Community-Based Primary Palliative Care Community of Practice Series

Managing Complex Pain

Project ECHO
Palliative Care - Canada
BY Pallium Canada

Presenters: Dr. Robert Baker & Elisabeth Antifeau

Date: March 2nd, 2022

Territorial Honouring

The Palliative Care ECHO Project

The Palliative Care ECHO Project is a 5-year national initiative to cultivate communities of practice and establish continuous professional development among health care providers across Canada who care for patients with life-limiting illness.

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Thank You

The Palliative Care ECHO Project is supported by a financial contribution from Health Canada. The views expressed herein do not necessarily represent the views of Health Canada.

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Disclosure

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- Not-for-profit
- Funded by Health Canada

Disclosure

This program has received financial support from:

- Health Canada in the form of a contribution program
- Generates funds to support operations and R&D from Pallium Pocketbook sales and course registration Fees

Presenters

- Dr. Robert Baker: Nothing to declare
- Elisabeth Antifeau: Nothing to declare

Disclosure

Mitigating Potential Biases:

- The scientific planning committee had complete independent control over the development of course content

Welcome & Reminders

- Please introduce yourself in the chat! Let us know what province you are joining us from, your role and your work setting
- Your microphones are muted. There will be time during this session for questions and discussion.
- You are welcome to use the chat function to ask questions, if you have any comments or are having technical difficulties, but also please also feel free to raise your hand!
- This session is being recorded and will be emailed to registrants within the next week.
- Remember not to disclose any Personal Health Information (PHI) during the session
- This 1-credit-per-hour Group Learning program has been certified by the College of Family Physicians of Canada for up to **11 Mainpro+** credits.

How ECHO Works

General Format:

- Introduction
- Presentation
- Q&A
- Interactive, Case-Based Discussion
- Session Wrap Up

Be a case presenter!

- If you would like to submit a case for one of our upcoming sessions, you can:
  - Let us know in the chat
  - Send us an e-mail us at echo@pallium.ca
  - Let us know in your feedback survey after today's session

Overview of Sessions

Session #	Session Title	Date/ Time
Session 1	Symptom Management	Feb. 16, 2022 from 1-2pm ET
Session 2	Managing Complex Pain	Mar. 2, 2022 from 1-2pm ET
Session 3	Managing the Last Hours of Life in the Home	Mar 16, 2022 from 1-2pm ET
Session 4	Beyond the Essential Communication Skills- Part 1	Mar 30, 2022 from 1-2pm ET
Session 5	Beyond the Essential Communication Skills- Part 2	Apr 13, 2022 from 1-2pm ET
Session 6	Beyond the Essential Communication Skills- Part 3	Apr 27, 2022 from 1-2pm ET
Session 7	Grief and Bereavement: Identifying and Managing Complex Grief	May 11, 2022 from 1-2pm ET
Session 8	Teamwork in Primary Palliative Care	May 25, 2022 from 1-2pm ET
Session 9	Grief in Children	Jun 8, 2022 from 1-2pm ET
Session 10	Community Palliative Resources	Jun 22, 2022 from 1-2pm ET
Session 11	Organizing Practices to Provide Primary Palliative Care	Jul 6, 2022 from 1-2pm ET

Introductions

Facilitator

Dr. Nadine Gebara, MD CCFP- PC

Clinical co-lead of this ECHO series
Palliative Care Physician at Toronto Western Hospital, University Health Network
Family Physician at Gold Standard Health, Annex

Panelists:

Dr. Haley Draper, MD CCFP- PC

Clinical co-lead of this ECHO series
Palliative Care Physician at Toronto Western Hospital, University Health Network
Family Physician at Gold Standard Health, Annex

Amanda Tinning, MN NP
Nurse Practitioner for the home Transitional Heart Failure Clinic
Division of General Internal Medicine
QEII Health Sciences Centre
Halifax, NS

Introductions

Panelists (continued):

Thandi Briggs, RSW MSW
Care Coordinator, Integrated Palliative Care Program
Home and Community Care Support Services Toronto Central

Elisabeth Antifeau, RN, MScN, CHPCN(C), GNC(C)

Regional Clinical Nurse Specialist (CNS-C), Palliative End of Life Care
IH Regional Palliative End of Life Care Program
Pallium Canada Master Facilitator & Coach, Scientific Consultant

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Introductions

Presenter

Dr. Robert Baker, MD CCSAM AAMRO CISAM

Medical Director, Palliative and End of Life Care, Interior Health Western Region
Medical Director, Kamloops Hospice House
Medical Director, Phoenix Centre Residential Detox, Kamloops
Medical Director, Sage Health Centre Residential Addiction Treatment, Kamloops British Columbia
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Managing Complex Pain in Palliative Care

Session Learning Objectives

Upon completing the session, participants will be able to:

- Describe the role of opioids in the management of pain.
- Discuss management of complex pain including methadone and other third line adjuvants.
- Identify alternate interventional procedures for complex pain management
- Discuss the care management needs of a patient experiencing complex pain

