

From acute to chronic pain

Jayne Gallagher

Consultant in Pain Medicine

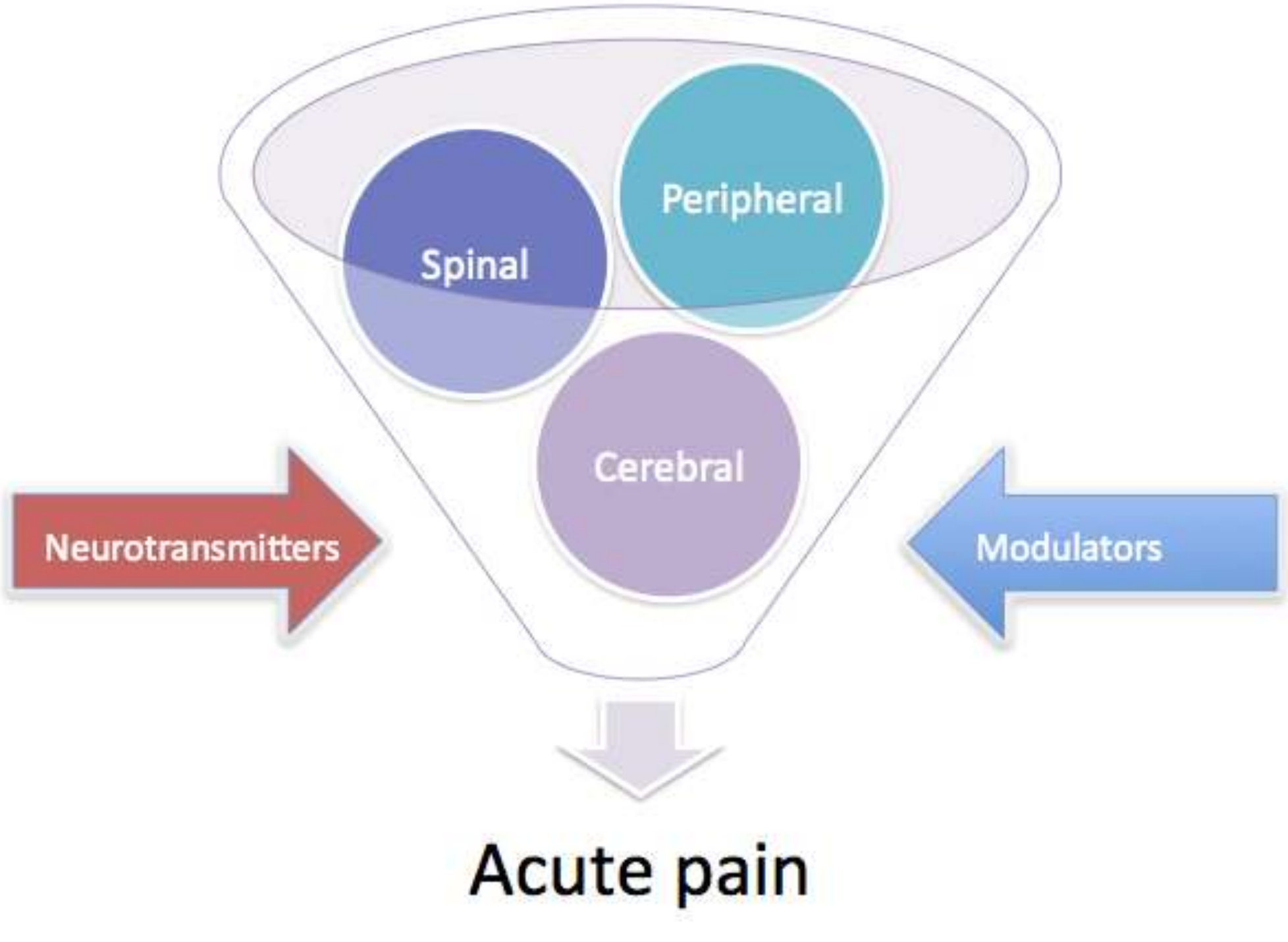
Barts Health NHS Trust

Acute pain

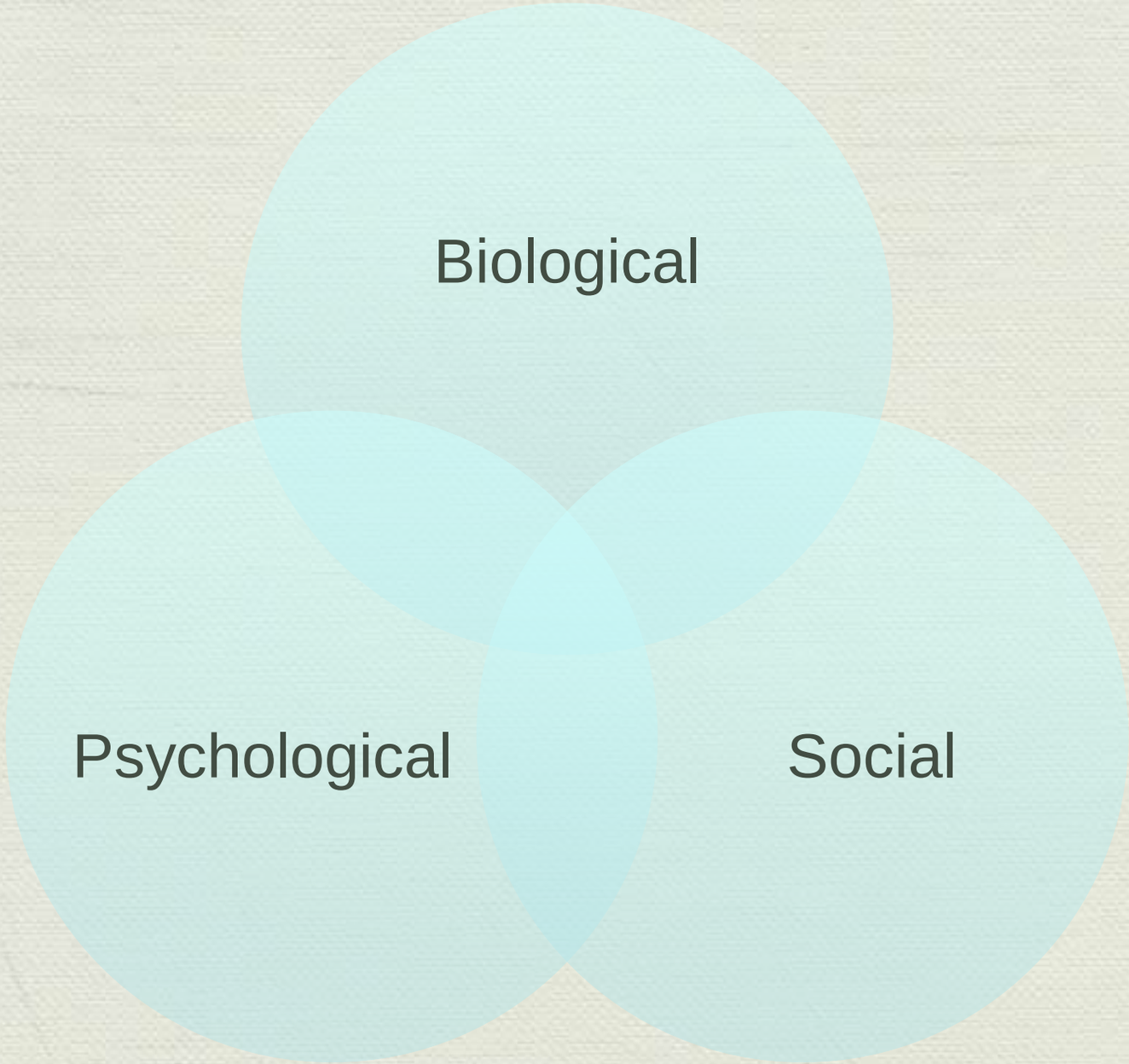
- Recent onset
- Probable limited duration
- Identifiable and causal relationship to injury or disease
- Transmitted in normal pain pathways as a result of nociceptive stimuli
- Useful warning of tissue damage

Chronic pain

- Pain present for more than 3 months
- Outlasts the original stimulus
- Usually serves no purpose
- Often accompanied by behavioural or mood changes


Peripheral
Spinal
Cerebral
Neurotransmitters
Modulators
Acute pain

Pain always has a context



The post-surgical model

What is CPSP?

