From acute to chronic pain

Jayne Gallagher
Consultant in Pain Medicine
Barts Health NHS Trust
<table>
<thead>
<tr>
<th>Acute pain</th>
<th>Chronic pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>➡️ Recent onset</td>
<td>➡️ Pain present for more than 3 months</td>
</tr>
<tr>
<td>➡️ Probable limited duration</td>
<td>➡️ Outlasts the original stimulus</td>
</tr>
<tr>
<td>➡️ Identifiable and causal relationship to injury or disease</td>
<td>➡️ Usually serves no purpose</td>
</tr>
<tr>
<td>➡️ Transmitted in normal pain pathways as a result of nociceptive stimuli</td>
<td>➡️ Often accompanied by behavioural or mood changes</td>
</tr>
<tr>
<td>➡️ Useful warning of tissue damage</td>
<td></td>
</tr>
</tbody>
</table>
Acute pain

- Spinal
- Peripheral
- Cerebral

Neurotransmitters
Modulators
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

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

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

*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 nature of the peripheral nerve injury.
- Lesions in the RVM regulate the duration of pain and its transition from acute to chronic.
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

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% Confidence Intervals</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEA (mg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>450+</td>
<td>6.14</td>
<td>4.92 to 7.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>226–450</td>
<td>3.69</td>
<td>2.86 to 4.73</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>141–225</td>
<td>2.69</td>
<td>2.15 to 3.36</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1–140</td>
<td>2.08</td>
<td>1.55 to 2.78</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>High severity</td>
<td>2.02</td>
<td>1.74 to 2.34</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>1.02</td>
<td>1.01 to 1.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.02</td>
<td>0.87 to 1.20</td>
<td>0.783</td>
</tr>
<tr>
<td>Tenure (yrs)</td>
<td>0.98</td>
<td>0.97 to 0.99</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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

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.

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

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

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

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

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

<table>
<thead>
<tr>
<th>3 months</th>
<th>Neuropathic pain</th>
<th>Allodynia</th>
<th>Hyperalgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregabalin</td>
<td>0%</td>
<td>2%</td>
<td>8%</td>
</tr>
<tr>
<td>Placebo</td>
<td>8.7%</td>
<td>12%</td>
<td>20%</td>
</tr>
<tr>
<td>p=0.001</td>
<td>p=0.002</td>
<td>p=0.009</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6 months</th>
<th>Neuropathic pain</th>
<th>Allodynia</th>
<th>Hyperalgesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregabalin</td>
<td>0%</td>
<td>0%</td>
<td>2%</td>
</tr>
<tr>
<td>Placebo</td>
<td>5.2%</td>
<td>8%</td>
<td>11%</td>
</tr>
<tr>
<td>p=0.014</td>
<td>p=0.002</td>
<td>p=0.006</td>
<td></td>
</tr>
</tbody>
</table>

OVERALL PAIN
Three months p = 0.0015
Six months p=0.02
Conclusions
Conclusions

- 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


- Kehlet H, Jensen TS, Woolf CJ. Persistant postsurgical pain: risk factors and prevention. Lancet. 2006; 367 (9522); 1618-25