

Nausea, Vomiting, Bowel Obstruction

Gordon J. Wood, MD, MSCI, FAAHPM
Coleman Palliative Care Intensive
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Objectives

- Describe a three step approach to the management of N/V at the end of life
- Identify strategies to manage refractory N/V in persons near the end of life
- Describe how to medically manage a malignant bowel obstruction



Mechanism-Based Therapy

1. Careful assessment to determine etiology
2. Use knowledge of pathophysiology to determine receptors underlying symptoms
3. Choose antiemetic to block implicated receptors

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Evaluation

- History
- Physical examination

...think “Head-to-Toe”

Evaluation

- Laboratory Testing
 - What labs should you consider?
- Radiology
 - What imaging should you consider?

Evaluation

- Confident in cause of N/V in 45 of 61 hospice patients
- Chemical abnormalities 33% (metabolic, drugs, infection)
- Impaired gastric emptying 44%
- Visceral and serosal causes 31% (bowel obstruction, GI bleed, enteritis, constipation)

Evaluation

- 40 patient episodes of nausea and/or vomiting on inpatient palliative care unit
- 59 reversible etiologies
 - 51% medications
 - 11% constipation

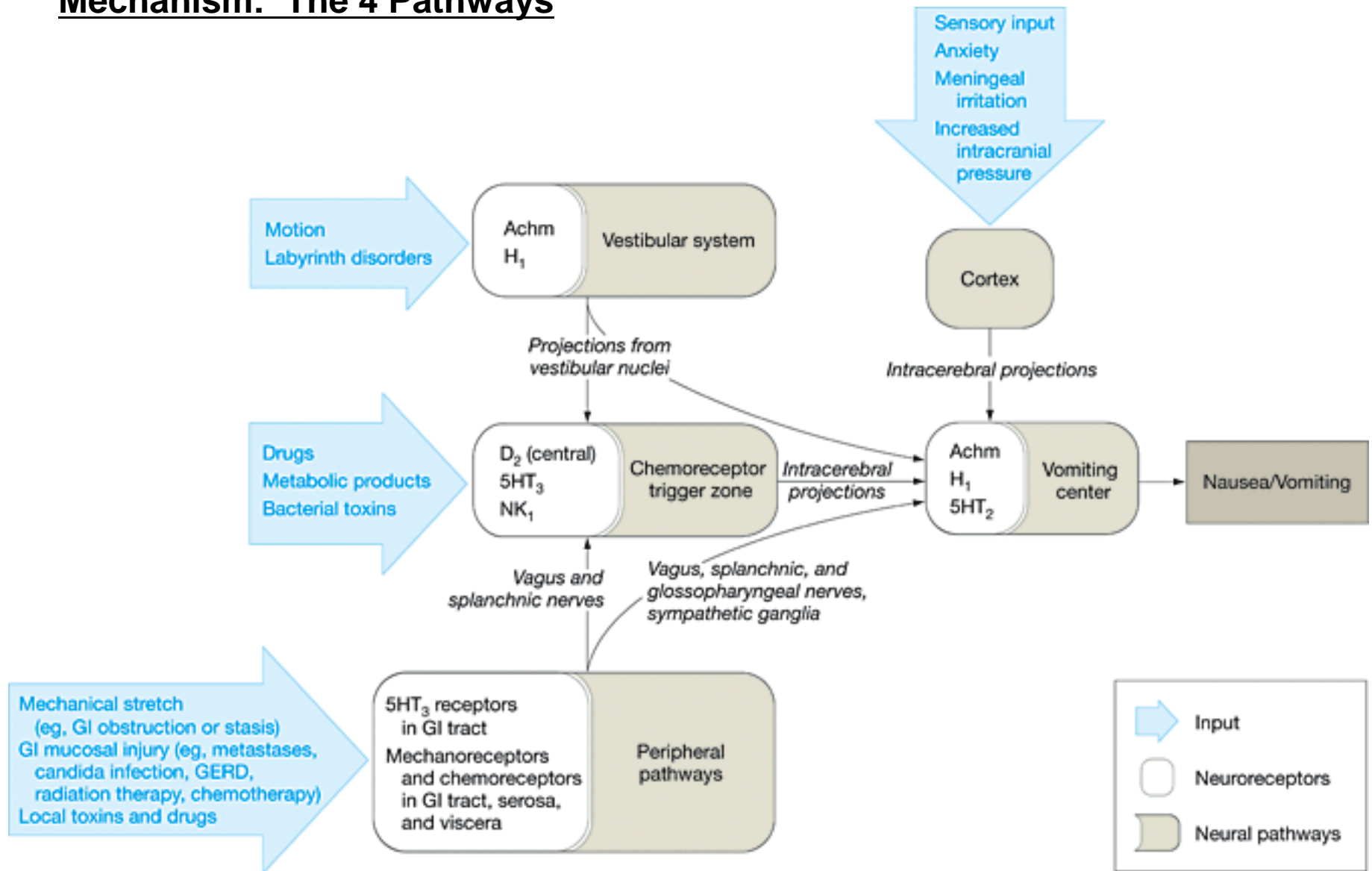
Mechanism-Based Therapy

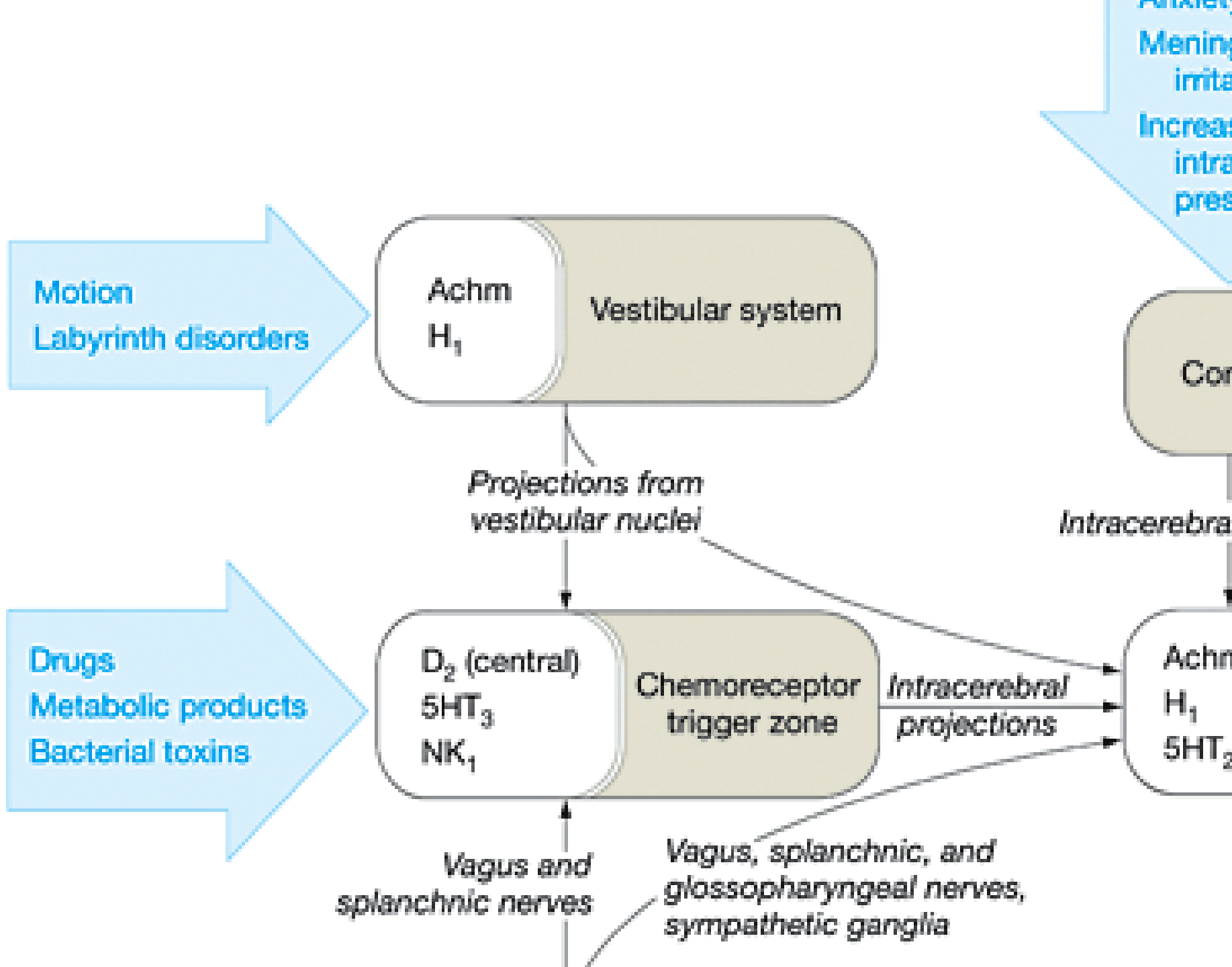
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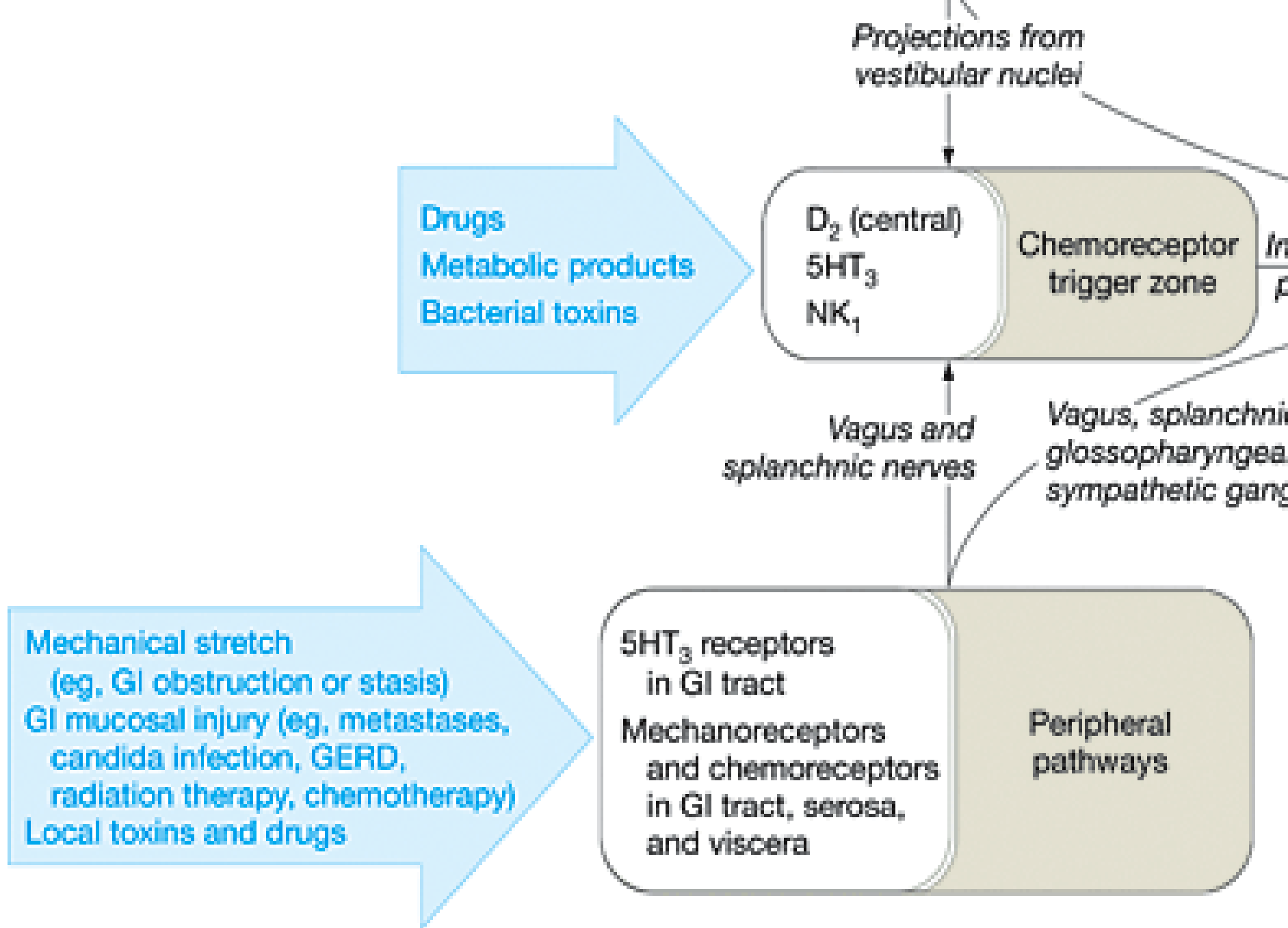
Mechanism: The 4 Pathways

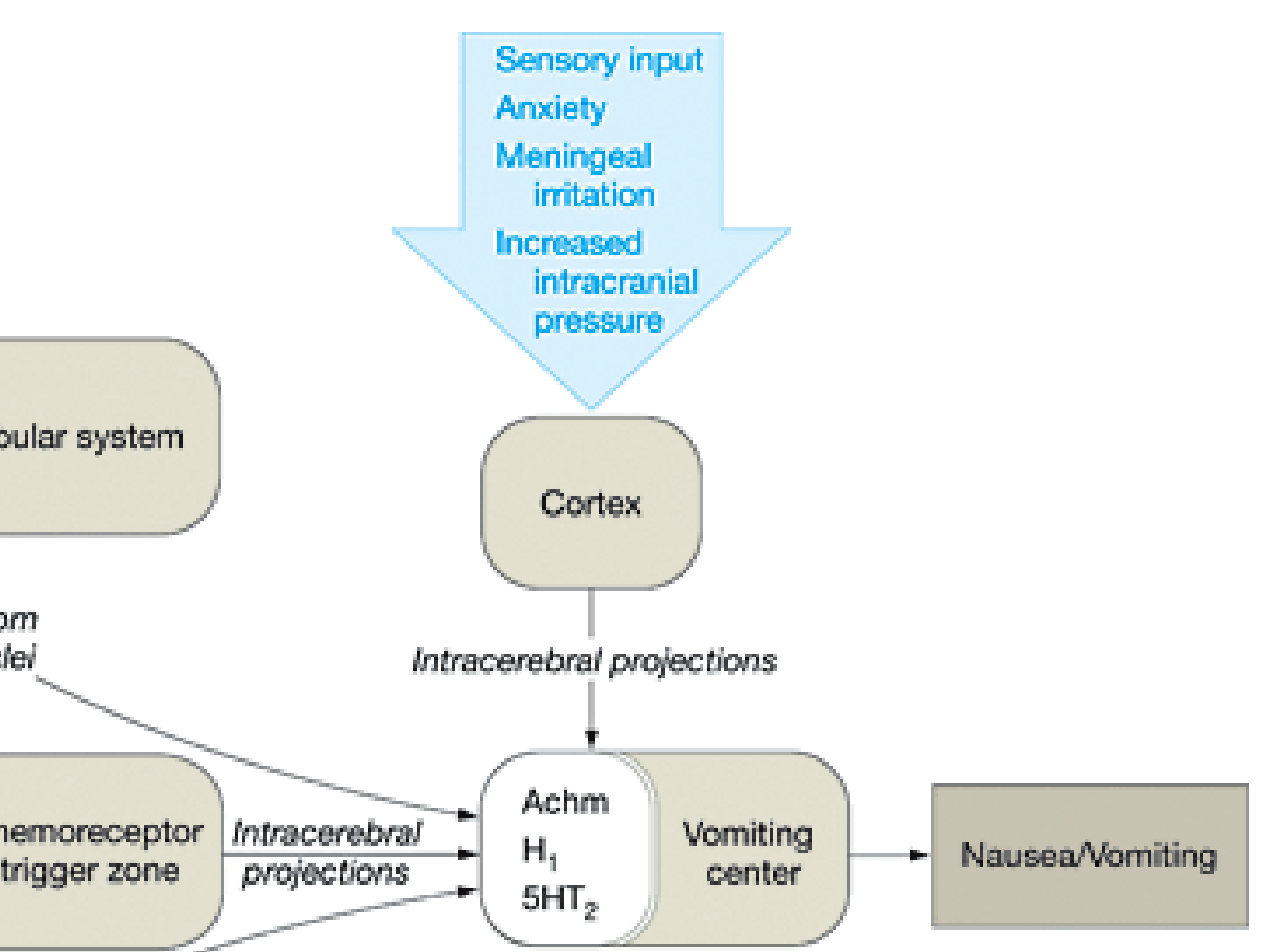
1. Chemoreceptor Trigger Zone
2. Cortex
3. Peripheral Pathways
4. Vestibular System

