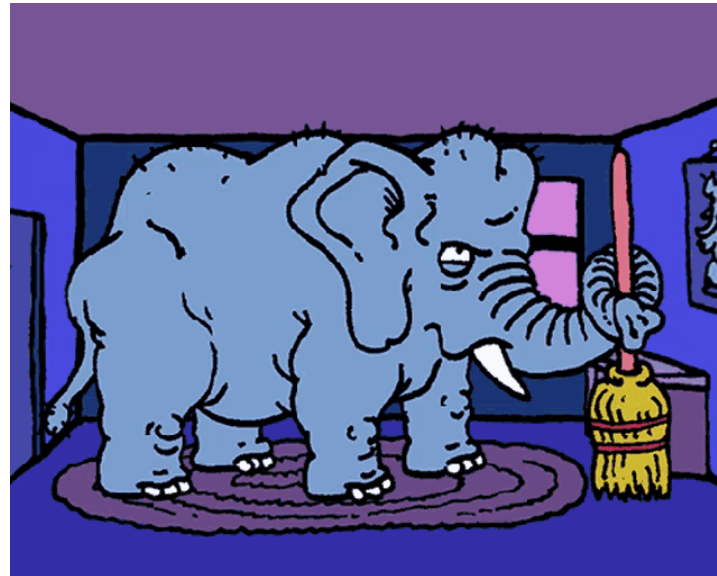
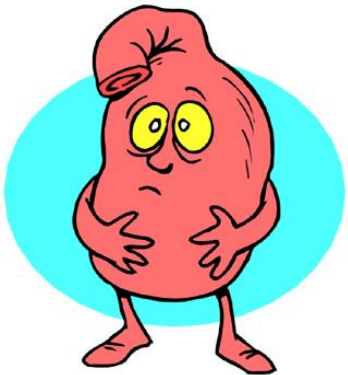


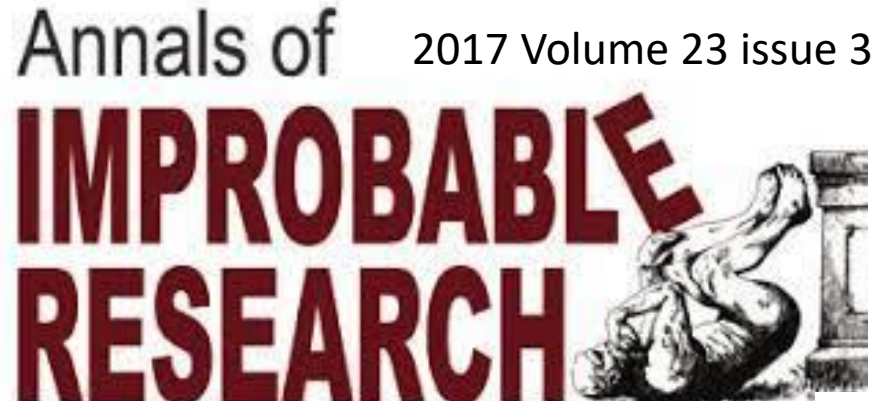
chronic abdominal pain

Dr Peter Paine:
NEPG Huddersfield 2024

1. Naming Pain
2. Framing Pain
- 3. Inflaming Pain**
4. Calming Pain



1. Naming Pain



Improbable Research Reviews*

Improbable Research: Bubble Wrap and Insignificance
Medical: Koch, Wrong, and Useless Ear Movement*
Improbable Sex: Smart Teens and Sex*
Ig® and Beyond: Hydrodynamics of Defecation; Chev
Boys Will Be Boys: Congestion, Comeuppance*
Dog Research: Dogs and Humans, Peeing*
Cats Research: String and Balls*
Smoking / Drinking / Drugs: Kissing Addiction, Beer
Icky Cutesy: Head Zapping, and an Extra Scalp*
Nominative Determinism: Paine on Pain, in Pain*



PAIN® 144 (2009) 236-244

PAIN®

www.elsevier.com/locate/pain

Research papers

Exploring relationships for visceral and somatic pain with autonomic control and personality

Peter Paine^a, Jessin Kishor^b, Sian F. Worthen^b, Lloyd J. Gregory^a, Qasim Aziz^{b,*}

^aDepartment of Gastrointestinal Sciences, Hope Hospital, University of Manchester, UK

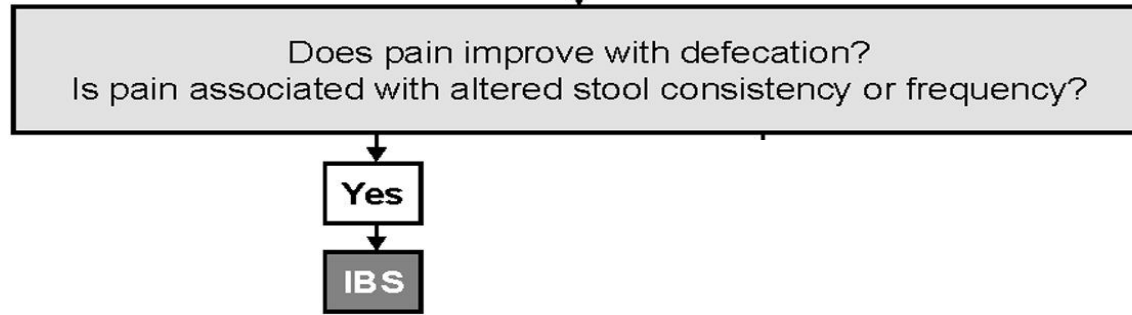
^bBarts and the London, Queen Mary School of Medicine and Dentistry, University of London, UK





“I’m afraid that your irritable bowel syndrome has progressed. You now have furious and vindictive bowel syndrome.”

Chronic abdominal pain



Review article: diagnostic and therapeutic approach to persistent abdominal pain beyond irritable bowel syndrome



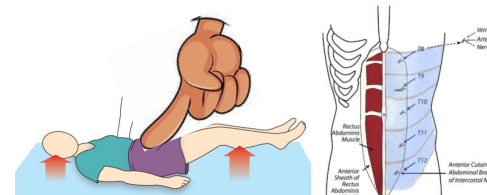
~~The "F" word~~

- FAPS → CAPS
- FGID → DGBI
- AD → GBNM

- *SOD 3*
- *Chronic pancreatitis*
- *IBS in IBD*

Centrally mediated

(ACNES)



Scylla or Charibdis?



Naming Pain: Pain Nosology

chronic pain as disease not just symptom

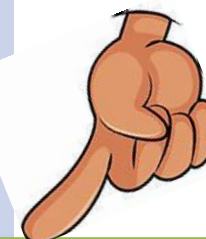
- IASP 2017 (mechanistic)
 - **Nociceptive** (normal)
 - (impending) tissue damage
 - **Neuropathic**
 - Nerve damage
 - **Nociplastic**
 - Nerves behaving badly!
- ICD 11 (diagnostic)
 - Primary – Pain as a disease
 - Secondary – Pain as a symptom

Diagnosing postoperative neuropathic pain: a Delphi survey

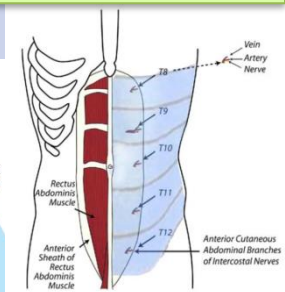
R. D. Searle^{1*}, S. J. Howell² and M. I. Bennett³ *British Journal of Anaesthesia* 109 (2): 240–4 (2012)

Table 2 Items achieving consensus after survey round 3

Important	Not important
Spontaneous	Paroxysmal
Shooting	Pulsing
Burning	Radiology
Dysaesthesia	Nerve conduction
Allodynia	
Hyperalgesia	
Difficult to manage pain	
Poor response to opioids	
Good response to anti-neuropathics	



ACNES: *finger focal*
Carnett's sign – rectus sheath
 pain on tensing



- 1. The pain is
 - 1a. Chronic (>3 mo);
 - 1b. Regional (rather than discrete) in distribution*;
 - 1c. There is no evidence that nociceptive pain (a) is present or (b) if present, is entirely responsible for the pain; and
 - 1d. There is no evidence that neuropathic pain (a) is present or (b) if present, is entirely responsible for the pain.†

- 2. There is a history of pain hypersensitivity in the region of pain.
 - Any one of the following:
 - Sensitivity to touch
 - Sensitivity to pressure
 - Sensitivity to movement
 - Sensitivity to heat or cold

3. Presence of comorbidities:

- Any one of the following:
 - Increased sensitivity to sound and/or light
 - Sleep disturbance with frequent nocturnal awakenings
 - Fatigue
 - Cognitive problems such as difficulty to focus attention, memory disturbances, etc.



nociplastic

- 4. Evoked pain hypersensitivity phenomena can be elicited clinically in the region of pain.
 - Any one of the following:
 - Static mechanical allodynia
 - Dynamic mechanical allodynia
 - Heat or cold allodynia
 - Painful after-sensations reported following the assessment of any of the above alternatives.

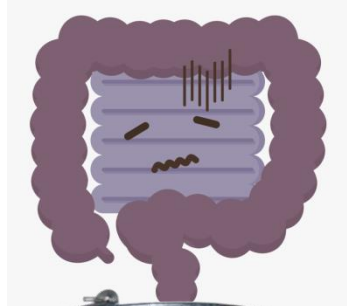


Possible nociplastic pain: 1 and 4.

Probable nociplastic pain: all the above (1, 2, 3, and 4)‡

2. Framing Pain

Adam's story



STRUCTURAL
Dilated bowel
Inflammation

legitimate

BODY



"nutter"
"junky"



NNO = 2

FUNCTIONAL
Normal scans
No Inflammation

MIND

"ill" - legitimate

Paradigm Paralysis



"I'm pink therefore I am"



Paradigm Transplant

"I think therefore I am"

