

Chronic Pain and Depression

Snehal Bhatt, MD

Assistant Professor, Psychiatry

Medical Director, Addiction and Substance Abuse Programs

University of New Mexico

June 1, 2016

Objectives

- Recognize the high co-morbidity between chronic pain and depressive disorders
- Appreciate how co-morbid depression effects chronic pain outcomes
- Understand some treatment strategies for addressing co-occurring depression and chronic pain

Depression-chronic pain dyad

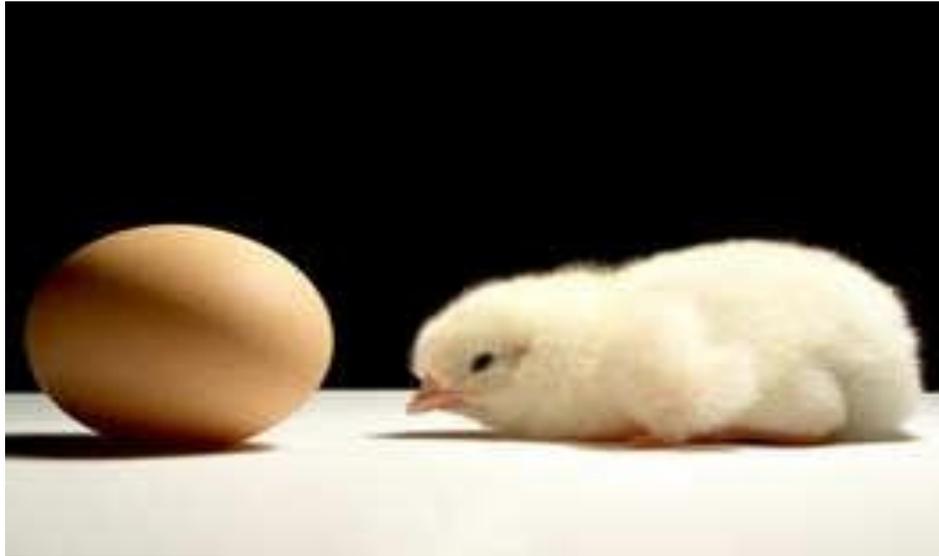
Pain

- Pain is the most common symptom reported in the general population and in general medical setting
- Pain complaints account for more than 40% of all symptom-related outpatient visits in the US
- Pain complaints account for over 100 million ambulatory encounters in the US each year
- Pain costs the US over \$100 billion each year in healthcare and lost productivity
- Pain is one of the most common reasons for temporary as well as permanent work disability

Depression

- Depression present in 10-15% of all patients attending primary care
- It is one of 5 most common conditions seen in primary care
- Nearly 10% of all primary care visits are depression related
- PCPs provide about 50% of all outpatient care for depressed patients
- Both conditions frequently undertreated

Pain and depression co-exist



Pain and depression co-exist

- Pain and depression frequently co-exist: 30-50% co-occurrence
- Pain is a strong predictor of onset and persistence of depression
- Depression is a strong predictor of pain, particularly chronic pain
- Relative to people with no pain, odds ratio for depression 1.8 with single site pain, and 3.7 with multi-site pain [Kroenke et al., 2009]
- Kroenke et al. [2011]: pain and depression have strong and similar bi-directional effects on one another when assessed longitudinally over 12 months

Co-occurrence = worse outcomes

- Pain negatively effects depression response to treatment, and vice versa
- Additive adverse impact on
 - Quality of life
 - Disability
 - Response to treatment
 - Pain outcomes, including chronicity
 - Patient satisfaction with treatment
 - Self-rated health
 - Functional limitations
 - Deteriorating social and occupational functioning
 - Greater use of medical services
 - Higher medical service costs
 - **Suicide attempts and completions**

Biopsychosocial models

- Biological: Genetics, Neurotransmitters, Cytokines, Peripheral sensory
- Sociocultural: gender, cultural beliefs, occupation, disability
- Psychological: Personality, anxiety, attribution
- Studies show positive association between negative pain beliefs, such as permanence and constancy, and pain chronicity
- Depression associated with learned helplessness, cognitive distortions, and pessimistic future beliefs
- Factors such as unemployment, inability work, and kinesiophobia all associated with worse pain outcomes [Ang et al., 2010]

