



OPEN Reversal of cerebral pseudoatrophy in normal pressure hydrocephalus after ventriculoatrial shunt placement

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Normal Pressure Hydrocephalus (NPH) is a syndrome in predominantly older adults, differential diagnoses include primary neurodegenerative diseases. The key radiological finding is ventricular enlargement, different from increased ventricular size associated with cerebral atrophy. After definitive surgical cerebrospinal fluid (CSF) shunting there appears to be increased brain tissue volume in patients' follow-up images which could indicate that imaging findings usually interpreted as cerebral atrophy may be reversible with appropriate treatment. A cross-sectional study was performed comparing pre and postoperative brain volume in magnetic resonance imaging (MRI) studies of NPH patients who underwent ventriculoatrial shunting at our institution between April 2016 and February 2022. Brain volumes were obtained using volBrain and vol2Brain software. 30 patients were included, and 60 MRI studies reviewed. The average age was 80.4 years (54–92 years). 20 patients (66.6%) were men and 10 women. Following CSF shunting, patients had a statistically significant increase in white matter ($p=0.043$), gray matter ($p=0.002$), and total brain parenchyma ($p=0.032$). The brain volume increased in postoperative MRI. We call this finding cerebral pseudoatrophy, which has not been previously described. Further studies are required to confirm this finding, which poses relevance for the accurate diagnosis of NPH.

Keywords Normal pressure hydrocephalus, Cerebral pseudoatrophy, Hydrocephalus, Ventriculoatrial shunt, Ventricles, Brain volume

Nearly 60 years ago, Doctor Salomón Hakim, a Colombian neuroscientist and neurosurgeon, described Normal Pressure Hydrocephalus (NPH)¹. This syndrome involves a symptom triad (cognitive decline, gait disturbance, and urinary incontinence) associated with enlargement of the cerebral ventricular system due to abnormal cerebrospinal fluid (CSF) accumulation, where, unlike other types of hydrocephalus, intracranial pressure remains normal^{1,2}. This condition is observed in individuals with an average age of 70 years, and it significantly affects their quality of life³. Differential diagnoses include primary neurodegenerative diseases such as Alzheimer's disease, which are very common in older adults and have similar clinical manifestations^{4–7}.

Neuroimaging is one of the vital criteria for establishing a NPH diagnosis. Magnetic resonance imaging (MRI) is the study of choice⁸, with the key finding of enlarged cerebral ventricles disproportionate to any sulcal dilation present⁹. In typical cases of NPH, disproportionately enlarged subarachnoid space hydrocephalus (DESH) has been described^{10–12}. DESH is a radiologic finding including ventriculomegaly, Sylvian fissure dilation (in spite of shrunken cortical subarachnoid spaces), and high convexity sulci tightness^{13–15}. DESH should be recognized

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Age (years) mean $\pm$ SD	80.4 $\pm$ 6.85
Gender n (%)	
Male	20 (66.6)
Female	10 (33.3)
Preoperative clinical findings n (%)	
Cognitive compromise	29 (96.7)
Gait disturbance	30 (100)
Urinary incontinence	24 (80)
Clinical improvement n (%)	
Cognitive (n = 29)	22 (75.9)
Gait	26 (86.7)
Urinary incontinence (n = 23)	17 (73.9)
Intracranial pressure (mmH ₂ O) mean $\pm$ SD	
Intraoperative	148.7 $\pm$ 34.11
Valve pressure at postoperative MRI acquisition	117.0 $\pm$ 39.79

Table 1. Demographic characteristics. *SD* standard deviation.

	White matter	Gray matter	CSF	Total parenchyma	Intracranial cavity*
Preoperative volume (cc) (Mean $\pm$ SD)	463.66 $\pm$ 126.11	601.29 $\pm$ 136.58	326.39 $\pm$ 96.24	1064.95 $\pm$ 171.56	1401.02 $\pm$ 167.87
Postoperative volume (cc) (Mean $\pm$ SD)	488.44 $\pm$ 146.30	620.81 $\pm$ 160.83	273.14 $\pm$ 99.42	1109.25 $\pm$ 160.62	1392.02 $\pm$ 168.12
Difference (cc)	24.78	19.52	− 53.25	44.30	− 8.99
p value	0.043	0.002	0.001	0.032	0.596

Table 2. Preoperative and postoperative brain volumes. *CSF* cerebrospinal fluid. *Intracranial cavity includes the sum of all white matter, gray matter and CSF.

and differentiated from cortical atrophy for the adequate diagnosis of NPH, with utility as a prognostic tool for CSF shunt surgery response, and to avoid misdiagnosis of co-existent neurodegenerative diseases^{16–18}. Similarly, enlargement of cerebral ventricles in NPH due to increased CSF volume should be differentiated from that seen in cerebral atrophy, secondary to the loss of brain tissue^{19,20}.

After definitive CSF shunting, the patient's postoperative follow-up brain MRI usually shows a reduction of ventricular size and subarachnoid space in the sylvian fissures and increase in cerebral convexity^{21,22}. However, years ago Doctor Salomón Hakim observed that in many MRI studies, there also appears to be an increase in brain tissue volume in addition to CSF changes, a finding we have continued to observe at our institution, which could correlate with symptom improvement. This is of utmost importance since this may indicate that the findings normally interpreted as atrophy in the preoperative MRI of NPH patients is not actual cerebral atrophy and may be reversible if patients are offered appropriate treatment. This is especially significant in NPH, an underdiagnosed disease that may be confounded with irreversible conditions such as primary neurodegenerative diseases^{7,23}, especially in the face of a radiology report that states cerebral atrophy is present. Therefore, this study aimed to identify and compare brain tissue volumes in preoperative and postoperative MRI studies of 30 patients with a diagnosis of NPH using a volumetric and segmented automatized software (volBrain), to determine whether an increase in cerebral volume is found after ventriculoatrial shunting.

