



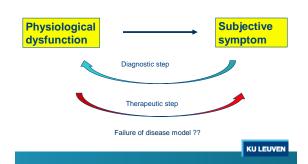
Health Psychology Lab – Leuven Psychology of aversive somatic experiences







## Disease model



## 3 main challenges

- · "Medically unexplained symptoms" (MUS)
  - Functional syndromes
    - · incl. various pain syndromes
  - o Somatization problems
- · Placebo/nocebo phenomena
- Poor (and highly varying) relationship between symptoms and bodily dysfunction

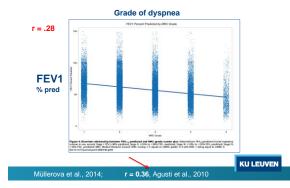
## Medically explained symptoms?

How well are self-reported complaints explained in diseases with known etiopathology?

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## Relation dyspnea - FEV1 in COPD



## Respiratory diseases

- r = .30 à .60 with relevant physiological disease indicators across respiratory diseases
- Asthma: ± 50% shows poor correlation with FEV1
- Trait NA is an important moderator of asthma symptoms



## Cardiac diseases

- r = ± .0 à 0.17: self-reported complaints with objective data (function measures; 24-hour holter data; data from implanted pacemakers/defibrillators)
- o 17 to 61.1% coincidence between actual and reported arrhythmia's
- 25 to 45% of patients with atrial fibrillation reported symptoms in the absence of tachyarrhythmias
- 40% of cardiac function measures for self-reported cardiac symptoms are "negative"
- (negative) emotional factors predict symptom reports better than objective measures of cardiac disease

"We need a complaint model rather than a disease model"

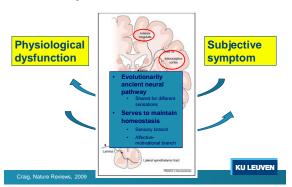
Kroenke, special issue on Symtoms, Annals of Internal Medicine, 2001

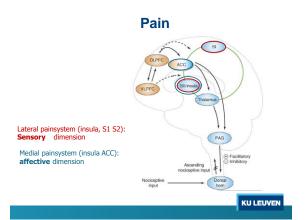
KU LEUVEN , 2005; Stickberger et al., 2005;

# **Complaint Model**

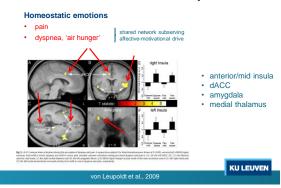


# Interoception

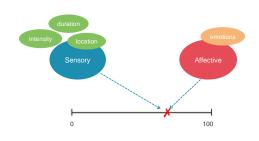




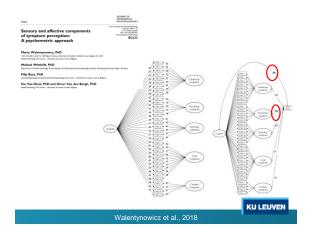
# **Breathlessness and pain**



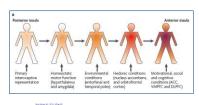
# What is a symptom ?? Dual process perspective



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Craig, 2003; Leventhal & Everhart, 1979; Price et al., 1983; Van den Bergh et al., 2015



# Critical role of insula





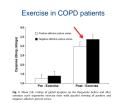
Overlapping activity in anterior insula during interoception and emotional experience

g, 2009

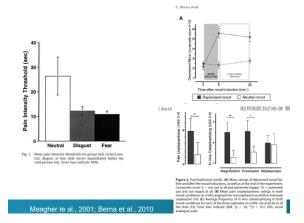
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## Dyspnea and emotional pictures

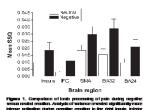




Von Leupokiti et al., 2006, 2009



## Painful esophageal stimulation and music



ense scheibur during regelier smalları in ihe righi insuls, infetor nini gyrun, SMA, und ACC (SA24 und BASZ).

