

# *Diagnosis of Neuropathic Pain*

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FRANCE

BPS, June 7, Brussels

## *Definition*

*Pain initiated or caused by a  
primary lesion or **dysfunction** in  
the nervous system*

*Bennett GJ: Neuropathic Pain: A Crisis of definition. Anesth Analg (2003)*

*Backonja MM: Defining Neuropathic pain. Anesth Analg (2003)*

*Hansson P: Difficulties in stratifying neuropathic pain by mechanisms.  
Eur J Pain (2003)*

## New Definition

*Pain initiated or caused by a primary lesion or ~~dysfunction~~ in the nervous system (IASP, 1994)*



*Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system (Treede et al., Neurology 2008)*

## Large variety of etiologies



Shingles



Syringomyelia



Radiculopathy



Trauma



Surgery

## *Clinical features of NeP*

### Positive symptoms

- Painful symptoms
- Non painful symptoms:  
Paresthesia  
Dysesthesia

### Negative symptoms

- Neurological Deficits :  
  
SENSORY ++  
Motor  
Cognitive...



*NO DIAGNOSTIC CRITERIA*

## *Diagnostic Strategies for NeP*



Diagnosis based on  
Symptoms  
(pain descriptors)



Diagnosis based on  
Signs  
(lesion/topography)

## *New Classification of neuropathic pain*

*Definite NP*  
*Probable NP*  
*Possible*  
*Unlikely*



*Level of certainty about the presence of a nerve lesion*

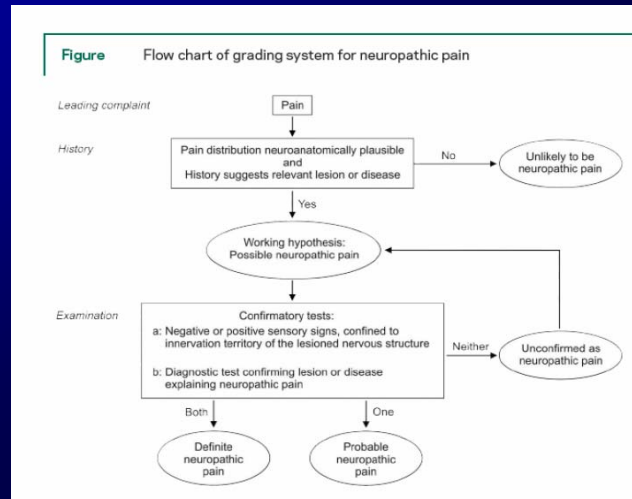
*Treede et al. 2008*

**Table** Grading system for neuropathic pain

Criteria to be evaluated for each patient

1. Pain with a distinct neuroanatomically plausible distribution\*
2. A history suggestive of a relevant lesion or disease affecting the peripheral or central somatosensory system\*
3. Demonstration of the distinct neuroanatomically plausible distribution by at least one confirmatory test†
4. Demonstration of the relevant lesion or disease by at least one confirmatory test§

*(Treede et al., Neurology 2008)*



*(Treede et al., Neurology 2008)*

## *Limitations of the new definition and criteria*

*The new criteria are too "neurological"*



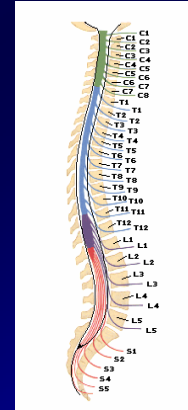
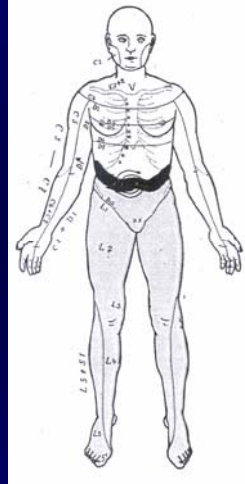
*Poorly applicable in daily practice, but interest for clinical research*

