# *Normal-Pressure Hydrocephalus (NPH)*

Last updated: January 12, 2024

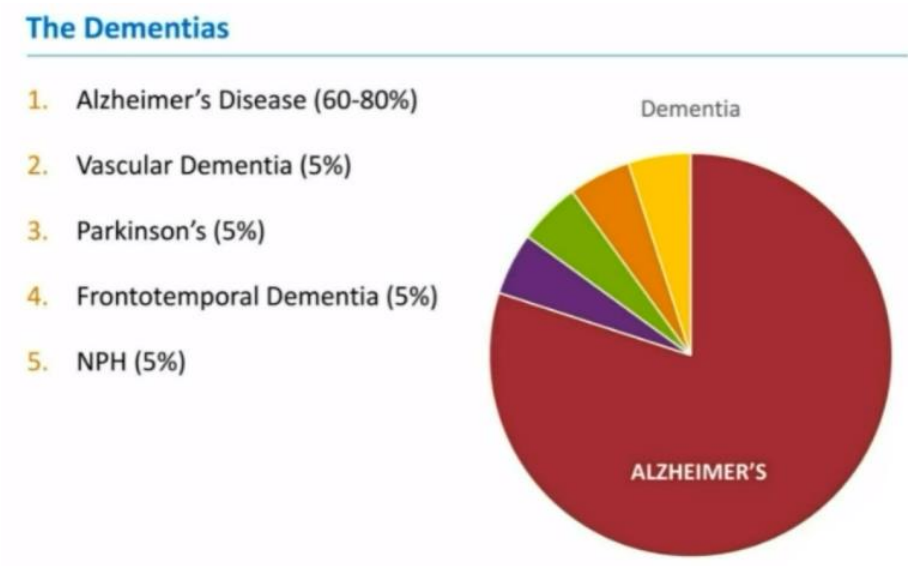


GAIT APRAXIA + DEMENTIA + INCONTINENCE
with high normal CSF pressure and dilated ventricles without brain parenchymal loss

- described by Hakim and then by Adams in 1965.

## EPIDEMIOLOGY

- highest PREVALENCE in late middle-aged and elderly groups (rare in patients < 60 years, peak incidence 60-80 yrs):
  1.6% in population-based studies (9-14% in SNF population)
  1/200 in patients > 60-70 yrs
- prevalence of iNPH in Asia, particularly in Japan, is higher than that in Europe or North America.
- accounts for ***5% of demented patients*** in older age group; true incidence is unknown and it is likely an underreported (in 2009, the incidence reported in Norway was 1.09 per 100,000 per year):




# PATHOPHYSIOLOGY

NPH - impaired CSF absorption in the absence of prior illness or injury - ***communicating hydrocephalus*** with *increased resistance to CSF outflow* (at *subarachnoid space* or *arachnoid villi* or *glymphatics*) and **normal ICP** (absence of headache & papilledema).

- normal ICP is maintained as result of apparent compensations.
- *ICP is not always normal* - transient ICP elevation may increase ventricular size and new fluid balance is reached with normal pressure but with higher force, based on Pascal's law of pressure in fluids.

Causes of subarachnoid space-arachnoid villi obstruction / scarring (i.e. secondary NPH):

1) SAH
2) meningitis
3) head trauma
4) CSF protein↑

N.B. large number of patients ***do not have identifiable cause*** (idiopathic NPH).

# PATHOLOGY

- there are no generally accepted neuropathological criteria for postmortem diagnosis.
- discrete abnormalities, such as arachnoid fibrosis, occur too infrequently.

# CLINICAL FEATURES

- **older patient** with insidious PROGRESSIVE TRIAD (in order of appearance; full triad is present in 60% of patients):

N.B. patients may appear *mildly parkinsonian*, but their tremor, if present, is postural, not resting.

N.B. reported symptoms should be corroborated by an informant familiar with the patient's premorbid and current condition!

1. **GAIT APRAXIA*** (94-100%) – most frequent first symptom: slow, unsteady, **wide-based "magnetic gait"** with small steps** + difficult turning (takes several steps), falls.

**difficulty picking feet off ground; freezings can happen

Other gait synonyms: "apraxic", "bradykinetic", "glue-footed", "parkinsonian", "short-stepped", and "shuffling".

NPH = "Lower-Body Parkinsonism"

- legs are bradykinetic (vs. Alzheimer disease – normal gait).
- disturbances in stance with tendency to lean forward and imbalance exacerbated by eye closure – "hydrocephalic astasia-abasia".
- falls are common.
- normal motor force, tone, and reflexes.

> N.B. upper motor neuron signs or lower limb weakness may be indicative of ***cervical myelopathy*** and ***lumbar canal stenosis***, respectively!

- *discrepancy between **walking** and **simulated walking*** (eliminates pyramidal lesion) - can move legs well and imitate walking while in chair, but becomes awkward and severely impaired as soon as attempts to walk.
- difficulty in handwriting and dressing.
- differentiation from parkinsonism:
  - Parkinson's patients are able to increase their stride length and walking cadence with aid of external cueing such as counting, command lines / landmarks; vs. patients with NPH have gait apraxia that does not respond to aids.
  - patients with NPH mobilize with relatively preserved arm swing.

Criteria to classify gait as "**probable NPH**" - at least two of the following should be present and not be entirely attributable to other conditions:

a. Decreased step height
b. Decreased step length
c. Decreased cadence (speed of walking)
d. Increased trunk sway during walking
e. Widened standing base
f. Toes turned outward on walking
g. Retropulsion (spontaneous or provoked)
h. En bloc turning (turning requiring three or more steps for 180 degrees)
i. Impaired walking balance, as evidenced by two or more corrections out of eight steps on tandem gait testing

Objective quantitative evaluation:

1) timed up & go test (TUG)
2) short-distance straight walking test

2. **COGNITIVE IMPAIRMENT** (78-98%) – progressive ***subcortical frontal dysexecutive syndrome***: psychomotor slowing, reduced attention, memory loss, difficulty planning, apathy → generalized cognitive impairment.

NPH – treatable dementia

- aphasia is uncommon.
- headache is uncommon (look for other causes of it).
- pathophysiologic mechanism - *compromised microcirculation*, due to increased intraparenchymal pressure (PET shows widespread glucose utilization defects in subcortical and cortical regions).

- differentiation from Alzheimer's disease: iNPH has milder disorientation and memory impairment, and greater frontal lobe dysfunction (attention impairment, declined psychomotor speed, impaired verbal fluency, dysexecutive syndrome).

Criteria to classify cognition as "**probable NPH**" - at least two of the following should be present and not be entirely attributable to other conditions:

a. Psychomotor slowing (increased response latency)
b. Decreased fine motor speed
c. Decreased fine motor accuracy
d. Difficulty dividing or maintaining attention
e. Impaired recall, especially for recent events
f. Executive dysfunction, such as impairment in multistep procedures, working memory, formulation of abstractions/similarities, insight
g. Behavioral or personality changes

Objective quantitative evaluation:

1) **Mini-Mental State Examination** – general cognitive evaluation
2) Wechsler Adult Intelligence Scale-III digit symbol coding and symbol search tasks – for psychomotor speed
3) Frontal Assessment Battery – frontal lobe function
4) Rivermead Behavioral Memory Test – memory testing

3. **URINARY INCONTINENCE*** (60-92%)
   - in urodynamic test, detrusor hyperactivity was seen in about 70% of patients, and bladder volume was approximately 200 mL, which is significantly smaller than the adult average.

Criteria to classify urinary continence domain as "**probable NPH**" – either one of the following should be present and not be entirely attributable to other conditions:

a. Episodic or persistent urinary incontinence
b. Urinary and fecal incontinence

Or any two of the following should be present:

a. Urinary urgency as defined by frequent perception of a pressing need to void.
b. Urinary frequency as defined by > 6 voiding episodes in an average 12-hour period despite normal fluid intake.
c. Nocturia as defined by the need to urinate > 2 times in an average night.

