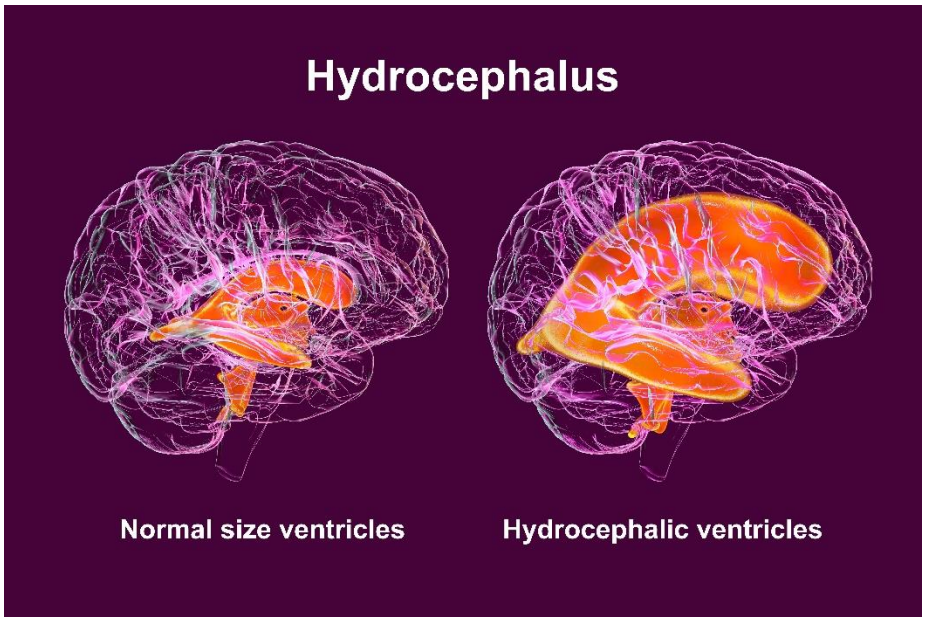


# Normal Pressure Hydrocephalus in Adults. How Does It Cause Damage if the Pressure is Normal?

**By**

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What is now known as normal-pressure hydrocephalus (NPH) was first discovered in the 1700s in autopsies of patients with enlarged cerebral ventricles. It then disappeared from the medical literature until it was "rediscovered" by Salomón Hakim in the mid-1960s.[1]

NPH consists of a syndrome of enlarged cerebral ventricles (ventriculomegaly) , cognitive impairment, urinary incontinence and a gait disorder (gait apraxia- an inability to lift the feet off the floor when walking as well as disequilibrium).

