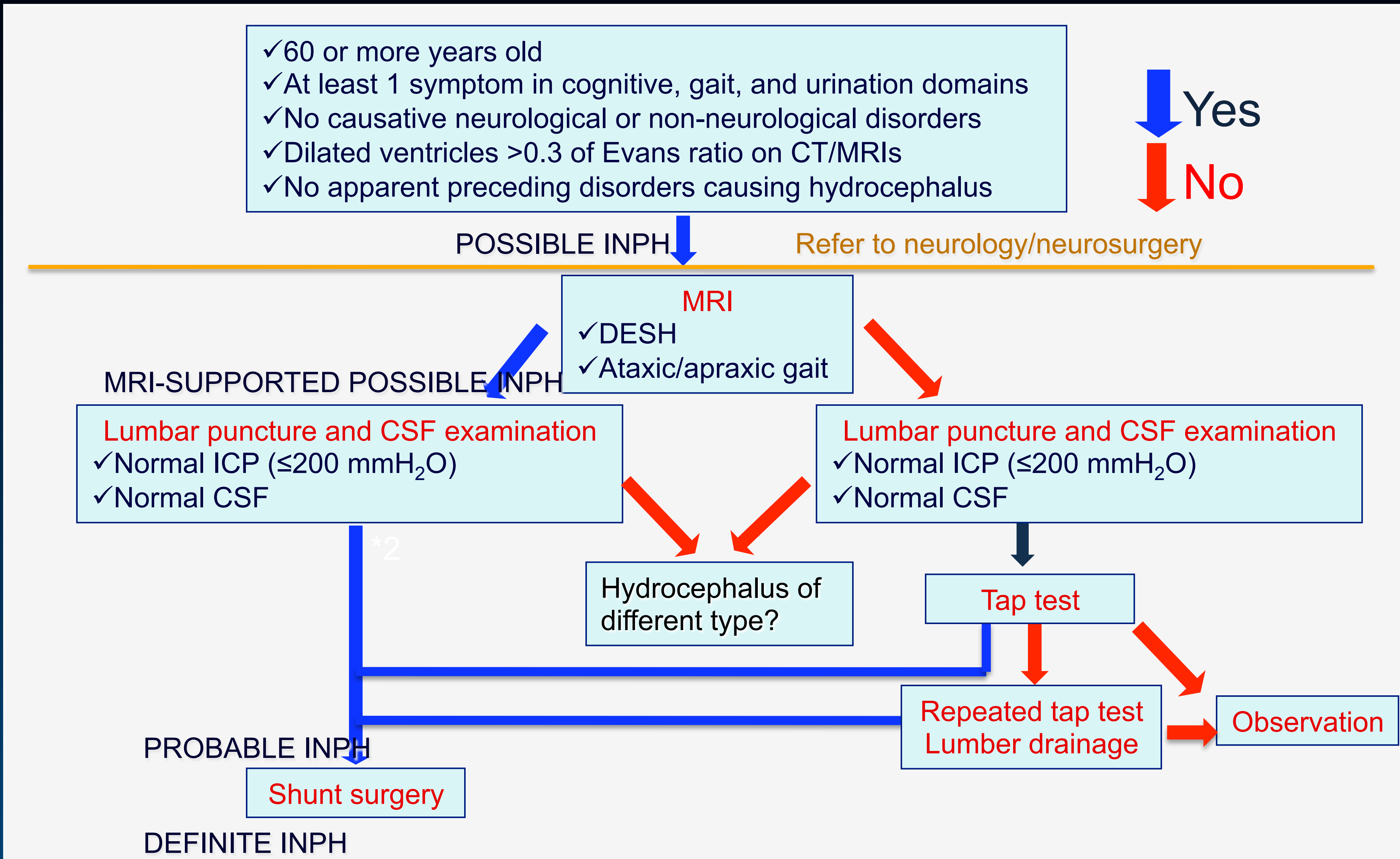
Neurol Med Chir (Tokyo) 52, 775～809, 2012

iNPH Guideline

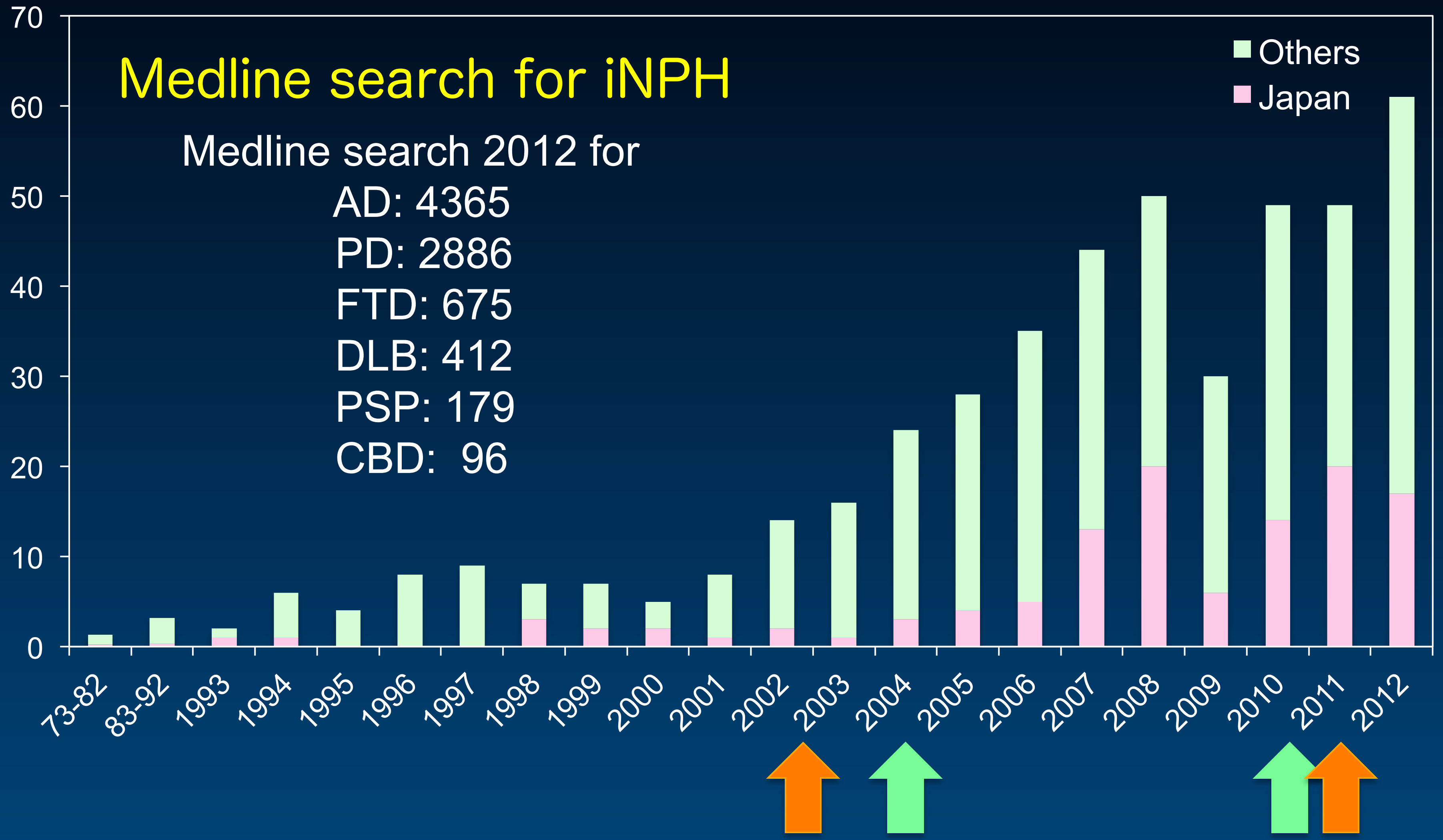
Guidelines for Management of Idiopathic Normal Pressure Hydrocephalus: Second Edition

Etsuro MORI,[1] Masatsune ISHIKAWA,[2] Takeo KATO,[3] Hiroaki KAZUI,[4]
Hiroji MIYAKE,[5] Masakazu MIYAJIMA,[6] Madoka NAKAJIMA,[6]
Masaaki HASHIMOTO,[7] Nagato KURIYAMA,[8] Takahiko TOKUDA,[9]
Kazunari ISHII,[10] Mitsunobu KAIJIMA,[11] Yoshihumi HIRATA,[12]
Makoto SAITO,[1] and Hajime ARAI[6]

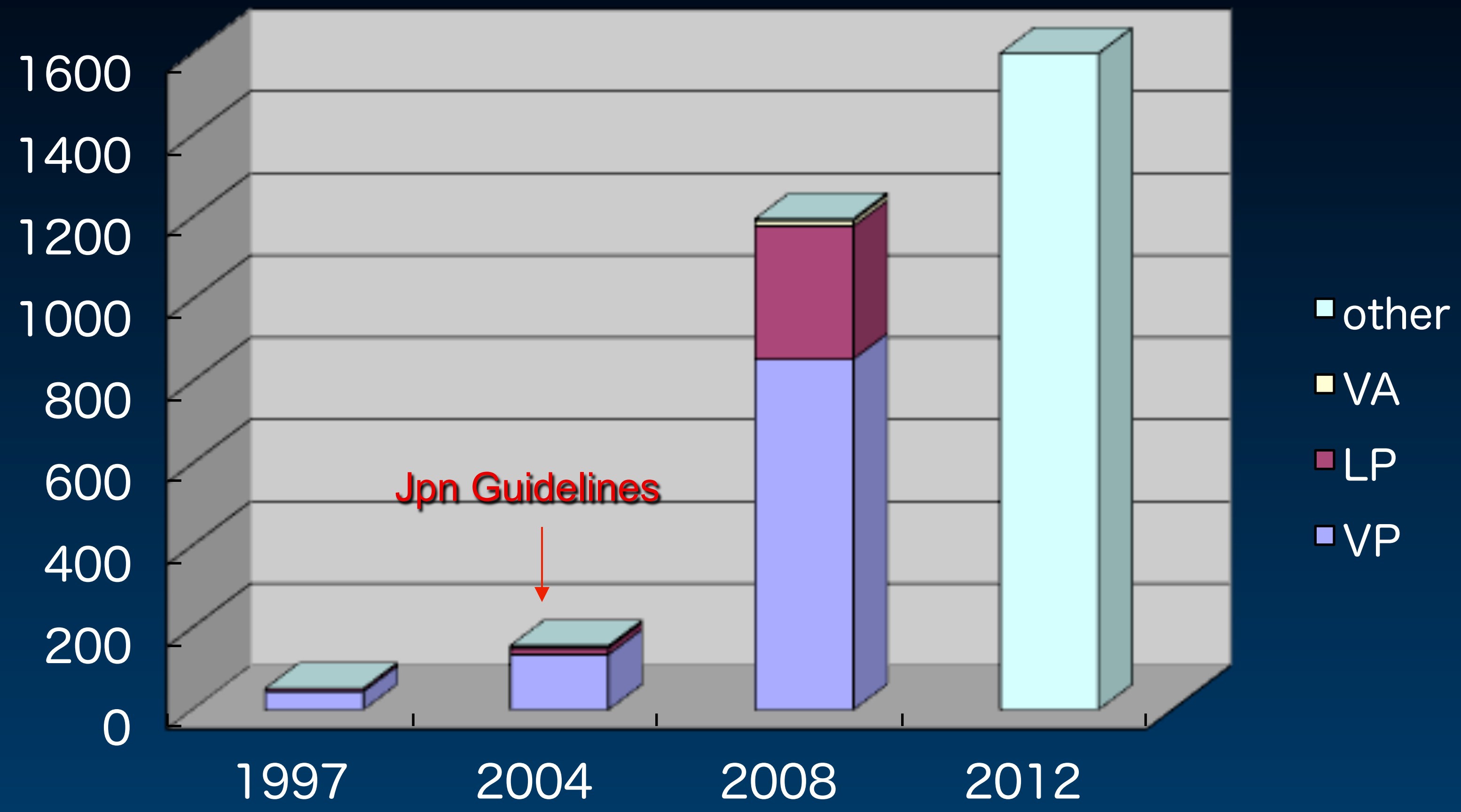
Flow of management



Number of papers

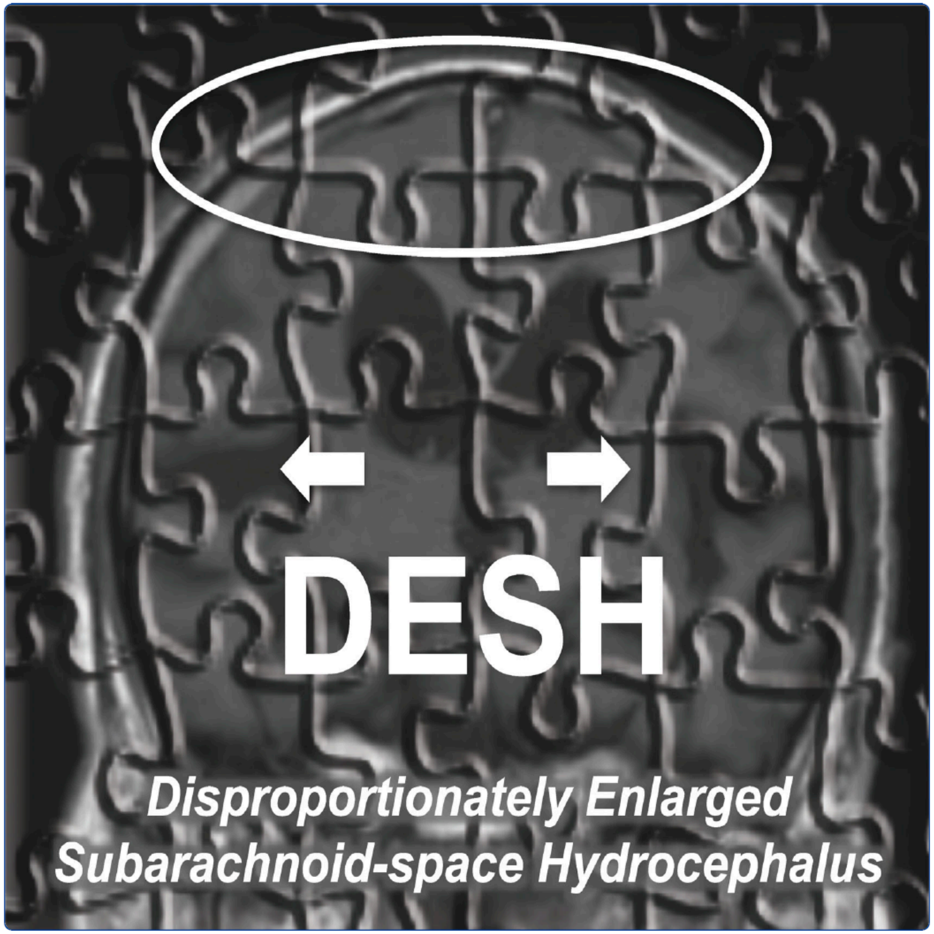


Number of surgery for iNPH in Japan



Based on the questionnaire surveys of the MHWL Research Project

CEREBROSPINAL FLUID RESEARCH



Diagnosis of idiopathic normal pressure hydrocephalus is supported by MRI-based scheme: a prospective cohort study

