

Introduction

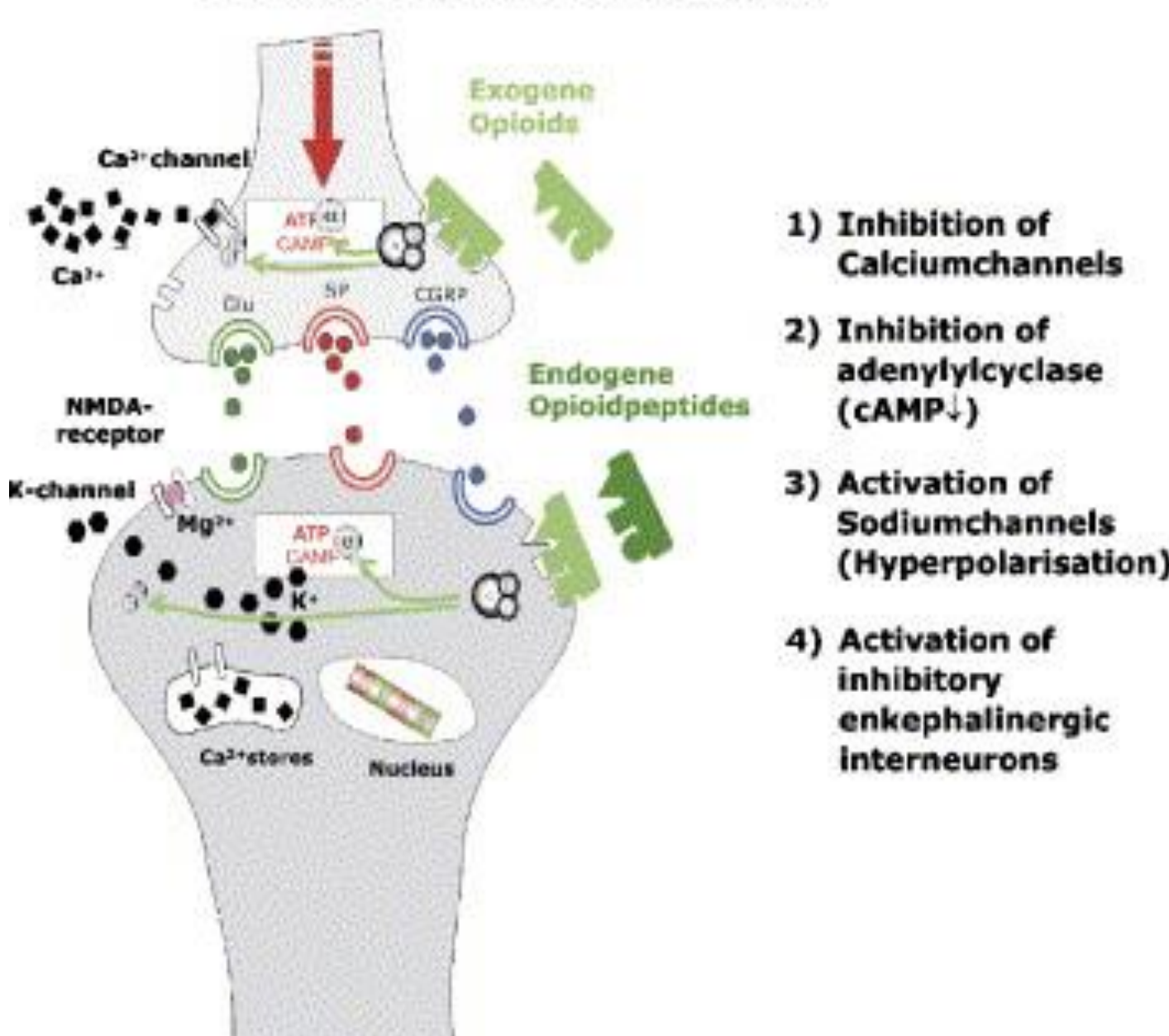
- Vaso-occlusive crises (VOC)** are a hallmark of **sickle cell disease (SCD)**, oftentimes, requiring patient-controlled analgesia (PCA) administration with opioids
- Escalating doses of opioids for VOCs run the **risk of opioid-induced hyperalgesia (OIH)**, a phenomenon where paradoxical administration of high-doses of opioids rather exacerbate pain¹
- Ketamine's use as an analgesic adjunct in OIH in SCD-VOCs is unknown, and data is sparse

