

Homburg

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In a Prospective observational cohort study Spielmann et al. investigates the association between cerebrospinal fluid (CSF) biomarkers (Tau, Phospho-tau, A β 42/A β 40 ratio) and neurocognitive outcomes following ventriculoperitoneal (VP) shunt surgery in patients with idiopathic normal pressure hydrocephalus (iNPH). 80 patients were assessed with neuropsychological tests before and after lumbar puncture, and at 6 weeks and 3 months postoperatively.

Strengths

- **Prospective design** with repeated neurocognitive assessments.
- **Relevant biomarker panel** (Tau, P-Tau, Aβ42/Aβ40) with potential prognostic value.
- Use of **sensitive cognitive tests** beyond MMSE (e.g., DemTect, TMT A & B).
- Suggests **personalized treatment strategies** based on CSF biomarker profiles.

Weaknesses

- No control group or randomization → **limits causal inference**.
- **Short follow-up** (3 months); long-term cognitive evolution not assessed.
- **Confounding factors** (age, comorbidities, baseline cognitive function) not clearly controlled.
- **No multivariate analysis** or statistical power calculations provided.
- MMSE used despite **low sensitivity** in detecting iNPH-related changes.
- **Biomarker thresholds** not standardized or validated.
- Functional and quality-of-life outcomes not reported.

Interpretation

- The **beta-amyloid ratio (Aβ42/Aβ40)** is associated with better cognitive outcomes after shunt surgery.
- **No significant improvement** observed in MMSE, but specific domains (executive function, psychomotor speed) showed gains.
- Suggests **Aβ42/Aβ40** as a possible **biomarker for patient selection**, but external validation is needed.

Conclusion

This study adds to growing evidence that CSF biomarkers, particularly the Aβ42/Aβ40 ratio, may help predict neurocognitive recovery after shunting in iNPH. However, **methodological limitations** reduce the strength of the conclusions. Larger, multicenter trials with **longitudinal follow-up** and **controlled design** are required to confirm its clinical utility.

Appraisal Summary

Category	Assessment
Study Design	❑ Prospective, but lacks control group or randomization
Sample Size	⚠ Modest (n=80), single-region cohort
Biomarker Relevance	❑ Strong focus on emerging prognostic markers
Cognitive Testing Battery	❑ DemTect and TMT used appropriately; MMSE underperforms
Statistical Analysis	⚠ Not robust; lacks multivariate models or biomarker threshold definition
Clinical Utility	⚠ Promising but not yet implementable
Innovation	❑ High—biomarker-guided prognosis in iNPH

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Spielmann H, Lepshokov M, Prajsnar-Borak A, Wagenpfeil G, Oertel J. Neurocognitive effects of CSF biomarkers in idiopathic normal pressure hydrocephalus patients undergoing VP shunt placement. Neurosurg Rev. 2025 Jun 5;48(1):484. doi: 10.1007/s10143-025-03609-8. PMID: 40471348.

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