Results

Of 66 patients with an NPH diagnosis who underwent surgical treatment during the study period, 30 patients fulfilled the study criteria. A total of 60 MRI scans of the 30 patients were processed with the volBrain and vol2Brain software; 30 preoperative and 30 postoperative studies. The average age was 80.4 years (54–92 years $\pm$ 6.85). 20 patients were men (66.6%) and 10 were women (33.3%) (Table 1). Postoperative MRI scans were performed an average of 9.3 months after the procedure (ranging from 4 to 15 months).

Following CSF ventricle shunting, patients had a statistically significant increase in white matter ($p=0.043$), gray matter ($p=0.002$), and total brain parenchyma ($p=0.032$), as well as a statistically significant decrease in CSF volume ($p=0.001$). There was an average increase of 5.35% in white matter volume, 3.25% in gray matter volume, 4.16% in total brain parenchyma, an average decrease of 16.31% in CSF volume, and an average decrease of intracranial volume of 0.64% which was not statistically significant ($p=0.596$) (Table 2), these changes can also be seen in Fig. 1. Although these were the general volumetric trends, there were some cases of decreased white (16/30, 53.3% patients) and gray matter volumes (10/30, 33.3% patients); as well as increased CSF volume (9/30, 30% patients). Figure 2 shows the pre- and postoperative MRI for one of the patients included in the

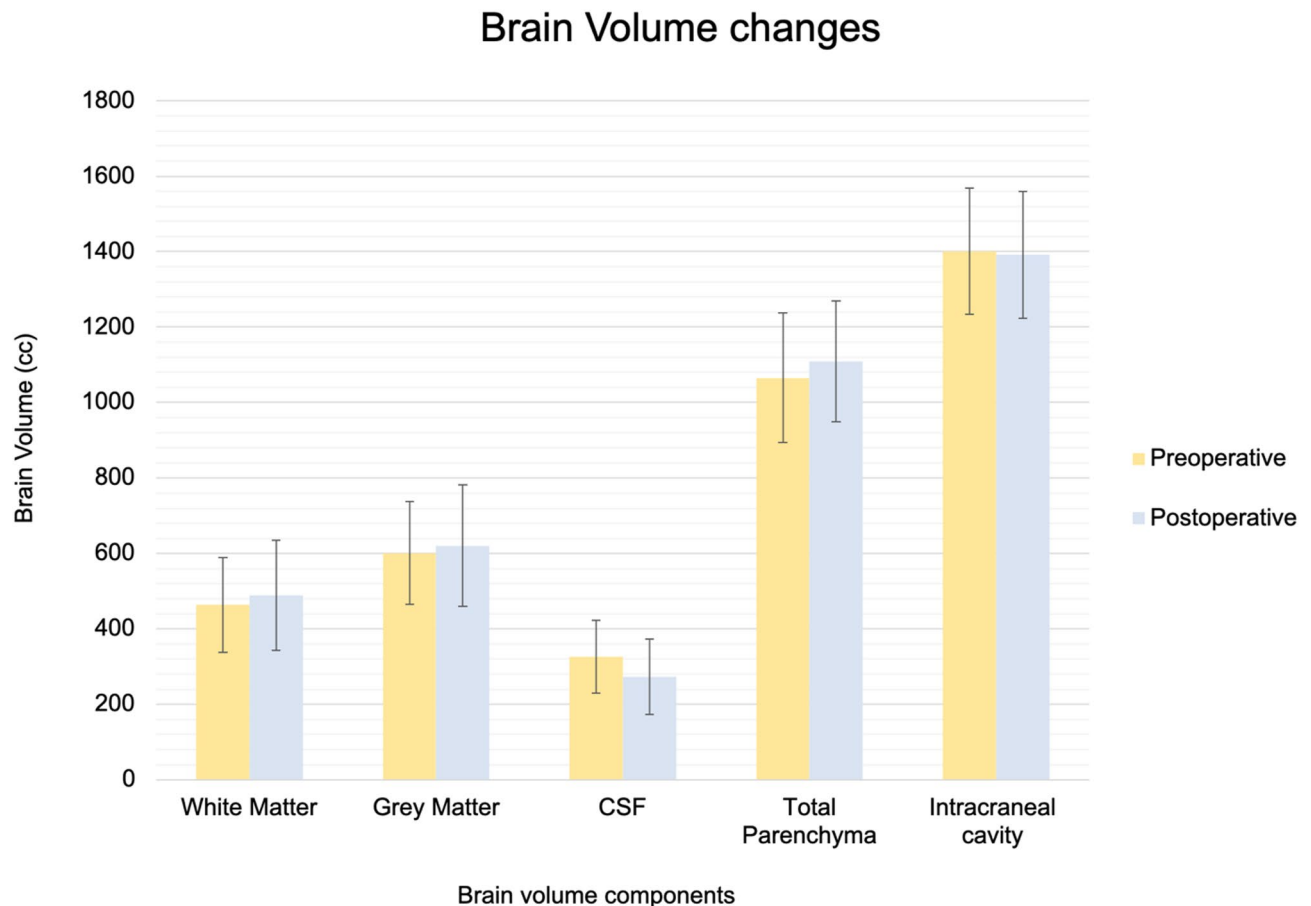


Fig. 1. Brain Volume changes by component between presurgical and postsurgical studies.

study. Figure 3 shows the volumetry performed in the vol2Brain software for another patient. More detailed information about pre- and post-volumetric analysis can be found as Supplementary material.

Clinical outcomes

22 patients (75.9%) improved in cognitive function, 26 (86.7%) in gait disturbance, and 17 (73.9%) in urinary incontinence (Table 1). One of the patients who initially presented with urinary incontinence had a cystostomy at follow-up, so symptom improvement couldn't be determined. The average intraoperative intracranial pressure was 148.7 mmH₂O, and the average valve pressure at MRI acquisition was 117.0 mmH₂O, with an average difference of 43.3 mmH₂O, ensuring effective CSF drainage.

