Neurología. 2017;xxx:xxx—xxx

SOCIEDAD ESPAÑOLA DE NEUROLOGIA

NEUROLOGÍA

www.elsevier.es/neurologia

REVIEW ARTICLE

Current concepts on the pathophysiology of idiopathic chronic adult hydrocephalus: Are we facing another neurodegenerative disease?☆

R. Martín-Láez[a,*], N. Valle-San Román[b], E.M. Rodríguez-Rodríguez[c], E. Marco-de Lucas[b], J.A. Berciano Blanco[c], A. Vázquez-Barquero[a]

[a] *Servicio de Neurocirugía, Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain*
[b] *Servicio de Radiología, Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain*
[c] *Servicio de Neurología, Hospital Universitario Marqués de Valdecilla, Instituto de Investigación Sanitaria IDIVAL, Centro de Investigación Biomédica en Red en Enfermedades Neurodegenerativas (CIBERNED), Universidad de Cantabria, Santander, Cantabria, Spain*

Received 27 October 2015; accepted 29 March 2016

KEYWORDS
Cerebrospinal fluid clearance;
Pathophysiology;
Cerebral blood flow;
Idiopathic chronic adult hydrocephalus;
Cerebrospinal fluid turnover;
Diffusion tractography

Abstract
Introduction: Since its description five decades ago, the pathophysiology of idiopathic chronic adult hydrocephalus (iCAH) has been traditionally related to the effect that ventricular dilatation exerts on the structures surrounding the ventricular system. However, altered cerebral blood flow, especially a reduction in the CSF turnover rate, are starting to be considered the main pathophysiological elements of this disease.
Development: Compression of the pyramidal tract, the frontostriatal and frontoreticular circuits, and the paraventricular fibres of the superior longitudinal fasciculus have all been reported in iCAH. At the level of the corpus callosum, gliosis replaces a number of commissural tracts. Cerebral blood flow is also altered, showing a periventricular watershed region limited by the subependymal arteries and the perforating branches of the major arteries of the anterior cerebral circulation. The CSF turnover rate is decreased by 75%, leading to the reduced clearance of neurotoxins and the interruption of neuroendocrine and paracrine signalling in the CSF.

☆ Please cite this article as: Martín-Láez R, Valle-San Román N, Rodríguez-Rodríguez EM, Marco-de Lucas E, Berciano Blanco JA, Vázquez-Barquero A. Actualización en la fisiopatología de la hidrocefalia crónica del adulto idiopática: ¿nos enfrentamos a otra enfermedad neurodegenerativa? Neurología. 2018. https://doi.org/10.1016/j.nrl.2016.03.010

* Corresponding author.
E-mail address: rmlaez@yahoo.es (R. Martín-Láez).

Conclusions: iCAH presents as a complex nosological entity, in which the effects of subcortical microangiopathy and reduced CSF turnover play a key role. According to its pathophysiology, it is simpler to think of iCAH more as a neurodegenerative disease, such as Alzheimer disease or Binswanger disease than as the classical concept of hydrocephalus.

PALABRAS CLAVE
Aclaramiento licuoral;
Fisiopatología;
Flujo sanguíneo cerebral;
Hidrocefalia crónica del adulto idiopática;
Recambio licuoral;
Tractografía por tensor de difusión

Actualización en la fisiopatología de la hidrocefalia crónica del adulto idiopática: ¿nos enfrentamos a otra enfermedad neurodegenerativa?

Resumen
Introducción: Desde la descripción hace 5 décadas de la hidrocefalia crónica del adulto idiopática (HCAi), su fisiopatología ha sido considerada básicamente relacionada con el efecto que la dilatación ventricular ejerce sobre las estructuras adyacentes al sistema ventricular. Sin embargo, las alteraciones en el flujo sanguíneo cerebral (FSC) y, sobre todo, la reducción en el recambio licuoral parecen emerger como componentes fisiopatológicos principales de esta enfermedad.
Desarrollo: En la HCAi se observa una compresión del tracto piramidal, de los circuitos cortico-subcorticales fronto-estriatales y fronto-reticulares, y de las fibras profundas del fascículo longitudinal superior. En el cuerpo calloso se objetiva un descenso en el número de fibras comisurales, que son reemplazadas por gliosis. El FSC se encuentra alterado, con un patrón de última pradera en la región subcortical adyacente a los ventrículos, correspondiente a la intersección entre las arterias subependimarias y las arterias perforantes dependientes de los grandes troncos arteriales de la circulación anterior. El recambio diario del LCR se ve disminuido en un 75%, lo que conlleva una reducción del aclaramiento de neurotóxicos y la interrupción de las señalizaciones neuroendocrinas y paracrinas que ocurren a través del LCR.
Conclusiones: La HCAi emerge como una entidad nosológica compleja, en la que los efectos de la microangiopatía subcortical y la disminución del recambio de LCR desempeñan un papel fundamental. Esta base fisiopatológica aleja la HCAi del concepto clásico de hidrocefalia y la acerca al perfil de otras enfermedades neurodegenerativas, como la enfermedad de Alzheimer o la enfermedad de Binswanger.

Introduction

Idiopathic normal-pressure hydrocephalus (iNPH) is a nosological entity characterised by the clinical triad of gait disturbance, cognitive impairment, and urinary incontinence, with neuroimaging findings of ventricular dilatation (Fig. 1) and in the absence of any other cause that may explain clinical findings.

Although this clinical syndrome had previously been described in the literature[1–5] (particular emphasis should be placed on the descriptions made by French neurologist Etienne Mouline[6] in 1819 and German pathologist Friedrich Dörner[7] in 1826), it was the late Colombian neurosurgeon Salomón Hakim Dow who provided a systematic description of the clinical and radiological features of iNPH in his doctoral thesis, written over 50 years ago.[8] Hakim, together with 2 renowned neurologists from the Massachusetts General Hospital, Raymond D. Adams and Charles M. Fisher, disclosed his findings in 2 articles, which were published simultaneously in the *New England Journal of Medicine*[9] and the *Journal of Neurological Sciences*.[10]

The classic triad of symptoms has traditionally been thought to be caused by the effect of ventricular dilatation on periventricular nerves[11–17] and vessels.[18–25] However, recent studies also suggest an inability of the CSF to remove waste products from the extracellular fluid as a causal factor for iNPH.[26–29]

We provide updated information on the pathophysiology of the disease, placing special emphasis on decreased CSF turnover, a novel factor which may have an impact on long-term prognosis. These findings challenge the classic concept of hydrocephalus, suggesting that iNPH is a neurodegenerative disease.

Development

Compression of periventricular subcortical fibres

Compression of the frontal projections descending close to the frontal horns of the lateral ventricles alters the