Chronic Pain and Depression

Snehal Bhatt, MD
Assistant Professor, Psychiatry
Medical Director, Addiction and Substance Abuse Programs University of New Mexico
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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 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

A biopsychosocial model [Casey et al., 2008]

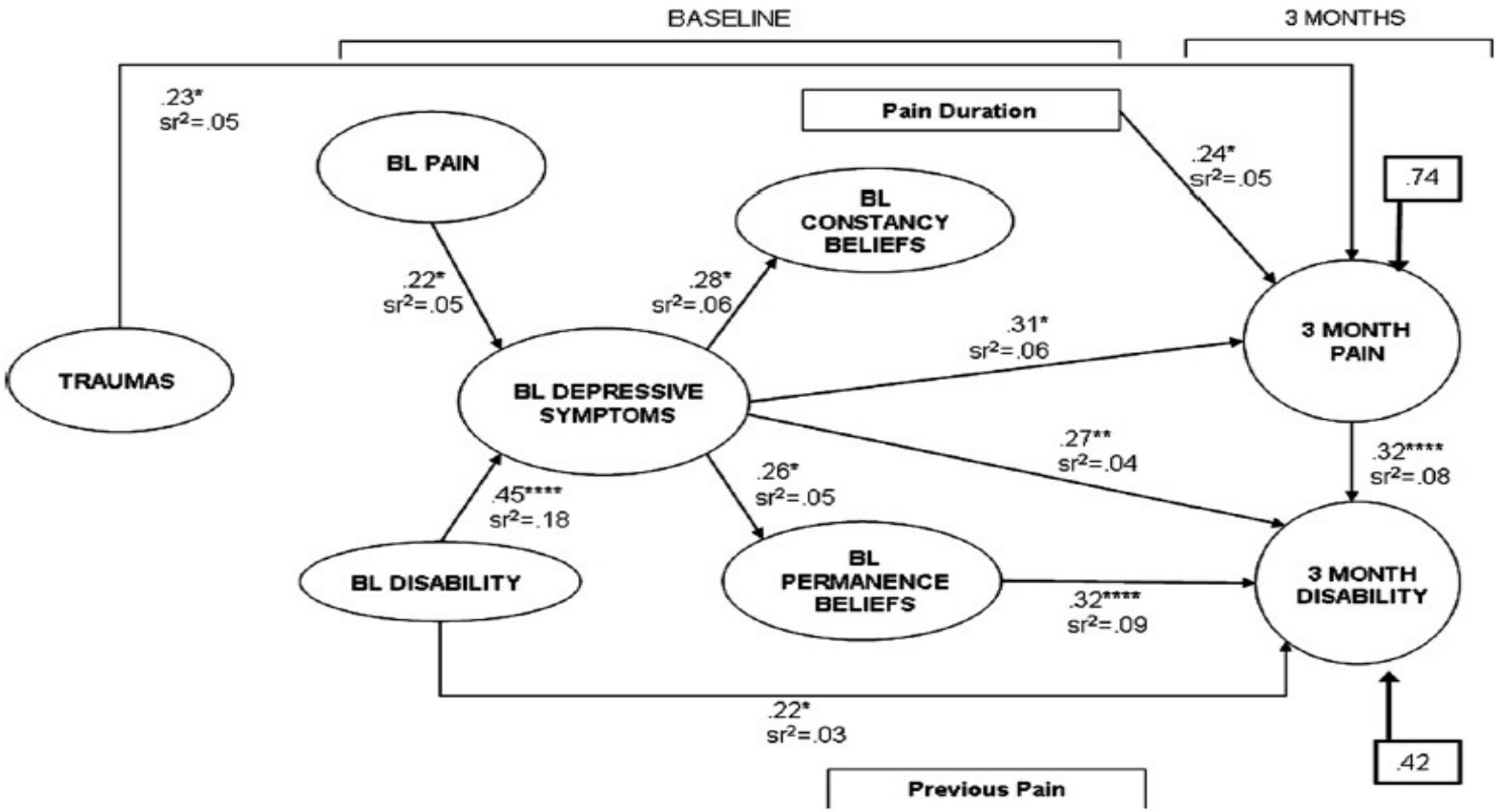


Fig. 2. Path analytic model of transition from acute to chronic pain and disability ($R^2 = .58$). *Note:* Standardized path coefficients (β) and squared semipartial correlations (sr^2) are reported for each path. "BL", baseline. Solid lines indicate $p < .05$ significant paths. Paths with associated p values $\geqslant .05$ are not depicted in this figure. $^{*}p < .05$. $^{**}p < .01$. $^{****}p < .0001$.

