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Radiological and Clinical Changes in idiopathic Normal Pressure Hydrocephalus

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Vita stråket 12, den 7 februari 2020, klockan 13.00

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Avhandlingen baseras på följande delarbeten

I. Jaraj, D, Agerskov, S, Rabiei, K, Marlow, T, Jensen, C, Guo, X, Kern, S, Wikkelsö, C, Skoog, I.
Vascular factors in suspected normal pressure hydrocephalus – a population-based study.
Neurology 2016; 86: 592-599.

II. Agerskov, S, Hellström, P, Andrén, K, Kollén, L, Wikkelsö, C, Tullberg, M.
The phenotype of idiopathic normal pressure hydrocephalus – a single center study of 429 patients.
Journal of the Neurological Sciences 2018; 391: 54-60.

III. Agerskov, S, Wallin, M, Hellström, P, Ziegelitz, D, Wikkelsö, C, Tullberg, M.
Absence of disproportionately enlarged subarachnoid space hydrocephalus, a sharp callosal angle and other morphologic MRI markers should not be used to exclude patients with idiopathic normal pressure hydrocephalus from shunt surgery.
American Journal of Neuroradiology 2019; 40: 74-79.

IV. Agerskov, S, Arvidsson, J, Ziegelitz, D, Lagerstrand, K, Starck, G, Björkman-Burtscher, I, Wikkelsö, C, Tullberg, M. MRI diffusion and perfusion markers in the mesencephalon and pons as markers of disease and symptom reversibility in idiopathic normal pressure hydrocephalus.
Submitted.

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Radiological and Clinical Changes in idiopathic Normal Pressure Hydrocephalus

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Abstract

Idiopathic normal pressure hydrocephalus (iNPH) is a treatable, neurological disorder affecting the elderly population causing gait, balance, cognitive and micturition impairments. Treatment results in a clinical improvement in up to 80% of patients. Unfortunately, the pathophysiology is still incompletely understood, the clinical picture needs to be clarified, and no reliable, predictive biomarkers exist. The overall aim of this thesis was to elucidate on the development and pathophysiology of iNPH by describing the clinical and radiological phenotype as well as the involvement of known vascular risk factors in the disease, and by investigating the specific role of the brainstem in iNPH. A further aim was to explore the predictive potential of several clinical and radiological biomarkers.

In Study I, radiological and clinical signs of iNPH were associated with vascular risk factors and white matter lesions in a large, population-based sample. Study II showed that a majority of patients have symptoms from at least three of four symptom groups at the time of diagnosis, but the severity is greatly varied. In addition, paratonia, a less well-recognized symptom is seen in most patients and should be considered a core finding of iNPH. Further, the postoperative improvement seen in the majority of patients involve all symptom groups. Study III showed that while all patients have ventriculomegaly, several other morphological MRI findings are seen only in a subgroup of patients and should not be required for the diagnosis. In addition, no morphological MRI marker had any predictive value, and, as such, they should not be used to exclude patients from shunt surgery. In Study IV, diffusion changes in the mesencephalon and pons were evident pre- and postoperatively in all patients, and responders showed a significant relative cerebral blood flow increase postoperatively, correlating to the degree of clinical improvement.

In conclusion, vascular changes are probably involved in the development of iNPH. While several clinical and radiological findings are characteristic of the disease, the severity is profoundly varied among patients and cannot be used for prediction. The brainstem seems to be involved in the core symptom generation in iNPH and further studies focusing on this area are warranted.

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