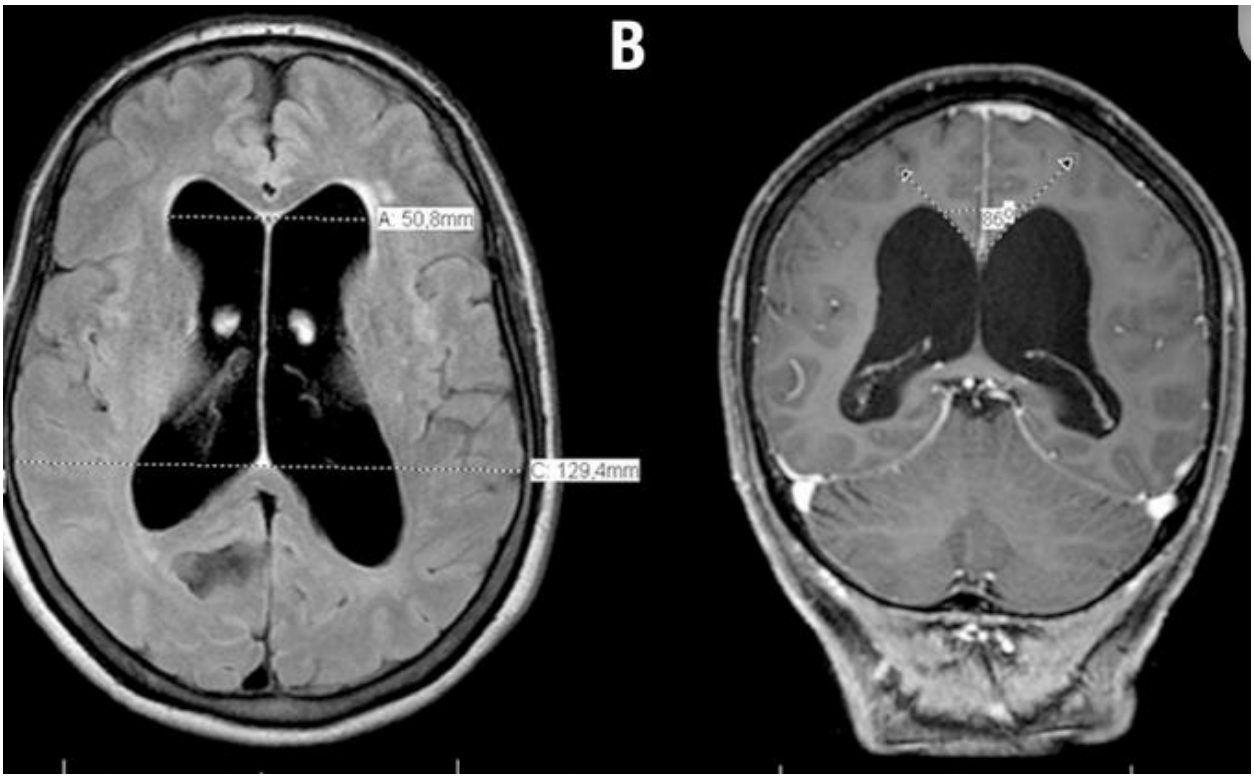
NPH can be idiopathic, which typically makes up about half of the cases. Other etiologies may include subarachnoid hemorrhage, meningitis, intracerebral hemorrhage, brain tumor or head trauma.[2]

The mechanism of NPH is typically cerebrospinal fluid (CSF) flow obstruction. One might expect that if there is outflow obstruction that the cerebrospinal fluid pressure would increase. But that does not occur in this disorder. Instead, the brain gets

compressed as the pressure increases which normalizes the intracranial pressure at the cost of increasing force on the brain and decreased brain arterial perfusion. It is explained by Pascal's law of hydrodynamics, where Force = Area x Pressure. As fluid accumulates, the pressure in the ventricles would normally increase, but instead normalizes due to increasing brain compression. As the ventricles enlarge, their area increases. As per Pascal's law, if the cerebrospinal fluid pressure remains the same, as the surface area of the ventricles increases, the compressive forces exerted on the brain will also increase. Using Pascal's law, ventricles that have increased their surface area by a factor of two will exert twice the force against the brain given the same normal cerebrospinal fluid pressure.[1,2] Increased force in the ventricles compresses the brain and increases the transmantle pressure (The difference between the ventricular pressure and the pressure over the brain surface), which produces a global decrease in cerebral perfusion. The most affected areas are the frontal cortex, periventricular white matter, basal ganglia, and the thalami.[2]