A biopsychosocial model [Casey et al., 2008]

- Patients with acute back pain followed 3 months
- Depression **Baseline depressive symptoms and pain permanence beliefs most powerful predictors of chronic disability**
- **Baseline depression also the strongest independent predictor of subsequent pain at 3 months**
- > passive coping style and avoidance > chronic disability
- Bi-directional relationship between disability and depression
- Acute disability due to pain > interference with relationships and activities > depression > loss of motivation > chronic disability
- **Acute pain intensity did NOT predict 3 month disability**

Therefore, must screen for depression in patients with chronic pain

Screening for depression

- Clinical interview = GOLD STANDARD
- “SIG E CAPS”
- HAM-D
- CES-D
- Beck Depression Inventory: 21 questions; self administered
- Zung self rated depression scale
- PHQ-9

PHQ-9

- Patient self-administered
- Quick
- Useful for monitoring change over time
- Scores of 10 or above 88% sensitive and 88% specific for MDD
- Remember 5, 10, 15, 20 [mild, moderate, moderately severe, and severe]
- 5 point decrease is significant improvement
- Response: a 50% decrease, or a score under 10
- Remission: score under 5

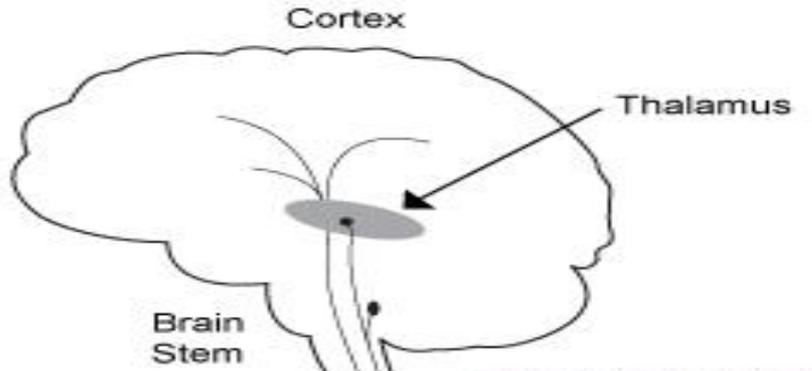
PHQ-9

- <10: reassurance, supportive therapy
- 10-15: watchful waiting, supportive therapy; antidepressant if no improvement in 1 month
- 15-19: counseling or antidepressant [patient preference]
- 20 or above: antidepressant, alone or with counseling

Treatment considerations

 = Click to Explore

PERCEPTION



DESCENDING MODULATION

CENTRAL TRANSMISSION

Spinal Cord

TRANSMISSION

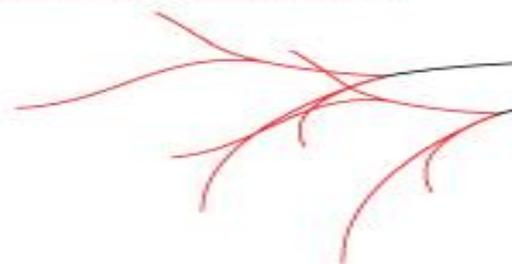
SYNAPTIC TRANSMISSION

TRANSDUCTION

PERIPHERAL TRANSMISSION

Dorsal Root Ganglion (DRG)

Peripheral Nerves (PNS)



TCA antidepressants

- Longest track record of any anti-depressants in the treatment of multiple pain conditions
- Typically, lower doses than used for anti-depressant effect, but titrating to higher doses may benefit a subset of patients
- *Analgesic effects even in the absence of depression or antidepressant effect*
- Benefits: long track record, low cost
- Risks: side effect profile [QTc prolongation, hypotension, sedation, falls in elderly, fatal in overdose]

