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Monitoring leptin concentration in the hypothalamus with intact blood-brain barrier using cerebral open-flow microperfusion (cOFM)

T. Birngruber[1], T. Altendorfer-Kroath[1], P. Kotzbeck[2], F. Sinner[1]
[1] Joanneum Research Forschungsgesellschaft m.b.H, Graz, Austria
[2] Medical University of Graz, Graz, Austria

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PURPOSE

AIM

- To test the cerebral open-flow microperfusion (cOFM) sampling technology [1, 2] regarding its capability to monitor leptin concentration in the hypothalamus of mice.

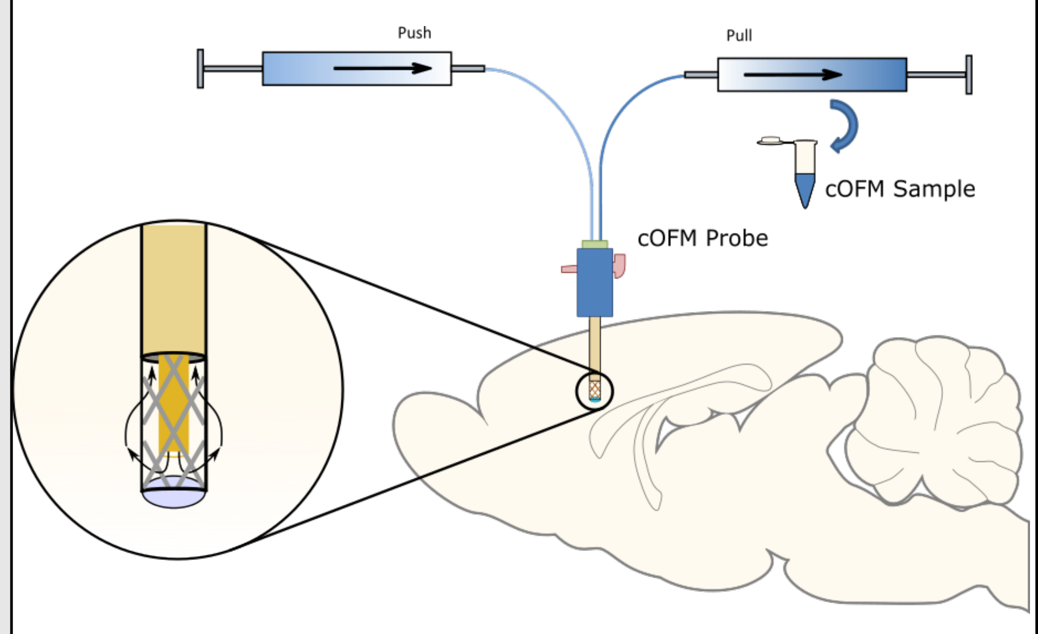
BACKGROUND

- Leptin is a hormone produced in adipocytes that regulates food uptake by inhibiting hunger.
- Leptin plays a significant role in energy homeostasis and obesity.
- Investigating and understanding the pathways of leptin signaling to the hypothalamus has been the subject of intensive research.

METHOD

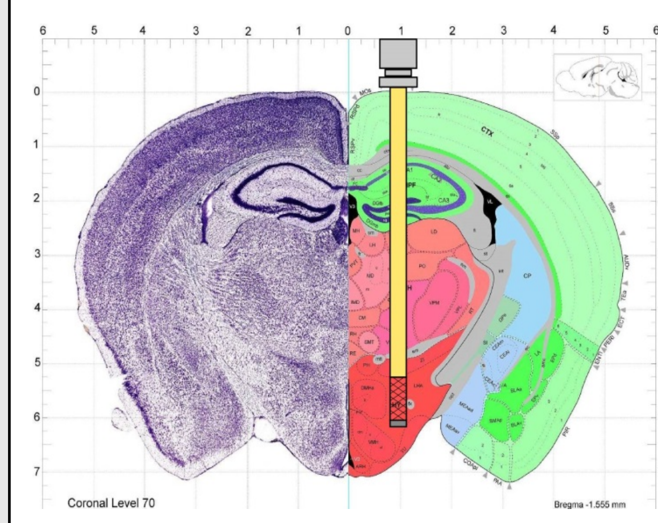
- cOFM sampling was performed in anesthetized C57BL/6 mice
- cOFM probe was implanted in the hypothalamus
- Blood-brain barrier was re-established after 14 days
- Leptin (2.5 mg/kg) was injected intraperitoneal (*i.p.*)
- cOFM and plasma were sampled at baseline
- cOFM and plasma were sampled hourly after leptin bolus
- Total sampling time was 6 hours
- Leptin was measured by using an ELISA kit

cOFM working principle



Perfusate is pumped through the cOFM probe by two syringe pumps in push/pull mode. At the tip of the probe the perfusate is mixed with hypothalamic interstitial fluid.