Regarding the relationship between brain volume and clinical outcomes, a statistically significant relationship was found between the expansion of brain parenchyma and the improvement in urinary incontinence ($p = 0.042$). Regarding the improvement in gait disturbances and cognitive impairments, a positive relationship was found, however, it was not statistically significant, with p -values of 0.4 and 0.3, respectively.

Discussion

While the classic clinical triad of cognitive decline, gait disturbance, and urinary incontinence is the cornerstone for diagnostic suspicion and confirmation of NPH, radiological findings are vital criteria for NPH diagnosis as well^{8,11}. In patients with suspected NPH, it is important to determine whether the observed ventriculomegaly is due to cerebral atrophy (ex vacuo hydrocephalus) or communicating hydrocephalus. Cerebral atrophy is a common radiological finding in older patients, especially those with primary neurodegenerative diseases such as Alzheimer's disease or vascular dementia. Atrophy speaks to the loss of brain cells, which is irreversible, as are the neurologic deficits associated with this phenomenon¹⁹. The neurosurgeon's main question for the neuroradiologist is whether the observed ventricular enlargement is proportionate to the degree of enlargement of the cortical sulci, which would indicate ex vacuo hydrocephalus due to cerebral atrophy in neurodegenerative diseases; or whether this ventricular enlargement is not proportional to atrophy and may be due to communicating hydrocephalus^{7,19}.

In typical NPH cases, the ventricles are disproportionately more dilated than the cortical sulci, which are narrowed or obliterated in the high convexity and midline; this is associated with local narrowing of the subarachnoid space in these areas, while there is enlargement of the subarachnoid space at the Sylvian fissure, a finding called DESH (disproportionately enlarged subarachnoid space hydrocephalus)^{11,12,21,22}. After a

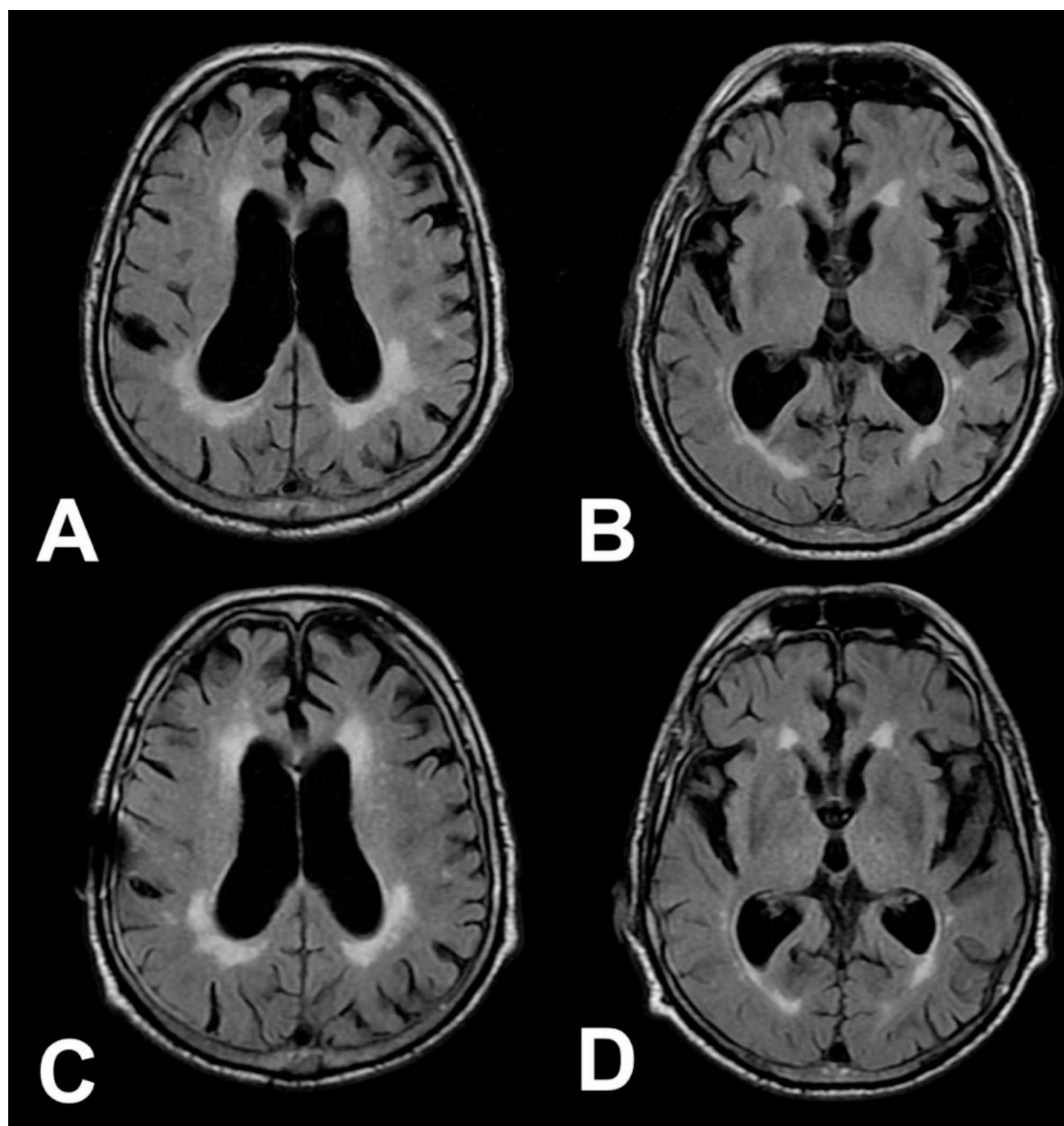


Fig. 2. Illustrative case. (A, B) Pre- and (C, D) postoperative fluid-attenuated inversion recovery (FLAIR) imaging demonstrating brain parenchyma and CSF volume changes.