- Pain should have developed after a surgical procedure
- Pain should be of at least 2 months' duration
- Other causes for the pain should be excluded
- Pain is not continuing from a pre-existing problem

Crombie IK, Linton S, Croft P, *et al*. IASP 1999

Problems in the research

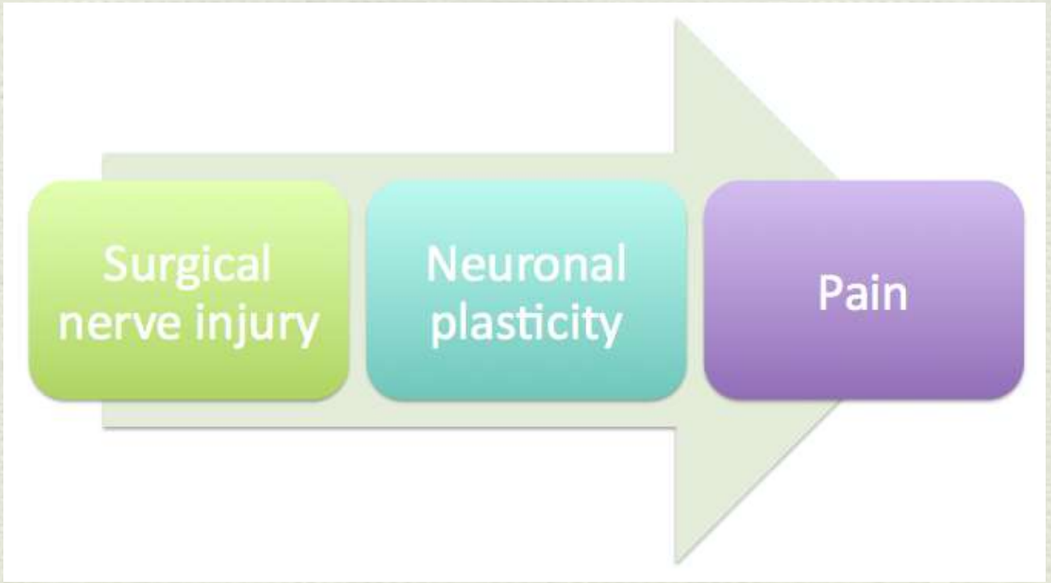
- No clear definition of CPSP
- Diversity of symptoms
- Use of questionnaires in large populations
- Relatively low incidence seen in the pain clinic