Mechanism: The 4 Pathways

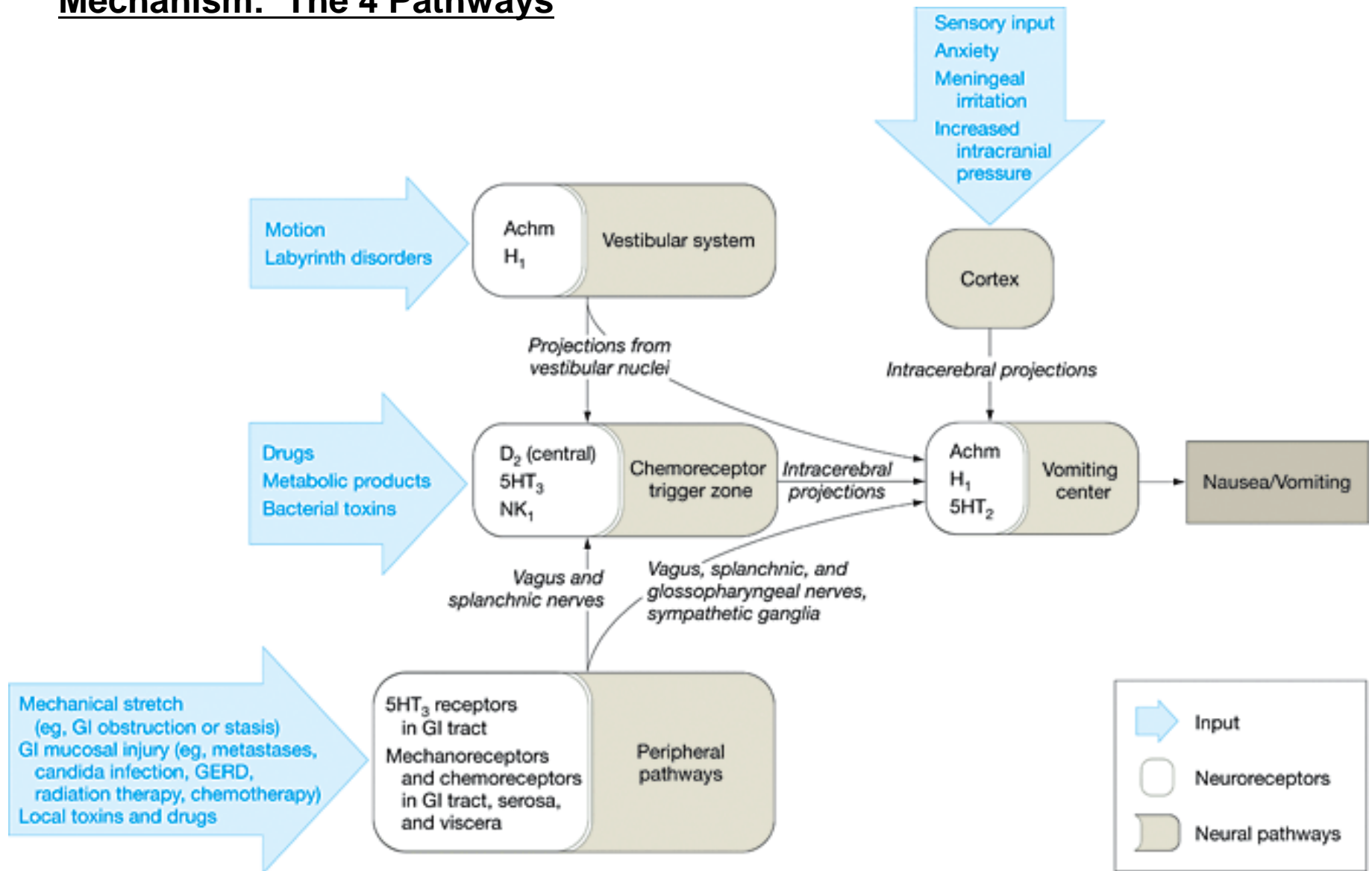








Mechanism: The 4 Pathways



Mechanism-Based Therapy

1. Careful assessment to determine etiology
2. Use knowledge of pathophysiology to determine receptors underlying symptoms
3. **Choose antiemetic to block implicated receptors**

Antiemetics

Antiemetic	Receptor Anatagonized
Metoclopramide (Reglan)	?
Haloperidol (Haldol)	?
Prochlorperazine (Compazine)	?
Chlorpromazine (Thorazine)	?
Promethazine (Phenergan)	?

Antiemetics: Continued

Antiemetic	Receptor Anatagonized
Diphenhydramine (Benadryl)	?
Scopolamine (Transderm Scop)	?
Hyoscyamine (Levsin)	?
Ondansetron (Zofran)	?
Mirtazapine (Remeron)	?

Mechanism-Based Therapy

- 40 patient episodes of N/V in inpatient palliative care unit
- Most common causes: gastric stasis/outlet obstruction (35%), chemical/metabolic (30%)
- Nausea resolved in 28 of 34 cases (82%)
- Vomiting resolved in 26 of 31 cases (84%)
- Total symptom control in mean of 3.4 days

Empiric Treatment

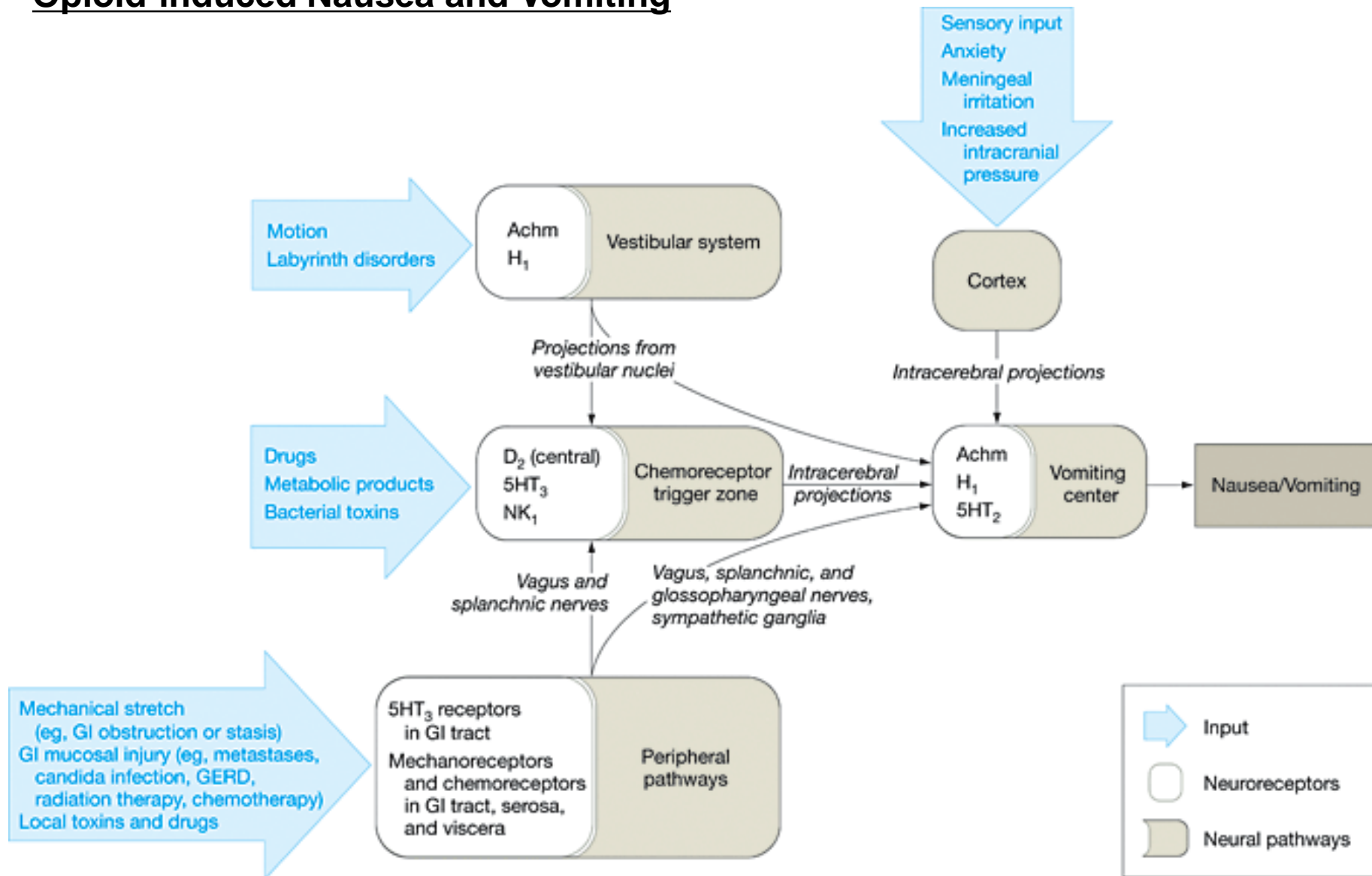
- Mechanism-based therapy effective^{1,2}
- Some advocate empiric D2 antagonists³ in all cases
- No head-to-head comparison
- D2 antagonists are our first choice in acutely symptomatic patients undergoing workup

1. Stephenson J et al. Support Care Cancer. 2006;14(4):348-353.
2. Lichter I et al. J Palliat Care. 1993;9(2):19-21.
3. Bruera E et al. J Pain Symptom Manage. 1996;11(3):147-153.

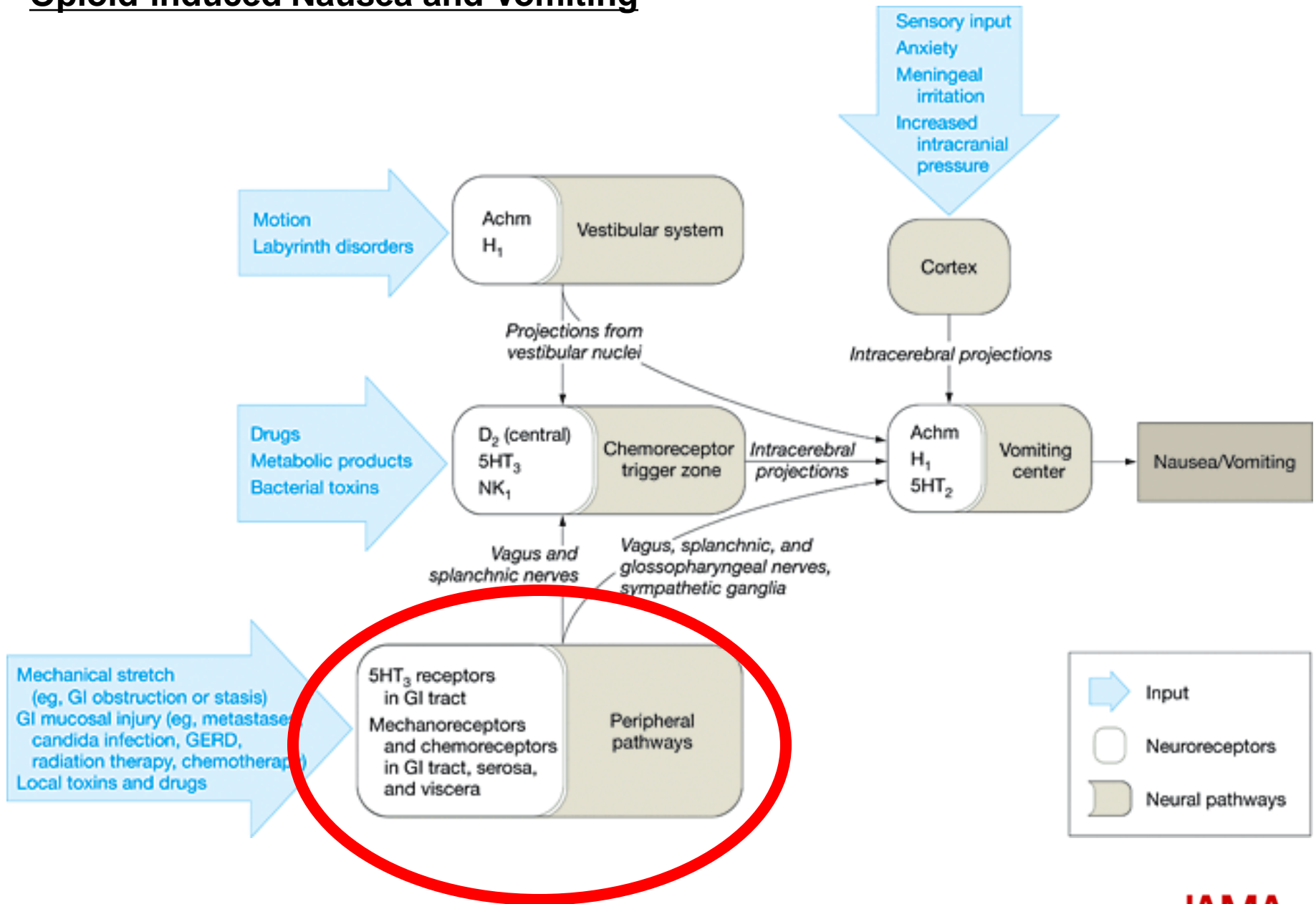
Benefits of mechanism-based therapy

- Potentially more effective in certain scenarios
- Facilitates systematic approach that identifies all possible contributors
- Guides treatment of underlying causes
- Informs choices of second and third antiemetics
- Minimizes risks of side-effects