STRUCTURAL
Dilated bowel
Inflammation

BODY

FUNCTIONAL
Normal scans
No Inflammation

MIND

legitimate

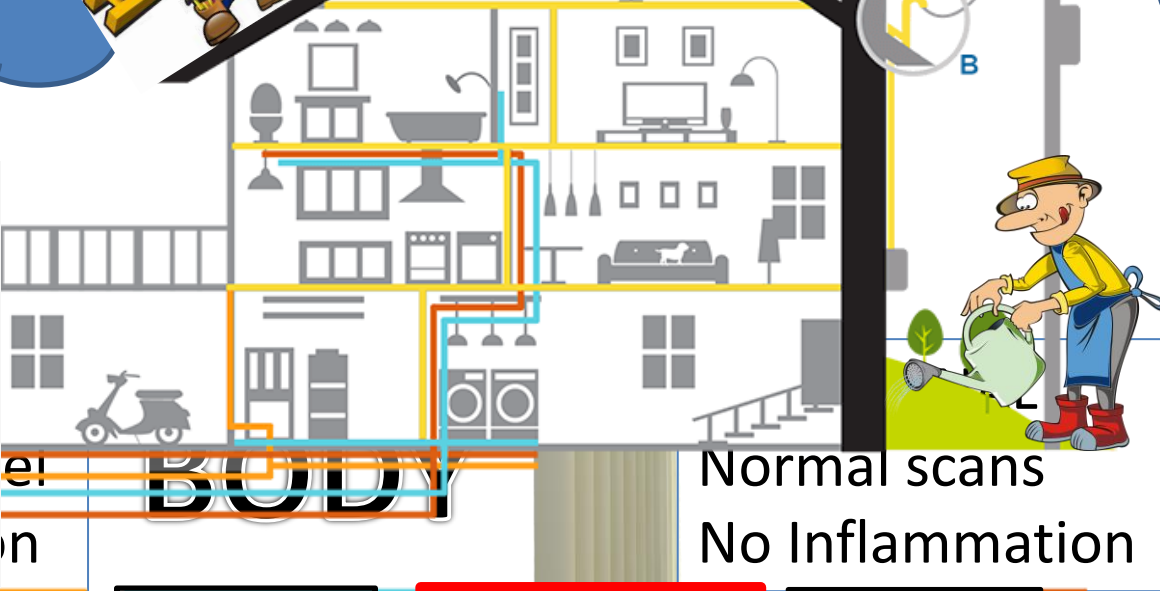
"ill" - legitimate

Cartesian Dualism

plumbing

wiring

The Psyche



legitimate

GAS LINES WATER LINES

ELECTRIC LINES

SEWER LINES "ill" - legitimate

Normal scans No Inflammation

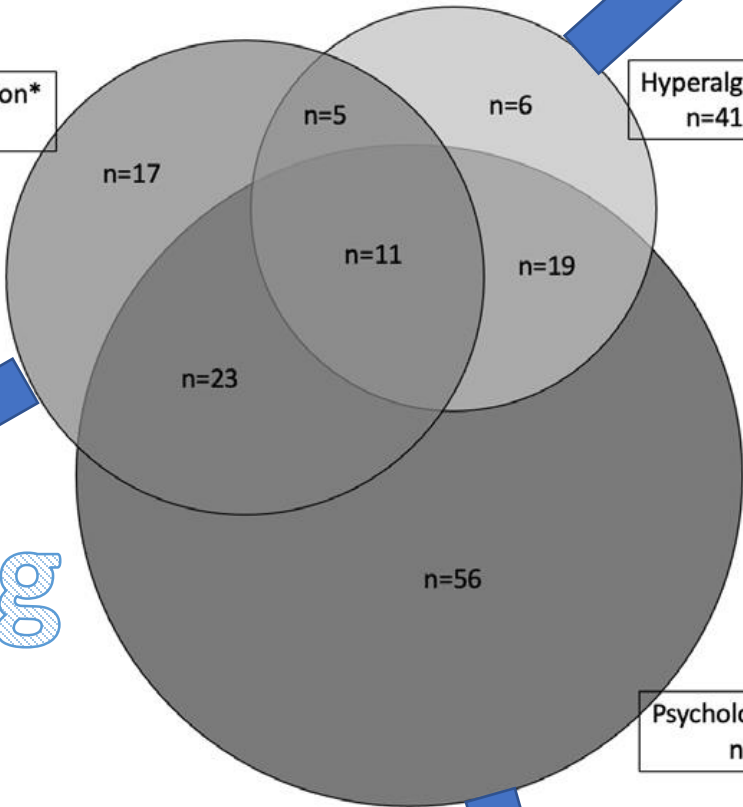
M

wiring

Pancreatic duct obstruction*
n=56

Hyperalgesia
n=41

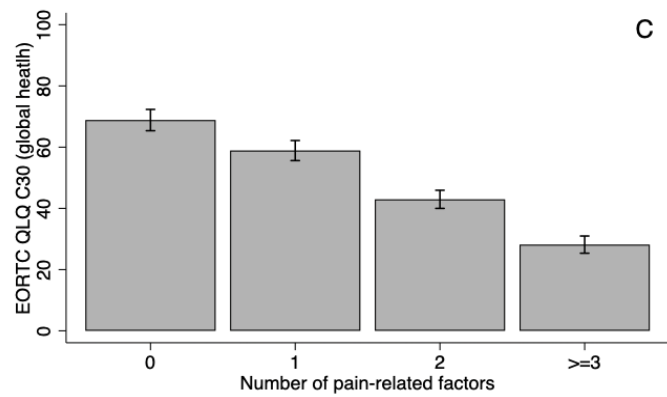
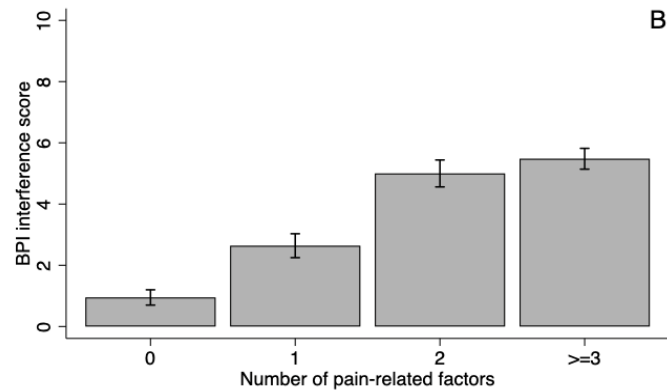
Psychologic distress
n=109



plumbing

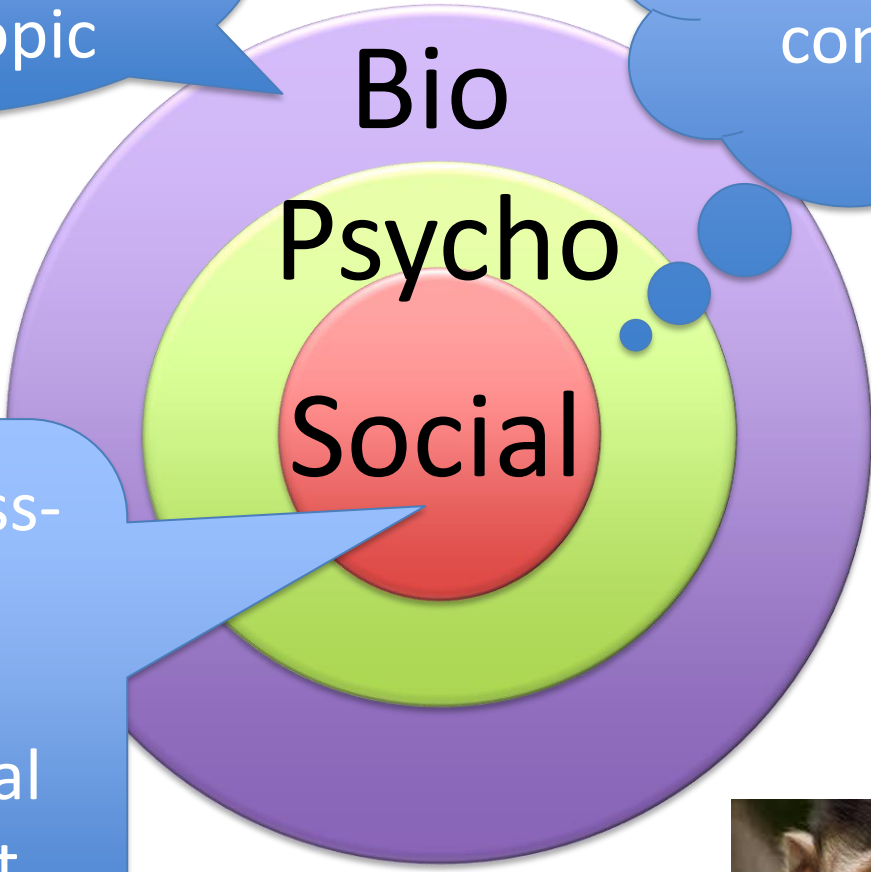
psychosocial

Olesen et al, Gut 2022

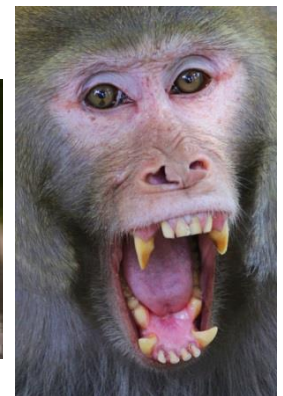
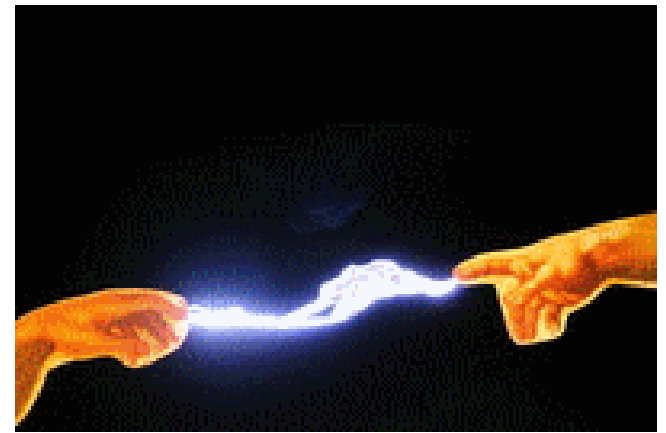


Body-minded
brain: visceros &
somato-topic

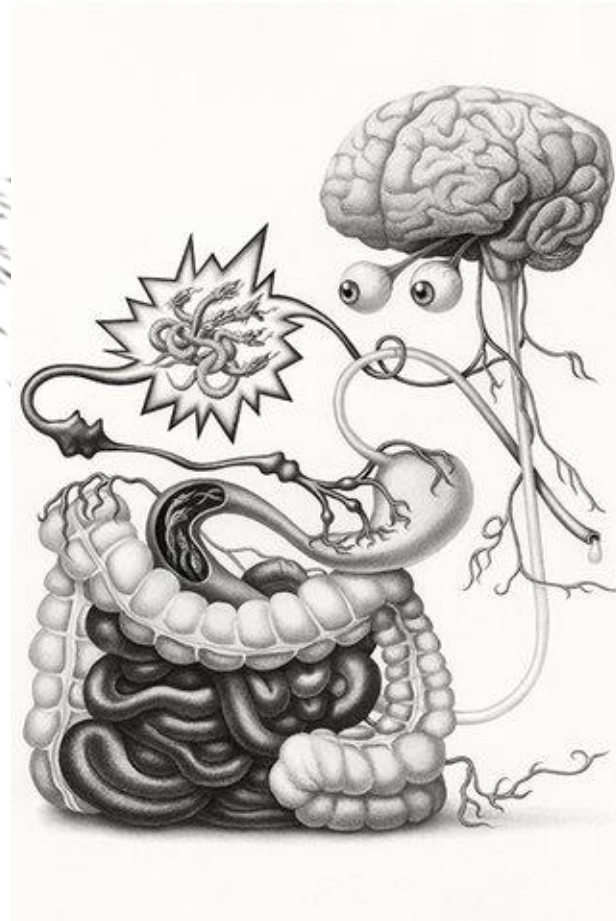
Embodied mind:
interoception &
consciousness



