



**PITTSBURGH  
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# **Malignant Hypothermia**

**PWSA.USA Scientific**

**Orlando, Florida**

**November 11, 2011**

# Hypothermia in PWS

- Several case reports in middle-aged PWS
  - Recurrence risk
  - No gender bias
  - Hypothermic response to ambient cold temperature challenge
- Faulty homeostatic mechanisms
  - Abnormal pain/temperature perception (known)
  - Abnormal central sensor threshold (suspected)
  - Impaired insight and judgment
  - Cognitive inflexibility limits capacity for change

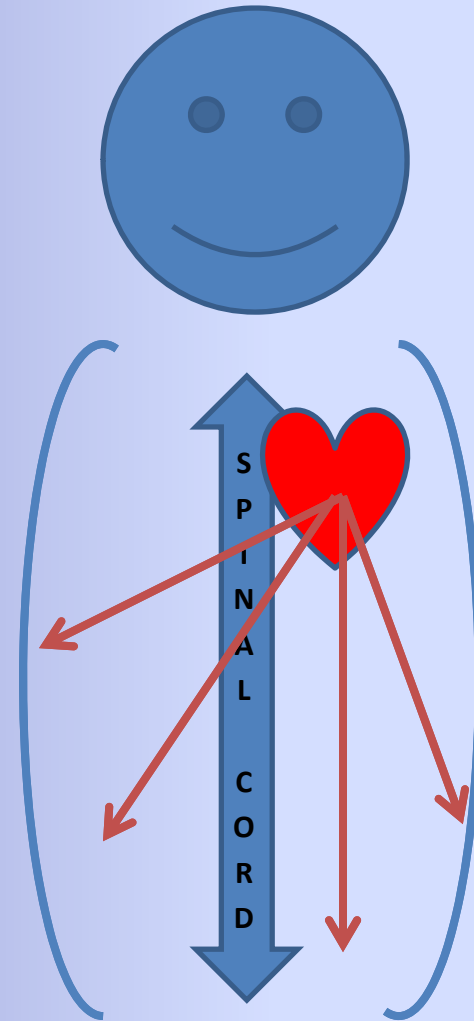
# Hypothermia in PWS

- Neurobiology of thermoregulation
- Causes of hypothermia
- Somatic findings secondary to hypothermia
- Morbidity associated with hypothermia
- Case presentations
- Treatment
- Prevention

# Mechanisms of Heat Loss

## Radiation

- 60% total heat loss
- core to surface via circulatory system



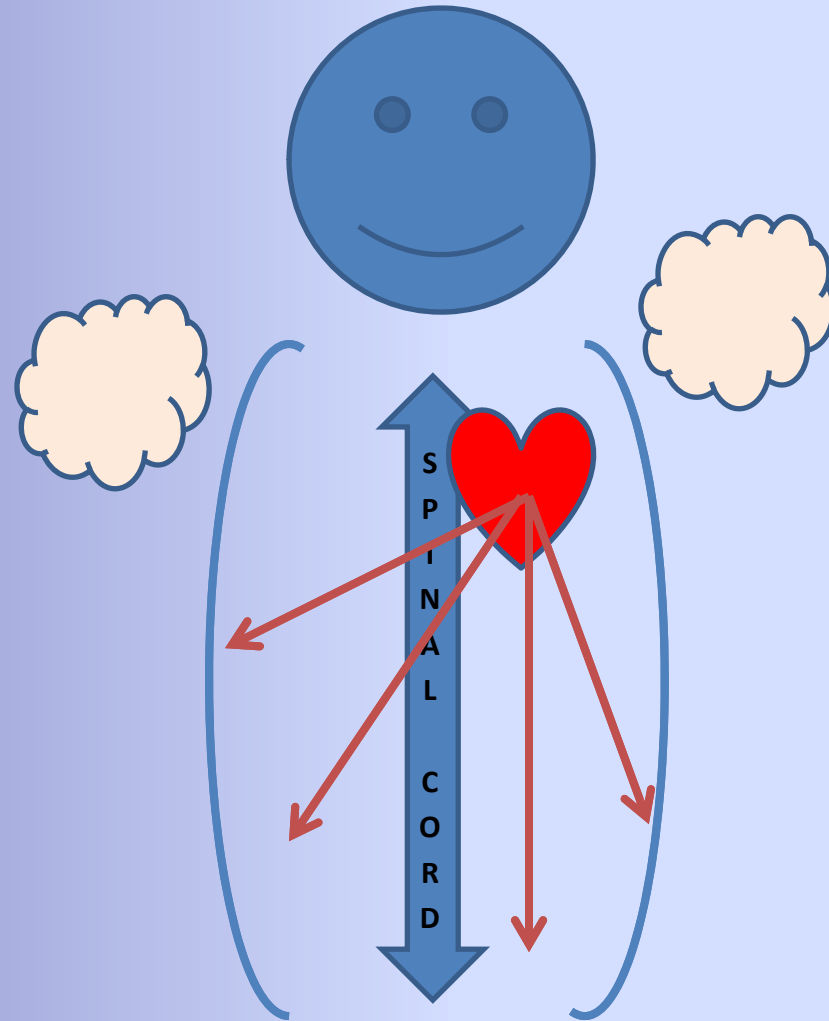
# Mechanisms of Heat Loss

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- core to surface via
- circulatory system