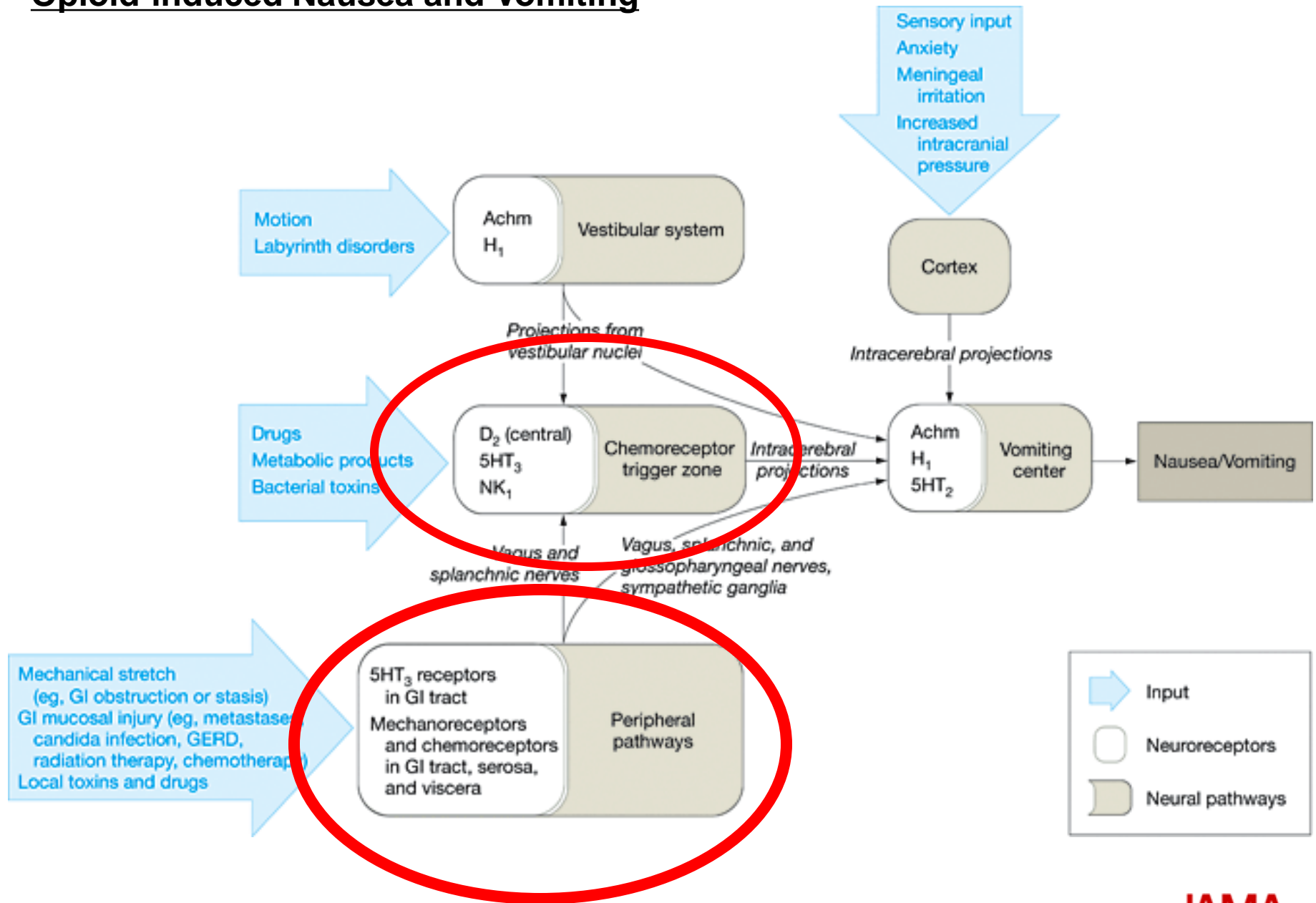
Opioid-induced Nausea and Vomiting



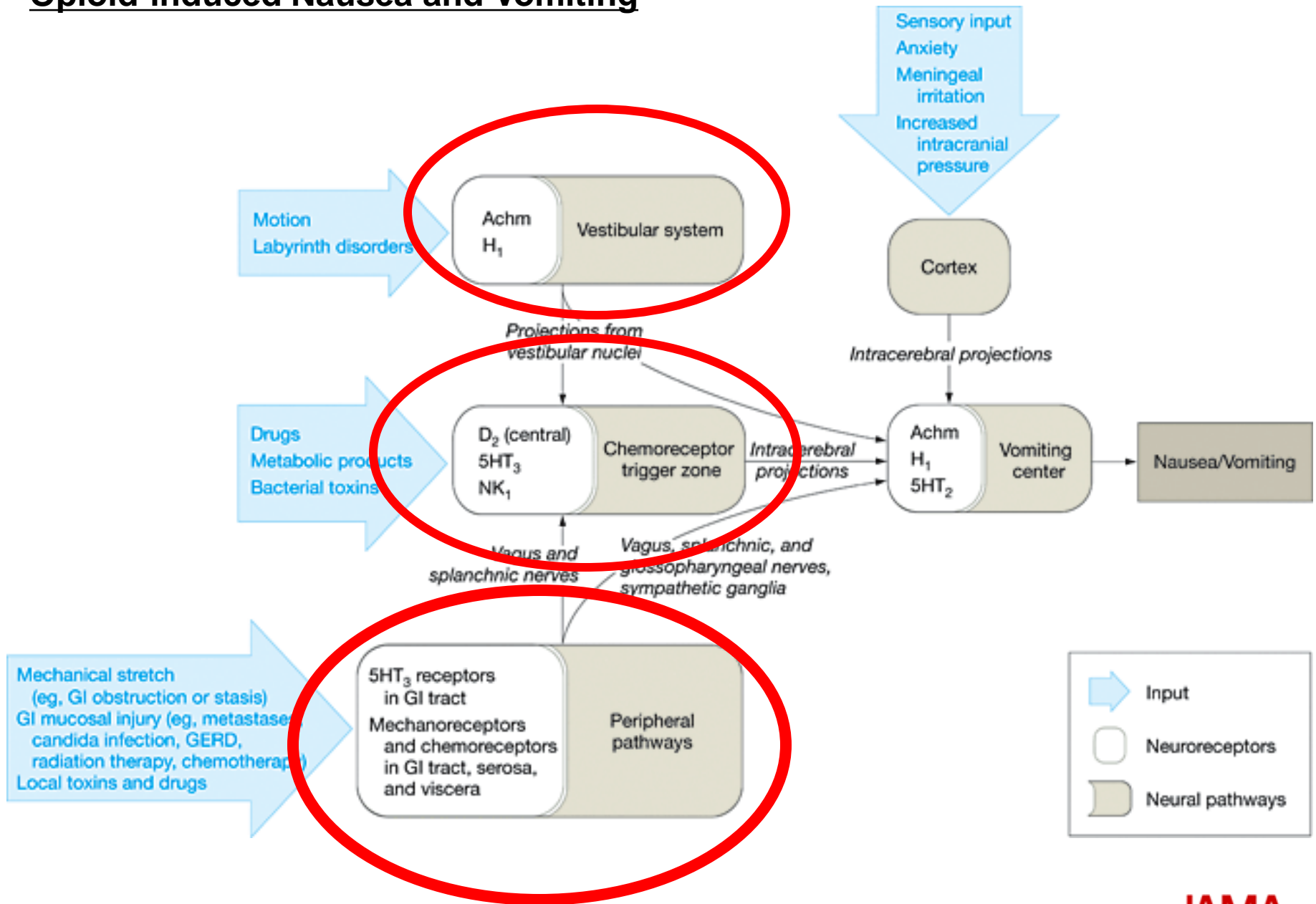
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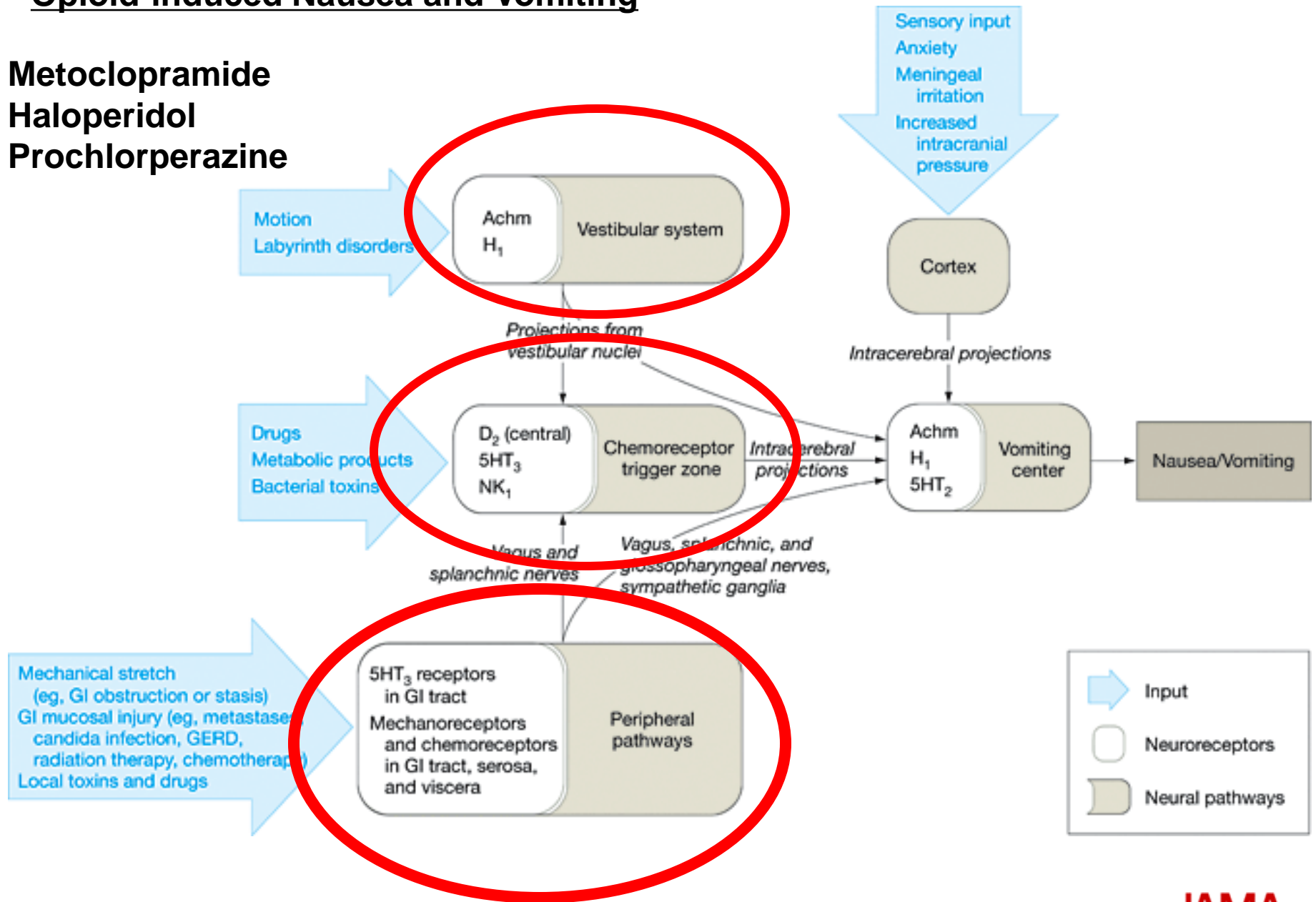
Opioid-induced Nausea and Vomiting



Wood, G. J. et al. JAMA 2007;298:1196-1207.

Opioid-induced Nausea and Vomiting

Metoclopramide
Haloperidol
Prochlorperazine



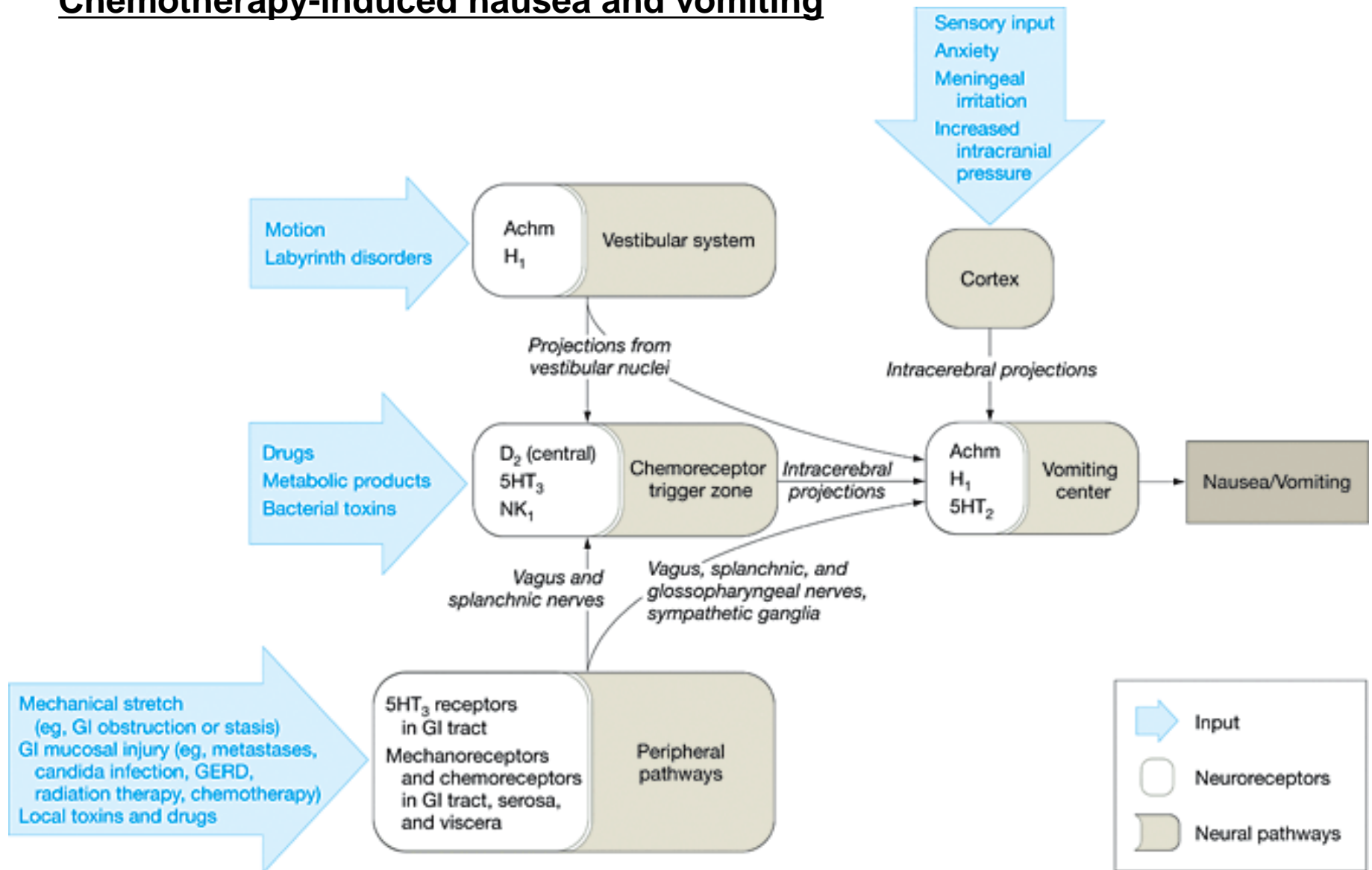
Opioid-Induced N/V

- D2 antagonists first-line
- Generally resolves within 3-5 days of continued use
- 10-20% dose reduction may alleviate nausea without loss of analgesia¹
- Opioid rotation also effective²

