Lecture 10: Other Factors Affecting AR

I. Gonadal

Modulate AR response to catecholamines

1) ***estrogen & progesterone → catecholamine metabolism***

2) oviduct & uterine smooth muscles response:

a) a-AR → contraction: ↑ estrogen → uterus

b) ß-AR → relaxation: pregnancy/↑ progesterone → uterus

II. Adrenal Steroid Hormones

glucocorticoid

permissive role → cAMP mediated effects on liver/other organs

e.g. catecholamines in adrenalectomized rats?

↓ gluconeogenesis/glycogenesis & lipolytic response of adipose

~cardiovascular response

III. Thyroid Hormones (TH)

↑TH → catecholamine effect enhanced

↓TH → catecholamine effect depressed

} → sympathetic neurons

Sympathoadrenal Functions

I. Constancy of homeostasis

A) ↓ blood pressure, glucose, O_2 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

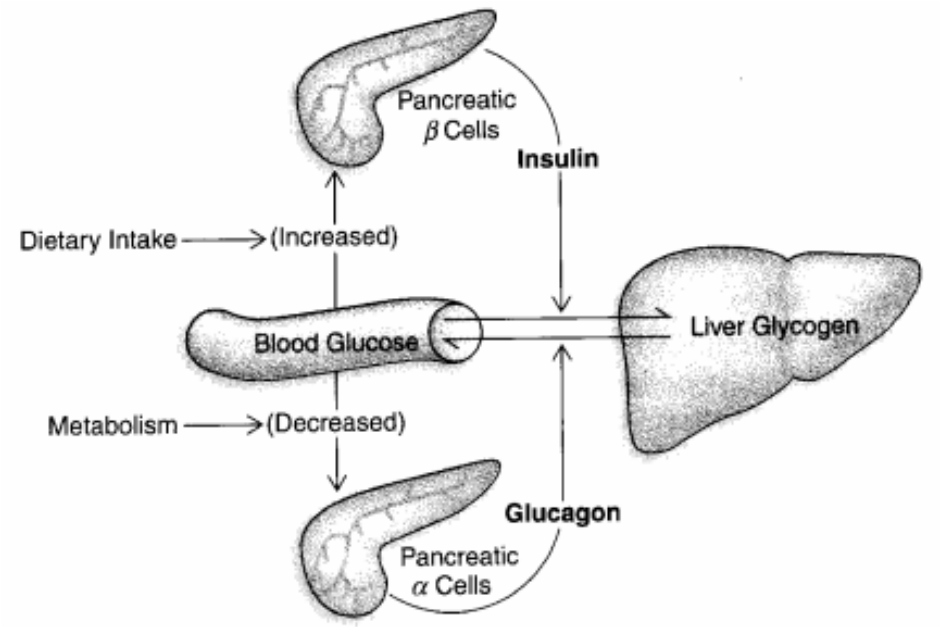
II. Dependent on the AR types at effectors

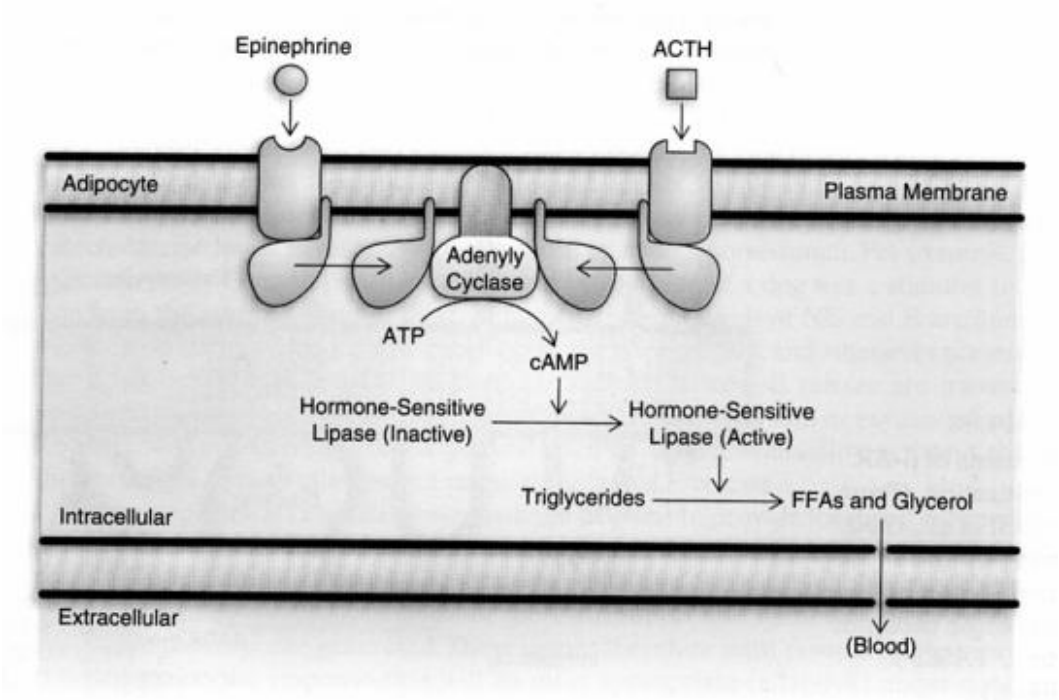
A) Receptors of autonomic effector cells
   1) α-AR & ß-AR
   2) only ß-AR with cholinergic receptors

