Total cerebral blood volume changes drive macroscopic cerebrospinal fluid flux in humans

Juliana Zimmermann[1,2,3†], Clara Boudriot[1†], Christiane Eipert[1†], Gabriel Hoffmann[1], Viktor Neumaier[1], Moritz Bonhoeffer[1], Christine Preibisch[1,3], Christian Sorg[1,4,*‡], Benedikt Zott[1,5,6,*,‡]

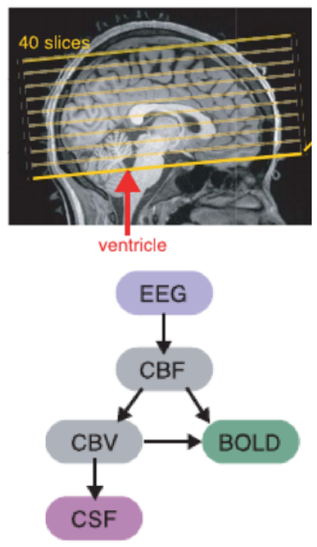
Tum School of Health and Medicine, Technical University of Munich, Germany, [1] Department of Neuroradiology, [2] Department of Anesthesiology, [3] Department of Neurology, [4] Department of Psychiatry, [5] Institute for Neuroscience, [6] Institute for Advanced Study, [+,‡] equal contribution, correspondence: benedikt.zott@tum.de, christian.sorg@tum.de

Introduction

- Directed motion, i.e. flux, of cerebrospinal fluid (CSF) is instrumental for the removal of waste products from the brain.

- Periodic processes like respiration and heartbeat have been identified as drivers of CSF flux.

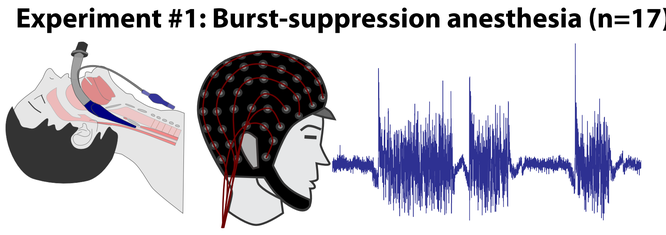
- Accumulating evidence indicates that CSF flux is associated with fluctuations in global cerebral blood volume (CBV) induced by concerted changes of neuronal activity. but direct evidence is still lacking.

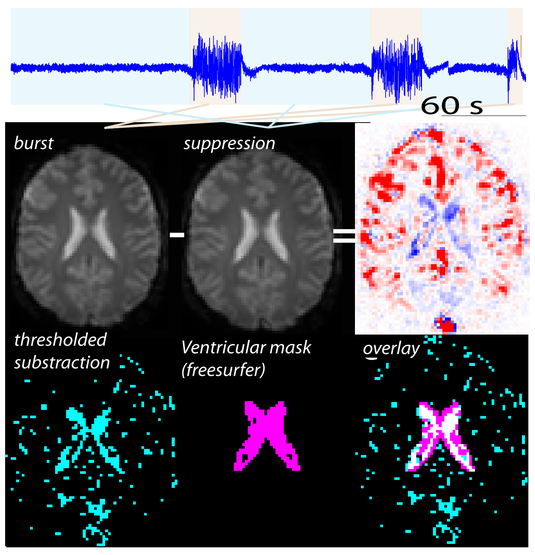


Fultz et al, Science 2019

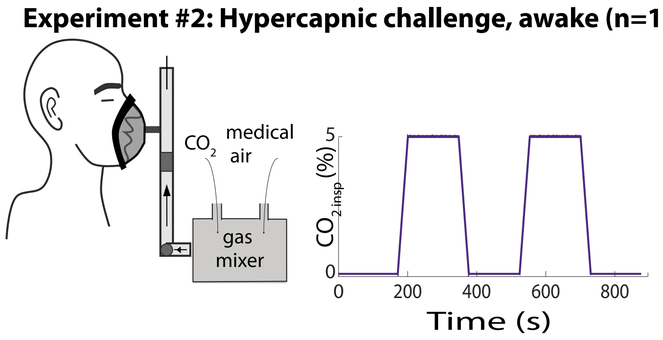
Methods

Experiment #1: Burst-suppression anesthesia (n=17)