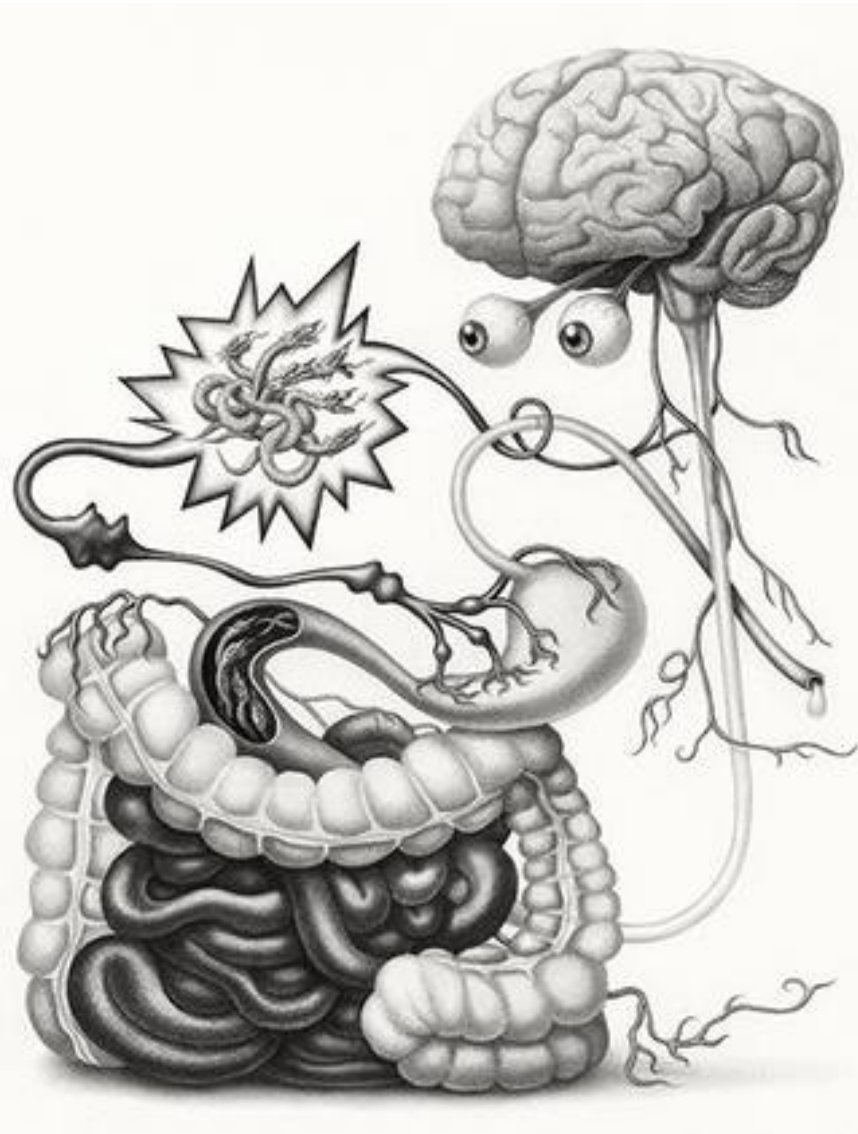
(Threat) Stress-
Defence
↕
(Safety) Social
Engagement
System



WANTED: Enteric Electricians!

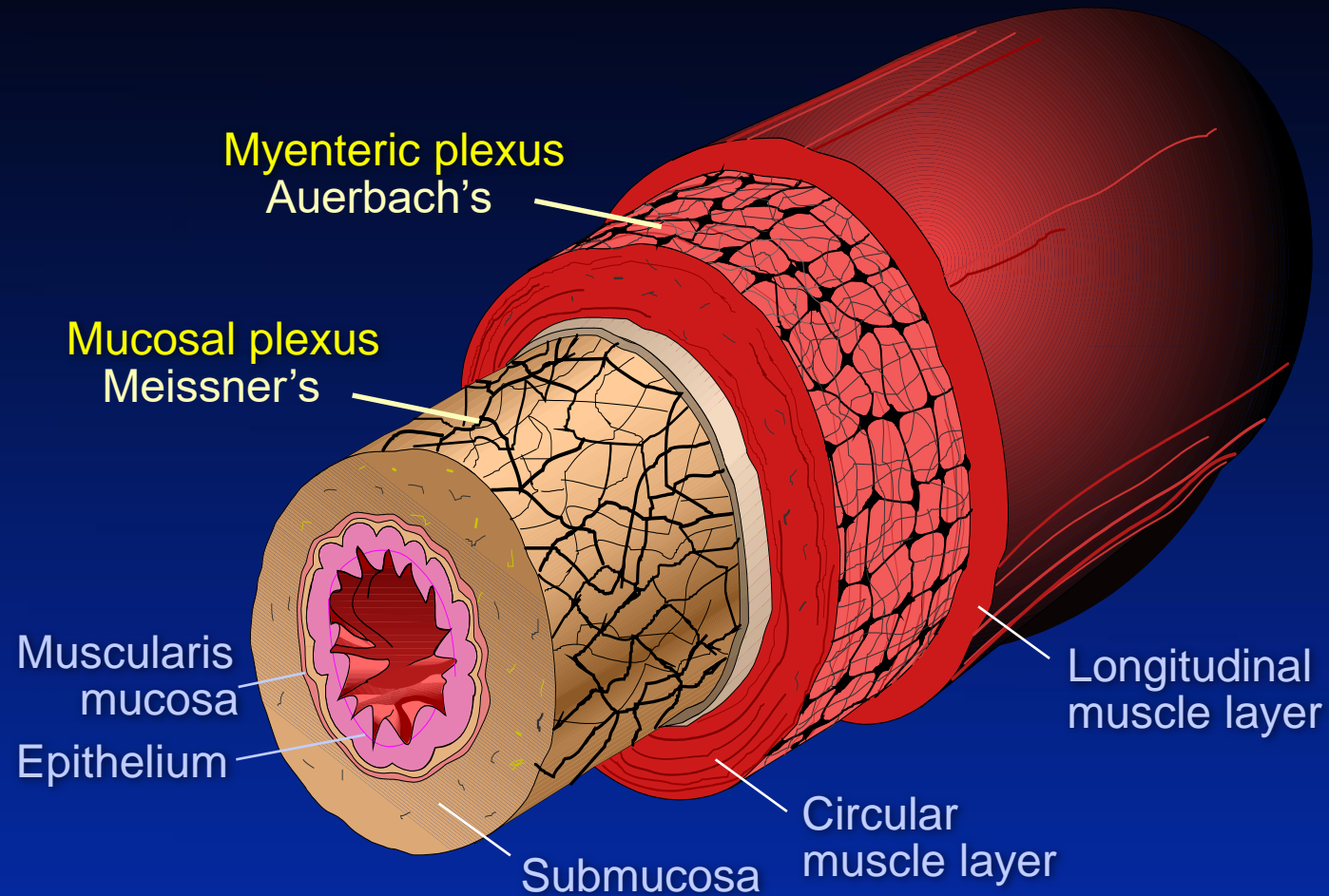


What is NGM?

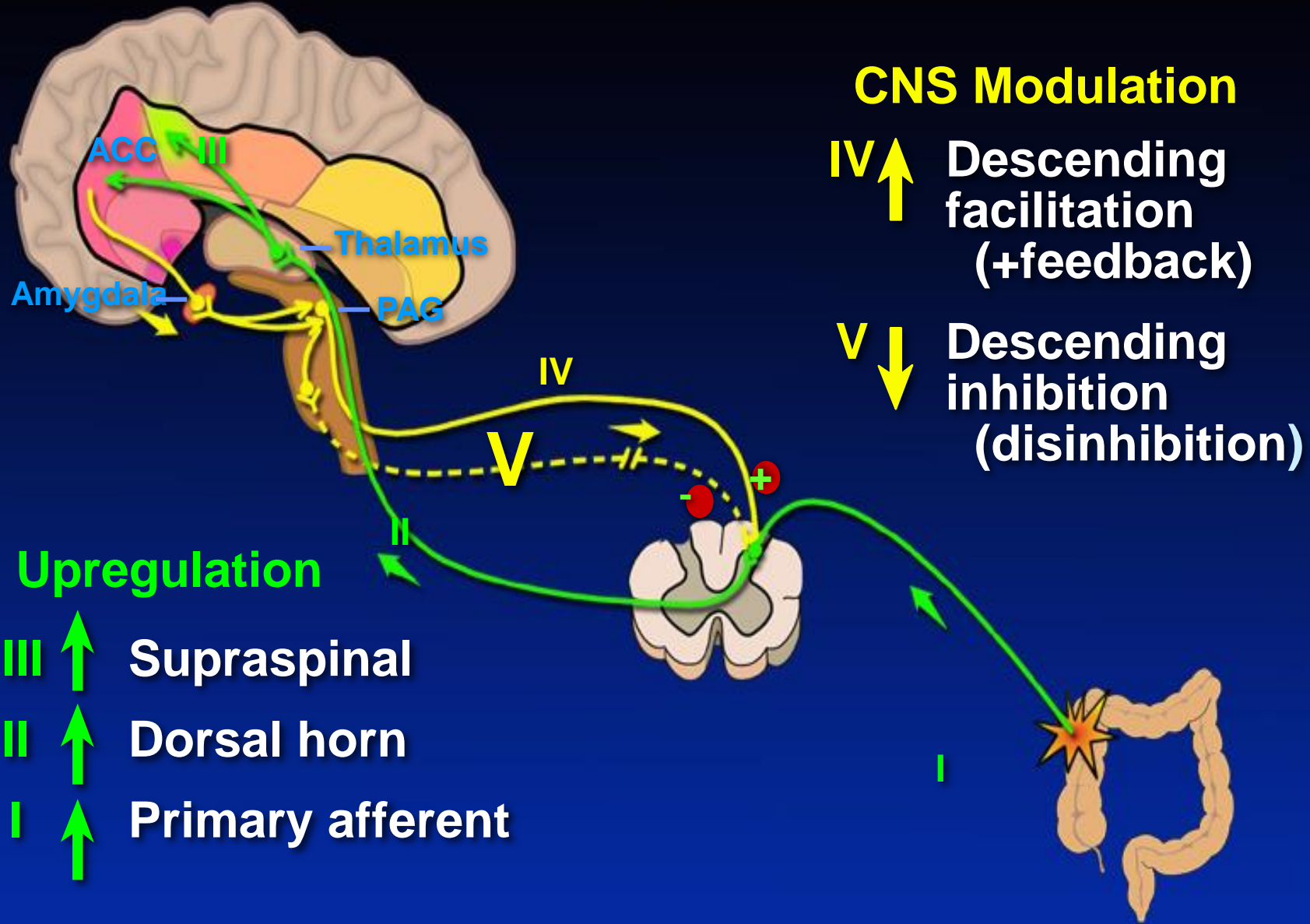


- Subspecialty (chair to 2021)
- “Functional”/DGBI gastrointestinal disorders from mouth to anus
- Biggest caseload
 - 10% primary care
 - 40% secondary care
- Least popular section
 - IBD & endoscopy “big-beasts”
 - 20-30 self-proclaimed NGM subspecialists in UK
 - Perceived as difficult and depressing and dangerous (complaints etc)

