Cerebral open flow microperfusion (cOFM) – long-term sampling of cerebral interstitial and cerebrospinal fluid

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Background

Cerebral open flow microperfusion (cOFM) is a membrane-free sampling technique for long-term sampling of cerebral interstitial fluid (cISF) and cerebrospinal fluid (CSF).

Macroscopic openings in the cOFM probe avoid membrane-related problems such as biofouling, protein clotting, high molecular weight cut-off and the exclusion of large and lipophilic substances.

➨ **cOFM is uniquely suited for monitoring any substance in the cerebral interstitial fluid.**

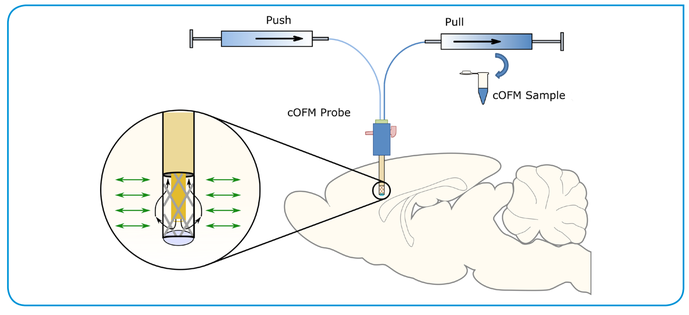

Figure 1: cOFM working principle.

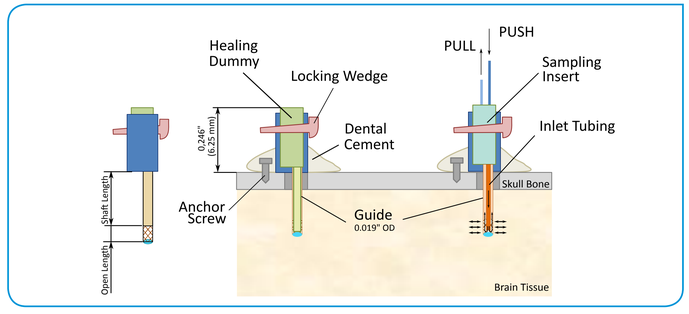

Figure 2: Schematic representation of cOFM.

Motivation

Similar to other probe-based sampling techniques in the brain, cOFM probe implantation causes tissue trauma which leads to a disruption of the blood brain barrier (BBB), but substance transport can only be reliably assessed with an intact BBB.

We thus investigated BBB permeability at different time points after implantation using **Evans Blue (EB**, $MW_{unbound}$ = 1 kDa, MW_{bound} = 66 kDa) and **sodium fluorescein** (**Naf**, 376 Da).

- **membrane-free long-term sampling of cISF**
- **monitoring transport across the intact BBB**
- **monitoring BBB permeability**

Experiment 1: When does the BBB re-establish after cOFM implantation?

EB was injected into the tail vein at different time points after cOFM probe implantation: 5, 7, 9, 11, 15 days (n = 6 each). Positive control animals were sacrificed directly after cOFM implantation (n = 6). Negative control animals did not receive an EB injection (n = 6). Animals were intravascularly perfused with PBS and whole brains were collected, fixed and fluorescence was measured.

➨ **BBB is re-established 11 days after implantation.**

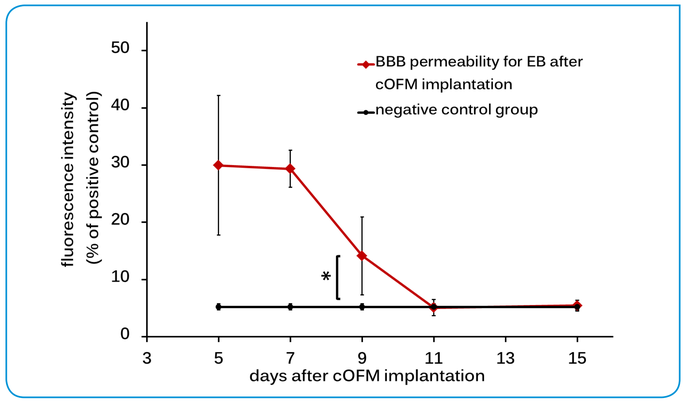

Figure 3: BBB permeability for EB [1].

Experiment 2: Can cOFM be used to monitor BBB permeability?

Fifteen days after cOFM implantation, cOFM sampling was performed in 12 rats. Naf was infused continuously into the femoral vein to maintain constant concentration in the blood. Naf concentration was measured in cOFM and plasma samples. Half of the animals (group 2) additionally received hyperosmolar mannitol in the cOFM perfusate to open the BBB.

➨ **cOFM monitors BBB permeability sensitively.**

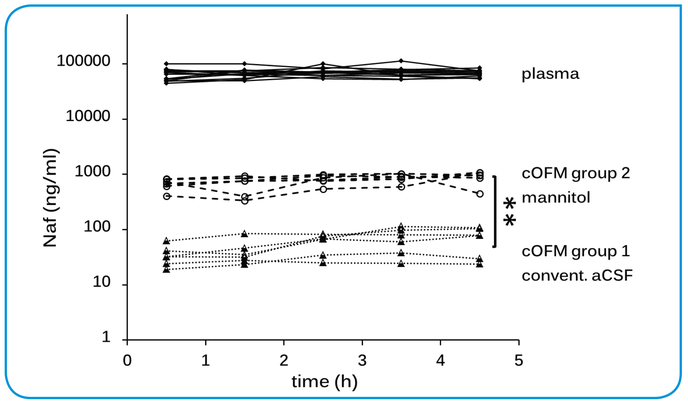

Figure 4: Naf concentration in plasma and cOFM samples [1].

References

[1] Birngruber et at. (2013)
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40, 864–871