

Chronic Pain and Neuropsychology

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Chronic Pain and Neuropsychology

- Pain and neuropsychological conditions comingle.
- The rich body of knowledge about chronic pain provides a helpful context and specific hypotheses for understanding the nature of excessive disability in some neuropsychological conditions.

Topics

- Overlap of pain and neuropsychology phenomenon.
- Incidence of pain and pain-related disability.
- Psychophysics of normal and abnormal pain experience.
- The roles of personality and cognitive processing in normal and chronic pain experience – the primacy of attention.
- The nature of some common interventions.
- Medicines, pain, and cognitive processing.



**BEHAVIORAL METHODS
FOR CHRONIC PAIN
AND ILLNESS**

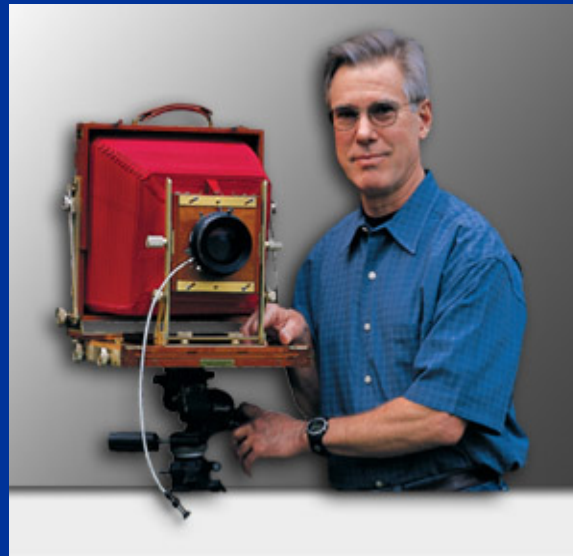
WILBERT E. FORDYCE



Jim Moore, Ph.d



Thomas
Williamson-
Kirkland, MD



Steve Fey, Ph.D.

Intersection of Pain and Neuropsychology

Symptom Complaints

	Medical <u>Outpatients</u> (n=50)	Stress <u>Claimants</u> (n-170)
Headache	62%	88%
Back Pain	48%	80%
Neck Pain	30%	74%
Memory	20%	53%

Lees-Haley & Brown, 1993

Head Injury and Chronic Pain

	<u>Mild</u>	<u>Mod/Sev</u>
■ Headache	89%	18%
■ Neck/Shoulder	51%	4%
■ Back	45%	2%
■ Other	20%	2%

Uomoto & Esselman, 1993

Cognitive Complaints with Chronic Pain

Patients rating
at least moderate
pain

- | | |
|-------------------------------|-------|
| ■ Trouble remembering | 17.6% |
| ■ Having to recheck things | 14.4% |
| ■ Difficulty Making Decisions | 14.4% |
| ■ Mind Going Blank | 15.3% |
| ■ Trouble Concentrating | 18.5% |

Roth et al., 2005

Cognitive Complaints with Chronic Pain

- 62% of those with at least mod. pain endorsed at least one cognitive complaint.
- 28% endorsed all five.
- BDI depression scores explained the largest proportion of cognitive complaints variance.
- Ratings of pain severity lose their association with cognitive complaints after controlling for pain catastrophizing and anxiety.

Cognitive Impairment and Chronic Pain

- Pain (experimental and chronic) is weakly associated with performance on neuropsychological tests (attention?).
 - Limited studies with small n's.
 - Small effect sizes.
 - Significant within pain group variability in test performance.
 - Multiple confounds in clinical groups (mood, meds, demographics, disability status, definition of pain).
 - Varying test batteries, not all measures impacted.
 - Simulated and probable “pain” malingers produce the lowest scores.

Cognitive Impairment and Chronic Pain

- FMS < controls (WMS-R mem. indices, pasat): Grace et al., 1999
- Mal < CP & EP < controls (WAIS-III PSI): Etherton et al., 2006a
- Community elderly, CP < NoP (mental flex.) Karp et al., 2006
- FMS, RA & CMSP < controls: Dick et al., 2002
- HA, MHA & CMSP > MTBI: Bell et al., 1999
- Mal < EP, CMSP, controls WAIS-III WMI: Etherton et al., 2006b

Cognitive Impairment and Chronic Pain

- A disruption of attention is a purported mechanism of impaired test performance.
- Pain is similar to other nonspecific influences on neuropsychological scores: mood, fatigue, meds.
- In motivated, not overly medicated or depressed, patients the nature of neuropsychological tests are such that pain influences on scores are likely minimal, but...
- In some patients, acute or chronic pain can impact cognitive efficiency. For a specific patient it is difficult to know.

MMPI and Chronic Pain

- Number of MMPI studies of chronic pain

3.98×10^{13}

MMPI and Chronic Pain

- In general, about half of MMPI profiles of chronic pain populations can be statistically “clustered”.
- Slesinger et al., 2002 – 2pt frequencies for patients admitted for chronic pain management. (n=209, valid profiles)