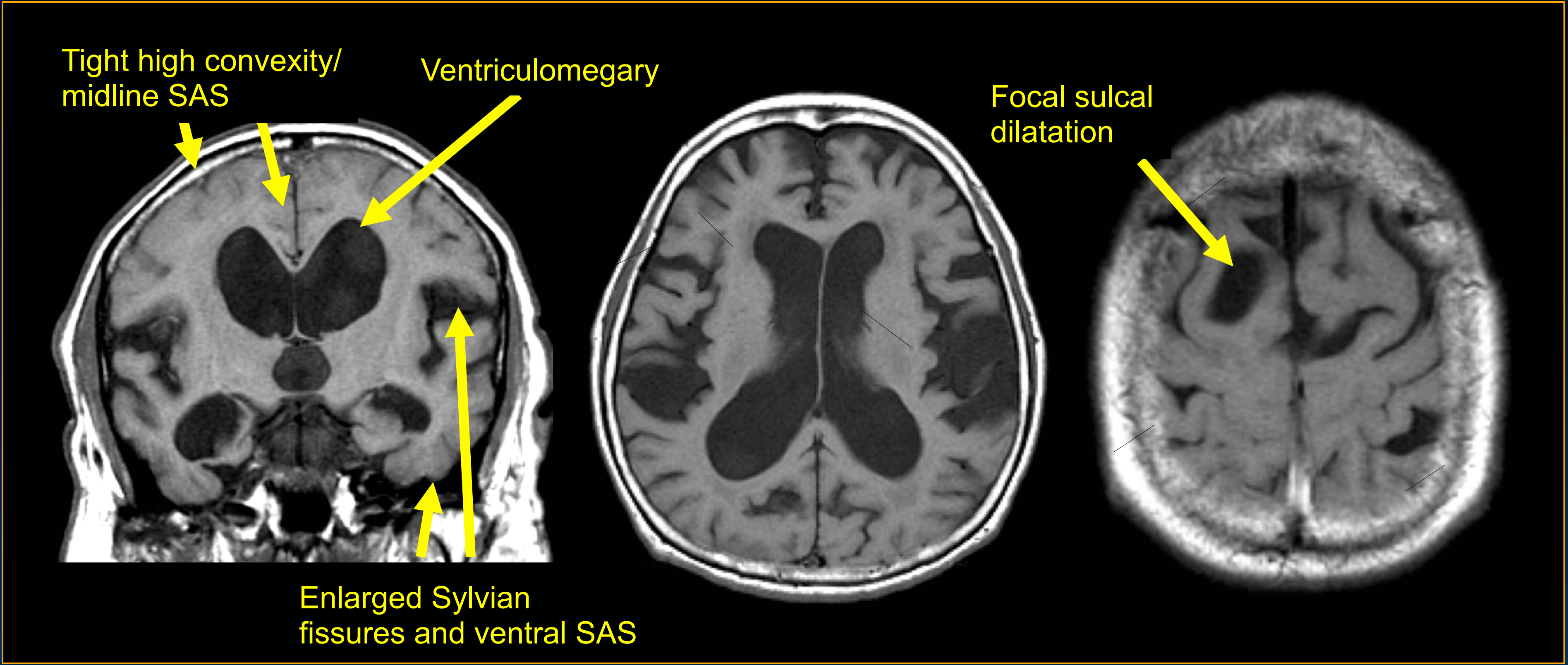
Hashimoto *et al.*

BioMed Central

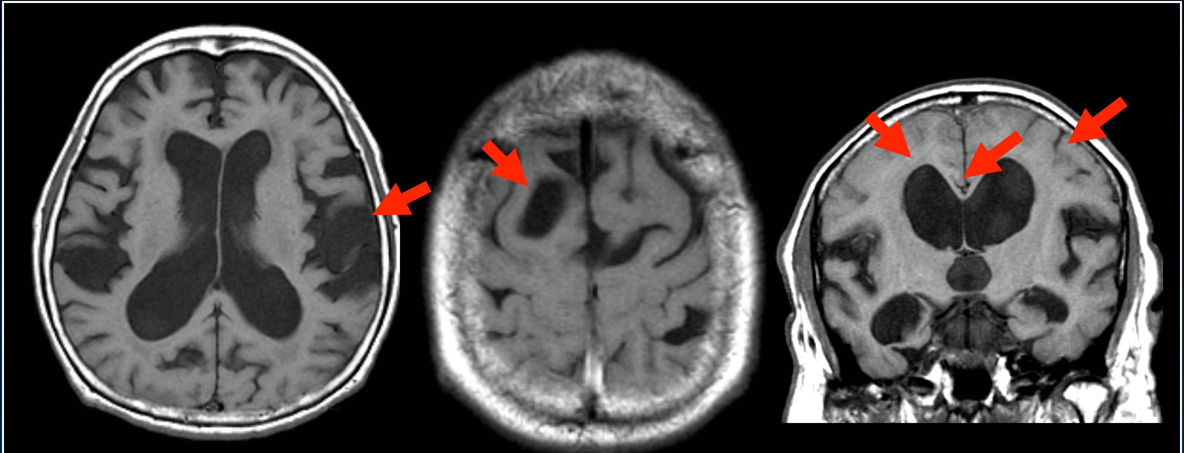
Hashimoto *et al. Cerebrospinal Fluid Research* 2010, **7**:18
http://www.cerebrospinalfluidresearch.com/content/7/1/18 (31 October 2010)

- SINPHONI
  - Tight high-convexity and medial subarachnoid spaces and enlarged Sylvian fissure associated with ventriculomegaly
- Guidelines 2nd Ed.
  - CSF is distributed disproportionately between the superior and inferior subarachnoid spaces

DESH


Tight high convexity/
midline SAS
Ventriculomegary
Focal sulcal
dilatation
Enlarged Sylvian
fissures and ventral SAS

MRI features of iNPH



iNPH

Brain atrophy

- Disproportionate ventriculomegary
  - Tightened high-convexity/midline subarachnoid spaces
  - Dilated Sylvian fissures
  - Focal sulcal dilatation
- Acute callosal angle

- Proportionate ventriculomegary
  - Ventricles and subarachnoid spaces including Sylvian fissures are evenly dilated

Tight high-convexity/midline subarchnoid spaces and large Sylvian fissures

AJNR Am J Neuroradiol 19:1277–1284, August 1998

CSF Spaces in Idiopathic Normal Pressure Hydrocephalus: Morphology and Volumetry

Hajime Kitagaki, Etsuro Mori, Kazunari Ishii, Shigeru Yamaji,
Nobutsugu Hirono, and Toru Imamura

SINPHONI
Study of INPH On Neurological Improvement

- Aims: validation of MRI-based diagnosis
- Study design: prospective cohort study

Hashimoto *et al. Cerebrospinal Fluid Research* 2010, **7**:18
http://www.cerebrospinalfluidresearch.com/content/7/1/18

CEREBROSPINAL FLUID RESEARCH

RESEARCH Open Access

Diagnosis of idiopathic normal pressure hydrocephalus is supported by MRI-based scheme: a prospective cohort study

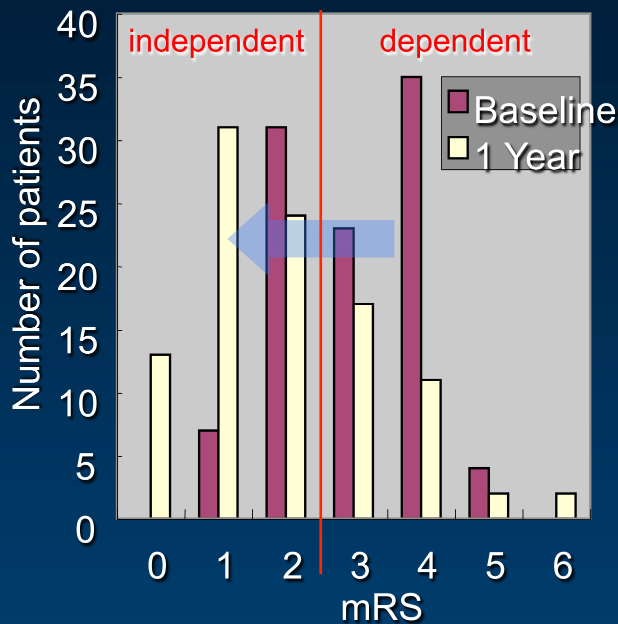
Masaaki Hashimoto[1*], Masatsune Ishikawa[2], Etsuro Mori[3], Nobumasa Kuwana[4],
The study of INPH on neurological improvement (SINPHONI)

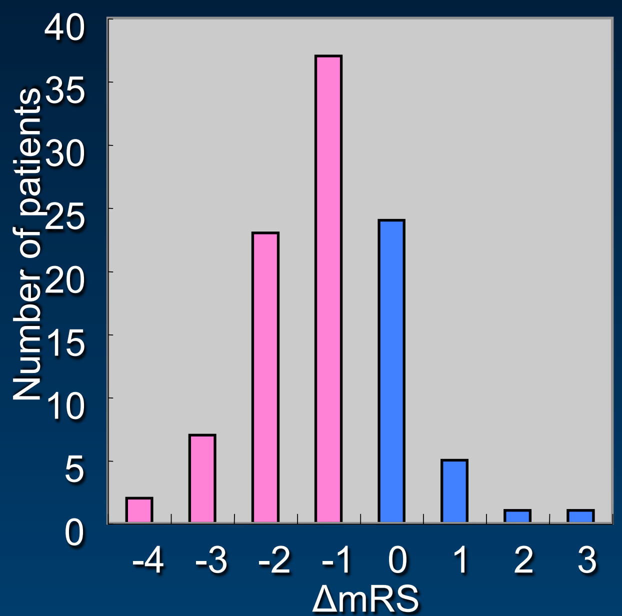
SINPHONI

- Cohort study design
  - 100 pts, 1 year
- Inclusion
  - possible iNPH
  - Ventriculomegary of EI>0.3 and narrowing of high convexty/midline subarachnoid space on coronal MRI
- Intervention
  - VP shunt with CHPV
- End point
  - ≥1 level improvement on mRS

SINPHONI
Study of INPH On Neurological Improvement

- Inclusion criteria
  - (1) Jpn GL criteria possible iNPH
  - (2) Ventriculomegary of Evans index > 0.3 and tight high convexity/midline subarachnoid spaces

