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## **Cerebrospinal fluid iron**

- Ultrasensitive photoelectrochemical biosensor of amyloid-beta oligomer detection via porphyrinbased covalent organic frameworks enhanced by iron single-atom catalysts
- ZIP14 Deletion Disrupts Divalent Metal Homeostasis in Mouse Cerebrospinal Fluid
- Iron Hemostasis in Patients With Subarachnoid Hemorrhage and the Role of Early CSF Drainage
- From the Gut to the Brain: Transcriptomic Insights into Neonatal Meningitis <em>Escherichia coli</em> Across Diverse Host Niches
- Extracorporeal Blood Purification Therapy to Deal a Deferasirox Induced Life-Threatening Hepatic Encephalopathy in a Septic Child With Sickle-Cell Disease: A Case Report
- Idiopathic Intracranial Hypertension With Papilledema and Iron Deficiency Anemia in a 14-Year-Old Female Patient: A Case Report of First Presentation in the Middle East
- Vascular Contribution to Cerebral Waste Clearance Affected by Aging or Diabetes
- Reactive astrocyte-derived exosomes enhance intracranial lymphatic drainage in mice after intracranial hemorrhage

Cerebrospinal fluid (CSF) iron is an important neurological health and disease marker. The concentration of iron in the CSF can provide insights into various conditions affecting the central nervous system. Elevated or decreased levels of CSF iron may be associated with a range of disorders, including neurodegenerative diseases, infections, and hemorrhagic conditions.

Here are some key points:

1. Role of Iron in the CNS: Iron is essential for brain function and involves various metabolic processes. However, its dysregulation can lead to oxidative stress and neuronal damage.

2. Diagnostic Use: Measuring iron levels in the CSF can help diagnose conditions like multiple sclerosis, Alzheimer's disease, and brain hemorrhages. Elevated iron levels might indicate bleeding or inflammation, while low levels could be related to iron metabolism disorders.

3. Research and Studies: Studies are ongoing to understand the exact role of CSF iron in neurological diseases and how it might be used as a biomarker for early diagnosis or monitoring of disease progression.

Mahaney et al. previously showed hemoglobin and ferritin to be elevated in the lumbar puncture cerebrospinal fluid (CSF) of neonates with PHH. They evaluated CSF from serial ventricular taps to determine whether neonates with PHH following severe initial ventriculomegaly had higher initial levels and prolonged clearance of CSF hemoglobin and hemoglobin degradation products compared to those in neonates with PHH following moderate initial ventriculomegaly.

In this observational cohort study, CSF samples were obtained from serial ventricular taps in premature neonates with severe IVH and subsequent PHH. CSF hemoglobin, ferritin, total iron, total bilirubin, and total protein were quantified using ELISA. Ventriculomegaly on cranial imaging was assessed using the frontal occipital horn ratio (FOHR) and was categorized as severe (FOHR > 0.6) or moderate (FOHR  $\leq$  0.6).

Ventricular tap CSF hemoglobin (mean) and ferritin (initial and mean) were higher in neonates with severe versus moderate initial ventriculomegaly. CSF hemoglobin, ferritin, total iron, total bilirubin, and total protein decreased in a nonlinear fashion over the weeks following severe IVH. Significantly higher levels of CSF ferritin and total iron were observed in the early weeks following IVH in neonates with severe initial ventriculomegaly than in those with initial moderate ventriculomegaly.

Among preterm neonates with PHH following severe IVH, elevated CSF hemoglobin, ferritin, and iron were associated with more severe early ventricular enlargement (FOHR > 0.6 vs  $\leq$  0.6 at first ventricular tap)<sup>1)</sup>.

## **Experimental animal studies**

Evidence indicates that erythrocyte-derived iron and inflammation both play a role in intraventricular hemorrhage-induced brain injury including hydrocephalus. Many immune-associated cells, primarily stromal macrophages, reside at the choroid plexus where they are involved in inflammatory responses and antigen presentation. However, whether intraventricular iron impacts those stromal cells is unknown. Bian et al. evaluated the relationship between choroid plexus stromal macrophages and iron-induced hydrocephalus in rats and the impact of minocycline and clodronate liposomes on those changes. Aged (18-month-old) and young (3-month-old) male Fischer 344 rats were used to study choroid plexus stromal macrophages. Rats underwent intraventricular iron injection to induce hydrocephalus and were treated with either minocycline, a microglia/macrophage inhibitor, or clodronate liposomes, a macrophage-depleting agent. Ventricular volume was measured using magnetic resonance imaging, and stromal macrophages were guantified by immunofluorescence staining. They found that stromal macrophages accounted for about 10% of the total choroid plexus cells with more in aged rats. In both aged and young rats, intraventricular iron injection resulted in hydrocephalus and increased stromal macrophage number. Minocycline or clodronate liposomes ameliorated iron-induced hydrocephalus and the increase in stromal macrophages. In conclusion, stromal macrophages account for  $\sim 10\%$  of all choroid plexus cells, with more in aged rats. Treatments targeting macrophages (minocycline and clodronate liposomes) are associated with reduced iron-induced hydrocephalus<sup>2)</sup>

## 1)

Mahaney KB, Buddhala C, Paturu M, Morales DM, Smyser CD, Limbrick DD, Gummidipundi SE, Han SS, Strahle JM. Elevated cerebrospinal fluid iron and ferritin associated with early severe ventriculomegaly in preterm posthemorrhagic hydrocephalus. J Neurosurg Pediatr. 2022 May 27;30(2):169-176. doi: 10.3171/2022.4.PEDS21463. PMID: 35916101.

Bian C, Wan Y, Koduri S, Hua Y, Keep RF, Xi G. Iron-Induced Hydrocephalus: the Role of Choroid Plexus Stromal Macrophages. Transl Stroke Res. 2023 Apr;14(2):238-249. doi: 10.1007/s12975-022-01031-6. Epub 2022 May 11. Erratum in: Transl Stroke Res. 2024 Sep 11. doi: 10.1007/s12975-024-01294-1. PMID: 35543803; PMCID: PMC9794223.

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