Incidence of chronic pain after surgery

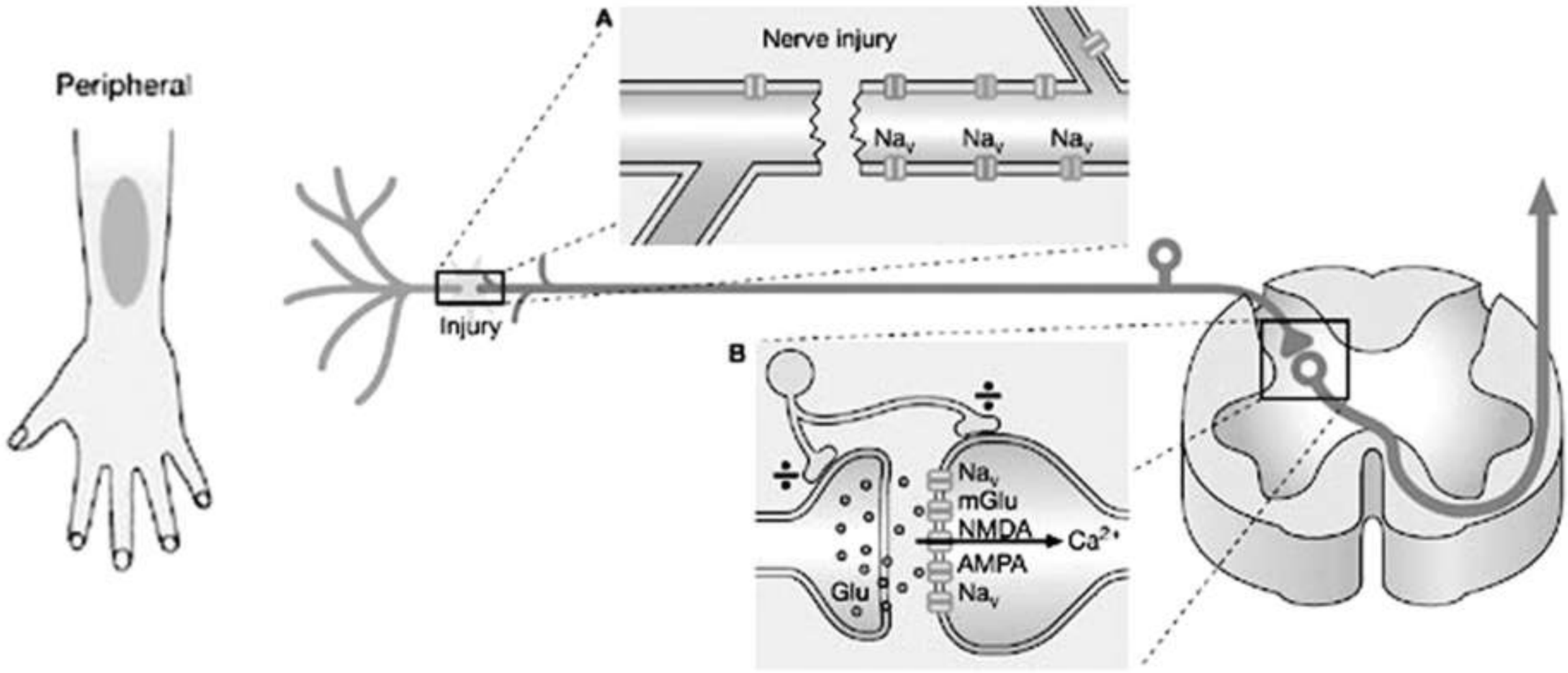
Type of operation	Incidence of chronic pain	Number of operations in UK in 2005-6*	Number of operations in USA in 1994
Mastectomy	20-50%	18 000	131 000
Caesarean section	6%	139 000	858 000
Amputation	50-85%	15 000	132 000
Cardiac surgery	30-55%	29 000	501 000
Hernia repair	5-35%	75 000	689 000
Cholecystectomy	5-50%	51 000	667 000
Hip replacement	12%	61 000	
Thoracotomy	5-65%		660 000

*Based on Hospital Episode Statistics

Mechanisms of CPSP



- Peripheral injury leads to increased excitability in peripheral nociceptors
  - PRIMARY HYPERALGESIA
- Prolonged excitability of CNS nociceptors leads to increased sensitivity to painful stimuli in areas of normal tissue removed from the site of injury
  - SECONDARY HYPERALGESIA
- Depolarisation of injured nociceptors may result in a pacemaker function
- Most medications used to treat postoperative pain have minor effects on secondary hyperalgesia



Central sensitisation

Predictive factors for CPSP

- Pre-operative pain (knee surgery)
- Greater continuous acute postoperative pain (thoracotomy)
- Age (increases with thoracotomy, decreases with mastectomy)
- Gender
- Cultural effects
- Pre-operative anxiety and catastrophising

Genetic polymorphisms

- Protective genotypes and phenotypes have been isolated
  - Homozygous carriers of a GTP cyclohydrolase 1 haplotype
  - Children born of mothers with a familial history of hypertension

Surgical factors

- Invasive procedures
  - Redo interventions
  - Surgery in a previously injured area
  - Particular surgical techniques
- Acute pain intensity is a strong predictor for developing CPSP

Anaesthetic factors

- A reduction in the nociceptive input to the spinal cord may reduce the incidence of acute and chronic pain after surgery (animal studies)
- There is confusing evidence for the effect of different anaesthetic and analgesic regimes
- Pre-emptive analgesia has not been shown to reduce phantom pain
- Preventative analgesia may be of benefit
- CPSP could be minimized by an aggressive perioperative multimodal approach to pain management

Is chronic pain an extended duration of acute pain?

Does chronic pain arise from fundamentally different factors?