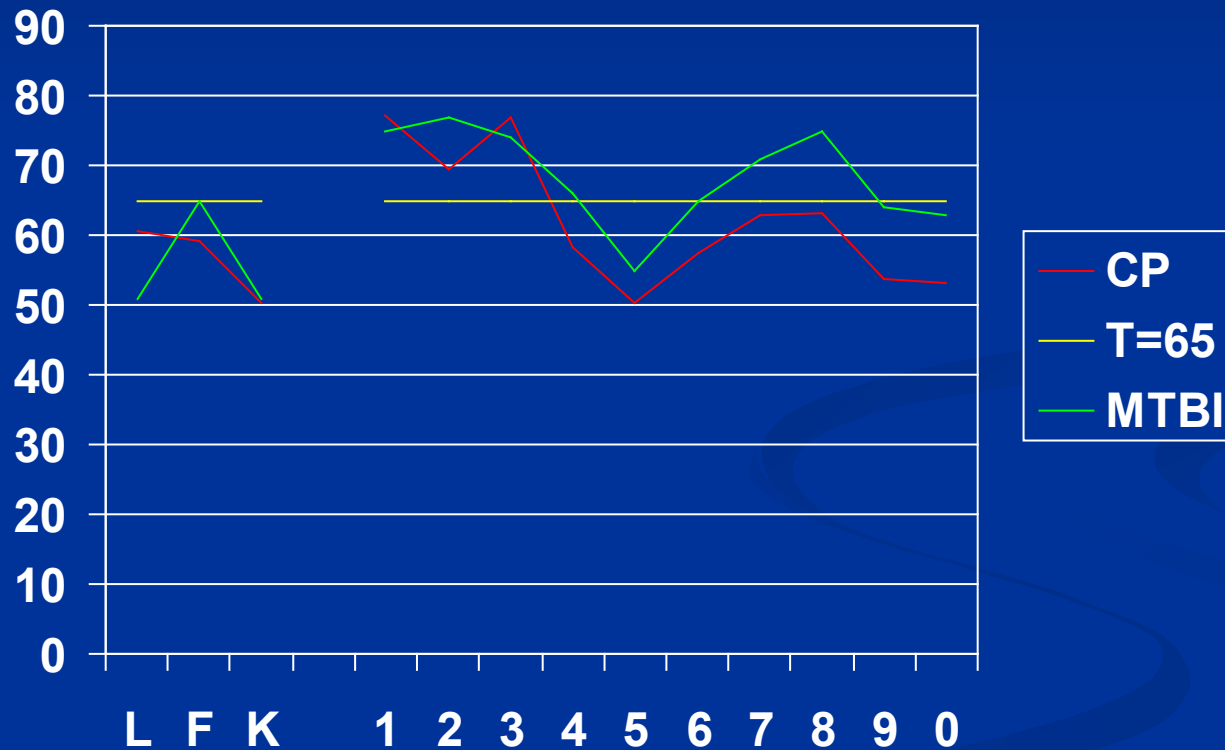
1-3/3-1 41%

2-3/3-2 10%

1-2/2-1 11%

MMPI-2 Chronic Pain

Slesinger et al, 2002, Leininger et al., 1991



Incidence of Pain and Pain-Related Disability

Pain Disability in US Workers

- “In the past two weeks...”
 - 52% of the workforce reported having headache, back pain, arthritis, or musculoskeletal pain
 - 12.7% lost productive time
 - 7.2% lost at least two hours of productive work time
 - 1.1% was absent from work for at least 1 day

Stewart et al., 2003 – Work & Health Interview, n=28,900

Pain Disability in US Workers

- % of workers with at least two hours of lost productivity due to pain in the last 2 weeks

■ Headache	2.72
■ Arthritis	1.23
■ Back	1.97
■ Other	1.32
■ Any	7.24

Stewart et al., 2003

Chronic Spinal Pain in the US

- 19% of the US adult population was estimated to have experienced chronic neck or back pain in the past 12 months.
- 29.3% reported a lifetime prevalence of chronic spinal pain.

Von Korff et al., 2005 – National Comorbidity Replication Study, n=5600

Chronic Spinal Pain in the US & Mental Disorder

	<u>12 Mo. Prev.</u>	<u>OR</u>
■ Major Depression	12.6%	2.5
■ Any Anxiety Dis.	26.5%	2.3
■ Alcohol Abuse	4.0%	2.0
■ Any Substance Abuse	4.8%	1.6
■ Any Mental Dis.	35.0%	2.3

Von Korff et al., 2005

Chronic Spinal Pain in the US & Medical Disorders

	<u>12 Mo. Prev.</u>	<u>OR</u>
■ Migraine	12.5%	5.2
■ Other Headache	14.6%	4.0
■ HTN	26.6%	1.5
■ IBS	1.9%	2.4
■ Cancer	.8%	.8
■ Diabetes	8.2%	1.2

Von Korff et al., 2005

12 Month Prevalence of Chronic Spinal Pain in the US

	<u>None</u>	<u>Any</u>
■ Other Chronic Pain	17.5%	48.3%
■ Chronic Disease	22.9%	38.9%
■ Mental Disorder	25.9%	40.8%

Von Korff et al., 2005

Reported Disability in Association with Chronic Spinal Pain

- % of reported normal/healthy vocational and/or avocational role performance over the past month
 - Spinal Pain: 76.5 vs. No Spinal Pain: 92.5
 - Regression estimates of reductions in role performance:
 - Spinal pain: -16%
 - Spinal pain adjusted for all comorbidities and demographics: 8%

Von Korff et al., 2005

Rising Low Back Pain Incidence?

- Rates of reported low back pain in North Carolina.

1992:	3.9%
2006:	10.2%

Freburger et al., 2009

Outpatient Musculoskeletal Pain Visits

	<u>1980</u>	<u>2000</u>
■ % of outpatient visits for MSP.....	9.6%	9.9%
■ % of specialty visits for chronic MSP.....	34%	49%
■ Major pain = HA	17%	9%
■ Major pain = LE	24%	32%

Caudill-Slosberg et al., 2004

Prevalence of Back Pain in a Primary Care Setting over 5 years

	<u>None</u>	<u>Mild</u>	<u>Mod</u>	<u>Sev</u>
Baseline	0.0%	18.5%	51.9%	29.7%
1 year	11.5%	34.9%	38.8%	14.7%
3 years	16.2%	35.8%	34.3%	13.8%
5 years	22.5%	35.0%	30.1%	12.4%

- Many patients get better
- Risk for future severe back pain was related to the presence of severe pain at the preceding time, levels of depression, presence of multiple pain sites, number of pain related disability days – but not mild/mod pain at baseline.

Von Korff & Miglioretti, 2005.

Back Pain Incidence

- Three year prospective study of 148 randomly selected veterans with no significant back pain 4 months prior to initial outpatient visit.
 - Patients with history of back diagnostic or interventional codes were excluded
 - 47% reported no previous back pain
 - 16% had more than 5 episodes of previous back pain

Jarvik et al., 2005

Back Pain Incidence

- 67% had back pain over the three years
- 44% reported their back pain was at least moderately bothersome
- Self reported depression at baseline was the single most powerful predictor of subsequent back pain (OR: 2.3)
 - (model: MRI, history of previous back pain, age, body mass index, smoking history, depression)