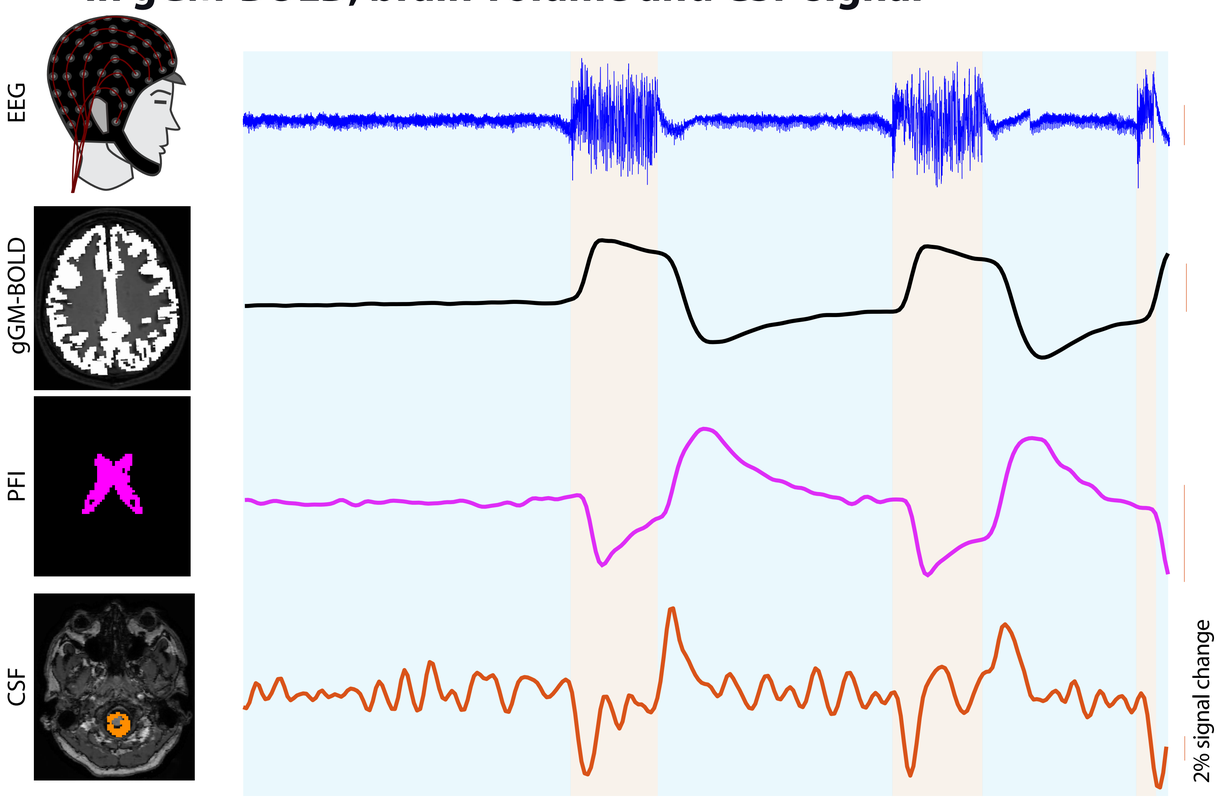
Experiment #2: Hypercapnic challenge, awake (n=17)



Design of the two experiments and generation of the masks to record the partial volume-effect-based signal at the parenchymal-fluid interface (PFI)