CSF shunting procedure, radiological changes are frequently observed in postoperative follow-up, mainly characterized by a decrease in the size of cerebral ventricles and total subarachnoid space^{24,25}. Additionally, decreased subarachnoid space in the Sylvian fissure and increased subarachnoid space in the high convexity and midline have been documented^{24–27}.

However, few studies have documented postoperative changes in brain volume, all of them after shunting to the peritoneum^{18,24,25,28,29}. In a study of 54 patients with NPH undergoing shunting, Yamada et al. documented an expansion of only 2% of the brain parenchyma one month after surgery, with no changes in further follow-up²⁴. Cogswell et al. documented a postoperative increase of 1.4% in cortical volume in a study of 22 patients¹⁸. Hiraoka et al. found no significant changes in the volume of cerebral hemispheres and infratentorial brains of 21 patients with shunt-responsive NPH²⁵. On the other hand, Singer et al. documented a significant increase in total brain volume following CSF drainage in 20 patients undergoing diagnostic lumbar puncture, providing

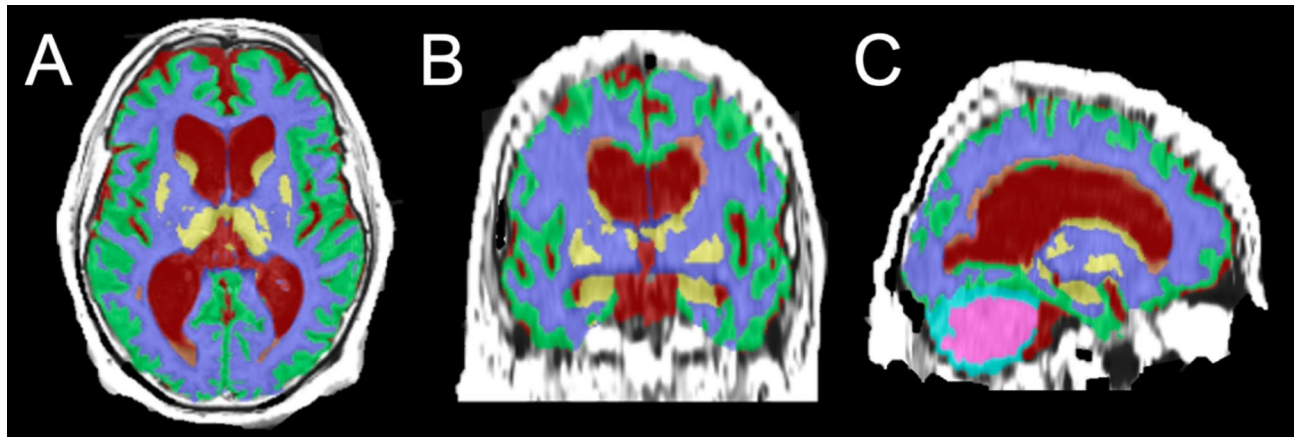


Fig. 3. Tissue segmentation for volumetric analysis in vol2Brain software. (A) Axial, (B) coronal, and (C) sagittal processed images are demonstrated. CSF volume is represented in red, cortical grey matter in green, and cortical white matter in purple.

evidence that CSF removal in patients with NPH results in a change of the brain volume rather than only a change of the brain's shape²⁸.

In this study, we objectively measured brain volume using automated software comparing pre and postoperative brain MRI scans of 30 patients who underwent a ventricular shunt to the atrium after having fulfilled clinical and imaging criteria for NPH diagnosis. To our knowledge, this is the largest series studying volumetrics and the only one using atrial shunting. There is a lack of literature regarding comparative volumetrics between shunting to the peritoneum versus the atrium.

As expected, we found a statistically significant decrease in CSF volume, owing to the direct effects of the shunting procedure. Additionally, there was a statistically significant increase in white and gray matter volume (5.35% and 3.25% respectively) and total brain parenchyma (4.16%), when comparing the pre and postoperative images. We suggest the radiological manifestation of this phenomenon be called cerebral pseudotrophy, and this present work intends to include this term in the neuroscientific knowledge. We believe that awareness of this phenomenon is of special importance in NPH patients, whose diagnosis may be confounded by the interpretation of imaging findings as atrophy, which is associated with primary neurodegenerative diseases and irreversible by nature.

Of note, a non-statistically significant mild decrease in total intracranial cavity volume was noted (0.64%) which could be attributed to random effects as it is expected for intracranial volume to be constant in adults²⁵. Other possible causes include volumetric changes due to unquantified venous sinus volume increases after postoperative fluid shifts, CSF flow through the shunt system, or even physiologic volume changes with aging as a known cause of progressive intracranial volume decrease (up to 0.4% annually, and required to be > 1.1% to be considered pathological)^{30,31}.

NPH pathophysiology remains subject of study, and while CSF dynamics have been thoroughly described, the role of parenchymal changes and their significance is still uncertain³². Mechanical models such as the viscoelastic or viscoelastoplastic models have been applied to understand the physiopathology processes involved in NPH^{32–34}. Particularly, the viscoelastic model can be applied to understand the development of NPH and the observed volume changes after CSF shunting. Viscoelasticity is a physical phenomenon seen in soft tissues, in which the material is viscous (deforms at a constant rate upon force, and remains in this state after force is removed) and elastic (deforms immediately upon force, but returns to previous state after removed)³⁵.