## Evaporation

- 22% total heat loss



# Mechanisms of Heat Loss

## Radiation

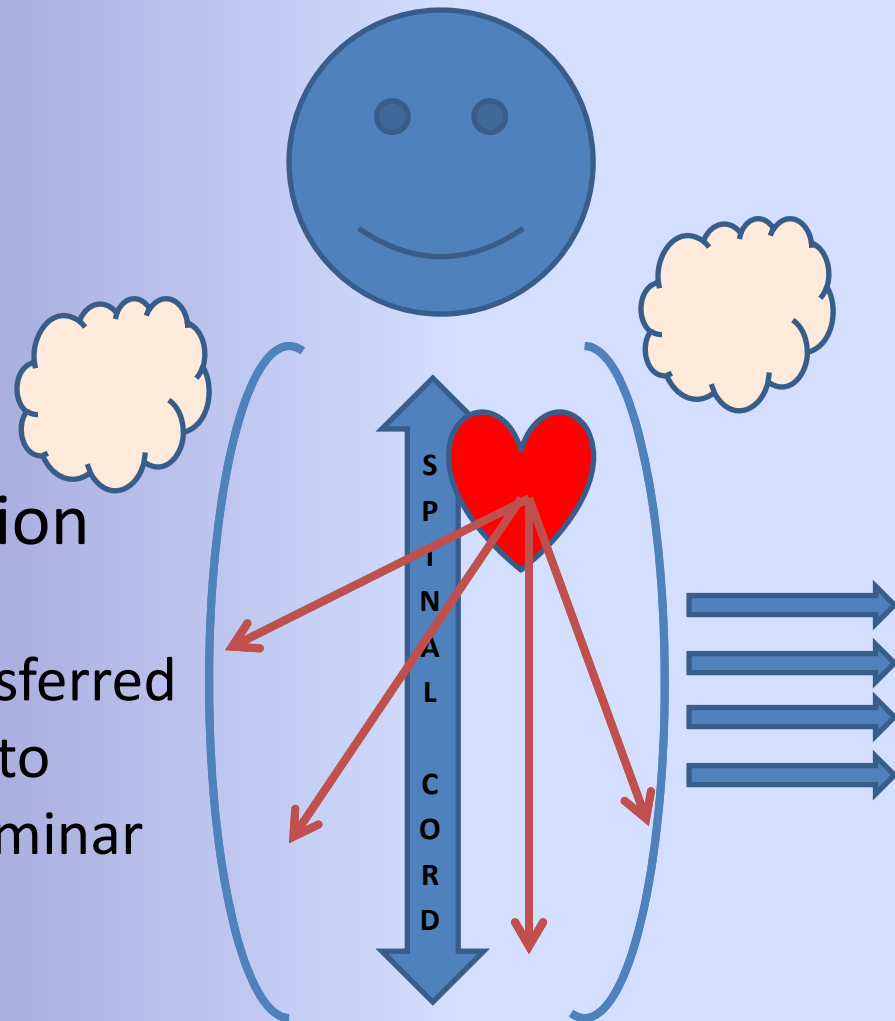
- 60% total heat loss
- core to surface via circulatory system