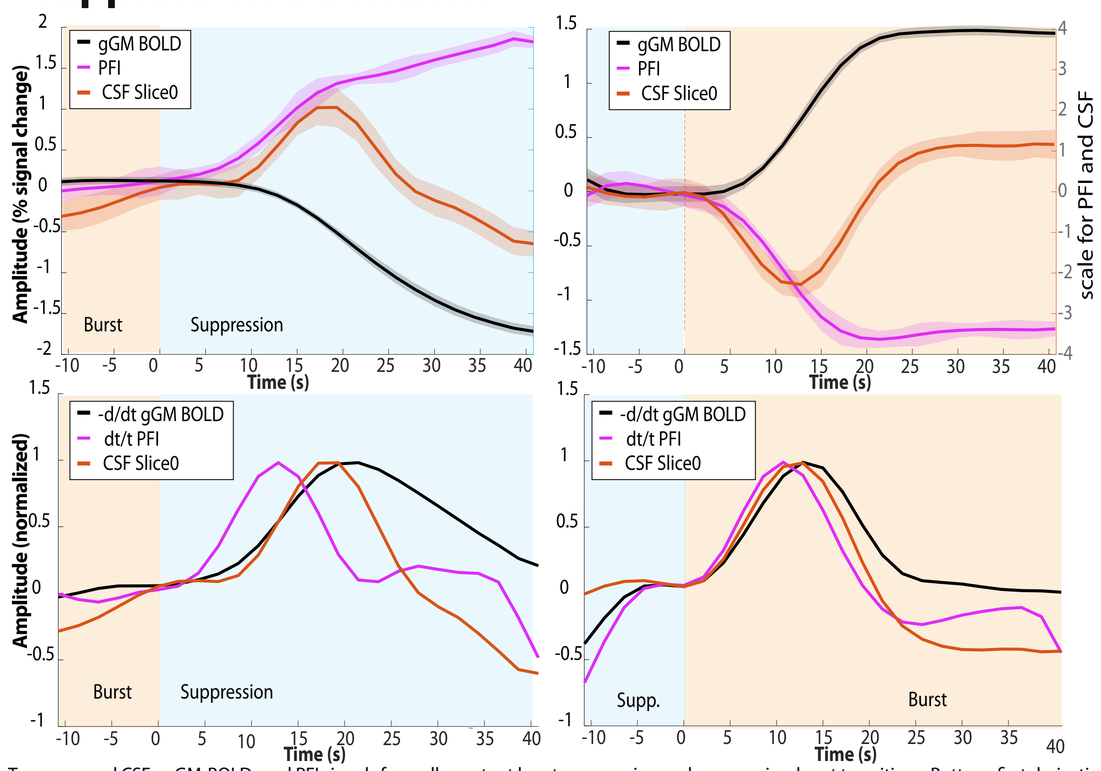
Results

1a Burst-suppression transitions are associated with changes in gGM-BOLD, brain volume and CSF signal



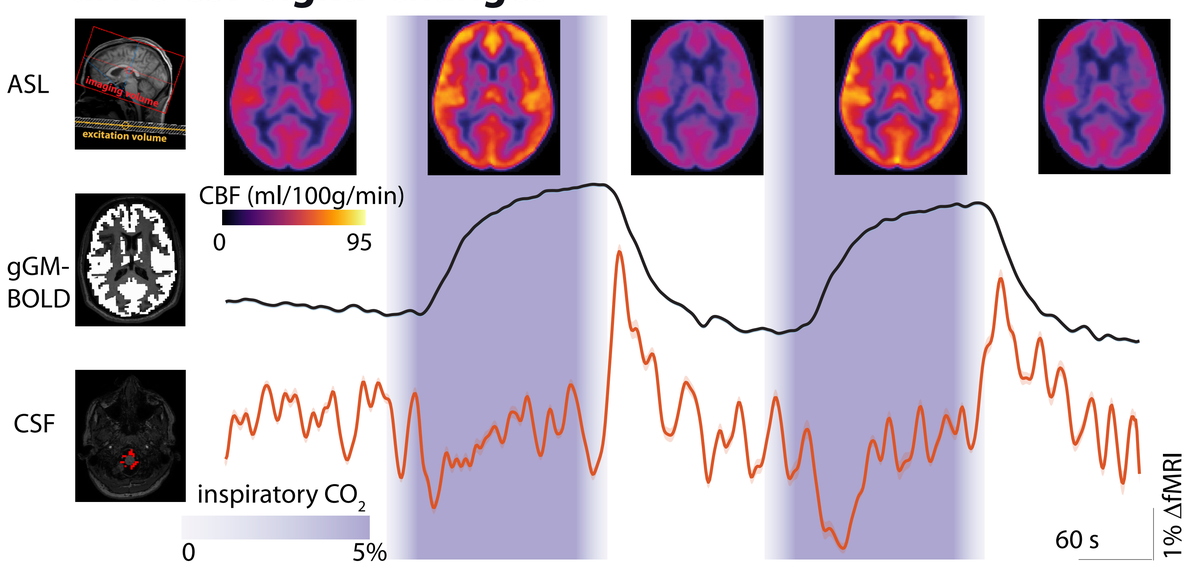
Simultaneous recordings of the electroencephalogram (EEG), the global grey matter (gGM-BOLD) signal, the PFI-signal and the CSF signal in slice 1 of the imaging volume, recorded in a healthy subject under deep sevoflurane anesthesia