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# (Negative) affect "invades" the perception of physical symptoms

- · More pain
- · More attention to pain
- · More avoidance of pain

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# **High trait NA persons**

- Over-reactive evaluative system
  - Increased activity in limbic areas when processing emotional stimuli
  - Decreased activity in parts of the ACC and PFC
- · Genetic basis
- Poor executive control function
- Poor emotion regulation
- Suppression
- Attentional and interpretational biases towards threatening stimuli
- Negative Repetitive Thinking



Hariri, 2009; Posner & Rothbart, 2000, Davidson, 2000; Yiend, 2010; Moberly & Watkins, 2008;



"interoceptive perception is largely a construction of beliefs that are kept in check by the actual state of the body (rather than vice versa)".

> Barrett & Simmons, Nature Reviews 2015,p. 424



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**Exaggerated affective** High NA responding Х

Somatic Events

Was It So Bad? The Role of Retrospective Memory in Symptom Reporting

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# Healthy Ss High HSR Low HSR 0.30s 30-60s 60-90s 90-120s 120-150s 150-180s 180-210s 210-240s 210-240s 270-300s 300-330s Short trial Healthy Controls

## **Exaggerated affective responding**

- · Brain imaging in different MUS groups
  - greater activation of the affective networks when processing interoceptive stimuli
  - o failure to adequately activate inhibitory systems to counter-regulate unpleasantness

Abnormal Affective Modulation of Somatosensory Brain Processing Among Patients With Fibromyalgia

Pedro Montova, PhD, Carolina Stiges, MS, Manuel García-Herrera, MD, PhD, Raúl Izquierdo, MD, Magdalena Truyols, MS, Nicole Blay, BS, and Dolores Collado, MD

Psychosomatic Medicine 67:957–963 (2005)

## Central sensitization?

Central Sensitization: Explanation or Phenomenon?

Emanuel N. van den Broeke<sup>1</sup>, Diana M. Torta<sup>1,2</sup>, and Omer Van den Bergh<sup>2</sup> <sup>1</sup>Institute of Neuroscience, Université Catholique de Louvain, and <sup>3</sup>Health Psychology, Paculy of Psychology and Educational Sciences, University of Leuven

Central sensitization and pain hypersensitivity: Some critical considerations. [version 1; referees: awaiting peer review]

Emanuel N. van den Broeke ©

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'There is no simple, direct "There is no simple, direct relationship between the wound per se and the pain experienced. The pain is in very large part determined by other factors, and of great importance here is the significance of the wound, i.e. reaction to the wound" (p. 165)

From Beecher, H.K. (1959). Measurem subjective responses: quantitative effec drugs. New York, NY, US: Oxford Univ

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# Interpretation/meaning matters!

## Catastrophic interpretations of pain

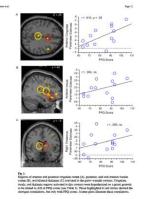
## **Pain Catastrophizing Scale**

When I am in pain...

- · I constantly wonder whether the pain will stop.
- · that is awful and I think it will never get better
- · I become afraid the pain will get worse
- I wonder whether anything serious might happen

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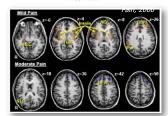
## Pain-related fear



## Catastrophic interpretations of pain

Cortical responses to pain in healthy individuals depends on pain catastrophizing

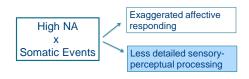
David A. Seminowicz, Karen D. Davis \*

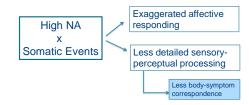


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## Effects of pain catastrophizing

- · Predictor of future pain, even when controlling for level of medical
- · Hampers the effects of distraction from pain
- · Dysregulation of the endogenous opioid pain-control system.
- Increased pro-inflammatory cytokine (IL-6)
- · Amplification of cortical activation in the context of pain





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# **Body - symptom correspondence**