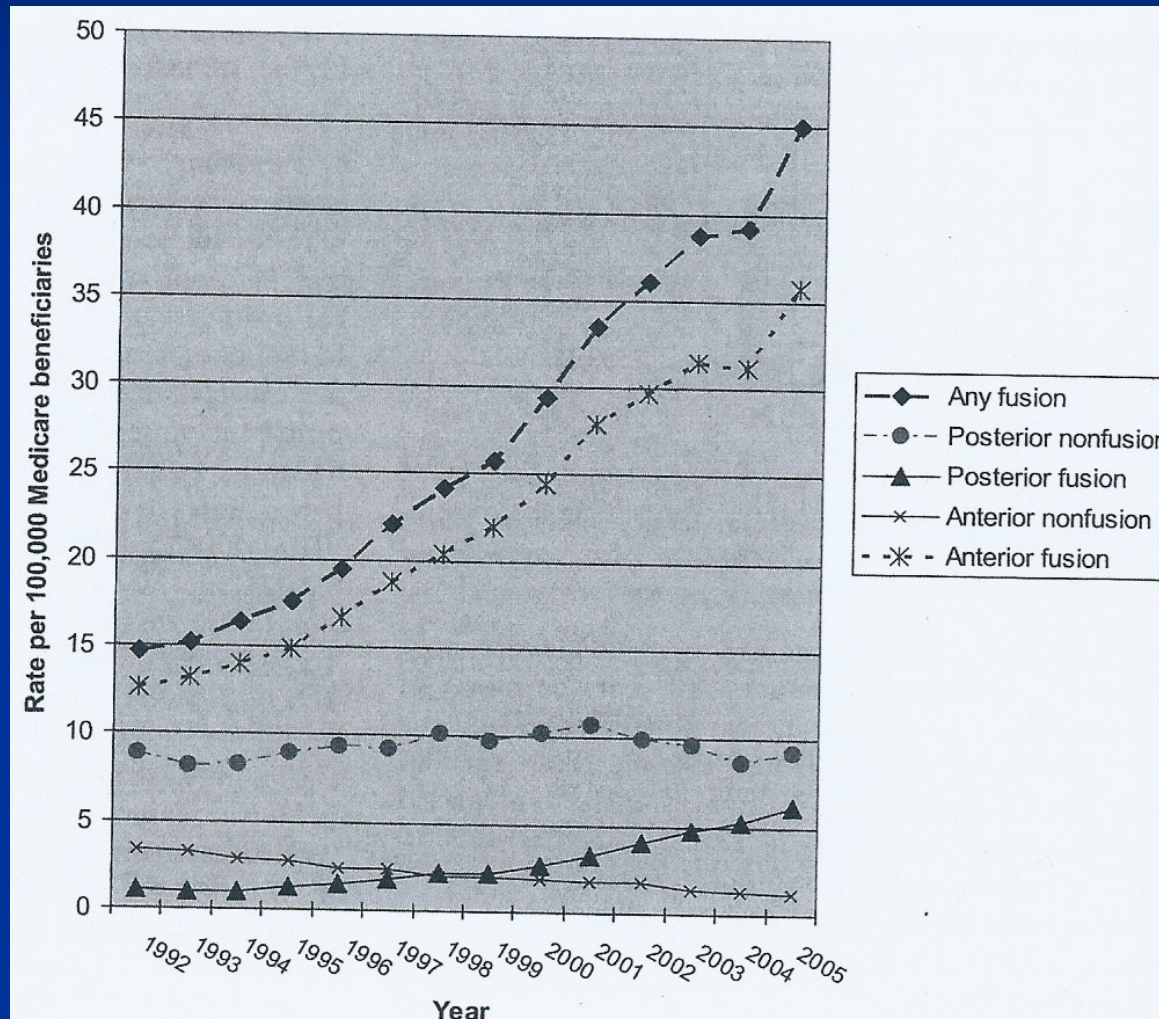
Back Pain Incidence

- Positive MRI findings were infrequent initially and at followup
 - Patients with evidence of stenosis or nerve root contact reported pain
 - Disc protrusions were associated negatively with the onset of back pain
 - Few changes over time

Jarvik et al., 2005

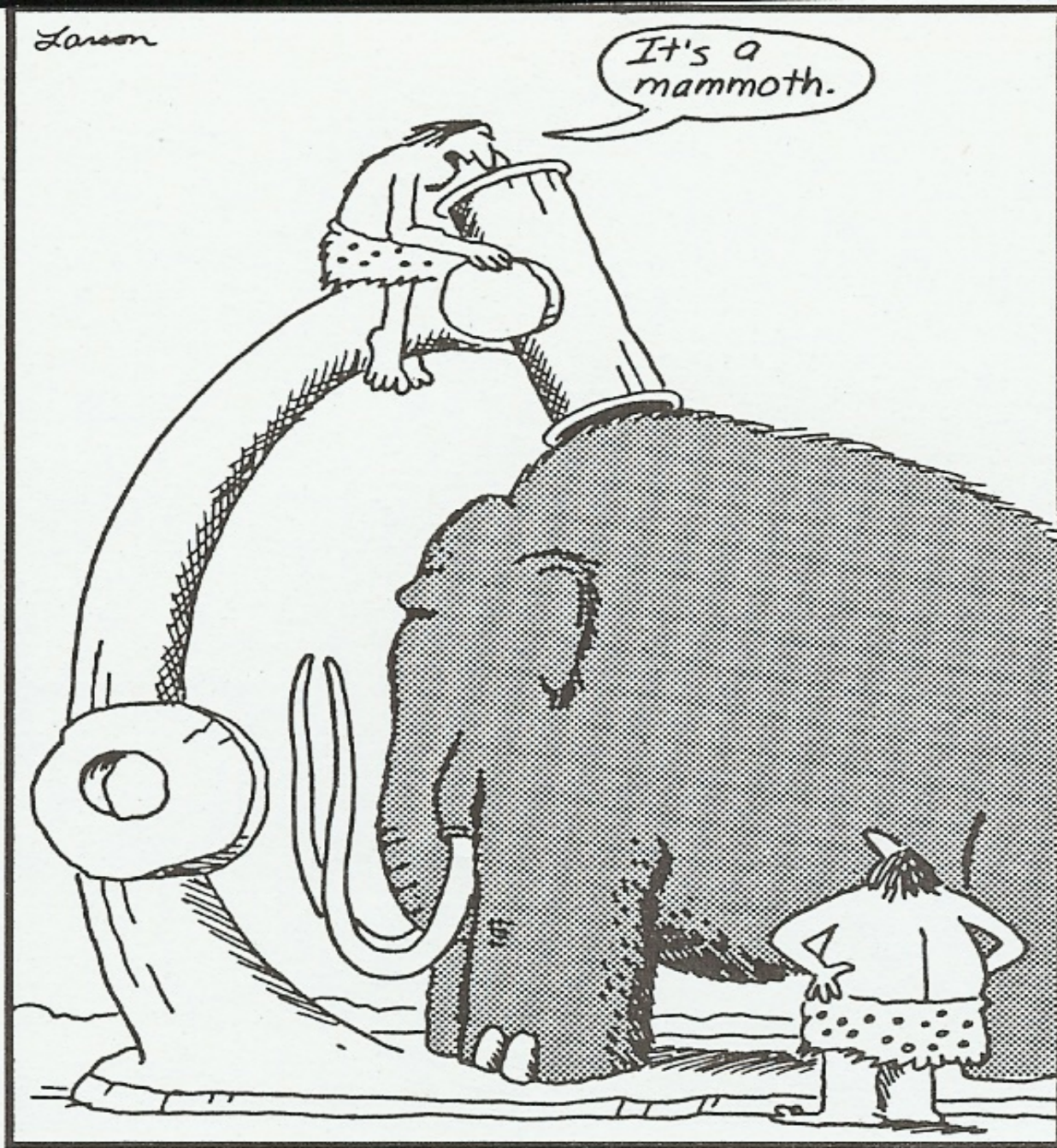
Rates of Spinal Surgery for Medicare Beneficiaries: 1992-2005

Wang et al., 2009.



Pain Psychophysics

Larson



Early microscope

Heritability of Pain Tolerance

- Pain sensitivity varies significantly between families
- Pain sensitivity shows similarities between relatives

Birklein et al., 2008

Heritability of Pain Tolerance

- Norwegian Twin Study of Experimental Pain Sensitivity (MZ=53, DZ=39)
 - 60% of the variance in cold-pressor pain ratings were genetically mediated
 - 26% of the variance in heat pain ratings were genetically mediated

Nielsen et al., 2008

Pre-Injury Pain and One Year Injury Outcome

- Pre-collision unspecified pain (not neck pain) predicted post whiplash work disability and the presence of chronic neck pain.
- Pre-collision psychologic distress predicted significant neck pain, but not work disability.