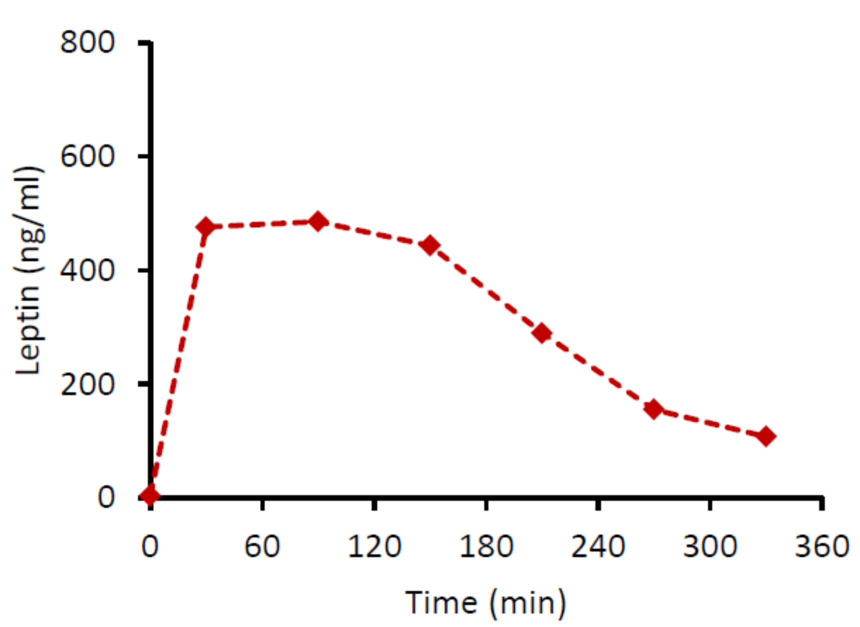
cOFM implantation plan



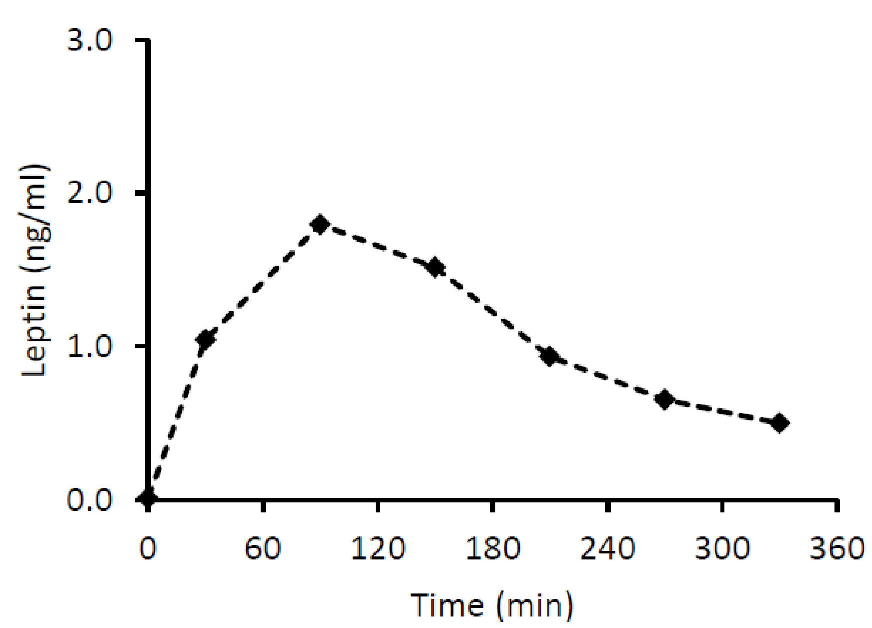
The cOFM probe is implanted with its tip placed in the hypothalamus of c57BL/6 mice.

RESULTS

Leptin level in plasma after *i.p.* bolus injection



Leptin level in cOFM samples in hypothalamus



Leptin concentration profile in the hypothalamus was similar to the blood but at a considerably lower level.

CONCLUSION

- cOFM allows monitoring of leptin concentration in the hypothalamus of mice with intact blood-brain barrier after *i.p.* injection.
- The cOFM sampling technology is a new type of experimental set-up which can be used to investigate hormones and other obesity and diabetes related substances in the brain.

REFERENCE

[1] T. Birngruber et al. "Cerebral open flow microperfusion - a new in vivo technique for continuous measurement of substance transport across the intact blood-brain barrier", *Clinical and Experimental Pharmacology & Physiology; 2013, Vol. 40*
[2] T. Birngruber et al. "Long-Term Implanted cOFM Probe Causes Minimal Tissue Reaction in the Brain", *PLoS ONE; 2014, Vol. 9*