## Evaporation

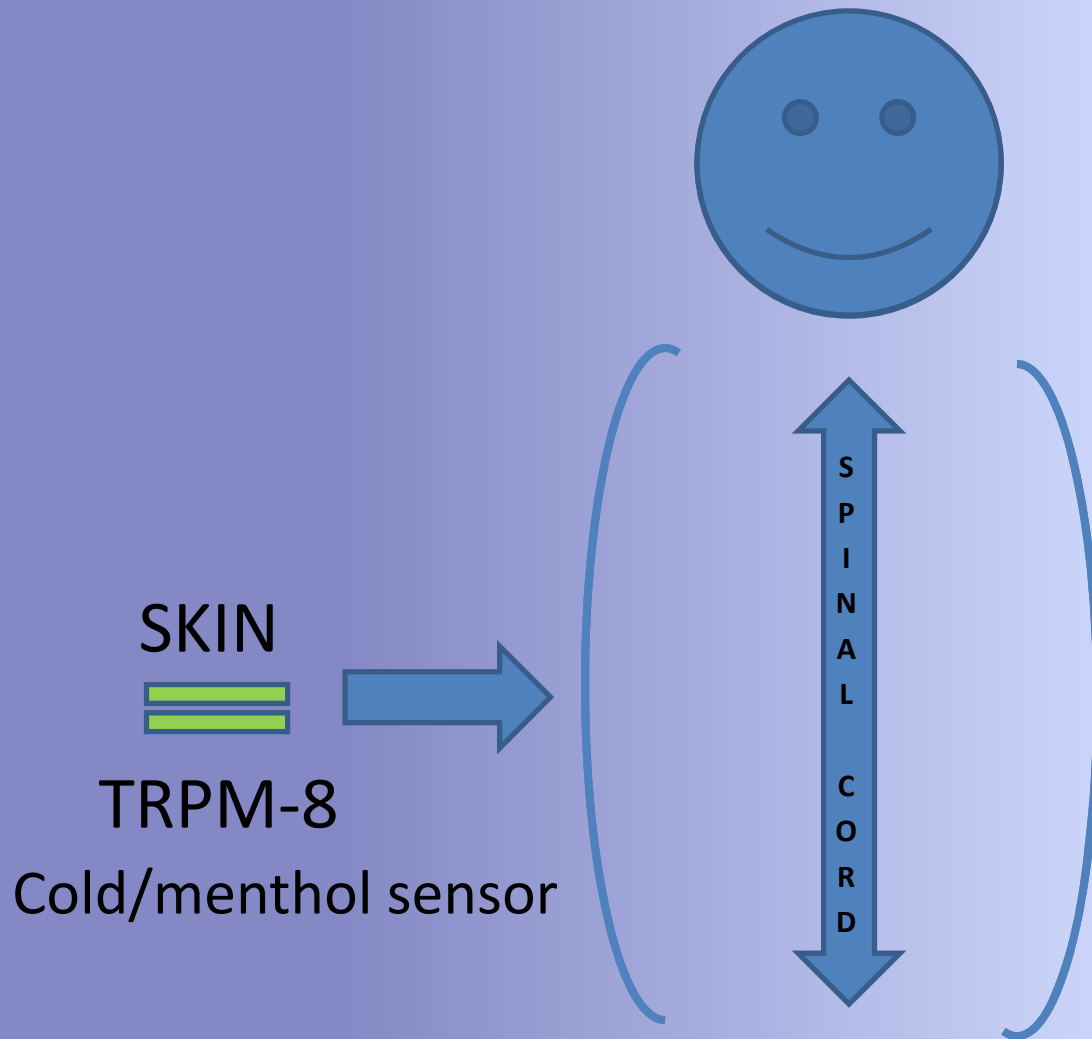
- 22% total heat loss

## Conduction & Convection

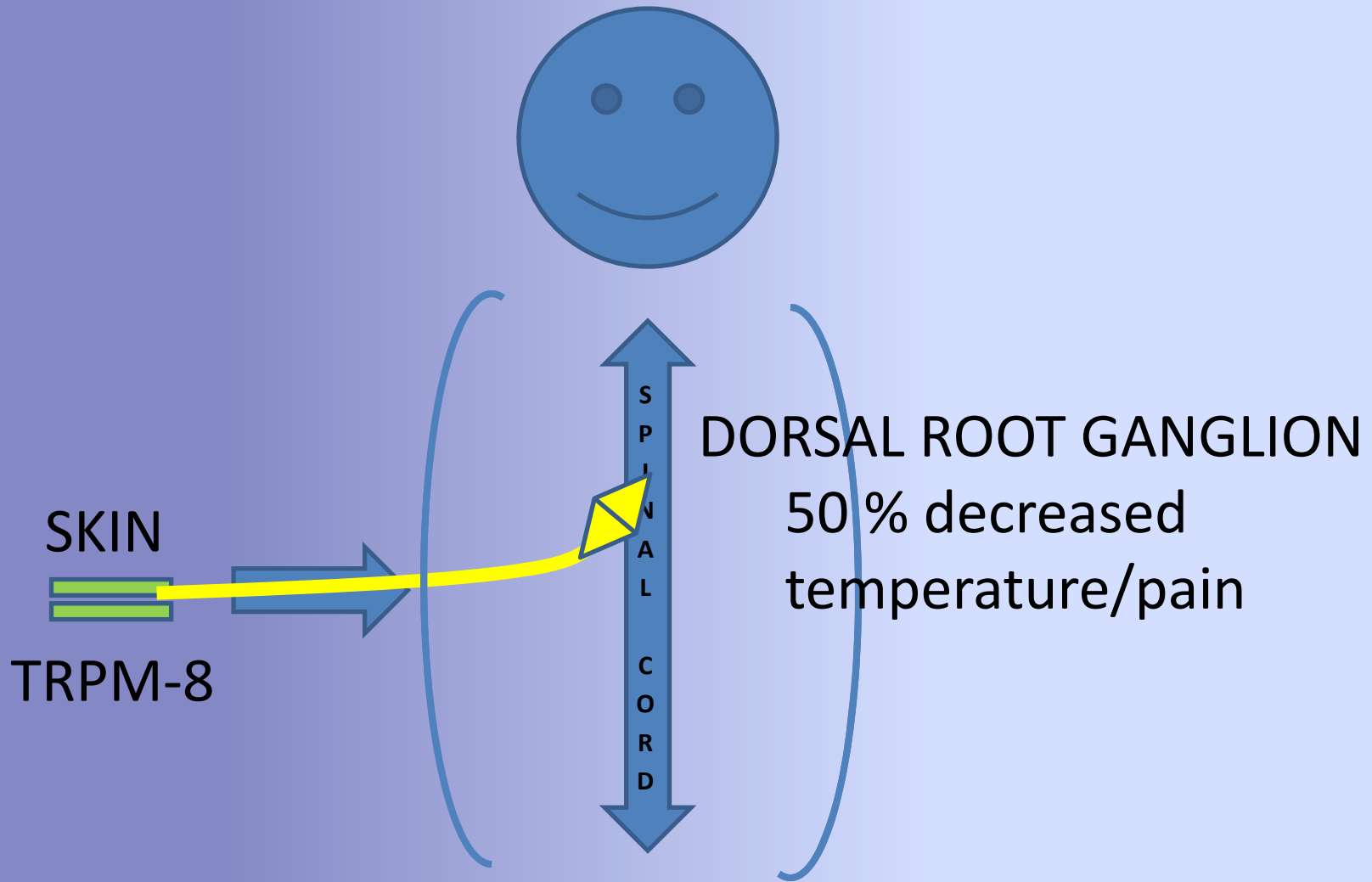
- 15% total heat loss
- kinetic energy transferred from body surface to environment via laminar air/water flow