## Limitations of the new definition and criteria

*Symptoms are not taken into account*



*Problems in patients with nociceptive pain in a deficit area*

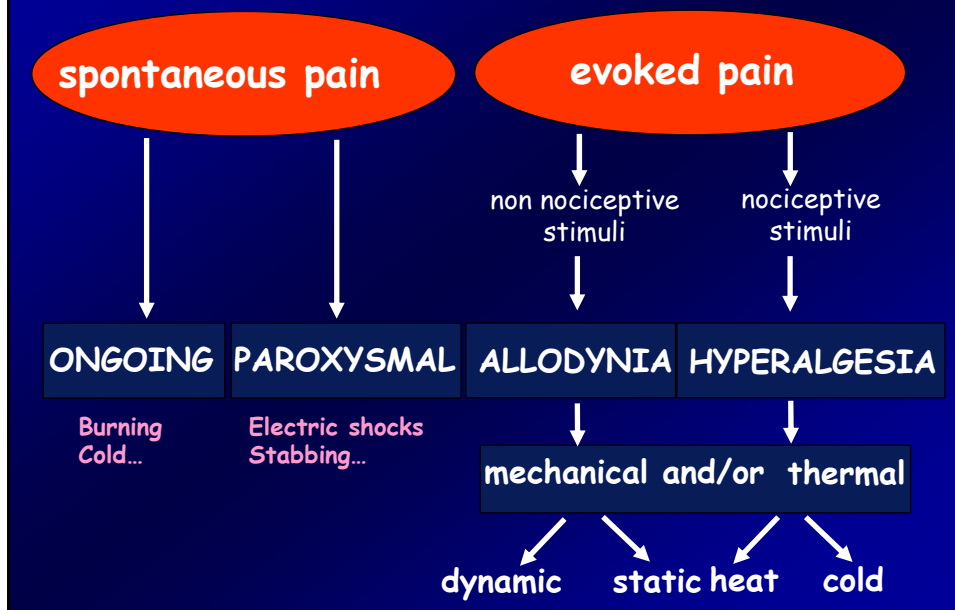


## Diagnostic Strategies for NeP

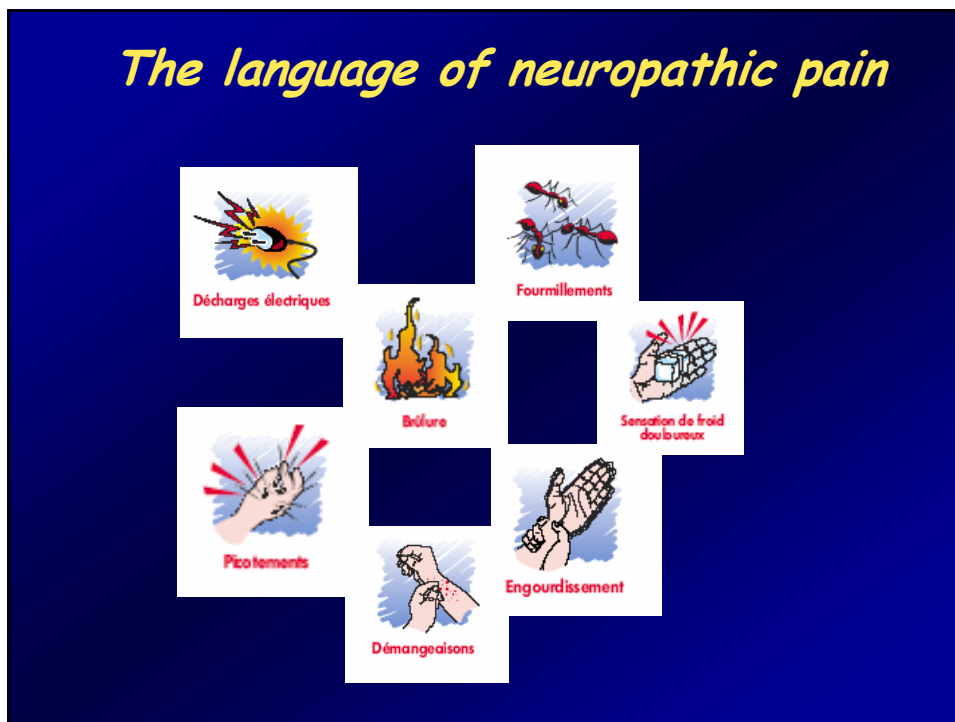
Diagnosis based on Symptoms  
(pain descriptors)

Diagnosis based on Signs  
(lesion/topography)

## Multiple symptoms



## The language of neuropathic pain



*Diagnosis based on symptoms?*



*Identification of discriminant  
pain descriptors*



*Development of diagnostic tools*

## New Neuropathic pain Questionnaires

### Screening/diagnosis

LANSS Pain Scale  
Bennett, Pain, 2001

Neuropathic Pain  
Questionnaire (NPQ)  
Krause & Backonja, CIJ Pain, 2003

DN4  
Bouhassira et al., Pain 2005

ID Pain  
(Portenoy, 2006)

Pain detect  
(Freynhagen et al., 2006)