It will all make sense in the end

A bit of everything that will all come together by the end…

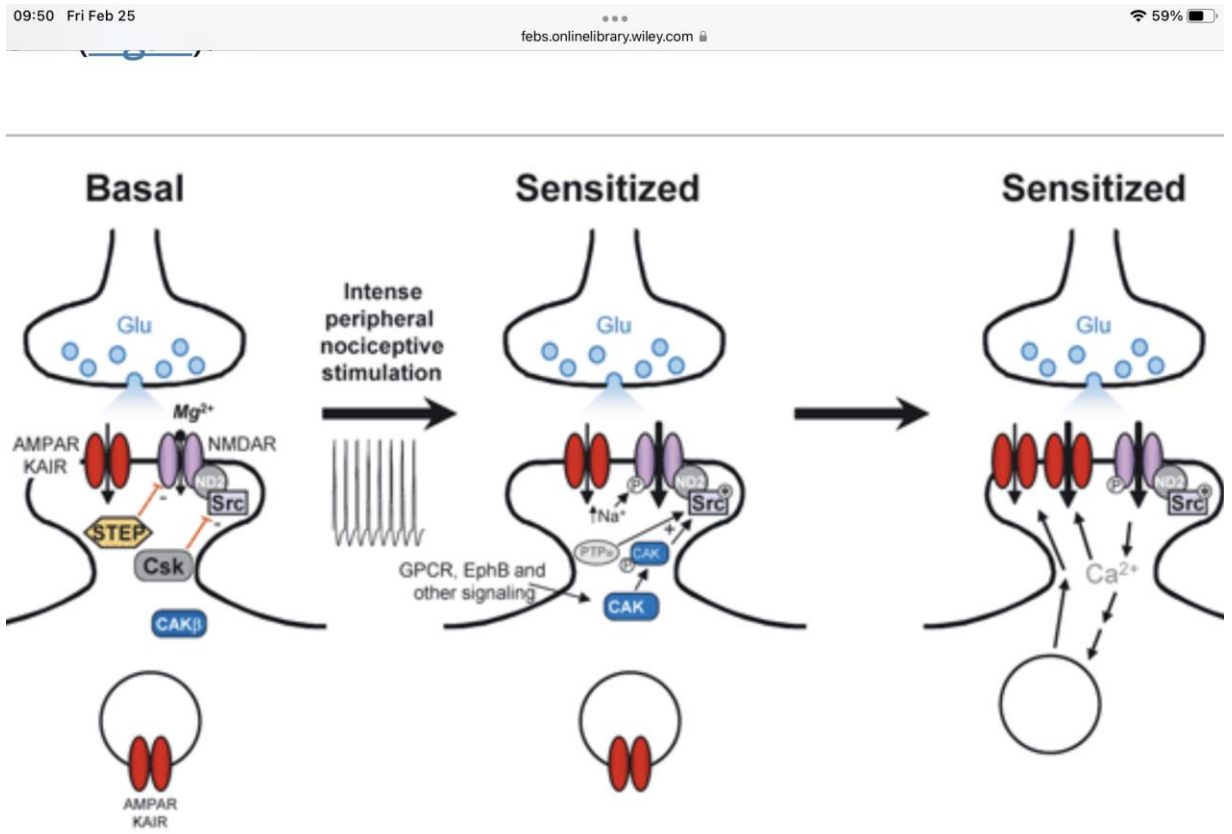
Opiate Therapy Basics

- Opiates do NOT have a ceiling effect; the dose can always be raised to meet the need
- Effect can be maximized by using scheduled dosing with PRN for Break Thru Pain (BTP) (10-15% of total daily dose Q1H)
- They do however have side effects, pruritus, constipation, and opioid toxicity likely due to the accumulation of neuro-active metabolites.
- They do cause tolerance, often coincident with disease progression and the need for greater analgesia

Is the distinction between Chronic Non-Cancer Pain (CNCP) and Palliative pain control artificial?

- While our various regulatory bodies maintain a distinction between palliative symptom management and CNCP…..
- Virtually all palliative pain is chronic pain
- Chronic pain is defined as pain that has a duration of greater than six months or much longer than would be expected by the underlying aetiology
- Chronic pain strategies can have therapeutic value in palliative settings that we often fail to take full advantage of