# Temperature Regulation: Afferent

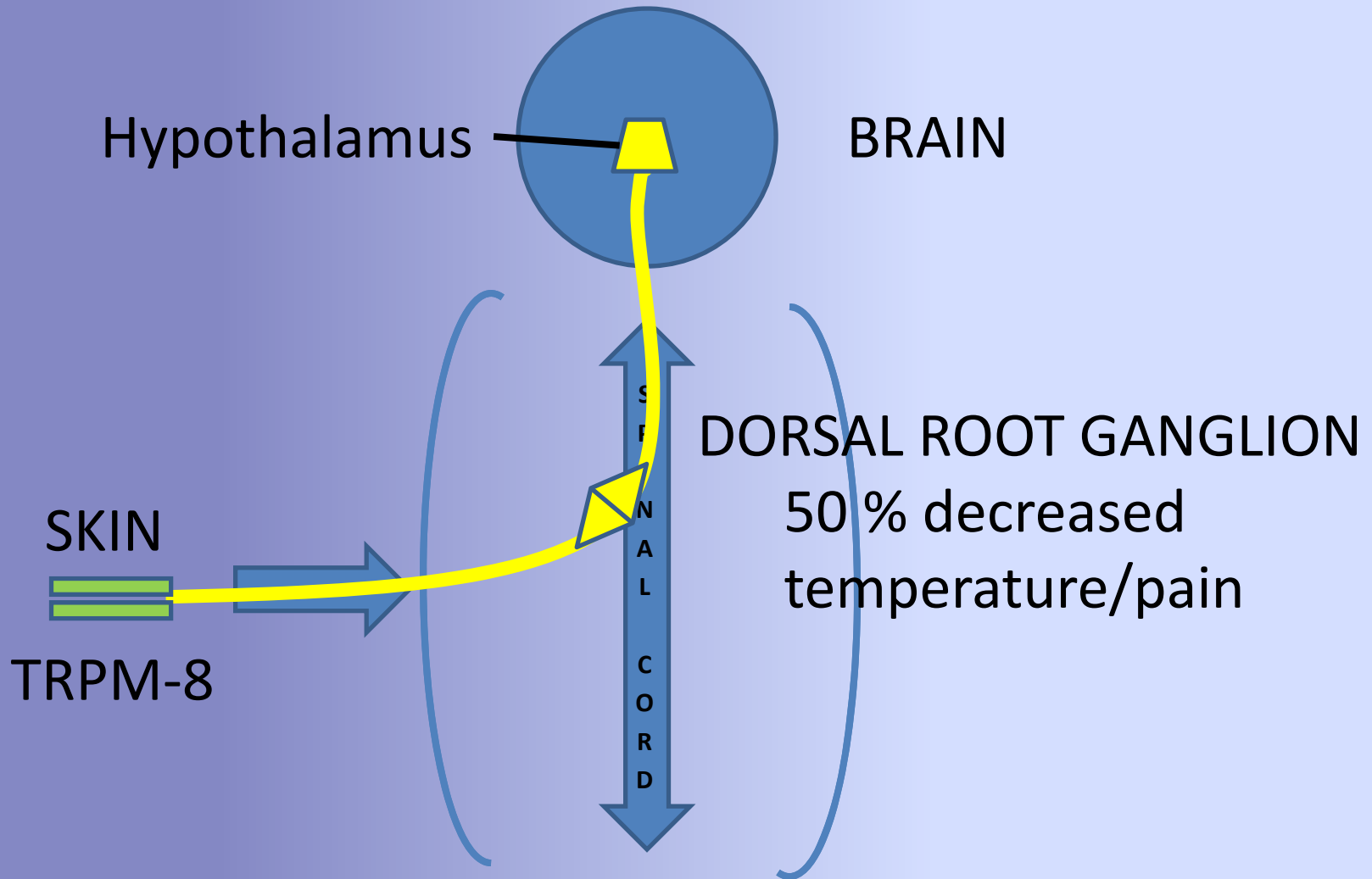


# Temperature Regulation: Afferent

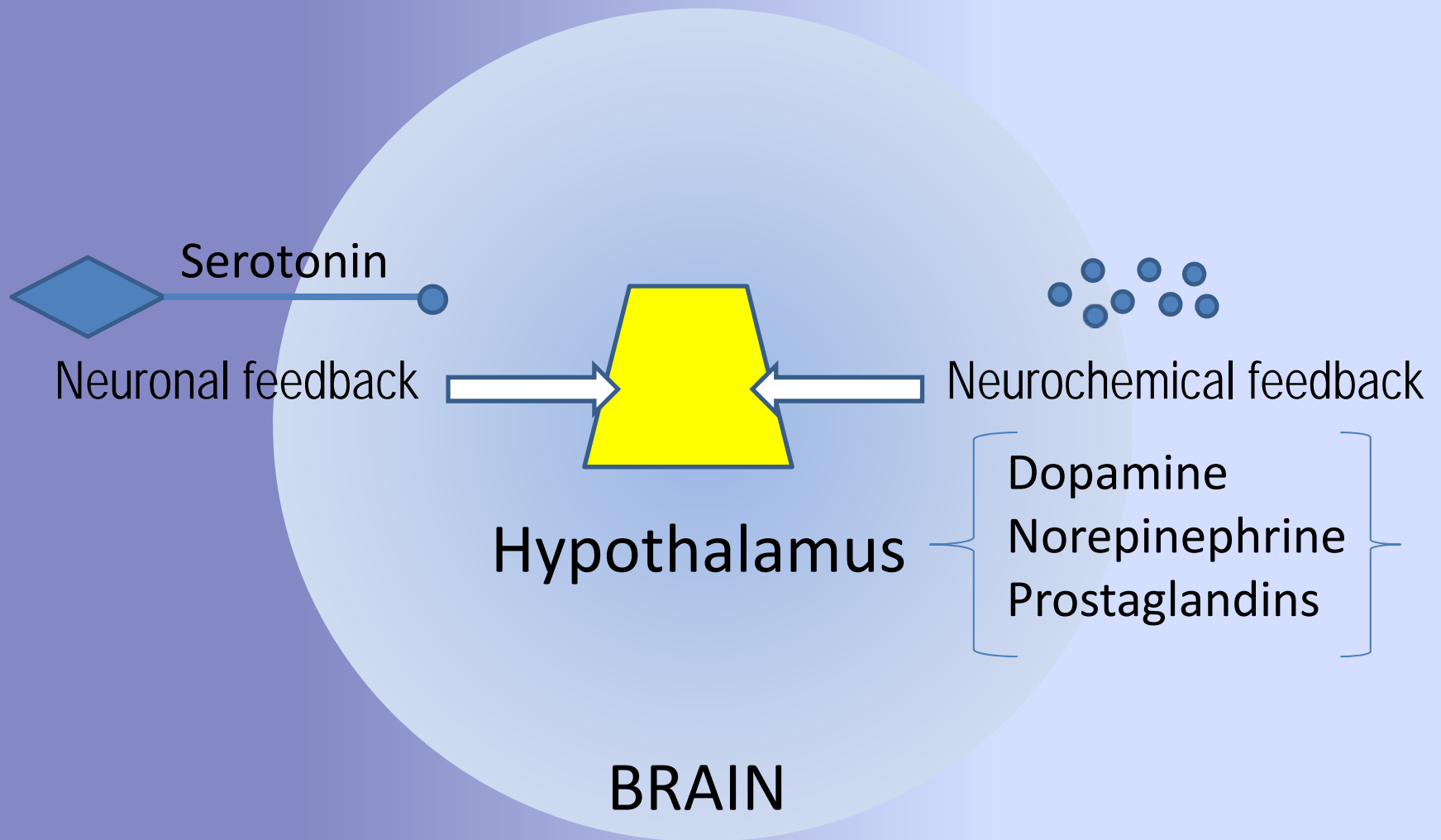




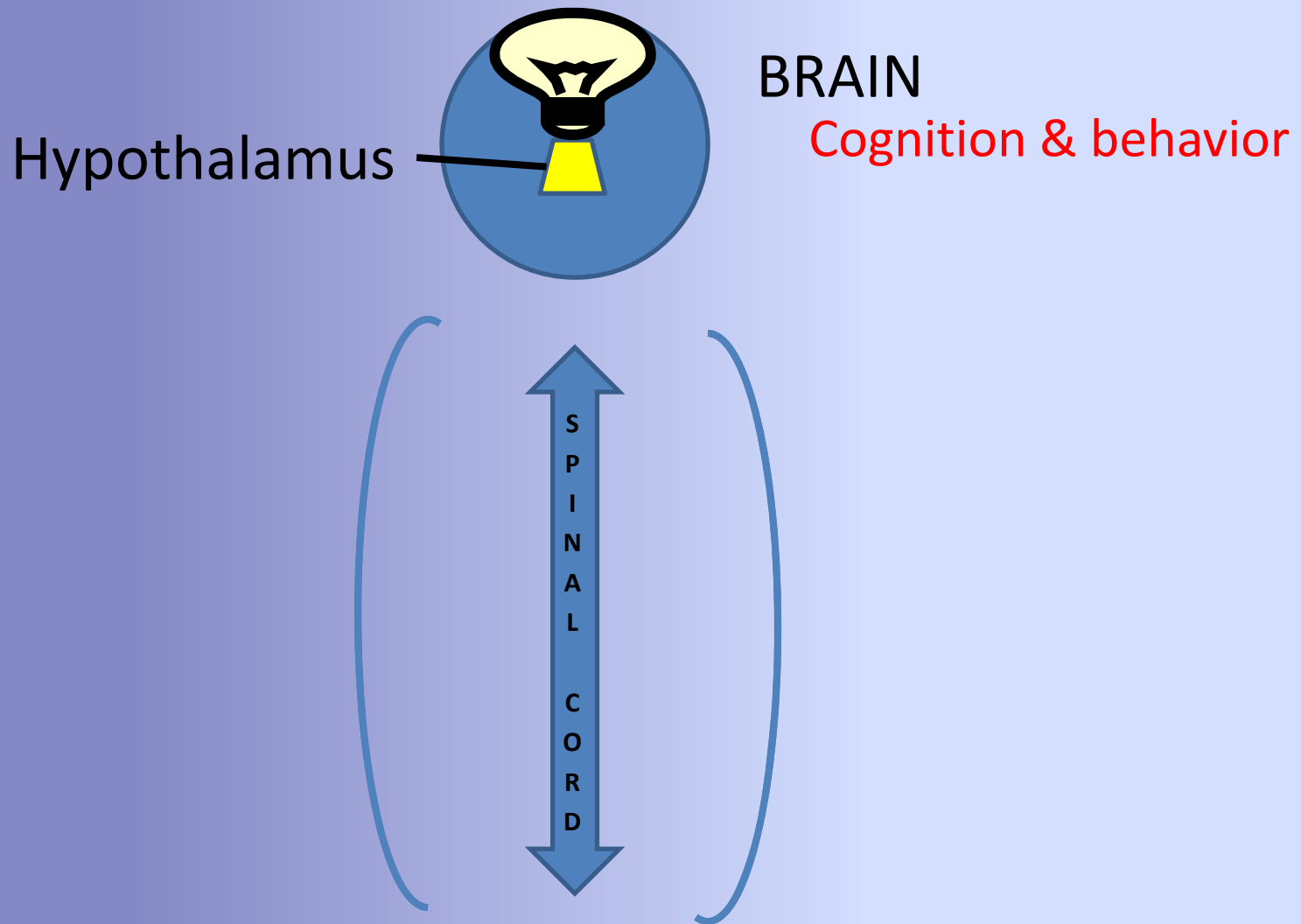
# Temperature Regulation: Afferent



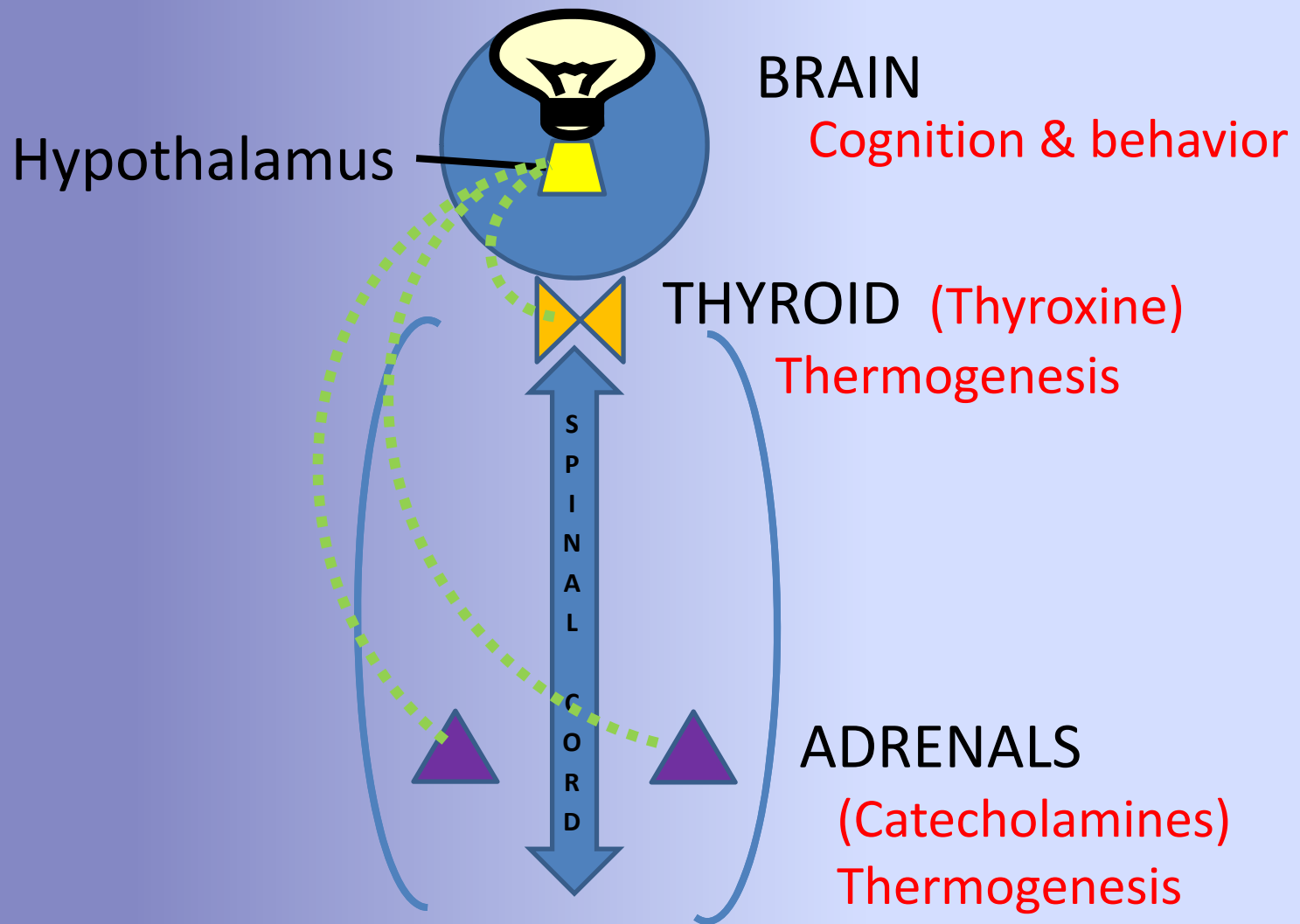
# Central Temperature Regulation



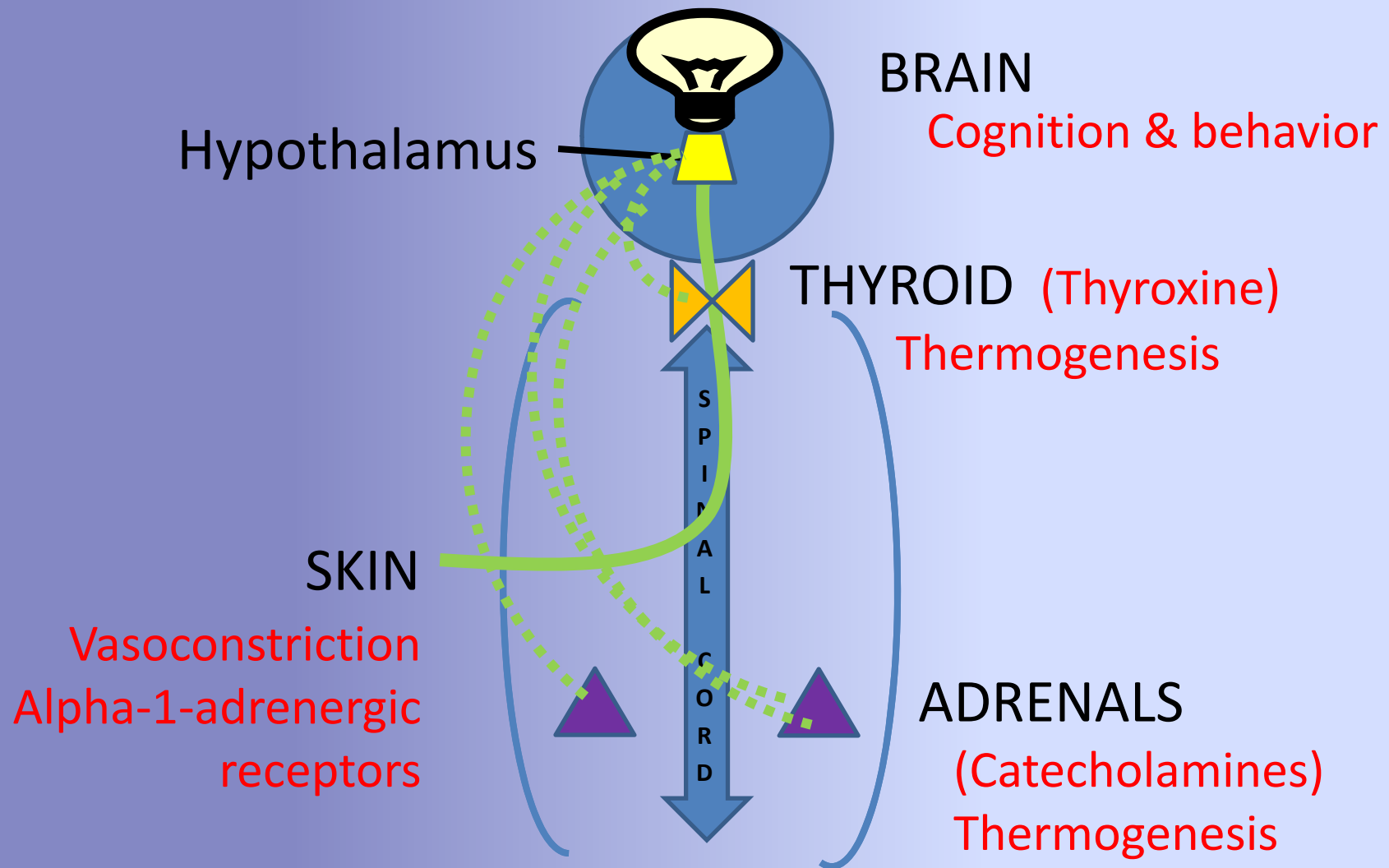
# Temperature Regulation: Efferent



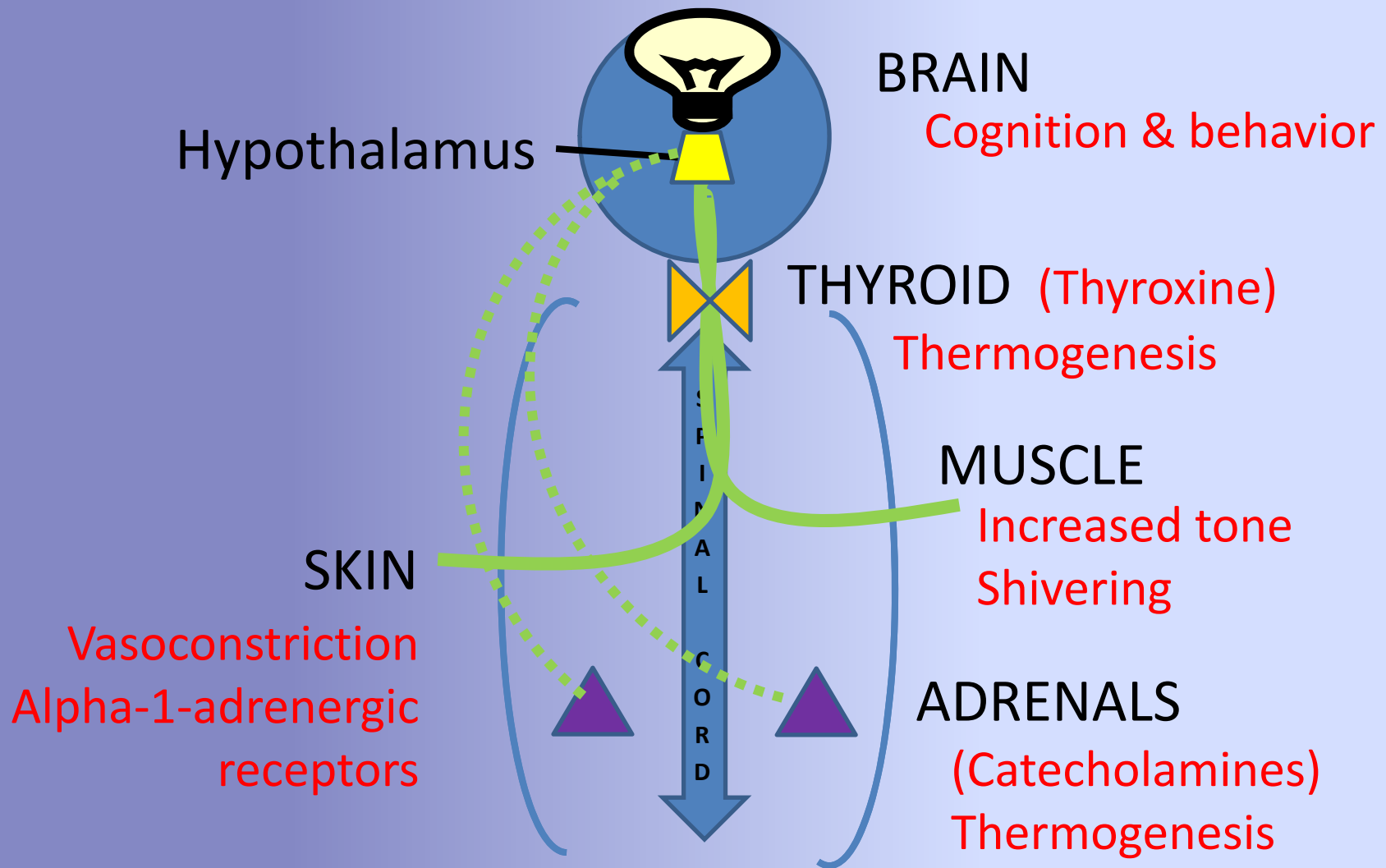
# Temperature Regulation: Efferent



# Temperature Regulation: Efferent



# Temperature Regulation: Efferent



# Causes of Hypothermia

- Central nervous system dysfunction
  - Focal, structural, generalized
  - Impaired intellectual capacity and judgment
- Metabolic disorders
  - Hypothyroidism , adrenal insufficiency, diabetes mellitus
- Age
  - Very young and very old
- Toxic effects
  - Alcohol
- Iatrogenic effects

# Causes of Hypothermia

- Iatrogenic causes (medications)
  - Opioids (decrease sympathetic outflow, increase vasodilatation, increased threshold for temperature regulation)