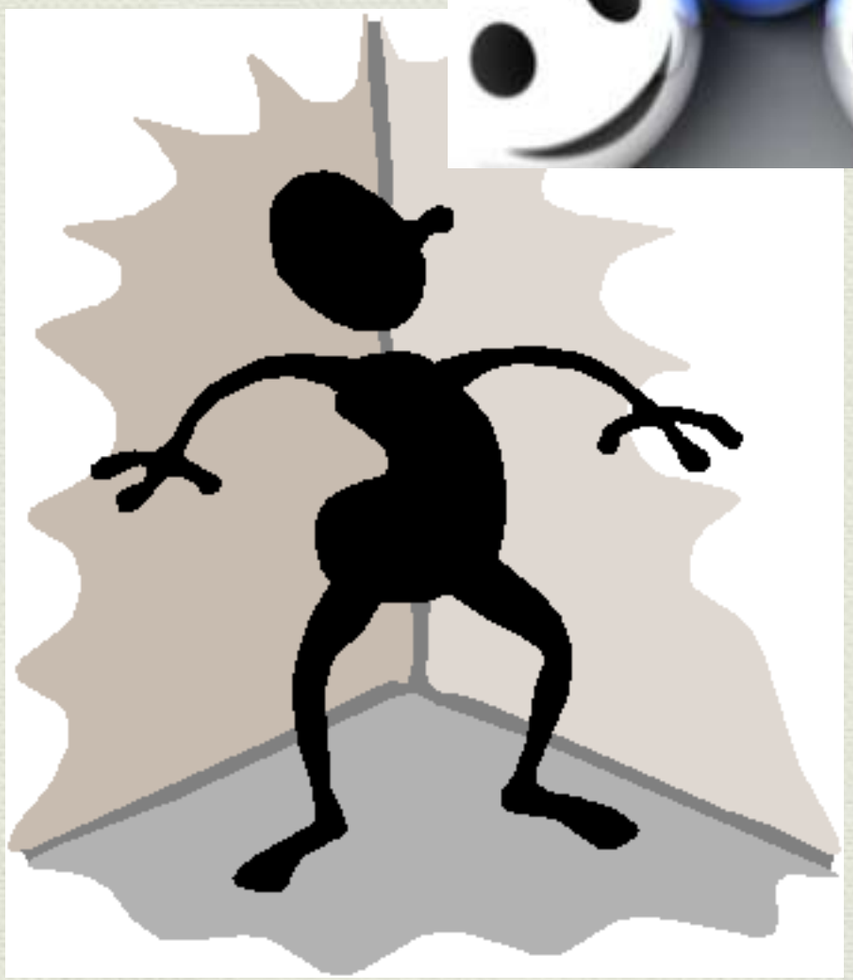
Animal data

Animal data

- CNS and brain play a crucial role in determining the persistence of pain
- The duration of pain is controlled by supraspinal systems from the rostral ventromedial medulla (RVM) of the brain to the spinal cord (rat studies)
  - ‘On’ and ‘off’ cells that facilitate and inhibit pain transmission
  - Supraspinal CNS processes are more determinant in the persistence of pain rather than the the nature of the peripheral nerve injury
  - Lesions in the RVM regulate the duration of pain and its transition from acute to chronic

Human data

Human data



- Fear and catastrophising play a central role in the duration of pain
  - Avoidance behaviour may delay pain resolution
- Level of anxiety correlates with severity of pain from nociceptive stimuli
- Anxiety and depression may increase pain duration
  - 30-65% of patients with chronic pain have depression
  - Pain durability or new pain incidence is altered rather than pain thresholds or pain severity

Psychophysical approaches

Quantitative sensory testing

- QST has yielded varying results
- Sustained peripheral nervous system dysfunction following surgery is common
- The relationship between this dysfunction, pain duration and the incidence of chronic pain is unclear
- Altered central nervous system function (seen as peripherally as temporal summation) may have better predictive value

Role of opioids

- Opioid-induced hyperalgesia has been demonstrated in animal studies, and in human subjects
- Dose-response relationship between the early use of opioids for low back pain and elevated risk of chronic opioid use
- Early use of opioids may be a marker of disease severity
- Opioids may prolong the duration of pain

Table 5. Logistic Regression Model Examining Association Between Morphine Equivalent Amount (MEA) and Late Opioid Use After Controlling for Severity, Age, Gender, and Job Tenure