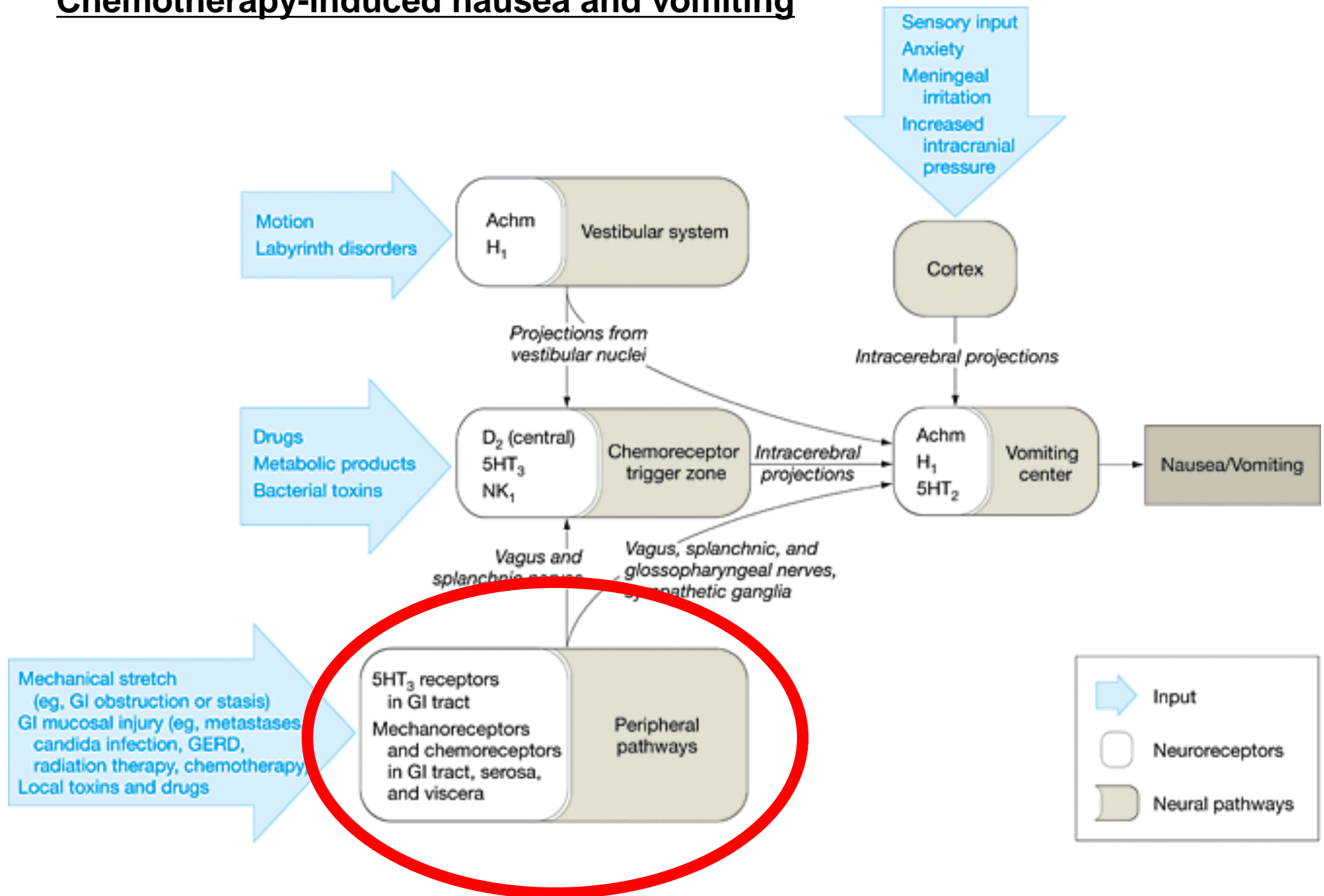
1. Fallon MT et al. BMJ. 1998;317(7150):81.

2. De Soutz ND et al. J Pain Symptom Manage. 1995;10(5):378-384.

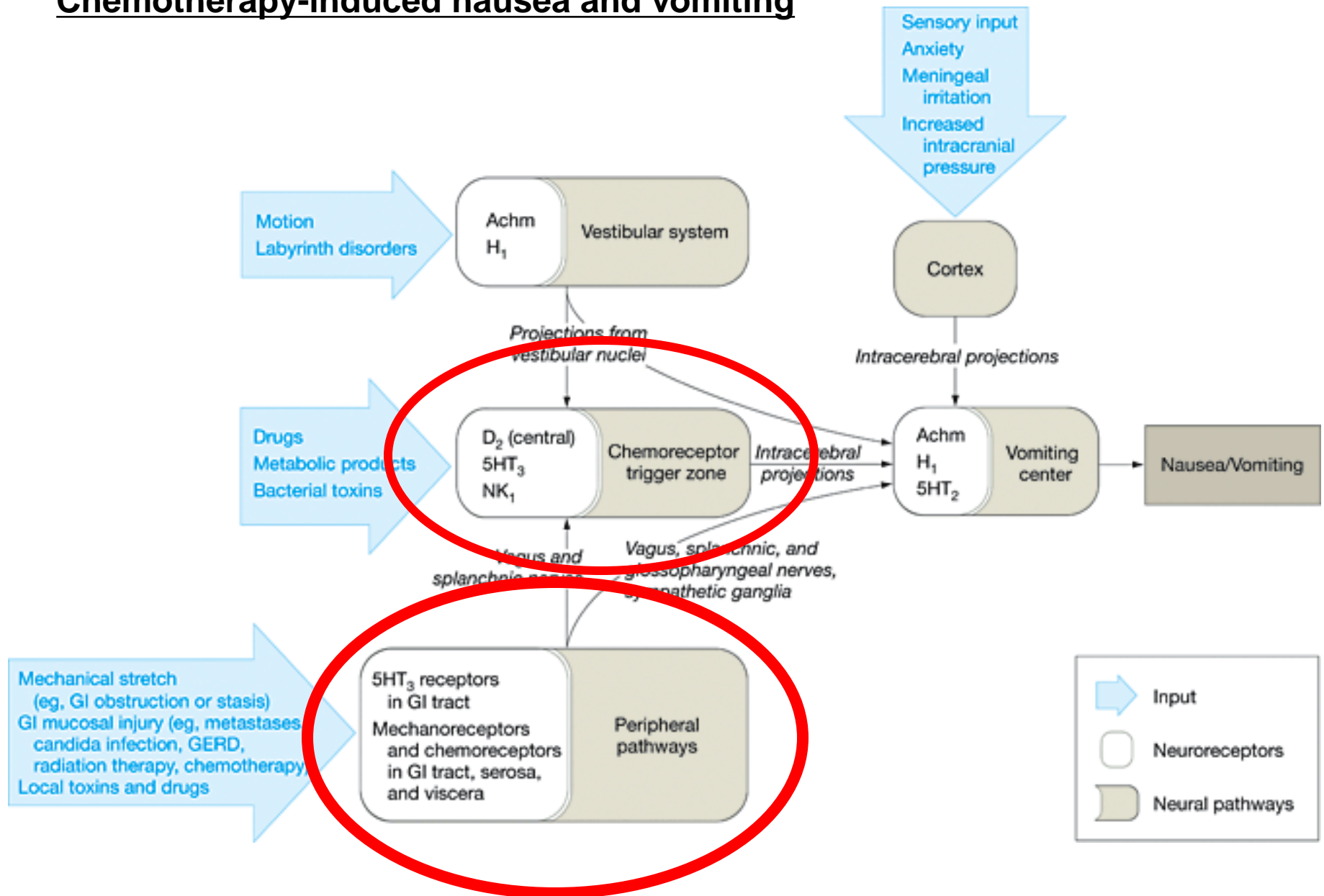
Chemotherapy-induced nausea and vomiting



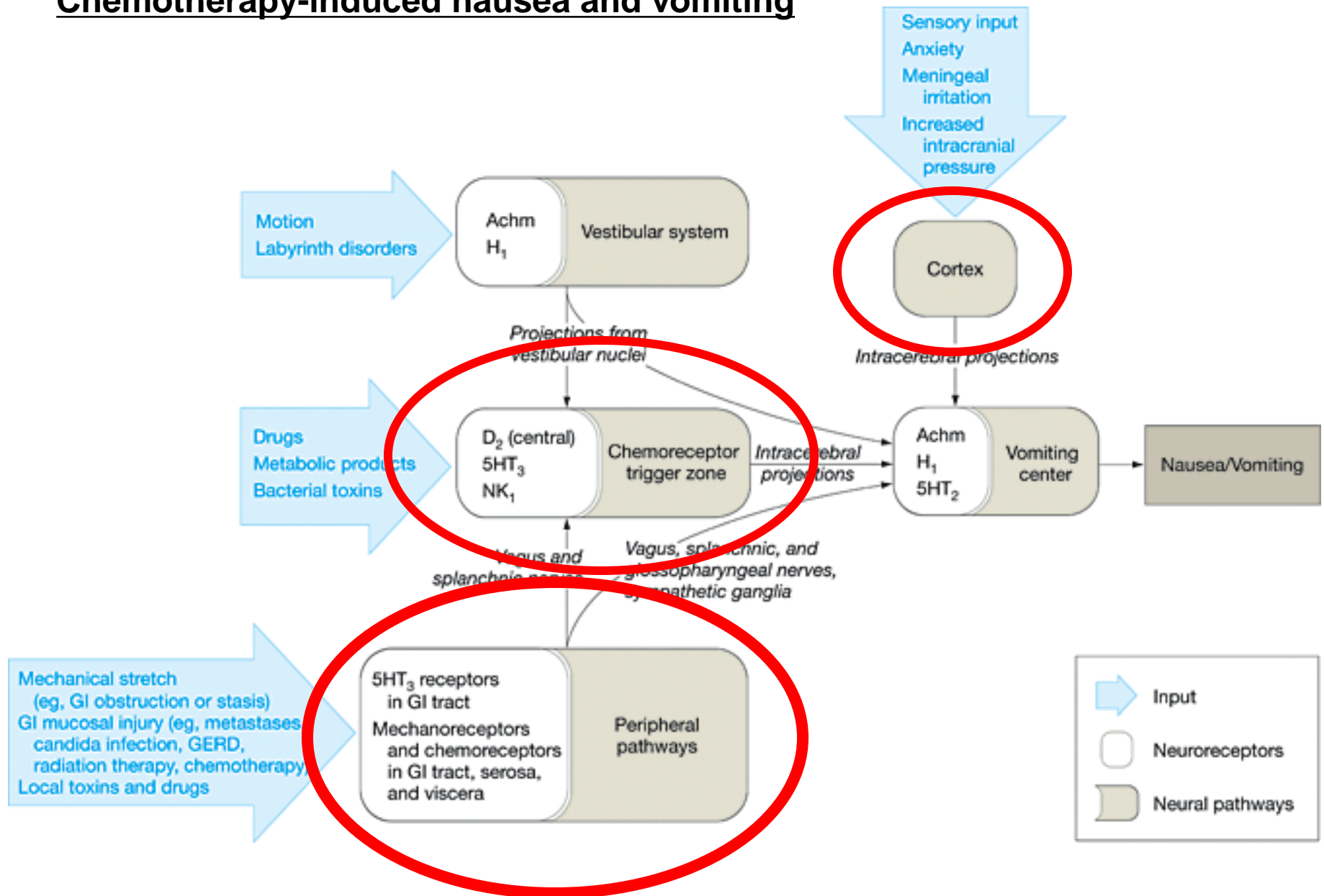
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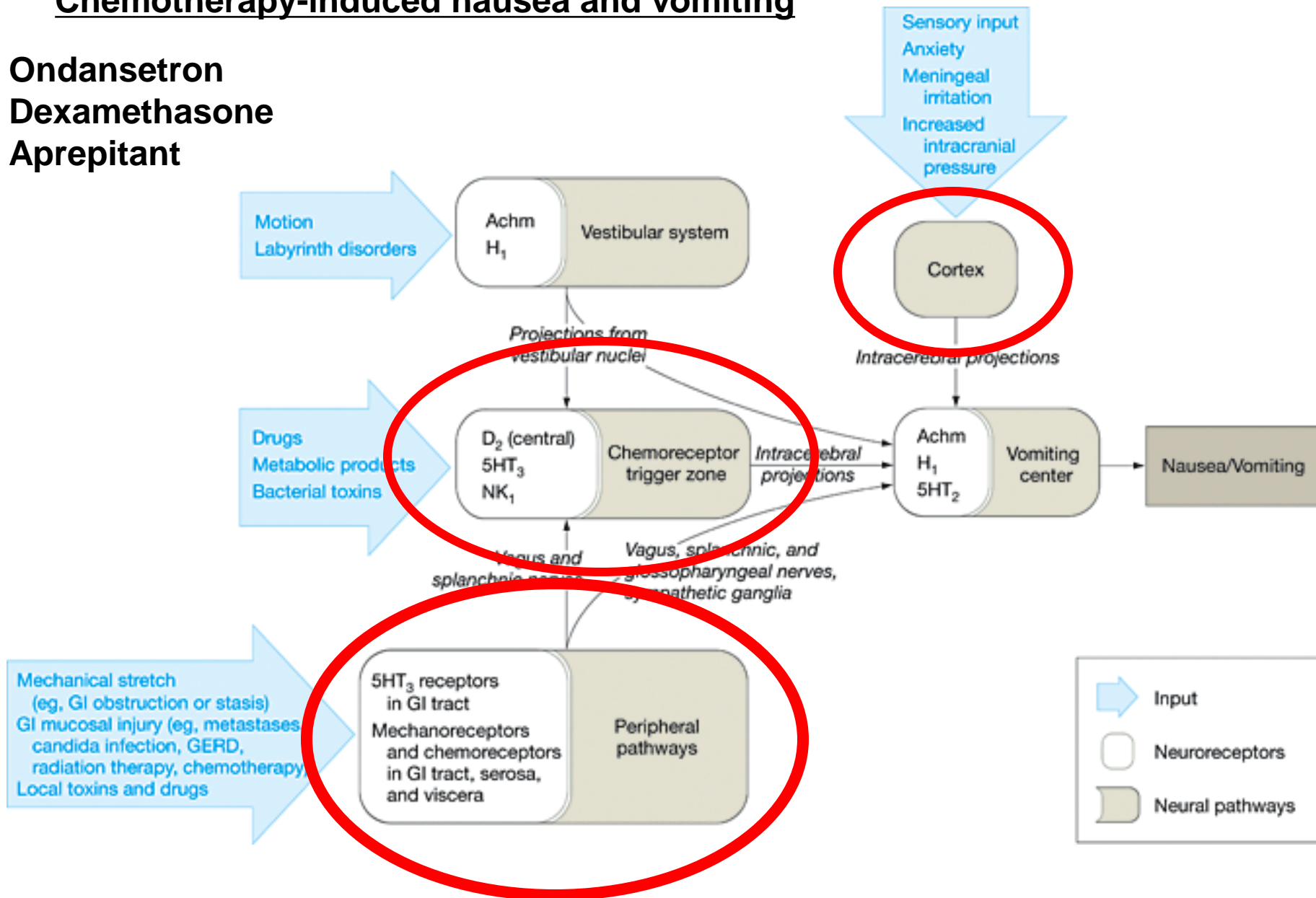