Case Description

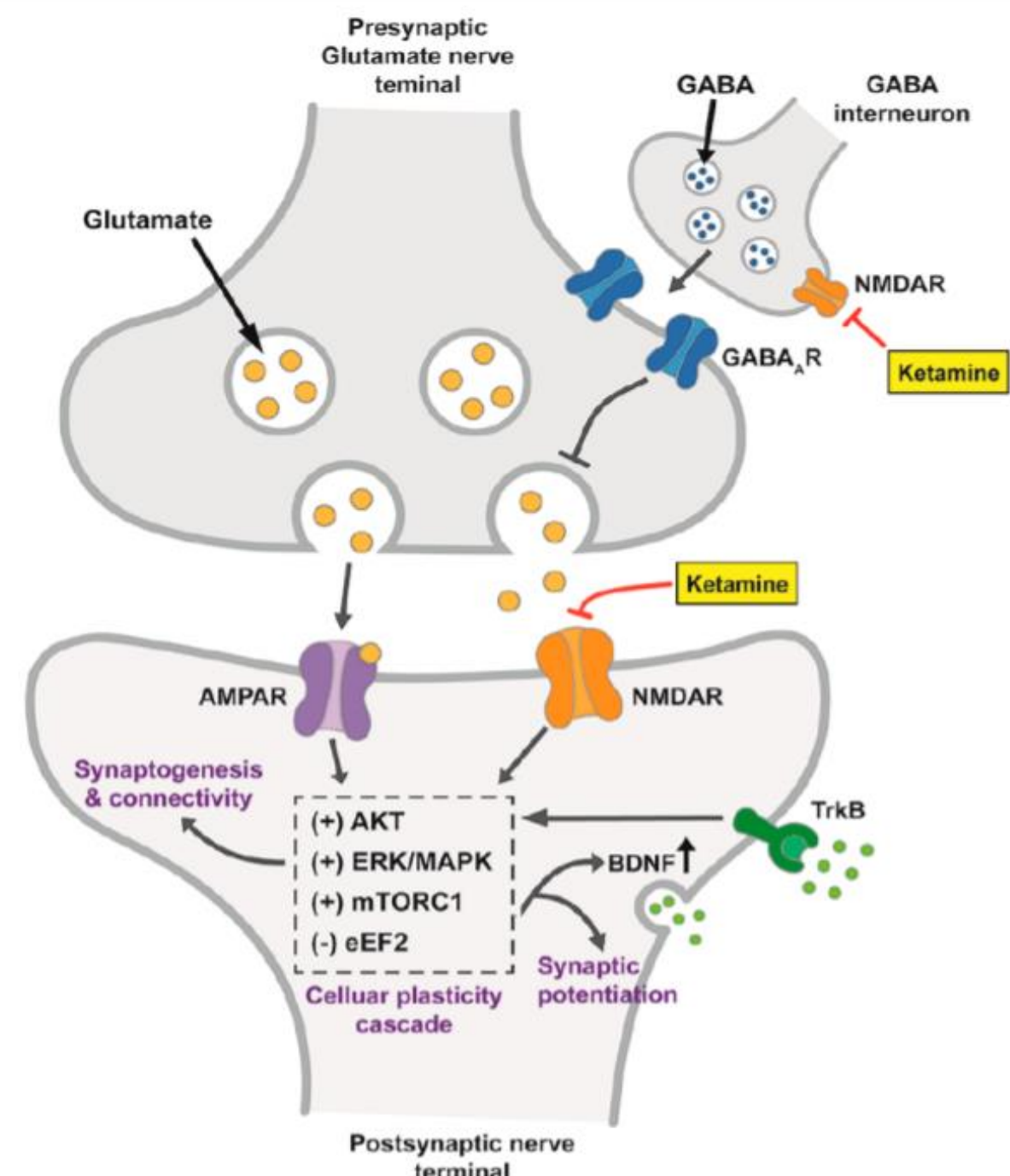
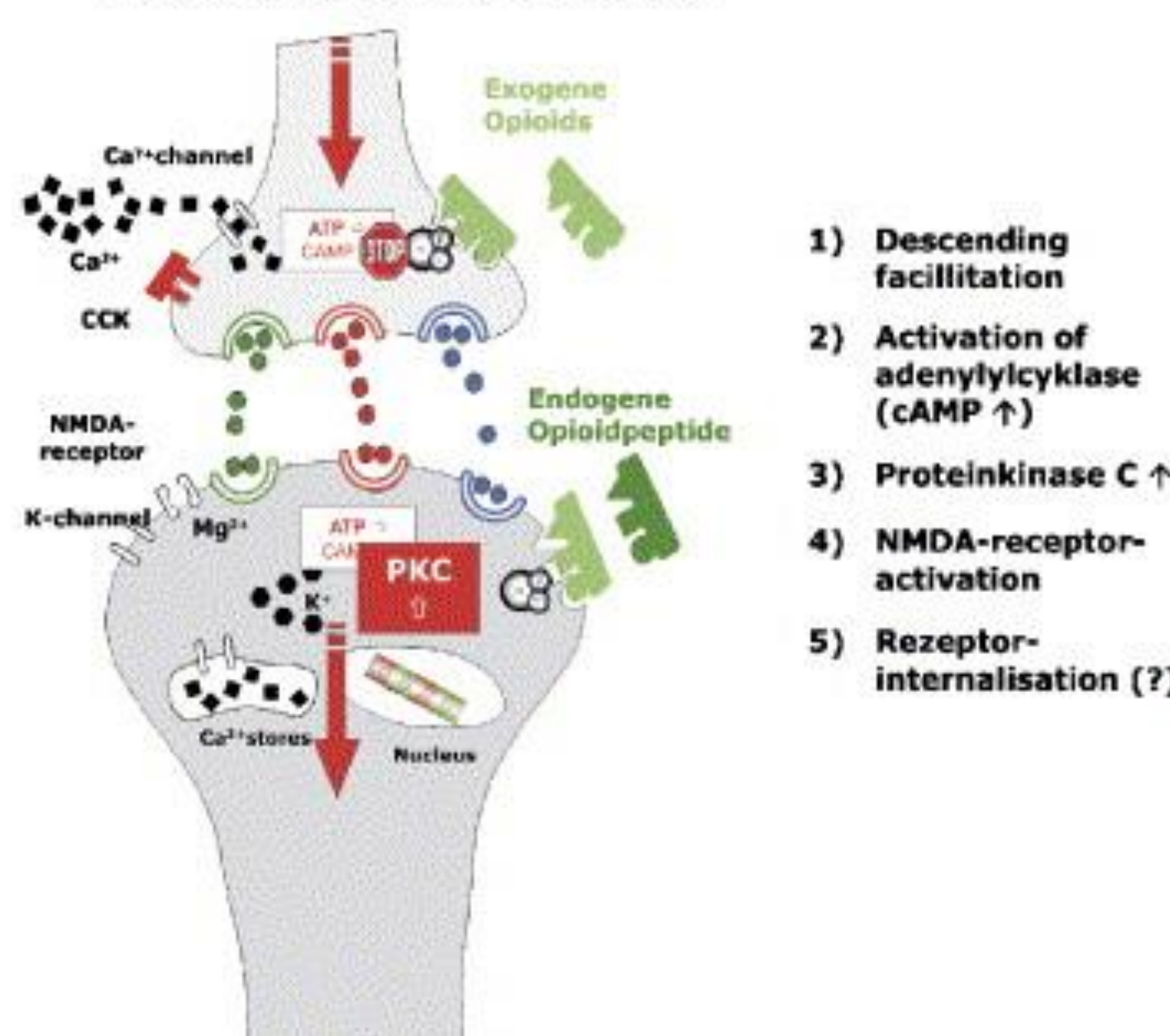
- A **female in her 30s with SCD** and asthma presented to the ED with 9/10 **back pain and 3-day history of cough and chest tightness**
- Home pain regimen (630 morphine milligram equivalent – MME)
 - Oxycodone extended-release (ER) 120mg q12hr
 - Oxycodone immediate-release (IR) 30mg q4hr
- Labs showed she was **RSV positive** with stable hemoglobin.
- She was **admitted for VOC pain management**. She received 1L fluids, 6mg IV hydromorphone, oxycodone-ER 120mg, gabapentin 300mg, albuterol nebulizers, and IV ketorolac
- Hydromorphone PCA was initiated** at 0.8mg loading and 0.7mg demand q15mins
 - She received 11mg hydromorphone in the first 24 hours
- By **days 2–3, pain scores improved to 7/10**, and chest symptoms subsided. PCA demand dose was changed to 1mg q20mins and later spaced to q60mins by day 4, and Oxycodone-IR 30mg q4hr standing and PRN were added
- Overnight, she developed left leg and right arm pain requiring boluses of IV hydromorphone with up-titrations of PCA to 1mg q20mins, and 0.5mg/hr basal. Ultrasounds were negative for thrombosis, and labs were unchanged
- Despite regimen up-titrations, her pain worsened. **Ketamine infusion was initiated** at 0.2mg/kg/hr and increased to 0.3mg over 12 hours. **Her PCA was weaned over days 7-9**
- By day 10, ketamine was tapered to 0.1mg, PCA basal was discontinued, and demand remained at 3mg q90mins
- Orals were restarted and increased to wean her off PCA for discharge