TCA antidepressants

- A meta-analysis evaluated 55 RCTs involving TCA for treatment of somatic symptoms [a majority involved pain]: 76% of trials [41 trials] showed some benefits [O'Malley et al., 1999]
- Consistent evidence in treatment of diabetic neuropathy, postherpetic neuralgia
- Also evidence for central pain, post-stroke pain, tension headaches, migraines, chronic oral-facial pain
- Less consistent data on arthritic pain and low back pain
- Overall NNT 2-4 for 50% pain reduction [Lynch, 2001]

TCA tips

- Focus on side effect profiles
- Amitriptyline and Doxepin very sedating
- *Nortriptyline less sedating and more tolerable in elderly*
- Start low [10-25 mg nightly] and increase dose slowly
- May go up 25 mg every week until dose reaches 75-100 mg
- Higher doses may be needed for depression
- Caution in elderly
- Avoid if cardiac risk factors present

SSRIs

- Overall, disappointing results in terms of analgesia
- Headaches: only 3 placebo controlled trials- all negative
- Diabetic neuropathy: 3 RCTs: the largest one found no difference between fluoxetine and placebo; 2 smaller ones found positive effect for paroxetine and citalopram
- Fibromyalgia: a small study showed analgesic effect with fluoxetine; another larger study did not; another negative trial for citalopram

SSRI vs TCA

- Imipramine better than paroxetine at treating painful diabetic neuropathy [Sindrup et al., 1990]
- Despiramine and amitriptyline help diabetic neuropathy, but fluoxetine does not [Max et al., 1992]
- Amitriptyline helps tension headaches, but citalopram does not [Bendson et al., 1996]

SNRI

- Duloxetine superior to placebo in three RCTs for painful diabetic peripheral neuropathy
- 90% of analgesic effect due to direct analgesia, with 10% secondary to antidepressant effect [Perahia et al., 2006]
- NNT 5 for 50% pain reduction
- FDA approved for pain secondary to fibromyalgia
- Venlafaxine superior to placebo in treating diabetic neuropathy [Rowbotham et al., 2004]
- Duloxetine showed significant improvements in both pain AND depression
- [Brecht et al., 2007]

SNRI tips

- **Duloxetine**
 - Usual dose 60 mg/day
 - No additional efficacy shown in doses more than 60 mg
- **Venlafaxine**
 - Extended release formulation available
 - GI side effects common- take with food
 - May increase blood pressure slightly
 - Start at 37.5 or 75 mg; need to go to at least 150 mg; up to 225 mg

Neuropathic pain

- Duloxetine approved by FDA
- Duloxetine superior to placebo in three RCTs for painful diabetic peripheral neuropathy
- Venlafaxine superior to placebo in treating diabetic neuropathy [Rowbotham et al., 2004]
- Several studies showing efficacy for TCAs
- Limited data for efficacy of SSRIs
- [Kroenke et al., 2009]

