Lecture 9: Other Factors Affecting AR

I. Gonadal
   A) Modulate AR response to catecholamines
      1) estrogen & progesterone → catecholamine metabolism
      2) oviduct & uterine smooth muscles response:
         a) α-AR → contraction: ↑estrogen → uterus
         b) β-AR → relaxation: pregnancy/↑progesterone → uterus

II. Adrenal Steroid Hormones
   A) glucocorticoid
      permissive role → cAMP mediated effects on liver/other organs
      catecholamines in adrenalectomized rats?
         ↓ gluconeogenesis/glycogenesis & lipolytic response of adipose
         ~cardiovascular response

III. Thyroid Hormones (TH)
   \[ \uparrow \text{TH} \rightarrow \text{catecholamine effect enhanced} \]
   \[ \downarrow \text{TH} \rightarrow \text{catecholamine effect depressed} \]
   sympathetic neurons

**Sympathoadrenal Functions**

I. Constancy of homeostasis
   A) ↓blood pressure, glucose, O₂ availability → ↑catecholamines
   B) stress any condition → elevated plasma catecholamines
      ↑E: dogs: barking
      ↑E & NE: humans → exercise, standing, post surgery, low glucose
   C) E
      adrenal: humoral messenger → stimulus to autonomic effectors
   D) NE
      sympathetic neurons → local control autonomic effectors
II. Dependent on the AR types at the effectors

A) Receptors of autonomic effector cells
   1) α-AR & β-AR
   2) only β-AR with cholinergic receptors

B) Smooth muscle
   1) α-AR contraction (except intestines): Ach → relaxation
   2) β-AR relaxation (except cardiac): cholinergic receptors contraction

C) Domination: α-AR > β-AR

D) Cellular secretion
   1) α-AR inhibitory
   2) β-AR stimulatory
Carbohydrate Metabolism

E → 1) β-AR: hepatic glycogenolysis & glucose release
   a) skeletal glycogen
   b) β-AR: glycogen → lactic acid
   c) lactic acid → liver → glucogenesis → glucose

Cat → 2) α-AR
   a) inhibitory pancreatic B cell insulin secretion

Cat → 3) β-AR: stimulatory pancreatic A cell glucagon secretion

denervation → anesthesia → 4) adrenal gland: blocked Cat response to hypoglycemia?
   suggest brain glucoreceptors regulating sympathoadrenal response
   research → caudal forebrain

Fat Metabolism

Adipose tissue
Cat adrenal/sympathetic β-AR →↑lipolysis FFA & glycerol

FFA →
1) brain/cardiac: energy source (glucose-sparing)
2) liver: conversion to glucose

Paradox: lean individuals do not gain weight when overfed

1) metabolic defect → obesity
2) genetic: conversion of food → body fat

   stimulants for sympathetic nervous system (SNS)
   diet-induced thermogenesis ↓ NE
**Protein Metabolism**

- E → β-AR & cAMP
- ↓ skeletal muscle release of AAs
- ↓ skeletal muscle proteolysis

**E** important short-term response in fight/flight response

- ↑ lactate/glycerol/glucose
- AA substrate not needed

---

**Thermogenesis**

Mammals (rats)

1) fasting:
   - sympathetic activity conserve calories
     - metabolic activity/heat production

2) feeding:
   - ↑ sympathetic activity expend calories
     - metabolic activity/heat production

3) shivering:
   - a) shivering thermogenesis → piloerection (goose bumps)
     - 1) SNS → primary effects: heat production
     - 2) muscular activity → secondary effects: heat production
   - b) nonshivering thermogenesis →
     - 1) NE → β-AR: brown adipose tissue (BAT)
       - a) metabolic heat production
       - b) dietary-induced
       - c) mitotic division of BAT humans??
Nonshivering Thermogenesis

exposure to cold $\rightarrow$ NE $\rightarrow$ β-AR: BAT $\rightarrow$ **mitochondrial uncoupling protein (MUP)**

a) uncouple oxidative phosphorylation
b) utilize substrates to quickly generate heat rather than ATP
   1) WAT: hydrolysis of triglyceride $\rightarrow$ fatty acid + glycerol
   2) BAT: fatty acid + MUP $\rightarrow$ oxidation of fatty acid $\rightarrow$ heat production
c) neonates (unswaddled newborns) infrared detection heat
   fat deposits neck & interscapular regions
d) premies leading cause of deaths
   $\uparrow$ S/V $\rightarrow$ heat loss
   $\downarrow$ S of head (which is seldom cloth-covered)
   $\downarrow$ musculature & inability or reluctance to shiver
   $\downarrow$ thermal insulation, e.g. subcutaneous fat & fine body hair
   $\downarrow$ nervous system development $\rightarrow$ respond slower to cold
   (e.g. contracting skin blood vessels
e) animals coming out of hibernation
### Adipose Tissue Hormones & Enzyme

1. **Adiponectin**
   - Modulates metabolism: glucose regulation & fatty acid catabolism
   - Type 2 diabetes
   - Atherosclerosis
   - Obesity
   - Non-alcoholic fatty liver disease

2. **Resistin**
   - **??** link between obesity & diabetes mellitus type 2
   - **a) mice:**
     - Correlation between resistin titers & blood glucose levels
   - **b) humans:**
     - No link: resistin & obese humans with diabetes mellitus type 2

3. **Angiotsensin**

4. **Plasminogen activator inhibitor-1 (PAI-1):**
   - Breakdown clots

5. **TNFα (tumor necrosis factor):**
   - Systemic inflammation

6. **IL-6 (interleukin):**
   - Acute inflammation reaction

7. **Leptin**
   - Regulation of appetite & metabolism
   - Modulates metabolism: glucose regulation & fatty acid catabolism
   - Obesity
   - Atherosclerosis
   - Non-alcoholic fatty liver disease
   - Type 2 diabetes

### Cardiovascular Response to Stress

| E → β-AR | 1) Force of heartbeat |
|          | 2) Rate of heartbeat |
|          | 3) β-AR: vascular smooth muscular of coronary arteries |
|          | Selective shunting of blood from |
|          | Skin/ mucosa/ connective/ kidneys |
|          | Kidneys?? |
|          | Glucose via urine |
|          | 4) Spleen α-AR |
|          | ↑erythrocyte plasma conc |
|          | ↑oxygen capacity |
|          | 5) β-AR bronchial smooth muscles → relaxation: dialation |
|          | 6) Clotting ← E |
|          | ↑adhesiveness |
|          | ↓clotting time |
### Sympathoadrenal Pathophysiology

1) adrenal chromaffin tumors  
   early life
   
   CAT hypersecretion →
   
   a) hypertension  
   b) hyper basal metabolism/ oxygen consumption  
   c) weight loss  
   d) psychosis  
   e) tremulousness

2) asthma
   
   ↓ pulmonary function  
   ?? β-AR bronchial smooth muscles receptor uncoupling & numbers

3) heart disease  
   fat cell metabolism → lipogenesis / lipolysis
   
   a) α-AR → fat storage  
   b) β-AR → catabolism
   c) sexual difference  
      females: #s & size of fat cells in buttocks/ hips/ thighs
      males: "couch potatoes"
   d) anatomical: upper body adipose  
      ↑ hypertension/diabetes /stroke?