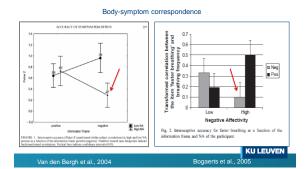
CO<sub>2</sub>-inhalation

within-subject correlation across a number of breathing trials



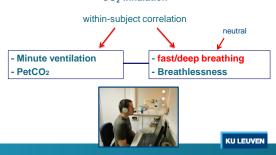
## **Negative affective context**

negative vs positive odor + info



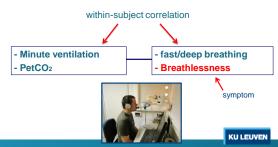
# **Body-symptom correspondence**

## CO<sub>2</sub>-inhalation

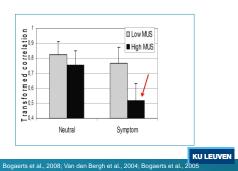


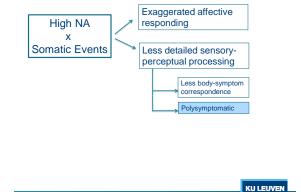
# **Body-symptom correspondence**

## CO<sub>2</sub>-inhalation

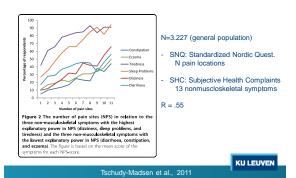


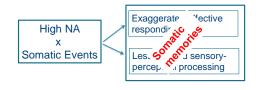
# **Body-symptom correspondence**



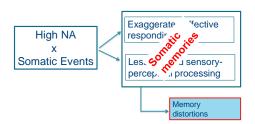


## Pain locations and nonpain symptoms





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Group	Patients (n = 30) Mean (SD)	Controls (n = 24) Mean (SD)	Statistics		
			Significant Effects	F (p)	ηĝ
Specific memories			Group	13.63 (.001)	.21
Total	7.13 (2.87)	9.42 (1.06)			
Positive cues	3.73 (1.51)	4.67 (0.76)			
Negative cues	3.40 (1.61)	4.75 (0.53)			
Overgeneral categoric memories			Group	7.62 (.008)	.13
Total	0.93 (1.17)	0.21 (0.59)			
Positive cues	0.33 (0.55)	0.13 (0.45)			
Negative cues	0.60 (0.77)	0.08 (0.28)			
Overgeneral extende	d memories		Group	8.70 (.005)	.14
Total	1.00 (1.23)	0.21 (0.51)			
Positive cues	0.43 (0.63)	0.13(0.34)			
Negative cues	0.57 (0.86)	0.08 (0.28)			
Same event*	0.07 (0.25)	0.00 (0.00)			
No memory*	0.63 (1.22)	0.13 (0.34)			
Omission <sup>a</sup>	0.23 (0.63)	0.04 (0.20)			

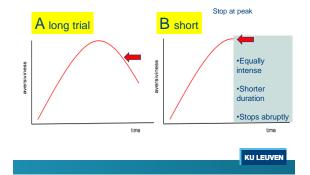
## Peak-end rule

## Encoding of somatic events

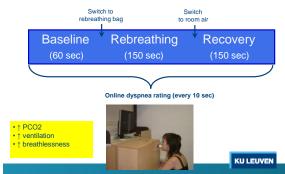
- · in the form of transitions and critical moments
  - 。 Segment that felt most intense (peak)
  - o Sensations in the final segment (end)
- · Relative duration neglect
- > Bias requires sensory-perceptual processing of events

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## Which trial caused greatest discomfort?



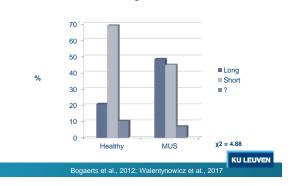
# Rebreathing test (Read, 1967)