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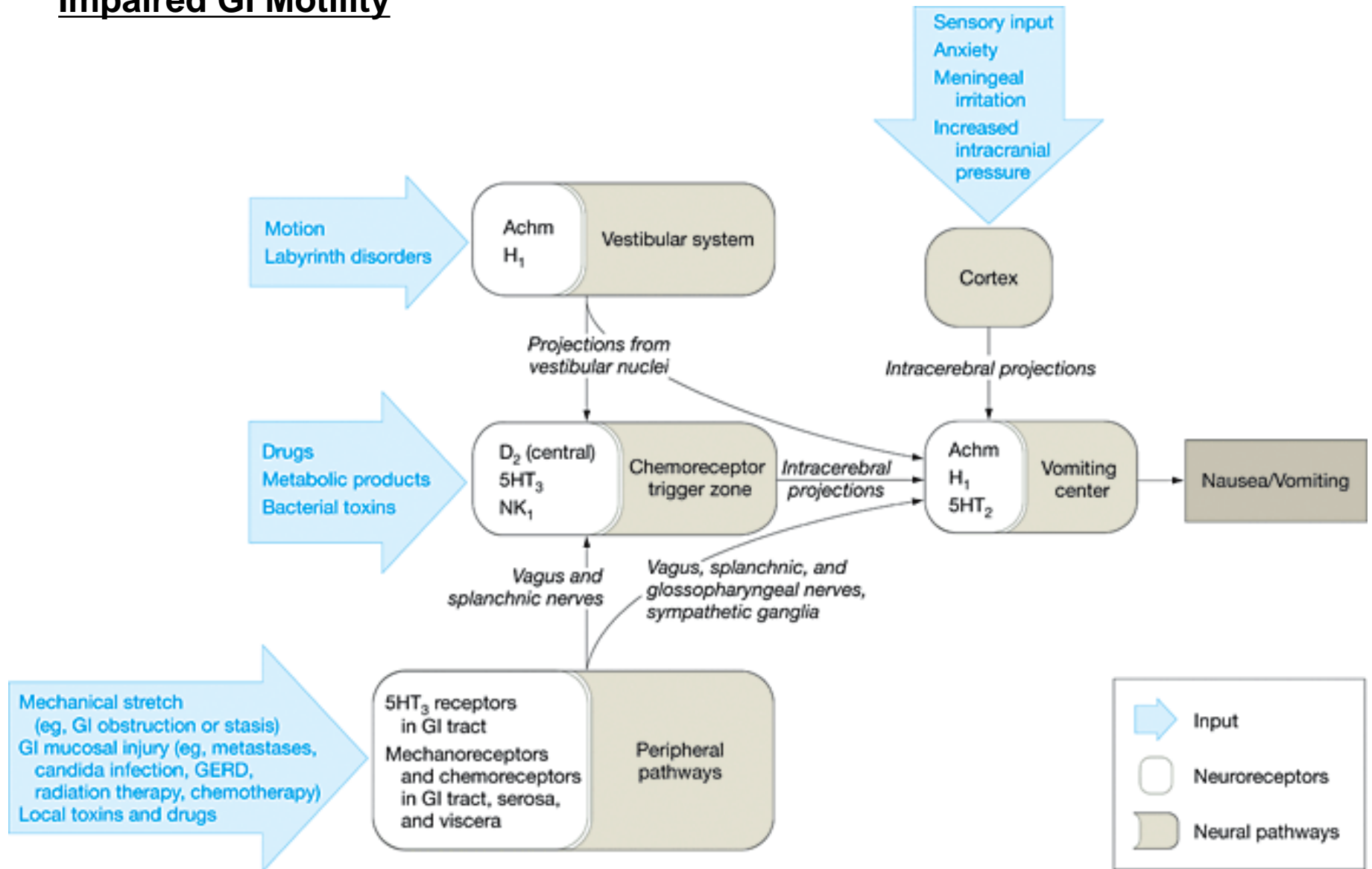


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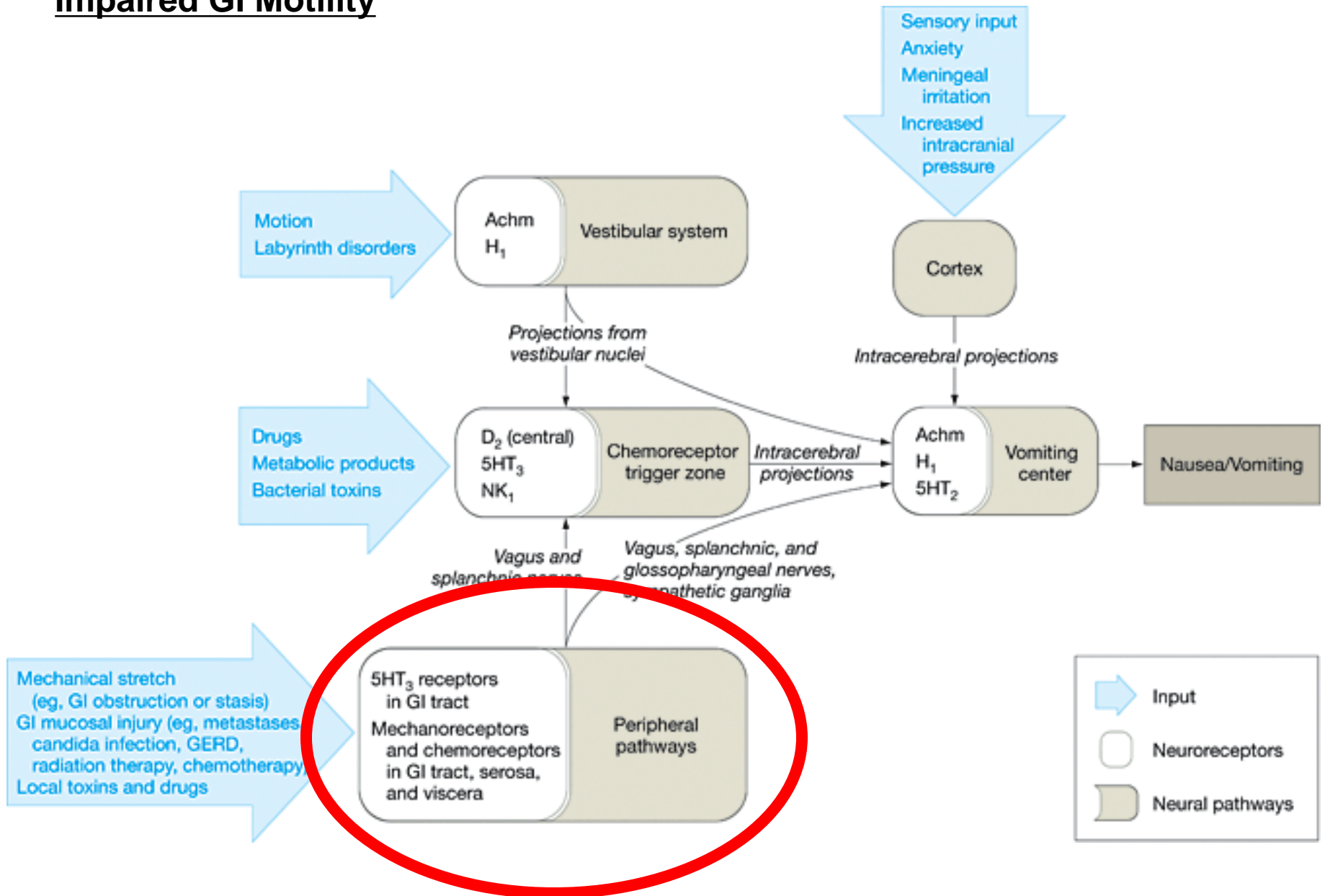
Ondansetron
Dexamethasone
Aprepitant