*relate to *stretched fibers* innervating legs and sphincters that project through *vicinity of frontal horns* of ventricular system;

— early hypothesis suggested that enlargement of the ventricles led to compression and/or deformation of the upper motor neuron fibers passing through the medial portion of the corona radiata.
— EMG evidence reveals contraction of antagonistic muscle groups and abnormally increased activity in the antigravity muscles acting on hip and knee joints - gait disorder of NPH is a disturbance in the phased activation of muscle groups (*disorder of subcortical motor control* rather than a primary pyramidal disturbance).

## CLINICAL COURSE

- origin after age 40 yr (International iNPH guidelines 2005) with average age of onset around 75 years.
- insidious onset (versus acute)
- minimum duration of > 3-6 mo

- progression over time
- gait disturbance should precede cognitive decline.

## SEVERITY GRADES

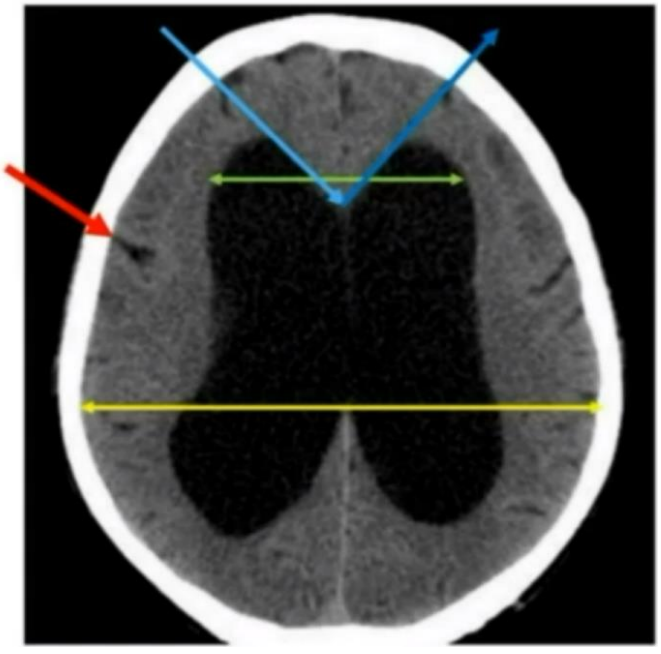
Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH) - **iNPH grading scale:**

| Grade | Gait disturbance | Dementia | Urinary incontinence |
|---|---|---|---|
| 0 | Normal | Within normal range | Absent |
| 1 | Unstable, but independent gait | No apparent dementia but apathetic | Absent but with pollakiuria or urinary urgency |
| 2 | Walking with a cane | Socially dependent but independent at home | Sometimes at night |
| 3 | Walking with two canes or a walking frame | Partially dependent at home | Sometimes during the day |
| 4 | Walking not possible | Totally dependent | Frequent |

## DIAGNOSIS – IMAGING

- hydrocephalus with little or no cortical atrophy (vs. Alzheimer disease) + no evidence of obstruction to CSF flow (look for flow voids on MRI in aqueduct)

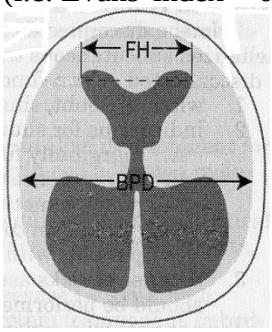
Evans' index > 0.3 (z-Evans' index > 0.42)
Callosal angle < 90 degrees
DESH



## VENTRICULOMEGALY

maximal width of ***frontal horns*** measure > 30% of maximal biparietal diameter on the same slice

(i.e. Evans' index > 0.3)

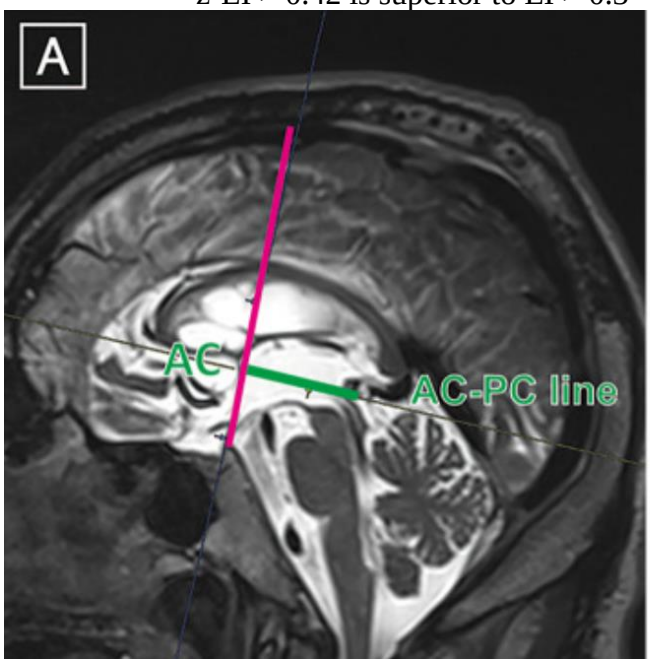


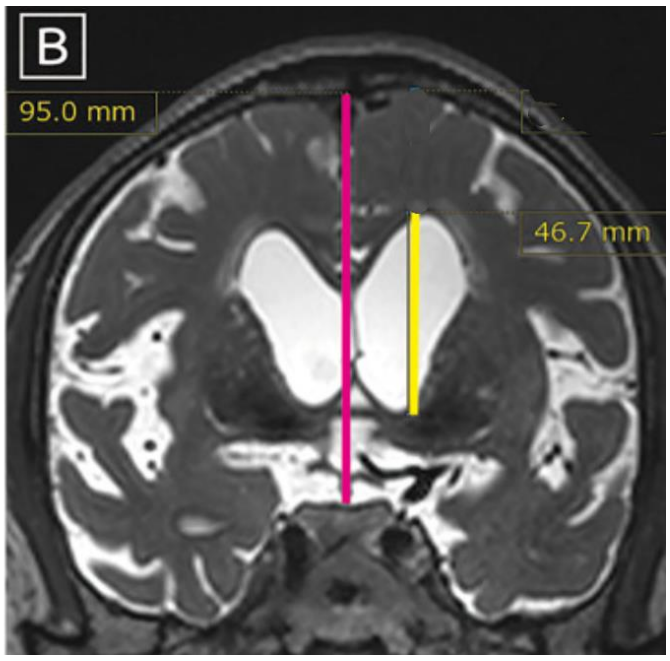

ventricular ***temporal horns*** are > 2 mm (not entirely attributable to hippocampus atrophy)

- although not common, transependymal CSF flow occasionally can be seen.
- diameter of corpus callosum decreases in many cases as the dorsal surface of the ventricle domes upward.
- sometimes ventriculomegaly is mild (e.g. Evans' index < 0.3).
- ventricular enlargement usually occurs vertically on the coronal plane (z-axis) rather than along the axial plane (x-axis).

  z-EI = height of the frontal horns of the lateral ventricles in the z-axis direction divided by the midline diameter of the skull.