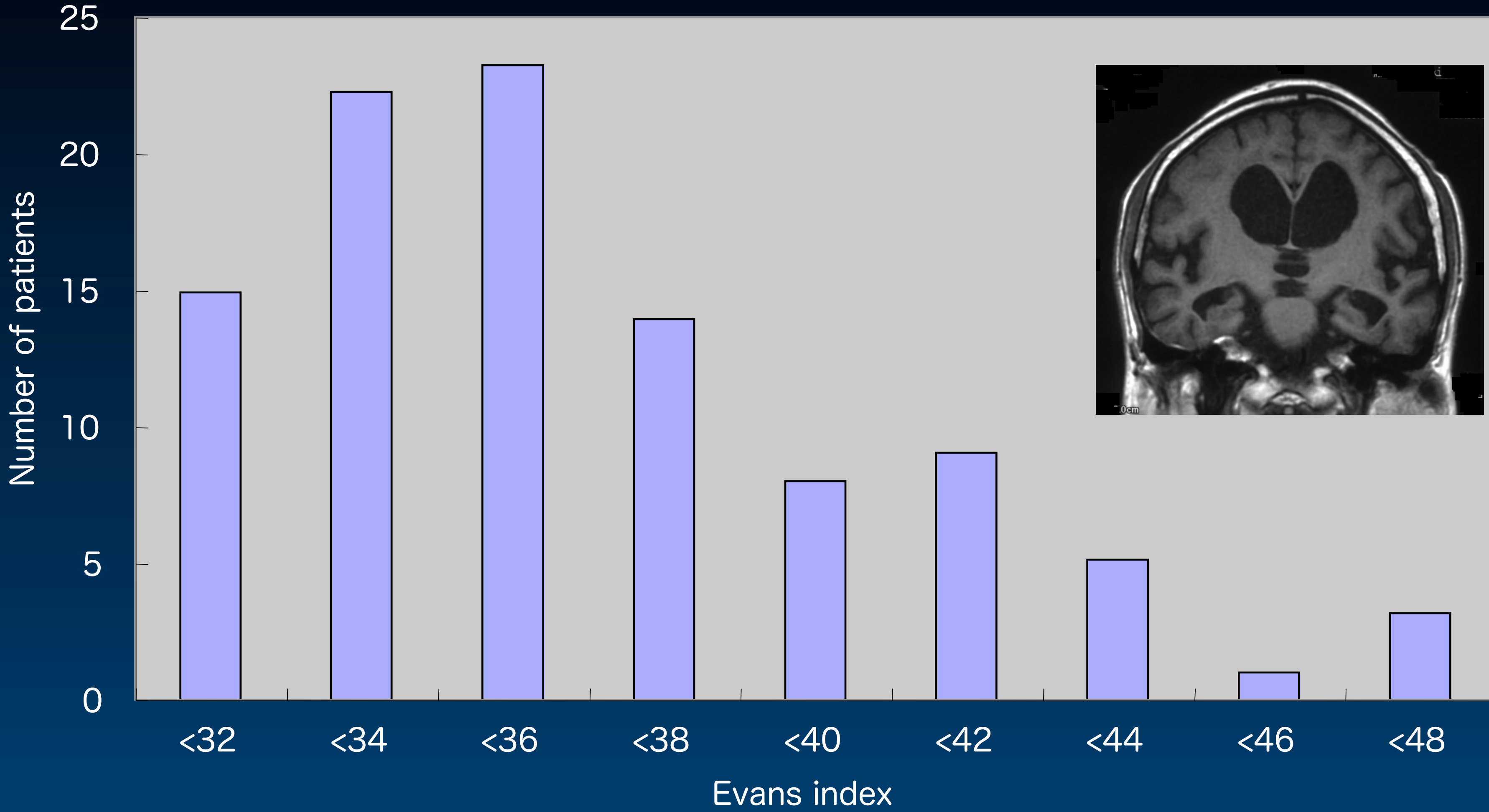




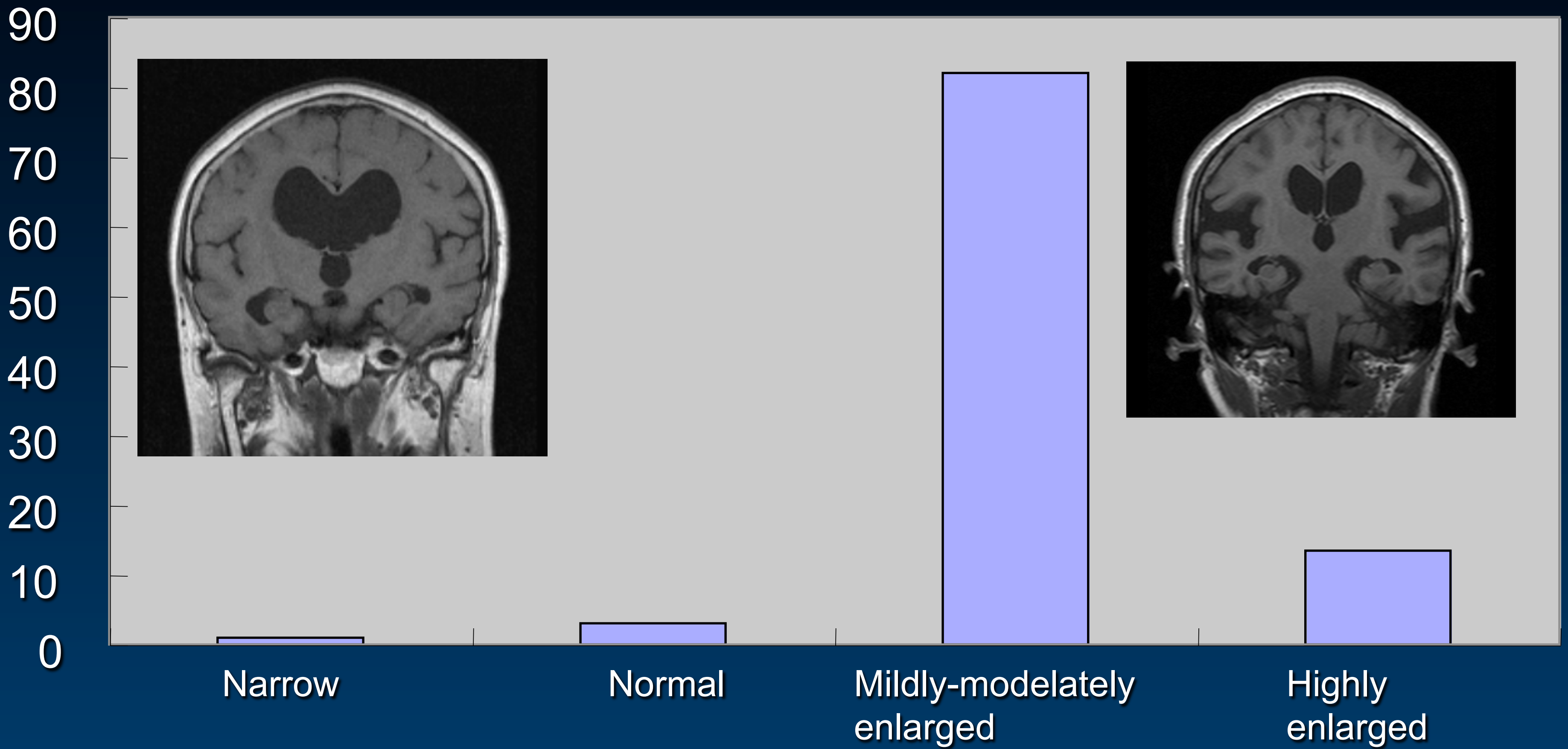
Favorable outcome = net benefit of whole procedure = 69%

Shunt responder = positive predictive value = 80%

Evans index


Number of patients
25
20
15
10
5
0
<32
<34
<36
<38
<40
<42
<44
<46
<48
Evans index