The brain's viscoelasticity seems to be affected in NPH. There is extracellular water shift from the brain parenchyma due to cortical stresses (compression) throughout the whole parenchyma, due to ventricular dilation leading to a loop of over-compressed and distorted parenchymal structure^{34,36}. These compression forces need to be diminished for water to re-enter the parenchyma so ventricle size is reduced, and viscoelasticity is restored.³⁴ Following definitive shunting in NPH, these brain tissue alterations are thought to be repaired progressively secondary to mechanical tissue reorganization, meaning the micromechanical connections are restored in spite of decayed tissue strength³². This could also be understood stemming from the notion that the brain is adaptable like an open-cell "sponge", described originally by Doctor Salomon Hakim et al.; the brain tissue's water content can shift upon stress, and this is reversible^{20,36,37}.

We hypothesize that pressure changes in NPH, as well as CSF accumulation, lead to brain tissue compression which confers the atrophic appearance observed in brain MRI, which is subsequently reversed after definitive shunting. Cogswell et al. hypothesized the increase they observed in cortical volume indicated post-shunt decompression of the cortex and sulci¹⁸. In addition to these findings, we hypothesize that there is a generalized gray and white matter reorganization as part of the tissue repair process³² in possible association to viscoelasticity changes, which is represented in volumetric changes. Therefore, after shunting, while ventricle size decreases the brain structure partially reverts, without parenchymal loss³⁷.

Likely, these changes impact the whole connectome. These data need to be further investigated. Volume changes as well as morphometric features may provide not only structural^{36,37} but also functional reorganization,

which is implicit in clinical improvement. We suggest preoperative volumes may predict clinical outcomes. Furthermore, the measurement of intracranial volume changes could have utility as an indicator of tap test response in the preoperative period and even shunt function in the postoperative period; this is particularly relevant as it has been described that visual evaluation alone can be inaccurate in comparison to automatic volumetric tools^{38,39}. This is a research gap that must be assessed in future studies.

In this sense, changes in brain volume may correlate with postoperative clinical improvement, since they may indicate decompression of structures and pathways involved in the pathophysiology of the symptom triad of NPH⁴⁰. Most patients included in our study showed improvement in these symptoms: 86.7% improved in gait disturbance, 75.9% in cognitive impairment, and 73.9% in urinary incontinence. However, although a correlation has been found between clinical improvement and changes in imaging indices such as the brain per ventricle ratio²⁴, previous studies have not examined the possible association between volumetric changes and symptom improvement^{18,24,25,28}.

Limitations

This study is limited by its restricted follow-up in a long-term manner. The limited sample size represents the main restriction for analysis. Nonetheless, this is one of the largest series of NPH patients analyzed for this hypothesis. The time for acquisition of postoperative MRI is variable and this may also affect the results presented. We suggest a long-term follow-up for further studies in order to evaluate if additional changes can be observed over time. Moreover, the study of connectomics in these patients would provide remarkable additional information to the data obtained in this study that could be correlated with clinical outcomes.

Conclusions

We observed an increase in the volume of both gray matter and white matter and, consequently, total brain parenchyma in the volumetric analysis of pre and postoperative brain MRI studies of patients with a NPH diagnosis who underwent definitive ventricular shunting. We have called this finding cerebral pseudoatrophy. More studies are required to characterize this finding, which has important implications for accurate diagnosis and treatment, that may impact successfully on the neurological outcomes of NPH patients.

Methods

Clinical features

A before-and-after cross-sectional study was performed. Pre and postoperative brain MRI studies were analyzed. MRI was performed according to the standard brain MRI protocol used in our institution. A superconducting unit with a magnetic field strength of 1.5 Tesla was used for the preoperative and postoperative imaging. A multiplanar imaging approach was used, with the standard brain protocol radiofrequency pulse sequences to obtain T1, T2, diffusion, and susceptibility-weighted imaging. Axial T2 FLAIR images were acquired with an oblique slice orientation, covering the entire brain (sequence type: Axial T2 FLAIR; acquisition type: 2D; slice thickness = 4.0 mm; spacing between slices = 1.0 mm; number of slices = 32; matrix = 288 × 192; field of view (FOV) = 24.0 cm; voxel size = 0.8 × 1.2 × 4.0 mm). The timing parameters included a repetition time (TR) of 9000 milliseconds (ms), an echo time (TE) of 120 ms, and an inversion time (TI) of 2570 ms. The acquisition was performed with a number of averages (NEX) of 1.00. Acquisition time was 2:52 min. The standard head coil was used for all patients.

Our institution has available a 3.0 Tesla MRI unit, nonetheless, due to the magnetic properties of the ventricular shunt valve, the use of this unit is avoided in order to prevent pressure changes. For the postoperative MRI imaging, a cranium x-ray was taken previous to MRI imaging to confirm the pressure, and after MRI, another cranium x-ray was taken to confirm no changes > 100 mmH₂O occurred. If this was the case, pressure adjustment for the valve was done to return it to baseline values.

Patients of all ages with a confirmed NPH diagnosis (according to the criteria of our specialized center for NPH) who underwent ventriculoatrial shunt (VA) placement in University Hospital Fundación Santa Fe de Bogotá between April 2016 and February 2022, and who had pre- and postoperative MRI studies, were included. Pre and postoperative white matter, gray matter, CSF, and total brain parenchyma volumes were measured using volBrain and vol2Brain software (<http://volbrain.upv.es/>)^{41,42}. This program allows automatic analysis of MRI data, performing a segmentation that provides volumetry of intracranial cavity components⁴¹. MRI studies not compatible with the software were excluded, as well as patients with postoperative complications (infection, valve removal, valve dysfunction, and/or subdural hematomas that required surgical evacuation) given the bias to interpret imaging. Other clinical and radiological data were also collected.

Clinical outcomes of improvement in triad symptoms were measured using the following tools: ICIQ scale for urinary incontinence⁴³; FIM⁴⁴ scale as a determinant for functionality, Minimental-35⁴⁵, MOCA, and INECO⁴⁶ scales to measure cognitive disorders; 10 m test and time up and do for gait disturbances⁴⁴, and ZARIT⁴⁷ scale to determine caregiver burden⁴⁸. The study was conducted following the Declaration of Helsinki. This study protocol was approved by the Institutional Review Board of the Hospital Universitario Fundación Santa Fe de Bogotá (*Comité Corporativo de Ética en Investigación—CCEI*), which waived the requirement to obtain informed consent because of the retrospective design. No experimental or additional interventions other than those established in our specialized center for NPH were carried out.