  z-EI > 0.42 is superior to EI > 0.3



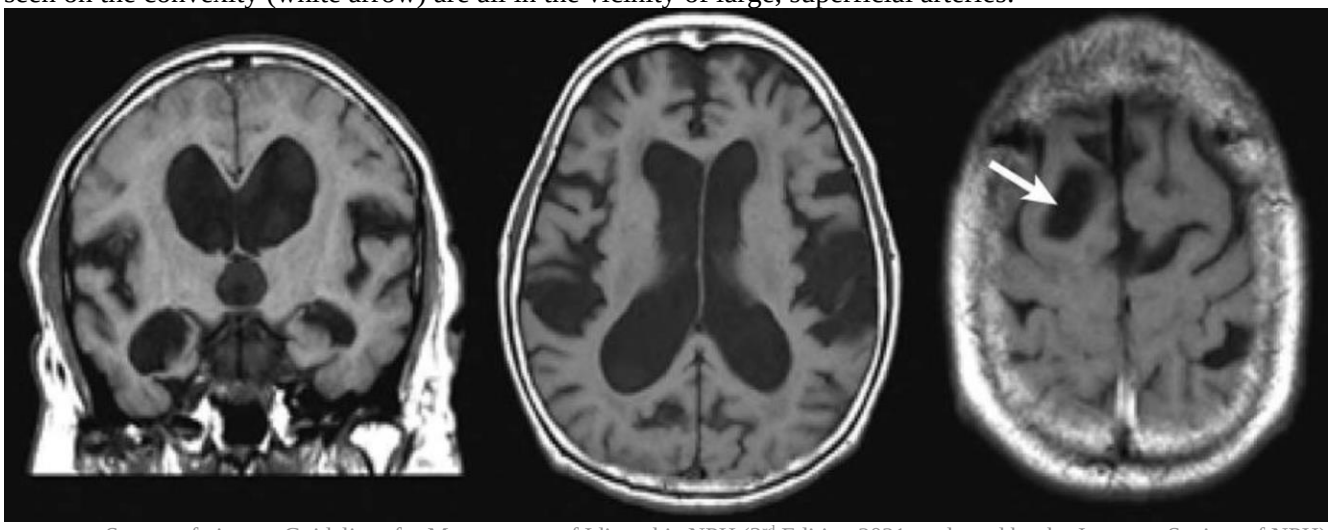




## DISPROPORTIONATELY ENLARGED SUBARACHNOID-SPACE HYDROCEPHALUS (DESH)

- imaging hallmark of iNPH: ventricular enlargement accompanied by shrinkage of the subarachnoid space at cerebral high convexities ("high-convexity / midline tightness") + Sylvian fissure enlargement.

- best seen on coronal MRI.
- good indicator that iNPH will respond to treatment.
- DESH findings normalize after shunting.

DESH - narrowing of the CSF spaces near the vertex + widening of the Sylvian fissure; few wide sulci that are seen on the convexity (white arrow) are all in the vicinity of large, superficial arteries:

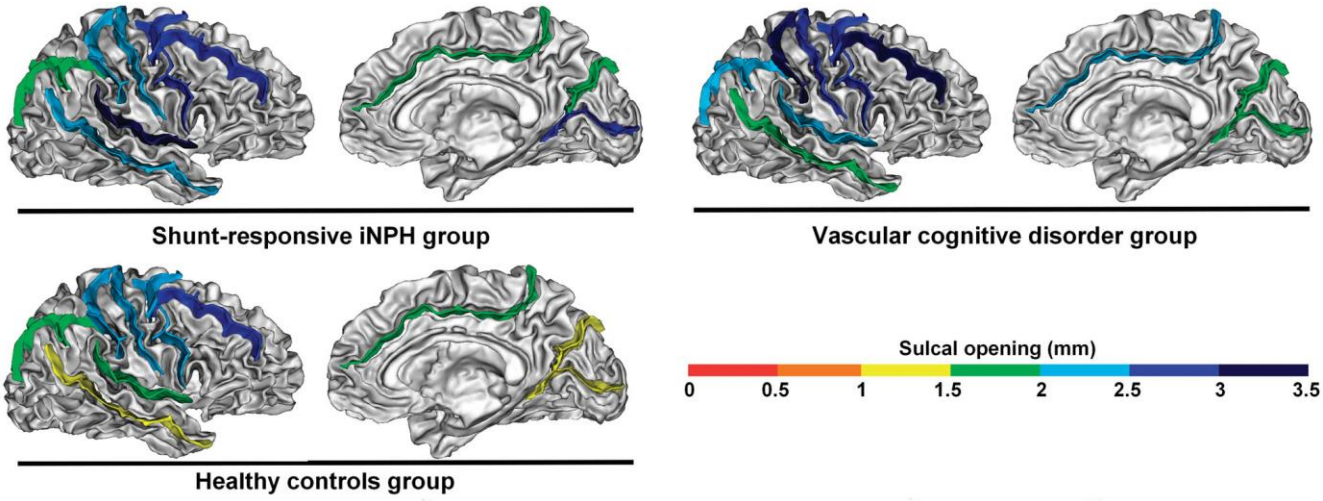


Source of picture: Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH)

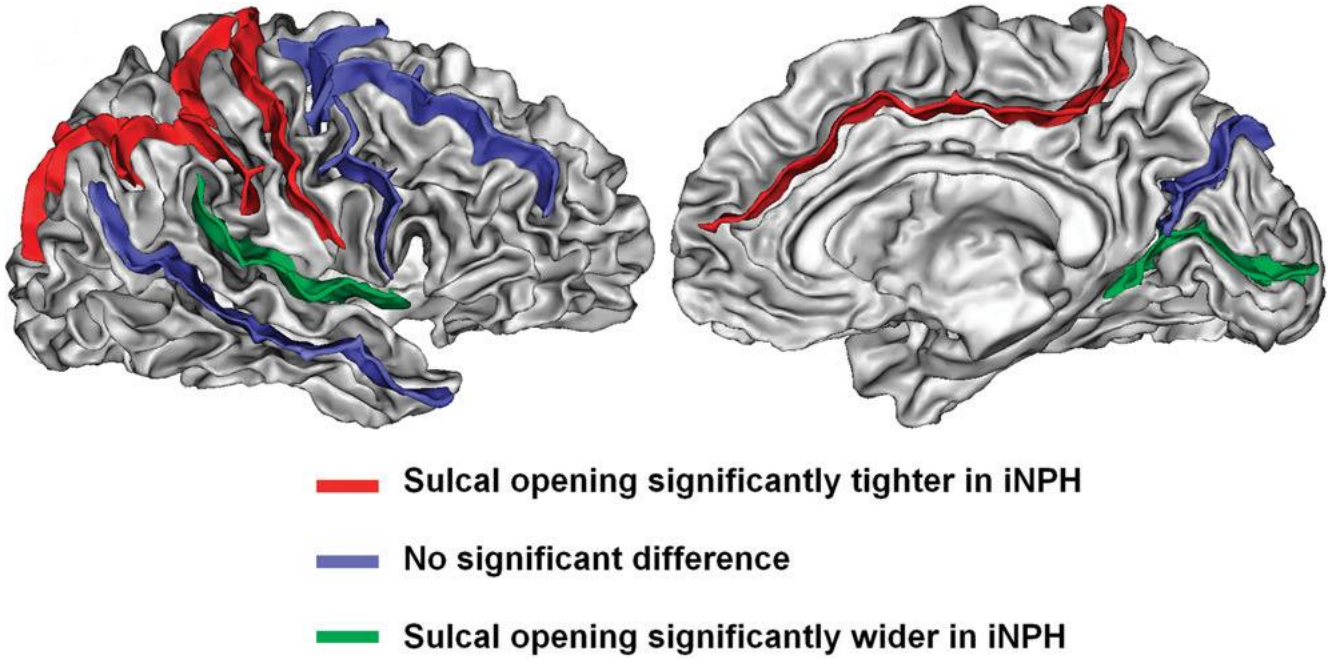
## Sulcal Morphometry

*Grégory Kuchcinski et al. Idiopathic Normal-Pressure Hydrocephalus: Diagnostic Accuracy of Automated Sulcal Morphometry in Patients With Ventriculomegaly. Neurosurgery 85:E747–E755, Oct 2019*

"NPH stretches lateral ventricles superiorly so superior sulci get compacted vs. inferior sulci stretched"

