## Introduction

The cerebral venous system might play a critical role in the pathophysiology of neurological disorders involving disturbed cerebrospinal fluid (CSF) dynamics. However, the physiology of the venous system, such as flow and pressure, remains poorly understood, specifically, how it functions in health and disease.

Essential to brain health is the homeostasis between three main constituents competing for space inside the scull: the brain tissue, the arterial – and - venous blood, and the CSF. Any volume increase in one of these constituents requires an equal decrease in volume in another. If not, intracranial pressure (ICP) will rise. This is known as the Monroe-Kelly doctrine and this principle is the basis for understanding the pathophysiology CSF- and hemodynamic disorders such as idiopathic normal pressure hydrocephalus (INPH) and idiopathic intracranial hypertension (IIH). The venous system may play a critical role in both these diseases since it interacts with the CSF- system during each cardiac cycle: With each heartbeat, expansion of the arterial pulse leads to a transient intracranial pressure rise that propagates through the CSF and compresses CSF-immersed veins, expelling blood toward the dural sinuses. Conversely, the dural sinuses are the principal site of CSF absorption. Consequently, sinus pressure sets the lower limit of CSF pressure (i.e., ICP) required for CSF outflow.

Part of this interplay can be studied by studying the arteriovenous interplay. With four-dimensional flow MRI (4D-flow) arterial and venous flow can be assessed simultaneously across the cardiac cycle. 4D-flow MRI enables assessment of both the configuration of the brain's venous system and its flow and pulsatility. While the anatomy of the venous system is highly variable and well documented, little is known about how anatomical variability affects venous hemodynamics. Moreover, knowledge of the hemodynamics of veins that interact directly with CSF, such as the cortical veins and the vein of Galen, are limited as well. Specifically, what constitutes normal flow patterns and which features characterize signs of pathology remain unclear. Large population-based studies are scarce and are needed to establish reference data for future research.

This study aimed to assess venous blood flow in a large population-based cohort using 4D-flow MRI, including CSF-immersed veins—such as cortical veins and the vein of Galen—and the major outflow pathways of the dural sinuses. Specifically, we quantified venous flow rates relative to total arterial inflow across common anatomical variants. The secondary aim was to identify flow patterns characteristic of iNPH-like gait disturbances.

## Methods

4D-flow MRI examinations of 762 volunteers from a population-based cohort of older adults (mean age 75 ± 5 years; 52% female) with self-reported gait disturbances were included in this study. Following neurological examinations, 689 had no neurological gait disorder (Group 1) and 73 had INPH-like gait disorder (Group 2). Blood flow, pulsatility and cross-sectional areas were assessed at the following brain sites. Arterial inflow was defined as the sum of the flows in the internal carotid arteries (ICAs) and the basilar artery (BA). The venous system was assessed at several locations along the dural sinuses and major outflow pathways, from the rostral-most segment of the superior sagittal sinus to the mid segment of the sigmoid sinus. In addition, large

cortical veins (typically the vein of Trolard and the vein of Labbé) and the vein of Galen were assessed.

## Results/Discussion

The distribution of transverse sinus drainage patterns—70% symmetrical, 25% right-sided dominant, and 5% left-sided dominant—was consistent with previous anatomical studies and did not differ between groups. The proportion of blood flow in relation to arterial inflow was higher in symmetrical than in asymmetrical drainage patterns, indicating greater reliance on accessory outflow pathways for the latter.

The cross-sectional areas of the intracranial sinuses were larger in Group 1 than those previously reported in younger cohorts<sup>1</sup> (areas estimated from diameter). This finding, combined with the fact that total cerebral blood flow declines with age<sup>5</sup>, suggests that dural sinus pressure may decrease with increasing age. This finding is particularly interesting because elevated dural sinus pressure is strongly associated with IIH, a disorder that predominantly affects women of childbearing age and is rare in the elderly. Similarly, when comparing flow and cross-sectional areas between the Group 1 and Group 2, comparatively smaller cross-sectional areas were found in Group 2 while demonstrating equal flow rates between the groups. This suggests higher dural sinus pressure in Group 2, which has been suggested previously in INPH, leading to reduced intracranial compliance. Further evidence of elevated venous pressure in Group 2 were larger cross-sectional areas of the cortical veins compared with Group 1. Since the cortical veins drain into the dural sinuses, increased dural sinus pressure will propagate back inflating the veins.

## Conclusion

To our knowledge, this is the first study to present venous blood flow and pulsatility in relation to common dural sinus configurations and large cerebral veins in a large, population-based cohort. We present reference values for flow, pulsatility, and cross-sectional areas across the cerebral venous system. Participants with iNPH-like gait disturbances exhibited signs consistent with elevated dural sinus pressure, whereas those with non-neurological gait disorders showed the opposite pattern.

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