

Is normal pressure hydrocephalus becoming less idiopathic?

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Normal pressure hydrocephalus (NPH) has posed a challenge to neurologists for 5 decades.¹ Difficulties in understanding its pathophysiology have hindered efforts to diagnose it and to develop a better approach to selecting patients for shunt surgery.

We know that many patients with NPH have CSF absorption difficulty as measured by resistance to CSF outflow (R_{out}).² The problem is that many with normal R_{out} also improve with shunt surgery, so other factors are important in NPH pathogenesis. We also know that more than 10% of patients presenting clinically with NPH have congenital chronic hydrocephalus. Congenital hydrocephalus may become symptomatic in older age, as evidenced by the fact that more than 10% of patients with NPH have a head size above the 98th percentile.^{3,4}

There is now increasing evidence that vascular risk factors are associated with hydrocephalus. As long ago as 1959, Bering demonstrated that intraventricular pulse pressure can induce the development of hydrocephalus. He showed that, in a dog model of hydrocephalus, ligation of the choroid plexus in one ventricle (removing the intraventricular pulse pressure in that ventricle) produced hydrocephalus in only the other ventricle. This observation has been approximated in humans recently. In the Atherosclerosis Risk in Communities Study, ventricle size was measured on 2 brain MRI scans 10 years apart. Baseline systolic blood pressure and pulse pressure were associated with increased ventricular enlargement.⁵ There are several other reports that indicate an association of hypertension, diabetes, and heart disease with NPH.^{6–9}

The important question is whether persons who have normal R_{out} but vascular risk factors improve with shunt surgery; this was addressed in the only double-blind, randomized, prospective treatment study in NPH.¹⁰ Patients ($n = 14$) who did not have an absorption problem (R_{out} was normal), but had severe brain white matter change and vascular risk factors, underwent shunting. Half had the shunt tube tied in the neck and left closed for 3 months. Those with an open shunt improved in the first 3 months and those who had occluded shunts did not, but when the shunt was opened, they too improved.

In this issue of *Neurology*®, vascular risk factors associated with NPH in a population-based study are described.¹¹ The authors found that, of 1,235 persons older than 70 years, 55 had imaging findings of NPH and, of these, 26 fulfilled the International Guidelines¹² for the diagnosis of NPH. Each case was matched to 5 controls on age, sex, and study cohort. Radiologic hydrocephalus was associated with hypertension (odds ratio [OR] 2.7; 95% confidence interval [CI]: 1.1–6.8), moderate to severe white matter lesions (OR 6.5; 95% CI: 2.1–20.3), and diabetes mellitus (OR 4.3; 95% CI: 1.1–16.3). Important strengths of this population-based study are that the controls came from the same population and exposure data were collected prospectively. An important limitation is that this is a cross-sectional study, so we do not know whether white matter changes cause hydrocephalus, hydrocephalus causes white matter changes, or it is bidirectional.

The associations between vascular risk factors and radiologic or clinical NPH have important implications. Perhaps early effective intervention treating vascular risk factors may reduce the incidence of NPH. Vascular risk factors are clearly associated with NPH, but further prospective studies will be needed to show whether they are causative.

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DISCLOSURE

The author reports no disclosures relevant to the manuscript. Go to Neurology.org for full disclosures.

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