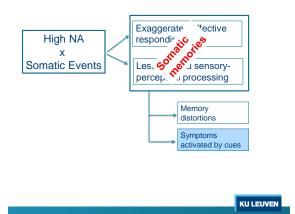


# Rebreathing test (Read, 1967)

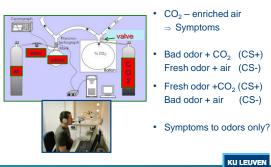


## Which trial caused greatest discomfort?

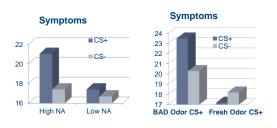




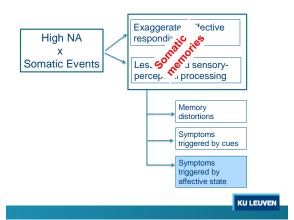
## MUS in the lab Odor-CO<sub>2</sub>-inhalation conditioning paradigm



## MUS in the lab Odor-CO<sub>2</sub>-inhalation conditioning paradigm



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## Pictorial cues (IAPS)

Series of 20 pics, 8 sec/pic



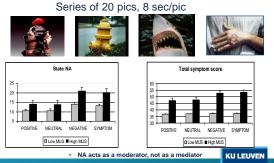
Positive Neutral Negative - threat Negative- symptom

- tightness of the chest
- pounding of the heart
- · not able to breathe deeply · rapid heartbeat
- - stomach or abdominal cramps nausea
- · dizziness
- headache
- fatigue
- · muscular pain

1 – 9 intensity ratings per item

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## Pictorial cues (IAPS)



## Fibro and CFS (N=90)



# Symptom Trigger Effect (diff negative – neutral pics)

## Somatovisceral illusions



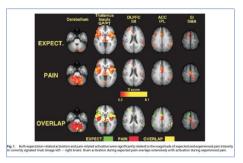


"Activating a 'mental representation' of an impending sensory event can significantly shape neural processes that underlie the actual sensory experience"

- Brain areas and neurotransmitters
- Peripheral (psycho-)physiology

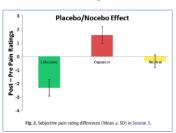
The subjective experience of pain: Where expectations become reality
Tetsuo Koyama\*, John G. McHaffle\*, Paul J. Laurienti\*, and Robert C. Coghill\*\*

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- Nocebo correlated with changes in the thalamus, insula, prefrontal cortex, anterior cingulate cortex, and other brain regions... (Koyama et al., 2005)
- Deactivation of the dopaminergic and opioidergic systems...(coloca 2012)
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# Heat pain



- · Same heat stimulus
- Administration of "sham" Lidocaine and Capsaicin

reeman et al., 2015

## **Heat pain**

## Nocebo effect

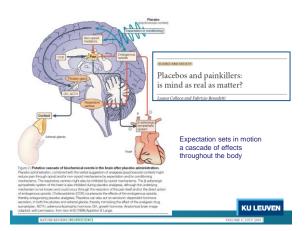
 significant fMRI signal changes in the insula, orbitofrontal cortex, and periaqueductal gray

### Placebo effect

significant fMRI signal changes in the striatum.

Positive and negative expectancies engage **different brain networks** to modulate our pain experiences caused by the same stimuli





## Nocebo effect sizes - pain

• moderate to large g= 0.62 to 1.03 (Hedges' g)

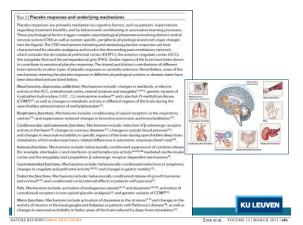
highly variable g=0.43 to 4.05similar to placebo d=0.81

verbal suggestions smaller than verbal PLUS conditioning

 $_{\circ}$  Verbal alone g = 0.64 to 0.87

Verbal PLUS g = 0.76 to 1.17



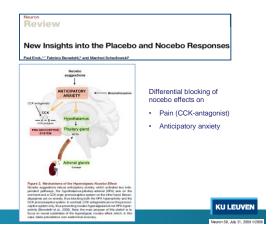


# Direct Evidence for Spinal Cord Involvement in Placebo Analgesia

Falk Eippert, 1x Jürgen Finsterbusch, 1 Ulrike Bingel, 2 Christian Büchel 1

... direct evidence that psychological factors can influence nociceptive processing at the earliest stage of the central nervous system, namely the dorsal horn of the spinal cord.