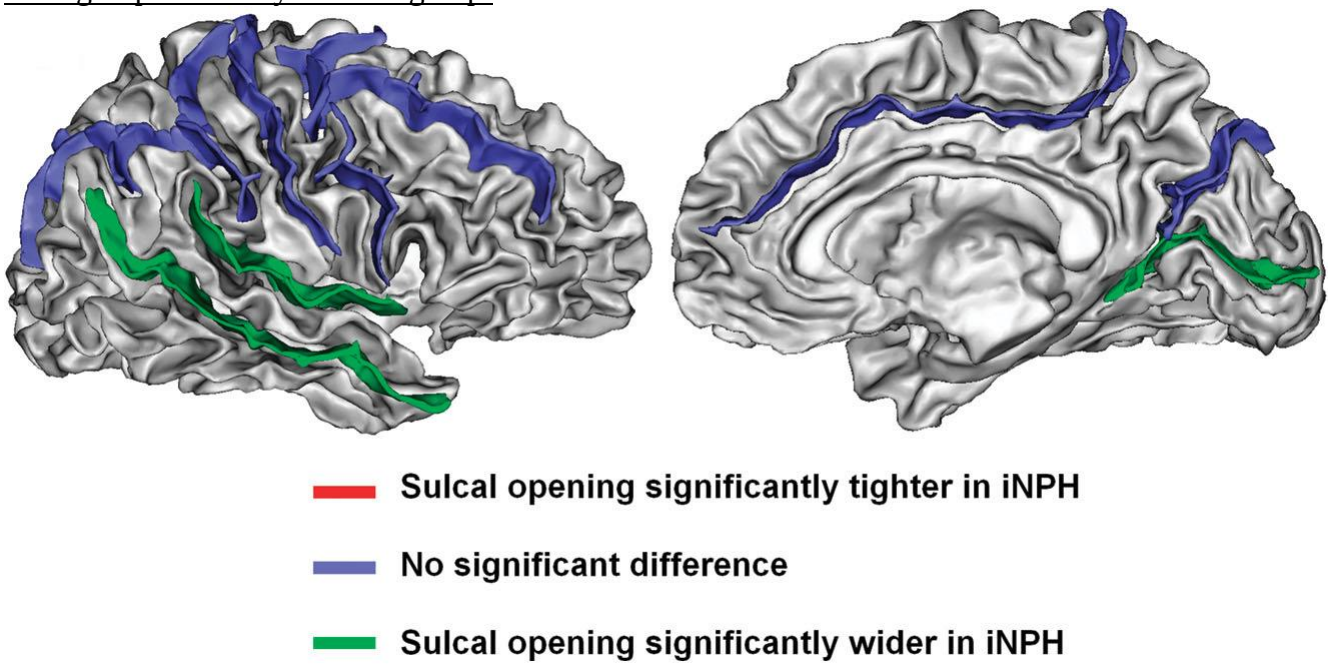



NPH group vs vascular cognitive disorder group:




- calcarine/cingulate ratio ≥ 0.96 had an excellent sensitivity (96.8%, 30/31) and a good specificity (80.0%, 28/35) whereas a lateral/intraparietal ratio ≥ 1.49 had a fair sensitivity (77.4%, 24/31) and an excellent specificity (97.1%, 34/35).

NPH group vs healthy controls group:



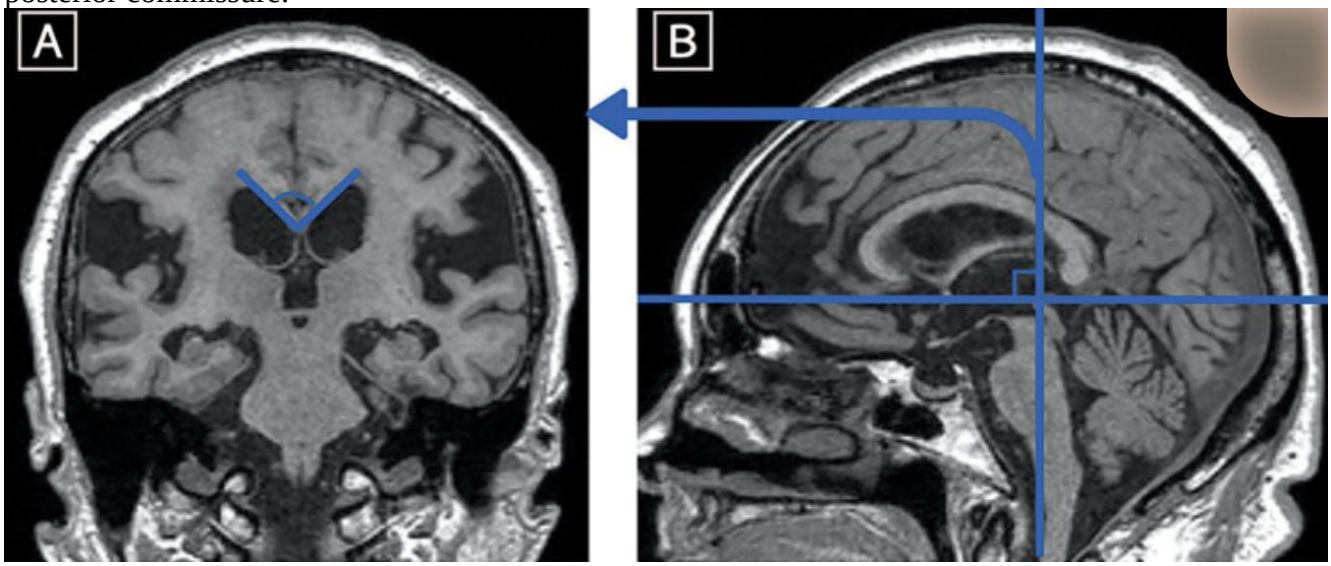

- the best parameter to differentiate NPH patients from healthy controls was the calcarine/cingulate ratio (AUC = 0.96; 95% CI = 0.91, 1.00); cut-off value ≥ 0.95 had a sensitivity of 96.0% (24/25) and a specificity of 88.0% (22/25).

Conclusion - the best parameter to discriminate shunt-responsive NPH from vascular cognitive disorder and healthy controls was the ratio between ***calcarine sulcus*** and ***cingulate sulcus*** opening with an area under the curve of 0.94 (95% CI: 0.89, 0.99); cut-off value of 0.95 provided the highest sensitivity (96.8%) and specificity (83.3%).

## STEEPENING OF CALLOSAL ANGLE

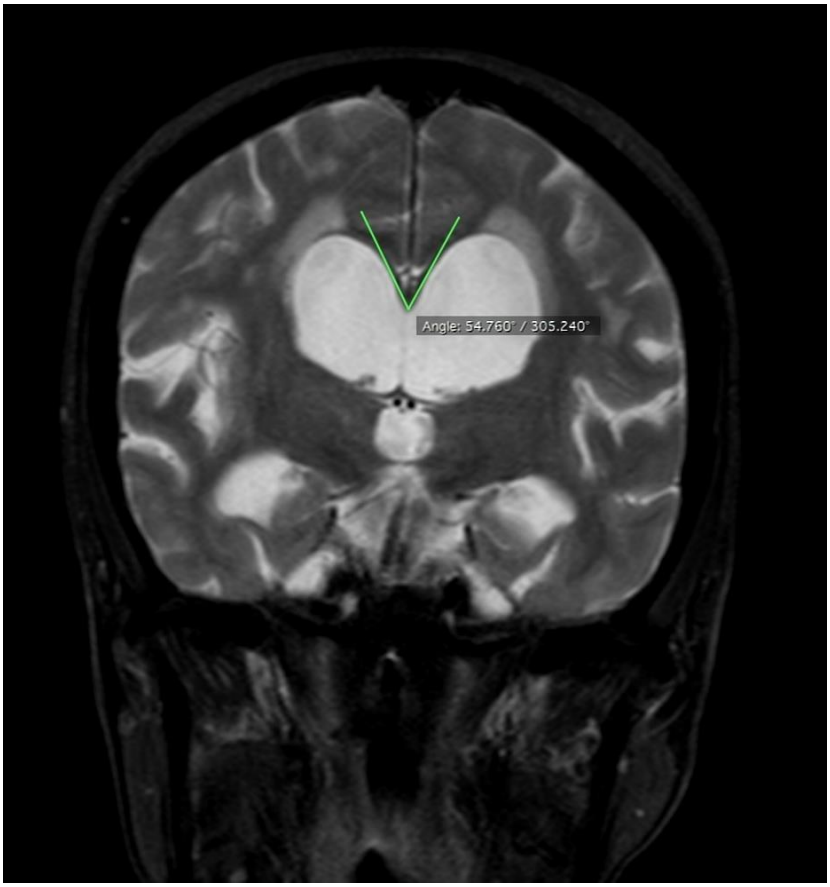
NPH stretches lateral ventricles superiorly – grows Mickey Mouse ears