Enteric Nervous System Anatomy



IBS - Neural Alterations Leading to Increased Pain

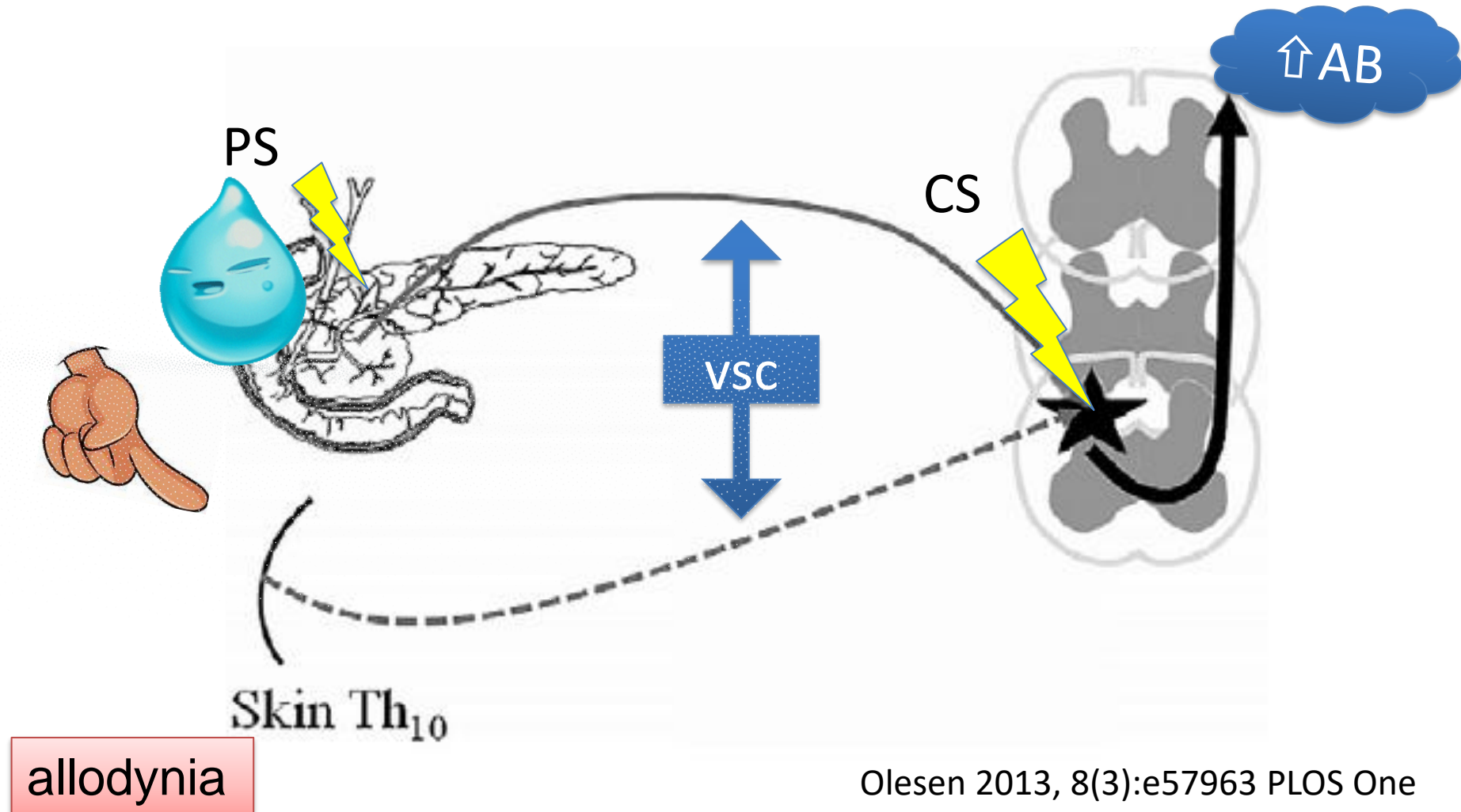


Centrally mediated pain

Criteria	CCAP, total N = 103
Rome IV CAPS criteria	
(Nearly) Continuous, n (%)	103 (100)
No relationship to gastrointestinal physiological events, n (%)	53 (51)
Function loss, n (%)	100 (97)
Not feigned, n (%)	103 (100)
Not explained by an alternative diagnosis, n (%)	103 (100)
3-6 months, n (%)	103 (100)

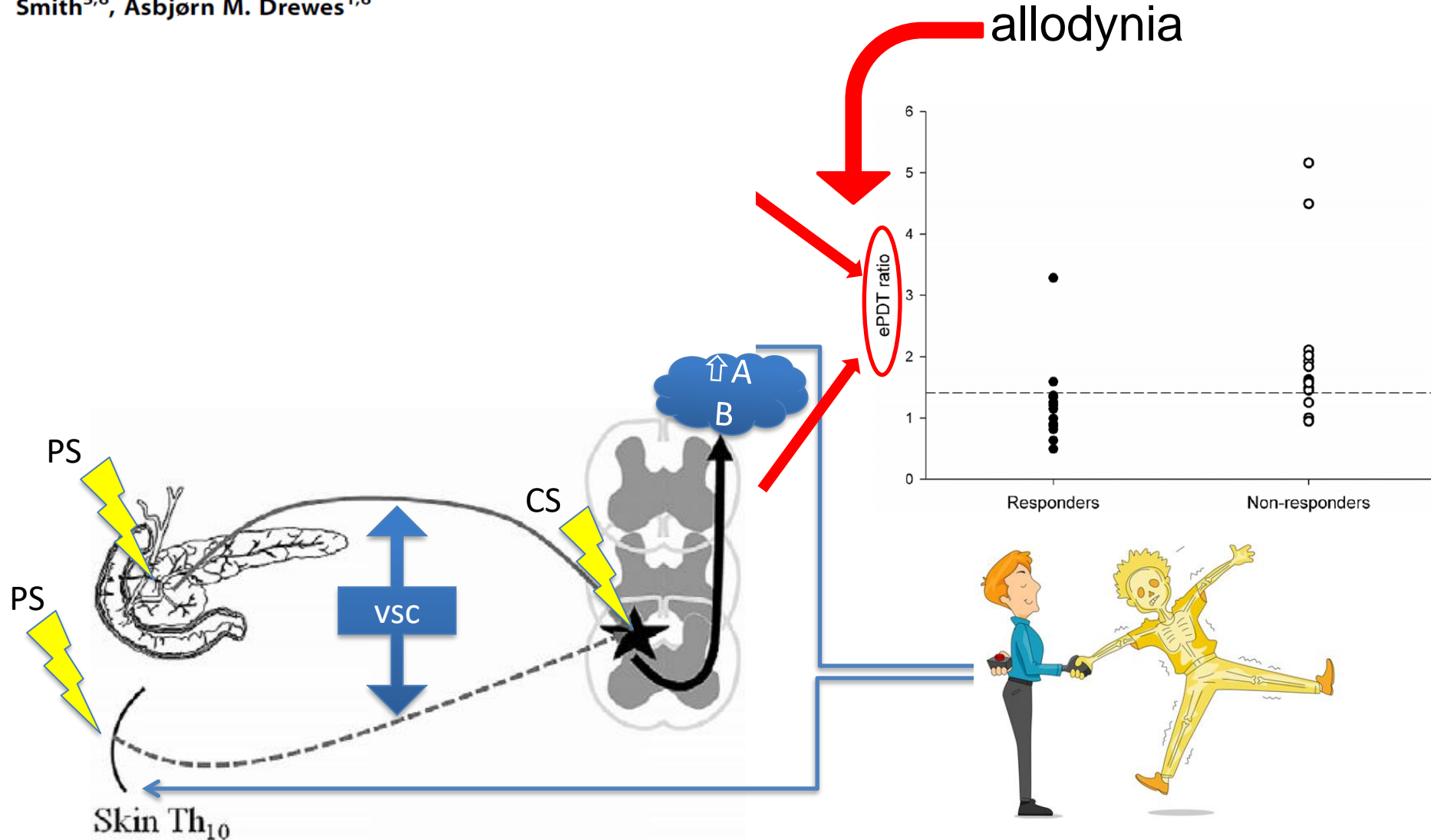
Neuropathic pain criteria	
Spontaneous, n (%)	100 (97)
Difficult to manage, n (%)	102 (99)
Allodynia, n (%)	83 (81)
Poor opioid response, n (%)	61 (59)
Shooting, n (%)	13 (13)
Burning, n (%)	12 (12)
Dysaesthesia, n (%)	9 (9)
Hyperalgesia, n (%)	7 (7)
Good response to neuropathic agents, n (%)	35 (34)

Viscerosomatic convergence



Quantitative Sensory Testing Predicts Pregabalin Efficacy in Painful Chronic Pancreatitis

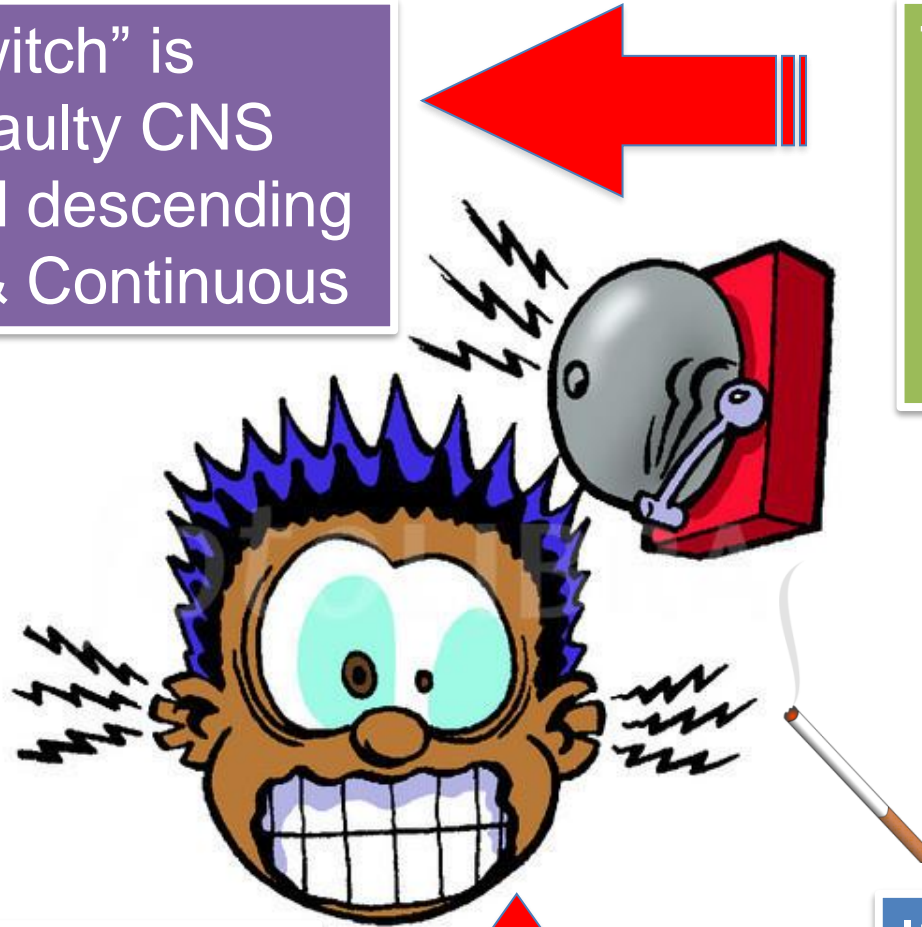
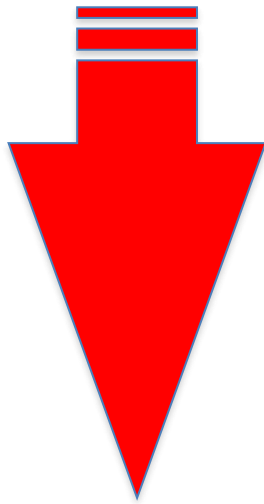
Søren S. Olesen^{1*}, Carina Graversen^{1,2,3}, Stefan A. W. Bouwense⁴, Harry van Goor⁴, Oliver H. G. Wilder-Smith^{5,6}, Asbjørn M. Drewes^{1,6}



The broken fire alarm: a wiring problem

The “off switch” is broken:- Faulty CNS gating and descending inhibition & Continuous

The volume is turned right up/amplified:- Central sensitisation, cutaneous allodynia (VSC) & hyperalgesia



It's driving me mad!:- Coping strategies over-whelmed – for any sane person

It's on a “hair trigger”:- Peripheral sensitisation & visceral allodynia

Adam's story: epilogue



- Diagnosis: CAPS & NBS
 - Settled well with opioid reduction and gabapentin and TCA over next several months
 - Weaned off all analgesics but now wants pouch!
-
- Option 1 To minimise the chances most -Do not have the operation
 - Or if he does he has to accept there is a risk that he will have on going pain which may not settle second time around

British Journal of Anaesthesia 99 (6): 775–86 (2007)
doi:10.1093/bja/aem316

BJA

REVIEW ARTICLE

Beyond Neuropathic Pain

Gabapentin Use in Cancer Pain and Perioperative Pain

Gabapentin: a multimodal perioperative drug?

