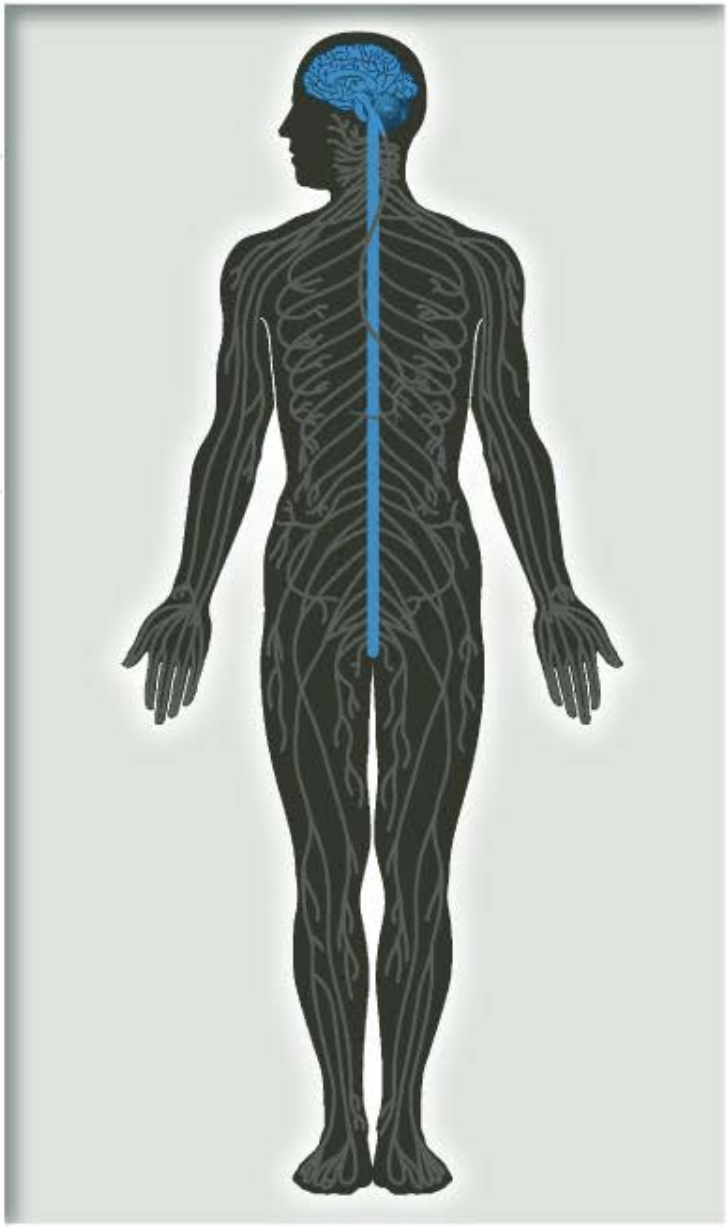
The Nervous System

The Nervous System consists of:

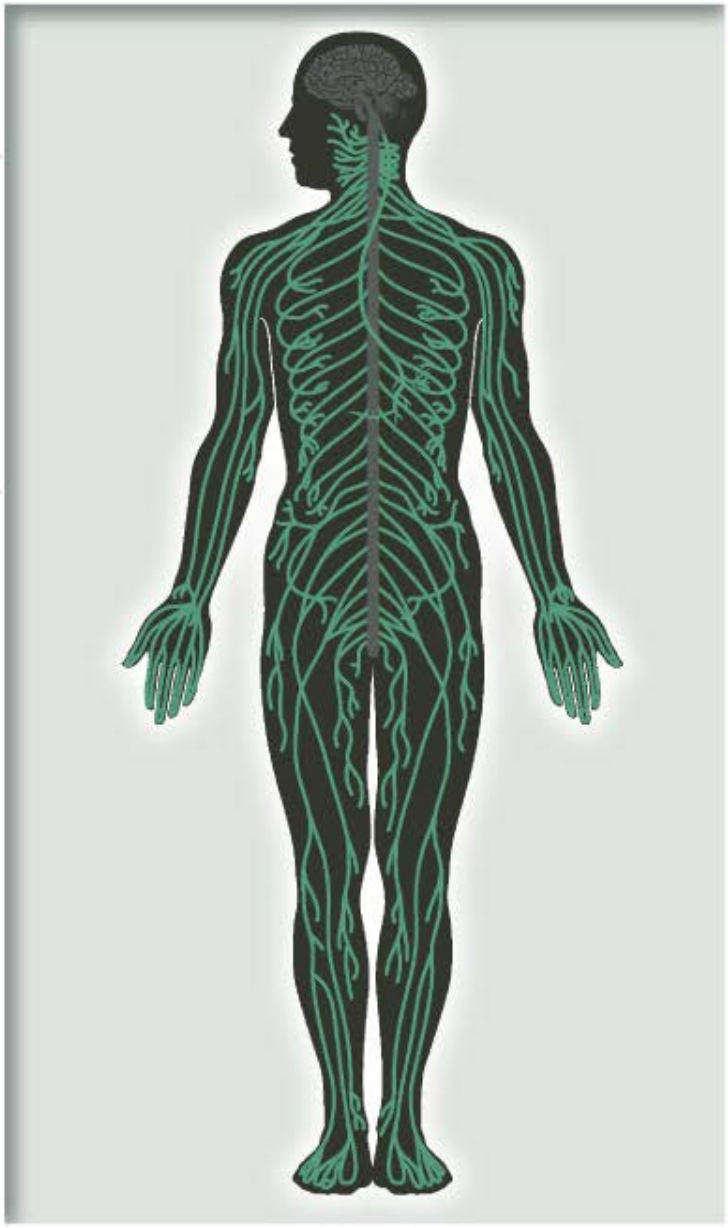
- **The Central Nervous System (CNS)** consists of:
  - brain
  - spine
- **The Peripheral Nervous System (PNS)** consists of:
  - neurons located outside the brain and spinal cord; i.e. nerves that enter and leave the CNS
  - enteric system: part of the PNS that is in the gastrointestinal tract



The Nervous System

The Nervous System consists of:

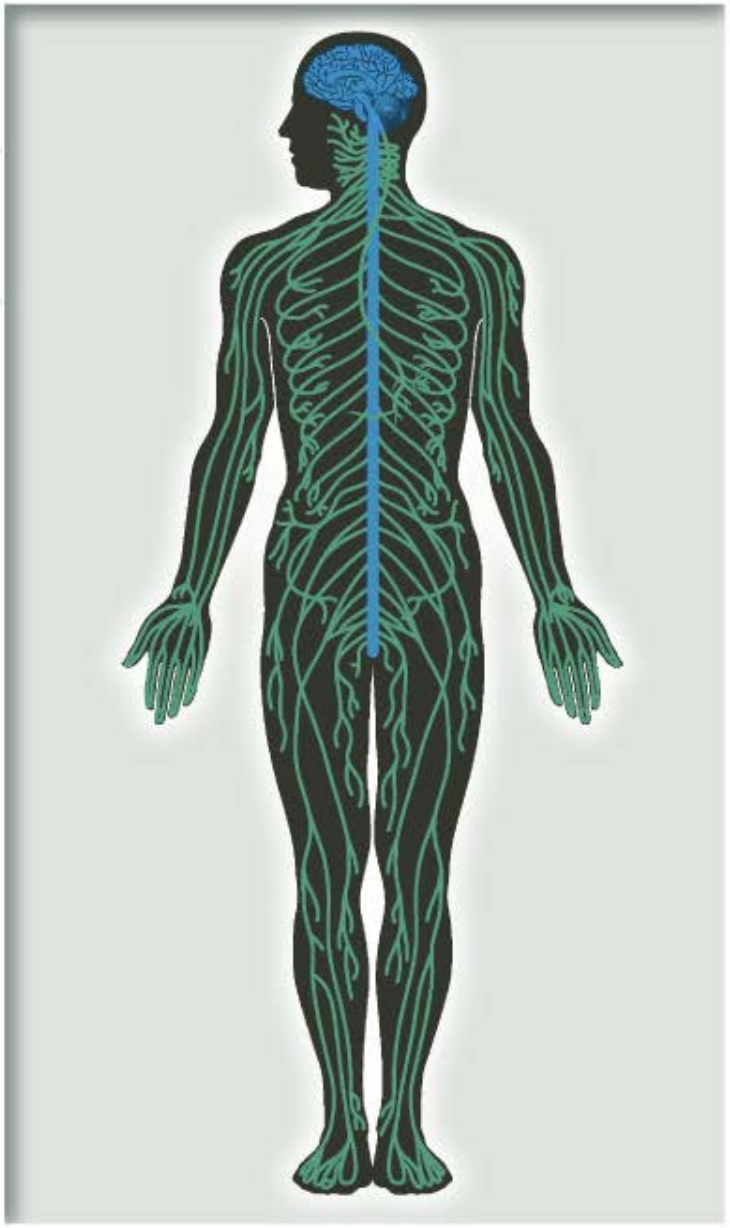
- The Central Nervous System (CNS) consists of:
  - brain
  - spine
- **The Peripheral Nervous System (PNS)** consists of:
  - neurons located outside the brain and spinal cord; i.e. nerves that enter and leave the CNS
  - enteric system: part of the PNS that is in the gastrointestinal tract



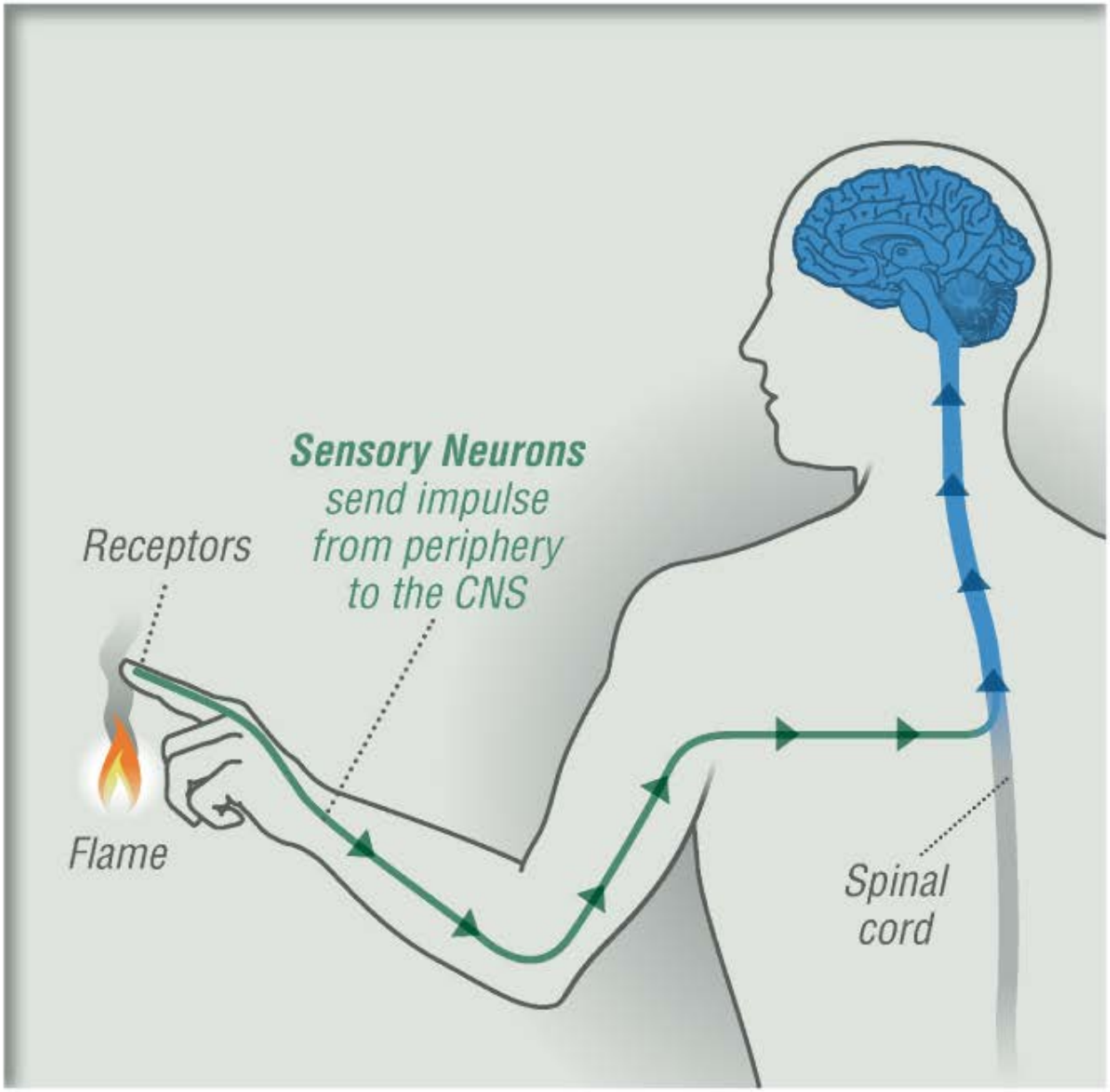
The Nervous System

The Nervous System can be divided into:

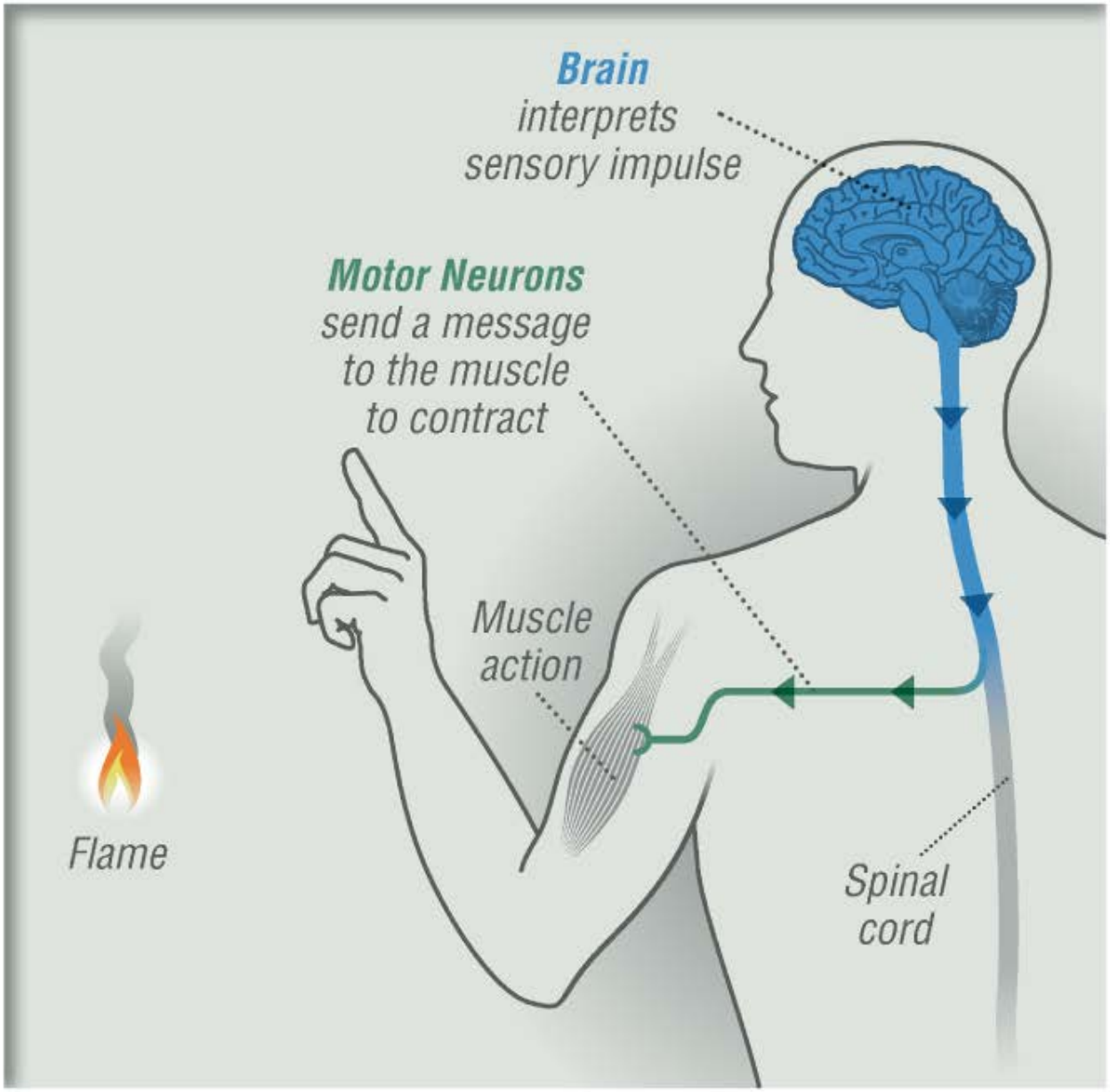
- **Somatic system**
  controls ***voluntary*** action
- **Autonomic system**
  controls ***involuntary*** action
  - **Sympathetic:** adjusts responses to stressful situations
  - **Parasympathetic:** maintains essential bodily functions