Variable	Odds Ratio	95% Confidence Intervals	P
MEA (mg)			
450+	6.14	4.92 to 7.66	<0.001
226–450	3.69	2.88 to 4.72	<0.001
141–225	2.89	2.25 to 3.69	<0.001
1–140	2.08	1.55 to 2.78	<0.001
0	—	—	—
High severity	2.02	1.74 to 2.34	<0.001
Age (yr)	1.02	1.01 to 1.02	<0.001
Female gender	1.02	0.87 to 1.20	0.783
Tenure (yr)	0.98	0.97 to 0.99	<0.001

Webster BS, Verma SK, Gatchel RJ. Spine 2007

Recent publications of interest

Prognostic indicators for acute and chronic low back pain

- Comparison of two large prospective cohort studies (n=258 for acute and subacute pain, n=68 for chronic pain)
- Being unemployed, having widespread pain, a high level of Chronic Pain Grade, and catastrophising, were prognostic indicators for disability at 12 months
- Fear of pain was significantly associated with disability in chronic low back pain
- It may be possible to screen and target patients with prognostic indicators

Grotle M, Foster NE, Dunn KM, *et al.* Pain. 2010; 151 (3): 790-797.

Predictors of pain severity 3 months after serious injury

- Prospective cohort study (n=242)
- Patients were assessed for pain severity (VAS) over the past 24 hours at 3 months
- Older age, female gender, past alcohol dependence, lower physical role function, pain severity, amount of morphine equivalents administered on the day of assessment, and pain control attitudes predicted pain severity at 3 months
- These patients may warrant increased monitoring and early triage to specialist pain services

Holmes A, Williamson O, Hogg M, *et al*. Pain Med. 2010; 11 (7): 90-1000

Predictors of pain 12 months after serious injury

- Prospective cohort study (n=238)
- Not working prior to injury, total Abbreviated Injury Scale, initial pain severity, and initial pain control attitudes predicted the presence of chronic pain at 12 months
- Patients in high-risk groups may warrant more clinical attention

Holmes A, Williamson O, Hogg M, *et al*. Pain Med. 2010; 11 (11): 1599-1611

The transition from acute to subacute to chronic low back pain

- Follow-up study (n=366)
- Low back pain influences disability and quality of life more than referred pain
- Disability is predicted by pain duration
- Quality of life is predicted by disability
- Pain severity predicts neither
- Changes related to determinants of disability and quality of life appear 14 days after the onset of pain

Kovacs FM, Abraira V, Zamora J, *et ai*. Spine. 2005; 30 (15): 1786-1792.

Predictors of chronic pain after cardiac surgery

- Prospective panel study (n=53)
- Patients who reported chronic pain 3 months after surgery had a pattern of increasing pain about 10 days after surgery, and held negative beliefs about opioid use

Lee W, Yan YY, Jensen MP, *et al.* Pain Med. 2010; 11 (12): 1849-1858

Transition from acute to chronic pain and disability: a model including cognitive, affective and trauma factors

- Data was collected from patients with acute back pain (n=84)
- Greater exposure to past traumatic life events and depressed mood were more predictive of chronic pain
- Depressed mood and negative beliefs were most predictive of chronic disability
- More cumulative traumatic life events, higher levels of depression in the early stages of a new pain episode, and early beliefs that pain may be permanent, significantly contribute to increased severity of subsequent pain and disability

Casey CY, Greenberg MA, Nicassio PM, *et al.* Pain. 2008; 145: 69-79

Pregabalin reduces the incidence of chronic neuropathic pain after TKR

- Randomised, double-blinded, placebo-controlled trial (n=240)
- Incidence of neuropathic pain, allodynia and hyperalgesia at 3 and 6 months were significantly reduced in the pregabalin group compared to placebo

3 months	Neuropathic pain	Allodynia	Hyperalgesia
Pregabalin	0%	2%	8%
Placebo	8.7%	12%	20%
	p=0.001	p=0.002	p=0.009