MRI volume analysis

The pre- and postoperative MRI of the patients who fulfilled all the inclusion criteria were analyzed using volBrain software⁴¹. volBrain is a software for the automatic analysis of previously anonymized data from brain MRIs, in a Nifti format that yields a PDF report with the tissue volumes of the cranial vault; specifically gray

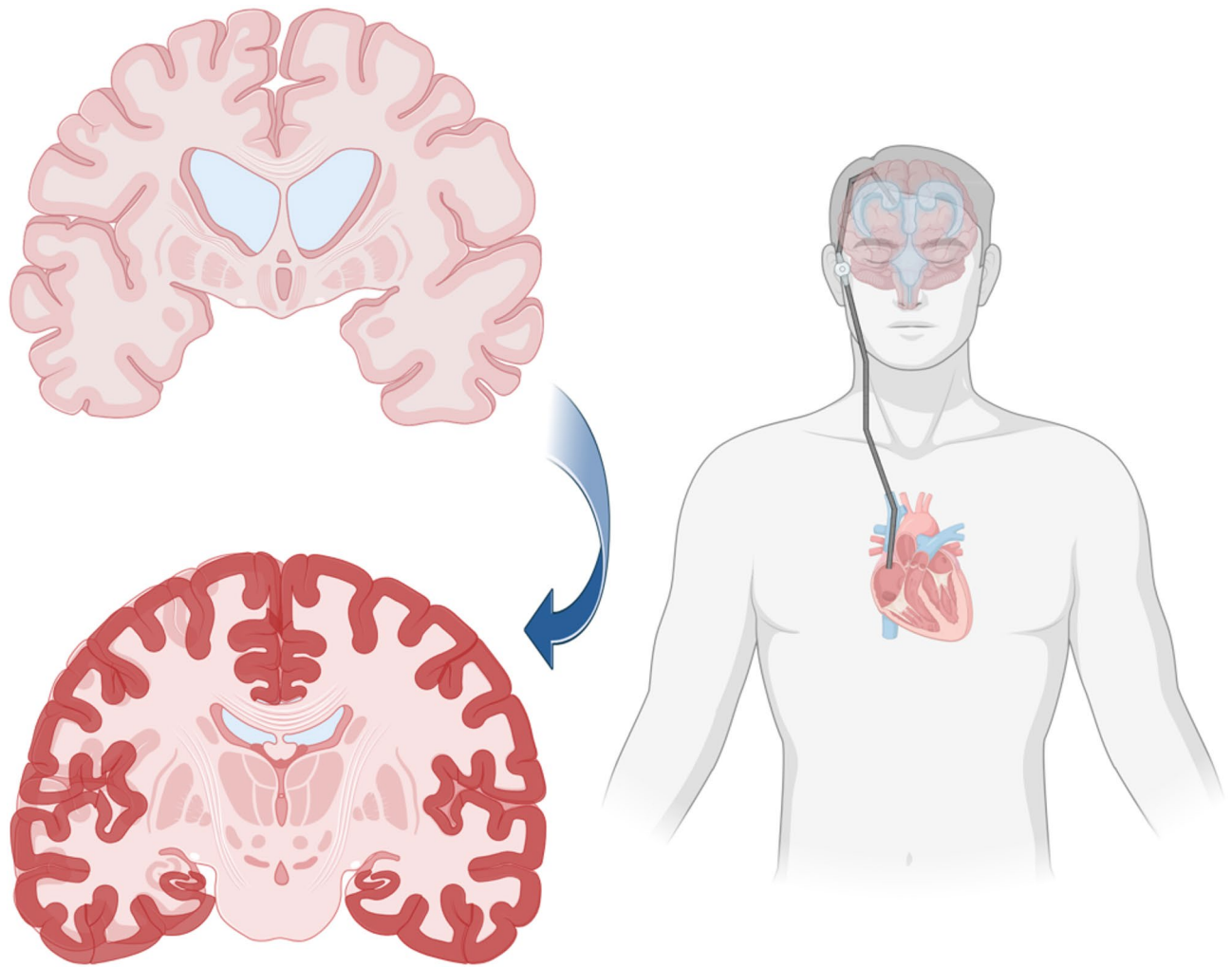


Fig. 4. Schematic illustration of volumetric changes after VA shunting. In the upper left side, an NPH brain with dilated ventricles is illustrated. In the down left side, the ventricle size is restored, and the cortical volume increase is enhanced in red. On the right side, a VA shunt is schematized. Created in <https://BioRender.com>.

matter, white matter, and CSF volume⁴¹. It also provides information about certain macroscopic structures including: cerebral hemispheres, cerebellum, brainstem, and lateral ventricle volumes⁴¹. Lastly, an automatic subcortical segmentation is carried out, with volumes and tag maps⁴¹. The anatomical levels of segmentation are done automatically with the spatial reference for segmentations in axial, coronal and sagittal acquisition orientations previously being standardized based on neurological orientation in the MNI152 space³⁸. The average time for processing of this study is approximately 12 min.