- indirect index of DESH findings.
- proposed as a useful marker of idiopathic NPH in distinguishing from those with ***ex-vacuo ventriculomegaly***.
- angle should be measured on a coronal image perpendicular to the AC-PC plane at the level of the posterior commissure:




- patients with NPH have smaller angles than those with ventriculomegaly from atrophy or normal controls.
  - normal angle is 100-120°
  - in NPH angle is 50-80°
  - ability to differentiate iNPH from Alzheimer's disease has a sensitivity of 97%, a specificity of 88%, and a positive predictive value of 93% at a cutoff value of 90°
  - in one study, symptomatic NPH patients who responded to shunting had a significantly smaller mean preoperative callosal angle (59°, 95% CI 56-63°) compared with those who did not respond (68°, 95% CI 61-75°).

    *Virhammar J, Laurell K, Cesarini KG et-al. The callosal angle measured on MRI as a predictor of outcome in idiopathic normal-pressure hydrocephalus. J. Neurosurg. 2014;120 (1): 178-84*




Case courtesy of Dr Bruno Di Muzio >>

## DIAGNOSIS – CSF DYNAMIC TESTS

Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH): CSF drainage test (tap test) is useful for diagnosing iNPH and predicting the therapeutic effect of a shunt intervention. ***Recommendation Grade 1, Level of Evidence B***.
It is recommended that the CSF tap test is evaluated (e.g. iNPHGS) within 24 hours after CSF removal and multiple evaluations should be done for up to a week. Cognitive impairment and urinary dysfunction are expected to improve subsequently after gait improvement, but there is no established evidence regarding the timing of this. ***Recommendation Grade 2, Level of Evidence C.***

Minimum battery to use with CSF dynamic tests:

1. 10-meter gait velocity (may add: number of steps for 10-meter walk, number of steps to turn 180 degrees)
2. TUG
3. MoCA (rather than MMSE)

Additional tests: SDMT (symbol digit modalities test), BDI-II, Lawton ADL, OAB-Q (bladder) score, Tinetti Balance, QOL (Eq-5D-5L) evaluation

1. Lumbar puncture "tap test" – high-normal CSF pressure (6-24 $cmH_2O$), normal CSF composition.

**Removal of 30-50 ml CSF** → transient clinical *improvement in cognitive & gait dysfunction*!

- sensitivity of 58% (26–87%), specificity of 75% (33–100%) in systematic reviews; 73-100% positive predictive value to indicate better prognosis with shunting.

- may have 50% placebo effect!
- if a tap test does not result in any improvement, iNPH cannot be excluded.
- there is no difference in the positive detection rate, sensitivity, and specificity with respect to the amount of CSF removed, in the range of 30–50 ml.
- evaluation method and timing of assessing changes in clinical symptoms are more important than the volume of CSF removed - evaluation should be performed:
    1) 2–4 hours after the tap test;
    2) on the following day (approximately 24 hours later) - symptoms may improve from the following day onward;
    3) multiple times within the first week.
    - in a single-center retrospective observational study, walking function improved on day 2 (48 hours later) after the tap test → degree of improvement decreased after day 3.
    - in SINPHONI-2 study, cognitive impairment and urinary incontinence tended to improve later than gait disturbance and were evaluated within one week of the tap test; in addition, although there is a report stating that MMSE did not improve the day after the tap test but improved 1 week later.

2. Prolonged external lumbar drainage (in excess of 300 mL, e.g. 3 days at 5 mL/hr) – highest sensitivity (50-100%), specificity (80%), and positive predictive value (80-100%); there is no known negative predictive value.

- Japanese guidelines state: it has not been established whether continuous CSF drainage test is more predictive of shunt efficacy than CSF tap test.

Practically:

a) if LP helps or if opening pressure > 15-20 cmH2O (in old patient it is too much) → **shunt**.
b) otherwise → **lumbar drain trial**.

# DIAGNOSIS – ANCILLARY TESTS

- diagnosis of NPH is complicated by the variability in its clinical presentation and course.
- these test are not required routinely but may increase confidence in the diagnosis in selected cases.

## CFS BIOMARKERS

**CSF biomarkers for distinguish iNPH from normal control (NC) and Alzheimer's disease (AD):**

| | Differential diagnosis | Predict poor CSF shunt effect |
|---|---|---|
| **Aβ42** | No change compared to AD, lower than NC | Low value |
| **p-tau** | Lower than AD, no change compared to NC | High value |
| **t-tau** | Lower than AD, no change compared to NC | High value |
| **NFL** | Higher than NC | High value |
| **LRG** | Higher than NC | High value |
| **Aβ38** | No change compared to AD, lower than NC | |
| **Aβ40** | No change compared to AD, lower than NC | |
| **PTPRQ** | Higher than NC | |
| **Brain-type transferrin** | Lower than NC | |

Aβ: amyloid β protein, LRG: leucine-rich α2-glycoprotein, NFL: neurofilament light chain, p-tau: phosphorylated tau, PTPRQ: protein tyrosine phosphatase receptor type Q, t-tau: total tau.

## ICP MONITORING

- rarely used for diagnosing iNPH.
- monitoring time is 12–48 hours, mainly at night.
- measurement site is most commonly the lumbar cistern.
- main parameters of ICP monitoring:
  (1) Intracranial **basal pressure** - is set at around 7–15 mmHg, and most patients with iNPH have an upper limit of normal pressure; value is controversial: when basal pressure is high, the efficacy of a shunt intervention is assumed to be also high but there are cases in which there is no correlation
  (2) Intermittent pressure **B-waves** (decreased brain compliance → slowly increase ventricular size → ischemic damage) - appear more frequently during REM sleep; the more frequently they appear (≥ 15% of all records), the more effective shunt intervention has been reported to be but there are also reports stating that there is no correlation.
  (3) **CSF pulse pressure** - in the effective shunt intervention groups, increase in amplitude and decrease in latency were observed and the average value (high wave relative frequency) of the three highest wave amplitudes was often ≥ 9 mmHg (positive prediction rate of 96%); correlation between amplitude and pressure is considered to be high.

## INFUSION TEST / CSF OUTFLOW RESISTANCE

- thought to reflect CSF absorption pathways.

- saline is injected into CSF space (e.g. ventricles or lumbar sac) either by rapid bolus or continuous infusion.
- CSF outflow resistance can then be calculated with pressure-volume study and used to assess CSF circulation for signs of disturbance.
- main parameters:
  (1) **CSF outflow resistance (Rout)**
  Efficacy of shunting is high when Rout is high
    - shunting lowers Rout
    - Rout has been found to be significantly higher in effective shunt intervention groups (positive prediction rate ≥ 80%)
    - reports state that the absolute value of Rout and the effective/ineffective threshold is around 14–20 mmHg/mL/min (positive prediction rate 80–92%), however, Rout measured in the spinal CSF compartment may not correctly reflect the Rout of the cerebral ventricular space or the entire cerebrospinal space.
    - there are cases in which a shunt intervention was effective even though the Rout was low.
  (2) **CSF outflow conductance (Cout)** is significantly lower in effective shunt intervention groups.
    - Cout effective/non-effective threshold is said to be 0.08 mL/min/mmHg (positive prediction rate of 74–76%).
    - there is no high-level evidence showing that it is useful for diagnosing iNPH.

