Sweeter than surgery: characterizing the effects of anesthetics on perioperative glycemic control

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Perioperative Hyperglycemia defined often as >11.1 mmol/L

Very common with incidence 17-66%

Perioperative Hyperglycemia is associated with:
* Surgical site infections
* Prolonged length of stay
* Thrombus formation
* Myocardial ischemia
* Stroke
* Death
* Etiology appears multifactorial:

* Risk factors include advanced age and obesity
* Type and extent of surgery
* Type of anesthesia

- Characterized by a period of acute insulin resistance
Glucose → Pancreas → Insulin

"Normal" Glycemic Control

- Enzymatic activation
- Protein Translocation
- Gene transcription

Insulin Receptor → Target Cell

*Background*
Glucose

Pancreas

Insulin

Insulin Receptor

Target Cell

- Enzymatic activation
- Protein Translocation
- Gene transcription

Surgical Glycemic Control

Background
Christian Rask-Madsen, and C. Ronald Kahn
Arterioscler Thromb Vasc Biol. 2012;32:2052-2059

*Targets*
Christian Rask-Madsen, and C. Ronald Kahn
Arterioscler Thromb Vasc Biol. 2012;32:2052-2059
The overriding hypothesis of these preliminary investigations is that anesthetic drugs will disrupt normal hepatic glycemic control.
*Mouse Primary Hepatocytes* will be treated for 2h with a range of clinically relevant doses of anesthetics:

- Isoflurane 0.26mM (=1MAC)
- Sevoflurane 0.26mM (=1MAC)
- Ketamine 10-50μM
- Propofol 10-50μM
- Intralipid 25μM

- Cell culture medium, and hepatocyte RNA and proteins will be isolated for subsequent analysis
Drug Treatment

Gene Expression
- SOCS-3
- G6PASE
- PEPCK
- IL-6
- TNFα

Protein Secretion
- IL-6
- TNFα

Enzymatic Activity
- Akt
- AMPK
- ACC

+ METFORMIN 0.1mM or SALSALATE 1-3mM

*Anticipated Responses*
* By characterizing the influence of anesthetics on hepatic metabolism it may allow for the identification of potentially therapeutic strategies

- Next steps will be to test the effects of anesthetics in vivo using both healthy and diet-induce models

- Eventual goal would be to test whether insulin sensitizers could feasibly be used perioperatively

**Summary**
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