V. K. F. Kong and M. G. Irwin*

*Peter Z. Yan, MD, Paul M. Butler, MD, PhD, Donna Kurowski, MD,
and Michael D. Perloff, MD, PhD*

- Option 2 600mg gabapentin as a premed
- Chose option 2 and successful pouch with no post-op pain

3. Inflaming Pain

Surgeons: friend or foe?



- “*all the operations were necessary – except the first!”*”

Sir Miles Irving
Prof of surgery
IFU, Hope Hospital

IBS and surgery

Avoiding unnecessary surgery in irritable bowel syndrome

George F Longstreth Gut 2007



Protecting patients with IBS from the risks and costs of unnecessary surgery

- 3x cholecystectomy rate
- 2x hysterectomy rate
- 2x appendicectomy rate
 - (IBS OR 2.17 for negative appendicectomy)
- Increased colon resection
- Increased back surgery

POST-SURGICAL NEUROPATHIC PAIN

ANZ J. Surg. 2008; 78: 548–555

EDWARD SHIPTON

- Neuropathic pain prevalence post-op
 - Post-thoracotomy 35%
 - Post-inguinal hernia 7-20%
 - C-Section 10%
- Laparotomy 18%
 - Re-ops → increased pain intensity
 - Mostly moderate-severe neuropathic pain
 - Lap adhesiolysis → 5% serious complications, 1% mortality
 - Most studies → adhesion & pain recurrence

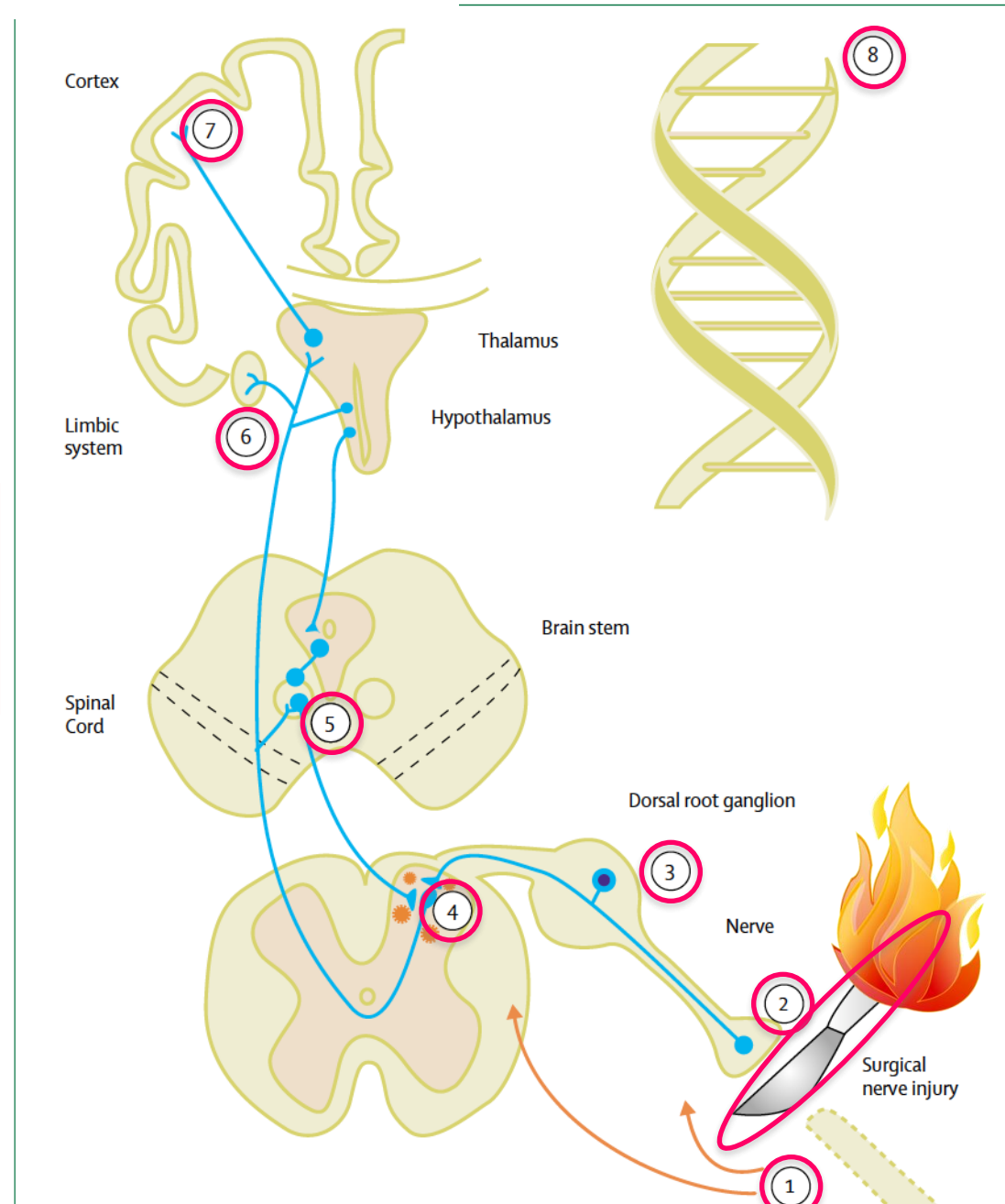


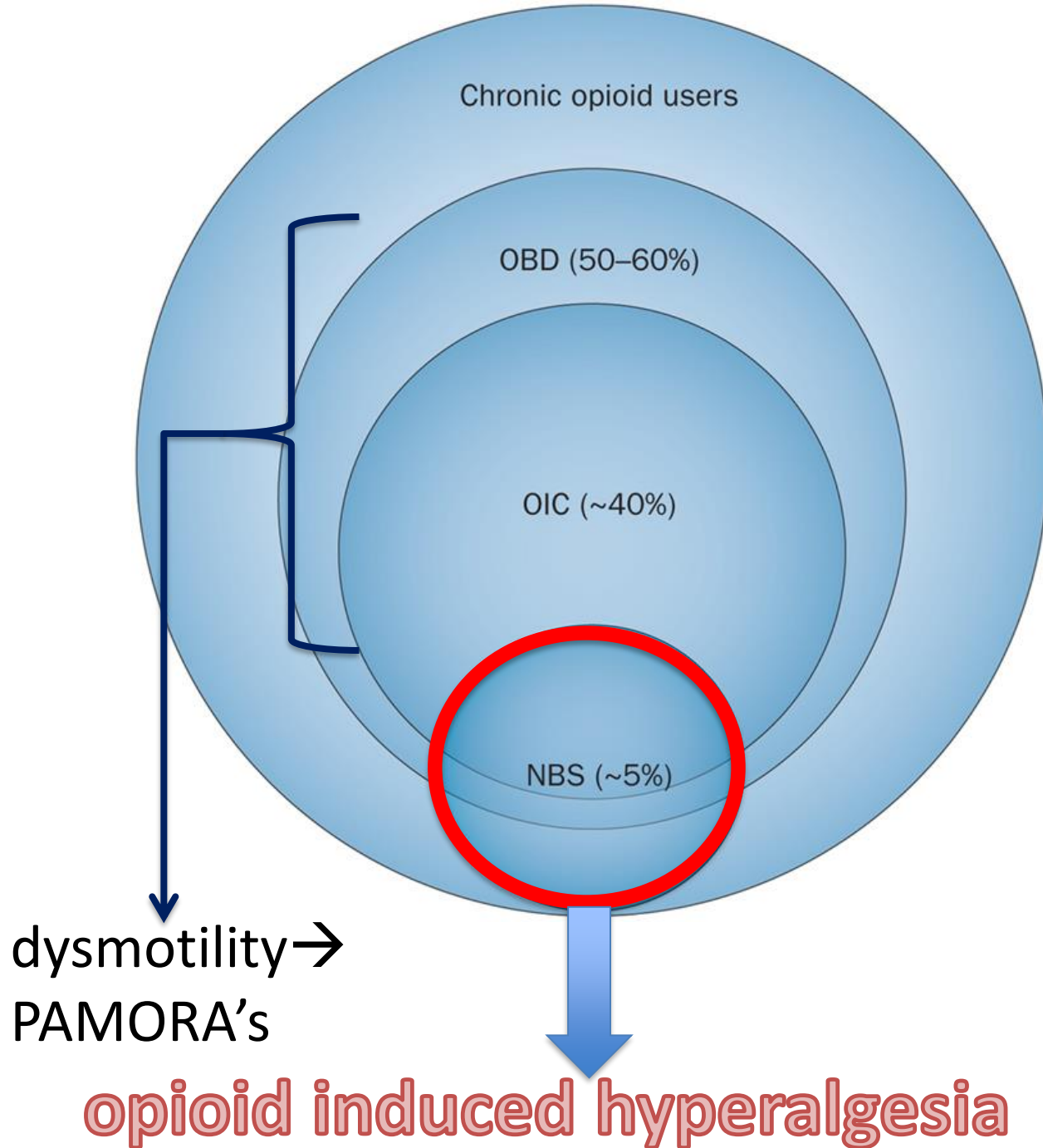
Persistent postsurgical pain: risk factors and prevention *Lancet 2006; 367: 1618-25*

Henrik Kehlet, Troels S Jensen, Clifford J Woolf

Sites & mechanisms of chronic post-surgical neuropathic pain

1. Peripheral sensitisation (distal chemicals)
2. Neuroma at injury site (ectopic excitability)
3. DRG gene expression (excitability)
4. Central sensitisation (dorsal horn gene expression, inhibitory interneurone loss, microglia activation)
5. reduced DNIC (brainstem)
6. Limbic & hypothalamus (emotion, behaviour, ANS)
7. Cortex (cognitive-evaluative)
8. Genomic DNA predisposition & Rx responsiveness?





Opioids can ruin your life

I manipulated doctors into prescribing me painkillers and various types of surgery that I did not need. Anon.