## SPECT-ACETAZOLAMIDE CHALLENGE

**Convexity apparent hyperperfusion (CAPPAH)** - reflects the morphological changes of DESH: decreased CBF around Sylvian fissure and relatively increased CBF around the high parietal region.

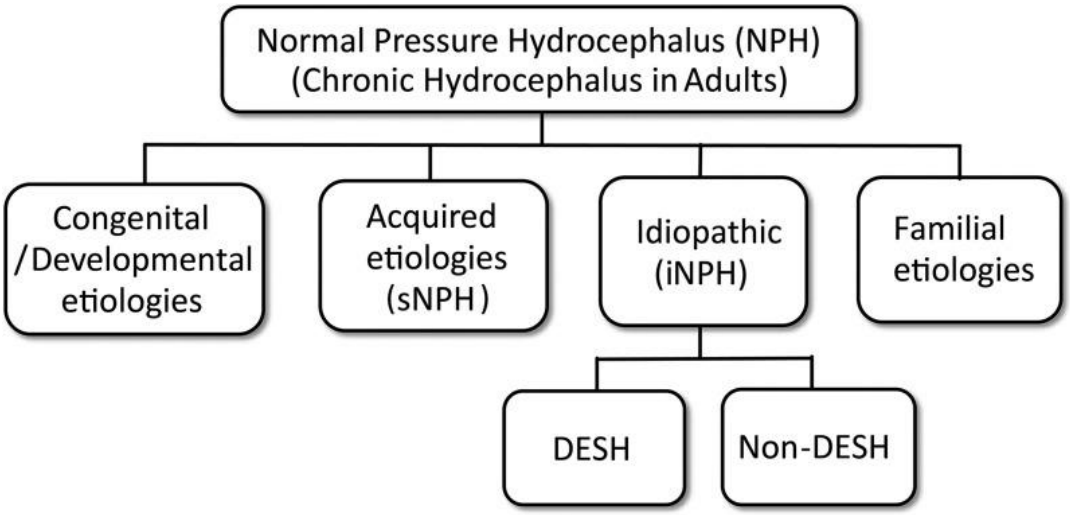
- acetazolamide-enhanced SPECT showed that increase in CBF after acetazolamide administration could predict improvement in cognitive function after shunting.

Historical tests:
**Radioisotope cisternography** (not particularly specific) - isotope injected intrathecally:
***normal*** - isotope is seen around brain convexity within 48 hours;
***NPH*** - isotope reflux into ventricles and stasis beyond 48 hours; delayed clearance of radiotracer over the cerebral convexities after 48–72 h

### BRAIN BIOPSY

- consider it during shunting procedure – to differentiate from Alzheimer disease.

## CLASSIFICATION




### NPH SUBTYPES

– respond to VPS or ETV.

1) **longstanding overt ventriculomegaly in adults (LOVA)** - severe lateral and third ventriculomegaly, features of chronic intracranial hypertension (e.g. enlarged head circumference, sella turcica enlargement and erosion). NPH-like symptoms start to appear in adulthood.
   N.B. most cases of LOVA are non-communicating hydrocephalus accompanied by aqueductal stenosis!
2) **panventriculomegaly with a wide foramen of Magendie and large cisterna magna (PaVM)**;
   - majority of cases exhibit pontine arachnoid septation and restricted CSF dynamics in the pontine cistern.
   - frequently co-occurs within families, suggesting a genetic component.
3) **asymptomatic ventriculomegaly with features of iNPH on MRI (AVIM)** - asymptomatic cases that exhibit iNPH features on brain MRI; high risk of progressing on to iNPH – patient should be monitored carefully.

## DIFFERENTIAL DIAGNOSIS

NPH can resemble, or occur in combination with, various disorders that are prevalent in the elderly, such as cerebrovascular disease*, neurodegenerative disorders (e.g., Alzheimer's, Parkinson's, Lewy body disease), primary urological disorders, spinal stenosis.
N.B. these coexistences may make patients not to respond to shunt (false-negative response)!

*bilateral multiple lacunar strokes (état lacunaire) can give all three symptoms!!! see p. Vas3 >>

Ventriculomegaly + absence of full triad symptoms = generally not NPH

No any single component of clinical triad = unlikely NPH

No ventricular enlargement even if with some or all of the triad symptoms = unlikely NPH

Papilledema or ICP↑ = unlikely NPH

GAIT DISTURBANCE

*Vascular*
- Cerebrovascular disease
- Stroke
- Multi-infarct dementia
- Binswanger's disease

*Neurodegenerative*
- Parkinson's disease
- Alzheimer's disease
- Progressive supranuclear palsy
- Frontotemporal dementia

*Miscellaneous*
- Peripheral neuropathy
- Cervical myelopathy
- Lumbar canal stenosis
- Diabetic neuropathy
- Autonomic dysregulation
- Spinal neoplasm

DEMENTIA

*Vascular*
- Cerebrovascular disease
- Stroke
- Multi-infarct dementia
- Binswanger's disease
- CADASIL (cerebral autosomal dominant arteriopathy, subcortical infarcts, and leukoencephalopathy)

*Neurodegenerative*
- Parkinson's disease
- Alzheimer's disease
- Progressive supranuclear palsy
- Frontotemporal dementia
- Corticobasal degeneration

| Cognitive skills | Alzheimer's disease | Idiopathic normal-pressure hydrocephalus |
|---|---|---|
| Impaired | Memory<br>Learning<br>Orientation<br>Attention concentration<br>Executive functions<br>Writing | Psychomotor slowing<br>Fine motor speed<br>Fine motor accuracy |
| Borderline impairment | Motor and psychomotor skills<br>Visuospatial skills<br>Language<br>Reading | Auditory memory (immediate and delayed)<br>Attention concentration<br>Executive function<br>Behavioral or personality changes |