Therefore, we 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

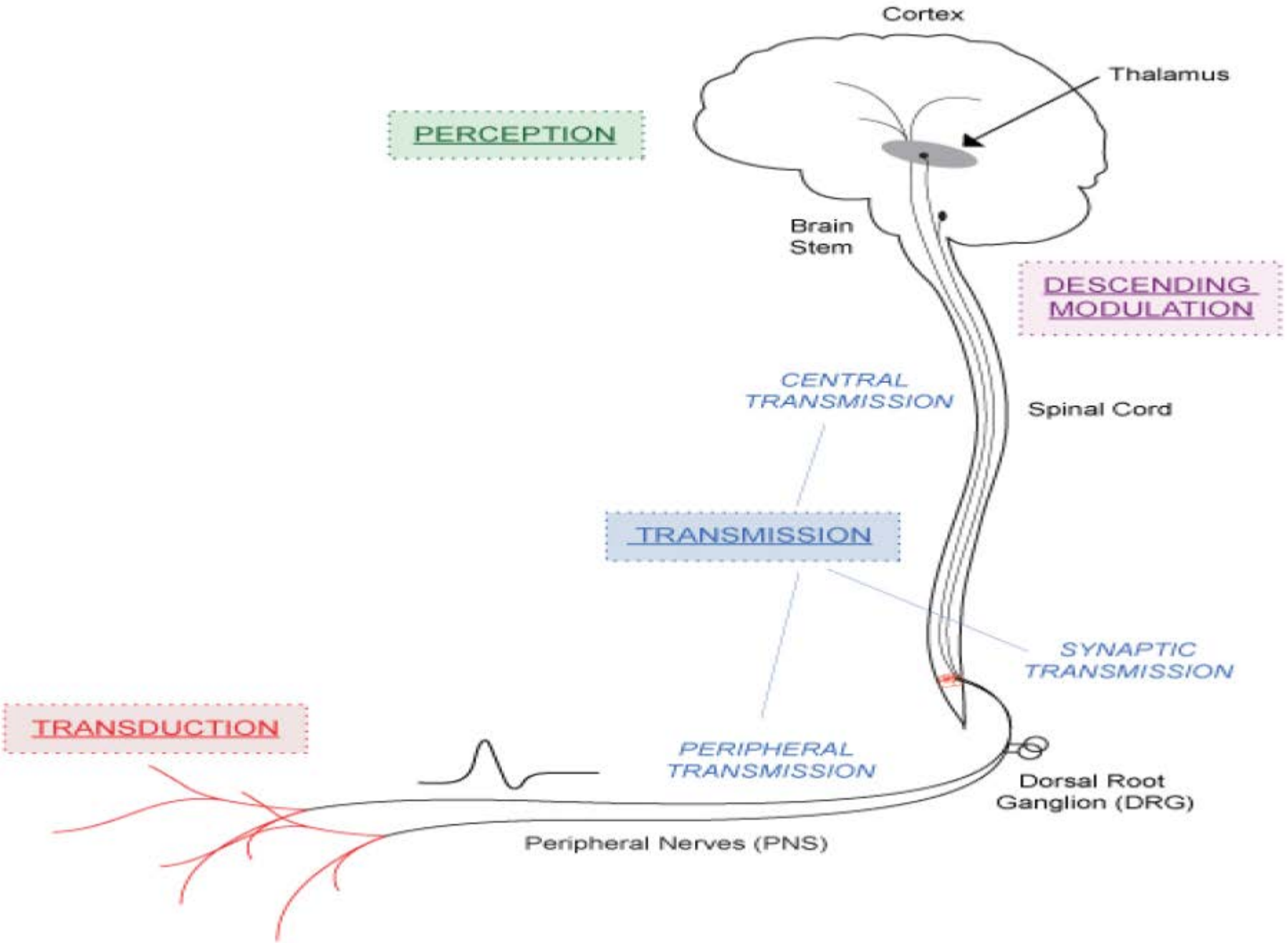
PHQ-9

- 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


Cortex
Thalamus
PERCEPTION
Brain Stem
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; upto 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 antidepresants 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 Musculoskelatal 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

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 (≥ 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