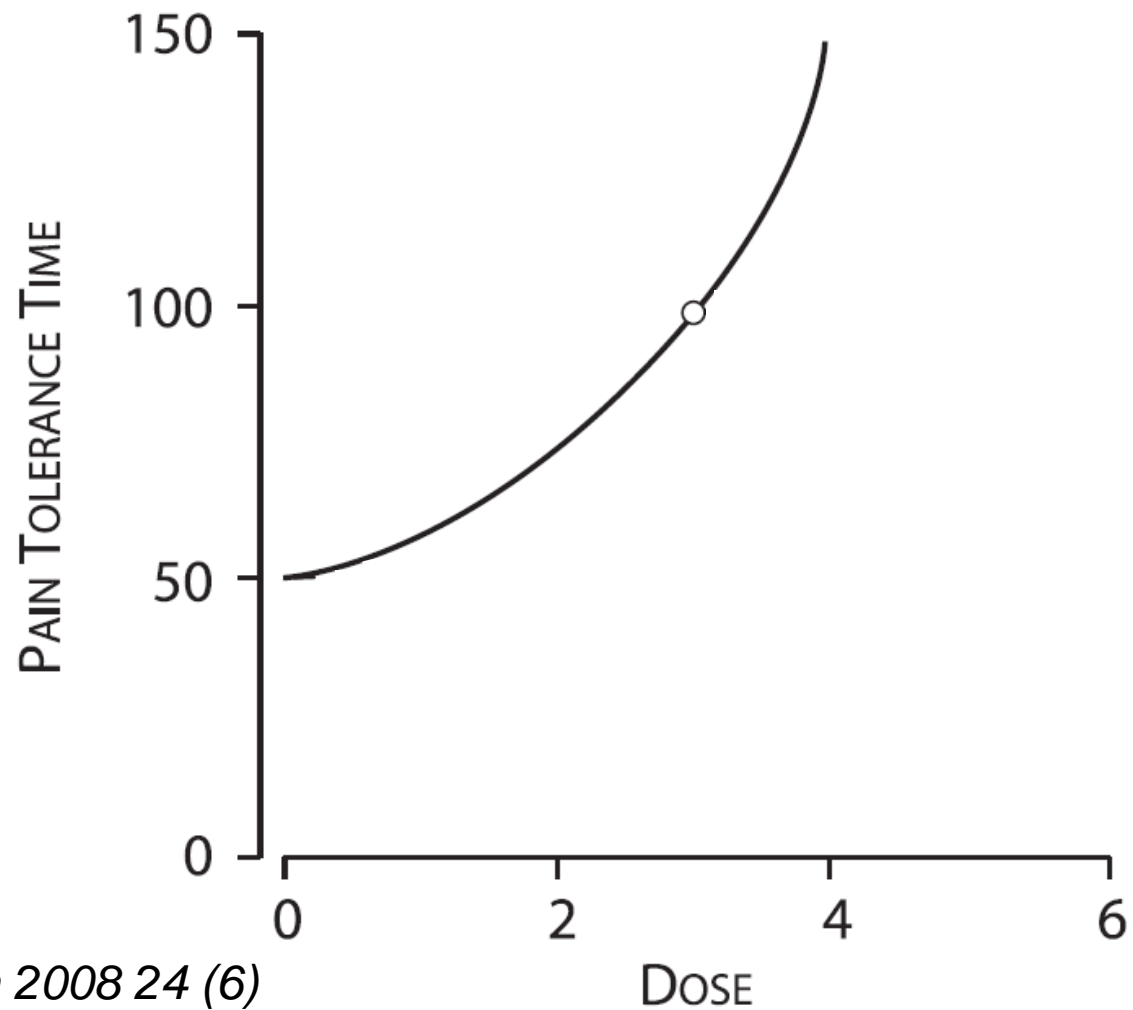
#opioidaware

YOUR MEDICINES. YOUR NHS





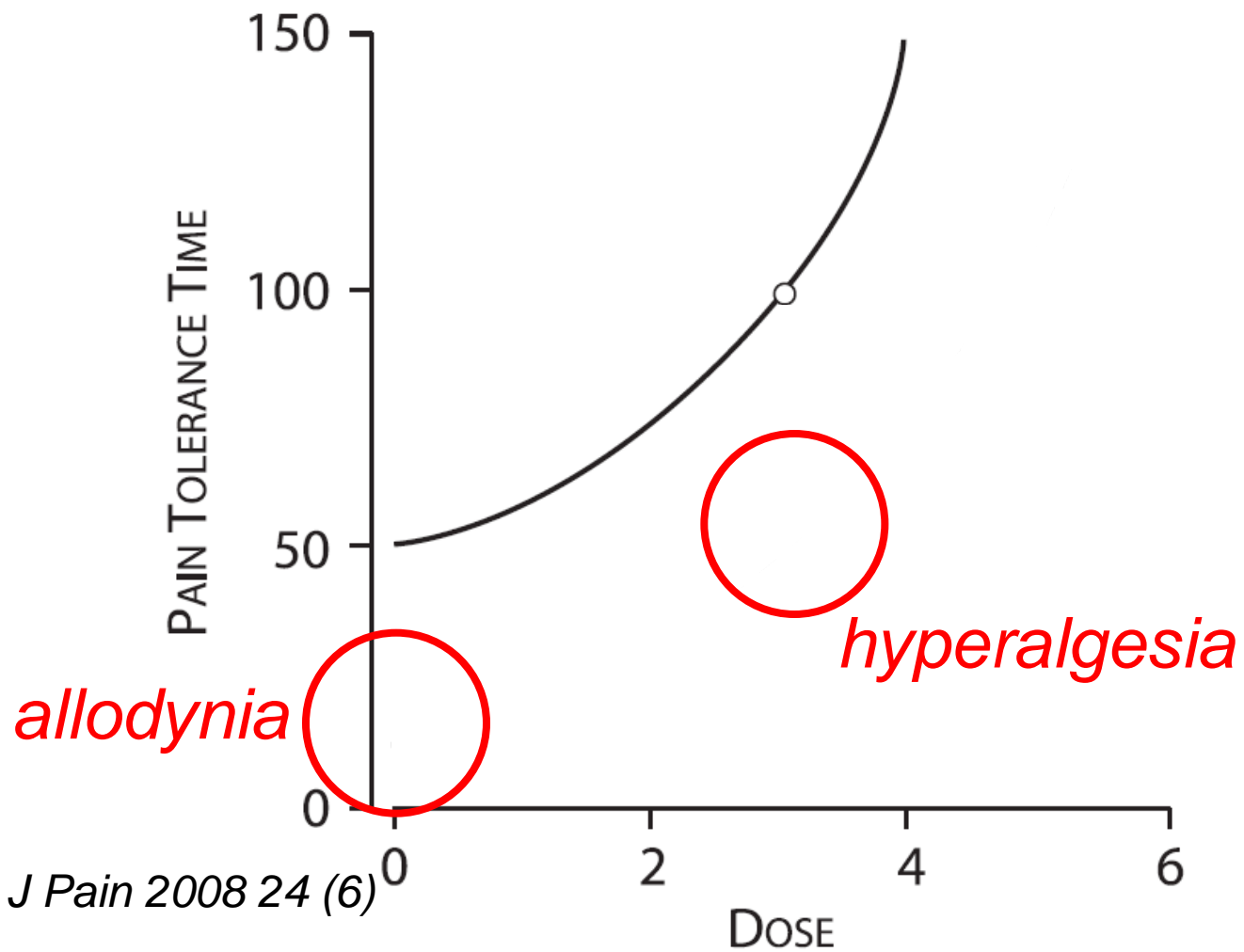
Opioid tolerance



*Chu, Clin J Pain 2008 24 (6)
479-496*

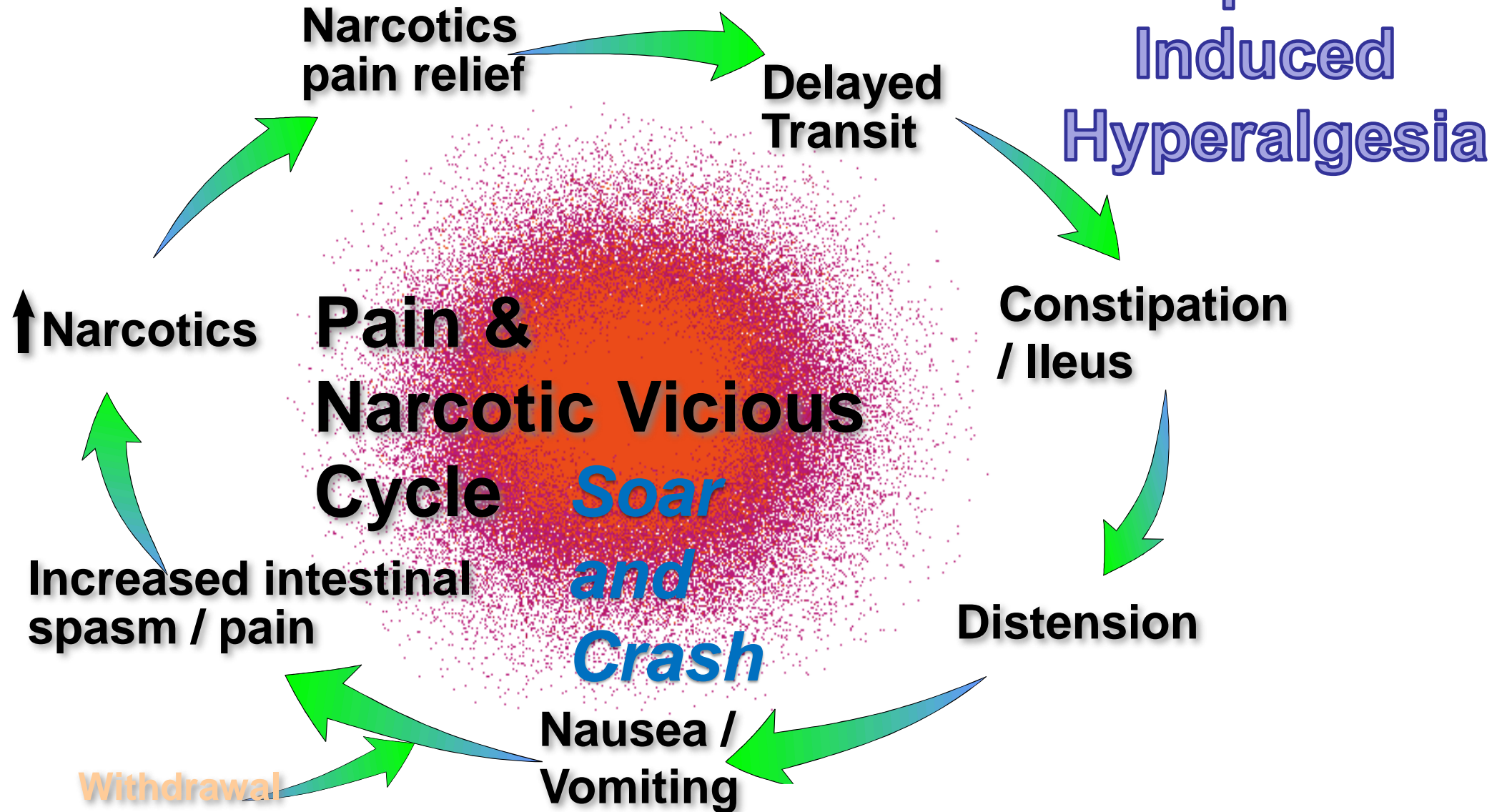


Opioid induced Hyperalgesia



Chu, Clin J Pain 2008 24 (6)
479-496

IBS - Narcotic Bowel Syndrome - dysmotility



Pain

**Vicious Cycle of
Patient - Physician
Interactions**

*Drossman
CGH 2008*

Opioid naïve vs previous vs current opioid

	OR	95% CI	P
Abdominal Allodynia			
Current	7.63	1.98-29.42	0.003***
Previous	1.05	0.22-5.00	0.951
N&V			
Current	1.15	0.34-3.71	0.810
Previous	0.54	0.11-2.55	0.433
Bloating			
Current	5.31	1.10-25.31	0.037*
Previous	8.40	1.27-55.39	0.027*
Weight loss			
Current	1.38	0.34-5.50	0.653
Previous	0.33	0.03-3.72	0.372
Above median pain score (4.5)			
Current	0.86	0.13-5.68	0.873
Previous	0.48	0.11-1.95	0.290
Trigger			
Current	2.38	0.61-9.37	0.214
Previous	1.83	0.31-9.37	0.498
Other gastrointestinal disease			
Current	0.96	0.29-3.21	0.951
Previous	0.90	0.18-4.56	0.899
Other functional diagnosis			
Current	0.95	0.18-4.95	0.959
Previous	1.20	0.14-10.11	0.867
Psychology referral			
Current	1.20	0.38-3.80	0.757
Previous	1.40	0.29-6.62	0.671

Any previous surgery			
Current	0.75	0.21-2.73	0.663
Previous	0.27	0.09-0.78	0.016*
Any surgery after diagnosis			
Current	2.76	0.78-9.82	0.117
Previous	0.35	0.11-1.17	0.089
2 or more tertiary appointments			
Current	1.43	0.43-4.79	0.561
Previous	0.72	0.25-2.02	0.528

Kilgallon... Paine
APT, 2019

Opioids Aware

<https://www.fpm.ac.uk/opioids-aware>

Key Messages

1. Opioids are very good analgesics for acute pain and for pain at the end of life but there is little evidence that they are helpful for long term pain.
2. A small proportion of people may obtain good pain relief with opioids in the long-term if the dose can be kept low and especially if their use is intermittent (however it is difficult to identify these people at the point of opioid initiation).
3. The risk of harm increases substantially at doses above an oral morphine equivalent of 120mg/day, but there is no increased benefit: tapering or stopping high dose opioids needs careful planning and collaboration.
4. If a patient has pain that remains severe despite opioid treatment it means they are not working and should be stopped, even if no other treatment is available.
5. Chronic pain is very complex and if patients have refractory and disabling symptoms, particularly if they are on high opioid doses, a very detailed assessment of the many emotional influences on their pain experience is essential.