Carstensen et al., 2008

Pre-Injury Pain and One Year Injury Outcome

- Female gender, lower educational level, employment status (unemployed or blue collar work) also impacted work status and neck pain ratings at one year.
- Injury severity and mild preinjury neck pain were not related to outcomes.
- Carstensen et al., 2008

Pain Attention Constructs

Perceptual amplification

Central sensitization

Increased somatic focus

Health anxiety

Pain related anxiety

Body vigilance

Kinesiophobia

Fear avoidance

Somatization disorder

Cognitive processing bias

Pain amplification syndrome

Dysfunctional spectrum synd.

Central sensitivity synd.

Multiple unexplained sxs

Central inhibition dysfunction

Augmented pain processing

Somatosensory amplification

Central hyperexcitability

Attentional capture

Preoccupation with pain sensations

■ From Rollman, 2009

Brain Activation in Response to Experimental Pain

- Bilateral insular cortices
- Bilateral primary somatosensory cortices
- Bilateral supramarginal gyri
- Bilateral supplemental motor areas
- Ipsilateral cingulate gyrus
- Bilateral thalamus

e.g., Owen et al., 2008

Hypervigilance

- Fibromyalgia (and chronic back pain) patients relative to normal controls
 - are generally hypervigilant to pain
 - have reduced thresholds and tolerance for experimental pain
 - rate greater intensity of tactile stimulation across the whole range of intensity levels (neutral to unpleasant)

e.g., Hollins et al., 2009

Pain Sensitivity in Chronic Pain

	<u>Controls(11)</u>	<u>FMS(16)</u>	<u>BP(11)</u>
■ McGill Pain	0	10.8	7.8
■ Pain Threshold	2.7kg	.7kg	.7kg
■ Mod Pain	5.3kg	2.2kg	2.7kg
■ Rated Pain at 2kg	1/20	6/20	6/20

Giesecke et al., 2004

At 2KG of Experimental Pressure

- FMS & CLBP patients:
 - Rated moderate levels of pain
 - Demonstrated increased fMRI signal:
 - in the contralateral primary somatosensory cortex
 - bilateral secondary somatosensory cortices
 - inferior parietal lobule
 - Cerebellum
- Giesecke et al., 2004

At 2KG of Experimental Pressure

- Healthy controls:
 - Rated faint pain
 - Demonstrated increased fMRI signal only in the contralateral somatosensory cortex

Giesecke et al., 2004

Equal Ratings of Experimental Pain

- All three groups demonstrated similar fMRI signals when equated for pain ratings in the:
 - Contralateral primary somatosensory cortex
 - Bilateral secondary somatosensory cortices
 - Contralateral anterior cingulate cortex
 - Contralateral insula
 - Cerebellum

Giesecke et al., 2004

Chronic Pain and Hyperalgesia

- Peripheral nerve injury and/or tissue inflammation innervates the dorsal horn system in the spinal cord.
 - Spinal cord NMDA receptors are activated ultimately leading to enduring increases in synaptic efficacy
 - With associated increases in spontaneous and stimulus induced neuronal discharges
 - With expansion of peripheral receptive fields

Mao et al., 1995

Chronic Pain and Hyperalgesia

- Functionally
 - Possible increase in spontaneous pain
 - Exaggerated responses to innocuous and noxious peripheral stimulation
 - Expansion of peripheral pain fields

Cognitive Processing, Personality, and Chronic Pain

Pain Catastrophizing

Pain Fear and Avoidance

Pain Memory

- Recall of pain is poorly correlated with actual pain ratings.
- Patients with chronic pain with high reported pain at the time of recall tend to over-report the level of pain previously recorded.
- Pain catastrophizing is positively correlated with the accuracy of pain memories.

Pain Anticipation

- Reliable expectation of future pain increases the rating of pain for higher intensity experimental pain, and lowers the reported pain in lower intensity stimulation relative to uncertainty.
- Pain expectation effects are mirrored in specific brain activation patterns.

Brown et al., 2008.

Pain Catastrophizing Scale

Sullivan et al., 1995

- I worry all the time about whether the pain will end.
- It's awful and I feel that it overwhelms me.
- I become afraid that the pain may get worse.
- I keep thinking about how much it hurts.
- There is nothing I can do to reduce the intensity of the pain.

Pain Catastrophizing

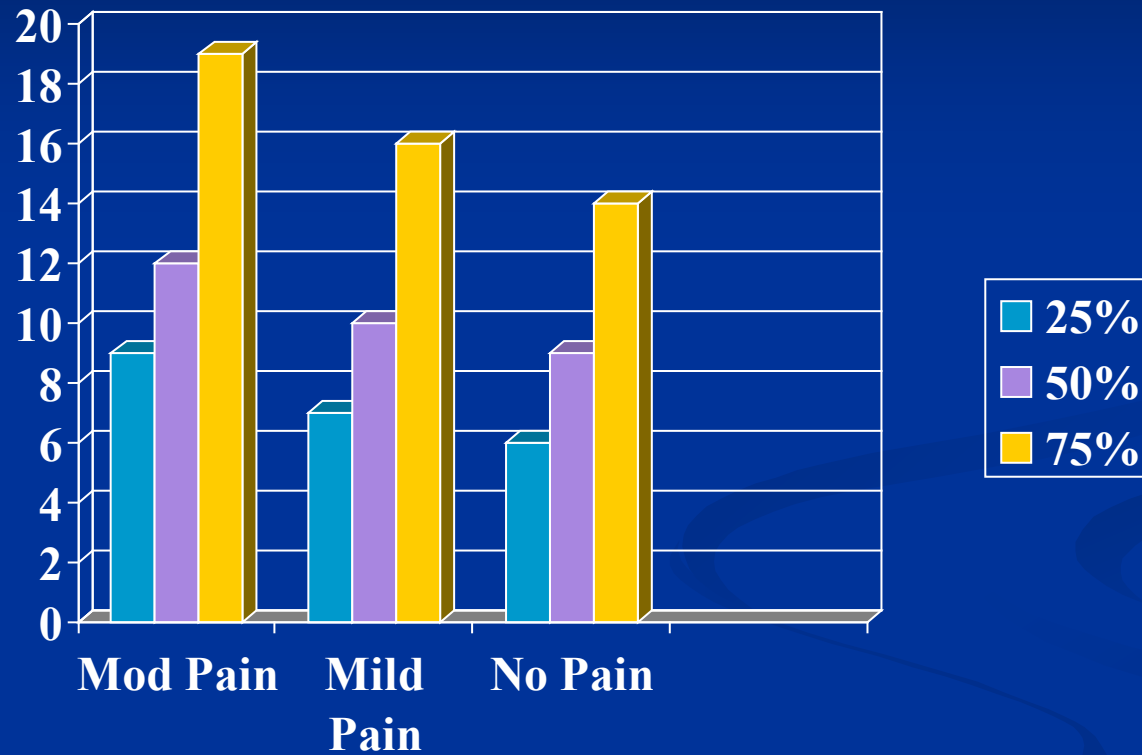
- Heterogeneous construct - PCS.
 - Rumination: “I can’t stop thinking about my pain”.
 - Magnification: “I fear something dangerous will happen”.
 - Helplessness: “There is nothing I can do to reduce my pain”.