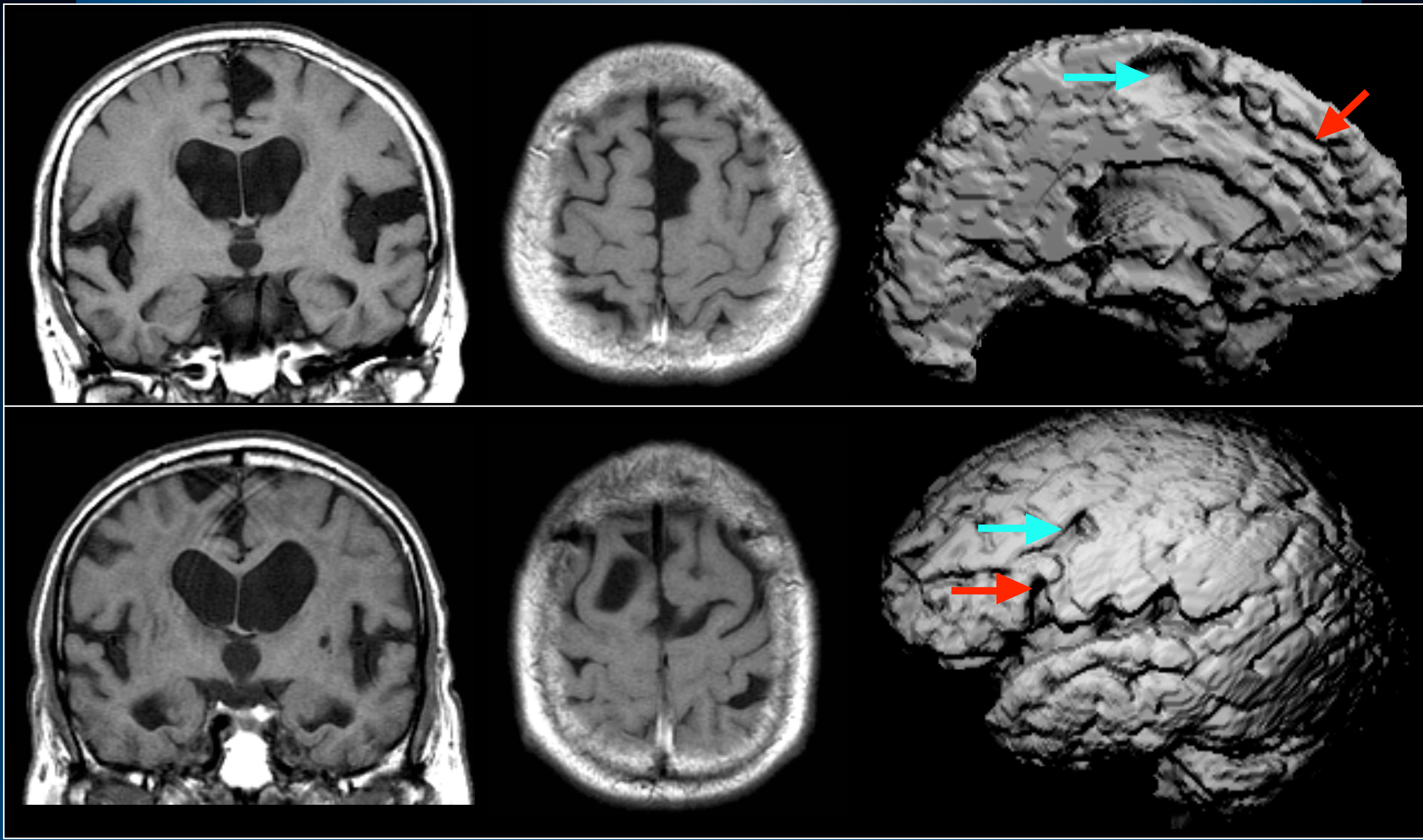
Sylvian fissures



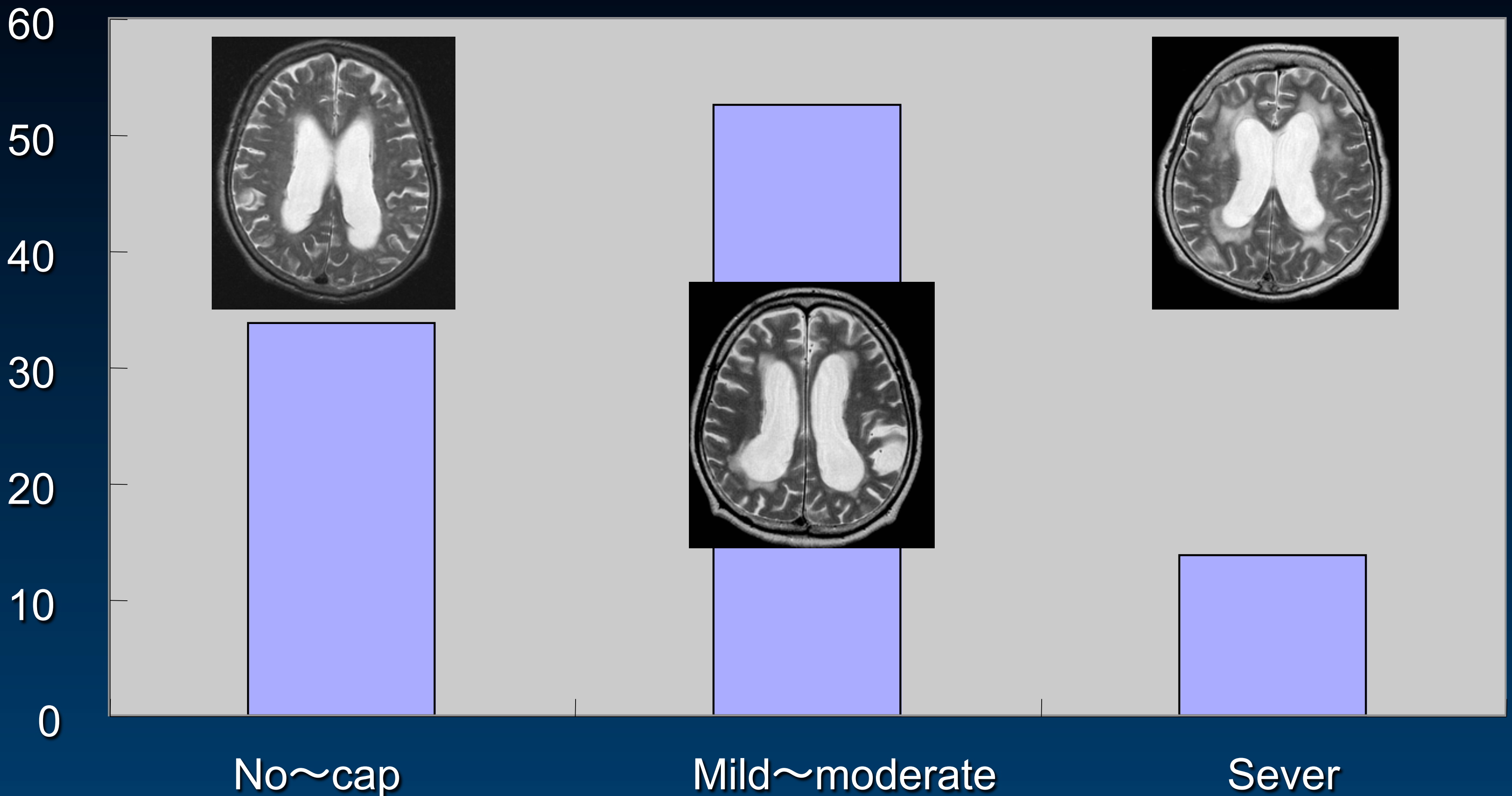
Sylvian fissures are dilated in 96%

Hashimoto M, et al. Cerebrospinal Fluid Res, in press

Focal sulcal dilatation: positive in 29%

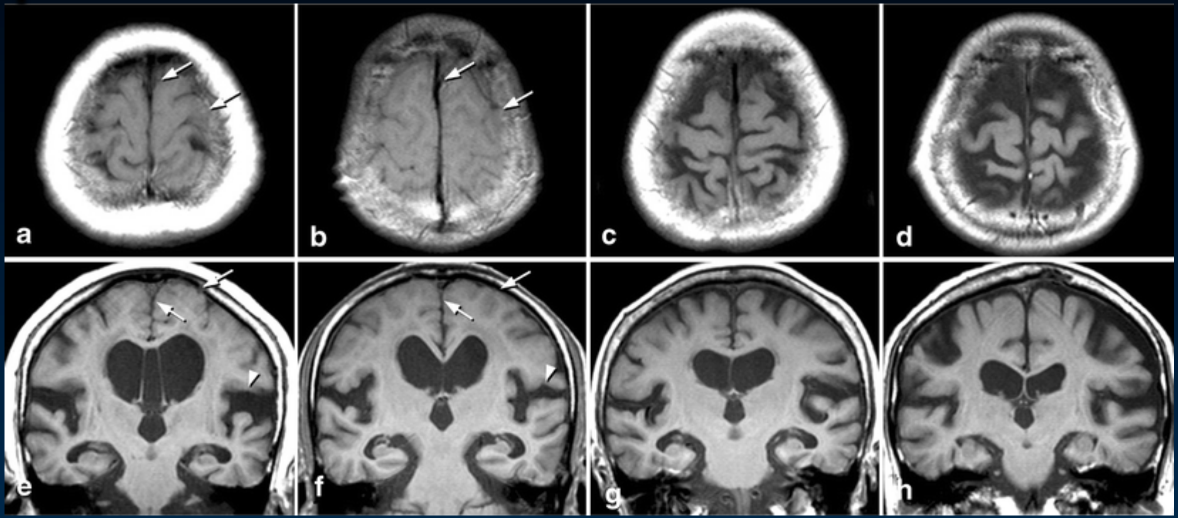


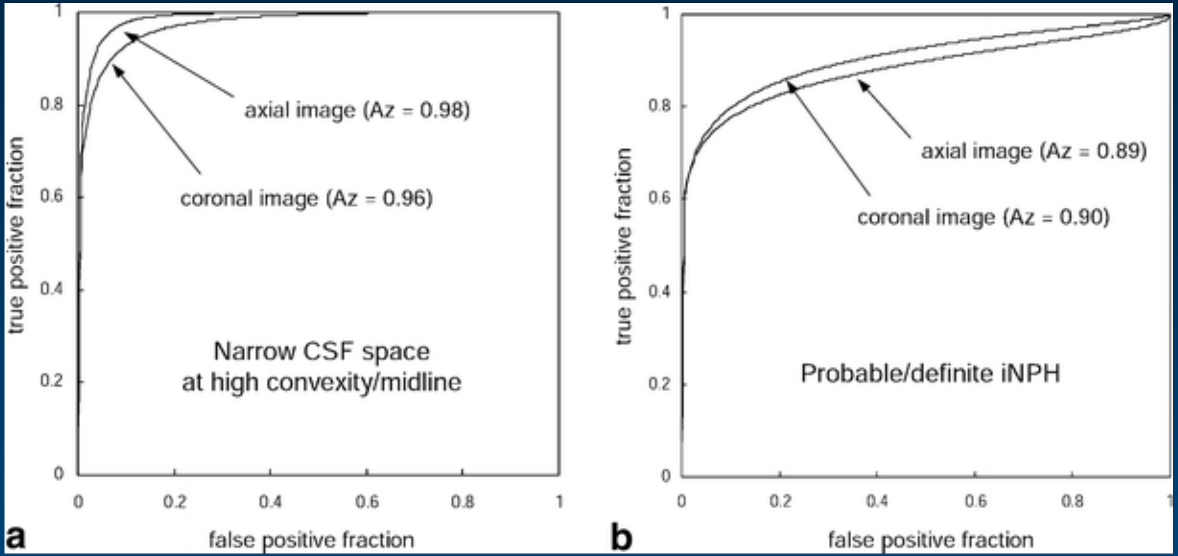
White matter changes



White matter changes lack in 33%

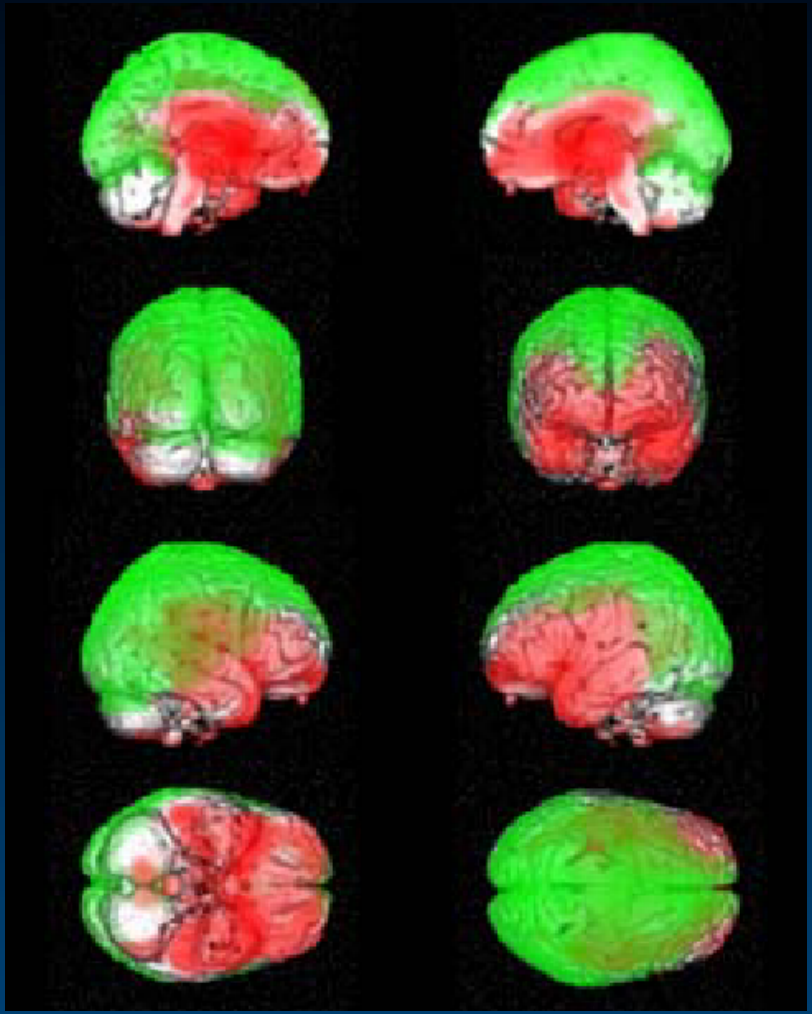
Axial MRI has an equal diagnostic performanceas coronal MRI





Sasaki M, et al.
Neuroradiology, 2008

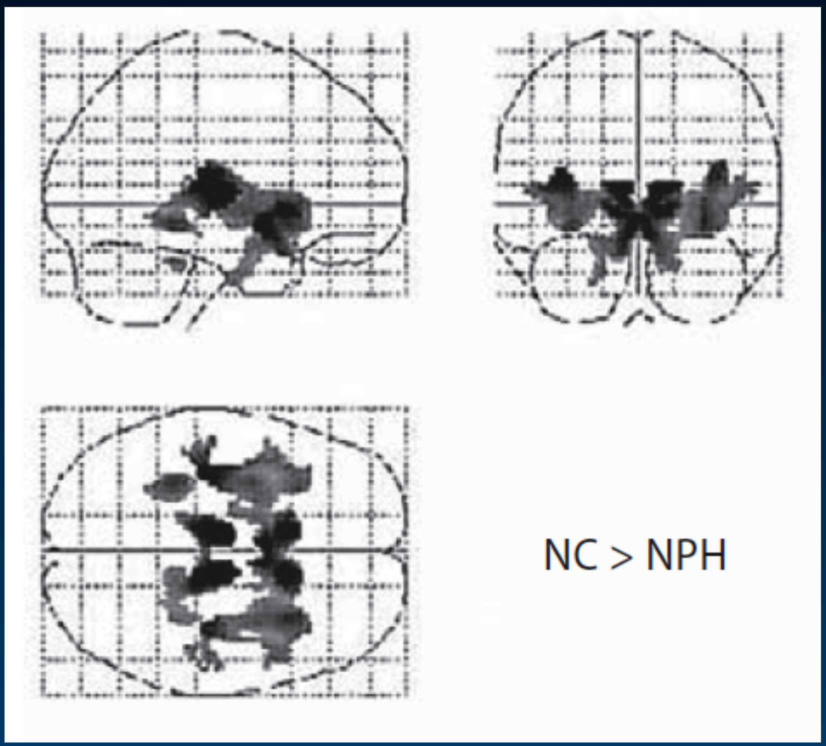
Statistical map of CSF

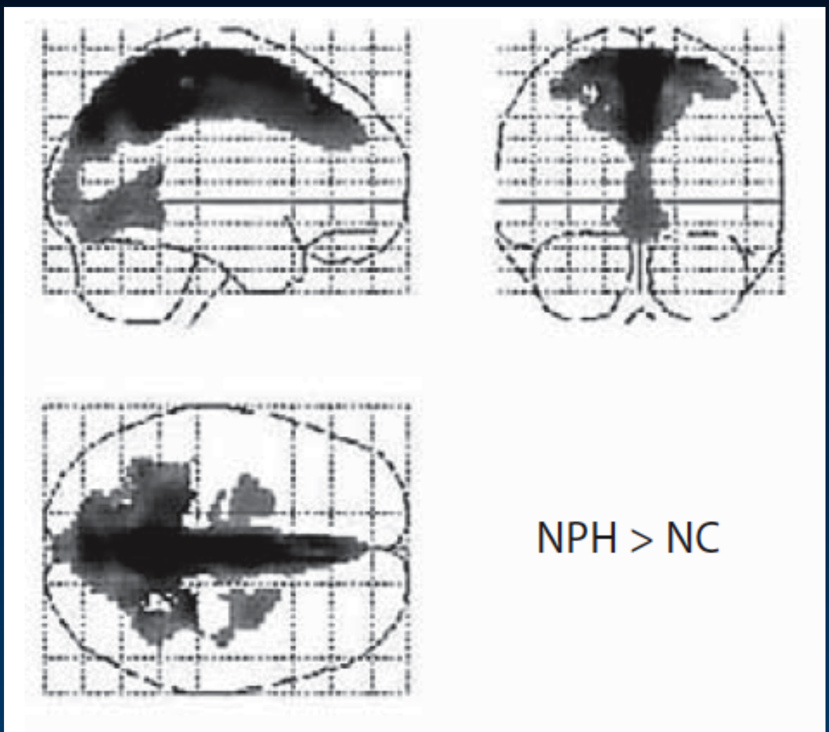


As compared with controls CSF volume is significantly
Decreased
Increased

Yamashita F, et al, Neuroradiology, 2010

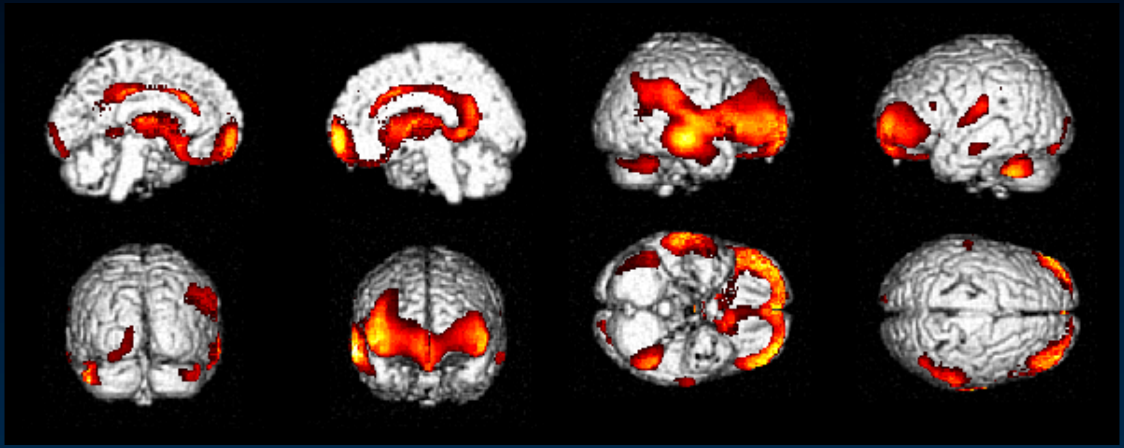
Statistical map of gray mater

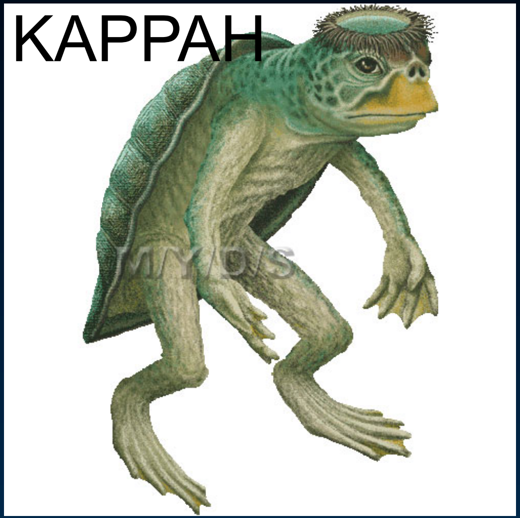




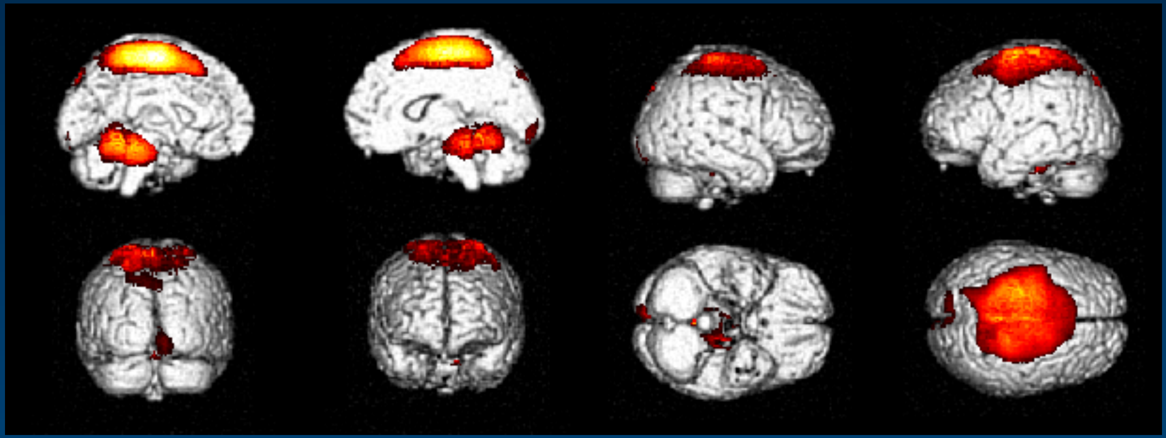
Ishii K, et al. Dement Geriatr Cogn Disord 2008