Opioids
can
ruin
your
life



I manipulated doctors into prescribing me painkillers and various types of surgery that I did not need. Anon.



#opioidaware

Narcotic bowel syndrome pain response to detoxification

Drossman, Am J G,
2012, 107, 1426-1440

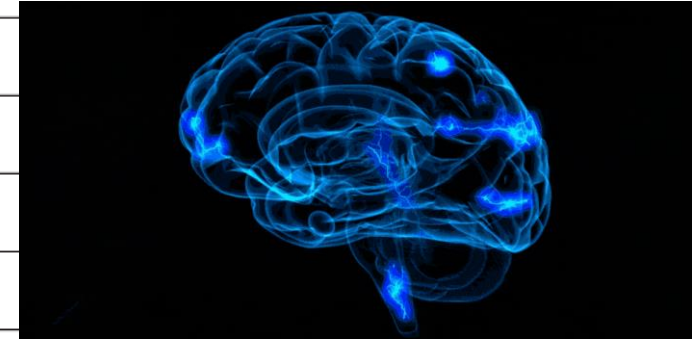
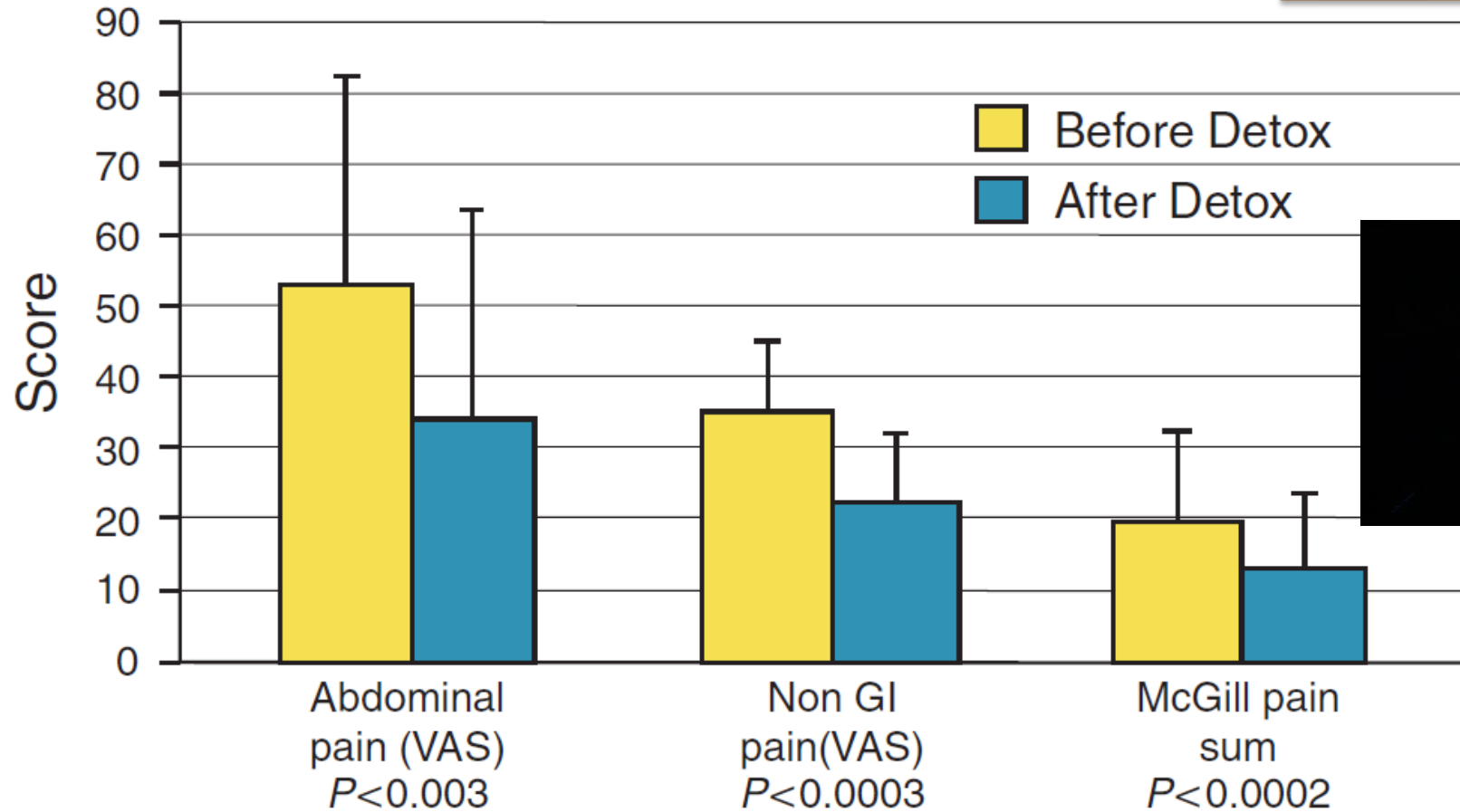


Figure 1. Pain response due to detoxification. The before and after detoxification levels of pain using a visual analog scale (VAS; 0–100) and the McGill Pain Questionnaire are shown. There is a statistically significant reduction in abdominal and non-gastrointestinal (non-GI)-related pain. This is also significant if one can define clinically meaningful response as >30% reduction (VAS abdominal pain 35%, VAS non-abdominal pain 42%, and McGill abdominal pain 31%).

NBS approach



- Recognition
- Relationship
- Replacement
 - TCA, Alpha 2 Delta ligands, SNRI (SSRI)
 - Linaclotide?
 - Psychological therapies
 - Tapentadol? (NRI-mu Opioid)
- Reduction
 - Rapid? (GA, drug & alcohol team)
 - Slow controlled patient driven
- Prevention? Toll Like Receptors 4 antagonists

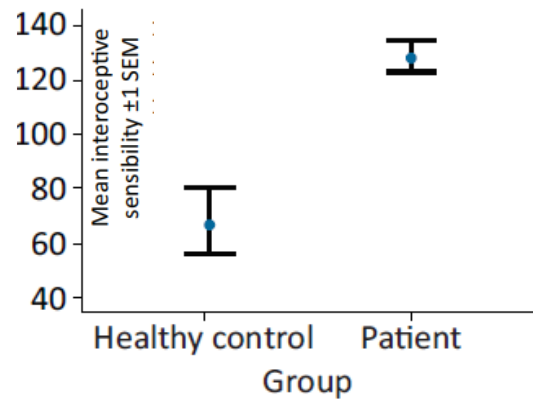
HSD/hEDS



- AD? But no genetic basis vs “classic” EDS
- **Recurrently** re-constructed phenotypes (bendy biomarkers) *Martin EJMG 2019*
- Unproven associations *Kohn, Clin Rev All & Imm 2020*

➤ 45/61 of participants in UK vs 11/93 of participants in other countries reported increased IFU referrals of hEDS ($P < .0001$) *Vasant NMO 2020*

pain + anxiety (+ disinformation)



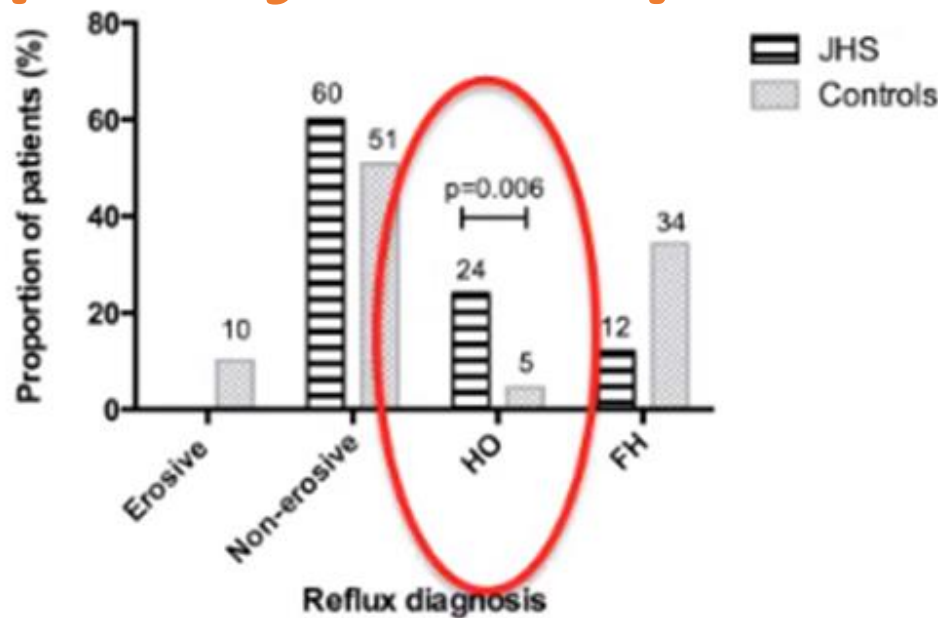
Interoceptive sensibility
p 0.005 (FM/CFS-ME + jHS)

Eccles, Clin Med, 2021

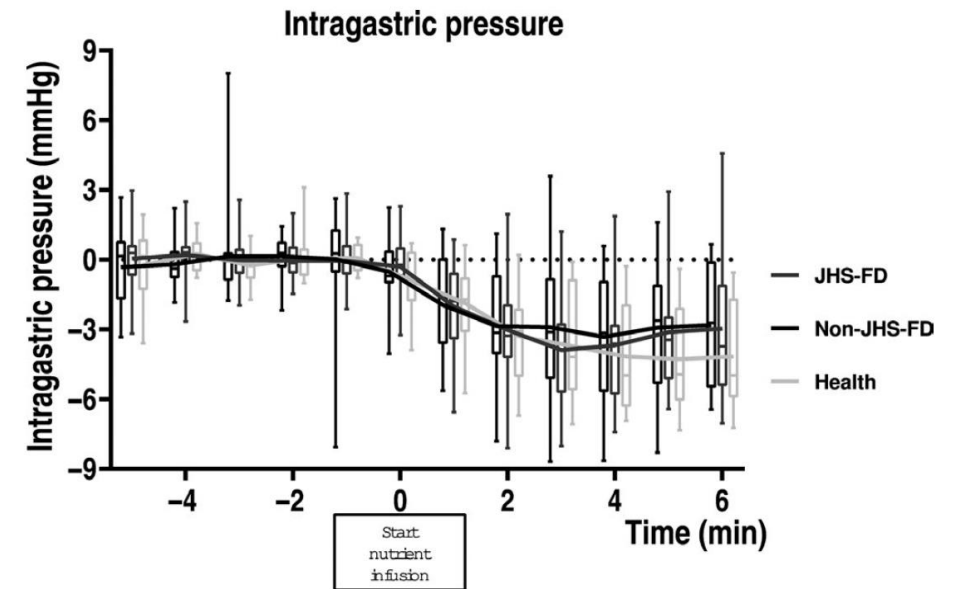
Large fibromyalgia overlap:

? nociplastic pain?