Impaired GI Motility

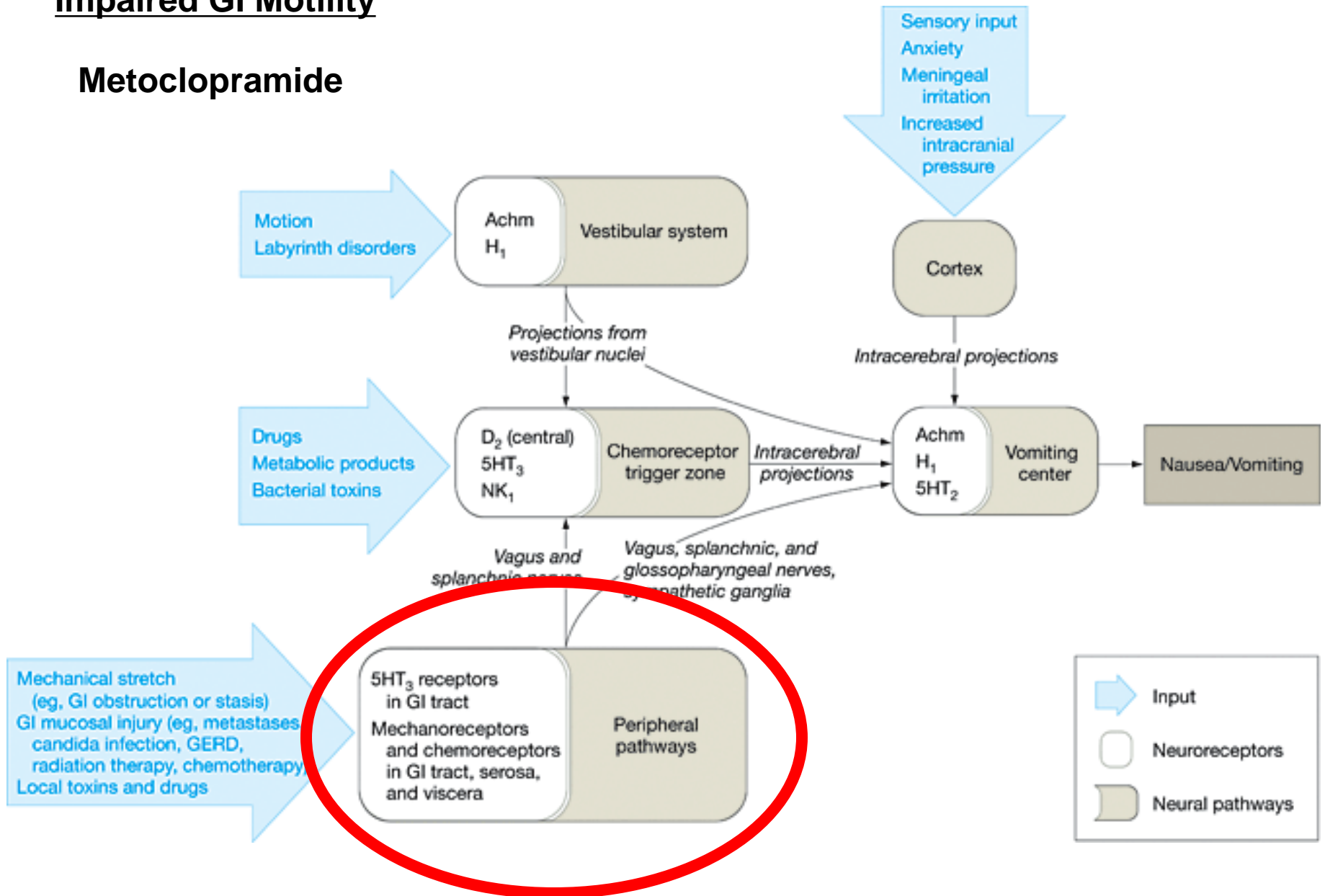


Impaired GI Motility

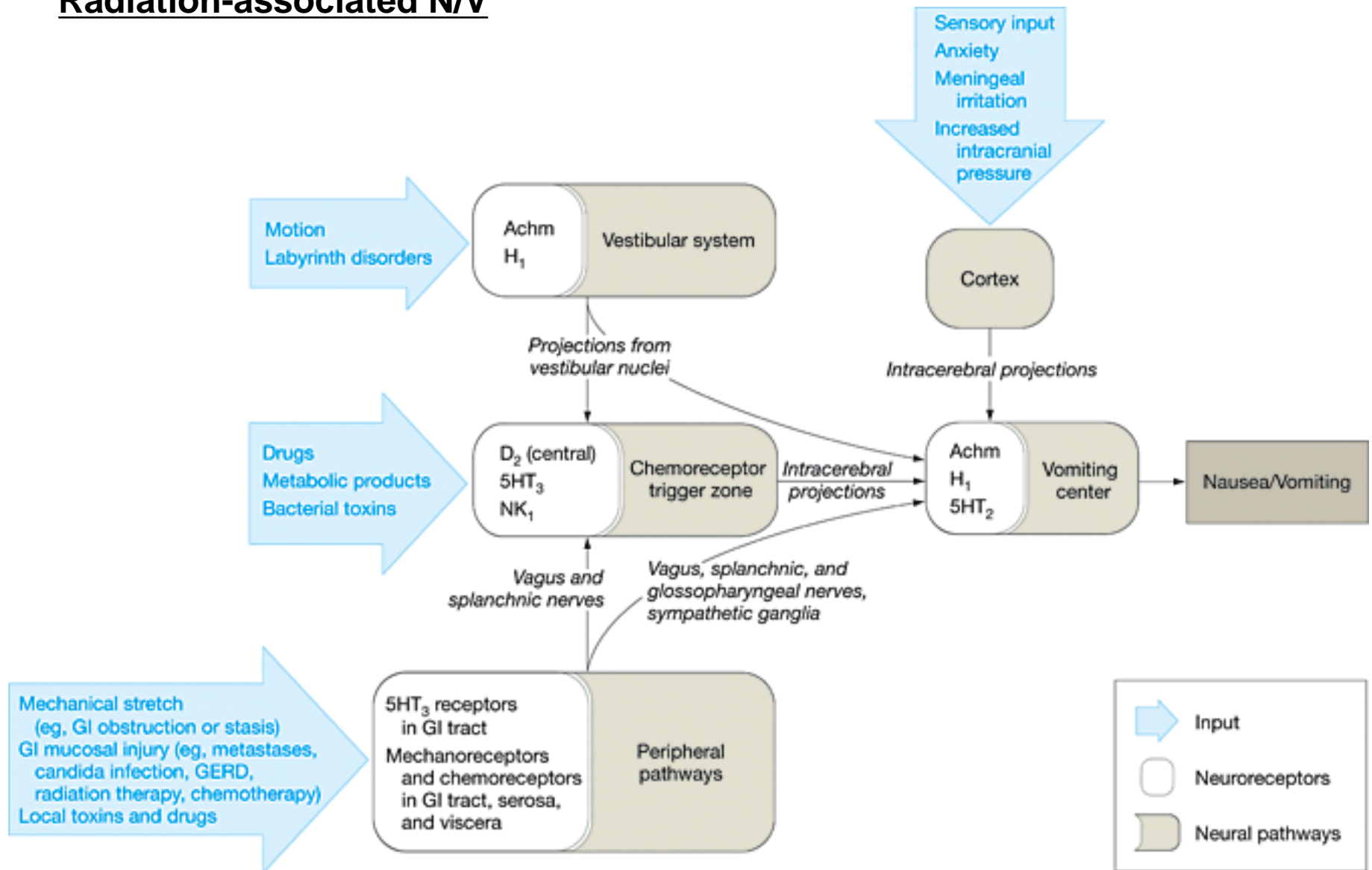


Impaired GI Motility

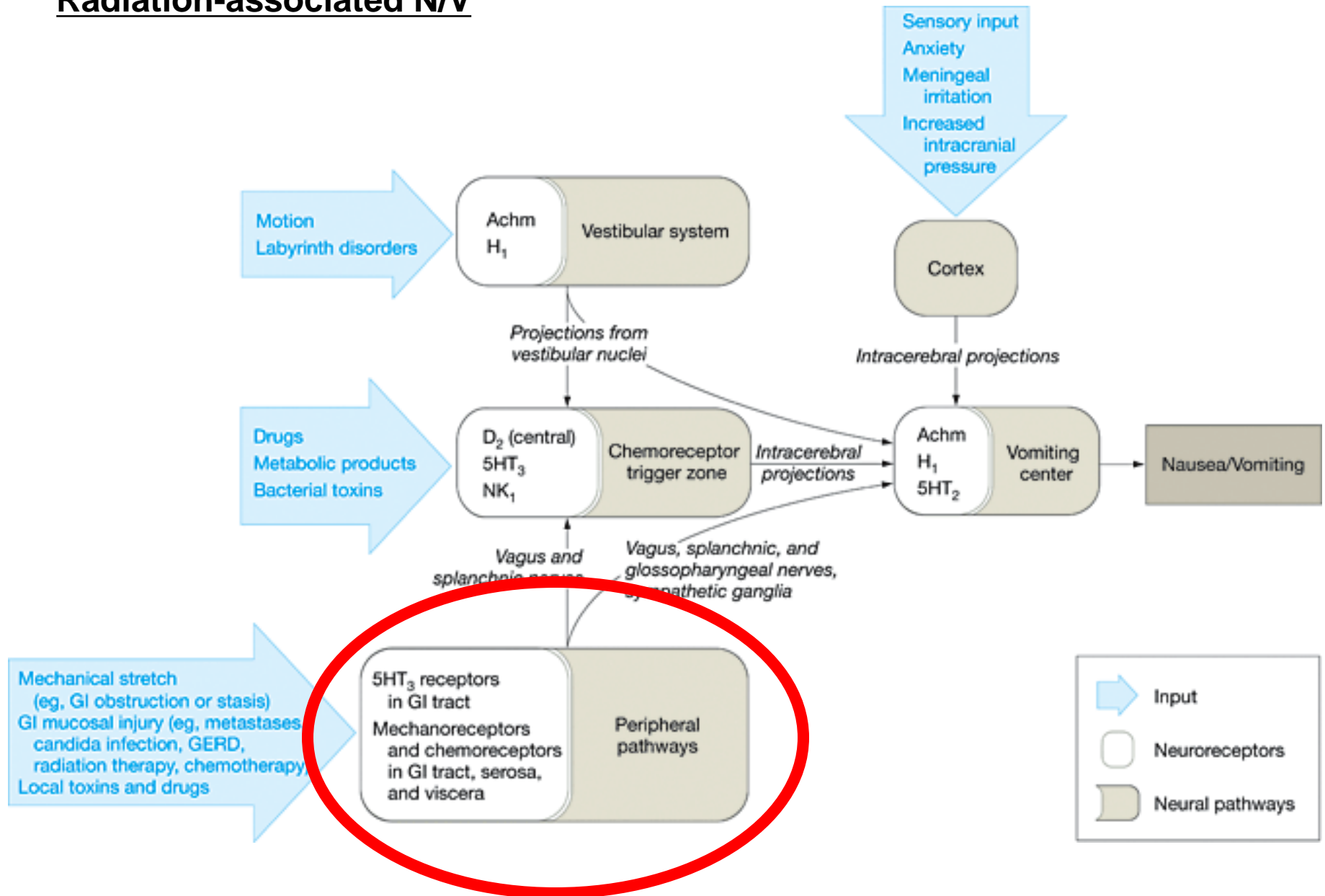
Metoclopramide



Radiation-associated N/V

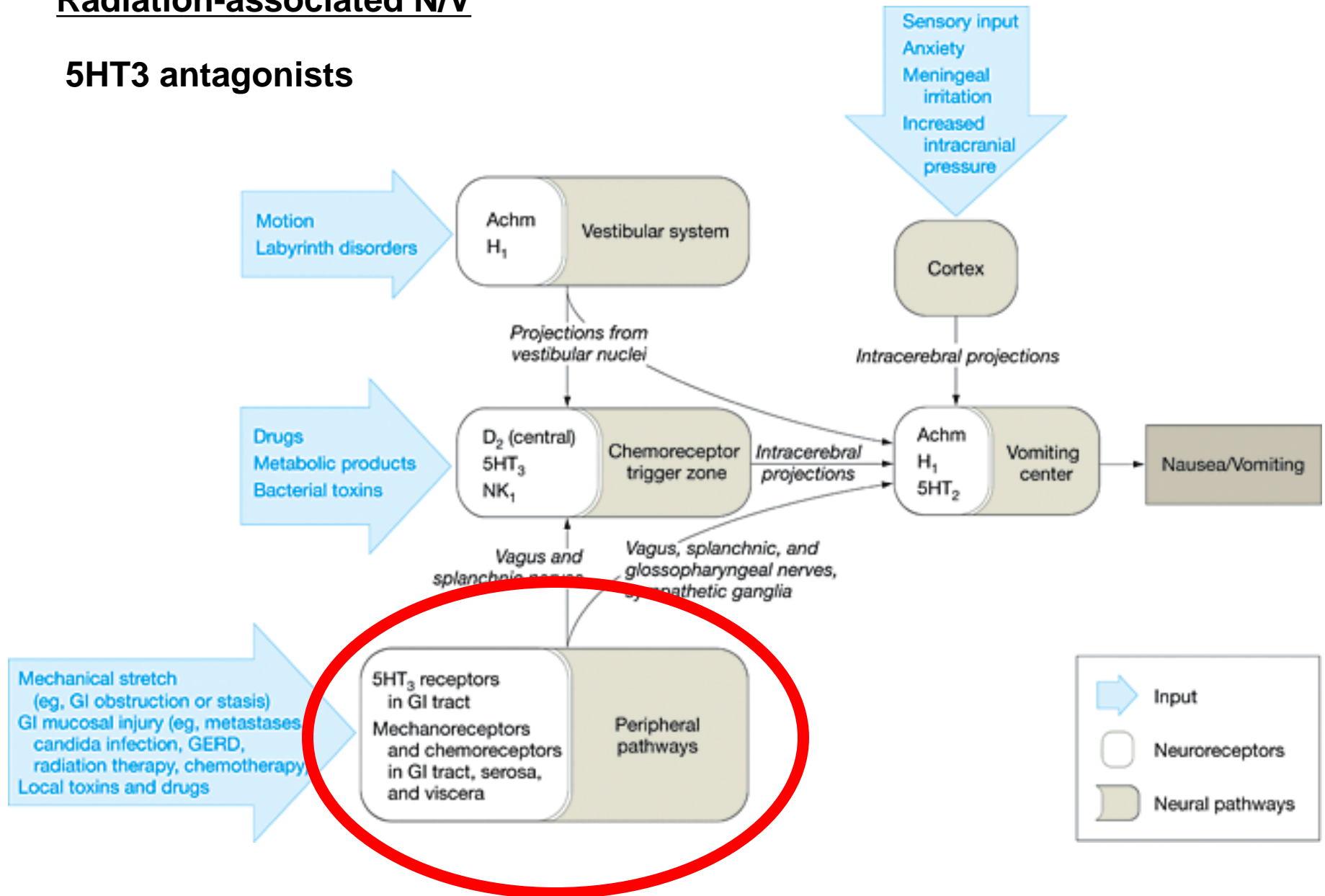


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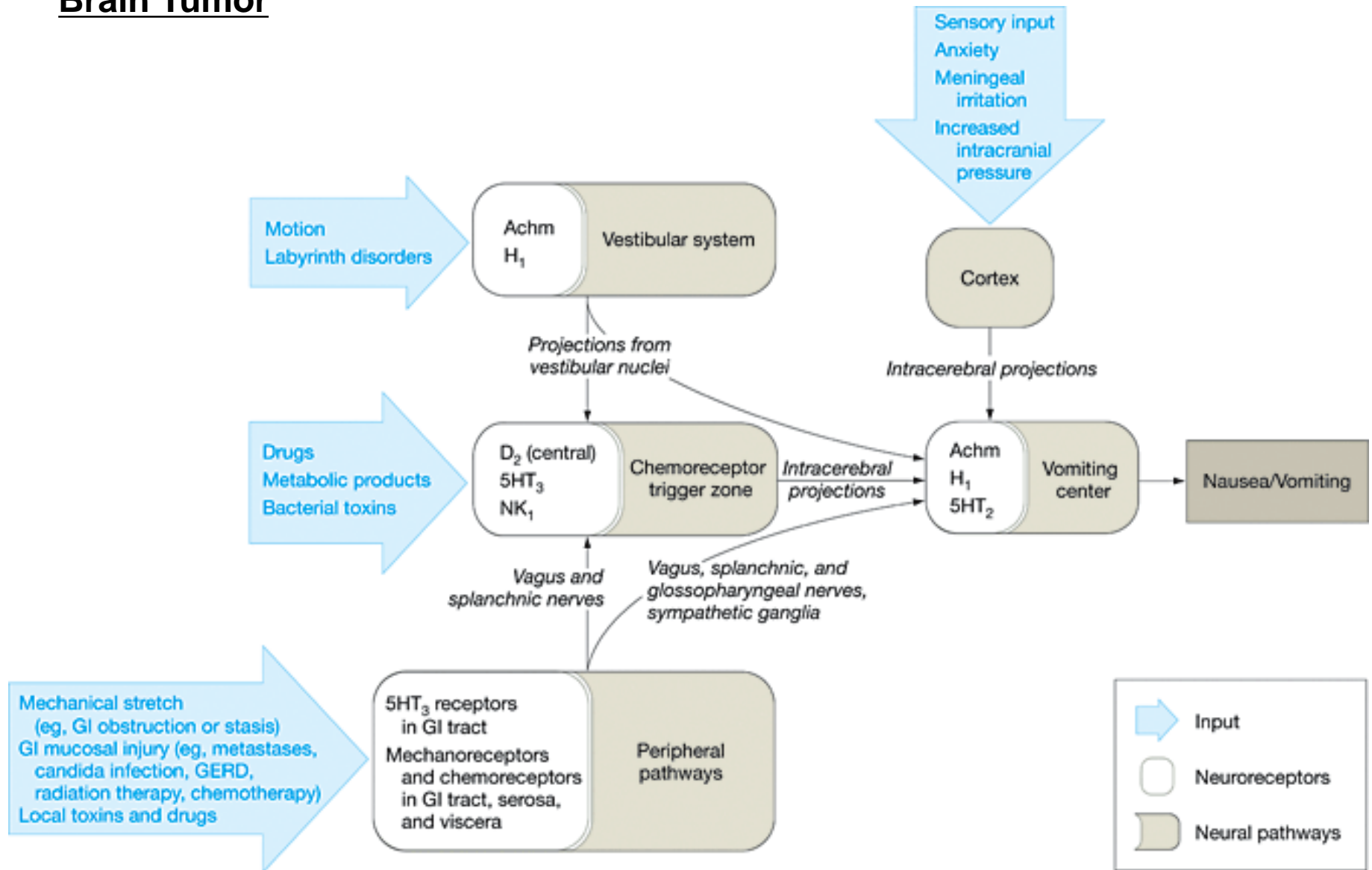