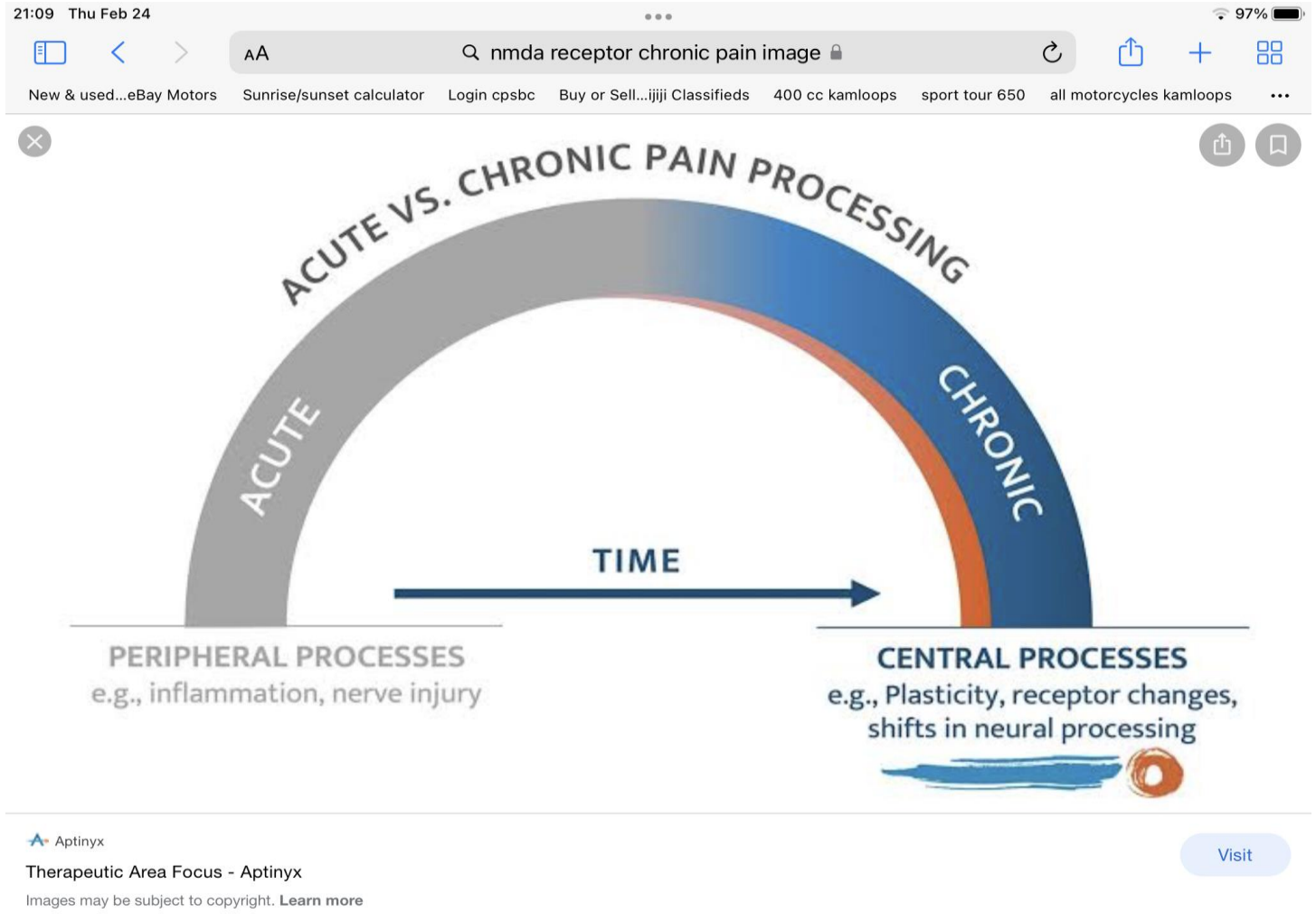
NMDA Receptor Role in Pain Sensitization