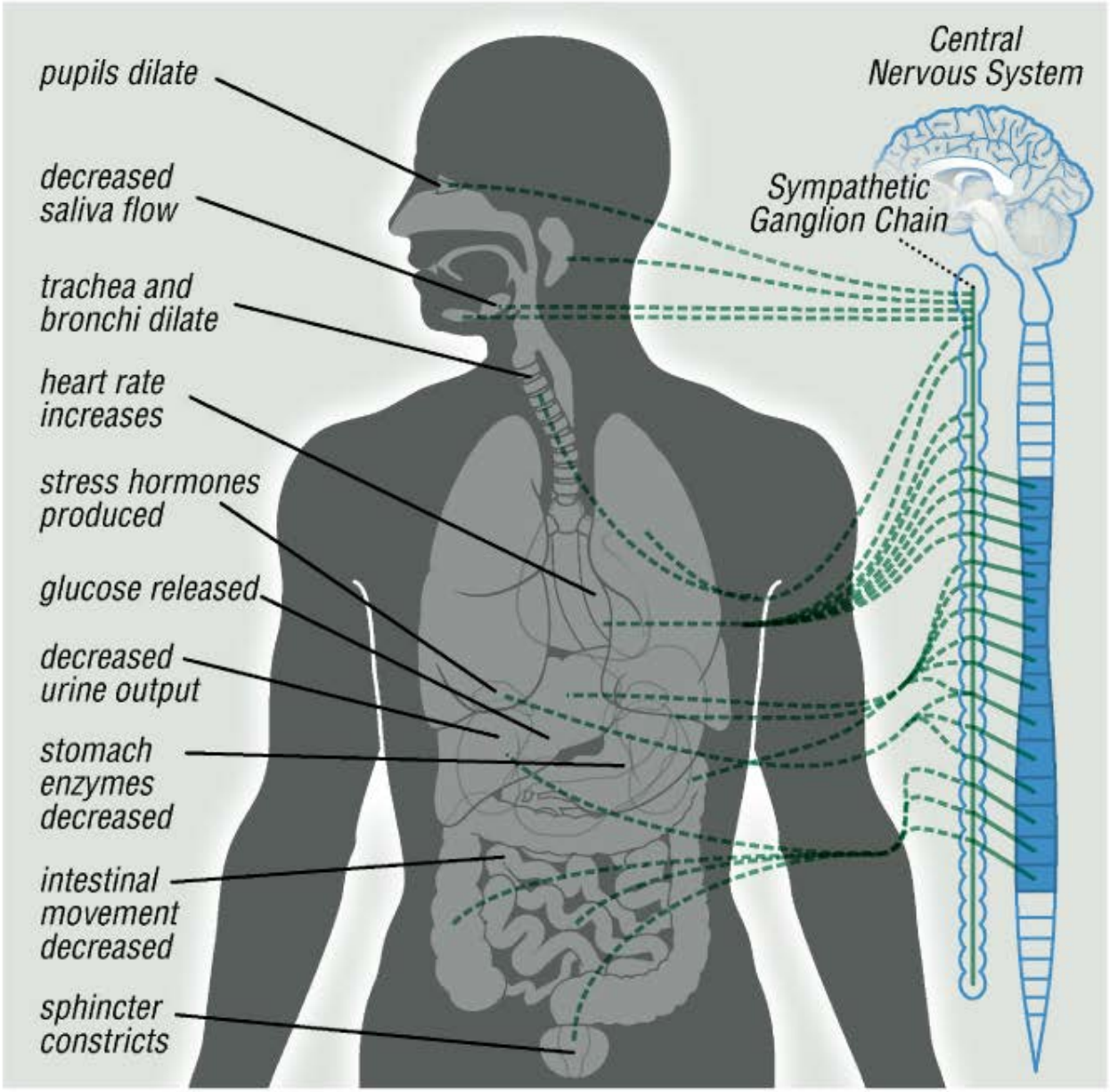
The Sensory-Somatic Nervous System Controls the Body's Relationship to the External Environment



The Sensory-Somatic Nervous System Controls the Body's Relationship to the External Environment



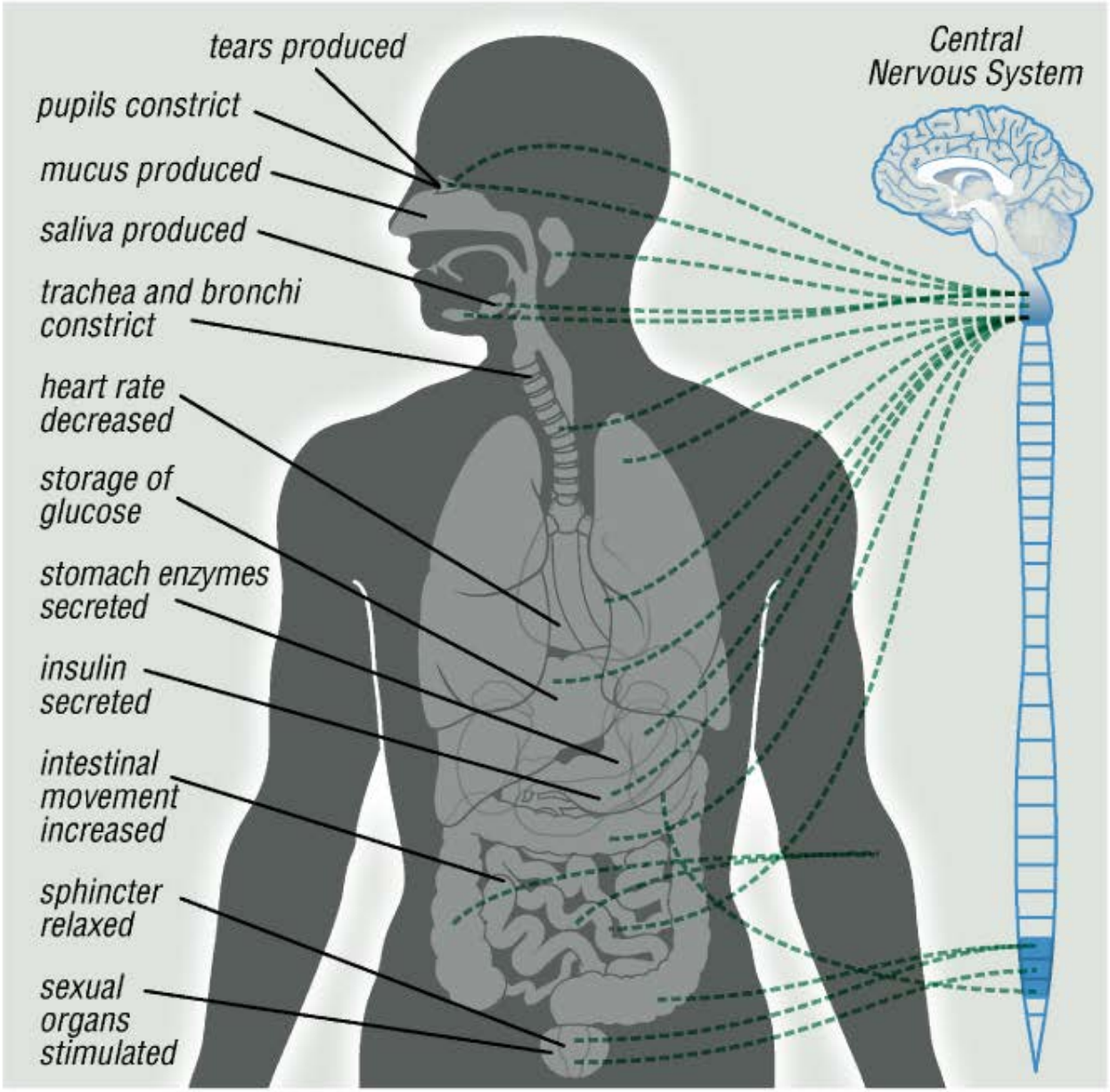
The Autonomic Nervous System Monitors and Regulates Conditions of the Internal Organs



SYMPATHETIC DIVISION

is principally an excitatory system that prepares the body for stress.

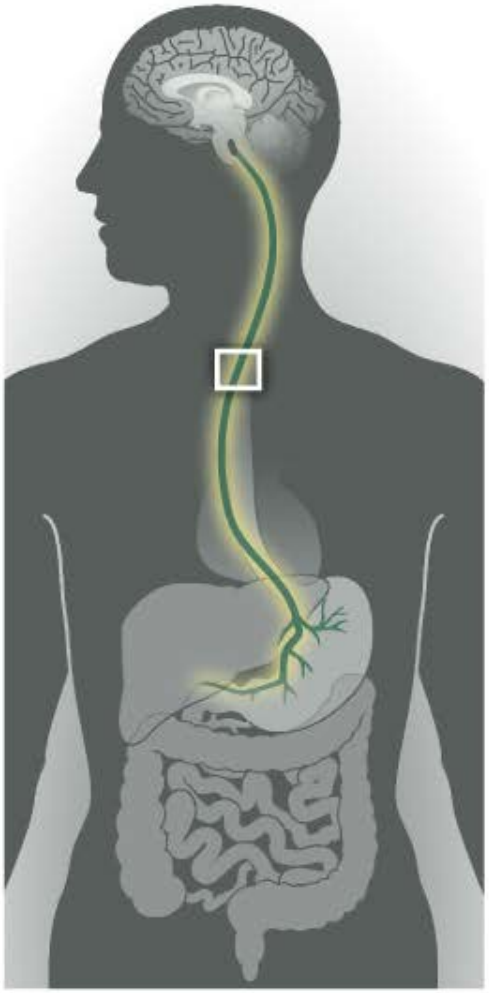
The Autonomic Nervous System Monitors and Regulates Conditions of the Internal Organs

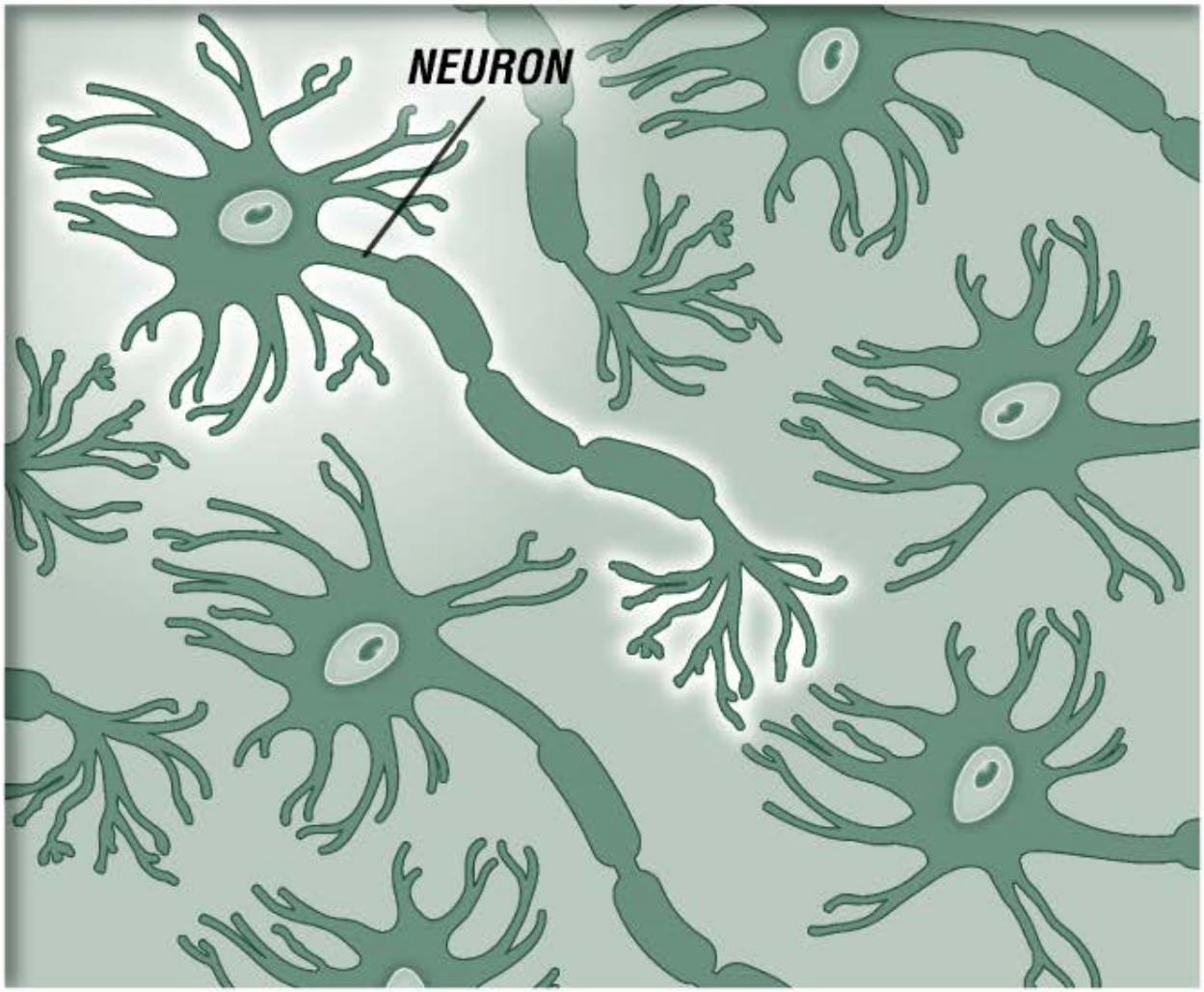


PARASYMPATHETIC DIVISION

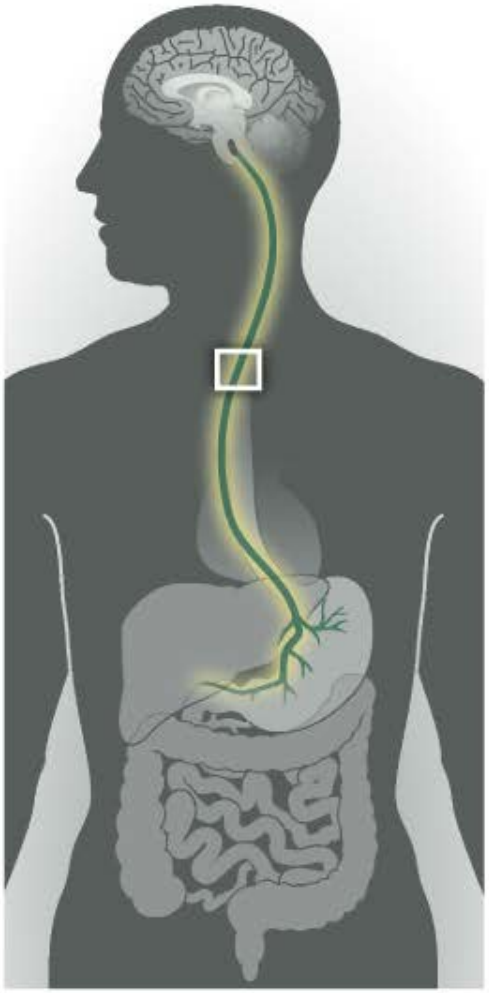
maintains or restores energy.

