Idiopathic Normal Pressure Hydrocephalus Etiology

- Causal associations between gut microbiota, metabolites, and idiopathic normal pressure hydrocephalus: a two-sample Mendelian randomization study
- Clinical Features and Diagnosis of Normal Pressure Hydrocephalus
- Single-cell elderly blood-CSF atlas implicates peripherally influenced immune dysregulation in normal pressure hydrocephalus
- Cerebrospinal Fluid Biomarkers in Idiopathic Normal Pressure Hydrocephalus: Bibliometric Analysis and Literature Review
- Anosmia and Upper Limb Rigidity-A Potential Phenotype of Idiopathic Normal Pressure Hydrocephalus with Cerebrospinal Fluid alpha-Synuclein Seeds
- The impact of perioperative aspirin utilization on postoperative hemorrhagic complications in idiopathic normal pressure hydrocephalus: a single-center retrospective analysis
- Beyond early motor response: Longitudinal cognitive and gait assessments after extended lumbar drainage in normal pressure hydrocephalus
- Long-term gait improvement following a CSF tap test in idiopathic normal pressure hydrocephalus patients: an analysis of clinical outcomes

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The etiology (cause) of idiopathic normal pressure hydrocephalus (INPH) is not well understood, as the term “idiopathic” indicates that the cause is unknown. However, several theories have been proposed regarding the underlying mechanisms and potential contributing factors to the development of INPH. Here are some of the proposed theories:

Impaired CSF absorption: One theory suggests that there is a disturbance in the absorption of cerebrospinal fluid (CSF) within the brain. CSF is produced within the brain's ventricles and normally flows through the ventricular system and is absorbed into the bloodstream. In INPH, there may be a dysfunction in the mechanisms responsible for CSF absorption, leading to its accumulation and resulting in hydrocephalus.

Reduced CSF circulation: Another theory suggests that there is a decrease in the circulation or flow of CSF within the brain. It is believed that impaired CSF flow can result from blockages or disruptions in the pathways through which CSF normally circulates, such as the cerebral aqueduct or the subarachnoid space.

Impaired drainage of interstitial fluid: Interstitial fluid is a fluid that surrounds and bathes the cells of the brain. Some researchers propose that impairment in the drainage of interstitial fluid, which is closely linked to CSF dynamics, may contribute to the development of INPH.

Age-related changes: INPH is more commonly observed in older individuals, suggesting that age-related changes in the brain may be involved. It is thought that alterations in the structure and function of the brain's blood vessels, as well as changes in the elasticity and compliance of the brain tissue, may play a role in the development of INPH.

Genetic factors: While most cases of INPH are considered sporadic (occurring without a family history), some studies have suggested a potential genetic predisposition. Certain genetic variations or

mutations may contribute to the development of INPH, although specific genes or pathways involved have not been conclusively identified.

It is important to note that these theories are still being investigated, and the exact mechanisms underlying INPH remain unclear. Further research is needed to gain a better understanding of the etiology and pathophysiology of INPH.

Studies signal the glymphatic system and classical cerebrospinal fluid absorption from the dural lymphatics as aetiological mechanisms of CSF retention. Research is also underway on imaging tests and biomarker developments for more precise diagnosis, shunting technique options with fewer sequelae and complications, and the influence of genetics. Particularly, the newly introduced 'suspected iNPH' in the third edition of the guidelines may be useful for earlier diagnosis. However, less well-studied areas remain, such as pharmacotherapy in non-operative indications and neurological findings other than the triadic signs [1)].

All patients with idiopathic normal pressure hydrocephalus (INPH) who underwent shunting in Sweden in 2008-2010 were compared to age- and sex-matched population-based controls. Inclusion criteria were age 60-85 years and no dementia. The 10 most important vascular risk factor (VRFs) and cerebrovascular and peripheral vascular disease were prospectively assessed using blood samples, clinical examinations, and standardized questionnaires. Assessed VRFs were hypertension, hyperlipidemia, diabetes, obesity, psychosocial factors, smoking habits, diet, alcohol intake, cardiac disease, and physical activity.

In total, 176 patients with INPH and 368 controls participated. Multivariable logistic regression analysis indicated that hyperlipidemia (odds ratio [OR] 2.380; 95% confidence interval [CI] 1.434-3.950), diabetes (OR 2.169; 95% CI 1.195-3.938), obesity (OR 5.428; 95% CI 2.502-11.772), and psychosocial factors (OR 5.343; 95% CI 3.219-8.868) were independently associated with INPH. Hypertension, physical inactivity, and cerebrovascular and peripheral vascular disease were also overrepresented in INPH. Moderate alcohol intake and physical activity were overrepresented among the controls. The population-attributable risk percentage was 24%.

The findings confirm that patients with INPH have more VRFs and lack the protective factors present in the general population. Almost 25% of cases of INPH may be explained by VRFs. This suggests that INPH may be a subtype of vascular dementia. Targeted interventions against modifiable VRFs are likely to have beneficial effects on INPH [2)].

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2)
Israelsson H, Carlberg B, Wikkelsö C, Laurell K, Kahlon B, Leijon G, Eklund A, Malm J. Vascular risk factors in INPH: A prospective case-control study (the INPH-CRasH study). Neurology. 2017 Jan 6. pii: 10.1212/WNL.0000000000003583. doi: 10.1212/WNL.0000000000003583. [Epub ahead of print] PubMed PMID: 28062721.