## Imaging for NPH

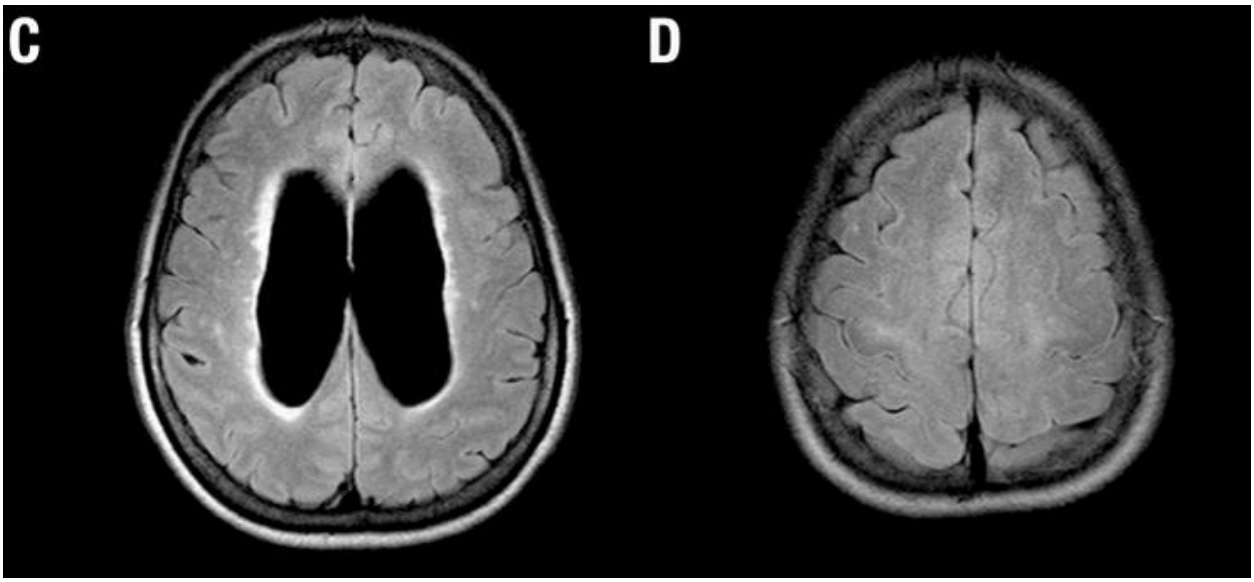
MRI is considered the best imaging test for NPH.




**Evans Index and Callosal Angle on MRI [2]**

Criteria for NPH include an Evan's index more than 0.3. The Evan's index is the ratio of maximal width of the frontal horns of the lateral ventricles and maximal internal diameter of skull at the same level on axial CT or MRI images. In the image above on the left, Evan's index is 50.8/129.4= 0.39

Another measurement of NPH severity is a callosal angle of greater than 40 degrees. As the ventricles enlarge, the callosal angle also increases. In the image above on the right the callosal angle is 86 degrees.[2]




**MRI Images of NPH[2]**

Image C above, is an axial FLAIR MRI scan with enlarged lateral ventricles and brightening in the surrounding white matter, suggestive of transependymal edema.

Image D above, illustrates Narrowing of the brain sulci and subarachnoid spaces in the frontoparietal regions seen in NPH.[2]

## Differential Diagnosis

When considering a diagnosis of NPH, other diseases that can cause dementia should be ruled out such as Alzheimer's disease, atypical Parkinsonism, dementia with Lewy bodies, progressive supranuclear palsy, and vascular dementia.[2] Other brain pathology such as tumor or stroke should also be considered.

## Gait in Hydrocephalus

An analysis comparing subjects with NPH versus normal controls reported that NPH patients had slower walking velocity due to shorter stride length, had outward rotation of the feet, wider step width, and were not able to lift their feet to a normal height

during the swing phase of walking. While walking, the feet of patients with NPH struck the ground flat and not with the normal heel strike as seen in the controls. There was also a decrease in the normal step-to-step variability of the walking pattern which led to poor compensation for body sway, which can cause problems with obstacle avoidance or on uneven walkways.[3]

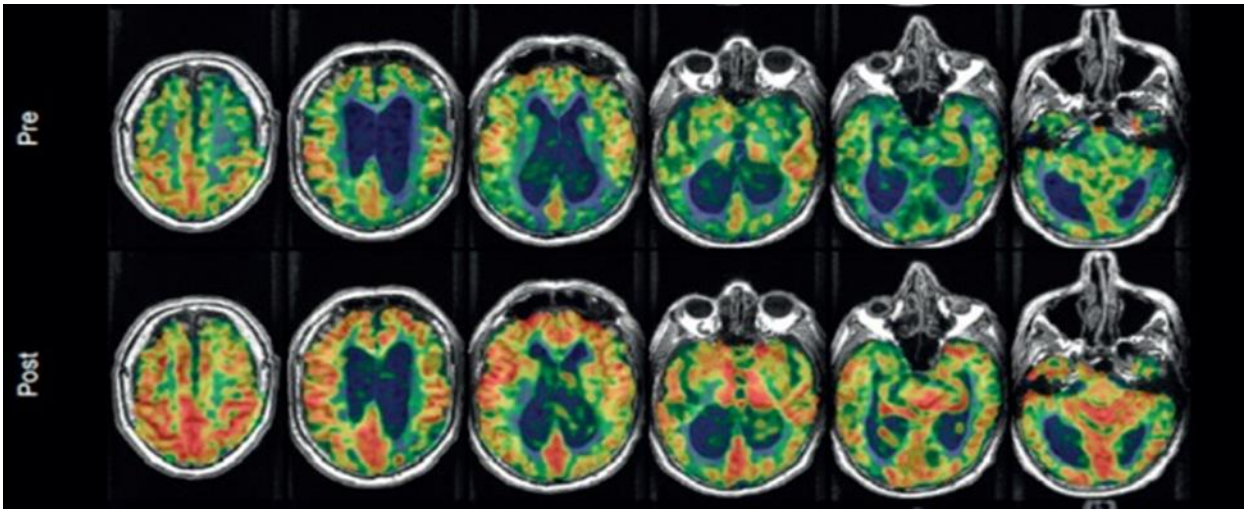
The typical gait of NPH is also known as magnetic gait as the patients walk as if their feet are glued to the floor.[4]