Pain Catastrophizing Scores

- Are widely distributed in normals.
- Are correlated with levels of rated pain, pain duration, and measures of depression, and trait neuroticism.
- Appear to contribute relatively small additional unique variance in reports of pain related disability.
- May impact overall disability through its contribution to pain fear and activity avoidance.

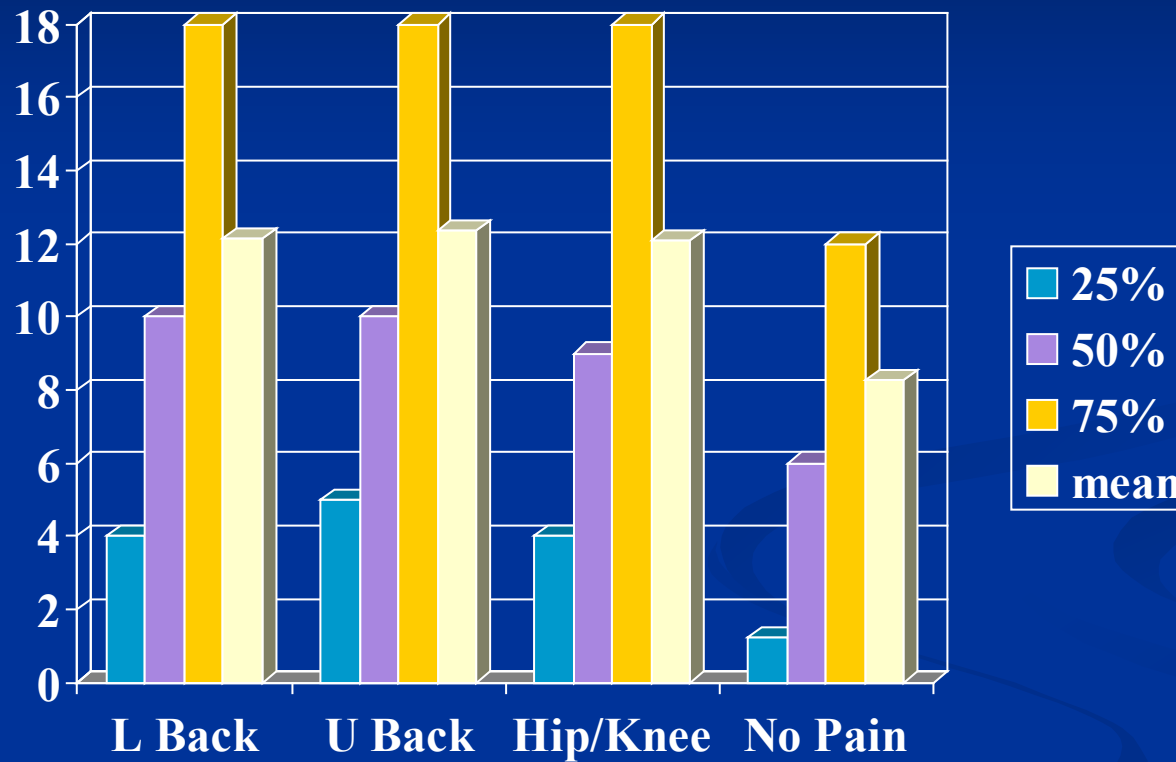
Sullivan et al., 1998; Severeijns et al, 2002; Buer & Linton, 2002.

Quartile Catastrophizing Scores in a Community Sample – Buer & Linton, 2002



Range: 0 - 52

Quartiles and Mean Catastrophizing Scores in a Community Sample – Severeijns et al., 2002



Range: 0 - 52

Pain Catastrophizing Scores

- Via zero-order correlations –
 - Accounts for up to 31% of the variance in pain ratings across a variety of subject groups,
 - e.g., low back pain, mixed chronic pain, RA, dental procedures, burn dressing changes, whiplash, experimental pain, population based samples

Sullivan et al., 2001

Pain Catastrophizing

- Ratings appear to be stable over time (test-retest correlations of .7 to .8).
- Yet PC scores and pain experience can be influenced by intervention (modifiable trait?).

Pain Catastrophizing

- Predict pain scores at a later period of time (PC is a primary cause of chronic pain)?
- PC scores can be higher in chronic pain populations.
- Is associated with higher levels of pain behaviors, frequency and duration of hospital and admissions and outpatient visits.

Pain Catastrophizing

- Scores are correlated with measures of depression, state anxiety, and trait anxiety.
- But do appear to offer independent predictive power to ratings of pain and, less so, pain-related disability.

Tampa Scale for Kinesiophobia

- I'm afraid I might injure myself if I exercise.
- Pain always means I have injured my body.
- It is not really safe for a person with a condition like mine to be physically active.
- No one should have to exercise when he/she is in pain.

Kori et al., 1990

Pain Fear – Activity Avoidance

- Fear avoidance beliefs are widely distributed in the normal population.
- PFA scores are correlated with pain catastrophizing scores.
- Pain catastrophizing appears to relate more to pain ratings.
- Fear avoidance scores appear more related to levels of disability (self report and actual performance).

e.g., Buer & Linton, 2002; Crombez et al., 1999.

Pain Fear – Activity Avoidance

- Levels of Pain Fear and Avoidance at the time of acute back injury in individuals without a history of significant previous back problems do predict pain and disability ratings at one year followup, but...
- Initial levels of emotional distress are a better predictor.

Grotle et al., 2006

Pain Fear – Activity Avoidance

- Pain fear avoidance was highly correlated with levels of initial reported pain in acute back (pain < 3 weeks) and moderately correlated with measures of depression and physical impairment (PT eval).
- Pain fear avoidance explained the largest portion of variance in 1 month pain related work disability.