1b Brain volume changes precede the CSF signal at burst-suppression transitions



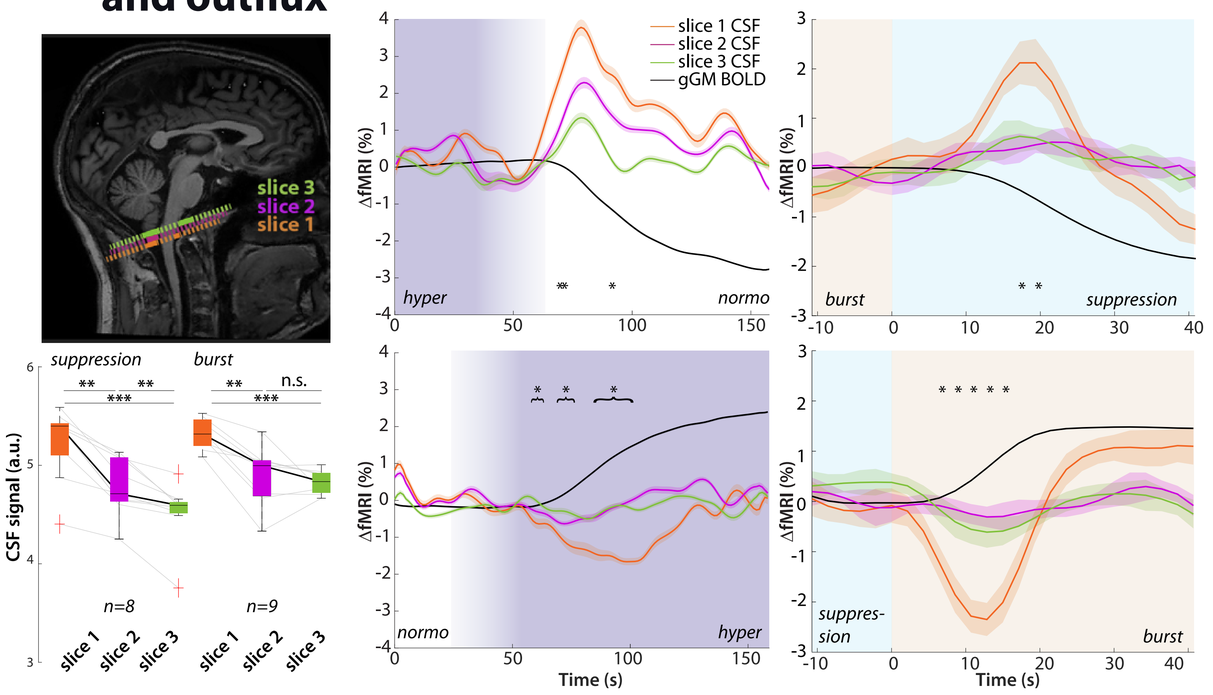
Top: averaged CSF-, gGM-BOLD- and PFI signals from all events at burst-suppression and suppression-burst transitions. Bottom: first derivative of the PFI signal, negative first derivative of the gGM-BOLD signal and CSF signal, averaged across all transitions.

2 Experimental manipulation of total brain blood volume drive CSF signal changes



Arterial spin labeling-derived CBF-maps, gGM-BOLD and slice 1 CSF signal during the hypercapnic challenge averaged across all 17 healthy subjects.

3 Changes in global brain blood volume mediate CSF in- and outflux



Analysis of the CSF signal across the lowest three slices of the imaging volume at burst-suppression or hyper-normocapnia transitions as well as during steady states. Plotted are the means from all experiments.

Conclusions and model

- **In burst-suppression anesthesia, neuronal activity-driven changes in total brain volume measured by PFI and gGM-BOLD are associated with CSF in-and outflux across the basal cisterna**
- **Experimental modulation of brain CBV by a hypercapnic challenge drives CSF in-and outflow across the basal cisterna**
- **We demonstrate tight mechanistic coupling between global neuronal activity, brain blood flow and volume, and macroscopic CSF flux**

Preprint:

Acknowledgments

DFG
Alzheimer Forschung Initiative e.V.