Ask Weber

Topic 18/19

Energy and metabolic pathways

Topic 18

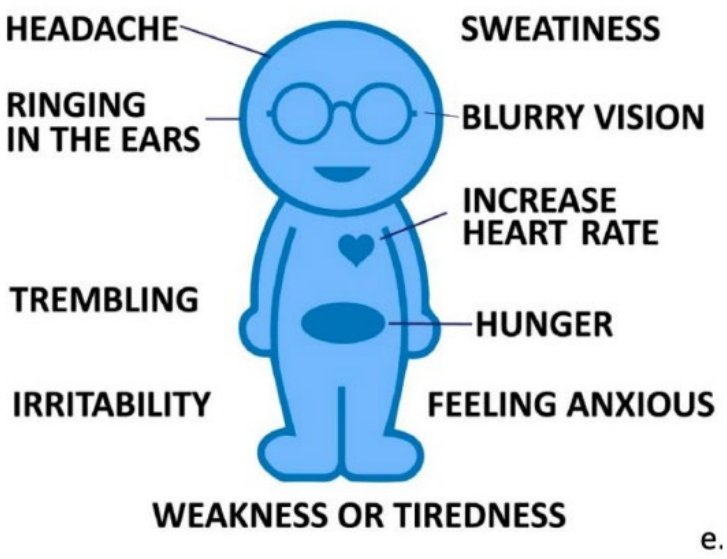
Fuels

THE UNIVERSITY OF
SYDNEY

Energy utilisation and sources

1. **What energy source does the brain, heart muscle and skeletal muscle use?**
   1. The brain uses glucose primarily (not in lecture, but brain can also function off ketone bodies when in starvation)
   2. cardiac muscle uses fatty acids, lactate, ketone bodies
   3. Skeletal muscle can use both glucose and fatty acids as well as ketone bodies

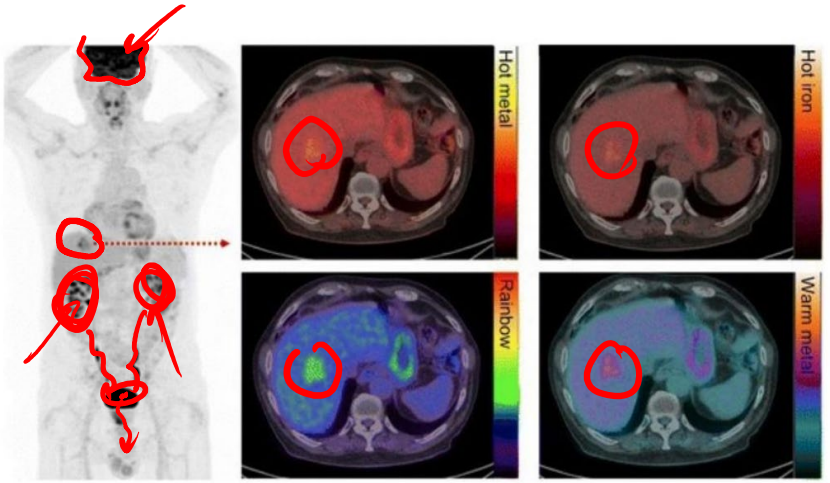
1. **What are the signs of hypoglycaemia?**
   - Headache, hunger
   - Sweatiness, blurry vision, anxiety, trembling, increased HR, irritability
   - Weakness/fatigue



Radiolabelling

How does the Warburg effect relate to radiolabelled imaging for cancers and metastases?

- Cancers primarily metabolise glucose (Warburg effect). By radiolabelling glucose (e.g. FDG) and injecting it into the patient, we can see regions of high glucose utilization. These areas will light up in the body scan. The scan itself is called a PET scan.



Energy generation from alternative sources

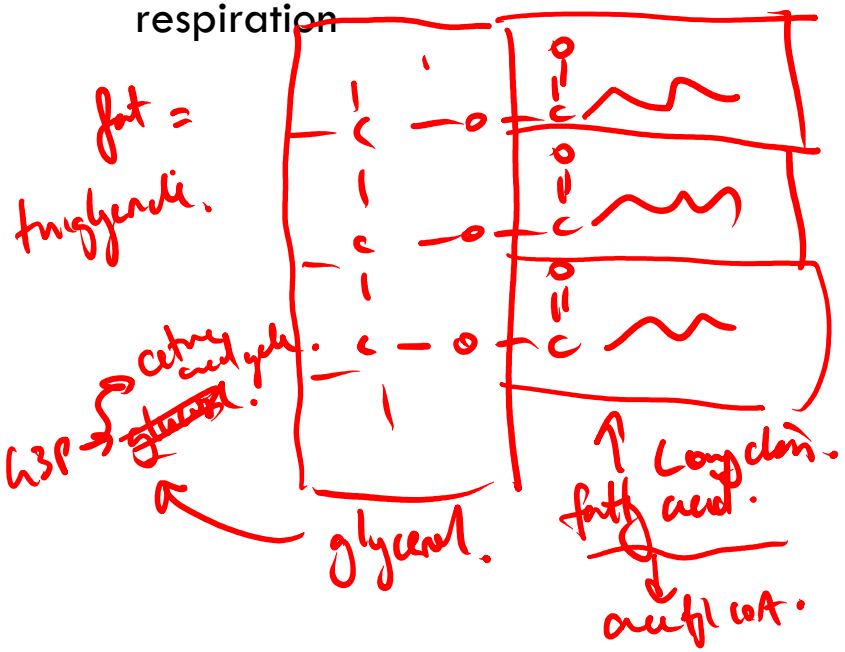
adipose tissue

How is energy generated cellularly (i.e. respiration) from glucose?