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

C) Domination α-AR > ß-AR

D) Cellular secretion
   1) α-AR inhibitory
   2) ß-AR stimulatory


Pancreatic
β Cells
Insulin
Dietary Intake
(Increased)
Blood Glucose
Liver Glycogen
Metabolism
(Decreased)
Glucagon
Pancreatic
α Cells


Epinephrine
ACTH
Adipocyte
Plasma Membrane
Adenyly
Cyclase
ATP
cAMP
Hormone-Sensitive
Lipase (Inactive)
Hormone-Sensitive
Lipase (Active)
Triglycerides
FFAs and Glycerol
Intracellular
Extracellular
(Blood)

Carbohydrate Metabolism

E → 1) ß-AR: hepatic glycogenolysis & glucose release

a) skeletal glycogen

b) ß-AR: glycogen → lactic acid

c) lactic acid liver → glucogenesis → glucose

Cat → 2) α-AR

inhibitory pancreatic B cell insulin secretion

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

denervation → 4) adrenal gland: blocked Cat response to hypoglycemia?

anesthesia ↗

→brain glucoreceptors regulating sympathoadrenal response

research → caudal forebrain

Fat Metabolism

Adipose tissue

Cat adrenal/sympathetic ß-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

***FFA = Free Fatty Acids**

Protein Metabolism

E → ß-AR & cAMP

↓ skeletal muscle release of FAAs

↓skeletal muscle proteolysis

E important short-term response in fight/flight response

↑ lactate/glycerol/glucose

FAA substrate not needed

***FAA = Free Amino Acid**

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

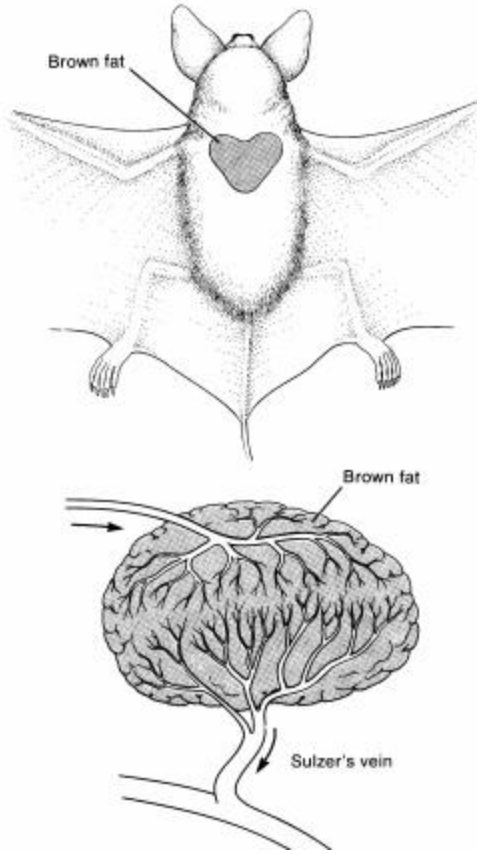
b) nonshivering thermogenesis →

1) NE → ß-AR: brown adipose tissue (BAT)