### Assessment/Evaluation

Neuropathic Pain Scale  
(NPS)  
Galer & Jensen, Neurology, 1997

Neuropathic Pain  
Symptom Inventory  
(NPSI)  
Bouhassira et al., Pain 2004



# *Clinical comparison of neuropathic and non-neuropathic pains*

*(French Neuropathic Pain Network)*

160 patients: 89 «pure» neuropathic pains  
71 non-neuropathic pains

- 1) Comparison of pain descriptors (9 items)
- 2) Comparison of clinical examination (8 items)



**Selection of discriminating items**

*Bouhassira et al. Pain (2005)*

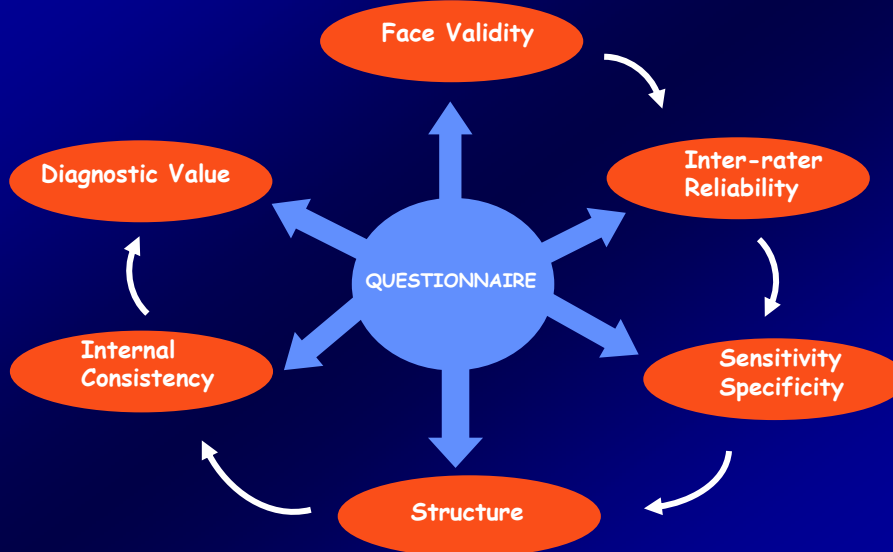
## *Comparison of descriptors frequency*

	Neuropathic pain (%)	Non-neuropathic pain (%)
« burning »	68 ***	30
« squeezing »	49	38
« cold pain »	26 **	10
« shooting »	65 ***	17
« lancinating »	76	65
« tingling »	60 ***	16
« pins and needles »	66 ***	17
« itching »	29 ***	6
« numbness »	66 ***	30

### Comparison of clinical examination

	Neuropathic pain (%)	Non-neuropathic pain (%)
« heat hypoesthesia »	70 ***	6
« cold-hypoesthesia »	67 ***	4
« touch hypoesthesia »	65 ***	6
« pressure hypoesthesia »	70 ***	10
« heat allodynia »	21 ***	4
« cold allodynia »	28 ***	4
« brush allodynia »	42 ***	5
« pressure allodynia »	46	45

### Psychometric Properties of the Questionnaire





**Score = 4/10**

**Specificity: 90%**  
**Sensitivity: 83%**

**Bouhassira et al. Pain (2005)**

**Question 1: Does the pain has one or more of the following characteristics**

	YES	NO
Burning		
Painful Cold		
Electric shoks		

**Question 2: Is the pain associated with one or more of the following characteristics in the same area**

	YES	NO
Tingling		
Pins and Needles		
Numbness		
Itching		

**Question 3: Is the pain located in an area where the examination reveals of the following characteristics:**

	YES	NO
Touch hypoesthesia		
Pincking hypoesthesia		

**Question 4: In the painful area, can the pain be caused or increased by:**

	YES	NO
Brushing		

	LANSS	NPQ	DN4	Pain-Detect	ID Pain
<b>Symptoms</b>					
Pricking, tingling, pins and needles	*	*	*	*	*
Electric shocks, shooting	*	*	*	*	*
Hot or burning	*	*	*	*	*
Numbness		*	*	*	*
Pain evoked by touching	*	*		*	*
Painful cold or freezing pain		*	*		
Pain evoked by heat or cold				*	
Pain evoked by changes in weather		*			
Pain limited to joints#					*
Autonomic changes	*				
<b>Clinical Examination</b>					
Brush allodynia	*	-	*	-	-
Raised soft touch threshold		-		-	-
Raised pin prick threshold	*	-	*	-	-

**Bennett, Attal, Backonja, Baron, Bouhassira, Freynhagen, Scholtz, Tölle, Wittchen, Jensen, Pain, 2007**

*DN4 could be used in multicenter  
International studies*

*translations already available:*

English	Thai	Norwegian
Spanish	Greek	Dutch
Italian	Portugese	Slovene...
Hungarian	Russian	
Arabic	Korean	



The language of neuropathic pain is universal ??