URINARY INCONTINENCE

*Structural*

Bladder outflow obstruction

Benign prostatic hypertrophy

*Bladder innervation*

Autonomic dysregulation

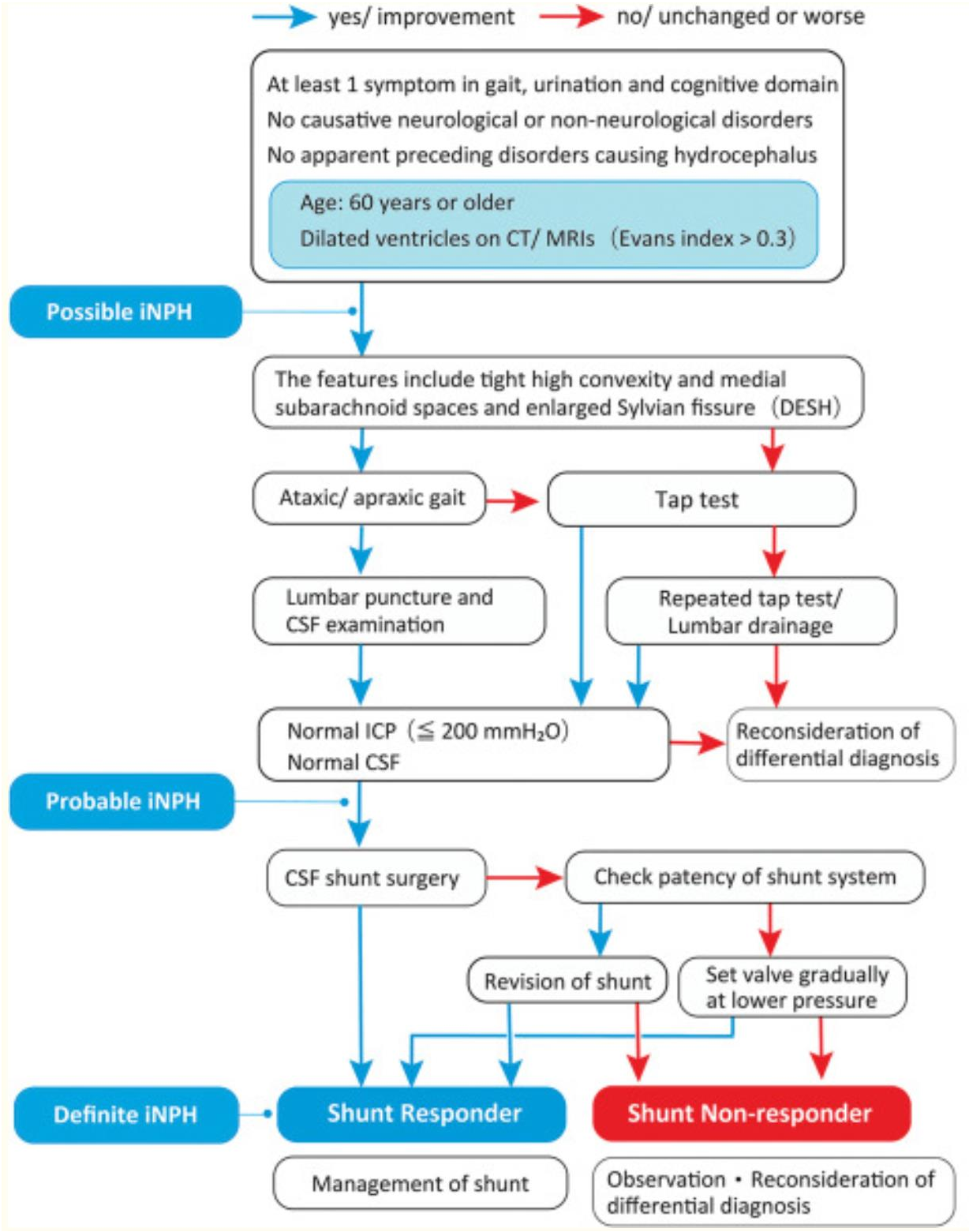
Lumbar canal stenosis

*Miscellaneous*

Medications—anticholinergics, diuretics

# DIAGNOSIS – ALGORITHM

Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH):




Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH):

**Possible iNPH** – unexplainable ≥ 2 symptoms in the clinical triad: gait disturbance, cognitive impairment, and urinary incontinence.

**Probable iNPH** = possible iNPH +

CSF pressure ≤ 200 mmH2O and normal CSF content

DESH with gait disturbance (small stride, shuffle, instability during walking, and increase in instability on turning)

OR

Improvement of symptoms after CSF tap and/or drainage

**Definite iNPH ("shunt responder")** - objective improvement after CSF shunt surgery.

# TREATMENT

- advance stages (> 2 years' duration) tend to be less responsive to treatment - *early treatment can be instrumental* in achieving an optimal treatment outcome and avoiding irreversible impairments.

Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH):
CSF shunt intervention is effective for treating iNPH. ***Recommendation Grade 1, Level of Evidence B***

a) **ventriculo-peritoneal (VP)** - should not be performed by free-hand; allows brain biopsy; frontal approach preferred by experts.
b) **lumbo-peritoneal (LP)** – most common choice in Japan; however, *serious adverse events* more common (22% vs 15% with VPS), *CSF over-drainage* is more common, greater likelihood of *need for shunt revision* (6.8% vs 1% for VPS) and more difficult to test patency (incl. shuntogram); in the elderly (frequent spinal degenerative disease), diagnostic imaging of the entire spine should be done before surgery.
c) **ventriculo-atrial (VA)** - occlusion and repeated interventions less common than with VPS, but *overdrainage (and SDH)* is more common.

- avoid in multi-infarct state - deep white matter T2 hyperintensities (marker of comorbidity); some studies showed inverse correlation with shunt responsiveness; other studies found no correlation.
- alternative methods of shunting:
  a) **ETV** - success rates generally reported around 50% (i.e. efficacy worse to that of VPS) and higher risk of complications than with VPS.
  b) **lumbar subcutaneous shunt** proposed by Mendelow's group.

Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH):
A programmable-pressure valve is recommended.

- patients with fixed-pressure valves require shunt revision and surgery for a subdural hematoma more often.

Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH):
If intracranial hypotension is detected and valve is set low, a mechanism (anti-siphon/gravity device, etc.) to prevent excessive drainage should be added. ***Recommendation Grade 1, Level of Evidence B***

- in a meta-analysis, no significant difference was observed in the symptom improvement rate, subdural fluid retention rate, and shunt revision rate between the single programmable-pressure valve with and without an over-drainage prevention mechanism.

Guidelines for Management of Idiopathic NPH (3rd Edition 2021, endorsed by the Japanese Society of NPH) – **programmable valve initial setting**:

a) initial high pressure setting with gradual decrease until clinical response or over-drainage symptoms are observed can be the proper approach.
b) setting initial pressure according to the body height and weight/gender table and implementing corrections if necessary.

***Recommendation Grade 2, Level of Evidence C***

- for many patients, **12-15 cmH2O** is adequate initial setting (but adjust based on intraop manometry – patient flat, pCO2 as close to normal as possible).
- in old days (fixed valve), some experts would keep patient flat for several days.
- while valve adjustments are made, keep patient off anticoagulants.

**Reference table for initial pressure setting of programmable valve**

| Women | BW (kg) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ht (cm) | 35 | 40 | 45 | 50 | 55 | 60 | 65 | 70 | 75 | 80 | 85 | 90 | 95 | 100 | 105 | 110 |
| 140 | 16 | 12 | 9 | 6 | 3 | | | | | | | | | | | |
| 145 | 19 | 16 | 13 | 10 | 7 | 4 | | | | | | | | | | |
| 150 | 23 | 19 | 16 | 13 | 10 | 7 | 4 | | | | | | | | | |
| 155 | 26 | 23 | 20 | 17 | 14 | 12 | 9 | 6 | 3 | | | | | | | |
| 160 | 29 | 27 | 24 | 21 | 18 | 16 | 13 | 11 | 8 | 5 | 3 | | | | | |
| 165 | 33 | 30 | 27 | 24 | 21 | 18 | 16 | 14 | 12 | 10 | 8 | 5 | 1 | | | |
| 170 | 36 | 34 | 31 | 28 | 25 | 23 | 20 | 18 | 15 | 13 | 11 | 9 | 6 | 4 | | |
| 175 | 39 | 37 | 34 | 31 | 29 | 27 | 24 | 20 | 18 | 16 | 14 | 12 | 10 | 8 | 5 | 3 |
| 180 | 42 | 40 | 37 | 35 | 33 | 31 | 28 | 26 | 23 | 20 | 18 | 16 | 14 | 12 | 10 | 8 |

| Men | BW (kg) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ht (cm) | 35 | 40 | 45 | 50 | 55 | 60 | 65 | 70 | 75 | 80 | 85 | 90 | 95 | 100 | 105 | 110 |
| 145 | 20 | 18 | 15 | 12 | 9 | 6 | 3 | | | | | | | | | |
| 150 | 23 | 20 | 18 | 15 | 12 | 9 | 6 | | | | | | | | | |
| 155 | 26 | 23 | 21 | 19 | 16 | 14 | 11 | 8 | 5 | 3 | | | | | | |
| 160 | 29 | 27 | 24 | 21 | 19 | 17 | 14 | 12 | 9 | 6 | 4 | 1 | | | | |
| 165 | 32 | 30 | 27 | 24 | 22 | 20 | 18 | 16 | 14 | 11 | 8 | 6 | 4 | 1 | | |
| 170 | 35 | 33 | 31 | 28 | 25 | 23 | 21 | 19 | 16 | 14 | 12 | 10 | 7 | 5 | 2 | |
| 175 | 38 | 36 | 34 | 31 | 29 | 27 | 25 | 23 | 21 | 18 | 16 | 14 | 12 | 10 | 7 | 5 |
| 180 | 41 | 39 | 37 | 34 | 32 | 30 | 28 | 25 | 23 | 21 | 19 | 17 | 15 | 13 | 11 | 9 |

**UNKNOWN VALUE**

ACETAZOLAMIDE to decrease CSF production (e.g. as diagnostic test) role is unknown.