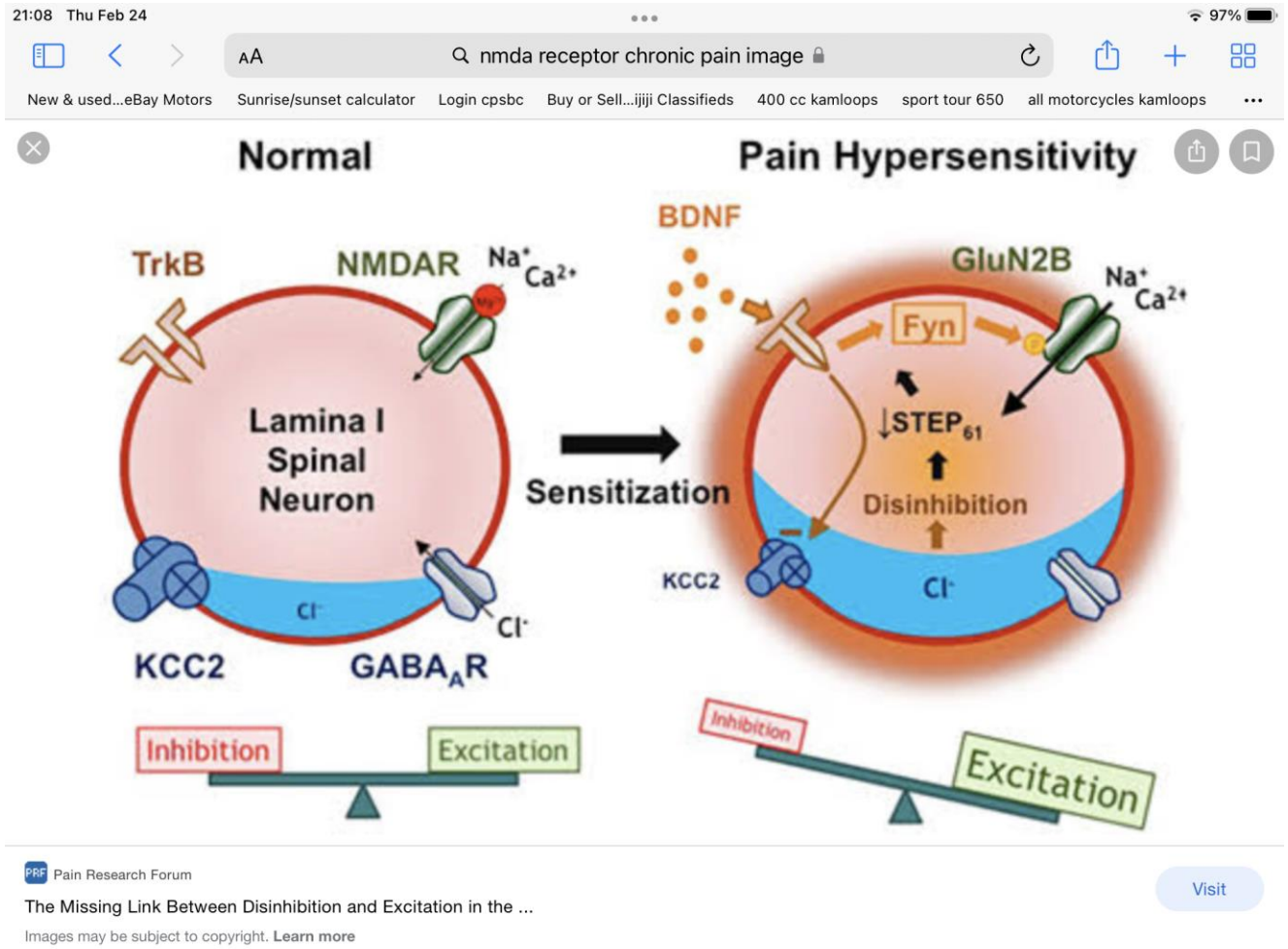
How is chronic pain management different? The role of the NMDA receptor

- Neuroplasticity
- Long-term potentiation (LTP) is the process by which synaptic connections between neurons becomes stronger with frequent activation i.e. learning and memory
- Practice leads to perfection, including in pain sensitivity, the so-called central sensitization syndrome
- NMDA receptors are critical in LTP or central sensitization
- NMDA receptors are associated with hyperalgesia thru LTP and therefore can present a target for chronic pain management in palliative care
- NMDA receptors play a crucial role in reduced opiate mu receptor sensitivity and the development of tolerance to opiates

NMDA Receptor blockade and chronic pain



Disturbed equilibrium



NMDA blocking potential benefits

- Prevent long-term potentiation (LTP) (i.e., “pain learning”)
- Prevent central sensitization syndrome
- Reduce mu receptor tolerance development