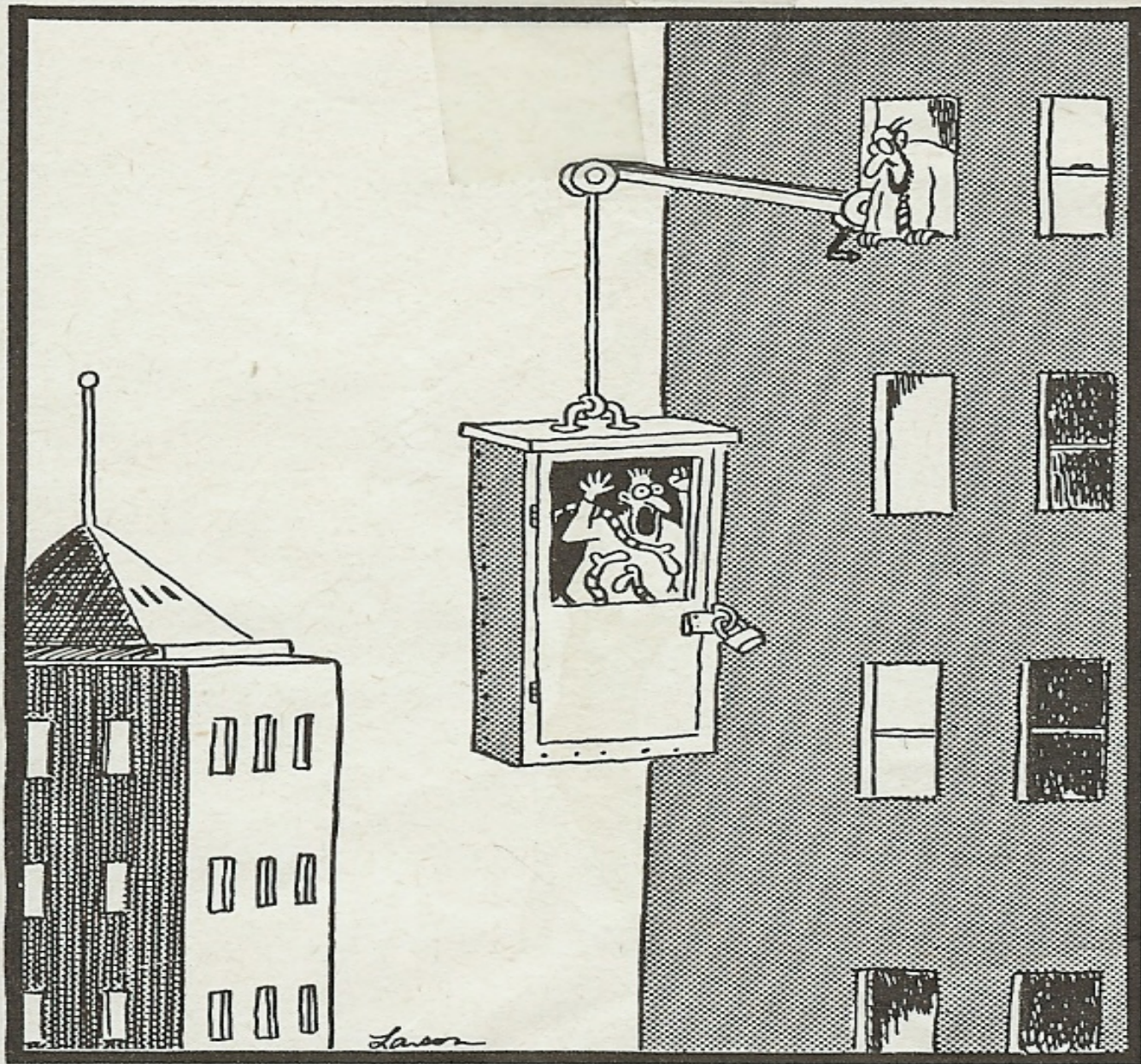
Pain Fear and Acute Injury Recovery

- In acute recovery from whiplash high levels of pain catastrophizing and movement fear are associated with more reported pain and disability.
- Pain ratings tended to decline with time.
- Daily measures of movement fear predicted the following day's pain ratings and overall levels of disability.
- Daily measures of pain minimally influenced the next days ratings of pain and movement fear.

Vangronsveld K et al., 2008.

Interventions

- Distraction
- Education
- Mood
- Contingency management
- EXPOSURE & ACTIVITY



Professor Gallagher and his controversial technique of simultaneously confronting the fear of heights, snakes, and the dark

Distraction

- In experimental pain paradigms distraction reduces subjective pain experience.
- E.g., Valet et al., 2004 – heat pain & stroop

	<u>no distraction</u>	<u>stroop</u>
Pain intensity	57/100	52/100
Pain unpleasantness	56/100	47/100

- Distraction activated cingulo-frontal cortex & posterior thalamus, deactivated primary pain encoding areas.

Virtual Reality Distraction

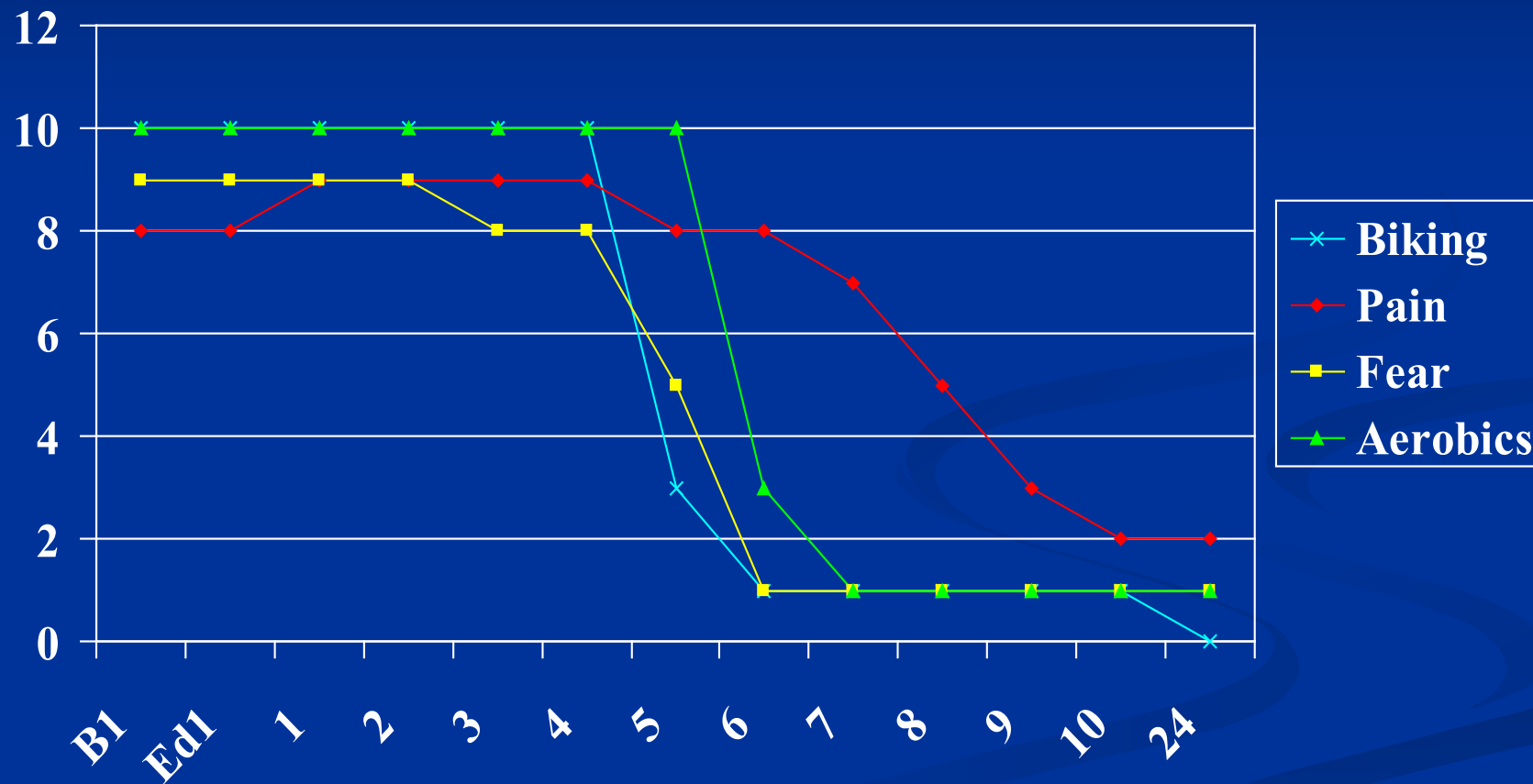
- 14 year old, burn pain during dressing changes (ratings from 0 to 100).