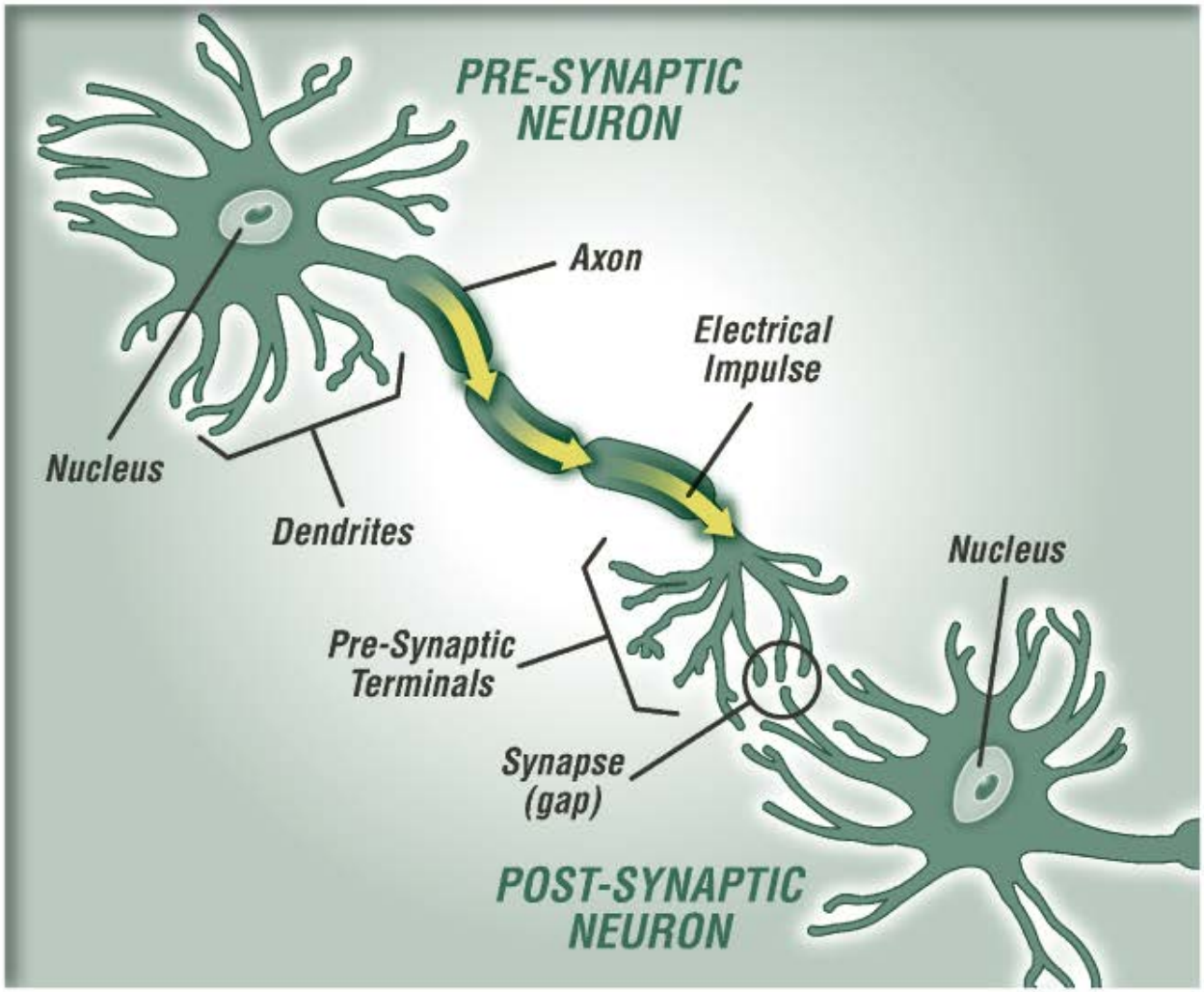
A Nerve Is a Bundle of Cells that Carries Signals between the Brain or Spinal Column and Other Parts of the Body



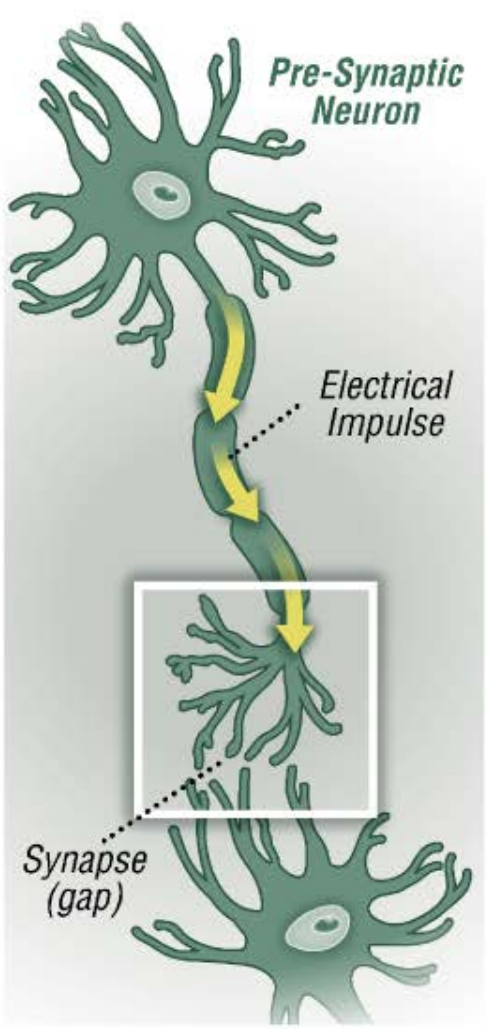


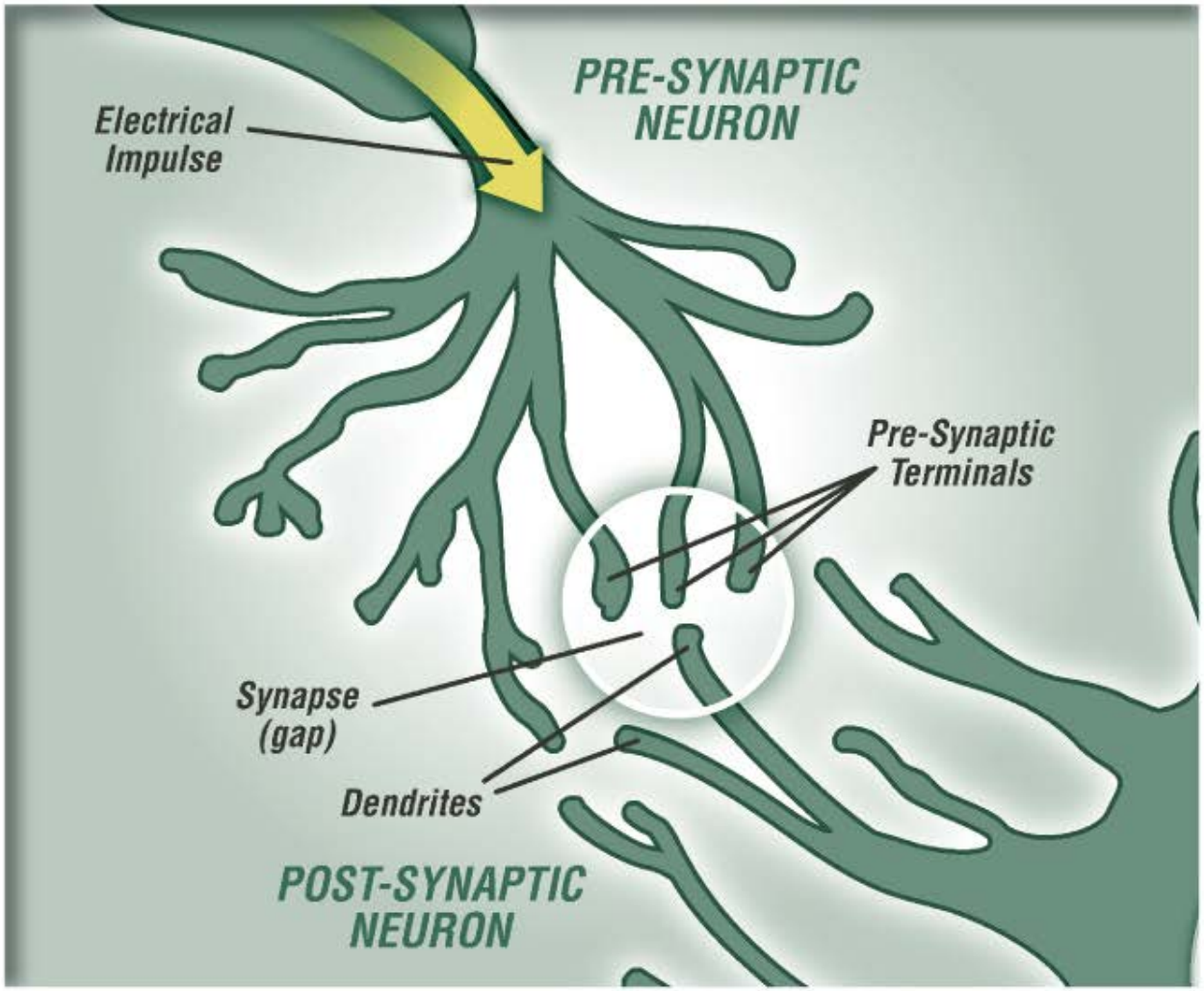
Principal Features of a Typical Neuron



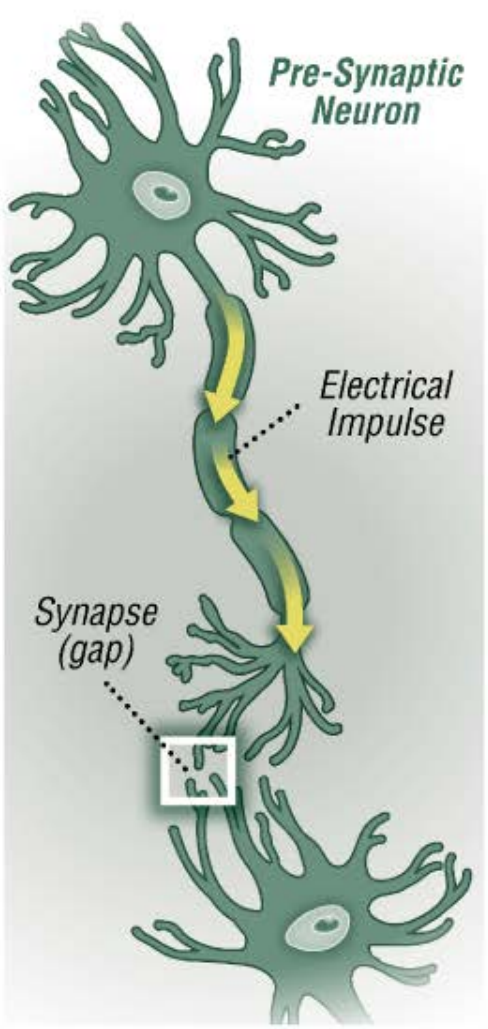


Principal Features of a Typical Neuron



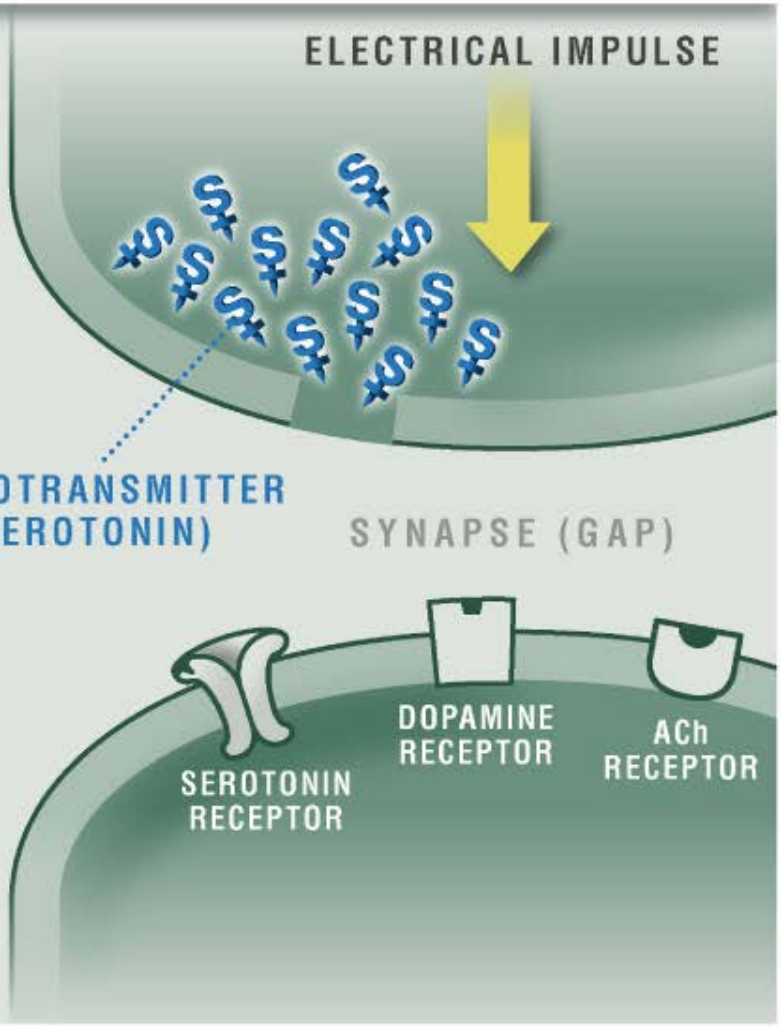


Neurotransmitters Cross the Synapse (Gap) between Nerve Cells, Triggering the Second Neuron into Action

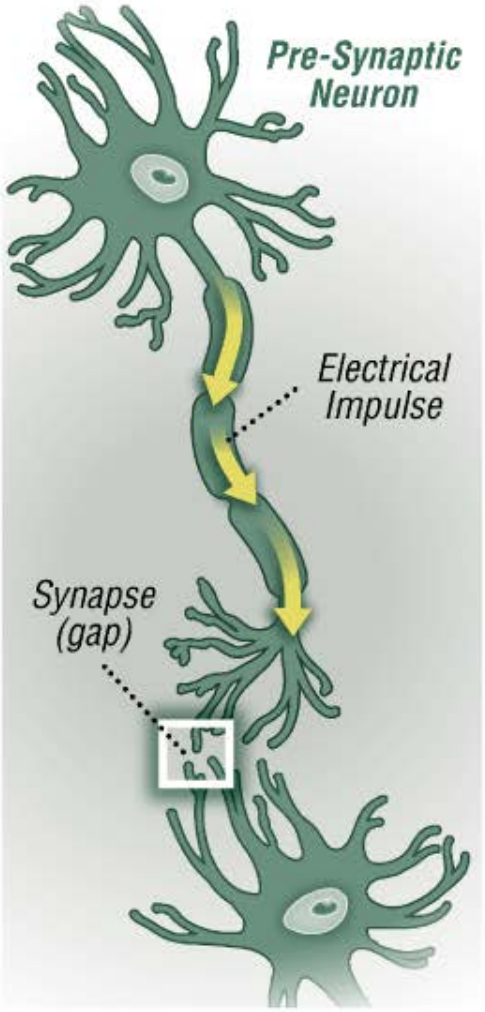


STEP 1:

Electrical impulse reaches the Pre-synaptic terminal.

