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Development of hydrocephalus and classical hypothesis of cerebrospinal fluid hydrodynamics: Facts and illusions

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ABSTRACT

According to the classical hypothesis of the cerebrospinal fluid (CSF) hydrodynamics, CSF is produced inside the brain ventricles, than it circulates like a slow river toward the cortical subarachnoid space, and finally it is absorbed into the venous sinuses. Some pathological conditions, primarily hydrocephalus, have also been interpreted based on this hypothesis. The development of hydrocephalus is explained as an imbalance between CSF formation and absorption, where more CSF is formed than is absorbed, which results in an abnormal increase in the CSF volume inside the cranial CSF spaces. It is believed that the reason for the imbalance is the obstruction of the CSF pathways between the site of CSF formation and the site of its absorption, which diminishes or prevents CSF outflow from the cranium. In spite of the general acceptance of the classical hypothesis, there are a considerable number of experimental results that do not support such a hypothesis and the generally accepted pathophysiology of hydrocephalus. A recently proposed new working hypothesis suggests that osmotic and hydrostatic forces at the central nervous system microvessels are crucial for the regulation of interstial fluid and CSF volume which constitute a functional unit. Based on that hypothesis, the generally accepted mechanisms of hydrocephalus development are not plausible. Therefore, the recent understanding of the correlation between CSF physiology and the development of hydrocephalus has been thoroughly presented, analyzed and evaluated, and new insights into hydrocephalus etiopathology have been proposed, which are in accordance with the experimental data and the new working hypothesis.

Contents

Abbreviations: BV, brain ventricle; CH, communicating hydrocephalus; CNS, central nervous system; CSF, cerebrospinal fluid; CM, cisterna magna; EH, external hydrocephalus; ISF, interstitial fluid; ICP, intracranial pressure; LV, lateral ventricle; SAS, subarachnoid space.

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1. Introduction

Based on current belief and knowledge, only a few physiological and pathological states are so strongly interconnected and affirm each other, as do the classical hypothesis of cerebrospinal fluid (CSF) secretion, circulation and absorption and the development of hydrocephalus. The classical hypothesis of CSF hydrodynamics presents CSF simply and schematically as a slow river which forms inside the brain ventricles, then flows unidirectionally along the CSF system toward the cortical subarachnoid space (SAS), and is then absorbed into the venous sinuses (see later). Nothing has influenced the perception of CSF dynamics and its correlation with the development of hydrocephalus more than Dandy's crucial experiment (1919) on the consequences of choroid plexecotomy in dogs. These findings are still considered relevant and are quoted even today (Rekate, 2009). If the choroid plexus of one lateral ventricle was removed, and if foramina of Monro of both lateral ventricles were obstructed, it was reported that the ventricle containing a choroid plexus would dilate and the ventricle lacking a choroid plexus would collapse. This observation led Dandy to conclude that this is "*the only absolute proof that cerebrospinal fluid is formed from the choroid plexus. At the same time, it is proven that the ependyma lining the ventricles is not concerned in the production of cerebrospinal fluid*." This experiment still points to a few more facts that are crucial in terms of forming a general hypothesis about CSF hydrodynamics. If the obstructed lateral ventricle containing a choroid plexus dilates, it is obvious that the choroid plexus actively produced (secreted) CSF. It is also obvious that the dilatation of the ventricle is possible only if the CSF absorption does not exist inside the brain ventricle. If CSF is absorbed outside the brain ventricles, it should flow (circulate) to the place of its absorption. If the CSF system is obstructed between the place of CSF secretion and the place of its absorption (foramina of Monro), the brain ventricles should, because of the continuity of CSF secretion by the choroid plexuses (CSF pumps), dilate and produce hydrocephalus. In other words, the classical hypothesis of CSF hydrodynamics was founded, and the development of hydrocephalus was explained with this experiment. At the same time, the postulated hypothesis offers a very reasonable explanation of hydrocephalus development, and the existence of hydrocephalus proves the authenticity of the classical hypothesis. Since that time, one has confirmed the other, and it is nearly impossible to research and discuss these two subjects separately. Therefore, until today this correlation persists with minor modifications in the same way as it did in Dandy's time.

Can we, after nearly a 100 years, still say that this is scientifically sustainable?

Recently, a new hypothesis regarding CSF hydrodynamics has been proposed (Bulat and Klarica, 2010; Klarica et al., 2009; Orešković and Klarica, 2010). According to this new hypothesis, CSF is not formed mainly by the choroid plexuses, and it does not then circulate to finally be absorbed, but it appears and disappears throughout the entire CSF system, depending on the hydrostatic and osmotic forces between the CSF, interstitial fluid (ISF) and blood capillaries. Osmotic and hydrostatic forces are crucial to the regulation of ISF–CSF volume. In terms of the capacity of fluid exchange, the cerebral capillaries are the dominant location, and the choroid plexuses are a less relevant place for this process. There is a permanent fluid and substance exchange between the CSF system and the surrounding tissue which depends on the (patho)physiological conditions that predominate within those compartments (see Section 4.2). In light of this new hypothesis, it would, of course, be necessary to reevaluate the generally accepted concept regarding hydrocephalus development. Therefore, the primary aim of this review is to attempt to critically evaluate the relationship between the classical CSF hypothesis and the development of hydrocephalus. This review will also make an effort to explain if and how the development of hydrocephalus can be incorporated into the new hypothesis. For the same reason, we will try to avoid any discussion about the epidemiology, pathology, classification, treatment, patient status, symptoms or mortality of hydrocephalus. We will make an exception for cases in which the same subjects would concern the aforementioned close correlation between the classical hypothesis and the development of hydrocephalus, and/or if they would allow us to further analyze that correlation.

The prevalent and crucial experimental data which support the classical hypothesis and explain the development of hydrocephalus have been observed in experimental animals. One should, of course, be extremely careful when the experimental results are extrapolated from animals to humans in any field, including the field of hydrocephalus development and CSF physiology. However, it is necessary to emphasize that the same principles of CSF hydrodynamics and the development of hydrocephalus in humans are present in other mammals. Furthermore, there are no mammalian species in which this matter is conceived outside the framework of the classical hypothesis. Thus, our analysis has not thoroughly explained the species-specific differences.

2. Classical hypothesis of cerebrospinal fluid hydrodynamics

According to experimental scientific interest and the first modern studies of CSF physiology from nearly a century ago (Cushing, 1914; Dandy, 1919; Dandy and Blackfan, 1914; Weed, 1914), CSF physiology is, after a 100 years of investigating, based on three key premises: (1) the active formation (secretion) of cerebrospinal fluid; (2) the passive absorption of CSF; and (3) the unidirectional flow of cerebrospinal fluid from the place of formation to the place of absorption (Fig. 1). Based on all of the above, CSF is referred to as the third circulation (the other two are