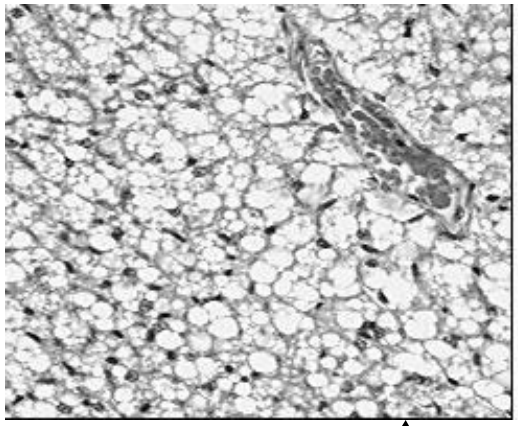
a) metabolic heat production

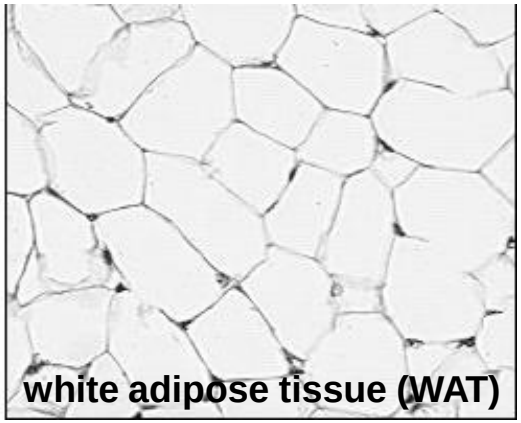
b) dietary-induced

c) mitotic division of BAT humans??

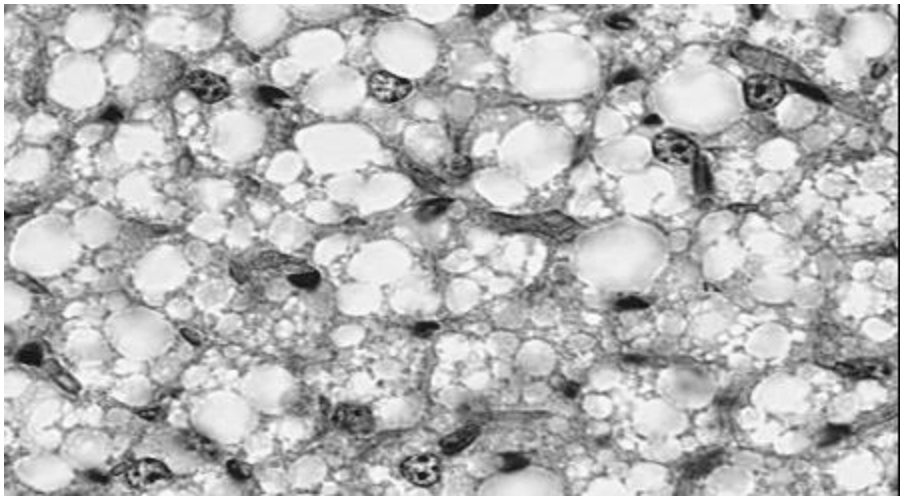


adipose tissue
- little cytoplasm
- lipid droplets





brown adipose tissue (BAT)



- ↑ variable sized lipid droplets
- ↑ capillaries
- ↑ mitochondria

Nonshivering Thermogenesis

exposure to cold → NE → ß-AR: BAT → **mitochondrial uncoupling protein (MUP)**

a) uncouple oxidative phosphorylation

b) utilize substrates to quickly generate heat rather than ATP

1) WAT: hydrolysis of triglyceride → fatty acid + glycerol

2) BAT: fatty acid + MUP → fatty acid oxidation → heat production

c) neonates (unswaddled newborns) infrared detection heat
fat deposits neck & interscapular regions

d) premies

↑ S/V ? heat loss

↑ S of head (which is seldom cloth-covered)

↓ musculature & inability or reluctance to shiver

↓ thermal insulation , e.g. subcutaneous fat & fine body hair

↓ nervous system development → 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) angiotensin

4) plasminogen activator inhibitor-1 (PAI-1): ↓ breakdown clots

5) TNFa (tumor necrosis factor) → systemic inflammation

6) IL-6 (interleukin) → acute inflammation reaction

7) leptin → regulation of appetite & metabolism

8) aromatase → estradiol

Cardiovascular Response to Stress

E → ß-AR 1) force of heartbeat

2) rate of heartbeat

3) ß-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
↑ oxygen capacity

5) ß-AR bronchial smooth muscles → relaxation: dilation

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 ?? ß-AR bronchial smooth muscles

receptor uncoupling & numbers

3) heart disease fat cell metabolismà lipogenesis/lipolysis

a) α-AR → fat storage

b) ß-AR → catabolism

c) sexual difference ↑ α-AR male couch potatoes

females: #s & size of fat cells in buttocks/ hips /thighs

d) anatomical: upper body adipose↑ hypertension/diabetes /stroke?