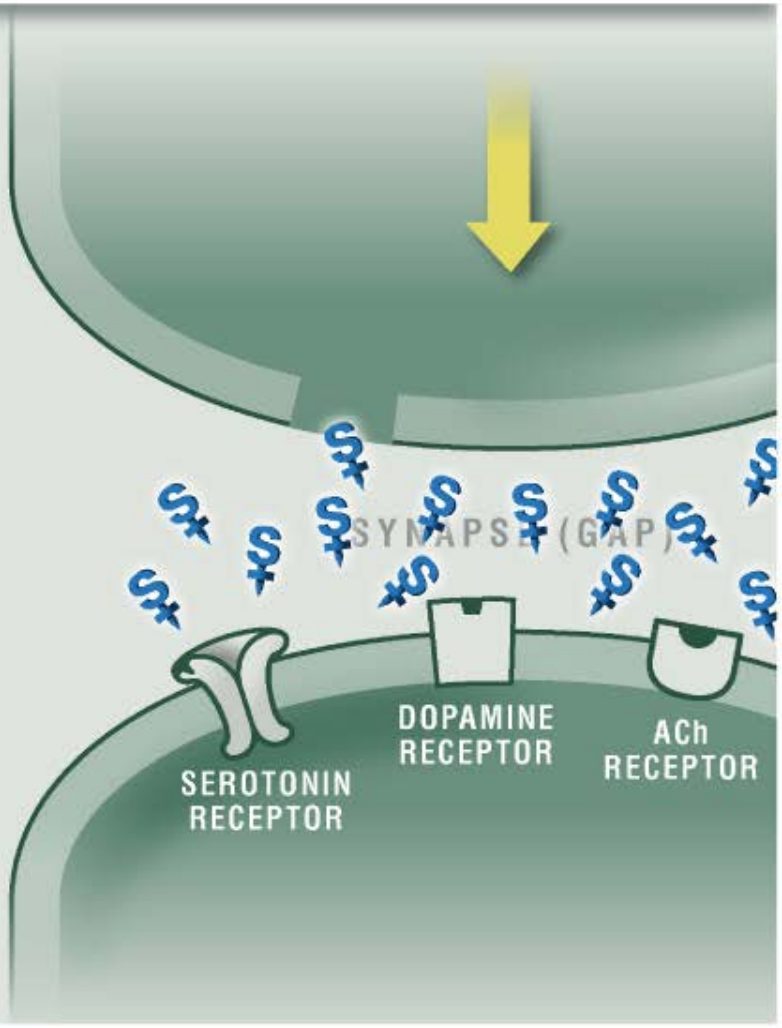


Neurotransmitters Cross the Synapse (Gap) between Nerve Cells, Triggering the Second Neuron into Action

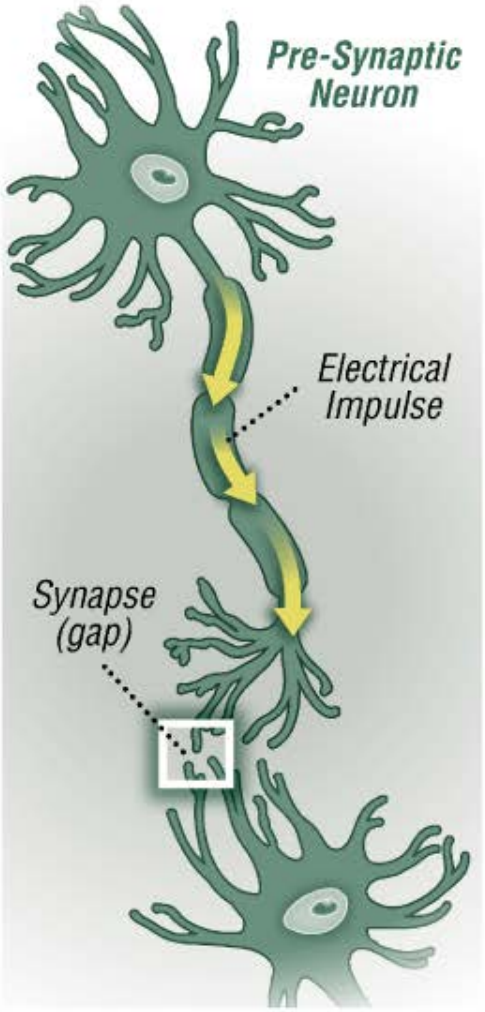


STEP 2:

Neurotransmitter (Serotonin) is released into the synapse (gap).

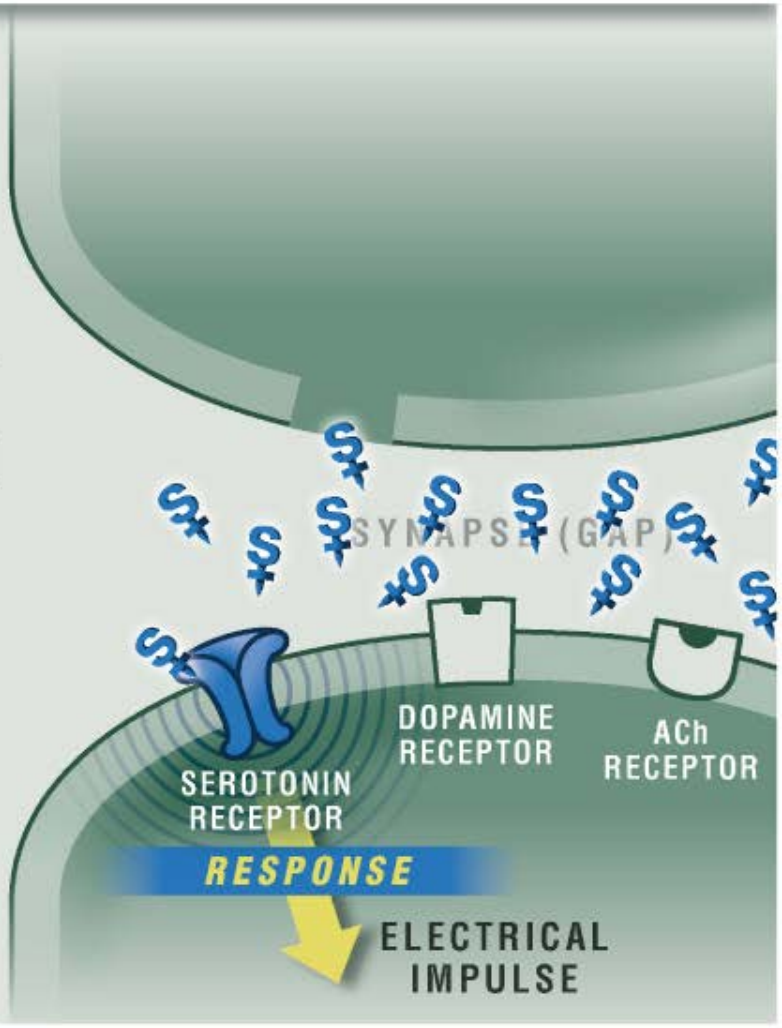


Neurotransmitters Cross the Synapse (Gap) between Nerve Cells, Triggering the Second Neuron into Action

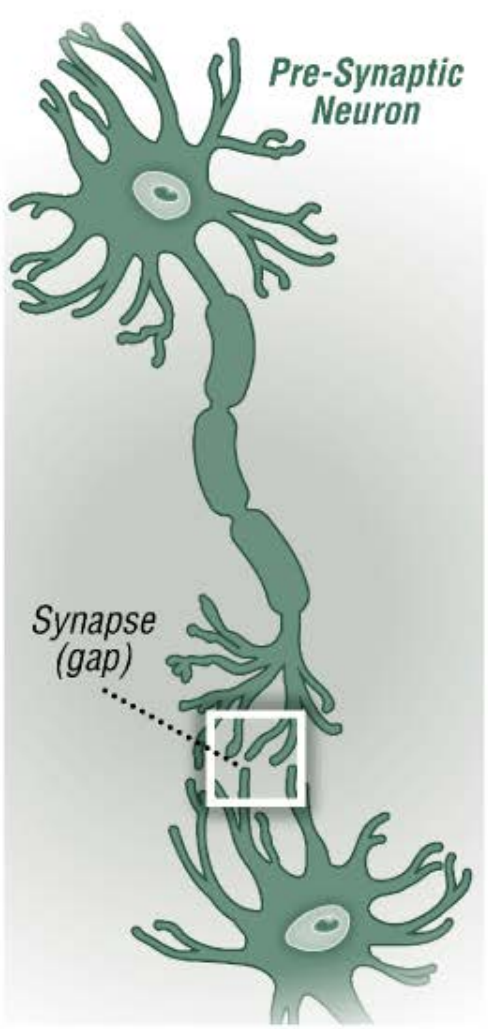


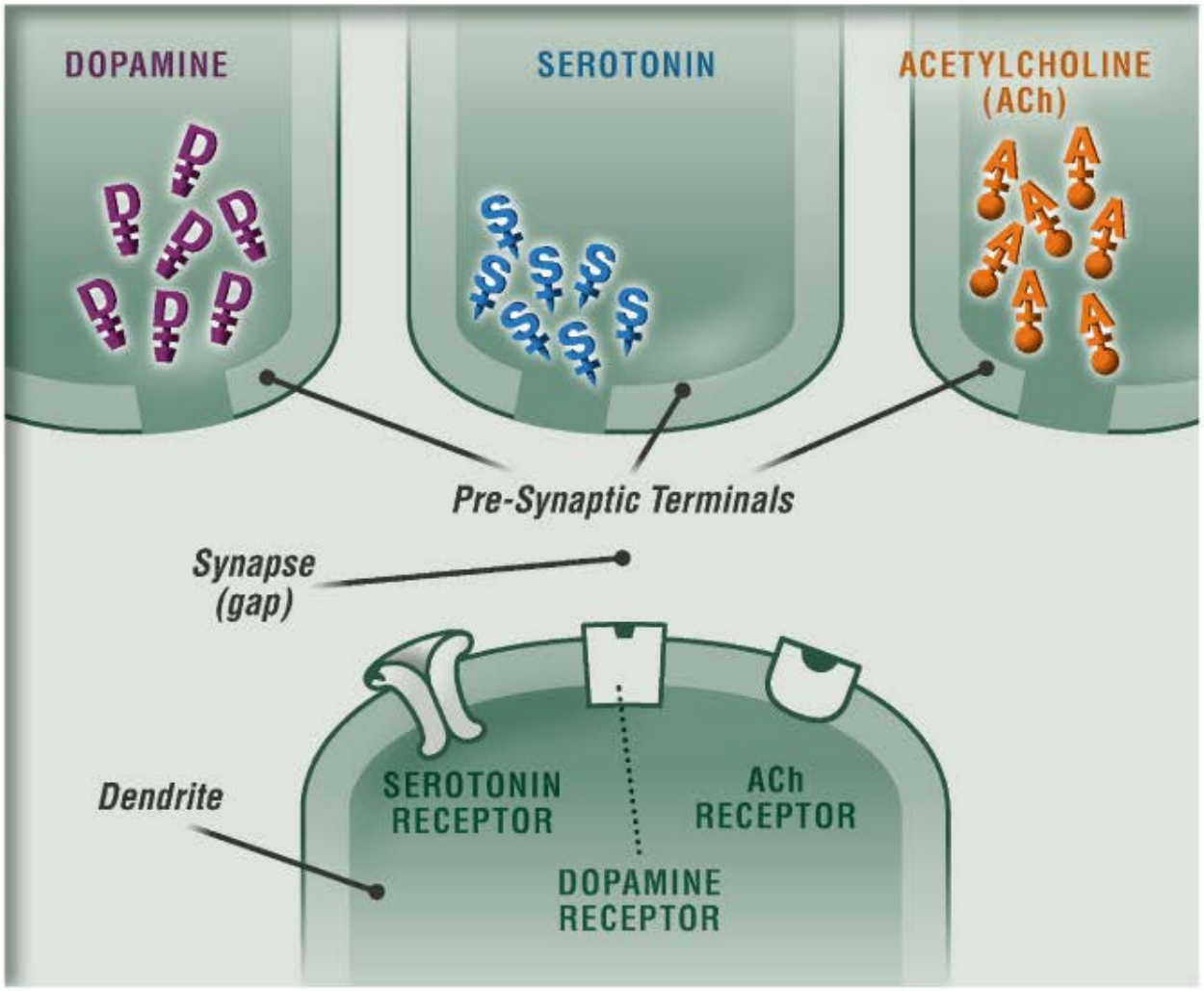
STEP 3:

Neurotransmitter (Serotonin) binds with the Serotonin receptor and the second cell is triggered into action.