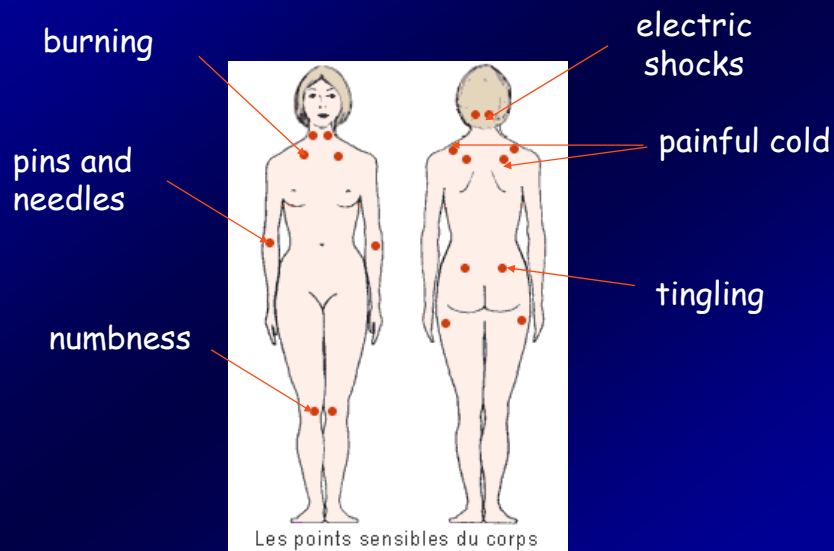
*Limitations of the diagnostic  
questionnaires*

- 1) Sensitivity-Specificity
- 2) Assessment of pain at one location
- 3) No information regarding the etiology/mechanisms



Questionnaires should not replace the clinical  
examination and etiological diagnostic tests  
(Bennett et al., Pain 2007; Hansson and Haanpää; EJP, 2007)

### *Screening tools should not be used in fibromyalgia*



### *Applications of NeP screening tools*

- 1) Daily clinical practice
- 2) Education/communication
- 3) Selection of patients in Clinical trials
- 4) Epidemiological Studies

## Applications

### 3) Communication, Education (doctors, patients)

The image displays three posters illustrating neuropathic pain symptoms. Each poster features a person with a specific, exaggerated physical manifestation of pain and includes a quote and a question in French.

- Poster 1 (Left):** A woman has a teapot on her head and another on her stomach. Quote: "J'ai la sensation horrible d'avoir les côtes marquées au fer rouge." Question: "EST-CE UNE DOULEUR NEUROPATHIQUE?"
- Poster 2 (Middle):** A woman has a large, spiky hairbrush on her head. Quote: "J'ai la sensation d'être une ligne à haute tension par temps d'orage." Question: "EST-CE UNE DOULEUR NEUROPATHIQUE?"
- Poster 3 (Right):** A man has a large, hairy arm on his left side. Quote: "J'ai la désagréable sensation d'avoir sous la peau une armée d'insectes." Question: "EST-CE UNE DOULEUR NEUROPATHIQUE?"

Each poster includes a small logo with the letters 'DN4' and a small text block at the bottom.

## Epidemiology

First epidemiological surveys in 3 UK cities using the S-LANSS (Torance et al., J Pain, 2006)

Response rate: 52.4%

Prevalence of chronic pain : 48 %



Prevalence of Pain of Predominantly Neuropathic Origin:  
8 %

## Epidemiology: DN4-Interview



**Score = 3/7**

**Specificity: 81%**

**Sensitivity: 78%**

*Bouhassira et al. Pain (2005)*

*Question 1: Does your pain has one or more of the following characteristics*

	YES	NO
Burning		
Painful Cold		
Electric shocks		

*Question 2: Is the pain associated with one or more of the following symptoms in the same area*

	YES	NO
Tingling		
Pins and Needles		
Numbness		
Itching		

## Study of the Prevalence of Neuropathic Pain (STOPNEP)

Representative sample of more than 30 000 subjects

Return rate : **81%**

Prevalence of chronic pain:

**31%** (for pain of any intensity)

**20%** (for pain of at least moderate intensity)

Chronic pain with Neuropathic Characteristics:

**6.9%** (for pain of any intensity)

**5.1%** (for pain of at least moderate intensity)

*Bouhassira et al., Pain 2008*

*Prevalence of painful polyneuropathy with or in patients with diabetes type 1 or 2*

Cross-sectional study in 40 centers in Belgium  
1111 patients included (70 % type 2)

Identification of neuropathy: **Neuropen test**

DPN with neuropathic characteristics : **DN4**



Neuropen test+ **AND** DN4 + = PDPN

VanAcker et al., submitted

## NEUROPEN<sup>®</sup>



### Tactile Sensation

Monofilament (10g)



Abnormal < 8/10

Sensitivity: 80-90%  
Specificity: 60-80%


### Pain Sensation

Neurotip (40 g)



Abnormal: no pain





### Questionnaire DN4

Répondre aux 4 questions ci-dessous en cochant une seule case pour chaque item.

**INTERROGATOIRE DU PATIENT**

**Question 1 :** La douleur présente-t-elle une ou plusieurs des caractéristiques suivantes ?

	OUI	NON
1 - Brûlure	<input type="checkbox"/>	<input type="checkbox"/>
2 - Sensation de froid/douleurs	<input type="checkbox"/>	<input type="checkbox"/>
3 - Décharges électriques	<input type="checkbox"/>	<input type="checkbox"/>

**Question 2 :** La douleur est-elle associée dans la même région à un ou plusieurs des symptômes suivants ?

	OUI	NON
4 - Fourmillements	<input type="checkbox"/>	<input type="checkbox"/>
5 - Picotements	<input type="checkbox"/>	<input type="checkbox"/>
6 - Engourdissement	<input type="checkbox"/>	<input type="checkbox"/>
7 - Démangeaisons	<input type="checkbox"/>	<input type="checkbox"/>

**EXAMEN DU PATIENT**


**Question 3 :** La douleur est-elle localisée dans un territoire ou l'examen met en évidence ?

	OUI	NON
8 - Hypoesthésie au tact	<input type="checkbox"/>	<input type="checkbox"/>
9 - Hypoesthésie à la pique	<input type="checkbox"/>	<input type="checkbox"/>

**Question 4 :** La douleur est-elle provoquée ou aggravée par :

	OUI	NON
10 - Le toucher	<input type="checkbox"/>	<input type="checkbox"/>

Score du Patient :  /10



### DN4 vragenlijst

Antwoord op de 4 onderstaande vragen door voor elk item één vakje aan te vinken.

**ONDERVRAGING VAN DE PATIËNT**

**Vraag 1 :** Vertoont de pijn één of meerdere van de volgende kenmerken?

	JA	NEEN
1 - Brandend gevoel	<input type="checkbox"/>	<input type="checkbox"/>
2 - Pijnlijk koudegevoel	<input type="checkbox"/>	<input type="checkbox"/>
3 - Elektrische schokken	<input type="checkbox"/>	<input type="checkbox"/>

**Vraag 2 :** Is de pijn in hetzelfde gebied geassocieerd met één of meerdere van de volgende symptomen?

	JA	NEEN
4 - Kriebelingen	<input type="checkbox"/>	<input type="checkbox"/>
5 - Tintelingen	<input type="checkbox"/>	<input type="checkbox"/>
6 - Gevoelloosheid	<input type="checkbox"/>	<input type="checkbox"/>
7 - Jeuk	<input type="checkbox"/>	<input type="checkbox"/>