NMDA receptor antagonists

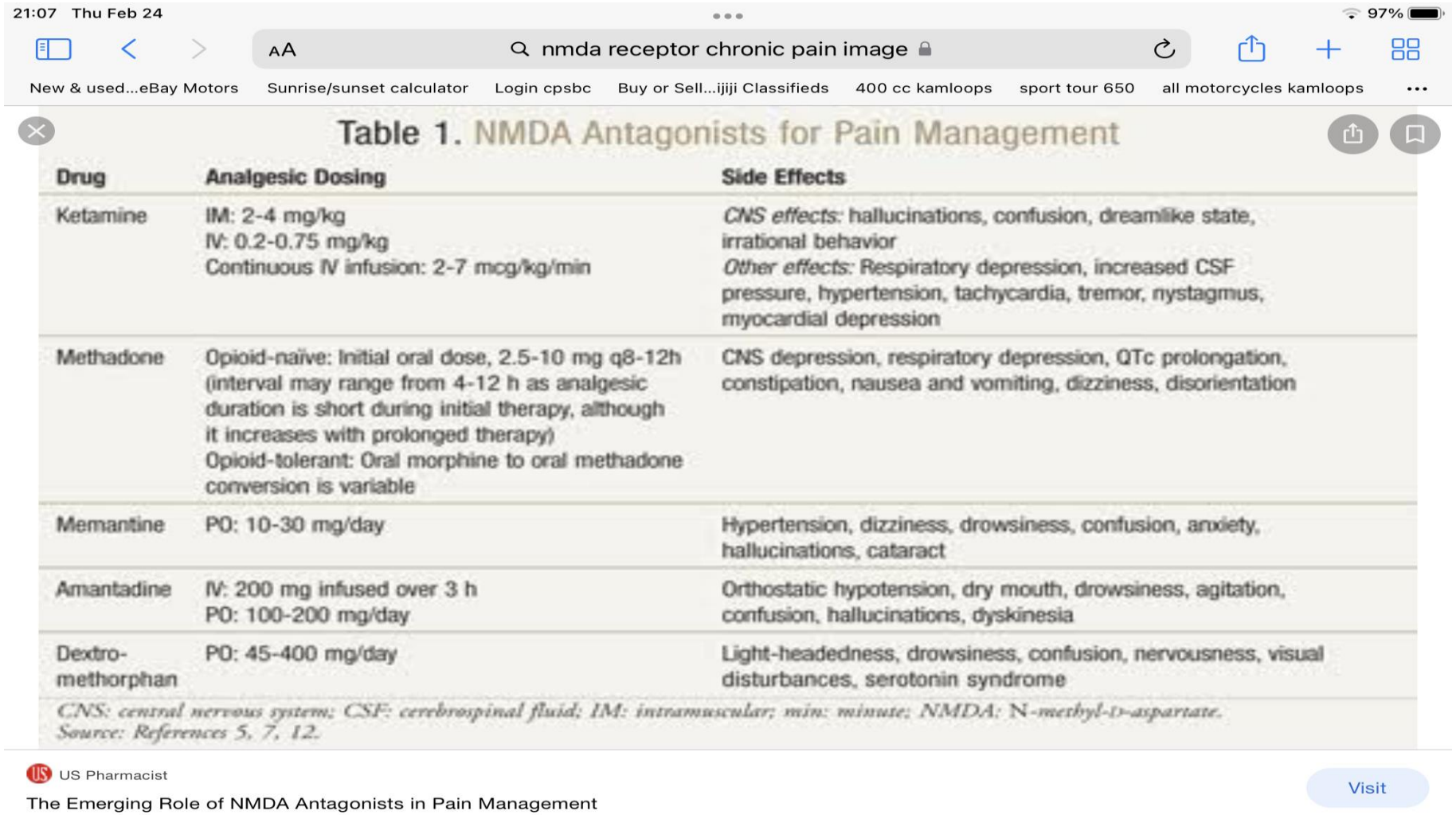


Table 1. NMDA Antagonists for Pain Management

Drug	Analgesic Dosing	Side Effects
Ketamine	IM: 2-4 mg/kg IV: 0.2-0.75 mg/kg Continuous IV infusion: 2-7 mcg/kg/min	*CNS effects:* hallucinations, confusion, dreamlike state, irrational behavior *Other effects:* Respiratory depression, increased CSF pressure, hypertension, tachycardia, tremor, nystagmus, myocardial depression
Methadone	Opioid-naïve: Initial oral dose, 2.5-10 mg q8-12h (interval may range from 4-12 h as analgesic duration is short during initial therapy, although it increases with prolonged therapy) Opioid-tolerant: Oral morphine to oral methadone conversion is variable	CNS depression, respiratory depression, QTc prolongation, constipation, nausea and vomiting, dizziness, disorientation
Memantine	PO: 10-30 mg/day	Hypertension, dizziness, drowsiness, confusion, anxiety, hallucinations, cataract
Amantadine	IV: 200 mg infused over 3 h PO: 100-200 mg/day	Orthostatic hypotension, dry mouth, drowsiness, agitation, confusion, hallucinations, dyskinesia
Dextro-methorphan	PO: 45-400 mg/day	Light-headedness, drowsiness, confusion, nervousness, visual disturbances, serotonin syndrome

CNS: central nervous system; CSF: cerebrospinal fluid; IM: intramuscular; min: minute; NMDA: N-methyl-D-aspartate.
Source: References 5, 7, 12.

NMDA antagonist: Methadone

- A pure mu agonist
- A potent NMDA antagonist
- Dual metabolic excretion liver or kidney
- No neuro-excitatory metabolites
- Excellent analgesia
- Much less risk of tolerance developing

- Cons
- Long half life 24- 96 hours
- Potent respiratory depressant
- QT prolongation

Methadone

- Medications generally require 4-5 half lives to achieve steady state
- Methadone can require a minimum of 4 days between dose adjustments …..start early in the disease process
- P.O. or rectal, no parenteral version in Canada
- Not suitable for BTP, will require a second opiate
- Difficult to convert but roughly equivalent in potency to hydromorphone
- For pain management as opposed to Opioid Agonist Therapy (OAT), best given TID
- Despite these challenges a very useful drug once familiarity is achieved

Dextromethorphan the DM in cough syrup

- Multiple sites of action
- Not a mu agonist
- Dissociative analgesia
- NMDA receptor blocker when used in high doses 300-600 mg/day
- Half-life variable 2-24 hours
- Side effects include agitation, hypomania, delusional disorders

Ketamine

- Very potent NMDA receptor antagonist
- Opiate sparing by reducing tolerance
- A potent antidepressant a useful activity in palliative care
- Ketamine burst therapy (full 5 days often not required)
- Day 1 100mg S/C infusion over 24 hrs
- Day 2 200 mg S/C infusion over 24 hrs
- Day 3, 300 mg S/C infusion over 24 hrs
- Day 4 400 mg S/C infusion over 24 hrs
- Day 5 500 mg S/C infusion over 24 hrs (we use a Baxter 2ml/hr infuser or CADD pumps)
- Protocol will often reduce opiate requirements and improve pain control for up to 4 weeks

Ketamine

- As a dissociative analgesic/anesthetic altered consciousness is possible including psychosis
- Dose related
- Haldol premedication?