■ Worst pain	75	30
■ Average pain	73	38
■ Unpleasantness	93	40
■ Anxiety	41	3
■ Time thinking of pain	84	32

Hoffman et al., 2000

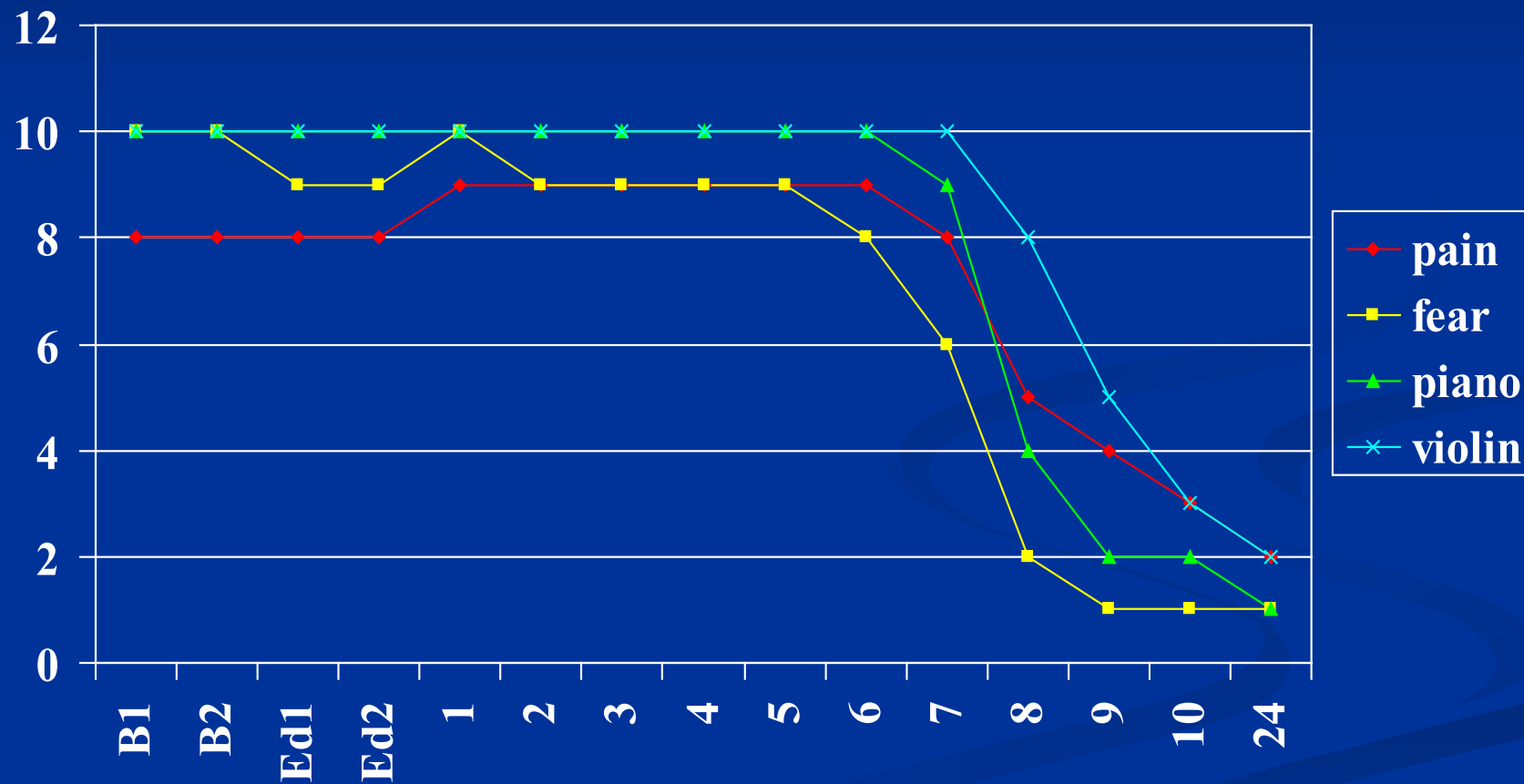
Graded Exposure in CRPS

De Jong et al., 2005



Graded Exposure in CRPS

De Jong et al., 2005



Opioids

- “The overriding therapeutic goals in the treatment of chronic nonmalignant pain are pain relief and improved functioning. Being “medication free” is no more appropriate a primary goal for patients with this type of medical problem than it is for patients with any other type of medical problem.”

Ridenberg & Portenoy, 1994

Opioid Prescriptions for Musculoskeletal Pain

	<u>1980</u>	<u>2000</u>
■ Opioid Rxs for chronic pain	8%	16%
■ Opioid Rxs for acute pain	8%	11%

Caudill-Slosberg et al., 2004

Opioid Prescriptions for Musculoskeletal Pain

	<u>1980</u>	<u>2000</u>
■ Strong Opioids for chronic pain	2%	9%
■ Strong Opioids for acute pain	1%	6%

Caudill-Slosberg et al., 2004

Patterns of Opioid Use in Denmark

- In the last two decades opioid treatment of non-cancer pain has increased 600%
- 66% of opioid prescriptions in Denmark are for non-cancer pain
- 3% of Danish population uses opioids on a regular or continuous basis
- 19% of the population reports chronic pain (≥ 6 mo.) & 12% of this group uses opioids

Ericksen et al., 2006

Patterns of Opioid Use in Denmark

- For those with chronic pain OR for opioid use:
 - 8.37 for “moderate to very severe” pain ratings relative to “none to mild”
 - 5.21 for “fair to very bad” self perceived health relative to “good to really good”
 - 1.68 for sedentary leisure activities vs active
 - 2.91 for disability pension vs none

Ericksen et al., 2006

Opioids

- Chronic pain patients taking long-term opioids generally report worse pain, higher healthcare utilization, and lower activity levels relative to non-opioid CP patients.
- Analgesic tolerance does stabilize in most patients and a stable dose can be achieved.
- Some patients report no improvement in pain in spite of escalating doses.
- Over half of patients in follow-up abandon opioid treatment due to lack of efficacy or side effects.
- Side effects (respiratory depression, nausea, sedation, euphoria/dysphoria, itching) generally subside with chronic use with the exception of constipation.

Ballantyne

Opioids and Time off Work in Low Back Pain

- 27% of all claimants remained off work ≥ 3 months
- 71% of those receiving opioids remained off work ≥ 3 months

Volinn et al., 2009.