  - ‘Beta blocker’ antihypertensives (block beta adrenergic receptors and shivering response)
  - Atypical antipsychotics (antagonize central 5-HT<sub>2A</sub> receptors, increase vasodilatation by blocking alpha adrenergic receptors in skin)
    - Risperidone, Clozapine, Olanzapine, Quetiapine, Aripiprazole, Ziprasidone
  - Anesthetics (increase vasodilatation and block central mechanisms)



# Somatic Effects of Hypothermia

- Altered mental status:
  - cognitive slowing, disorientation, decreased communication
- Coagulopathy (prolonged bleeding time)
  - impaired function of clotting factors
  - Impaired platelet aggregation
- Respiratory:
  - tachypnea
  - reduced alveolar concentration

# Somatic Effects of Hypothermia

- Myocardial morbidity (3X increase):
  - Mild hypothermia: tachycardia
  - Moderate hypothermia: bradycardia, dysrhythmia and ischemia
  - Pulses difficult to assess due to bradycardia and vasoconstriction
  - Dysrhythmias; atrial fibrillation
  - Conduction defects (prolonged PR, QRS, and QT) leading to heart block and ventricular fibrillation.
  - EKG can show J-waves imitating ischemic events.

# Somatic Effects of Hypothermia

- Impaired immune function
  - decreased blood flow due to vasoconstriction
  - decreased leucocyte mobilization
- Electrolyte abnormalities
  - acid/base fluctuations
- Renal insufficiency
  - cold diuresis
  - hypovolemia
- Decreased metabolism and clearance of medications
  - accumulation and toxicity

# Case 1: Overview

- 40 year old female
- PWS-unknown genetic subtype
- BMI = 37-40
- 4 ER admissions secondary to hypothermia-  
resulting in 2 inpatient stays and 9 related  
physician office visits over 2 months

*Hypothermia results in a high utilization (cost) of  
medical diagnostic and treatment services across  
all levels of care.*

# Case 1: Pertinent history

- Medical history:
  - Hypertension with elevated cholesterol
  - Bilateral Pneumonia (2010)
  - S/P Cervical (C5, C6) surgery (2010-MVA)
  - S/P Posterior spinal fusion with instrumentation (1980's-scoliosis)