- Aerobic respiration: Glucose undergoes glycolysis to form pyruvate
  - Pyruvate can be converted to acetyl CoA, and enter the citric acid cycle
- Anaerobic respiration: Glucose undergoes glycolysis to form pyruvate (which then forms lactate) – doesn't enter citric acid cycle, but generates 4 ATP (uses 2 in process – i.e. net 2 ATP production)

How is energy generated from fatty acids?

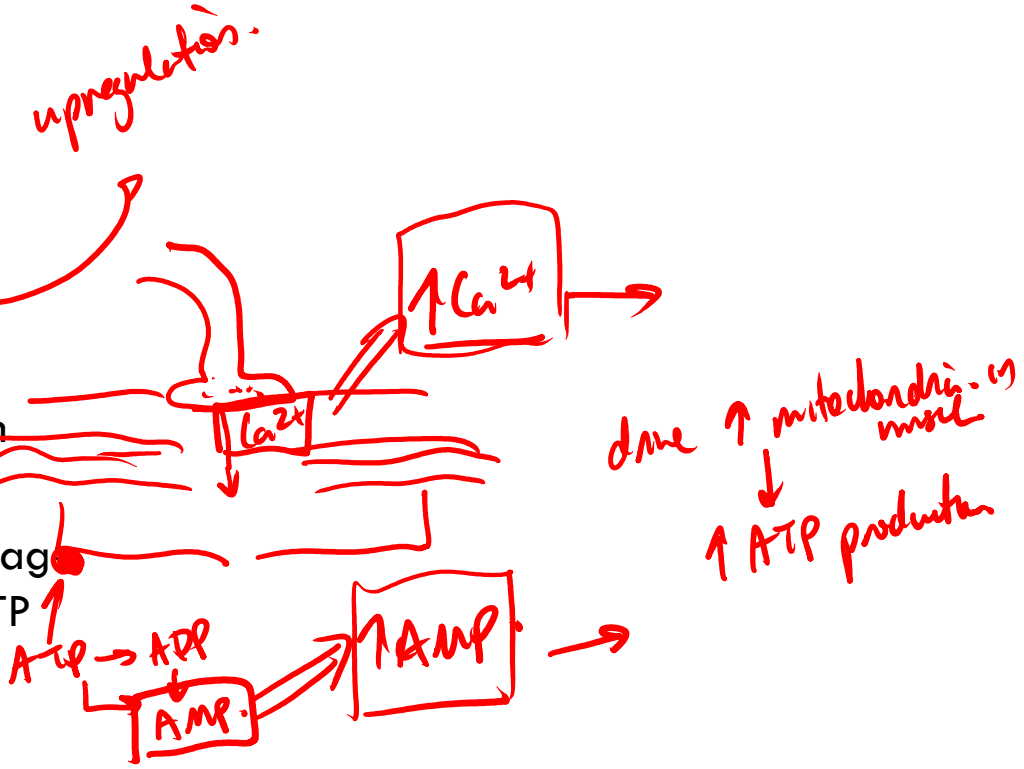
- Fatty acids can be broken down into Acetyl-CoA
- Acetyl CoA can enter the citric acid cycle to form ATP in aerobic respiration



ATP production rates

How is exercise proposed to increase ATP production in the long run?

- More exercise = more calcium in muscle (for contractions)
- More contraction = more ATP usage = more AMP in muscle (recall ATP can break down into AMP)
- More calcium AND more AMP = more mitochondrial production (via some upregulation mechanism?)



Feeding, fasting, starving

Describe the absorptive state in feeding

- Occurs 4h after a meal
- The meals TYPICALLY contain glucose (either directly or via carbohydrates)
- All tissues will utilize glucose in this state

Describe the post-absorptive state (fasting)

- Occurs 4-30h after a meal
- Glucose has either been initially utilized or is currently being stored (as glycogen)
- Tissues will reduce glucose utilization (except brain – brain always wants glucose when available)
- Glucose can be additionally re-utilized through breakdown of glycogen (glycogenolysis) and amino acids

Describe what happens to the body after 30 hours of no feeding (starving)

- Non-brain tissues stop using glucose (recall – brain ALWAYS wants sugar)
- Liver and kidney needs to remobilise glucose (from stored glucose – glycogenolysis and amino acids)
- If glucose runs too low, brain can start using ketone bodies (via ketogenesis – fatty acid breakdown)

Starvation

What is the order of biomolecular utilization in starvation?

- Fats are used first – fatty acids can be converted into Acetyl CoA, which can then be used in the citric acid cycle to produce ATP, as well as be used in the production of ketone bodies (ketogenesis). Ketone bodies can be used by the brain
- Amino acids (i.e. protein, muscle breakdown) can then be used – at this point, you will start looking cachexic. These amino acids get turned into pyruvic acid or acetyl - CoA, which can enter the citric acid cycle as well

What is ketogenesis?

In type 1 diabetics, patients are unable to produce insulin. If they don't take their insulin medication, a few things happen

- Glucagon levels increase – liver undergoes gluconeogenesis and glycogenolysis – this can form ketone bodies
- Adipose tissue will undergo lipolysis – this can form ketone bodies

The result of this is called diabetic ketoacidosis, as the ketone bodies and the process of production will acidify the blood. What clinical signs/symptoms do you expect to see in someone with DKA, and why?

1. Hyperglycaemia
2. Tachycardia
3. Fruity breath
4. Kussmaul breathing
5. Polyuria
6. Altered mental status