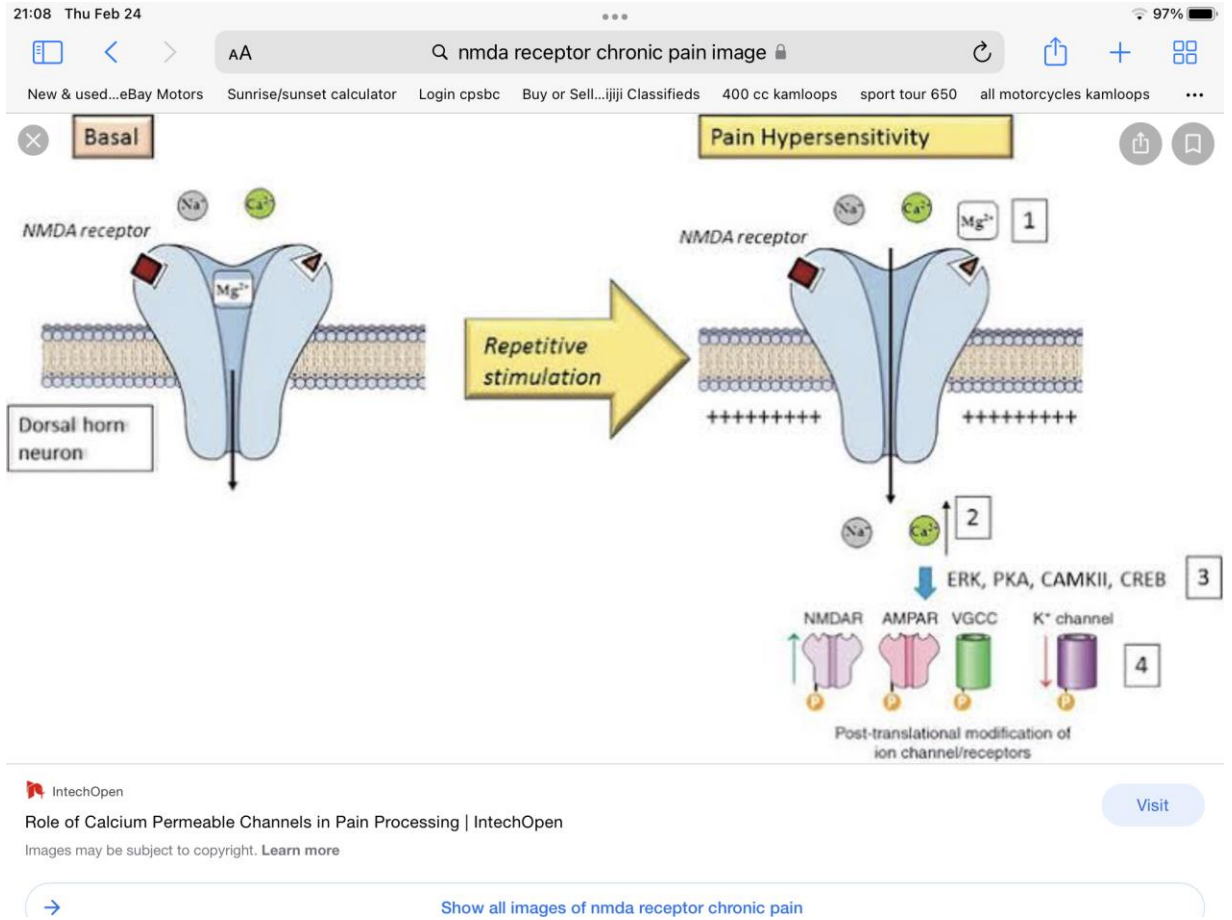
Other NMDA antagonists

- Memantine (Ebixa) used for dementia treatment as NMDA antagonism leads to increased acetylcholine release, pain studies however have shown a weak response
- Amantadine no longer used for influenza A, but veterinary use as an NMDA antagonist in dogs

Magnesium

- Magnesium citrate PO 150-600 mg /day divided doses is approximately 40% absorbed, with the remaining 60% non absorbed, the non absorbed 60% can act as an osmotic laxative similar to lactulose or Peg useful in constipation management
- In addition, magnesium stabilizes cell membranes, improving pain control and promoting uninterrupted sleep as well as a sense of ease
- Magnesium has a critical role in the NMDA receptors, serving as a “plug” blocking the NMDA receptor channel and preventing Ca from entering the cell and starting the cascade

The critical role of magnesium (deficiency is common with western diet)



Magnesium and NMDA activity

21:11 Thu Feb 24 ibshypo.com 96%

Magnesium and NMDA Receptors

Magnesium plays a central role in the activation of NMDA receptors. NMDA receptors are triggered after prolonged glutamate activation when a Mg^{2+} ion plug is replaced by a Ca^{2+} ion. The NMDA glutamate channel has a magnesium block.