There Are Many Different Types of Neurotransmitters





Neurotransmitters Within the Body

5HT – 5-hydroxytryptamine (serotonin)

ACH – Acetylcholine

ACTH – Adrenocorticotropic hormone

ADA – Adenosine

ADCYAP – ADYCYAP1, PACAP, adenylate cyclase activating polypeptide 1

ADM – Adrenomedullin

ATP – Adenosine triphosphate

AVP – Vp, Vsp, arginine vasopressin

CCK – Cholecystokinin

CGRP – Calcitonin gene-related peptide

DA – Dopamine

E – Epinephrine

EDN2 – Endothelin 2; ET2

ENK – Enkephalin

EST – Estrogen

GABA – Gamma-amino butryic acid

GIP – Gastric inhibitory polypeptide

GLP1 – Glucagon

GLU – Glutamate

GLY – Glycine

HCRT – Hypocretin; orexin

HIS – Histamine

INS – Insulin

MCH – Melanin concentrating hormone

NE – Norepinephrine

NGF – Nerve growth factor, beta polypeptide

NMU – Neuromedin U

NO – Nitric oxide

NPFF – Neuropeptide FF-amide peptide precursor; FMRFAL

NPFF – NEUROPEPTIDE FF-AMIDE PEPTIDE; FMRF-AMIDE-LIKE PEPTIDE PRECURSOR

NPY – Neuropeptide Y

PTH – Parathyroid hormone

SCT – Secretin

SST – Somatostatin

TAC1 – Tachykinin 1 (substance P)

TAC4 – Tachykinin 4 (HK1)

THC – Cannaninoids

TRH – Thyrotropin releasing hormone

TST – Testosterone

UTS2 – Urotensin II

VIP – Vasoactive intestinal peptide

Neurotransmitters Implicated in the Emetic Pathway

5HT – 5-hydroxytryptamine (serotonin)
ACH – Acetylcholine
ACTH – Adrenocorticotropic hormone
ADA – Adenosine
ADCYAP – ADYCYAP1, PACAP, adenylate cyclase activating polypeptide 1
ADM – Adrenomedullin
ATP – Adenosine triphosphate
AVP – Vp, Vsp, arginine vasopressin
CCK – Cholecystokinin
CGRP – Calcitonin gene-related peptide
DA – Dopamine
E – Epinephrine

EDN2 – Endothelin 2; ET2
ENK – Enkephalin
EST – Estrogen
GABA – Gamma-amino butryic acid
GIP – Gastric inhibitory polypeptide
GLP1 – Glucagon
GLU – Glutamate
GLY – Glycine
HCRT – Hypocretin; orexin
HIS – Histamine
INS – Insulin
MCH – Melanin concentrating hormone
NE – Norepinephrine
NGF – Nerve growth factor, beta polypeptide
NMU – Neuromedin U

NO – Nitric oxide
NPFF – Neuropeptide FF-amide peptide precursor; FMRFAL
NPFF – NEUROPEPTIDE FF-AMIDE PEPTIDE; FMRF-AMIDE-LIKE PEPTIDE PRECURSOR
NPY – Neuropeptide Y
PTH – Parathyroid hormone
SCT – Secretin
SST – Somatostatin
TAC1 – Tachykinin 1 (substance P)
TAC4 – Tachykinin 4 (HK1)
THC – Cannaninoids
TRH – Thyrotropin releasing hormone
TST – Testosterone
UTS2 – Urotensin II
VIP – Vasoactive intestinal peptide

Anti-Emetics Available as of 1985

DRUG CLASS	EXAMPLE
Substituted Benzamides	■ Metoclopramide
Phenothiazines	■ Compazine (Prochlorperazine) ■ Thorazine (Chlorpromazine)
Corticosteroids	■ Dexamethasone ■ Methylprednisolone
Butyrophenones	■ Haloperidol ■ Droperidol

In the 1980's, Researchers Were Focusing on Three Classes of Drugs for the Treatment of Chemotherapy Induced Nausea and Vomiting (CINV)

CLASS	COMPOUND	BRAND NAME	MANUFACTURER
Dopamine Antagonists	metoclopramide HCl	Reglan®	A.H. Robins
	thiethylperazine maleate	Torecan®	Roxane Labs
	trimethobenzamide HCl	Tigan®	SmithKline Beecham
	prochlorperazine	Compazine®	SmithKline Beecham
	haloperidol	Haldol®	Ortho-McNeil
	domperidone	—	—
Antihistamines	promethazine HCl	Phenergan®	Wyeth-Ayerst
	hydroxyzine HCl	Atarax®	—
	cinnarizine	—	—
	cyclizine	—	—
Anticholinergics	dazopride	—	A.H. Robins
	scopolamine	Scopace®	Hope Pharmaceuticals