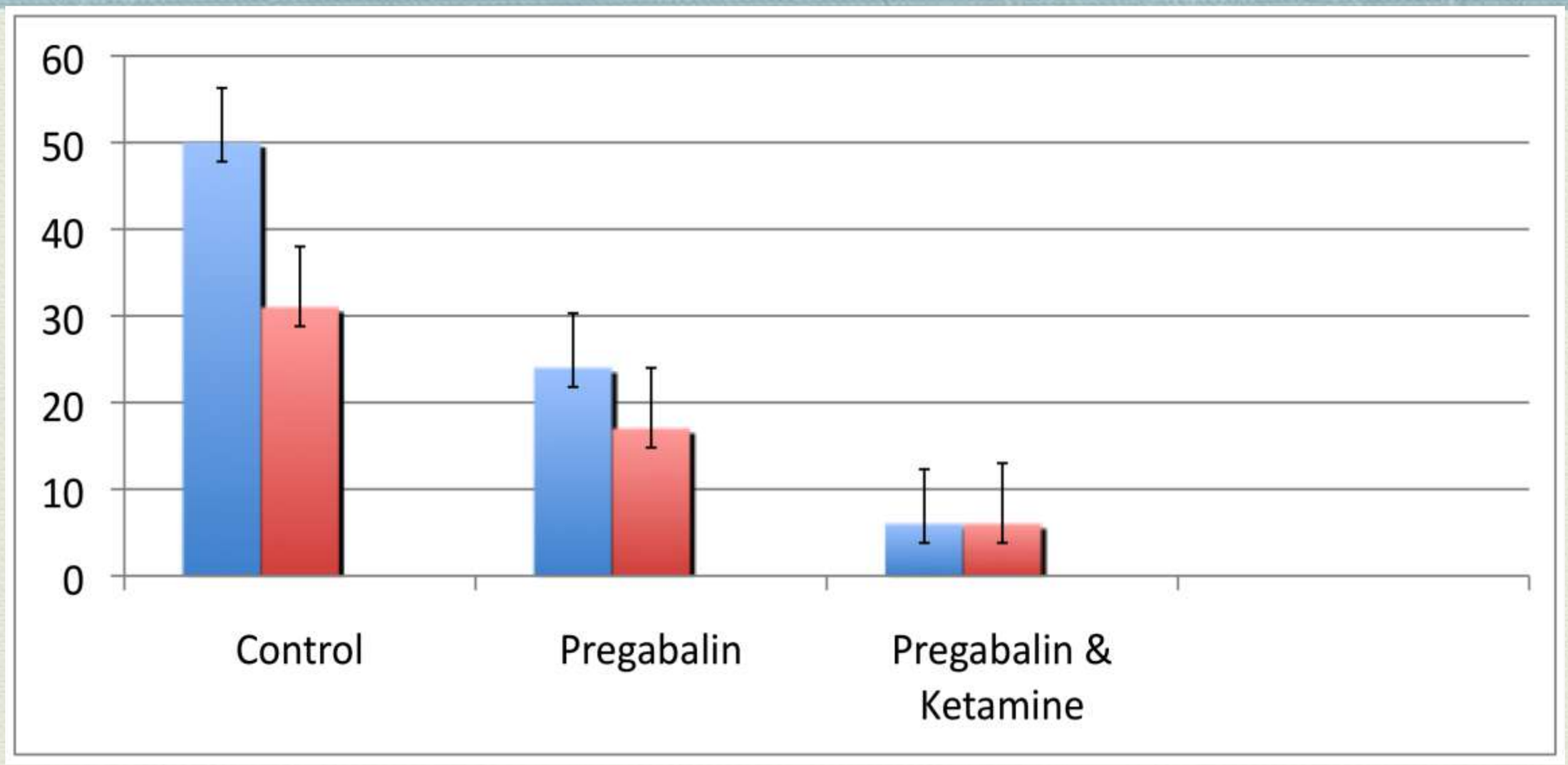
6 months	Neuropathic pain	Allodynia	Hyperalgesia
Pregabalin	0%	0%	2%
Placebo	5.2%	8%	11%
	p=0.014	p=0.002	p=0.006

Buvanendran A, Kroin JS, Della Valle CJ, *et al*. Anesth Analg. 2010; 110 (1): 199-207

OVERALL PAIN

Three months p = 0.0015

Six months p=0.02



Conclusions

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- Future research needs to explore the link between the reductions in pain duration and the incidence of CPSP
- More studies are required on therapeutic interventions in the management of acute and subacute pain after surgery
- It may be possible to characterise variables that may confer a risk of delayed pain resolution
- The perioperative setting should be used to investigate pain duration and the crucial transition from acute to chronic pain
- Anaesthetists should be involved in identifying and managing patients at risk of CPSP

References

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