CBF SPECT（SPM）

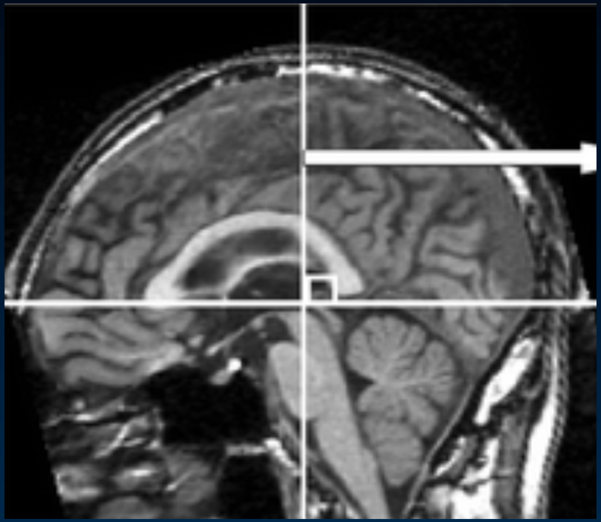


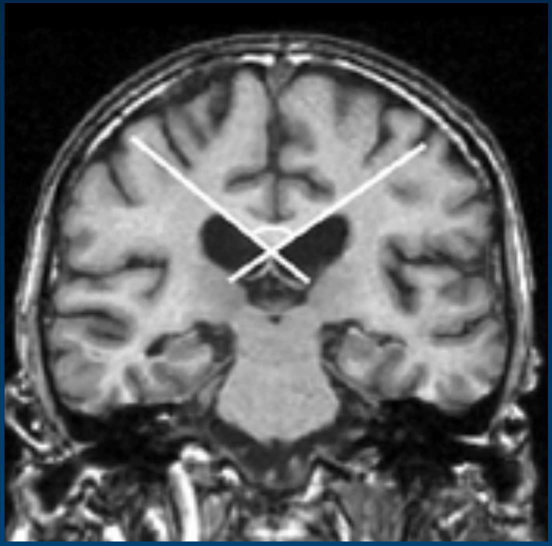


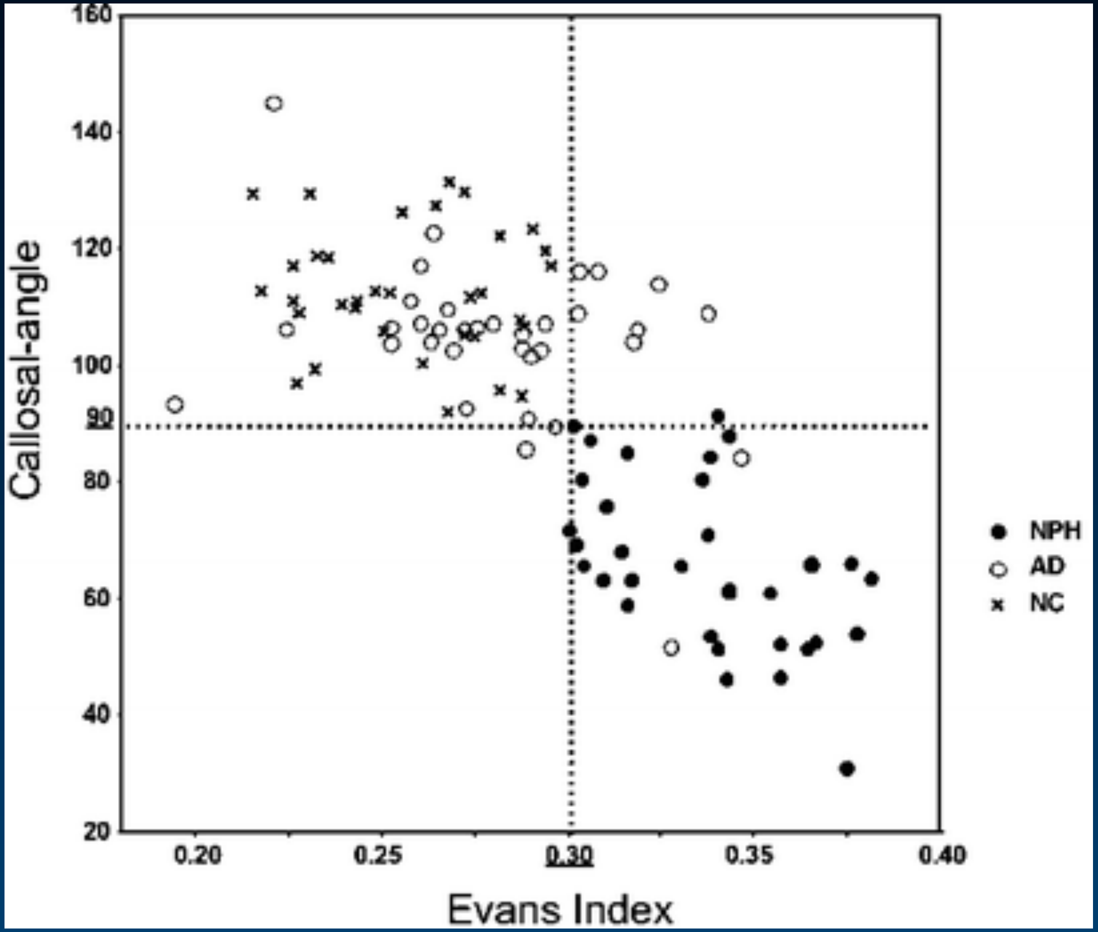
Convexity Apparent Hyperperfusion (CAPPAH) sign



Callosal angle

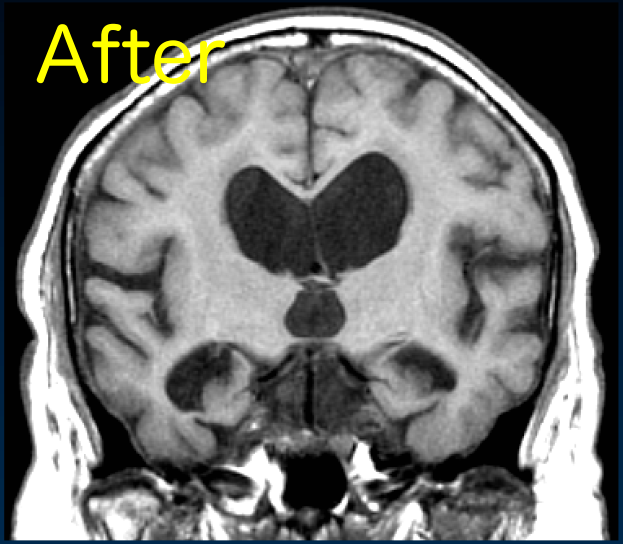






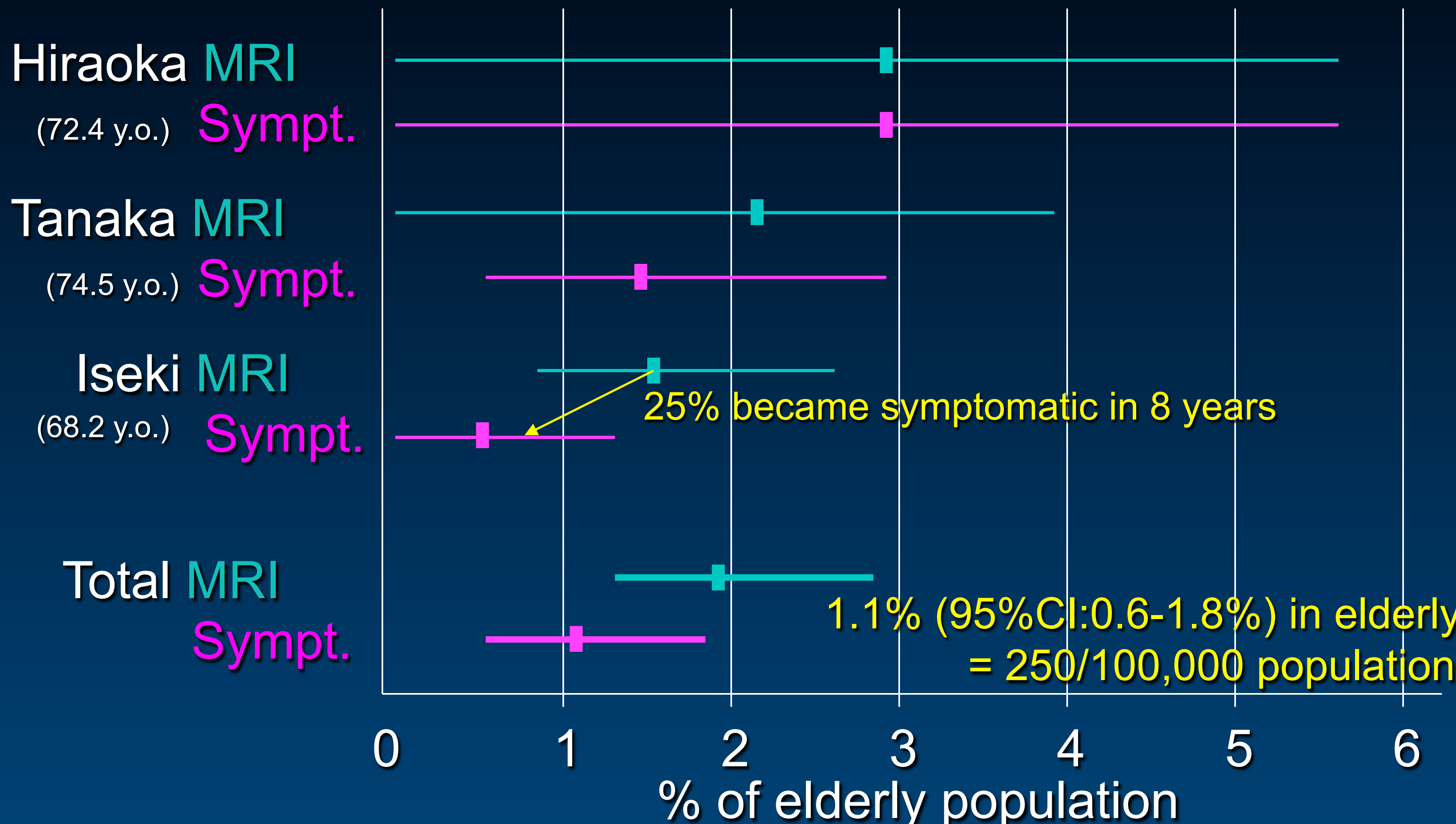
Ishii K, et al. Eur Radiol 2008

Volume changes after VP shunt



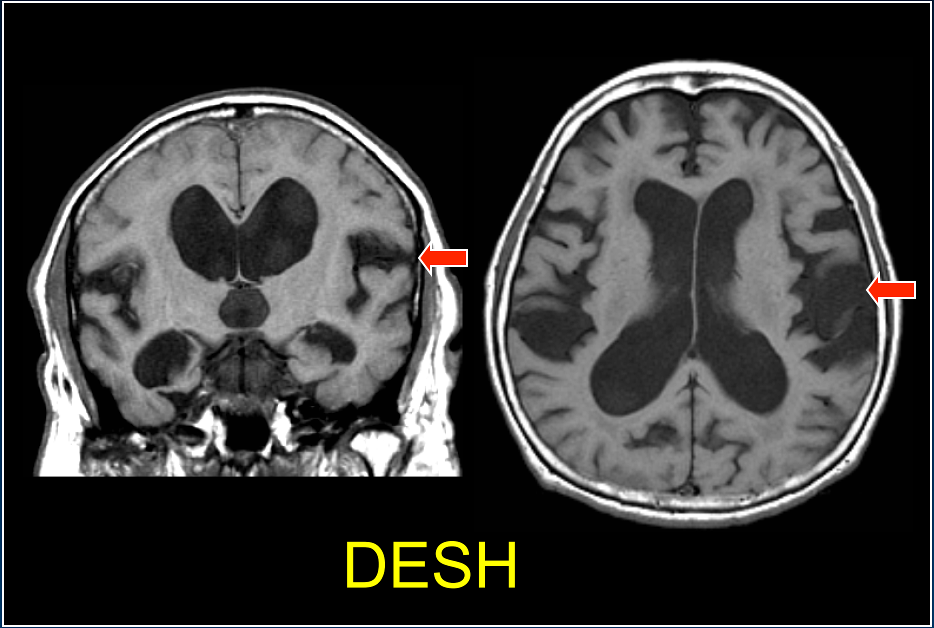
	Before	After	P Value
Ventricular CSF	144.5±29.8	95.4±27.3	0.015
Sylvian CSF	56.5±7.0	40.8±1.8	0.023
Basal CSF	39.5±7.5	34.5±11.7	0.057
Suprasylvian CSF	61.5±34.0	89.1±34.5	0.024