? SF neuropathic?



Fikree, NMO, 2016



Carbone, NMO, 2020

42% POTs **rapid** gastric emptying vs 20%

played in systematic review *Mehr, CAR, 2018*

DGBIs → Fear avoidance → ARFID

(Lam 2022 Frontline Gastro)

SPECIAL REPORT

Neuromodulators for Functional Gastrointestinal Disorders (Disorders of Gut–Brain Interaction): A Rome Foundation Working Team Report

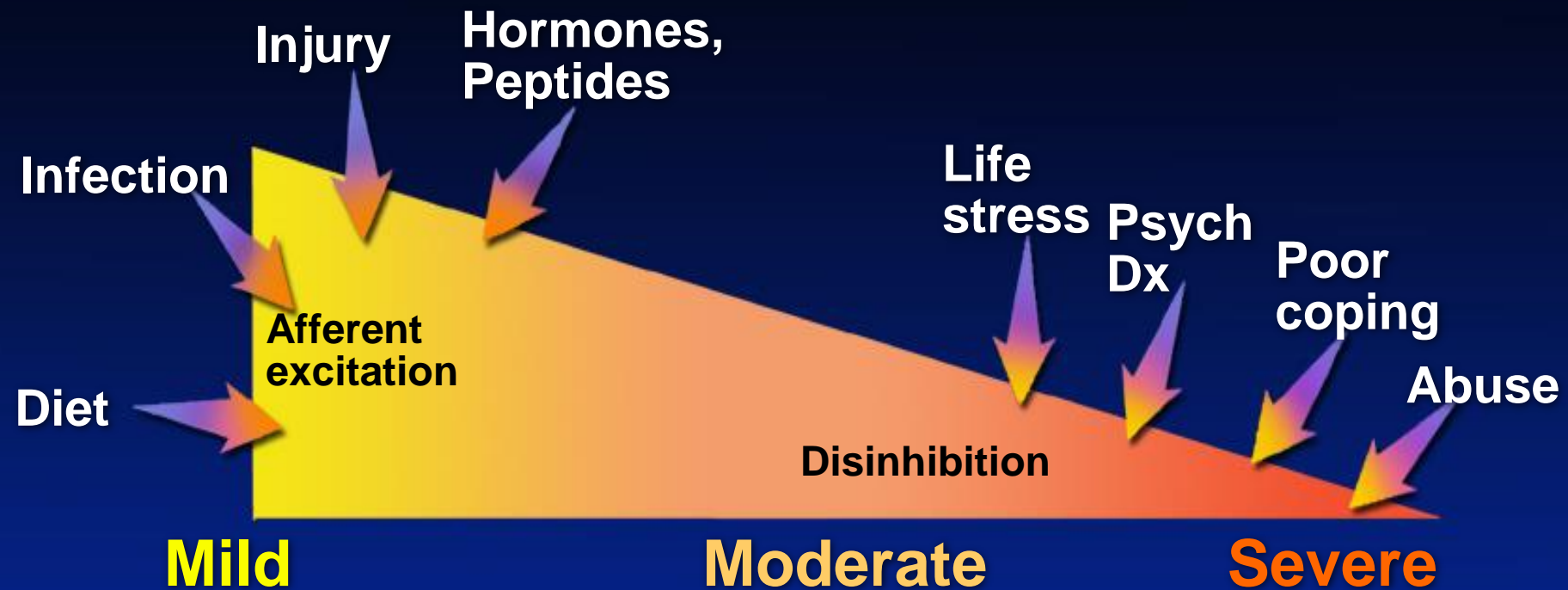


Douglas A. Drossman,^{1,2} Jan Tack,³ Alexander C. Ford,^{4,5} Eva Szigethy,⁶ Hans Törnblom,⁷ and Lukas Van Oudenhove⁸



4. Calming Pain

IBS – Brain-Gut Influences on Severity and Treatment



Lifestyle

Diet

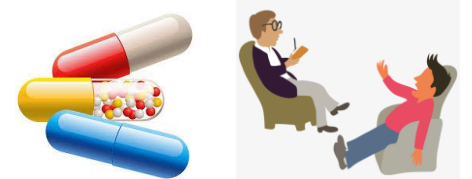
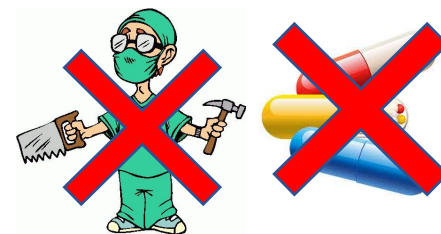
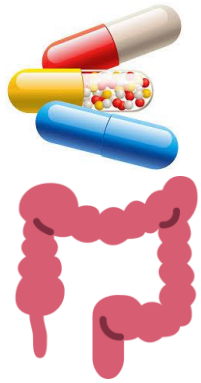
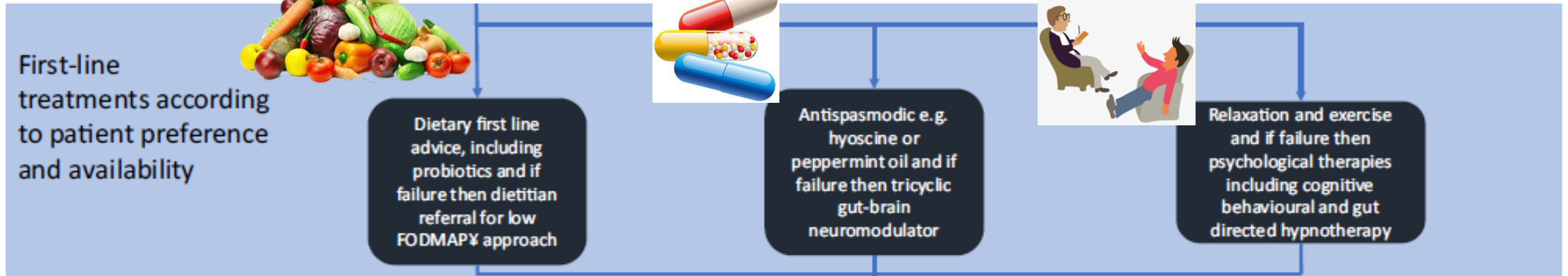
Gut medications

Behavioral Rx

Antidepressants



IBS pain



Gut-brain modulators for functional GI disorders

SSRIs

(paroxetine, fluoxetine, sertraline, citalopram, escitalopram)

When anxiety, depression, and phobic features are prominent with FGIDs

TCAs

(amitriptyline, nortriptyline, imipramine, desipramine)

First-line treatment when pain is dominant in FGIDs

Tetracyclic antidepressant

(mirtazapine, mianserin, trazodone)

Treatment of early satiety, nausea/vomiting, weight loss and disturbed sleep

SNRIs

(duloxetine, venlafaxine, desvenlafaxin, milnacipran)

Treatment when pain is dominant in FGIDs or when side effects from TCAs preclude treatment



Insufficient effect or dosage restricted by side effects

Augmentation

Azapirones (buspirone, tandospirone)
Dyspeptic features, anxiety prominent

Delta ligand agents

(gabapentin, pregabalin)
Abdominal wall pain, comorbid fibromyalgia

SSRI

When anxiety and phobic features dominant

Atypical antipsychotics

Pain with disturbed sleep (quetiapine), anxiety, nausea (olanzapine, sulpiride) additional somatic symptoms ("side effects"), comorbid fibromyalgia

Bupropion

Fatigue and sleepiness prominent

Psychological treatment

CBT when maladaptive cognitions and catastrophizing present

DBT, EMDR with history of PTSD or trauma

Hypnosis, mindfulness, relaxation as alternative treatments

chronic continuous abdominal pain



Kilgallon... Paine
APT, 2019

	OR	95% CI	P
Effectiveness			
Amitriptyline (%)	ref	ref	ref
Duloxetine (%)	8.00	2.04 - 31.37	0.003***
Gabapentin (%)	2.11	0.80 - 5.59	0.133
Linacotide (%)	4.33	1.35 - 13.92	0.014*
Nortriptyline (%)	0.95	0.27 - 3.41	0.940
Pregabalin (%)	1.90	0.62 - 5.81	0.258
Tolerance			
Amitriptyline (%)	ref	ref	ref
Duloxetine (%)	\$	—	0.998
Gabapentin (%)	1.43	0.51 - 4.00	0.490
Linacotide (%)	8.70	1.02 - 74.00	0.048*
Nortriptyline (%)	0.94	0.28 - 3.19	0.924
Pregabalin (%)	2.17	0.59 - 8.02	0.244

	OR	95% CI	P
Effectiveness			
Comb	21.0	2.28-192	0.007***
Comb + L	\$	—	0.998

abdominal symptoms

Occurrence of benign (if any) peripheral event

Pain experience

Sensory-discriminative dimension

Motivational-Affective dimension

Fear (*chronic* → *maladaptive*)

Fear Avoidance

Fear Confrontation

Catastrophising

Hypervigilance
& Attentional-
bias

Inflexibility

Disability

Cognitive
Behaviour
therapy

Mindfulness
Based
Stress
reduction

Acceptance
Commitment
therapy

Biofeedback

Hypnotherapy

Recovery

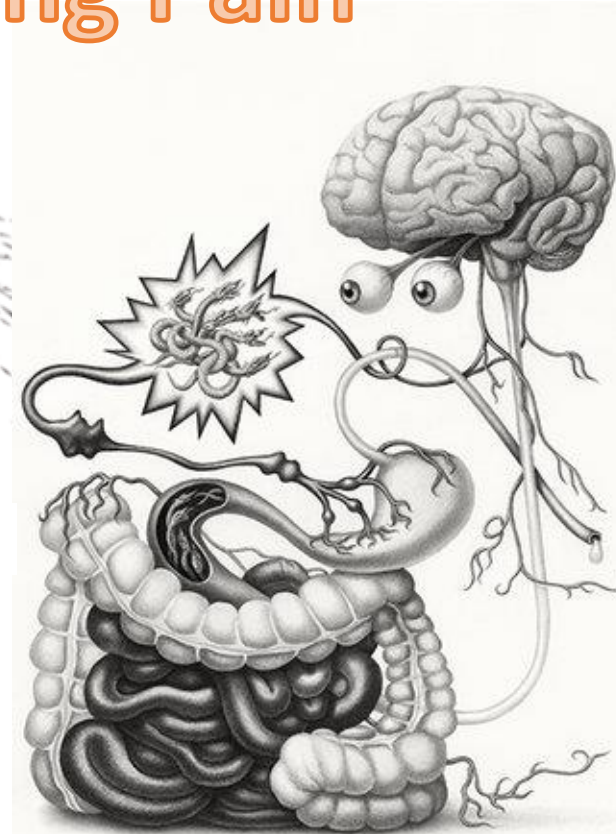
WANTED: Enteric Electricians!

1. Naming Pain

3. *Inflaming Pain*

2. Framing Pain

4. Calming Pain



YOU WOULDN'T GET THESE
STOMACH ACHES IF YOU CHEWED
YOUR FOOD PROPERLY.