Serotonin Receptors and Systems

1985

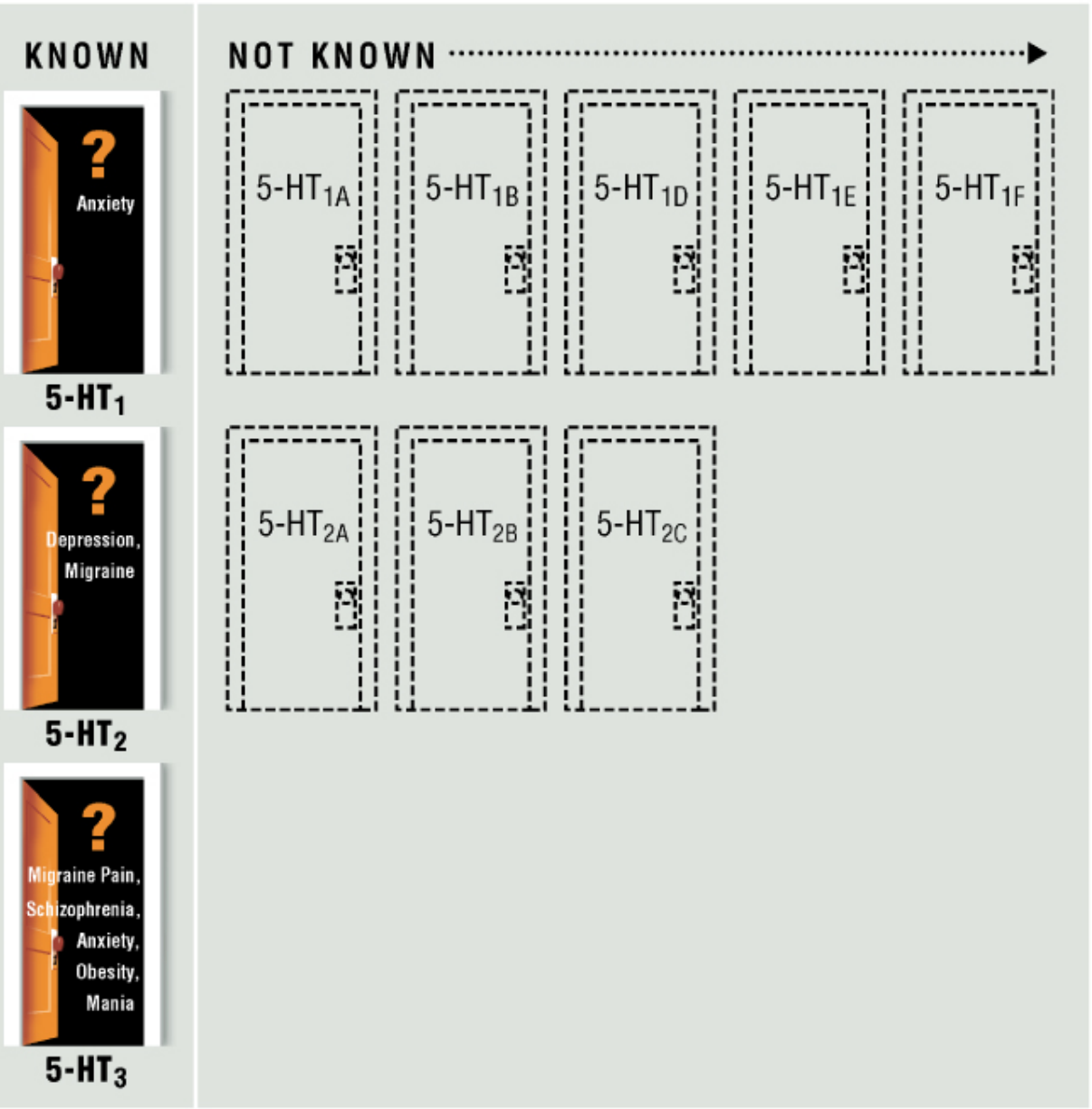
5-HT$_1$

5-HT$_2$

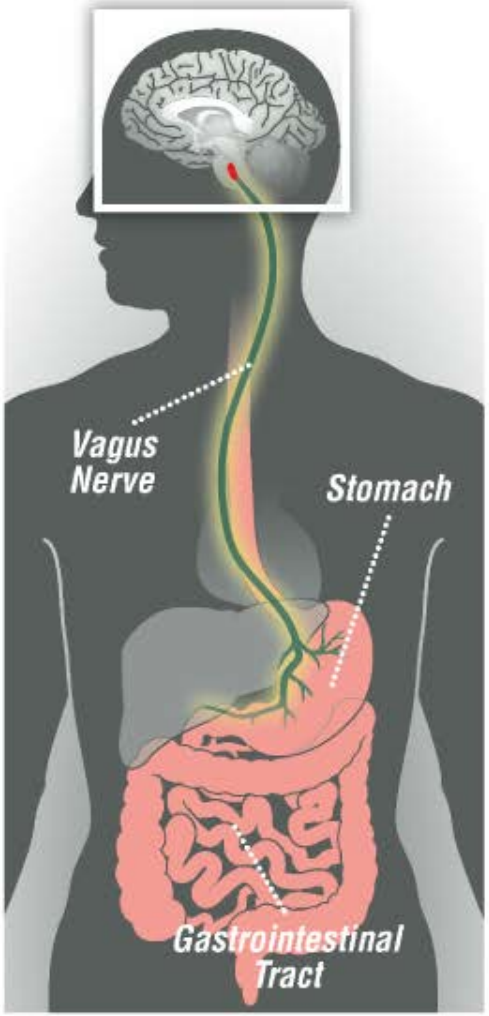
5-HT$_3$

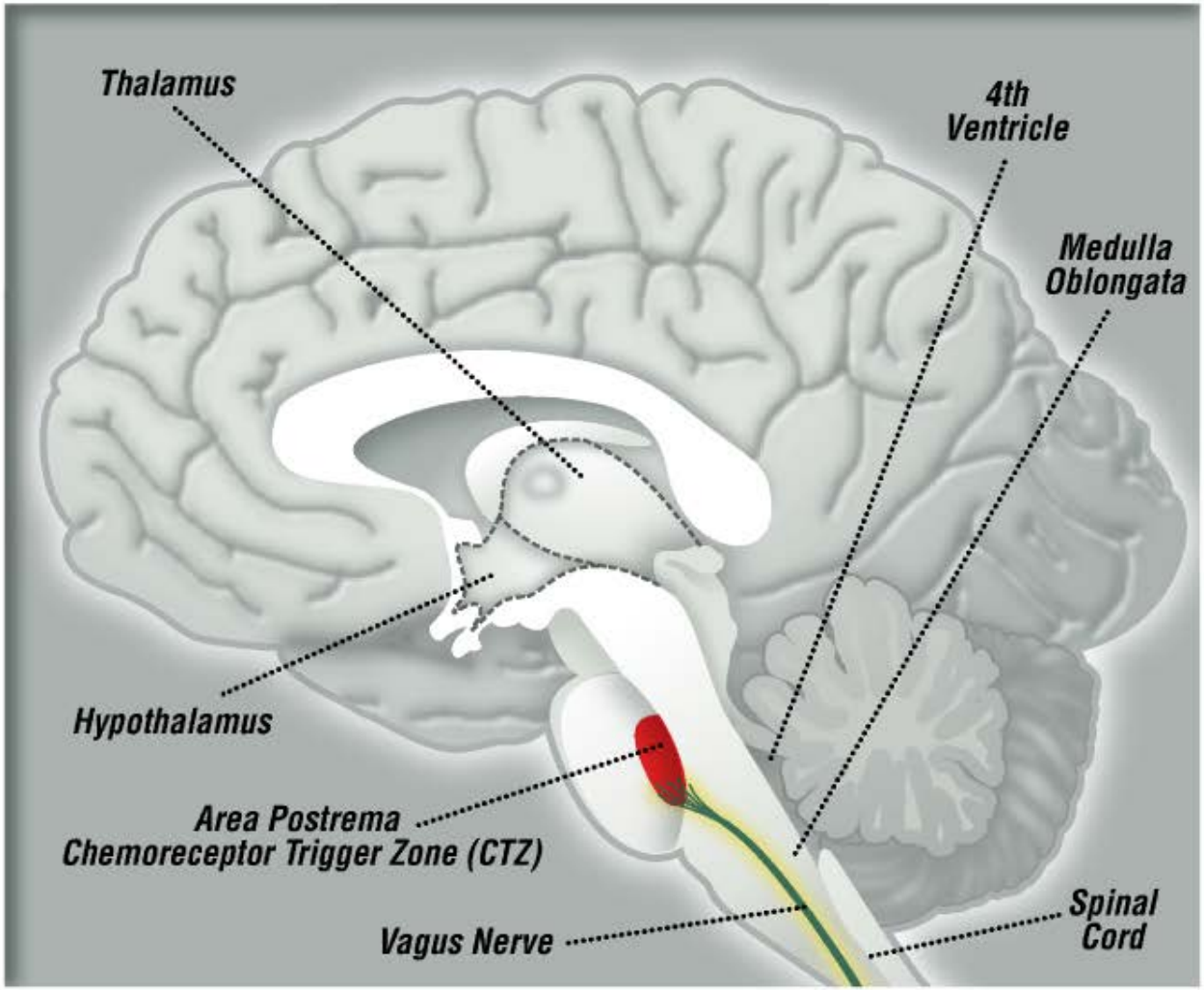
Serotonin Receptors and Systems

1985

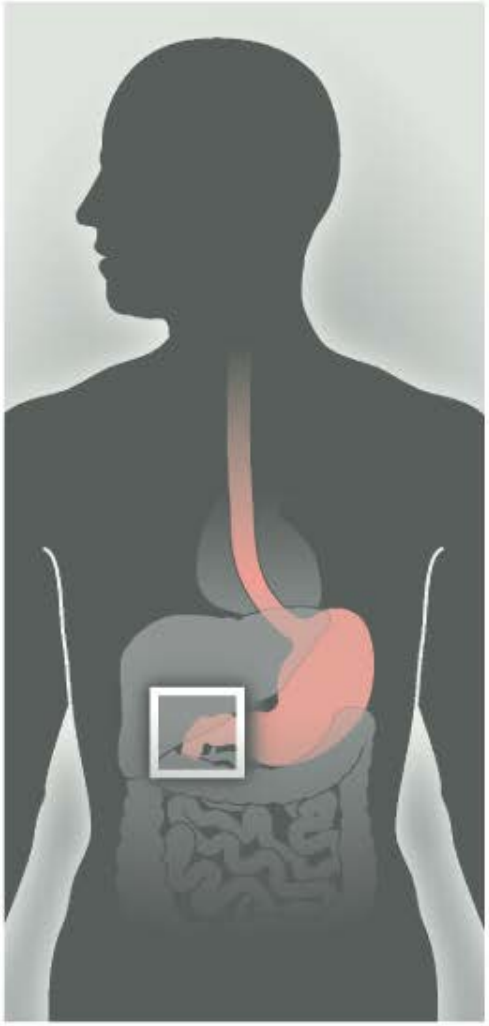


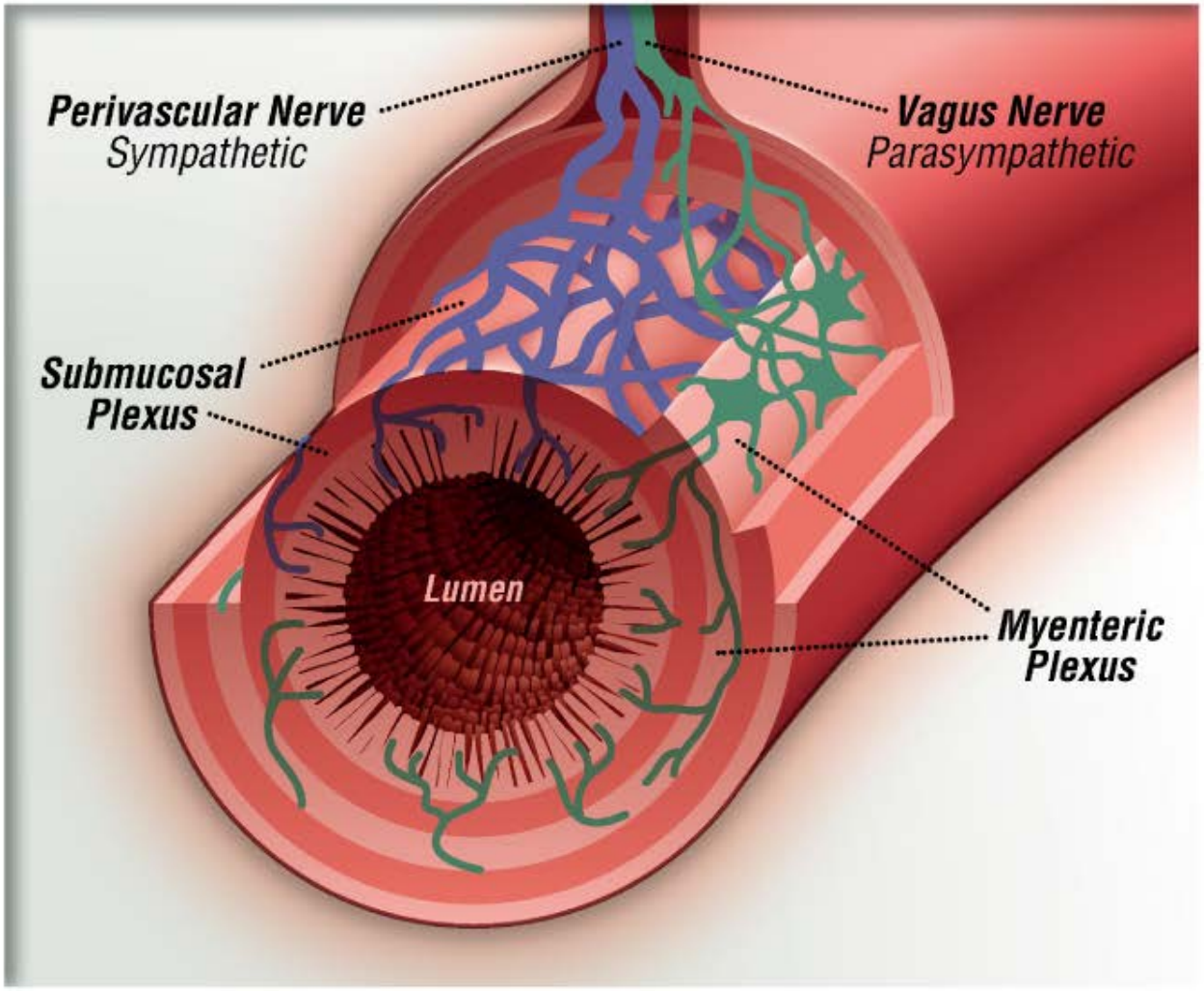
The Physiology of Emesis



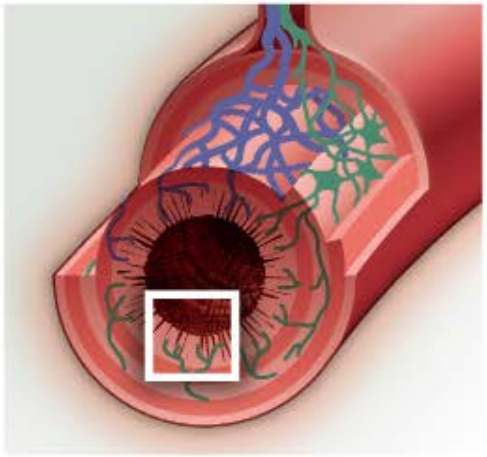


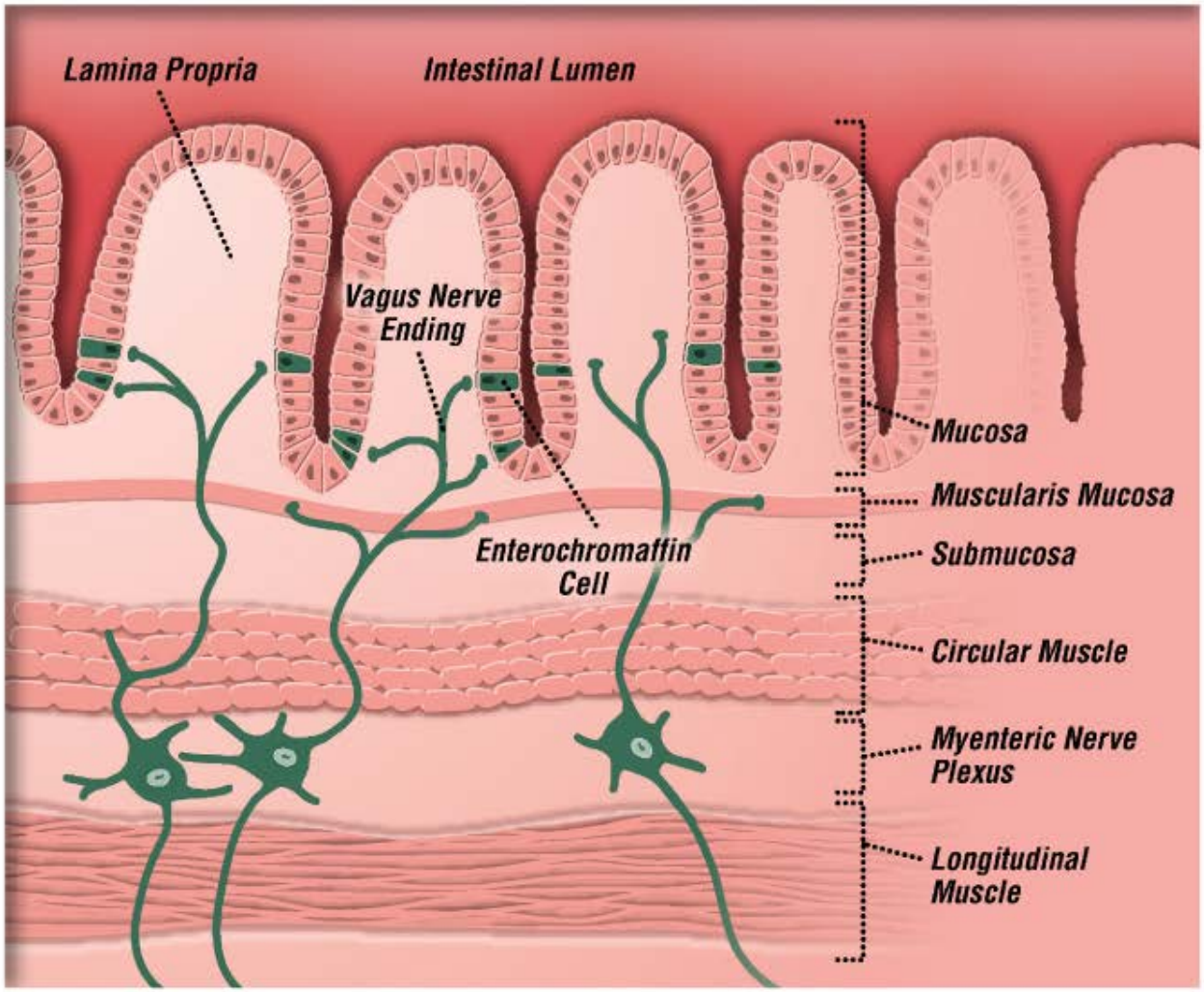
The Enteric Nervous System Is Composed of Two Ganglionated Plexuses





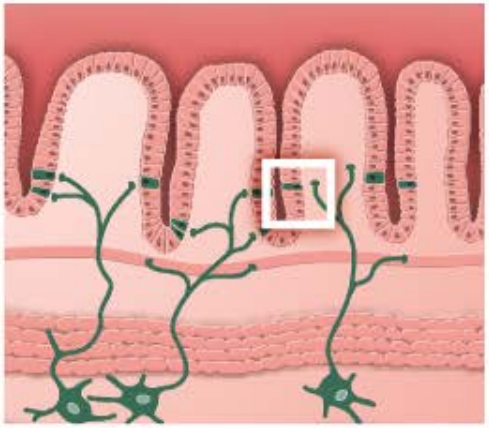
Specialized Cells in the Intestinal Wall

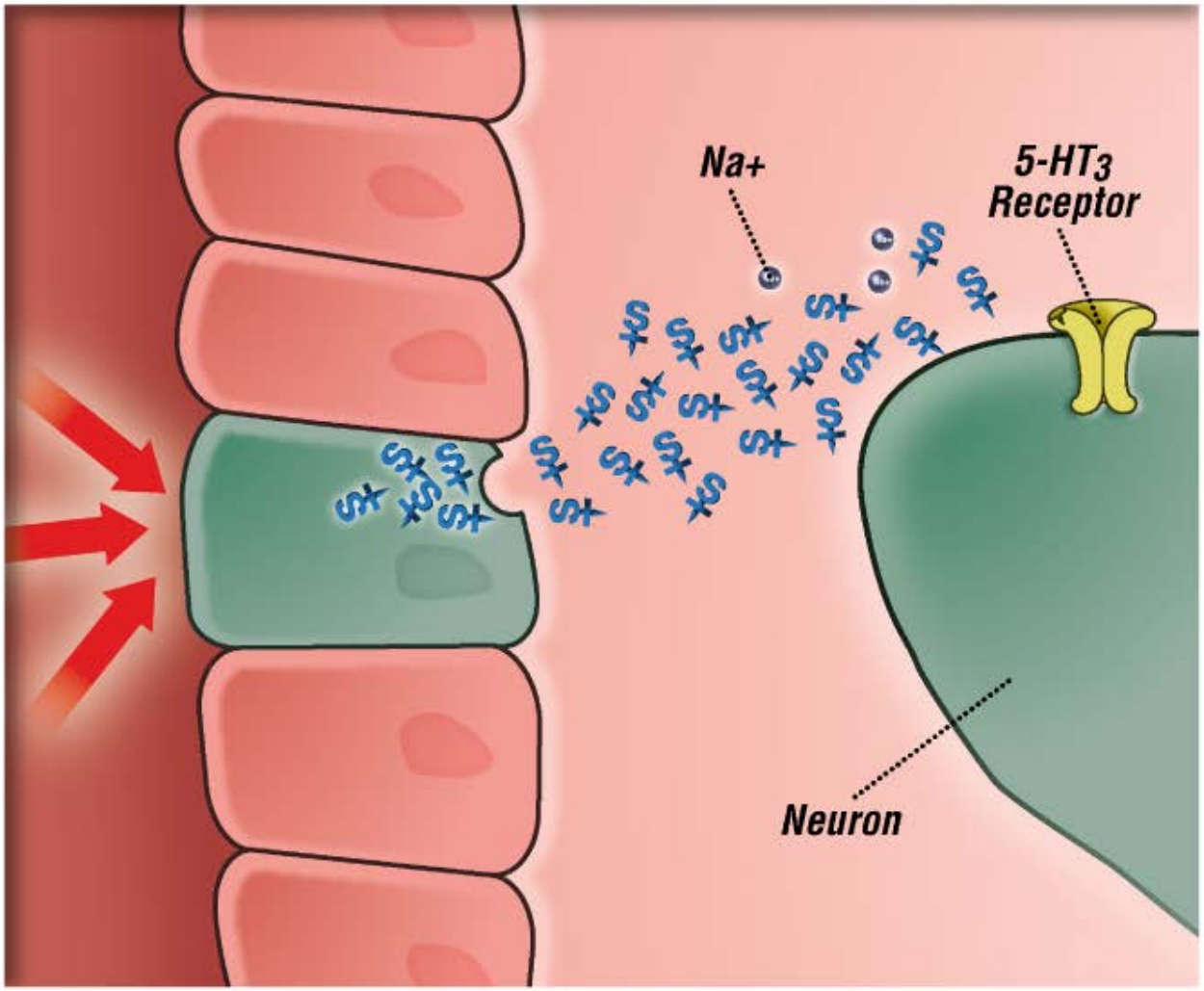




The Emetic Pathway

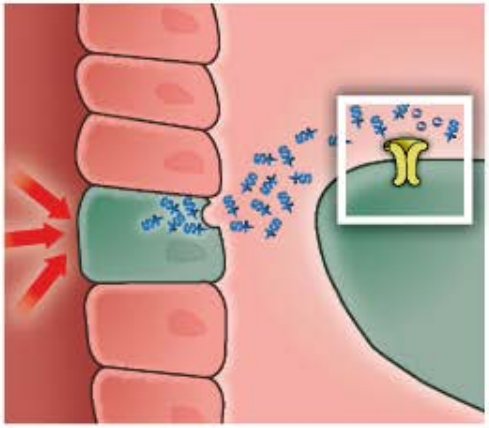
Chemotherapy agents and radiation cause the release of serotonin (5HT).