Fibromyalgia

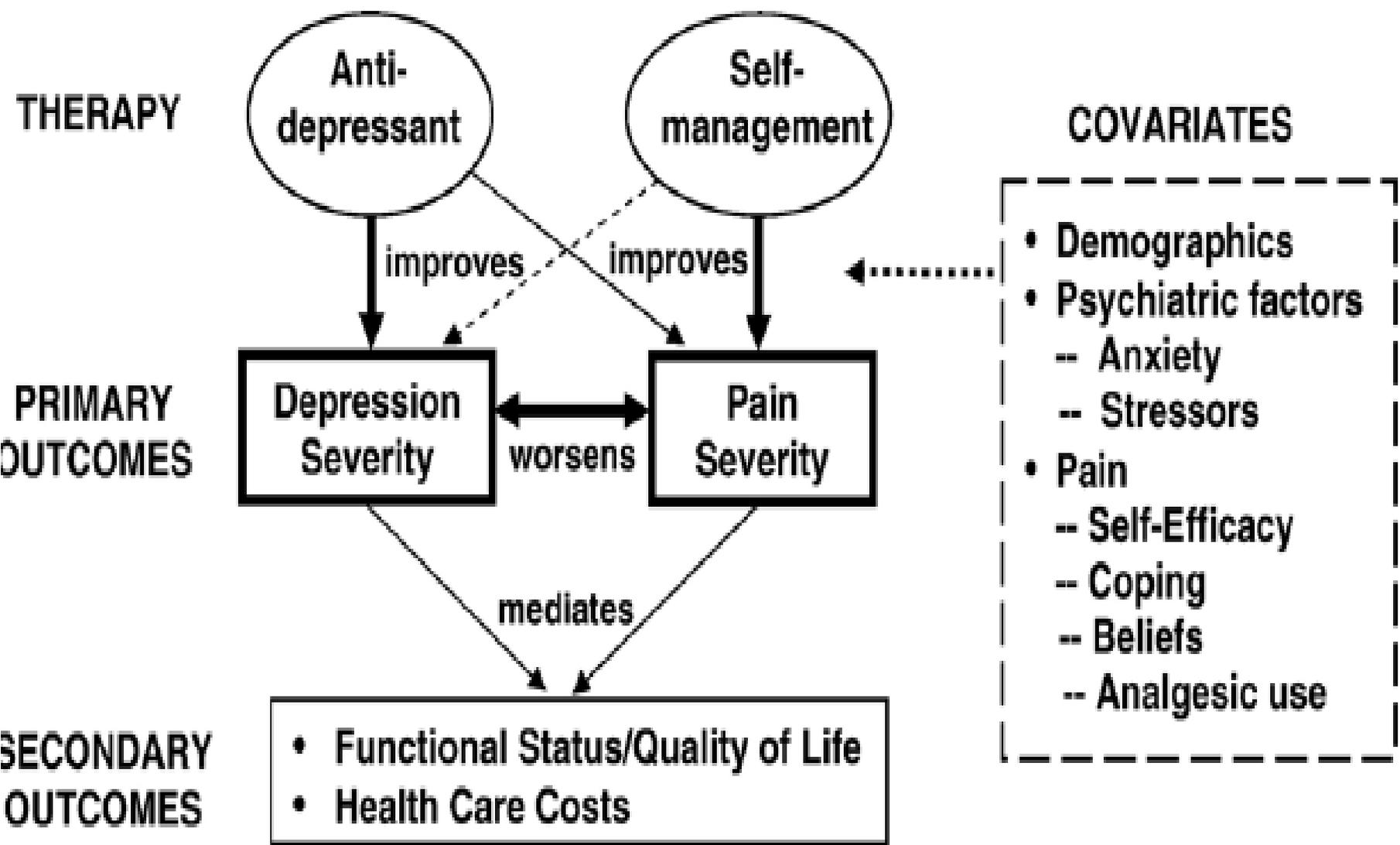
- Overall, antidepressants superior to placebo with NNT of 4
- Moderate effect sizes for pain, fatigue, sleep, and overall well being
- Symptom improvement and depression scores only correlated in one study
- Nine studies for TCAs
- Five for SSRIs: effect for fluoxetine
- Duloxetine positive in several trials; FDA approved
- Not enough evidence for venlafaxine yet
- [Kroenke et al., 2009]

Low back pain

- Ten trials included in 2 systematic reviews
- Tricyclic antidepressants consistently superior to placebo for pain relief
- Uncertain results for functional outcomes
- Moderate effect size [0.41 pooled]
- NO evidence for SSRI efficacy
- No data for SNRI meds
- [Kroenke et al., 2009]

Stepped Care for Affective Disorders and Musculoskeletal Pain [SCAMP study]

- NIMH sponsored RCT
- Population: 250 patients with clinically significant depression [PHQ > 10] and musculoskeletal pain of lower back, hips, knee AND 250 patients with no depression, but similar pain
- Follow over 12 months
- Depressed patients randomized to usual care OR stepped care intervention
- Stepped care participants receive 12 weeks of optimized anti-depressant management, followed by 6 sessions of pain self-management program



Conceptual model underlying the SCAMP trial. The thickness of each arrow indicates the postulated strength of effect.