## OUTCOMES

Untreated NPH – high morbidity and mortality!!!

87.5% 5-yr mortality for probable NPH (HR for death 3.8, CI 2.5-6.0)

Risk of dementia (in asymptomatic ventriculomegaly) HR 2.8 (CI 1.5-5.2)

## AFTER SHUNTING

- benefits may not be seen immediately → improvement in gait is the highest, followed by cognitive impairment and urinary dysfunction → symptom improvement may plateau (symptoms may worsen with UTI, URI).

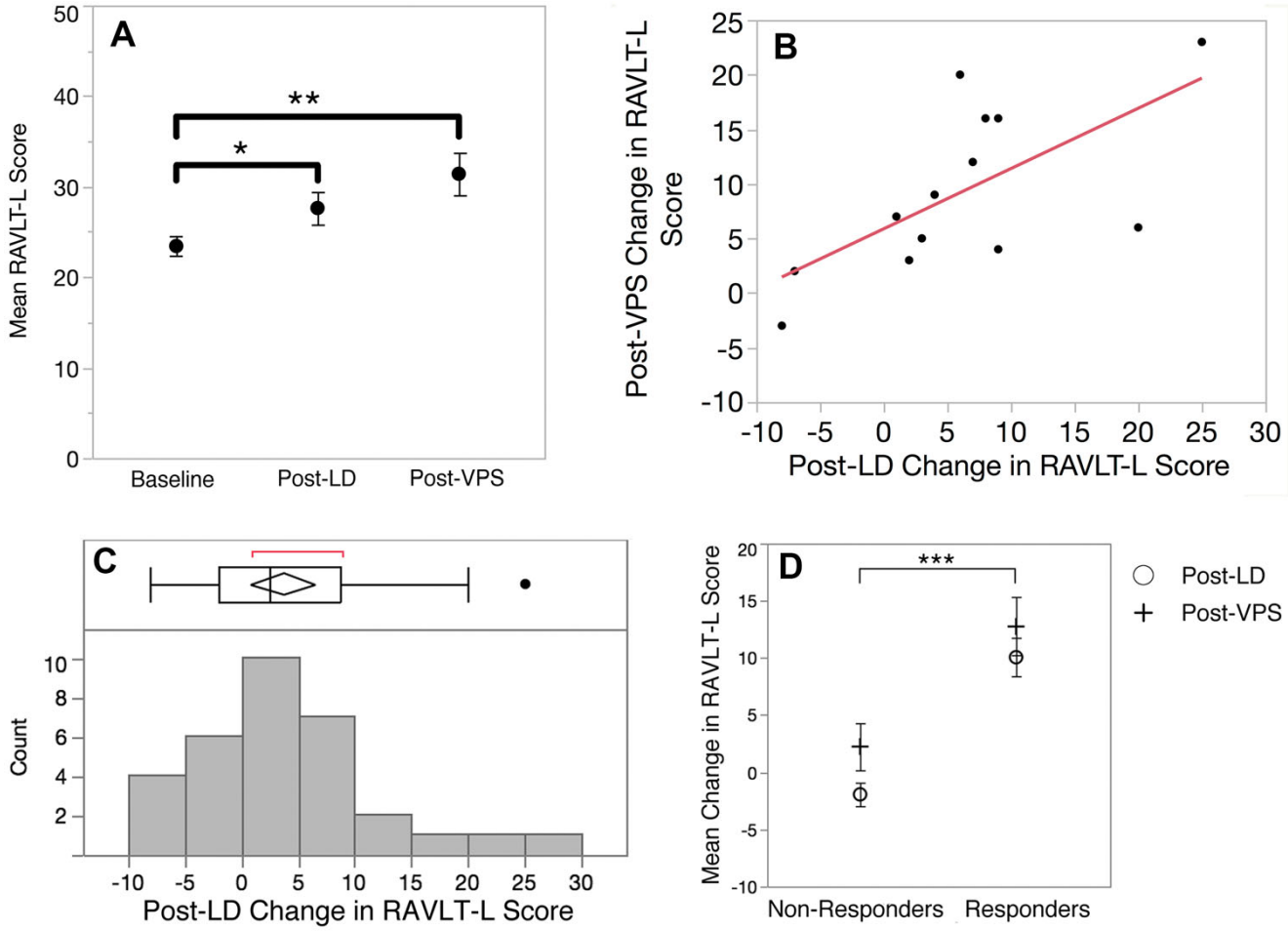
  N.B. all symptoms can improve!

- shunt benefits may last 10 years or more.
- ventricular size does not necessarily improve after shunting! (but may see changes in aqueductal CSF flow on MRI if shunt is working; may use ShuntCheck if question about shunt patency).
- even if patient selection is as good as it could be, the 60-80% rate of long-term benefit with shunting is expected; i.e. there are cases of probable NPH that are "shunt-nonresponsive"
- gait and balance are the most common symptoms to improve after both temporary and permanent CSF diversions, whereas cognition is generally recognized as the least likely symptom to improve in NPH.
- patients can cognitively improve after ventriculoperitoneal shunting; **Rey Auditory Verbal Learning Test-L (RAVLT-L)** was the only neuropsychological test to demonstrate statistically significant improvement both postlumbar drain and postshunt, i.e. improvement on the RAVLT-L postlumbar drain predicted improvement on the RAVLT-L postshunt!!!

  *Robert A.McGovern et al. Predicting Cognitive Improvement in Normal Pressure Hydrocephalus Patients Using Preoperative Neuropsychological Testing and Cerebrospinal Fluid Biomarkers. Neurosurgery 85:E662–E669, 2019*

  A multivariate logistic regression demonstrated that only RAVLT-L improvement after lumbar CSF drainage could predict post-VPS improvement. No other neuropsychological tests were helpful in determining cognitive improvement either post-LD or post-VPS.
  Even patients with relatively poor baseline cognition have the ability to improve after VPS as long as they demonstrate improvement post-LD - if the patient improves by approximately 5-10 words on the RAVLT-L portion after lumbar CSF drainage, expect post-VPS cognitive improvement regardless of other factors.
  Interestingly, though the RAVLT appears to be one of the best objective measures of cognitive improvement in NPH patients, it ***does not correlate with patients' subjective feelings on cognitive improvement*** as well as measures of visual memory

  Rey Auditory Verbal Learning Test-Learning (RAVLT-L) scores for NPH patients. A, Mean RAVLT-L raw score significantly improves both post-LD and post-VPS compared to baseline testing. ∗P = .047, ∗∗P = .0031, 1-sided t-test. B, Post-VPS RAVLT-L improvement is correlated with post-LD RAVLT-L improvement in a linear fashion (R2 = 0.43, P = .015). C, RAVLT-L improvement after lumbar CSF drainage (post-LD) follows a right-skewed normal distribution. D, When split into 2 groups based on RAVLT-L improvement (>3 points) post-LD, responders demonstrated a significant difference in RAVLT-L score post-VPS. ∗∗∗P < .0001, 2-sided t-test:




A multivariate logistic regression demonstrated that only RAVLT-L improvement after lumbar CSF drainage could predict post-VPS improvement

## Outcome trails – PENS, PENS 2

Codman Certas Plus valve at 4 versus 8 (virtual off)

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