## Predictive Tests of Treatment Response

The definitive treatment for NPH is placement of a ventriculoperitoneal shunt (VP shunt).

There are several tests that can be performed to assess whether inserting a VP shunt may help a patient with NPH.

The first test is a **large volume lumbar puncture** (**LVLP**) where 30 to 50 milliliters of CSF are removed. There is a pre-and post-procedure objective evaluation of gait, cognition, and urinary incontinence. A non-enhanced brain MRI with CBF-ASL (cerebral blood flow, arterial spin labeling ) can be done pre- and post-procedure to evaluate if perfusion has also improved. A VP shunt is recommended if post-procedure improvement is documented, although it is known that the test is not 100% accurate and in some cases there may be improvement even with a negative test.[2]




**Arterial spin-labeling perfusion MRI demonstrating increased brain arterial perfusion after a large volume spinal tap in a patient with NPH**.[2]

A study of 35 patients who had a positive LVLP test reported that 72% of the subjects had gait improvement, however there was no significant improvement in cognitive function.[5]

In the medical literature, the sensitivity of the LVLP test is 26% to 62% which means that some people who had negative tests will still improve with shunt placement. After a successful large volume lumbar puncture test, the positive predictive value of a VP shunt improving a patient's clinical status is 73% to 100%.[6]

**External lumbar drainage** (ELD) is another test that can be used when patients do not demonstrate any response to a LVLP. A lumbar spinal catheter is inserted and CSF is slowly drained over 72 hours.[7]

A study of 151 patients found that 100 patients or 66% had improved clinical status after the ELD procedure and 84 of them then went on to have VP shunt placement. 76 patients or 90.5% had a positive outcome after shunt placement. Eighteen patients who had a negative ELD test still decided to undergo shunt placement and four of them or 22% experienced clinical improvement after the shunt was placed.[6]

In a **lumbar infusion test** (**LIT**), fluid is infused into a lumbar spinal catheter and the intracerebral pressure monitored via another lumbar catheter. A rise in the pressure can indicate decreased fluid reabsorption from the CSF, (also described as resistance to CSF outflow or Rout) and may have positive prognostic value in determining which patients with NPH may benefit from a VP shunt.[8,9] One advantage of using the lumbar infusion test over ELD as a secondary test after a negative LVLP is that it is a 45-minute test rather than a 3-day test.

In one study the **LIT** was compared to **LVLP**. The LIT was found to have a positive predictive value of 80% for VP shunt success while the LVLP had a higher positive predictive value of 94%. However, the LIT missed 16% of patients who improved after shunt surgery, while the LVLP missed 58%. The authors concluded that the LIT is more sensitive while the LVLP was more specific and both tests were complementary to each other.[8] Another study comparing the two procedures concluded that routinely performing LIT and LVLP in patients with MRI findings and a clinical picture of NPH is not necessary, given that both tests will have significant numbers of false negatives. However, where there is some doubt of the NPH diagnosis, they may be helpful in helping to decide if a VP shunting procedure should be performed.[10]

## Ventriculoperitoneal Shunt

A VP shunt procedure involves making a hole in the skull and inserting a catheter into one of the cerebral ventricles. The catheter is then subcutaneously threaded down the neck and thorax and inserted in the peritoneum. There is a one-way valve to prevent reflux of CSF back from catheter into the ventricles.