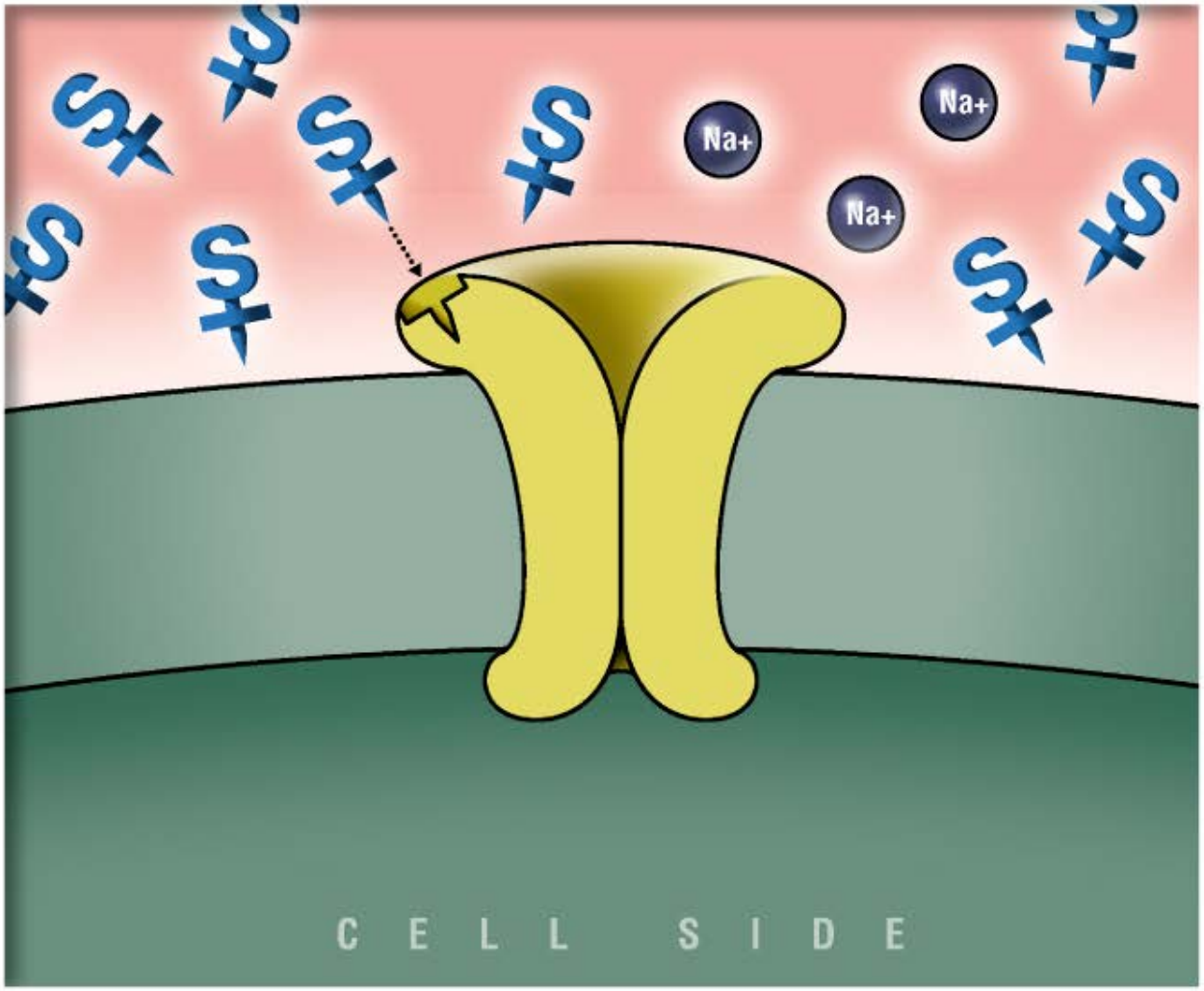




The Emetic Pathway

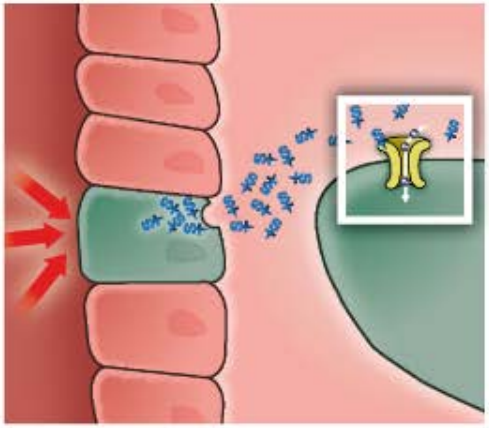
5-HT (Serotonin) binds to the 5-HT_3 receptor in the emetic pathway.

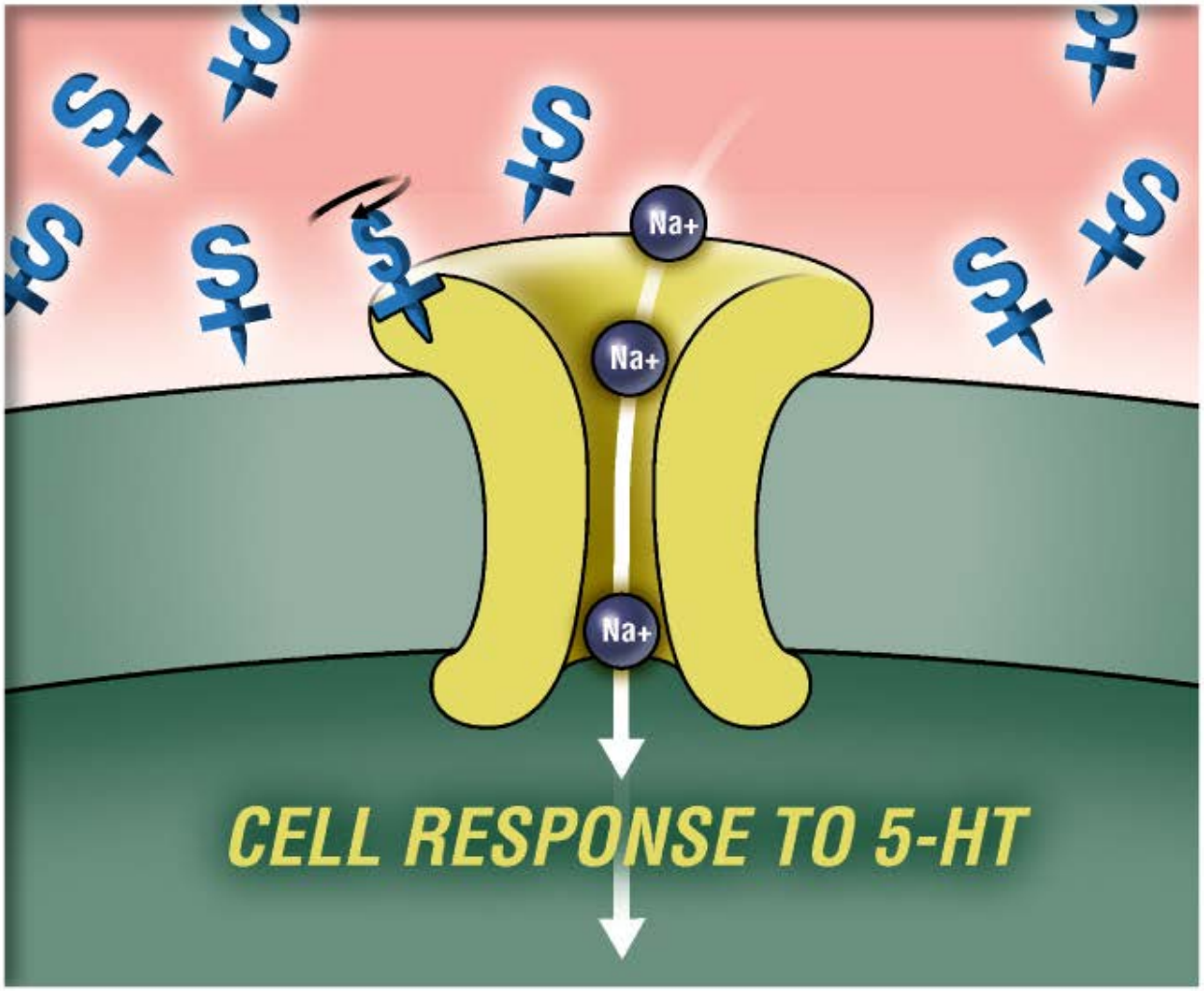




The Emetic Pathway

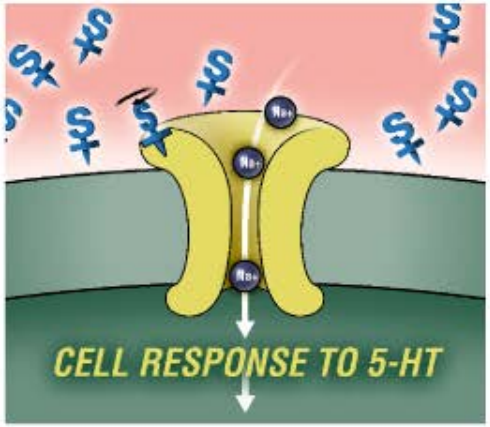
The 5-HT (serotonin) "key" opens the channel of the receptor, allowing charged particles to enter the cell.

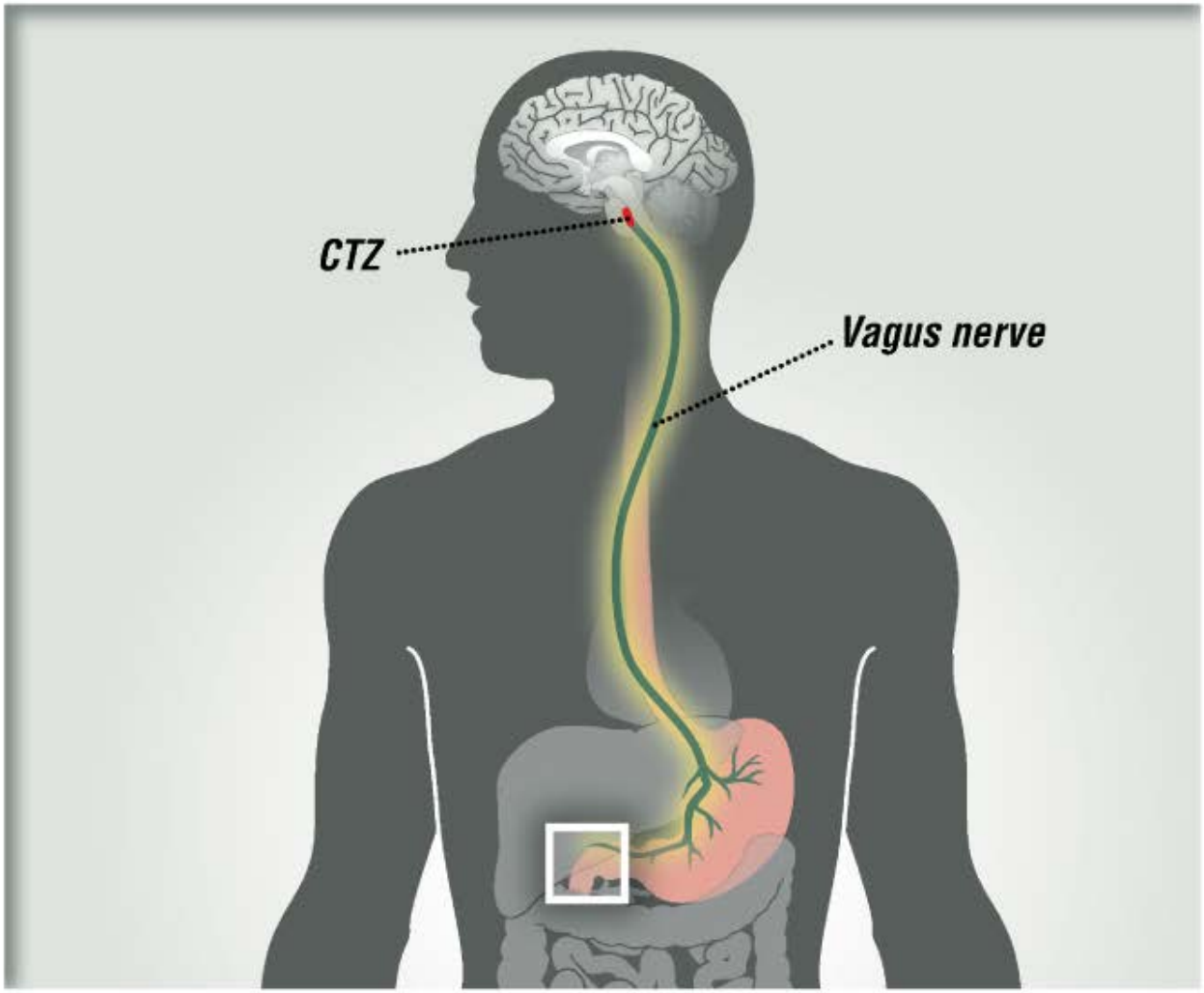




The Emetic Pathway

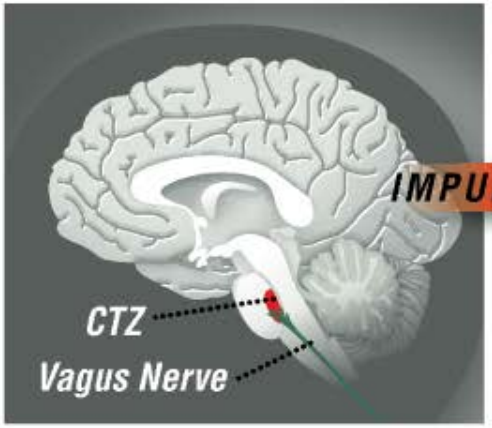
Activated vagal nerve cells send impulses (messages) to the CTZ (chemoreceptor trigger zone) in the vomiting center of the brain.

