Characterization of the **satellite glial cell (SGC)** in the extrinsic sensory innervation of the gut in rodent high-fat diet-induced obesity (DIO)

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Obesity epidemic warrants scientific attention

• In the U.S., 39.4% of adults were obese in 2011-2012 (68.6% overweight or obese)\(^1\)

• Canine obesity rates average 34-59% in developed nations \(^2\)

• Feline obesity rates average 19-52% in developed nations \(^3\)

• Obesity co-morbidities are often very detrimental to quality of life.

• Therefore, the study of **physiological regulation of food intake** is relevant for understanding obesity onset and identifying treatments.
The vagal afferent pathway communicates information about contents of the gut lumen to the hypothalamus

• Gut hormones target vagal afferent terminals, which relay sensory information to the brain.

• Anorexigenic hormones (eg leptin) signal satiety.

• However, consumption of a high-fat diet (HFD) leads to leptin resistance in vagal afferent neurons (VAN).

Anorexigenic:
- Cholecystokinin
- Glucagon-like peptide 1
- Peptide YY$_{3-36}$
- Leptin
Leptin resistance is characterized by cellular and electrophysiological changes in VAN.

- Leptin is ineffective in communicating the “fed” state of the gut to the brain.
- Changes in neuronal plasticity “lock” VAN in an orexigenic phenotype, and hyperphagia ensues.\(^{4,5}\)
Satellite glial cells (SGCs) envelop neuronal cell bodies in 3D space


NeuN Iba1 DAPI
SGCs envelop VAN in 3D space

Iba1

DAPI
SGCs have macrophagic properties

- Derived from monocytic lineage & share characteristics of microglia in CNS
- Have two distinct macrophage phenotypes:
  - M1: classically-activated, pro-inflammatory
  - M2: alternatively-activated, anti-inflammatory
- Become activated in systemic inflammation
- Respond to neuronal injury
- Respond to CCK, leptin, and ghrelin *in vitro*

Despite substantial investigation of SGC role in neuronal injury and pain, the potential role of SGCs in diet-induced obesity and associated inflammation has not been well examined.
SGCs examination is relevant to DIO studies

**Hypothesis:** SGC in the nodose ganglion mediate phenotypic changes in vagal afferent neurons (VAN) during diet-induced obesity (DIO).

**Specific Aim:** Characterize inflammatory phenotype of SGCs in response to short- and long-term HFD

*In particular,* do SGCs express the leptin receptor (LepR)?
Experiments

• Short-term HFD
  • 1-day HFD-induced inflammation in absence of obesity

• Long-term HFD
  • SGC phenotype & inflammatory response during development (4 wk) and after establishment (9wk) of DIO
Process of long-term HFD study

Start 4 wk. 9 wk.

LF x8

HF x8

x4 per group

x4 per group

Perform immunohistochemistry (IHC)

Section frozen tissue

Confocal Imaging & Quantitation of markers
Food intake and body weight of HFD-fed rats increase at ~3 wks

2-way ANOVA

- *p < 0.05
- ***p < 0.001

p-values are from Bonferroni post-tests
Markers analyzed with IHC

- **Iba1** (ionized calcium-binding adapter molecule 1)
  - SGC marker
- **Arg1** (arginase 1)
  - Alternatively-activated anti-inflammatory microglia (M2) marker
- **iNOS** (inducible nitric oxide synthase)
  - Classically-activated pro-inflammatory microglia (M1) marker
- **Leptin receptor**
  - Expressed on SGCs?
Iba1 is more highly expressed in rat NG of rats fed a HFD for 1 day. 

1 day chow

1 day HFD

p = 0.2631
n= 2
1-day HFD induces trend toward pro-inflammatory (M1) phenotype in SGCs.
Leptin Receptor (LepR) co-localizes with Iba1 on SGCs
Conclusions

• We have preliminary data demonstrating that SGCs respond to HFD-induced inflammation, highlighting a potential role of the SGCs in VAN phenotype in DIO.

• HFD induces a trend toward a pro-inflammatory (M1) phenotype in NG SGCs.

• The leptin receptor is expressed on SGCs. This is the first evidence in vivo of leptin receptor expression on SGCs in the nodose ganglion.
Future directions

• Conclude 9-wk HFD
• Continue quantititating inflammatory markers via IHC and qPCR
• Perform more extensive 3D analysis of SGC morphology
• Characterize leptin receptor expression on SGCs
• Repeat study to increase $n$
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Questions?
References