Experimental magnesium deficiency induces hyperalgesia, which is reversed by NMDA receptor antagonists.


NCBI Resources How To

PMC

Advanced Journal list

Journal List > Br J Pharmacol > v.134(6); 2001 Nov > PMC1573046

BJP British Journal of Pharmacology

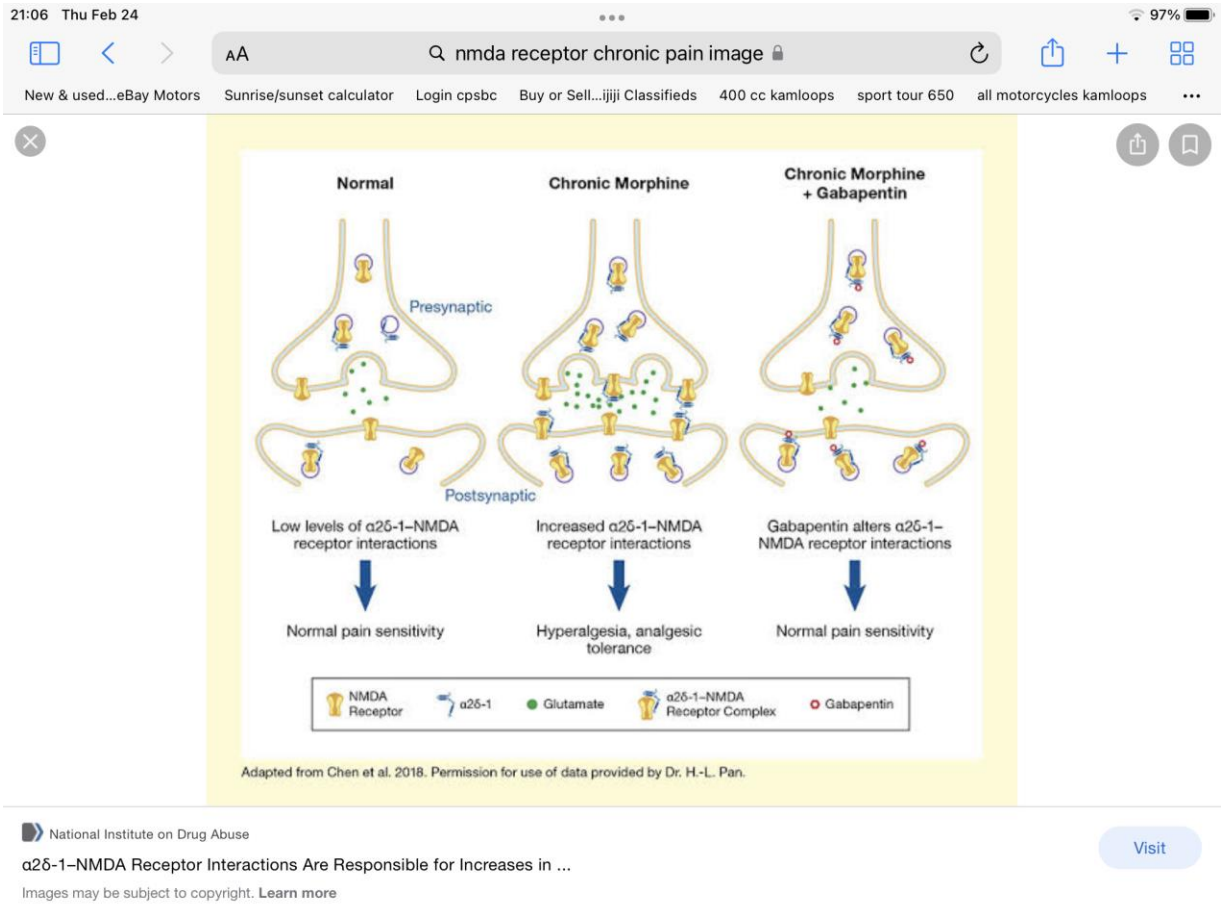
Br J Pharmacol. 2001 Nov; 134(6): 1227–1236. PMCID: PMC1573046
doi: 10.1038/sj.bjp.0704354 PMID: 11704642

Role of spinal NMDA receptors, protein kinase C and nitric oxide synthase in the hyperalgesia induced by magnesium deficiency in rats

Sophie Begon,[1] Gisèle Pickering,[1,*] Alain Eschalier,[1] André Mazur,[2] Yves Rayssiguier,[2] and Claude Dubray[1]

Magnesium supplementation has been shown to reduce post-operative pain and its addition to anaesthetics reduces anaesthesia requirements.