- Psychiatric diagnoses
  - Anxiety/Depression
- Allergies/ Sensitivities:
  - Lamictal (rash)
  - NSAIDS (GI upset)
  - Ultram

# Case 1: Medication list

## Medications prior to first episode of hypothermia:

- **Abilify 5 mg QHS**
- Provigil 200mg QAM
- Baclofen 20mg TID
- Pravastatin Sodium  
80mg QHS
- Furosemide 60mg QAM
- Lisinopril 20mg BID
- Loratadine 10mg QD
- Omega-3-fish oils 2 caps BID
- Alendronate sodium 70mg  
4 tabs Q month
- Antacid 1000mg BID
- Multivitamin 1 tab QD
- Ferrous Sulfate 325mg BID
- Vitamin D ½ tab BID
- Docusate Sodium 100mg BID
- Nasacort AQ 2 sprays ea.  
nostril QD

# Case 1: Time course

- 12/10/10: Temp 93.3°F (34°C); after warming temp 94.1°F (34.5°C); no action recorded at this time
- 12/15/10: MD visit- Dx: HTN, Hypothermia; Pulmonary consult for low O<sub>2</sub> sats ; Med changes: Increase Lisinopril to 40mg QD
- 12/28/10: Sent to ER for HTN, hypothermia & unusual behaviors (response delay, confusion, jerky head movements, argumentative with staff)