Surgical procedure: VA placement

Under general anesthesia, the patient is positioned supine, with cephalic rotation contralateral to the surgical site (usually on the right side). A fronto-pterional trichotomy and surgical site demarcation on the frontal and retroauricular region, and over the external jugular vein is performed using guidance by ultrasonography. Placement of sterile fields and iodized incision field is done. Under ultrasound guidance, the internal jugular vein is identified and using a Peel-Away® Fr.7 catheter, the catheter is advanced distal to the cavoatrial junction (Fig. 4). With fluoroscopic guidance adequate placement in the right atrium is confirmed and the catheter is secured. The valve is placed in the retroauricular region and connected to the distal catheter. Next, ventricular access is done and after CSF is obtained the opening pressure is measured with manometry (using an intravenous extension set and a sterile measuring tape). The ventricular catheter is connected to the valve and secured. Closure is done in regular fashion. For the register and as a parameter for programming the valvular system. The programmable valve (Codman® Hakim®) is advanced to the reatroauricular position and connected proximally and distally. The rest of the procedure is performed in a regular fashion.

Statistical analysis

STATA version 17 was used for statistical analysis. A univariate analysis was performed to describe the characteristics of each variable. Qualitative variables were determined with absolute and relative frequencies.

Quantitative variables were determined with central tendency and dispersion measures; for normal distribution (median and standard deviation) and abnormal distribution (median and interquartile range). Shapiro–Wilk test (significance of 5% ($p < 0.05$)) was used to analyze the quantitative variables.

Data availability

The datasets generated during and/or analyzed during the current study are available upon request to the corresponding author [FH].

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References

- Adams, R. D., Fisher, C. M., Hakim, S., Ojemann, R. G. & Sweet, W. H. Symptomatic occult hydrocephalus with normal cerebrospinal-fluid pressure: A treatable syndrome. *N. Engl. J. Med.* **273**, 117–126 (1965).
- Bräutigam, K., Vakis, A. & Tsitsipanis, C. Pathogenesis of idiopathic normal pressure hydrocephalus: A review of knowledge. *J. Clin. Neurosci.* **61**, 10–13 (2019).
- Sundström, N., Lundin, F., Arvidsson, L., Tullberg, M. & Wikkelsø, C. The demography of idiopathic normal pressure hydrocephalus: Data on 3000 consecutive, surgically treated patients and a systematic review of the literature. *J. Neurosurg.* <https://doi.org/10.3171/2022.2.JNS212063> (2022).
- Pyykkö, O. T. et al. Incidence, comorbidities, and mortality in idiopathic normal pressure hydrocephalus. *World Neurosurg.* **112**, e624–e631 (2018).
- Gallia, G. L., Rigamonti, D. & Williams, M. A. The diagnosis and treatment of idiopathic normal pressure hydrocephalus. *Nat. Clin. Pract. Neurol.* **2**, 375–381 (2006).
- Williams, M. A. & Malm, J. Diagnosis and treatment of idiopathic normal pressure hydrocephalus. *Contin. Lifelong Learn. Neurol.* **22**, 579–599 (2016).
- Iddon, J. L. et al. Specific patterns of cognitive impairment in patients with idiopathic normal pressure hydrocephalus and Alzheimer's disease: A pilot study. *J. Neurol. Neurosurg. Psychiatry* **67**, 723–732 (1999).
- Bradley, W. G. Magnetic resonance imaging of normal pressure hydrocephalus. *Semin. Ultrasound CT MRI* **37**, 120–128 (2016).
- Bradley, W. G. CSF Flow in the brain in the context of normal pressure hydrocephalus. *Am. J. Neuroradiol.* **36**, 831–838 (2015).
- Miskin, N. et al. Diagnosis of normal-pressure hydrocephalus: use of traditional measures in the era of volumetric MR imaging. *Radiology* **285**, 197–205 (2017).
- Damasceno, B. P. Neuroimaging in normal pressure hydrocephalus. *Dement. Neuropsychol.* **9**, 350–355 (2015).
- Yamashita, F. et al. Voxel-based morphometry of disproportionate cerebrospinal fluid space distribution for the differential diagnosis of idiopathic normal pressure hydrocephalus. *J. Neuroimaging* **24**, 359–365 (2014).
- Akiba, C. et al. The prevalence and clinical associations of disproportionately enlarged subarachnoid space hydrocephalus (DESH), an imaging feature of idiopathic normal pressure hydrocephalus in community and memory clinic based Singaporean cohorts. *J. Neurol. Sci.* **408**, 116510 (2020).
- Hashizume, Y. Macroscopic findings of brain with dementia. *Neuropathology* **42**, 353–366 (2022).
- Hladky, S. B. & Barrand, M. A. Regulation of brain fluid volumes and pressures: basic principles, intracranial hypertension, ventriculomegaly and hydrocephalus. *Fluids Barriers CNS* **21**, 57 (2024).
- McCarty, A. M., Jones, D. T., Dickson, D. W. & Graff-Radford, N. R. Disproportionately enlarged subarachnoid-space hydrocephalus (DESH) in normal pressure hydrocephalus misinterpreted as atrophy: Autopsy and radiological evidence. *Neurocase* **25**, 151 (2019).
- Jóhannsdóttir, A. M., Pedersen, C. B., Munthe, S., Poulsen, F. R. & Jóhannsson, B. Idiopathic normal pressure hydrocephalus: Validation of the DESH score as a prognostic tool for shunt surgery response. *Clin. Neurol. Neurosurg.* **241**, 108295 (2024).
- Cogswell, P. M. et al. Changes in ventricular and cortical volumes following shunt placement in patients with idiopathic normal pressure hydrocephalus. *Am. J. Neuroradiol.* **42**, 2165–2171 (2021).
- Fishman, R. A. & Dillon, W. P. Normal pressure hydrocephalus: new findings and old questions. *Am. J. Neuroradiol.* **22**, 1640–1641 (2001).
- Hakim, C. A., Hakim, R. & Hakim, S. Normal-pressure hydrocephalus. *Neurosurg. Clin. N. Am.* **12**, 761–773 (2001).
- Kitagaki, H. et al. CSF spaces in idiopathic normal pressure hydrocephalus: morphology and volumetry. *Am. J. Neuroradiol.* **19**, 1277–1284 (1998).
- Yamashita, F. et al. Detection of changes in cerebrospinal fluid space in idiopathic normal pressure hydrocephalus using voxel-based morphometry. *Neuroradiology* **52**, 381–386 (2010).
- Jaraj, D. et al. Prevalence of idiopathic normal-pressure hydrocephalus. *Neurology* **82**, 1449–1454 (2014).
- Yamada, S., Ishikawa, M., Yamaguchi, M. & Yamamoto, K. Longitudinal morphological changes during recovery from brain deformation due to idiopathic normal pressure hydrocephalus after ventriculoperitoneal shunt surgery. *Sci. Rep.* **9**, 17318 (2019).
- Hiraoka, K. et al. Changes in the volumes of the brain and cerebrospinal fluid spaces after shunt surgery in idiopathic normal-pressure hydrocephalus. *J. Neurol. Sci.* **296**, 7–12 (2010).
- Virhammar, J., Laurell, K., Cesarini, K. G. & Larsson, E.-M. Increase in callosal angle and decrease in ventricular volume after shunt surgery in patients with idiopathic normal pressure hydrocephalus. *J. Neurosurg.* **130**, 130–135 (2018).
- Wada, T. et al. Reversibility of brain morphology after shunt operations and preoperative clinical symptoms in patients with idiopathic normal pressure hydrocephalus. *Psychogeriatrics* **13**, 41–48 (2013).
- Singer, O. C. et al. MR volumetric changes after diagnostic CSF removal in normal pressure hydrocephalus. *J. Neurol.* **259**, 2440–2446 (2012).
- Kaye, J. A. Plasticity in the aging brain: reversibility of anatomic, metabolic, and cognitive deficits in normal-pressure hydrocephalus following shunt surgery. *Arch. Neurol.* **47**, 1336 (1990).
- Narayanan, S. et al. Brain volume loss in individuals over time: Source of variance and limits of detectability. *Neuroimage* **214**, 116737 (2020).
- Nerland, S. et al. A comparison of intracranial volume estimation methods and their cross-sectional and longitudinal associations with age. *Hum. Brain Mapp.* **43**, 4620–4639 (2022).
- Freimann, F. B. et al. Alteration of brain viscoelasticity after shunt treatment in normal pressure hydrocephalus. *Neuroradiology* **54**, 189–196 (2012).
- Hakim, C. A. *The Physics and Physiopathology of the Hydraulic Complex of the Central Nervous System. The Mechanics of Hydrocephalus and Normal Pressure Hydrocephalus* (Doctoral dissertation, Massachusetts Institute of Technology) (1985).
- Pang, D. & Altschuler, E. Low-pressure hydrocephalic state and viscoelastic alterations in the brain. *Neurosurgery* **35**, 643 (1994).
- Lan, P. S. Methods for Imaging Brain Function Using Bold and Viscoelastic Contrast. *ProQuest Dissertations and Theses* (Stanford University, 2021).