Gabapentin really can play a role, it just takes a long time (if ever) to appreciate it!



The role of gabapentin and its various analogues in NMDA receptor activation

- Gabapentin can block or reduce the influx of Ca when the Mg plug is removed thus contributing to less LTP and reducing the risk of opiate tolerance developing
- Subjectively patients may not “appreciate“ that the medication is working in the background

Think NMDA antagonism early

- Just as we have seen the benefits of an early palliative approach
- We should consider the critical role that the NMDA receptor can play in long term symptom control
- With the exception of ketamine therapy, other approaches can take time to have an effect
- Early use of magnesium citrate and gabapentin?

Opioid toxicity

- Codeine and morphine have neuro-excitatory metabolites that rely on renal excretion, if this is impaired by CKD or the far more common scenario of dehydration these metabolites can accumulate and lead to opiate toxicity
- Hyrdromorphone and oxycodone are much less likely to cause this and safer to use in CKD patients
- Fentanyl and methadone do not have neuro-excitatory metabolites and are even better choices

Incident Pain Management

- Fentanyl 50 mcg/ml (injectable) given sublingual, do not swallow for 2 minutes
- Quick in 5 minutes, quick out 15 minutes
- If significant opiate tolerance switch to sufenta (10 x fentanyl)

Thank you!

Questions & Discussion

Complex Pain Management Case Study

Mrs. MP

- 40 year old lady with extensive vulvar cancer and pelvic mets
- Received delayed treatment d/t anxiety and negative experiences with health system; now “palliative”, no further treatment options; PPS 60%
- Past history of neglect, abuse and substance mis-use
- Massive open fungating wound in her groin area; colostomy
- Unable to sit or lay for any length of time, always on her feet.

Social situation:

- Lives with spouse and 3 children (aged under 10) in remote rural property
- Limited formal home health services available (2x/week)

Current Medication Regime

- Methadone 150mg po daily
- Oxycodone 40mg every 3 hours
- Fentora (oral fentanyl*) 100mcg SL every hour PRN
- Pain 6 or 7/10, with 8-‘14’/10 incident pain; meds do not help her rest.
- Offered an epidural in past but the client is only wanting this as a last resort as this would mean she would be away from her young family

(*Note: Family Physician ordered fentora but not covered by palliative benefits. Client had a $1300 bill for a 4 day use, can’t afford and stopped fentora).

Current Situation and Medication Intervention

- Large increase in multi-symptom burden and distress:
  - Pain (7-14), Tiredness (10), Drowsiness (8), Nausea (0), lack of appetite (6), shortness of breath (0) depression (5); anxiety (9) and wellbeing (10).
  - PPS remains at 60%
- Consult with Palliative Physician (Dr. Baker/GP)
  - Started on Sufentanyl PCA S/C infusion at 20mcg/hr with 5mcg bolus every 15min for break through pain
  - Titrated q24 hrs: received 632 mcg/24 hrs: 31 bolus doses and 62 attempts.
  - Increased to 25mcg/hr and 6 mcg q15 mins; still poor effect, pain 8-9/10;
  - Increased to 30 mcg/hr and 7.5 mcg q10 mins, little relief
  - Moved to layer in Ketamine therapy – full 5 day burst – 500 mg on Day 5;
  - Improved pain 5-7/10, sleeping 5 hrs per night; still occasional incident pain 10-14/10
  - No adverse effects

Alternate Complex Pain Interventions Used: Whole Community Palliative Rounds Approach

- OT/PT consult for “nesting” options in the home
- OT/PT consult for energy conservation strategy (3 busy kids!)
- Palliative Social Worker consult for supportive counselling/housing
- Home Health Nursing increased visits from 2x/week- up to daily by exception.
- Skin/Wound Care Specialist consulted and a Lido/Flagyl spray added to regime

Outcomes:

- Rural based palliative team kept her home for another 6 weeks with variable pain control (5-7/10) and some sleep ~ 4-5 hours/night
- Eventually chronic pain issues were overwhelming; Family moved to larger urban centre + hospice (arranged by social worker to keep them together) to receive an epidural which provided complete pain relief
- Restored quality of life, stayed in urban hospice setting with family; rapid decline in condition and died 10 weeks later.
- Post debriefing and support with local team: failure or success?

Session Wrap Up

- Please fill out the feedback survey following the session! Link has been added into the chat
- A recording of this session will be emailed to registrants within the next week
- Please join us for the next session in this series:
  - Managing the Last Hours of Life in the Home
  - Presenter: Dr. Alissa Tedesco
  - March 16th, 2022 from 1-2pm ET
- Bring us your cases! There are several ways to initiate this process:
  - Contact our support team at echo@pallium.ca
  - Let us know in the feedback survey
  - Complete the case submission form- attachment has been added into the chat

Thank You

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