In one study of 17,035 patients who received a VP shunt, with a mean follow-up of 3.9 years, 23.8% had a complication, 6.1% suffered an infection and 22% needed a VP shunt revision. If non-traumatic subdural hematoma was included as a complication, the complication rate was 33.4%. (Nontraumatic subdural hematoma is a known potential complication of overdrainage from a VP Shunt.)[11]

In the medical literature, VP shunts have an estimated 98% failure rate over 10 years. Some causes of shunt failure include tissue, clots or infection causing obstruction, kinking, catheter migration, fracture of the catheter, valve malfunction, pseudocyst formation either in the brain or in the abdomen.[12]

## Endovascular Implantable Shunts

An alternative method of draining CSF fluid is now in initial trials. It is an endovascular implantable shunt that is placed via cannulation of the femoral vein and then threaded to the internal jugular vein. A needle is then advanced through the catheter into the vein wall and pushed into the cerebello-pontine angle cistern. A small device with a one-way pressure valve and a tube is inserted and anchored which can then drain CSF directly into the internal jugular vein. An advantage of this method is that there is no need to open the cranium and pass a catheter through brain tissue, as in a VP shunt.[13]

In April 2024, after 19 patients had received the shunt, an abstract about the study was presented at a scientific meeting. The subjects all had idiopathic NPH and percutaneous transdural implant placement with this new device. The abstract reported that there was a 32% to 39% significant gait improvement up to 180 days post-procedure, although there appeared to be a decrease in patients returning for follow-up exams over time. There was no discussion in the abstract of long-term complications or if cognitive ability or incontinence had specifically improved with the procedure. The abstract did report there were no technical complications during placement.[14] Clinical trials of this device are still ongoing and more details of this specific trial should be forthcoming if and when it is formally published.

## Endoscopic Third Ventriculostomy

Endoscopic third ventriculostomy (ETV) is a procedure where an endoscope is placed though a skull burr hole and under direct vision a hole is made in the 3$^{rd}$ ventricle. It has typically been used for obstructive hydrocephalus, but some researchers have tried it for idiopathic NPH. Some small studies have had good results with ETV, but there is apparently only one randomized controlled trial comparing VP shunt to ETV. In that study, 50% of the ETV group had improved after 12 months of follow-up compared to

76.9% of the VP Shunt group. 19% of the VP Shunt group had overdrainage and developed a subdural hematoma and needed corrective surgery.[15] A Cochrane review in 2015 reviewed that study and felt the data was inconclusive and the researchers had used a non-programmable valve in the VP shunt which was not standard practice. They concluded the evidence was low quality and more research was needed.[16] A meta-analysis in 2022 also concluded that current data regarding this procedure for idiopathic NPH is minimal.[17]

### Intracranial Shunt Draining Into the Internal Jugular Vein

Another experimental approach being evaluated is to insert an intracranial shunt similar to a VP shunt, but only brought down to the neck to drain into the internal jugular vein instead of into the peritoneal cavity.[18]

## Conclusion:

NPH is a progressive disease that can lead to urinary incontinence, dementia and gait disturbances, due to brain compression. It is most commonly idiopathic in adults but can occur after other brain disorders. Diagnosis is based on clinical suspicion and confirmed with MRI. Predictive tests for VP shunt placement effectiveness have good positive predictive value, but some patients with negative tests may still show improvement with the placement of a VP shunt.

VP shunts can be curative, but the degree of improvement may depend on how advanced the disease is, as well as the age of the patient and the presence of other concurrent disease processes. VP shunts are not risk-free and there is a significant complication rate.

More research is needed to see if the less invasive ETV is an acceptable modality for certain patients with idiopathic NPH.

Some newer procedures that drain CSF into the internal jugular vein are being trialed, including one that is inserted percutaneously and does not require opening of the skull to place the shunt. If that procedure turns out to be successful, without major complications, it would make inserting or replacing a shunt less invasive and be a major advance in the treatment of NPH.

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