36. Hakim, S., Venegas, J. G. & Burton, J. D. The physics of the cranial cavity, hydrocephalus and normal pressure hydrocephalus: Mechanical interpretation and mathematical model. *Surg. Neurol.* **5**, 187–210 (1976).
37. Penn, R. D. & Bacus, J. W. The brain as a sponge: A computed tomographic look at hakim's hypothesis. *Neurosurgery* **14**, 670 (1984).
38. Virhammar, J., Warntjes, M., Laurell, K. & Larsson, E.-M. Quantitative MRI for rapid and user-independent monitoring of intracranial CSF volume in hydrocephalus. *Am. J. Neuroradiol.* **37**, 797–801 (2016).
39. Ziegeltz, D. et al. Evaluation of a fully automated method for ventricular volume segmentation before and after shunt surgery in idiopathic normal pressure hydrocephalus. *World Neurosurg.* **181**, e303–e311 (2024).
40. Gavrilov, V. G. et al. Idiopathic normal pressure hydrocephalus (Hakim-Adams syndrome): Clinical symptoms, diagnosis and treatment. *Psychiatr. Danub.* **31**, 737–744 (2019).
41. Manjón, J. V. & Coupé, P. volBrain: An online MRI Brain volumetry system. *Front. Neuroinform.* <https://doi.org/10.3389/fninf.2016.00030> (2016).
42. Manjón, J. V. et al. vol2Brain: A new online pipeline for whole brain MRI analysis. *Front. Neuroinform.* <https://doi.org/10.3389/fninf.2022.862805> (2022).
43. Krzastek, S. C., Robinson, S. P., Young, H. F. & Klausner, A. P. Improvement in lower urinary tract symptoms across multiple domains following ventriculoperitoneal shunting for idiopathic normal pressure hydrocephalus. *Neurourol. Urodyn.* **36**, 2056–2063 (2017).
44. Feick, D. et al. Sensitivity and predictive value of occupational and physical therapy assessments in the functional evaluation of patients with suspected normal pressure hydrocephalus. *J. Rehabil. Med.* **40**, 715–720 (2008).
45. Mendes, G. A. S., de Oliveira, M. F. & Pinto, F. C. G. The timed up and go test as a diagnostic criterion in normal pressure hydrocephalus. *World Neurosurg.* **105**, 456–461 (2017).
46. Torralva, T., Roca, M., Gleichgerricht, E., López, P. & Manes, F. INECO frontal screening (IFS): A brief, sensitive, and specific tool to assess executive functions in dementia. *J. Int. Neuropsychol. Soc. JINS* **15**, 777–786 (2009).
47. Kazui, H. et al. Effect of shunt operation on idiopathic normal pressure hydrocephalus patients in reducing caregiver burden: evidence from SINPHONI. *Dement. Geriatr. Cogn. Disord.* **31**, 363–370 (2011).
48. Hakim, F. et al. Proposal for a normal pressure hydrocephalus syndrome center of excellence. *Interdiscip. Neurosurg.* **28**, 101506 (2022).

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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