Opioids and Time off Work in Low Back Pain

- 52% filled at least one opioid prescription
 - 71% schedule 3 and 4 opioids only
 - 29% filled at least one schedule 2 opioid

- 18% filled opioid prescriptions for ≥ 90 days

Volinn et al., 2009.

Opioids and Time off Work in Low Back Pain

■ Odd Ratios for chronic work disability

■ No opioids	1.0
■ Schedule 3-4	1.9
■ Schedule 2	6.1
■ Chronic Schd. 3-4	10.9
■ Chronic Schd 2	14.2

Volinn et al., 2009.

Chronic Opioid Use and Tolerance

- Opioid tolerance with prolonged use
 - Can reflect a reduction in number or turnover rate of opioid receptors, or desensitization of opioid receptors or both.
- Opioid induced abnormal pain sensitivity
 - Similar to the cellular conditions in neuropathic pain conditions (MNMDA receptor activation)
 - Changes in the dorsal horn cells of the spinal cord
 - In animals, some changes appear permanent

Ballantyne & Mao, 2004

Hyperalgesia and Opioid Tolerance

- Tolerance may reflect the paradoxical development of increasing levels of hyperalgesia with time, and increasing doses

Mao et al., 1995

Opioids and Cognition

- Stable moderate chronic opioid dosing does not appear to have a significant testable impact on cognition.
 - An increase in dose in chronic cancer opioid users does impact neuropsychological function (e.g., Bruera et al., 1989; Kamboj et al., 2005).
 - Cognition returns to baseline in one week? (Bruera et al., 1989).
 - A single dose of more powerful opioid (morphine) in a naive subject does produce impairment in recall (e.g., Hanks et al., 1995)
 - A single dose of a mild opioid in a naive subject may not impact cognition (eg, O'Neill et al., 1995).

Opioids and Cognition

Chronic high dose opioids can produce significant sedating and cognitive effects.

Morphine Dose Escalation and Cognition

Morphine Placebo

- Delayed Paragraph

Recall, Exposure Before

Treatment (# of Units) 4.8 6.0

- Delayed Paragraph

Recall, Exposure After

Treatment 4.0 6.5

- Trails B (secs)

177.4 186.4

Kamboj et al., 2005

Benzodiazapines and Cognition

- Evidence suggests general effects on a variety of cognitive functions in naive healthy subjects , particularly recall of information learned during drug exposure.
 - e.g., Hanks et al., 1995; Sellal et al., 1992; O'Neill et al., 1995

Benzodiazapines and Cognition

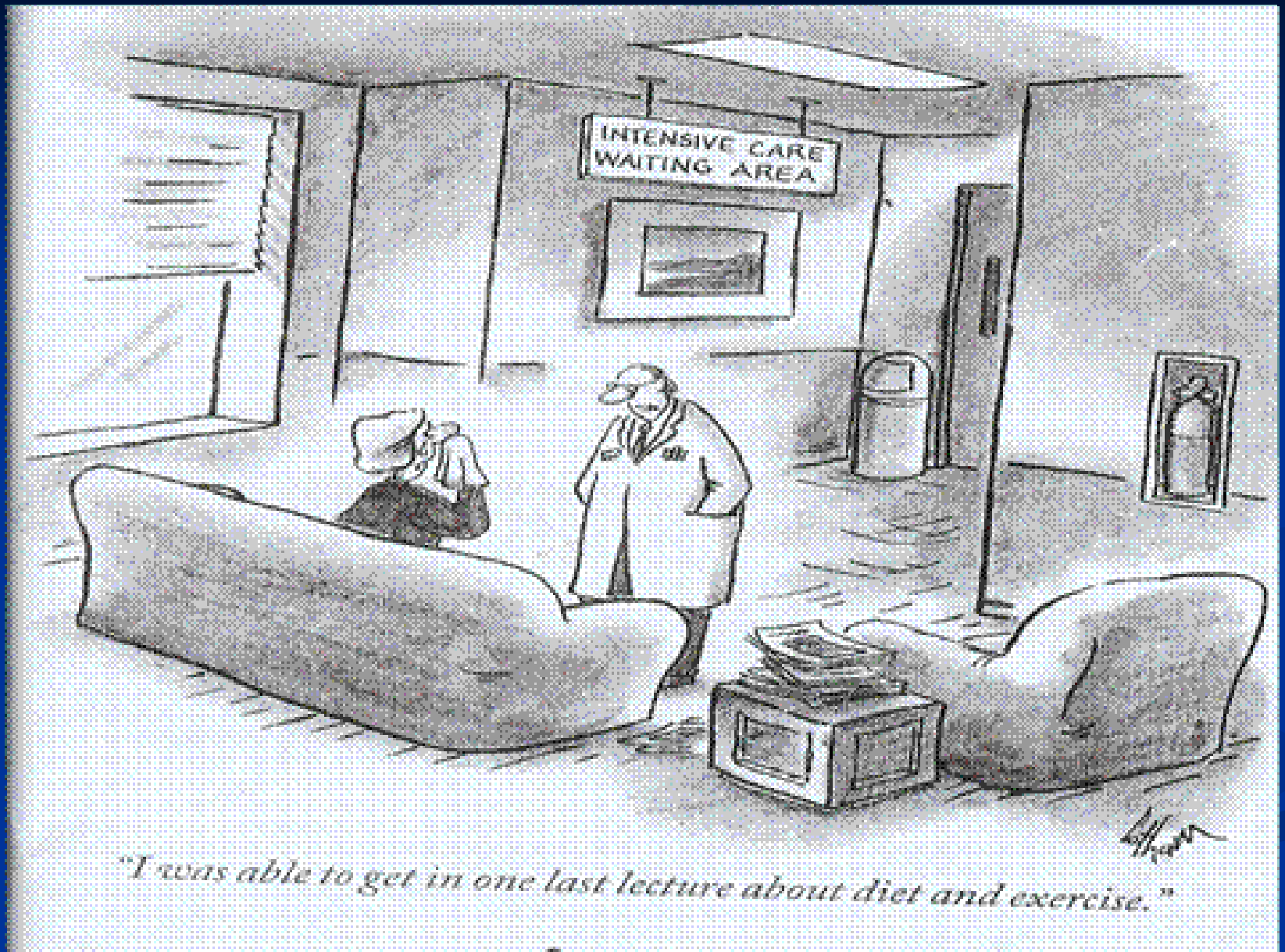
- Patients taking chronic benzodiazapines show cognitive impairment that improves when treatment stops
- Some patients do not appear to return to baseline following cessation

Stewart, 2005; Barker et al., 2004

Antiepileptics

- Some clearly impact cognitive function (Topamax, Dilantin).
- Gabapentin (Neurontin) and pregabalin (Lyrica) appear to have very mild cognitive effects, in general not statistically different from placebo.
- Many patients complain of sedation and problems with focus.

e.g., Salinsky et al., 2005, Aldenkamp et al, 2003.



"I was able to get in one last lecture about diet and exercise."