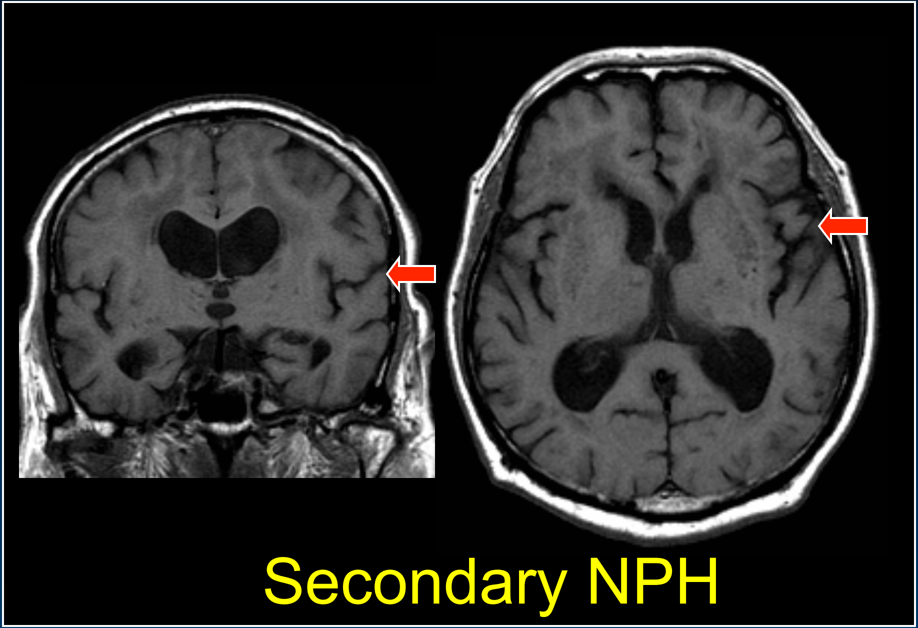
Prevalence of DESH: metaanalysis



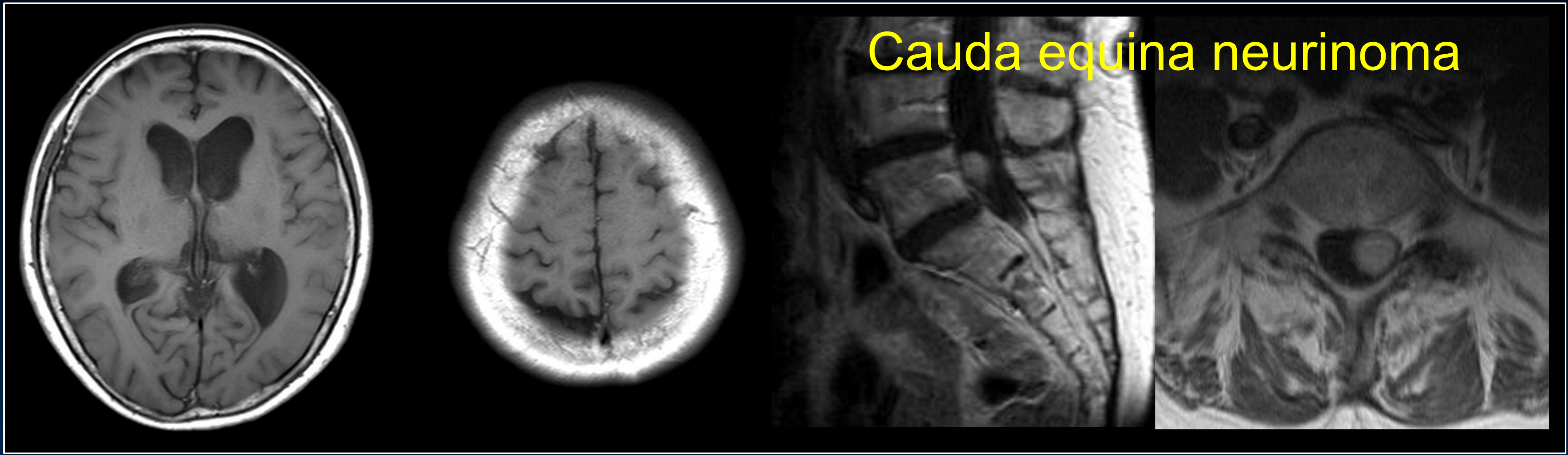
Behavioral Neurology & Cognitive Neuroscience, Tohoku University Graduate School of Medicine

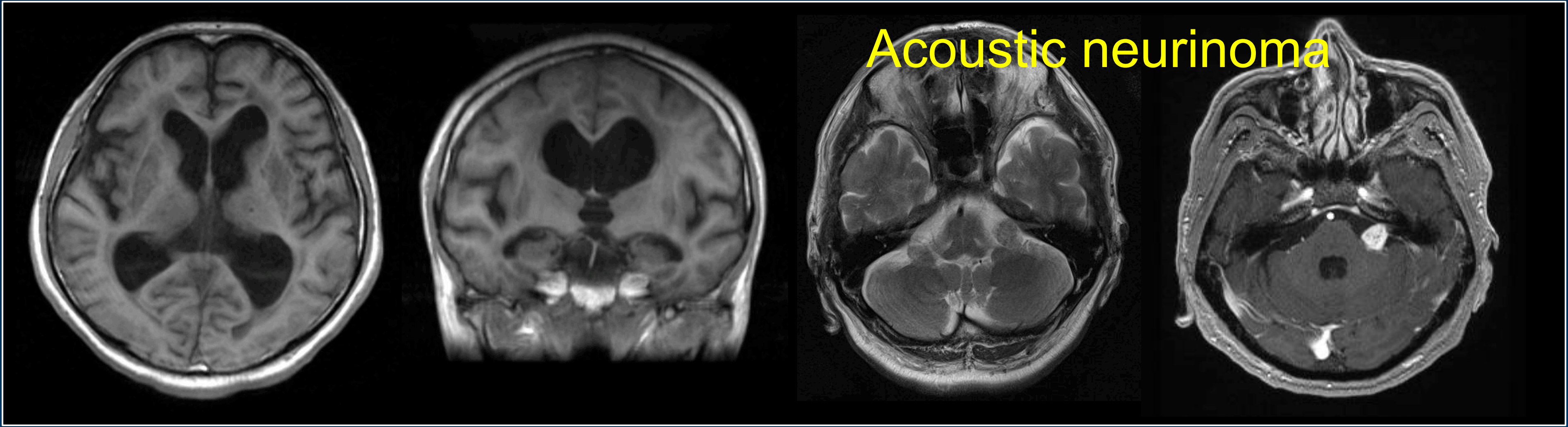
DESH is specific for iNPH



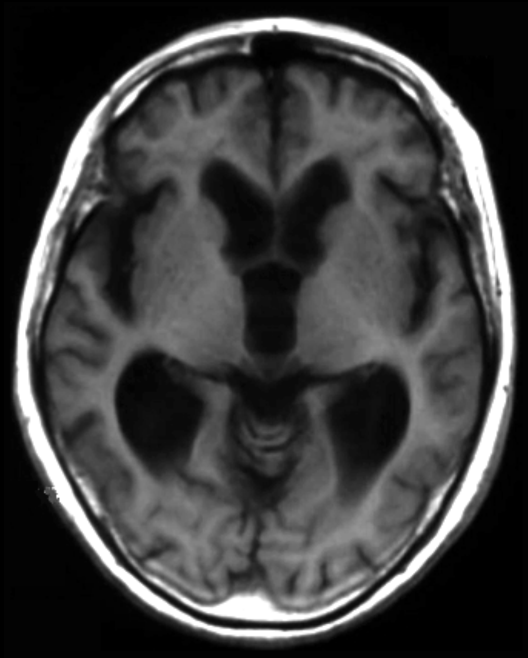


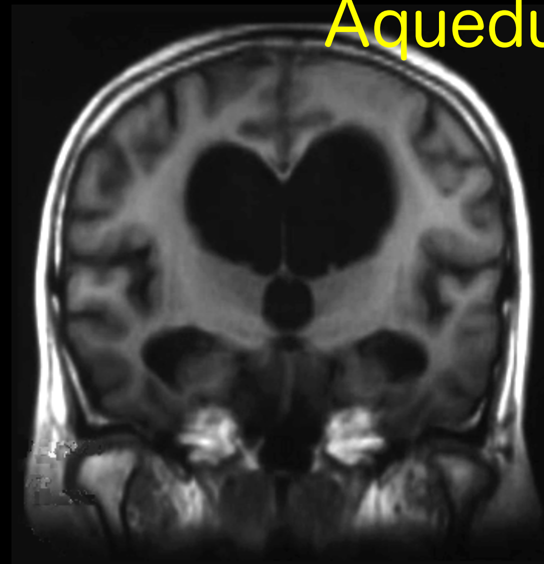
If not DESH

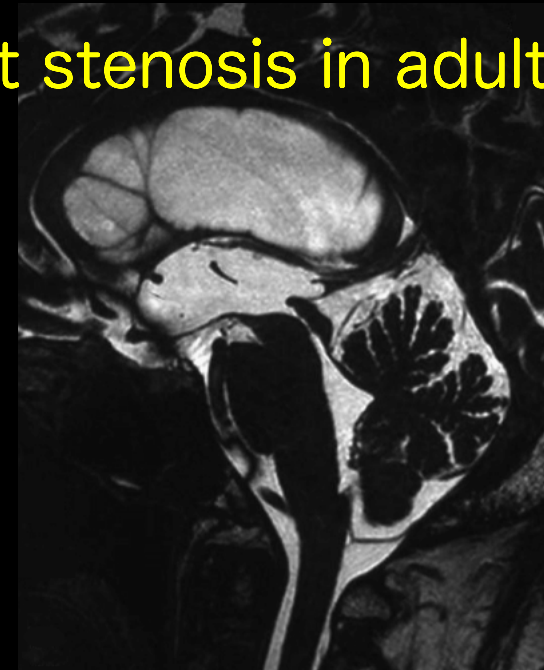




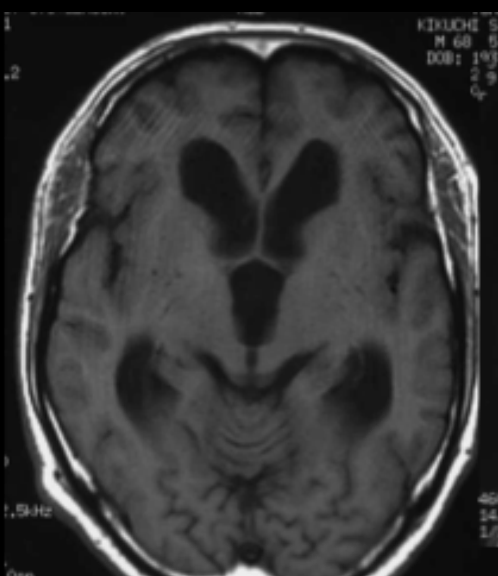
Aqueduct stenosis in adult

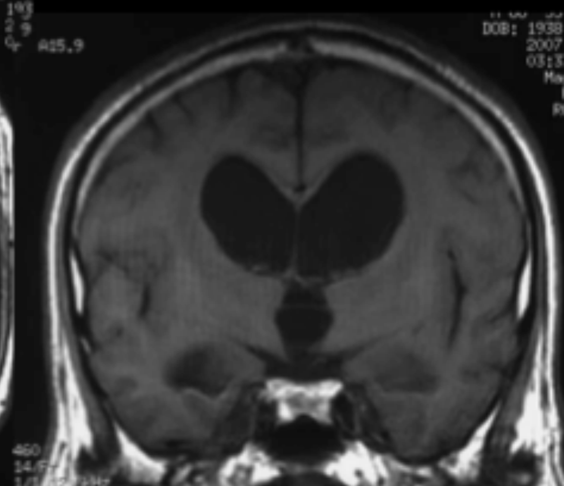




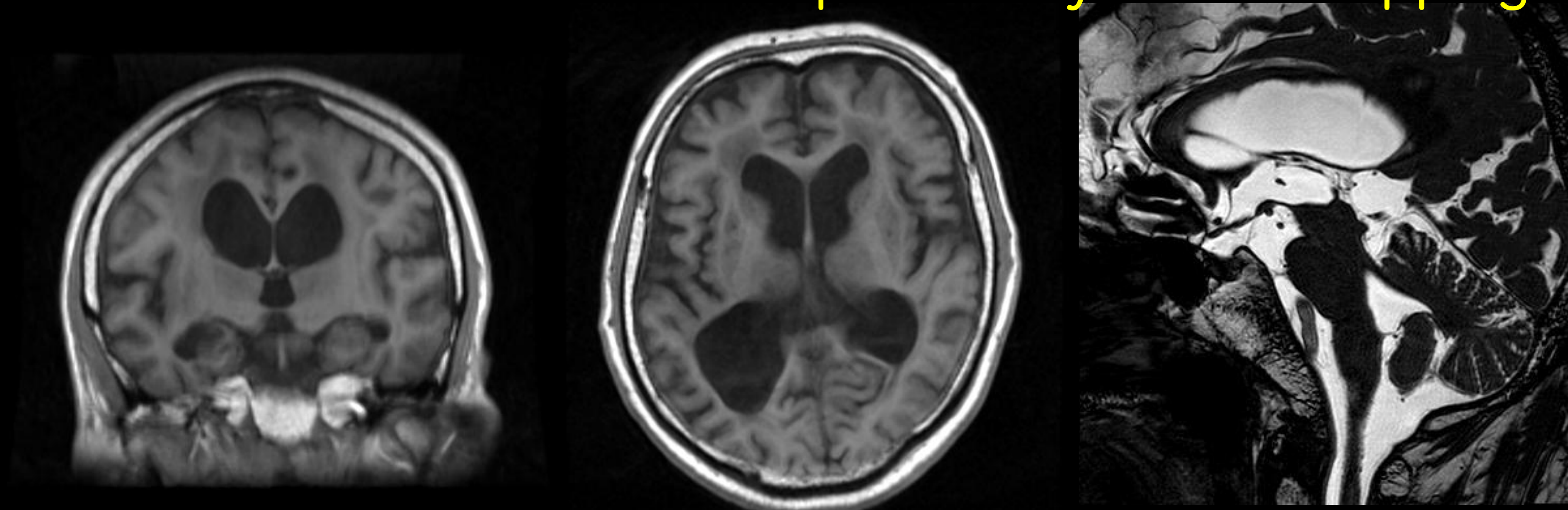


Blake’s pouch cyst in adult

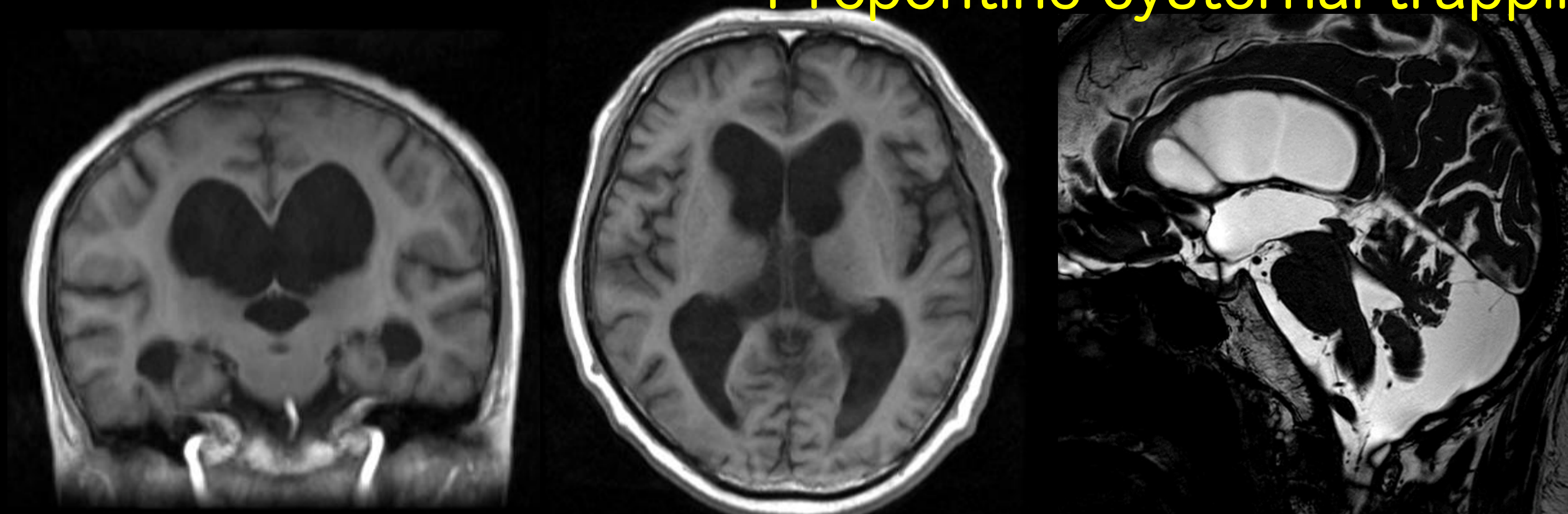




Prepontine cysternal trapping?