Radiation-associated N/V

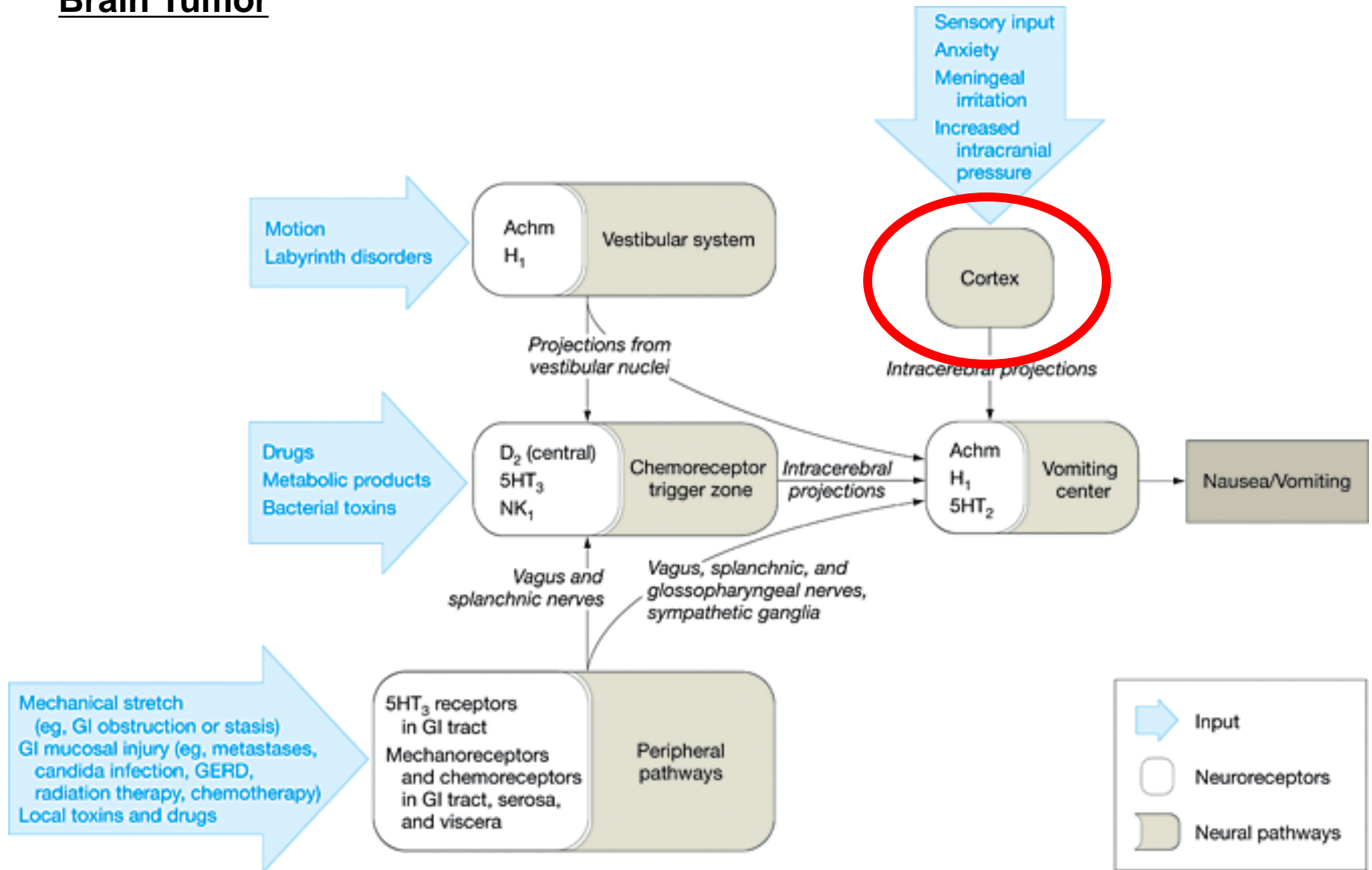
5HT₃ antagonists



Brain Tumor

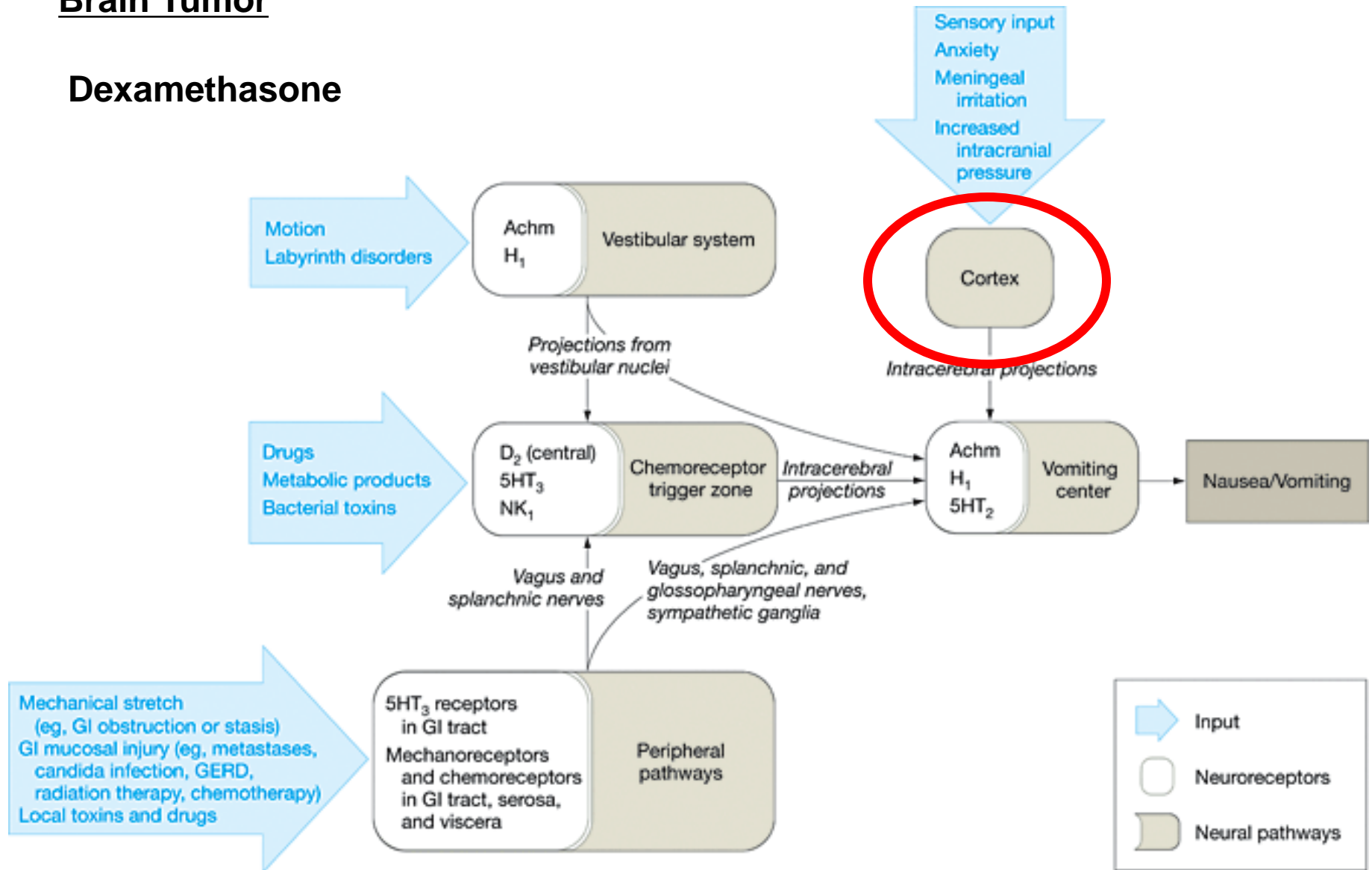


Brain Tumor

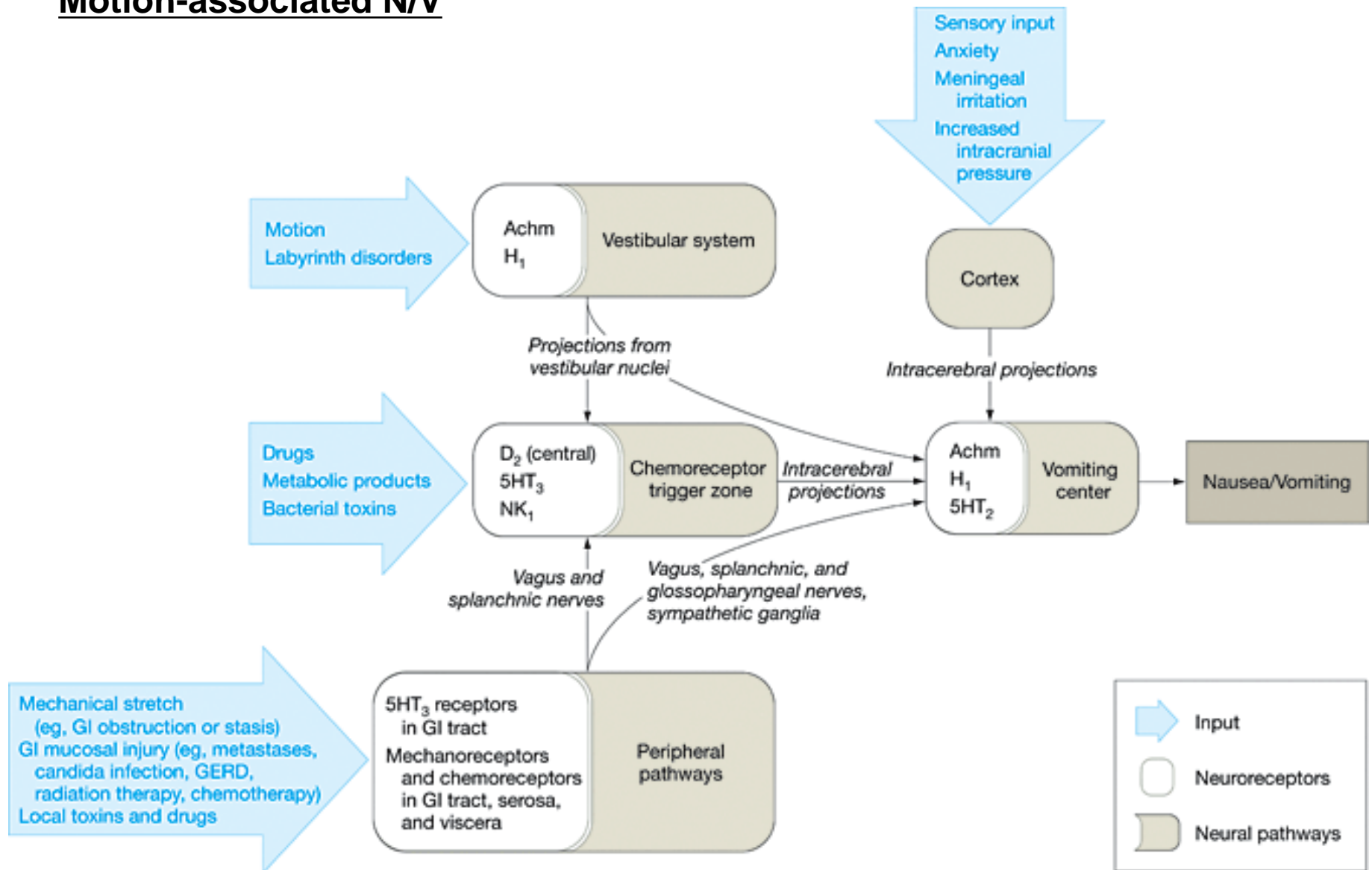


Brain Tumor

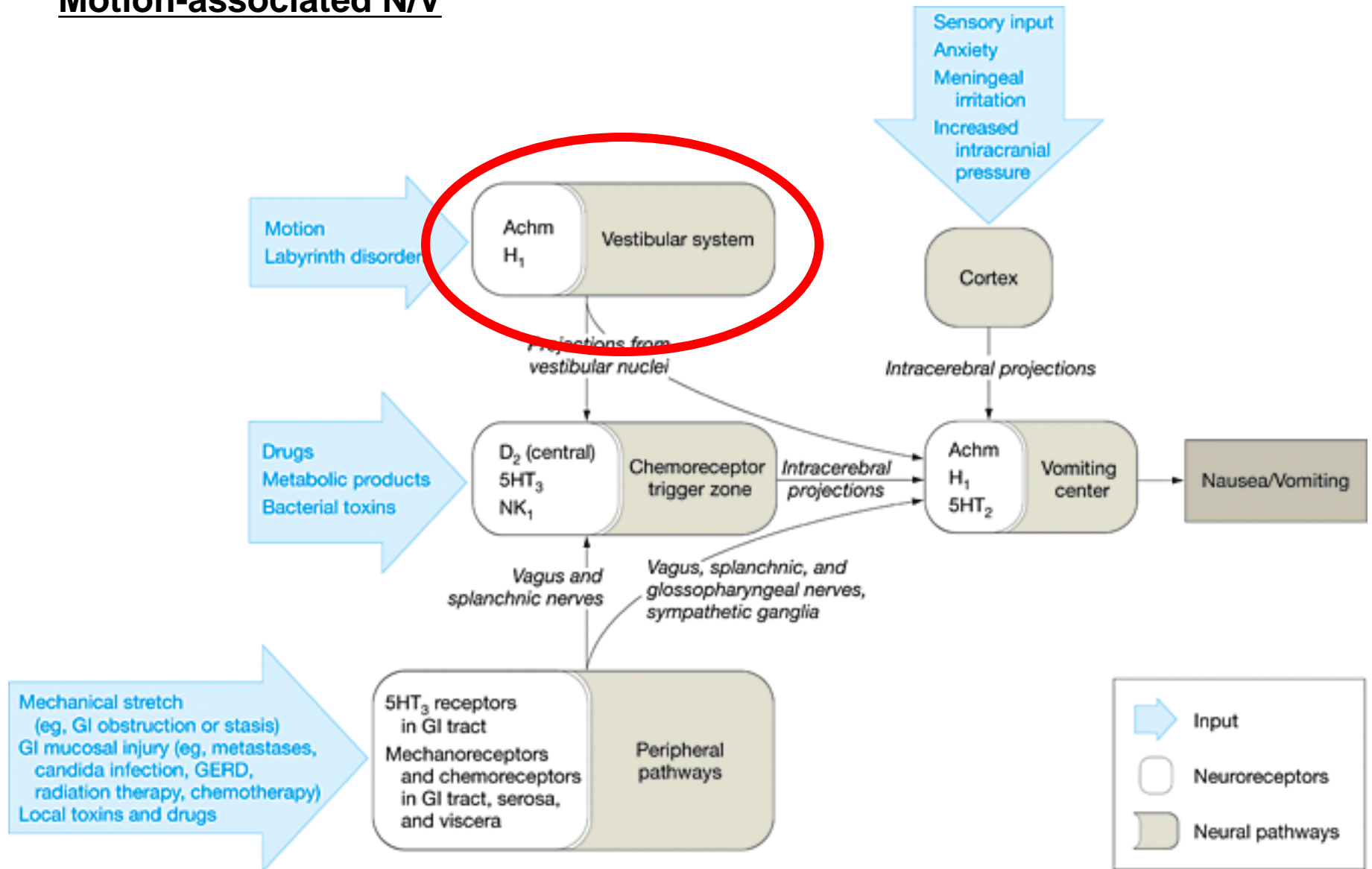
Dexamethasone



Motion-associated N/V

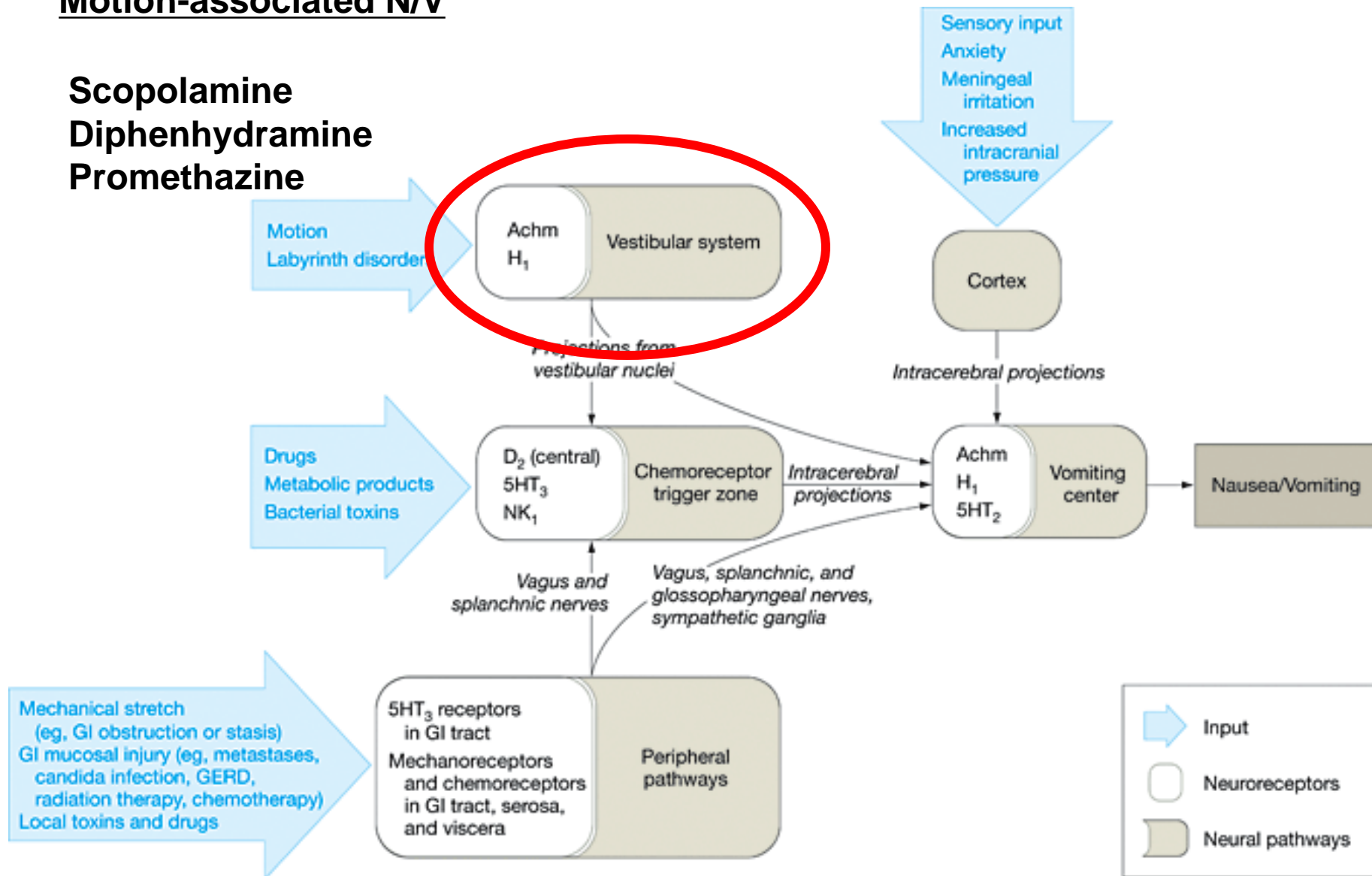


Motion-associated N/V

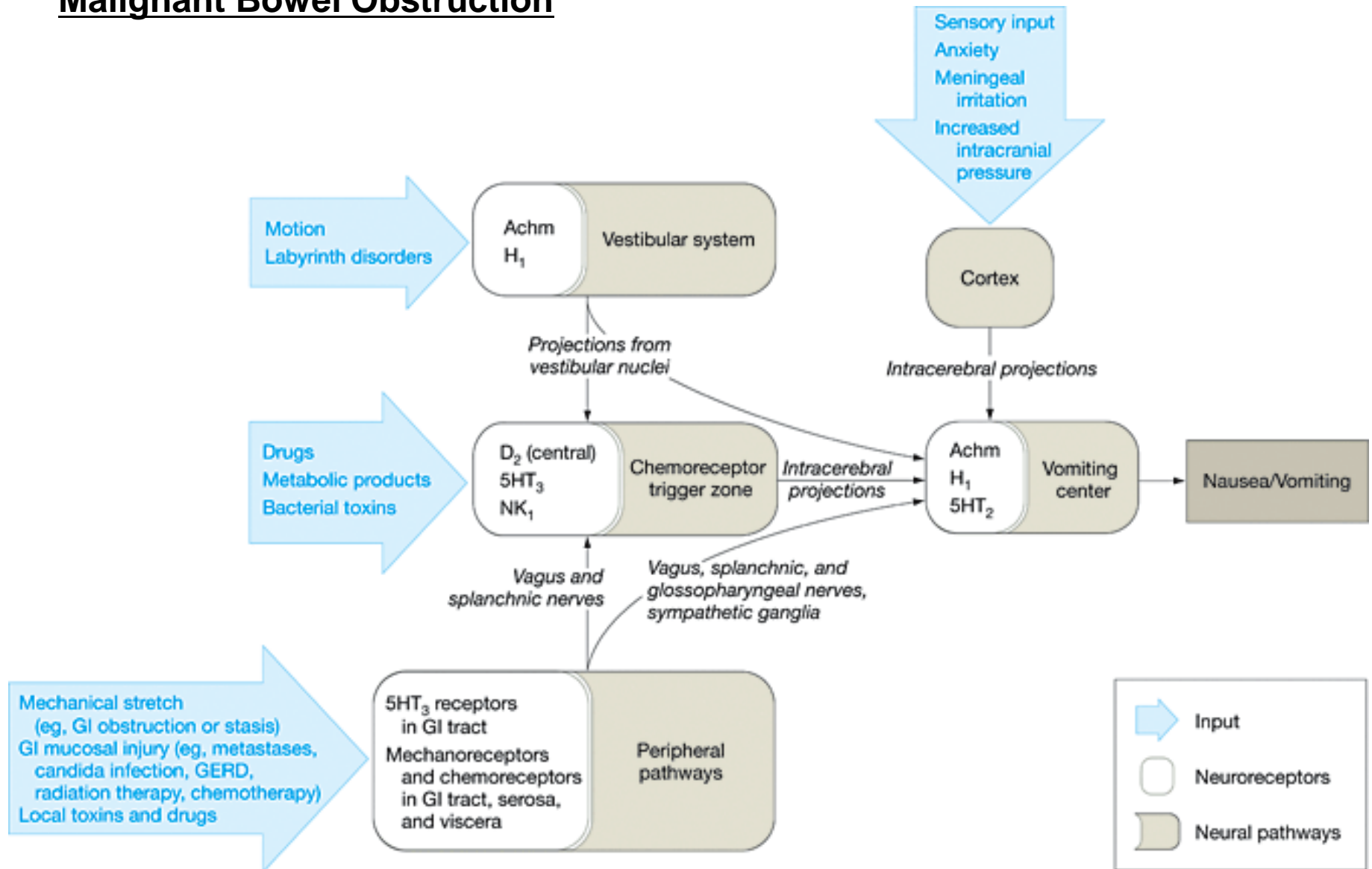


Motion-associated N/V

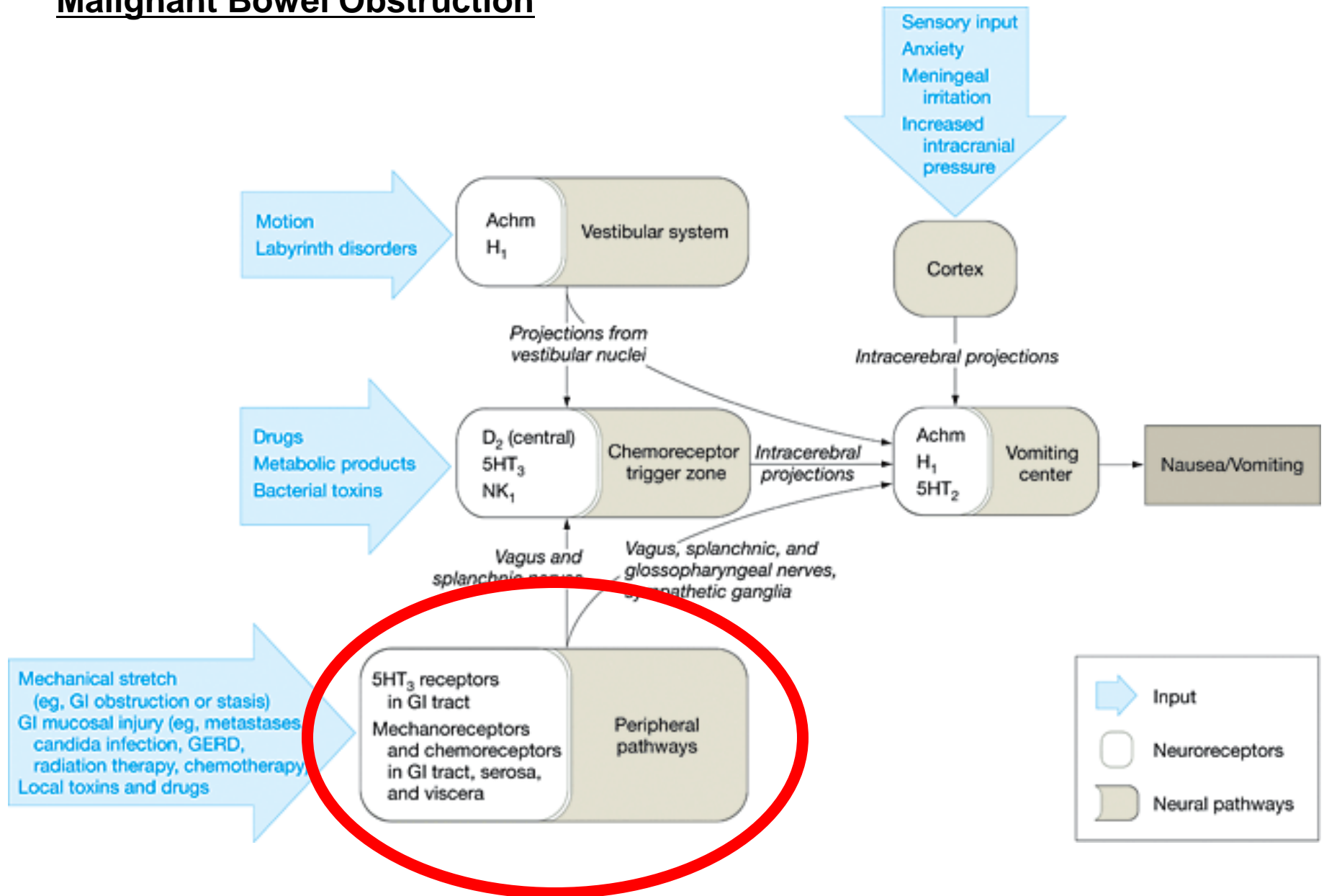
Scopolamine
Diphenhydramine
Promethazine



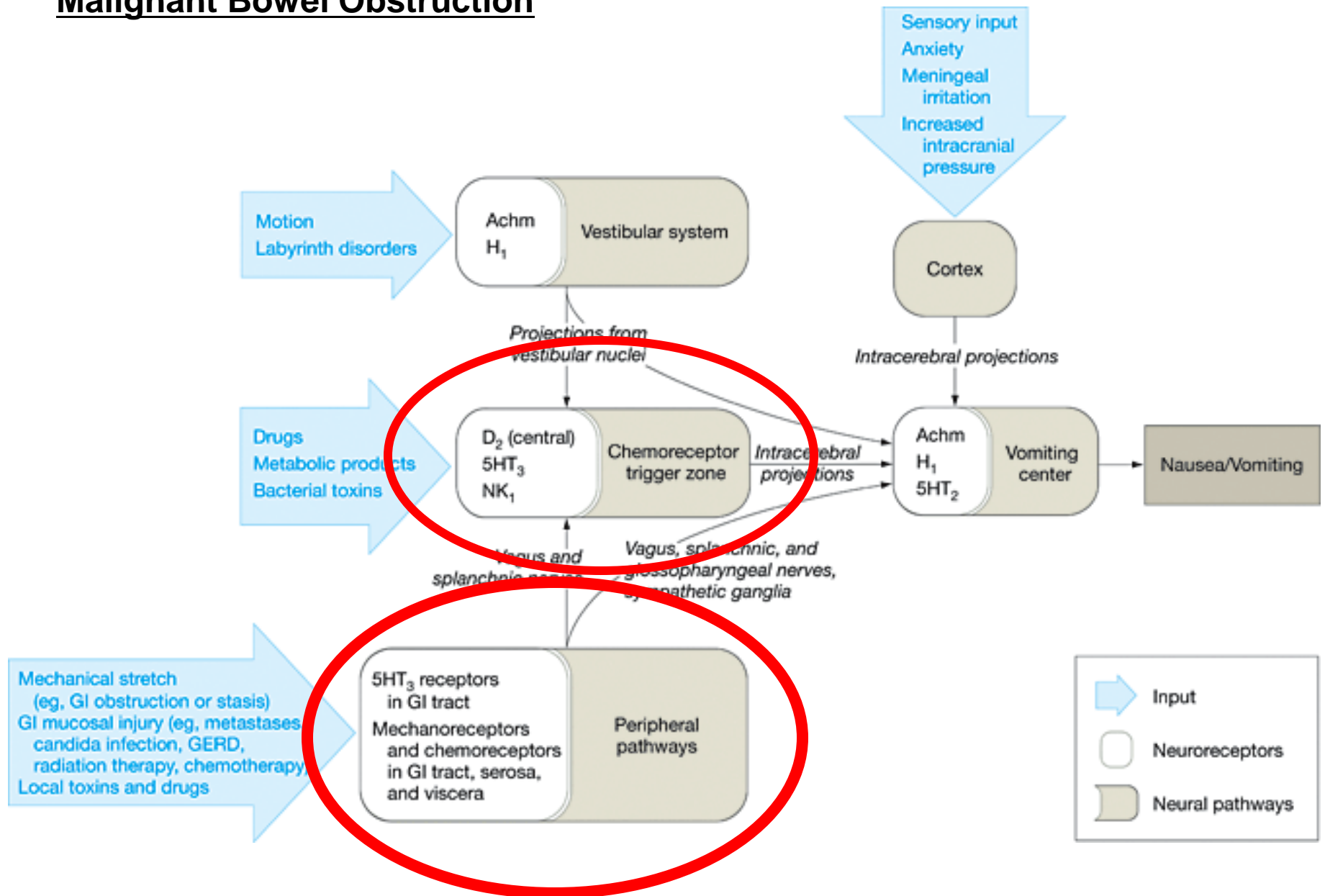
Malignant Bowel Obstruction



Malignant Bowel Obstruction

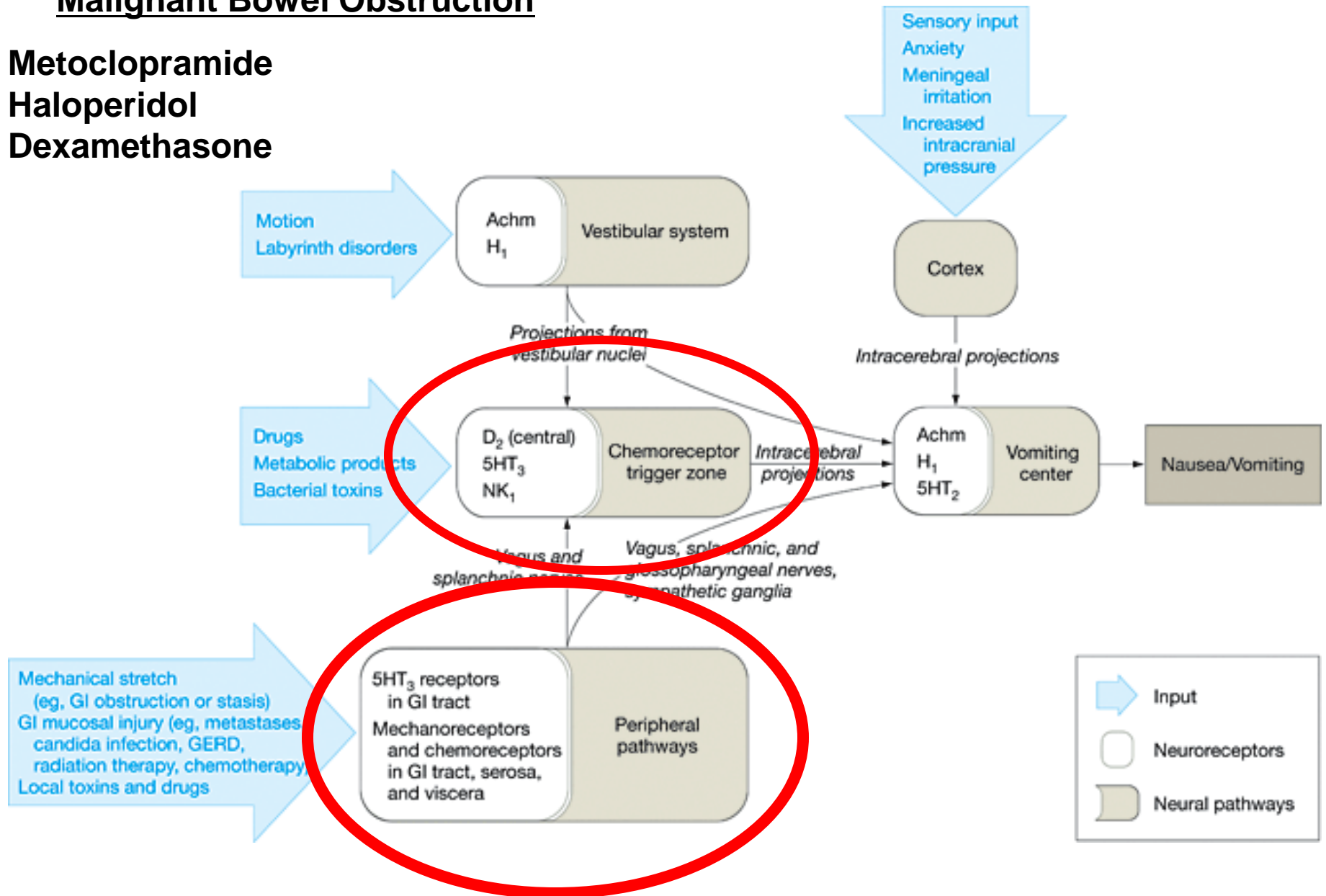


Malignant Bowel Obstruction



Malignant Bowel Obstruction

Metoclopramide
Haloperidol
Dexamethasone



Malignant Bowel Obstruction

- Most common in ovarian, colorectal CA
- Interventional management
 - Surgery if prognosis > 2 mos
 - Stent, NG tubes, venting PEG tubes
- Medical Management
 - Analgesic: opioid
 - Antisecretory: Octreotide/anticholinergic
 - Antiemetic: Metoclopramide/haloperidol
 - Steroid: Dexamethasone

Nonpharmacological Therapy

- Avoid strong smells or other triggers
- Small, frequent meals
- Limit oral intake during severe episodes
- Relaxation techniques
- Acupuncture and acupressure (P6 stimulation)¹

Refractory/Intractable N/V

Refractory/Intractable N/V

- Schedule around-the-clock
- Add second agent to block other implicated receptors