Opioid and Ketamine Mechanisms of Action

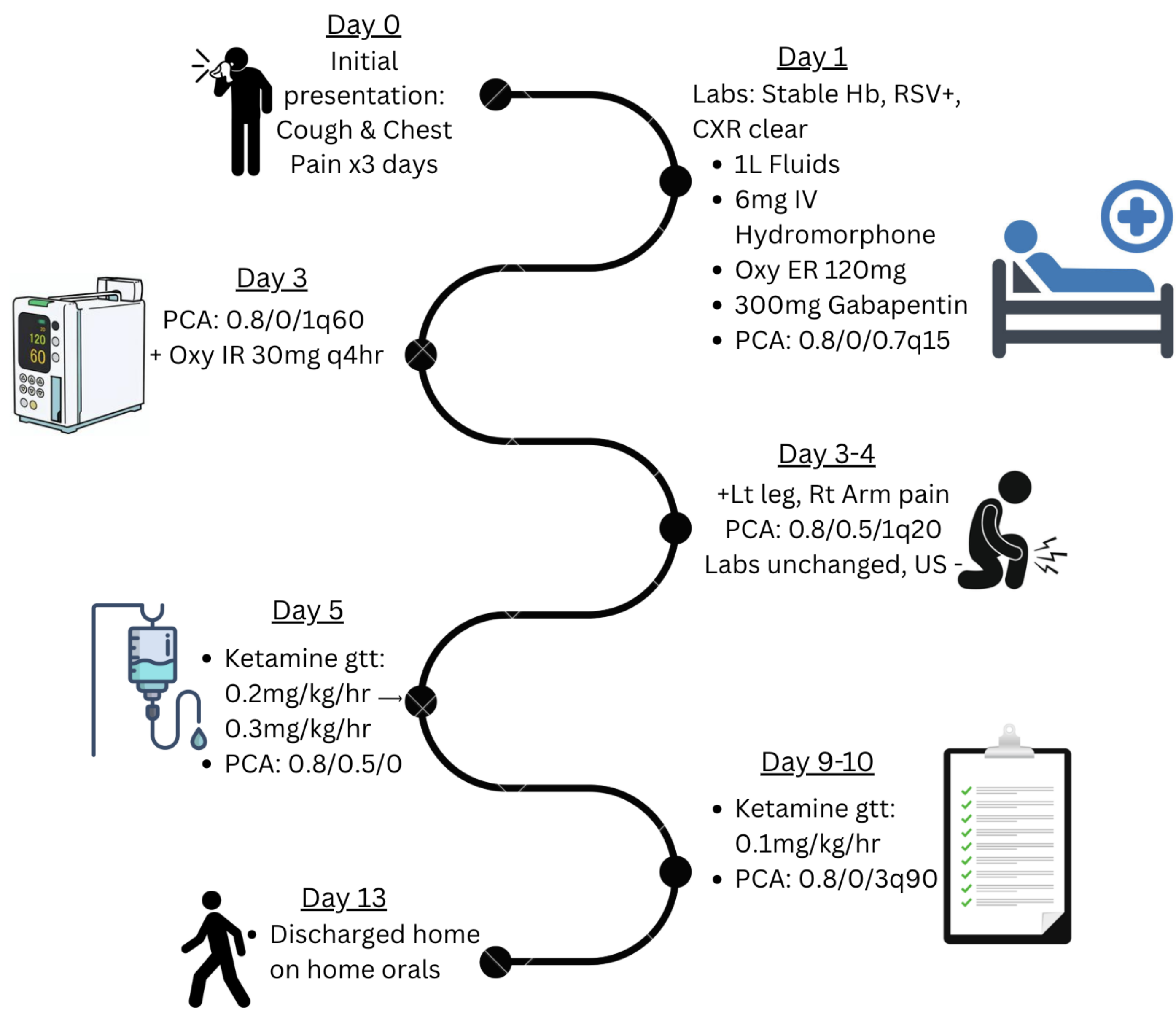
Antinociceptive mechanisms



Pronociceptive mechanisms



Timeline of Hospitalization



Timeline of Pain Regimen Titrations

Day	Hydromorphone (Total mg)	Oxycodone ER+IR (Total mg)	MME (total)	Ketamine (Total mg)	Average Pain score
0	6	120	210	0	9.5
1	19	240	455	0	7.0
2	24.55	240	482.8	0	7.0
3	35.8	360	719	0	8.0
4	25.33	420	756.6	0	9.0
5	66.33	180	601.6	42.7	9.3
6	32.3	0	161.5	65.7	10.0
7	24.48	0	122.4	65.6	Not Recorded
8	23.99	0	119.9	65.6	10.0
9	37.15	240	545.8	36	10.0
10	59.85	240	659.3	0	9.3
11	64.94	240	684.7	0	8.5
12	63.09	480	1035.5	0	7.7
13	22.94	300	564.7	0	7.0

Discussion / Conclusion

- The benefit of ketamine in SCD-VOCs is unclear due to a lack of standardized pain scales, distinct guidelines and dosing regimens²
- Our case highlights **ketamine's role as a subanesthetic adjunct for pain through the NMDA-receptor, a target distinct from opioids' u-MOR receptors**
- While our patient had no reductions in MMEs upon discharge, initiating ketamine during an episode of opioid-induced hyperalgesia subsequently plateaued her opioid requirements despite worsening pain

References

- Lee M, Silverman SM, Hansen H, Patel VB, Manchikanti L. A comprehensive review of opioid-induced hyperalgesia. *Pain Physician*. 2011;14(2):145-161.
- Ernesto Calderon Martinez, Stephin Zachariah Saji, Thomas Campos Carmona, Vaidarshi Abbagoni, Druvini Fernando, Nithin Karnan, Mohammad Salman, Suchita Mylavarapu, Mishell Estefania Llerena Vargas, Nathalia Schettino Samad, Arvapalli Lakshmi Sheethal, Sara Dost; Ketamine for Pain Relief in Sickle Cell Vaso-Occlusive Crises: A Systematic Review. *Blood* 2024; 144 (Supplement 1): 5356. doi: <https://doi.org/10.1182/blood-2024-211793>