Results

- At 12 months, 46 (37.4%) of the 123 intervention patients had a 50% or greater reduction in depression severity from baseline compared with 21 (16.5%) of 127 usual care patients (relative risk [RR], 2.3; 95% CI, 1.5 to 3.2)
- At 12 months, intervention group had a much lower number with major depression (50 [40.7%] vs. 87 [68.5%]; RR, 0.6; 95% CI, 0.4-0.6)
- a clinically significant ($\geq 30\%$) reduction in pain was much more likely in intervention patients (51 [41.5%] vs. 22 [17.3%]; RR, 2.4; 95% CI, 1.6-3.2)
- global improvement in pain also significantly more likely in intervention group (58 [47.2%] vs. 16 [12.6%]; RR 3.7, 95% CI, 2.3-6.1)
- combined improvement in both depression and pain also significantly more likely in intervention group (32 [26.0%] vs. 10 [7.9%]; RR = 3.3; 95% CI, 1.8 to 5.4)
- Also significantly better outcomes for pain related disability, quality of life, anxiety, and functional impairment

Take-home points

- Stepwise antidepressant treatment and pain self-management in patients with co-morbid depression and chronic pain can produce significant improvements in both depression and pain
- In this “real-life” population, SSRIs and SNRIs can play a greater role in treatment of these co-morbid conditions
- Further improvement with addition of CBT, optimized analgesic treatment?

Other strategies

Psychological therapies for management of chronic pain [excluding headaches] in adults- cochrane review, 2009

- Absence of evidence for behavioral therapy, except for pain immediately following treatment
- CBT = small, positive effects on pain, disability, and mood
- CBT and behavioral therapies effective at improving mood outcomes, and benefits may be maintained at 6 months

Acceptance based interventions

- Learn to live with pain and accept pain as part of daily life
- Mindfulness-based stress reduction program [MBSR]
 - “Mindfulness”: intentional and non-judgmental present moment awareness
 - Includes yoga, formal meditation practices, and mindfulness in everyday life
 - Ability to “disidentify from the contents of consciousness [i.e. thoughts] and view moment-by-moment experience with greater quality and objectivity” [shapiro et al., 2006]

Acceptance based interventions

- Mindfulness Based Cognitive Therapy [MBCT]
- Acceptance and Commitment Therapy [ACT]
 - Targets ineffective control strategies and experiential avoidance [such as kinesiophobia]
 - Learn to stay in contact with unpleasant emotions, thoughts, and sensations
 - Value clarification and committing to those values in daily life

Outcomes

- 10 controlled studies: small positive effect of MBSR and ACT on pain intensity
- Small positive effect of acceptance based therapies on depression
- ACT showed a large effect on depression in 1 study
- Effect sizes comparable to CBT, but much less data
- Matching?
 - Recurrent depression and RA more benefit from acceptance based therapies
 - Low meaning in life
 - Experiential avoidance

Conclusions

- Depression and chronic pain often co-exist
- Co-occurrence is associated with worse outcomes
- The relationship between the two is complex and bi-directional, with multiple additional mediating factors
- Depression screening is important in chronic pain patients
- Tricyclic antidepressants and SNRIs have more evidence compared to SSRIs in treatment of chronic pain; SSRIs can be helpful in fibromyalgia
- Treating depression through meds and therapy in co-occurring pain/depression is associated with positive outcomes on both pain AND depression measures

Question 1

- Which of the following was found to be the strongest independent predictor of chronic disability following acute back injury?
 - A. Pain at baseline
 - B. Pain at 3 months
 - C. Depression at baseline
 - D. Pain permanence beliefs
 - E. A and C
 - F. C and D

Question 2

- Which of the following regarding TCAs for treatment of chronic pain is true?
 - A. For chronic pain, they have a NNT of 6.
 - B. Their analgesic effects are largely secondary to their antidepressant effects
 - C. They require relatively high doses to treat chronic pain
 - D. Studies show their effectiveness in treating chronic back pain

Question 3

- Treating depression with an SSRI in a patient with chronic pain AND depression is not supported by data-

TRUE or FALSE