Prepontine cysternal trapping?



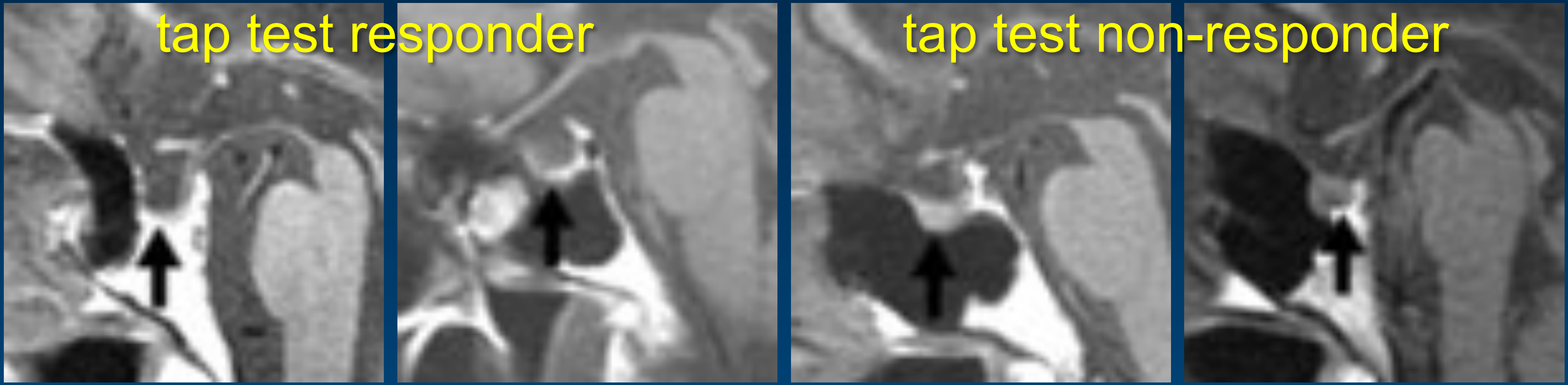
Diagnostic value of tap test under the condition of DESH

	Variables	TP	TN	FP	FN	Sensitivity (%)	Specificity (%)
1	GS-Gait-change	41	16	4	39	51.3	80.0
2	GS-Cogn-change	20	17	3	60	25.0	85.0
3	GS-Urin-change	30	17	3	50	37.5	85.0
4	GS-Total-change	57	13	7	23	71.3	65.0
5	TUG ≥10% (sec)[1]	26	14	5	50	34.2	73.6
6	MMSE≥3	51	6	14	29	63.8	30.0
7	Tap-any	74	4	16	6	92.5	20.0
8	GS-Total-change, CSFP≥15cmH_2O[2]	66	13	7	14	82.5	65.0

Ishikawa M, et al. Fluids Barriers CNS. 2012

DESH and tap test

MRI features	CSF-TT responder (%)	CSF-TT non-responder (%)	OR (95% CI)	*p* value[a]
Frontal convexity narrowing	38.1	38.1	1 (0.3–3.5)	1
Parietal convexity narrowing	57.1	47.6	1.5 (0.4–5.0)	0.76
Upward bowing of the corpus callosum	66.7	52.4	1.8 (0.5–6.3)	0.53
Narrowing of the CSF space at the high convexity	50.0	23.8	3.2 (0.9–11.8)	0.14
Marked dilatation of the Sylvian fissure	45.5	33.3	1.7 (0.5–5.7)	0.62
Empty sella	52.4	14.3	6.6 (1.5–29.4)	0.02
Disproportion between narrowing of the CSF space at the high convexity and dilatation of the Sylvian fissure ("mismatch" sign)	45.5	9.5	7.9 (1.5–42.5)	0.02
Empty sella or "mismatch" sign	72.7	19.0	11.3 (2.7–47.7)	0.001



Lee WJ, et al. J Neurol, 2010

False negative tap test

- Volume of CSF evacuation is insufficient
- Uncontrollable CSF leakage from puncture hole
  - Small puncture hole
  - Spinal canal stenosis
  - Traumatic tap (hemorrhage)
- Inadequate, insufficient measures
- Too few measuring points
- Back pain after lumbar puncture
  - Virhammar J, et al. Eur J Neurol 2012

Summary

- DESH is the key of the diagnosis of iNPH
  - The majority of iNPH is DESH
  - DESH differentiates iNPH from atrophy
  - DESH may be asymptomatic (AVIM)
  - If a condition mimicking iNPH is not DESH, secondary NPH or non-communicating hydrocephalus is suspected

Possible iNPH

meets all of the following five features

(1) Individuals who develop the symptoms in their 60s or older.

(2) More than one of the clinical triad: gait disturbance, cognitive impairment, and urinary incontinence.

(3) Ventricular dilatation (Evans' index > 0.3).

(4) The above-mentioned clinical symptoms cannot be completely explained by other neurological or non-neurological diseases.

(5) Preceding diseases possibly causing ventricular dilatation are not obvious, including subarachnoid hemorrhage, meningitis, head injury, congenital hydrocephalus, and aqueductal stenosis.

Possible iNPH supportive features

(a) Small stride, shuffle, instability during walking, and increase of instability on turning.
(b) The symptoms progress slowly; however, sometimes an undulating course, including temporal discontinuation of development and exacerbation, is observed.
(c) Gait disturbance is the most prevalent feature, followed by cognitive impairment and urinary incontinence.
(d) Cognitive impairment is detected on cognitive tests.
(e) The Sylvian fissures and basal cistern are usually enlarged.
(f) Other neurological diseases, including Parkinson’s disease, Alzheimer’s disease, and cerebrovascular diseases, may coexist; however, all such diseases should be mild.
(g) Periventricular changes are not essential.
(h) Measurement of CBF is useful for differentiation from other dementias.

Possible iNPH with MRI support

- Possible iNPH with MRI support indicates the condition fulfilling the requirements for possible iNPH, where MRI shows narrowing of the sulci and subarachnoid spaces over the high convexity/midline surface (disproportionately enlarged subarachnoid space hydrocephalus). This class of diagnosis can be used in circumstances where a CSF examination is not available, for example, in a population-based cohort study.

Probable iNPH

meets all of following three features

(1) Meets the requirements for possible iNPH.

(2) CSF pressure of 200 mmH_2O or less and normal CSF content.

(3) One of the following threeinvestigational features:

1. Neuroimaging features of narrowing of the sulci and subarachnoid spaces over the high convexity/midline surface (disproportionately enlarged subarachnoid space hydrocephalus) under the presence of gait disturbance.
2. Improvement of symptoms after CSF tap test.
3. Improvement of symptoms after CSF drainage test.

Definite iNPH

1. Improvement of symptoms after the shunt procedure.

The features of large Sylvian fissures and tight high convexity/midline subarachnoid spaces had been noticed but never been stressed

Commentary

MR Prediction of Shunt Response in NPH: CSF Morphology versus Physiology

William G. Bradley Jr., *Long Beach Memorial Medical Center, Long Beach, CA*

Clinical Perspective in Normal Pressure Hydrocephalus

In the commentary on our paper concerning shunt-responsive normal-pressure hydrocephalus (NPH) in the August issue of the *American Journal of Neuroradiology*, Dr. Bradley stressed the importance of clinical perspective in medical studies (1). We agree with his intention, but we do not accept his clinical perspective. Although it is very important to view a study from a clinical perspective, the issue is—what perspective is important for the management of NPH? In this context, his comments need to be examined closely.

Dr. Bradley advised that "anyone publishing a new sign should ensure the sign has not been previously published." He cited an article of George (2), and maintained that the finding of large Sylvian cisterns with NPH is not a new observation but a rehash of a previously reported finding, obtained this time with a "high-tech" tool. That article is

Reply

I have read Dr. Mori's letter concerning my commentary (1) on his article (2) and I wish to thank him for pointing out a mistake in a cited reference (3). Specifically, I had assumed that Dr. George's 1991 *AJNR* paper (3) contained information similar to his group's presentation (4) at the 1989 ASNR on large Sylvian cisterns in patients with NPH. Dr. Mori is correct in stating that large Sylvian cisterns are not mentioned as a feature of NPH in this article. On the other hand, the sign had been published by Dr. George 3 years earlier in a well-known textbook (5) in which he wrote, "Hydrocephalus, however, may coexist with large sulci and in particular with large Sylvian fissures. . . This oc-

in NPH; however, he never claimed priority. When I called him to confirm the references, he pointed out that Vassilouthis first described the sign in 1984 by using CT (6). Thus, I was correct in indicating

J Neurosurg 89:742–747, 1998

Focal dilation and paradoxical collapse of cortical fissures and sulci in patients with normal-pressure hydrocephalus

Andrei I. Holodny, M.D., Ajax E. George, M.D., Mony J. de Leon, Ed.D., James Golomb, M.D., Andrew J. Kalnin, M.D., and Paul R. Cooper, M.D.

Department of Radiology, University of Medicine and Dentistry of New Jersey–New Jersey Medical School, Newark, New Jersey; and Departments of Radiology, Psychiatry, Neurology, and Neurosurgery, New York University Medical Center, New York, New York

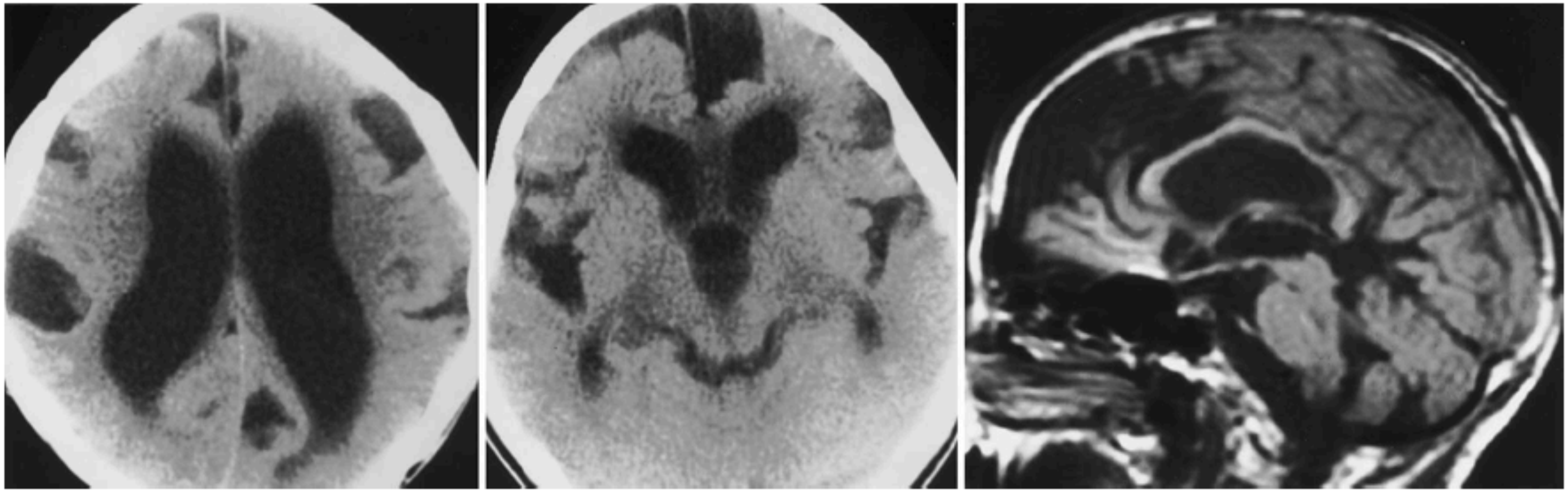


Fig. 1. Case 1. Axial CT scans obtained through the bodies of the lateral ventricles *(left)* and the third ventricle *(center)* and a paramidline sagittal T_1-weighted MR image *(right)* (TR 600 msec, TE 15 msec) demonstrating marked dilation of the lateral ventricles. The third ventricle is severely dilated and rounded. The fourth ventricle is also dilated. Evaluation of the sulci demonstrates marked dilation of the following sulci: the sylvian fissures bilaterally, the central sulci bilaterally, the anterior aspect of the interhemispheric fissure, the left parietooccipital fissure, and the left calcarine fissure. In addition, there is marked focal dilation of the sulcus cinguli on the right side, the precentral sulcus on the left side, and the frontal sulci bilaterally. There is also dilation of the suprasellar and quadrigeminal plate cisterns. The remaining sulci are compressed. The sagittal MR image demonstrates thinning and upward bowing of the corpus callosum. More caudal images demonstrated a moderate dilation of the temporal horns of the lateral ventricles; however, there is no evidence of dilation of the choroidal and parahippocampal fissures, hippocampal atrophy, or cerebellar or brainstem abnormalities.

J Neurosurg 61:501–509, 1984

The syndrome of normal-pressure hydrocephalus

John Vassilouthis, M.D.