- Prophylactic dosing
- Treat underlying cause if possible

Refractory/Intractable N/V

- Less traditional agents
 - Dexamethasone (Decadron)
 - Mirtazapine (Remeron)
 - Dronabinol (Marinol)
 - Olanzapine (Zyprexa)
 - Megestrol (Megace)
 - Thalidomide (Thalomid)

5HT3 Antagonists

- Effective for:
 - Chemotherapy-induced N/V¹
 - Radiation therapy-induced N/V²
 - Post-operative N/V³
 - Smaller studies suggest efficacy for nausea due to opioids⁴ or uremia⁵
- Otherwise, no more effective than cheaper D2 antagonists for most common causes of N/V⁶

1. Kris MG et al. J Clin Oncol. 2006;24(18):2932-2947.
2. Roberts JT et al. Oncology. 1993;50(3):173-179.
3. Gan TJ et al. Anesth Analg. 2003;97(1):62-71.
4. Sussman G et al. Clin Ther. 1999;21(7):1216-1227.
5. Ljutic D et al. Kidney Blood Press Res. 2002;25(1):61-64.
6. Weschules DJ et al. Am J Hosp Palliat Care. 2006;23(2):135-149.

Polypharmacy

- Most anti-emetics are centrally active
- Mechanism-based therapy prevents use of multiple medications antagonizing same receptor

Conclusions

1. Mechanism-based approach

- Careful assessment to determine etiology
- Use knowledge of pathophysiology to determine receptors underlying symptoms
- Choose antiemetic to block implicated receptors
- Also treat underlying etiology

2. Refractory/Intractable N/V

- Multiple agents, around-the-clock and prophylactically
- Less traditional agents

Questions?