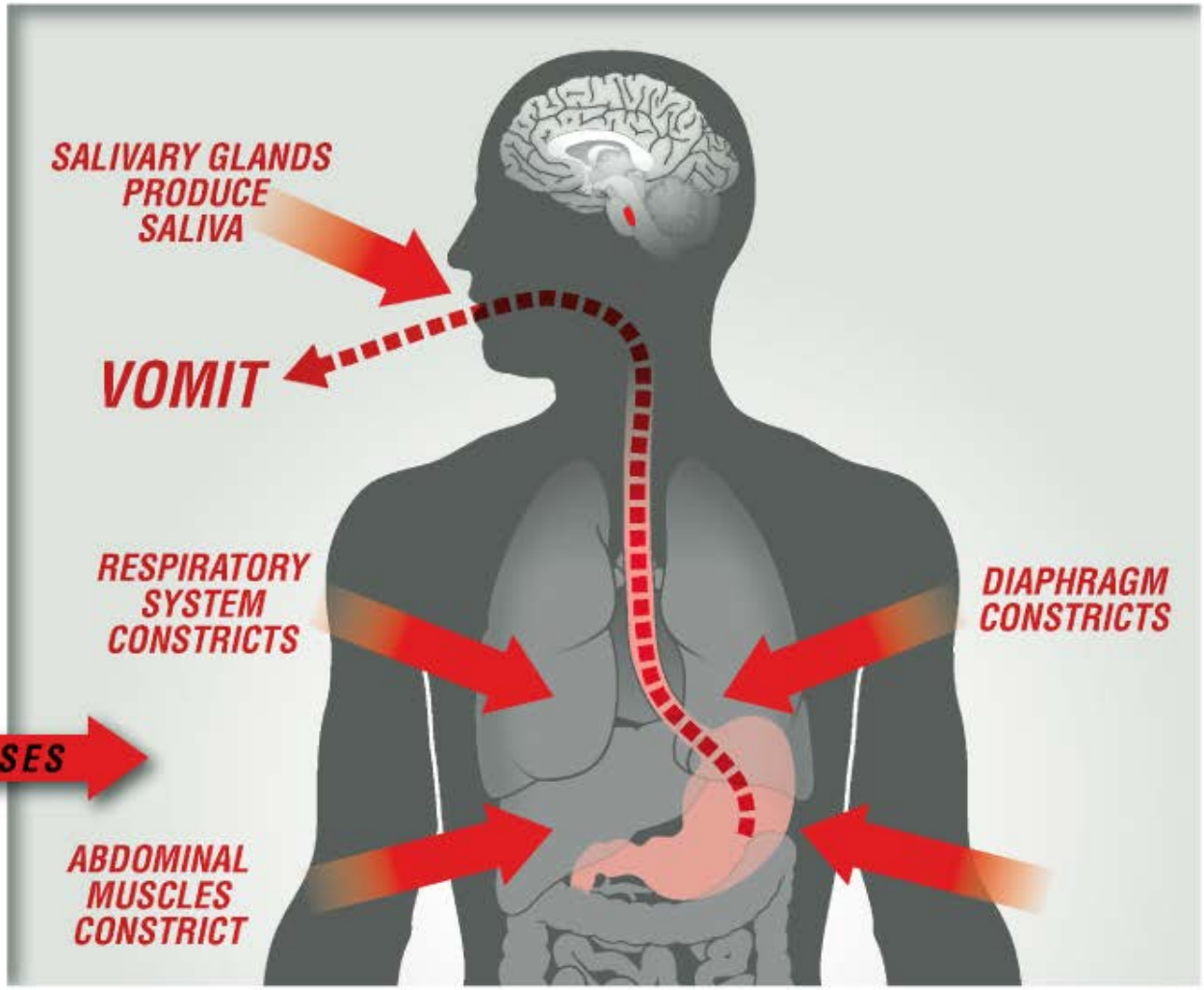




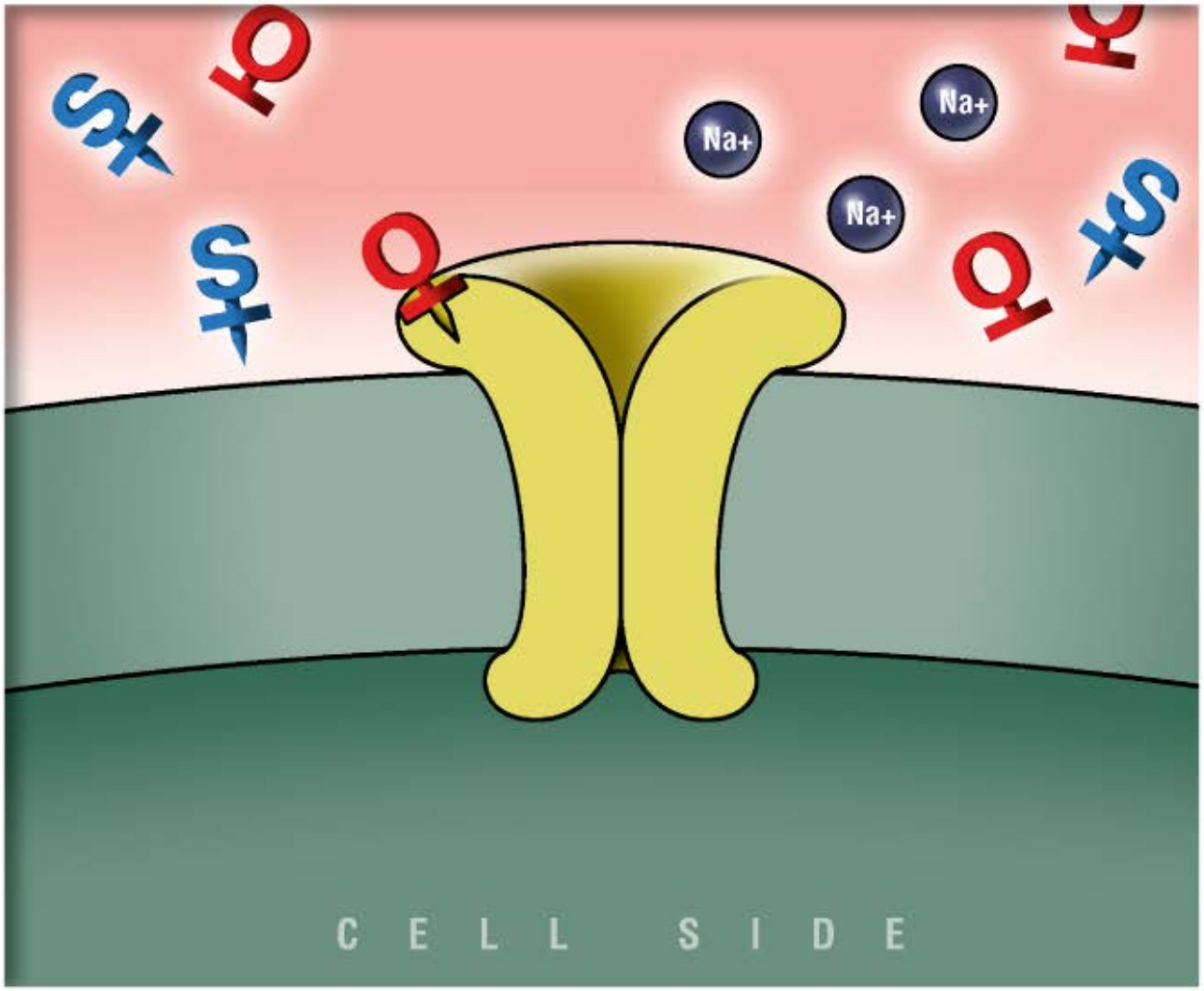
The Emetic Pathway

Impulses (messages) from the brain (CTZ) initiate the constriction of abdominal and respiratory muscles that cause emesis (vomiting).



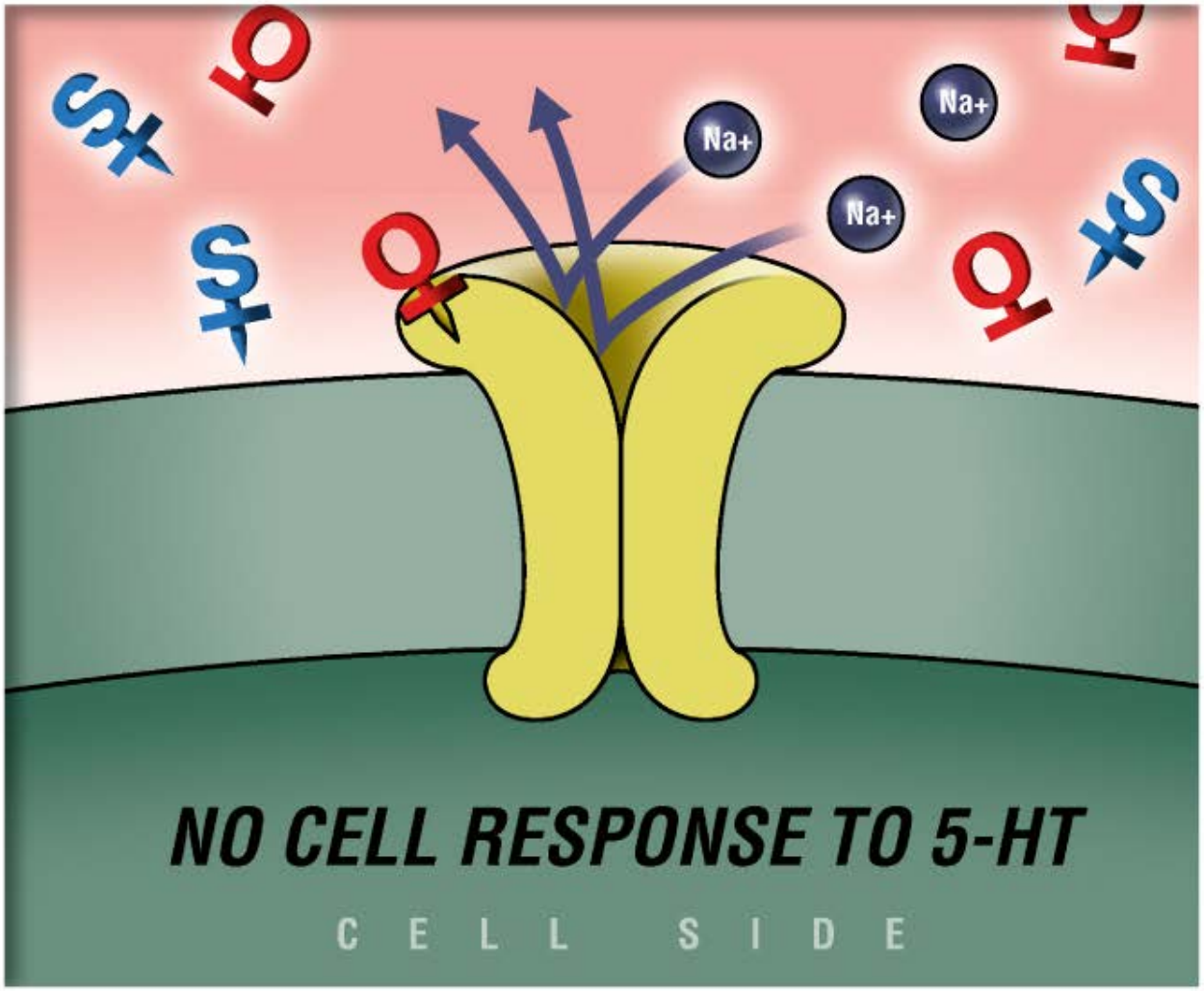


Ondansetron HCl Blocks the 5-HT_3 Receptor Inhibiting the Emetic Reflex



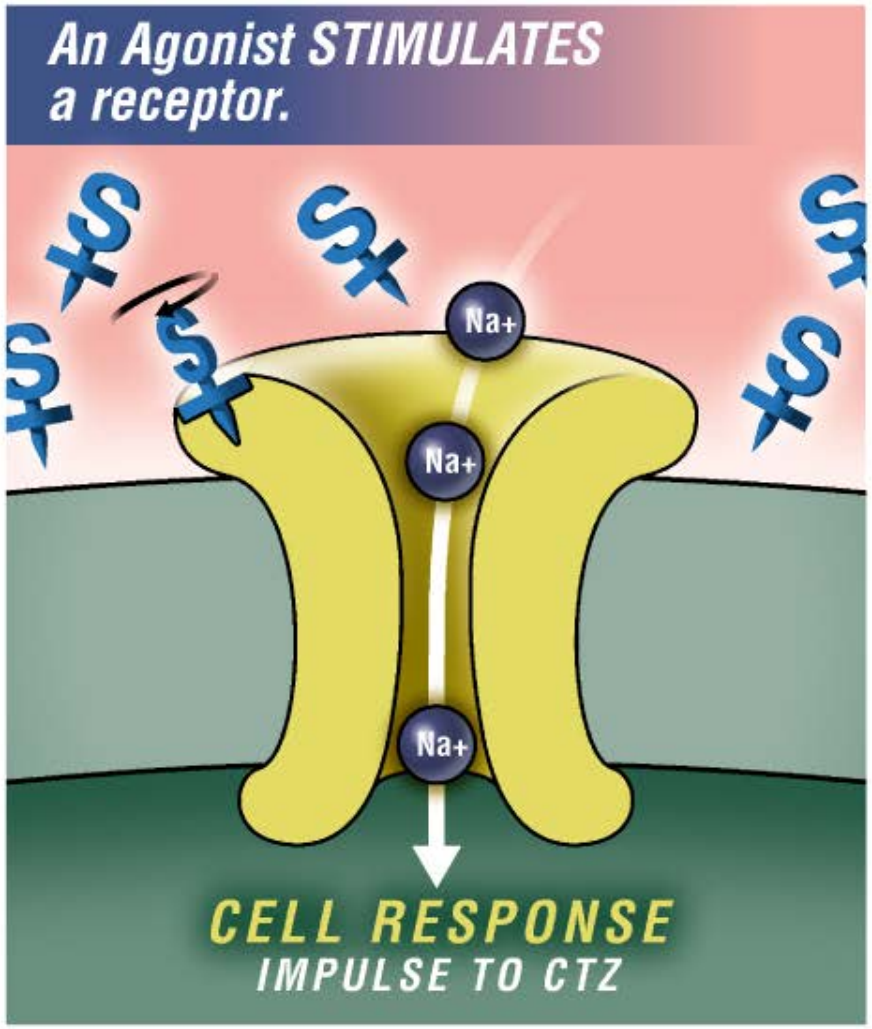
Ondansetron HCl Blocks the 5-HT_3 Receptor Inhibiting the Emetic Reflex

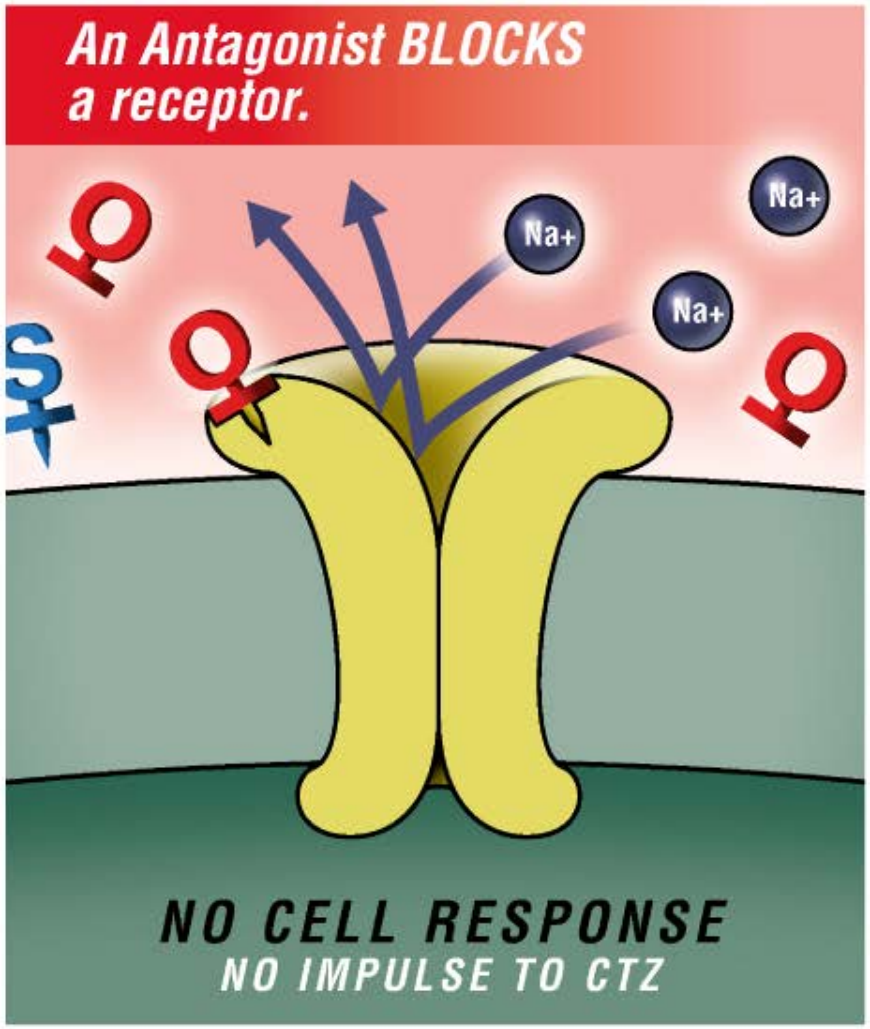
The 5-HT "key" cannot open the channel to the receptor. Charged particles ***CANNOT ENTER*** the cell.



Serotonin and Ondansetron HCl

Agonist versus Antagonist





Serotonin Receptors and Systems

2002

Jason Hannon, Daniel Hoyer; Acta Biol Szeged 46 (1–2): 1–12 (2002)