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Cerebral venous drainage and its impact on cerebrospinal fluid motion: a retrospective review of the work of the ISNVD

Clive Beggs^{1,2}

1. Buffalo Neuroimaging Analysis Center, University at Buffalo, 100 High St., Buffalo, NY 14203, NY, USA;
2. Institute for Sport, Physical Activity and Leisure, Leeds Beckett University, Leeds, LS1 3HE, UK

Since the inception of the Society, members of the ISNVD have pioneered work on the interaction between the cerebrospinal fluid (CSF) system and the cerebral venous drainage system, and its possible involvement in neurological disease. Initial investigations by ISNVD members involved the association between multiple sclerosis (MS) and increased CSF pulsatility in the Aqueduct of Sylvius (AoS) [1,2]. This was followed by a study that reported a similar phenomenon in healthy adults without neurologic disease [3], suggesting that increased aqueductal pulsatility might be primarily due to altered intracranial biomechanics associated with constricted cerebral venous drainage, rather than neuronal decay. This opinion was reinforced by Zivadinov et al., [4] who performed venous angioplasty on MS patients diagnosed with chronic cerebrospinal venous insufficiency (CCSVI) and found that the procedure normalized CSF pulsatility in the AoS. Independent work by Zamboni and co-workers [5] had already shown a 63% increase in the hydraulic resistance of the extracranial venous pathways in MS patients diagnosed with CCSVI [6]. As such, this body of work indicated a direct biomechanical link between cerebral venous outflow and the motion of the CSF pulse in the AoS, a link that was later confirmed by Lagana, Beggs and co-workers in a MRI study that demonstrated a strong positive correlation ($r=0.966$, $P<0.001$) between the intracranial venous blood volume and the aqueductal CSF volume in healthy young adults [7].

Although the clinical implications of this work are yet to be fully understood, increased CSF pulsatility in the AoS has been associated with early stage white matter damage (WM) in healthy individuals without neurologic disease [8]. As such, this appears to support the work of Chung et al [9], who found jugular venous reflux (JVR) to be associated with more severe age-related WM changes in the elderly. Collaborative work between Chung, Zivadinov, Beggs and their co-workers also revealed JVR to be associated with intracranial structural changes in Alzheimer's disease patients, which resulted in increased gray matter volume [10]. This unexpected finding, which has since been mirrored in a subsequent study investigating aging in healthy individuals [11], suggests that venous drainage anomalies may have far reaching neurological implications, leading to increased venous blood retention in the cranium, something that has the potential to alter the dynamics of the intracranial CSF system.

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