# Case 1: Time course

- 12/29/10: MD visit (ER follow-up)-Check for anemia, UTI; Temp 92.2°F (33.4°C) po, pulse 80, resp 16, BP 122/70; unable to obtain O<sub>2</sub> sats; after warming temp 97.9°F (36.6°C); Med changes: Decrease Furosemide to 20mg 1 QD, Increase Vitamin D 400u 1 BID, Bactrim DS 1 BID for 3 days; increase fluids (H<sub>2</sub>O)
- 1/3/11: Sent to ER-admitted; Dx: Hypothermia, R/O Adrenal Insufficiency; Temp range: 91.4-93°F (33°C-33.9°C) B/P 107/43-135/82, pulse 50-90 NSR, O<sub>2</sub> Sat 98% on RA; Med Changes: Decrease Lisinopril to 20mg daily; d/c Furosemide; Increase Lasix to 40mg QD; Begin Levothyroxine 50mcg QD; Magnesium oxide 1 tab QD; dc'd home 1/5/11



# Case 1: Time course, cont'd

- 1/10/11: Sent to ER-Dx: Hypothermia, Anemia; **Temp range: 92.3-92.8°F (33.5°C-33.8°C)**, pulse 47; EKG poor quality with artifact; Sinus bradycardia without ectopy
- 1/14/11: MD visit (ER follow-up) for hypothermia; Med changes: D/C Baclofen; Begin Robaxin 750mg TID
- 1/18/11: Sent to ER, Admitted; Dx: Hypothermia, etiology Hypothyroidism vs. Abilify; Outpatient pan-spinal MRI ordered to r/o spinal abscess (not completed as Neurosurgeon felt it was unnecessary due to absent clinical signs); Referral to hematology and endocrinology; Med changes: **d/c Abilify**; dc'd to home 1/20/11

# Case 1: Time course, cont'd

- 1/26/11: MD follow-up; Temp 96.3°F (35.7°C), pulse 50, resp 22, BP 124/84, O<sub>2</sub> sats 94% RA; No changes
- 2/10/11: New PCP (internal Medicine); Temp 97.8°F (36.6°C), pulse 61, BP 140/80-120/70, O<sub>2</sub> sats 94%; No changes
- 3/8/11: Endocrine, Dx: Sub-clinical hypothyroidism; No changes
- 3/15/11: Hematology, Temp 97.8°F (36.6°C), BP 137/95; No changes

# Case 2: Overview

- 47 year old female
- PWS-unknown genetic subtype
- Medical diagnoses:
  - Mild intellectual deficiency
  - Obesity
  - Sleep apnea
  - Hypothyroidism
  - Central adrenal insufficiency
- Weight 89 kg (196 lb)

## Case 2: Pertinent history

- Recurrent hypothermia-first episode 2 years ago; Required admission to MICU for treatment of **bradycardia, worsening mental status, cellulitis, pancytopenia**, and central adrenal insufficiency; Recovered with steroids, antibiotics; Discharged to rehab, and then, to group home.
- 5 similar episodes since then, presenting with **petechiae on chest and abdomen**; looks puffy (edema)with increased weight; **altered mental status** (less interactive; slurred speech; somnolent)

# Case 2: Pertinent history, cont'd

## Typical clinical course:

- To ER; hypotensive and hypothermic (**temp = 80's°F; 27-32°C**); **bradycardia** (required pacemaker x 1)
- Laboratory findings (typically):
  - Chem 8 and thyroid studies normal;
  - Transaminitis;
  - **Anemia, leukopenia;**
  - **Thrombocytopenia with abnormal clotting**
- Treatment: **stress dose of steroids + antibiotics**
- Discharge to rehabilitation with gradual recovery

## Case 2: Pertinent history, cont'd

- Medications at time of last episode:
  - Synthroid
  - Cortef 15 mg in AM and 5 mg in PM (double with stress)
  - Lisinopril
  - **Atenolol**
  - Nexium
  - Fosamax
  - Calcium and vitamins
- Last episode resolved after **Atenolol dc'd**

# Acute Warming Interventions

- Accurate measurement of core temperature
  - low reading rectal thermometer
- *Passive* warming
  - remove wet clothing (cold diuresis)
  - warm environment
  - re-dress in layers
- *Active* warming
  - forced air convection warming
  - insulation with warming blankets

# Prevention

- Manage recurrence risk
  - Seasonal monitoring of core body temperature
- Environmental interventions
  - Manage ambient temperature
  - Check for drafts
  - Limit exposure to cold
- Behavioral interventions
  - Appropriate dress for weather (layers, hats, scarves, gloves)
  - Educate, reinforce compliance with appropriate behavior



# Secondary Prevention

- Monitor (*LathamCenters Protocol, 2011*)
  - With seasonal changes; ambient temp < 45°F (7°C)
    - Temp/pulse/BP QD
  - If temp < 94.5°F (34.7°C) or pulse < 60
    - Temp/pulse Q6 hr
    - O2 sats Q6 hr
    - Call PCP
    - Warming interventions
  - If temp > 94.5°F (34.7°C), temp/pulse TID for
  - If temp > 96°F (35.6°C), temp/pulse BID for

# Secondary Prevention

- Warming interventions
  - Warm fluids
  - Knit hat
  - Ambient temperature > 75°F (23.8 °C)
  - Additional blankets on bed at night
  - Heating blanket when supervised

*Latham Centers Nursing Protocol , 2011*

# Tertiary Prevention

- Send to ER if:
  - Temperature cannot be maintained or  $<93^{\circ}\text{F}$  ( $34^{\circ}\text{C}$ )
  - Changes in cognition or behavior
  - Pulse  $<40$
  - Cyanosis
  - Petechiae
- Educate PCP/ER staff about effects of hypothermia in PWS

*Latham Centers Nursing Protocol, 2011*

# Summary: Hypothermia in PWS

- Faulty homeostatic mechanisms
  - Abnormal pain/temperature perception
  - Abnormal central sensor threshold
  - Atypical hypothermic response to ambient cold temperature challenge
  - Impaired behavioral response, insight/judgment and cognitive flexibility
- Increased susceptibility in middle-age
- Increased risk with medical/psychiatric co-morbidities
  - Thyroid, central adrenal insufficiency, diabetes mellitus
  - Psychosis/mood disorder/dementia
  - Hypertension/cardiopulmonary problems
  - Iatrogenic effects due to medications
- Recurrence risk must be managed



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**Thank you!**

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