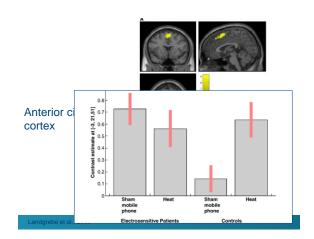


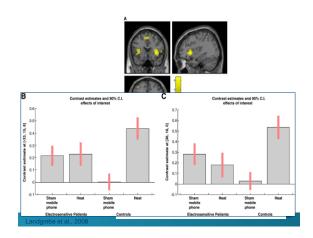
# Electrosensitivity and sham radiation

- Subjects
- Patients with electrosensitivity
- healthy controls
- Exposure
- heat
- sham radiation from mobile phones



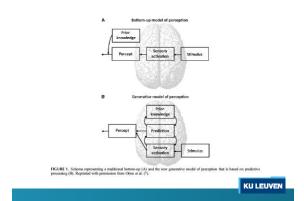
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# **Explaning placebo?**

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# We see things that are not there We don't see things that are there

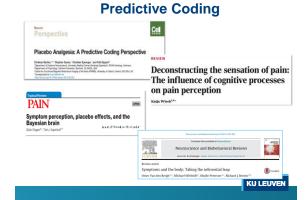
## Meaningful perception

Pattern detection - categorization



- · Complex inferential process
- Automatic/unconscious
- · Compelling percept of reality
- One cannot not see a chair

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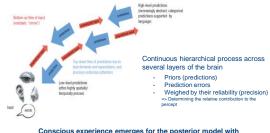


# **Predictive Coding**

- The brain has no direct access to the distal world it only has its own neural activity to make sense of
- A major task is pattern detection in its own neural activity
- To make a causal model of the (external and internal) world
- By "informed guessing" 
  o predictions using information
- · Criterion is adaptiveness/usefulness, not accuracy
  - An accurate model is mostly adaptive,
  - but bias can be more adaptive than accuracy (Lynn & Barrett, 2014) !!

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## Making a causal (posterior) model



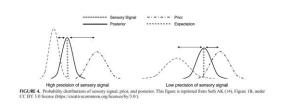
Conscious experience emerges for the posterior model with the lowest overall prediction error

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# **Rubber Hand Illusion**



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## **Lorimer Moseley**



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## Luana Collaca



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### REVIEW

Deconstructing the sensation of pain: The influence of cognitive processes on pain perception

Katja Wiech<sup>1,1</sup>

"The concept of pain as an actively constructed experience...has far-reaching implications for pain treatment and prevention."

Wiech, 2016, Science, 6312, p.587

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## **Critical questions**

- How could information be designed to optimally guide expectations for maximum treatment outcome?
- How could aberrant information processing be addressed using the framework of predictive coding?
- Future research should explore the translation of research on the inferential process underlying the perception of pain into clinical practice...
  - How can processes leading interoceptive illusions be modified to make them therapeutically useful?

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## **Breathlessness and Pain**

## • Pain

- o Refers to tissue damage
- Most adaptive response is behavioral escape/avoidance

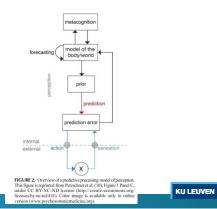
## Dyspnea

- o refers to impending death => panicogenic !!
- Most adaptive response is gasping
  - · a breathing response
- Plus behavioral escape/avoidance

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## **Breathlessness and Pain**

- Fear of pain does not create pain
  - **1**
- Fear of dyspnea may create dyspnea!!
  - Mismatch ventilatory drive actual ventilation
  - Respiratory muscles work harder
     Reduction of PCO<sub>2</sub>
    - => Vicious circles



## Conscious experience of a symptom

## ... unrelated to physiological dysfunction

- When the posterior model of the bodily state is completely determined by strong priors
- Symptoms experienced as true, real
  - Use the same machinery as in "objectifiable" symptoms





# **Treatment implications?**

- · Treating disability
  - o Avoidance behavior, catastrophizing..
  - o Modest treatment effects
- Treating pain perception/symptom perception ??
- Treating both.. ?