Neurosurgical Department, Army Veterans Administration Hospital (417 NITS), Athens, Greece

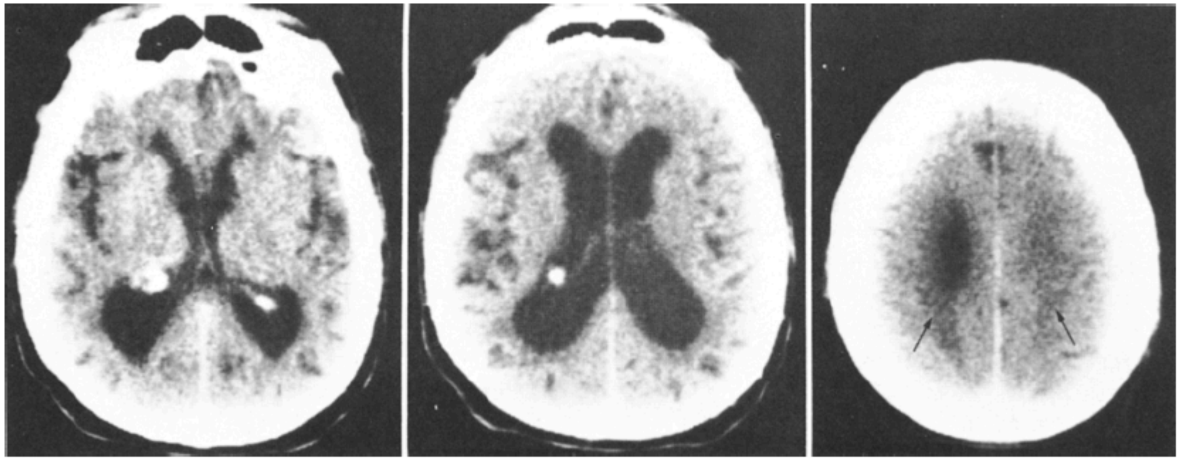


Fig. 2. Obliteration of the cerebral sulci *(arrows)* in a 72-year-old man with ventricular enlargement. Note the considerable dilatation of the subarachnoid spaces at the lower levels (including the Sylvian fissures).

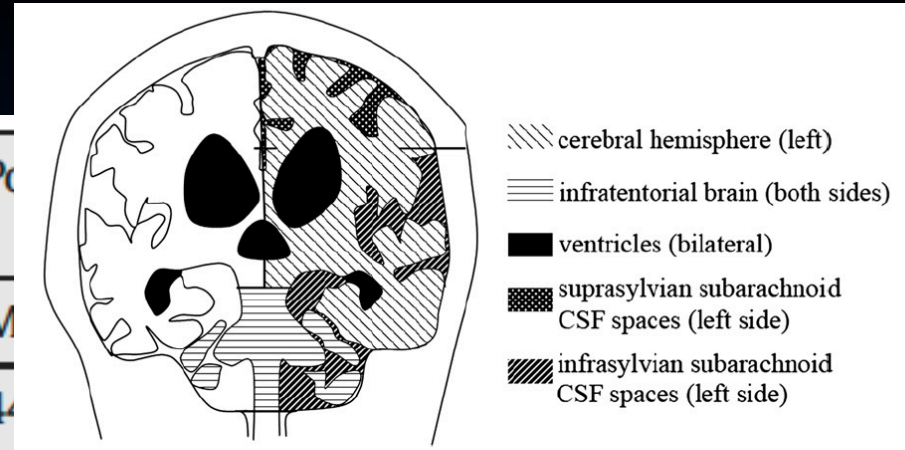
TABLE 2

*Computerized tomography characteristics in 40 patients with the NPH syndrome**

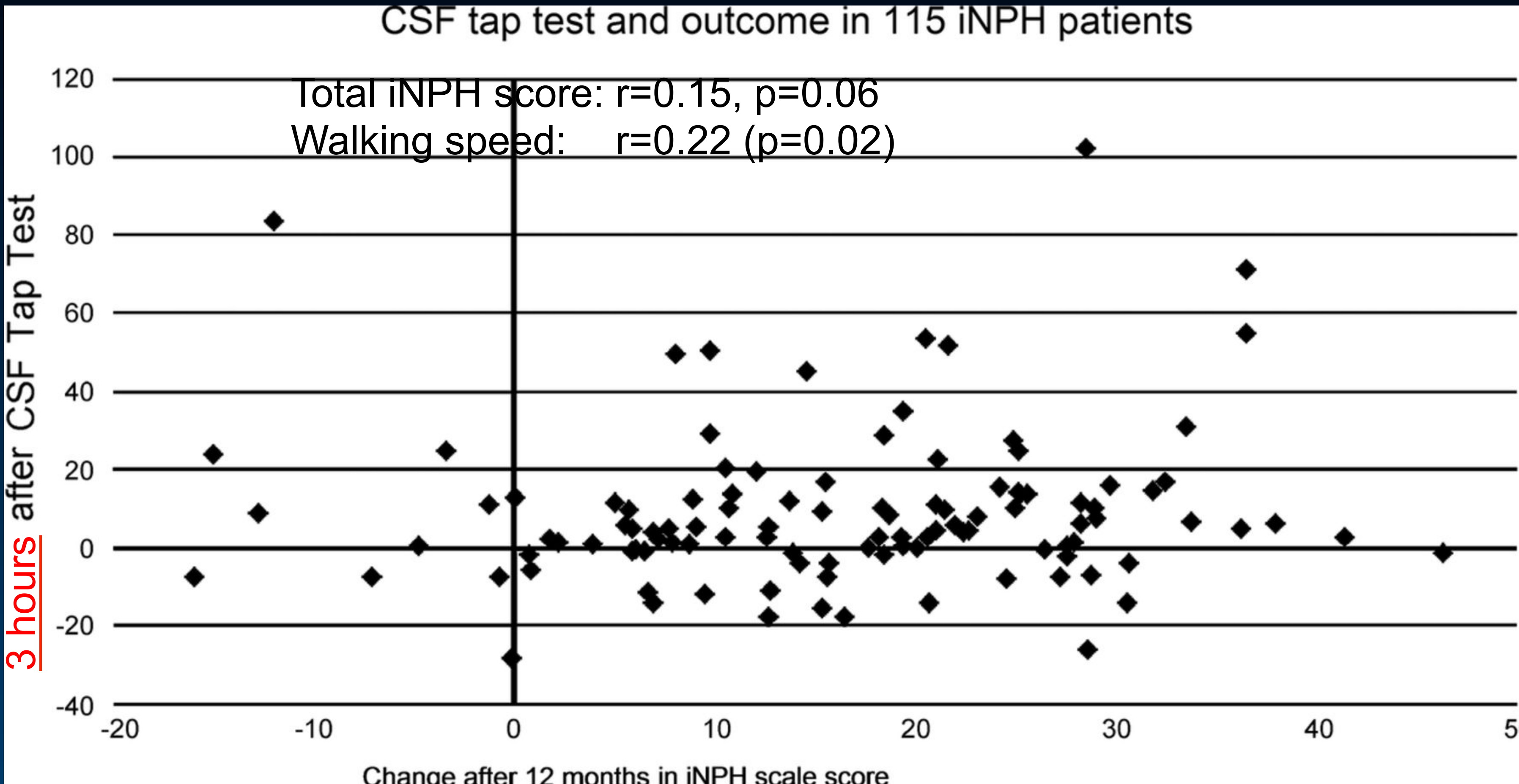
Etiology	No. of Cases	> Moderate Ventricular Enlargement	Obliteration of Cerebral Sulci	Periventricular Areas of Low Density	"Rounding" of Frontal Horns	Cortical Atrophy
SAH	10	10	8 (2)†	8	7	1
craniotomy	6	6	4 (1)†	5	5	1
CNS infection	3	3	3	3	3	–
head injury	5	5	4 (2)†	3	4	2
unknown (idiopathic)	16	16	12 (4)†	8	9	4
total cases	40	40	31 (9)†	27	28	8

* NPH = normal-pressure hydrocephalus; SAH = subarachnoid hemorrhage; CNS = central nervous system.
† Numbers in parentheses indicate cases with dilatation of the subarachnoid spaces at lower levels (Sylvian fissures included).

		Baseline		Po				
		Mean	SD	M				
Cerebral hemisphere		446.3	54.4	44				
Infratentorial brain		131.6	12.5	133.2	13.4	0.109	1.3	3.5
Ventricles		124.1	24.1	90.8	25.9	<0.0001	−26.1	19.7
Subarachnoid CSF spaces	Suprasylvian	33.5	11.8	44.8	9.5	<0.0001	43.5	38.8
	Infrasylvian	103.1	18.2	97.5	13.6	<0.05	−4.5	9.7
Total		838.5	89.9	810.2	89.0	<0.001	−3.4	3.2



Tap test and shunt outcome



Wikkelsø C et al. J Neurol Neurosurg Psychiatry, 2013

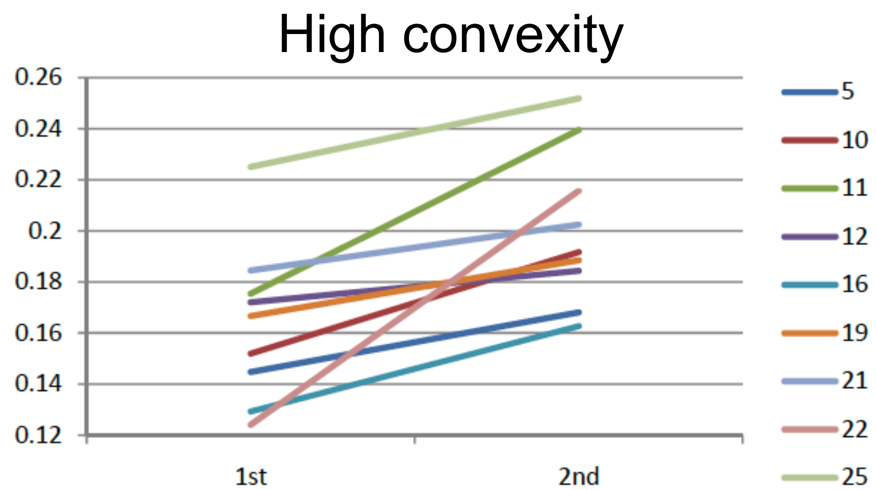
Predictive values of tap test and Rout

	CSF TT >5%	Rout >8	Rout >12	Rout >18	Rout>18, CSF TT>5%	Rout>12, CSF TT>5%
Sensitivity	52	92	70	31	18	36
Specificity	59	6	35	88	100	94
Positive pv	88	84	86	94	100	97
Negative pv	18	13	18	19	18	21
Accuracy	53	79	65	40	32	45

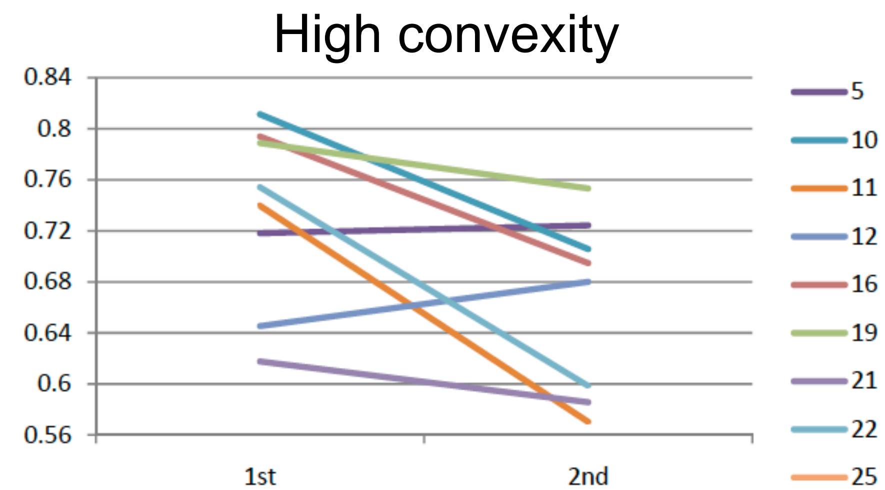
Outcome is measured by the Idiopathic Normal Pressure Hydrocephalus Scale.
CSF TT, CSF Tap Test; pv, predictive value.

Rout and CSF TT can be used for selecting patients for shunt surgery but not for excluding patients from treatment.

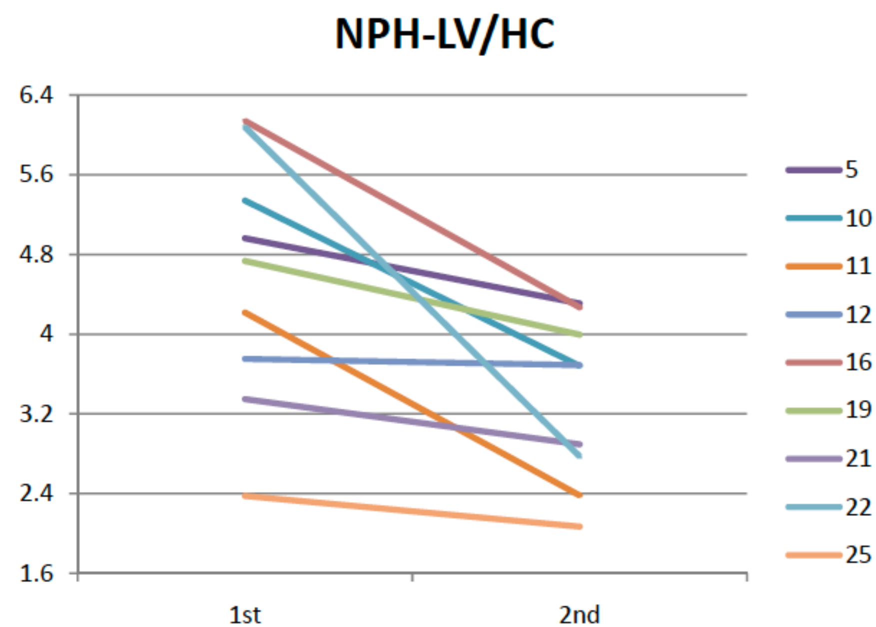
Wikkelsø C et al. J Neurol Neurosurg Psychiatry, 2013



High convexity
0.26
0.24
0.22
0.2
0.18
0.16
0.14
0.12
1st
2nd
5
10
11
12
16
19
21
22
25



High convexity
0.84
0.8
0.76
0.72
0.68
0.64
0.6
0.56
1st
2nd
5
10
11
12
16
19
21
22
25



NPH-LV/HC
6.4
5.6
4.8
4
3.2
2.4
1.6
1st
2nd
5
10
11
12
16
19
21
22
25