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## Fear ~ Attention

- a. Body Scanning
- b. Selective Attention
- c. Difficulty disengaging

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# Fear => Safety-seeking behaviors





- "A strategy intended to minimize or prevent a feared catastrophe"
  - →Total avoidance
  - →Escape
  - → Subtle within-situation avoidance behaviors

Tang et al, BRAT, 2007

## Fear and catastrophizing

~ physical performance and disability



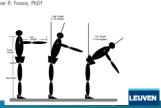
# Safety-seeking behaviors

	Description of the strategy	Rationale for the strategy		
1	"Lifting and loading the bag cautiously with back kept straight"	"To prevent pain and sudden jolt. Lifting could have put me out of circulation and my back would have seized up."		
2	"Standing with weight on one side"	"I can't stand still with both feet on the floor otherwise pain would have increased and I'd be in agony."		
3	"Holding and pushing my back to the 'good' side"	"So that no weight will be on my 'bad' side. This is to avoid something drastic from happening I'll panic. I'll die."		
4	"Constantly rocking. Shifting weight between my legs"	"To keep muscles in back moving otherwise tension will build up in my neck leading to severe headache."		
		RANU 2 MOVE		

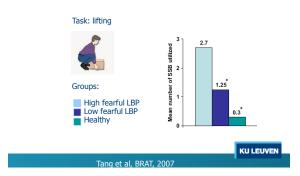
# Safety-seeking behaviors ~ poor behavioral performance

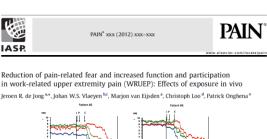
Pain-Related Fear Is Associated With Avoidance of Spinal Motion During Recovery From Low Back Pain

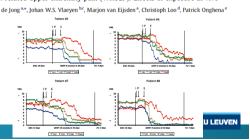
James S. Thomas, PhD,\* and Christopher R. France, PhD†

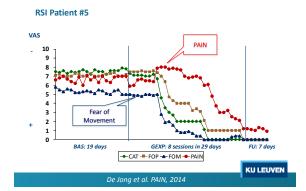


## Safety-seeking behaviors









# Complex Regional Pain syndrome





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Reduction of pain-related fear in complex regional pain syndrome type I: The application of graded exposure in vivo

Jeroen R. de Jong<sup>a,b,c,\*</sup>, Johan W.S. Vlaeyen<sup>b,d</sup>, Patrick Onghena<sup>e</sup>, Corine Cuypers<sup>f</sup>, Marlies den Hollander<sup>g</sup>, Joop Ruijgrok<sup>a</sup>



De Jong et al Pain, 2007

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## The health care provider?

"Patients' attitudes and beliefs (and thereby patients disability levels) may be derived from the projected attitudes and beliefs of health care providers"

(Rainville et al., Clin J Pain, 1995)

# Pain Attitudes and Beliefs Scale for HC providers (Ostelo

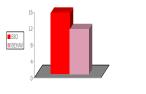
Sample item: "People would not have much back pain if there weren't something wrong with the back"

Dimensions: Biomechanical vs. Behavioral orientation

(Houben et al., EJP, 2005)

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## Health care providers attitudes







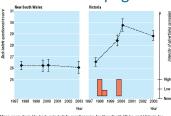
Back Pain patient vignette

Harmfulness of daily activities

Recommendation against work resumption

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Media Campagne



Mean score from the back pain beliefs questionnaire for New South Wales and Victoria for survey in August 1997, August 1999, February 2000, and December 2002 after media campaign ending in 1999. Error bars show 95% confidence interval. Bar chart shows media

Combined at al. (British Madical Jaures 2004)

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# Interoceptive exposure



- · Reduces anxiety for bodily sensations
- Increases sensory-perceptual details of somatic experiences