**ONDERZOEK VAN DE PATIËNT**

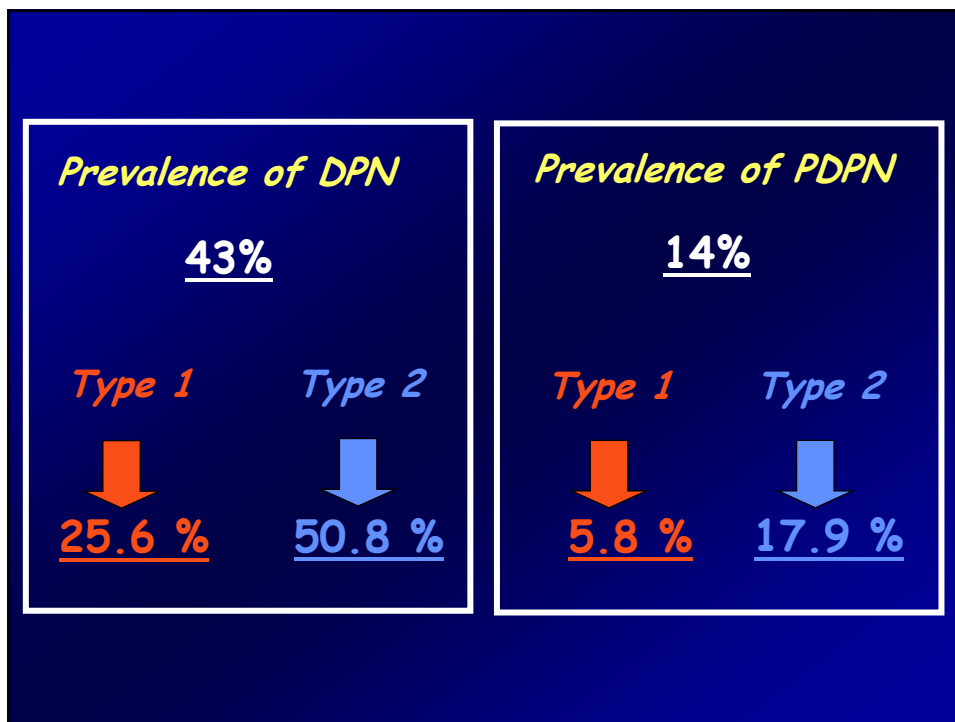
**Vraag 3 :** Is de pijn gelocaliseerd in een bepaald gebied of wijst het onderzoek op :

	JA	NEEN
8 - Hypo-esthesie bij aanraking	<input type="checkbox"/>	<input type="checkbox"/>
9 - Hypo-esthesie bij een prik	<input type="checkbox"/>	<input type="checkbox"/>

**Vraag 4 :** Wordt de pijn veroorzaakt of versterkt door :

	JA	NEEN
10 - Wrijven	<input type="checkbox"/>	<input type="checkbox"/>

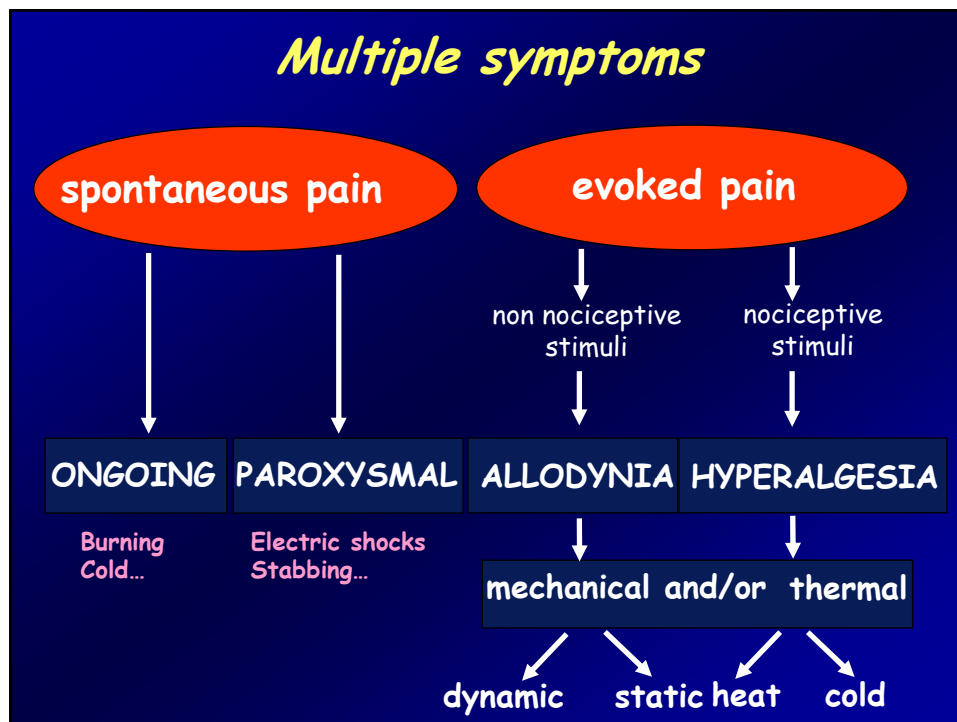
Score van de patiënt:  /10



## *Measurement of neuropathic pain*

### *Assessment: beyond the VAS*





## **Neuropathic Pain Symptom Inventory (NPSI)**

*Bouhassira et al., Pain, 2004*

### Main Objective :

Evaluation of the different components of NP:

- Spontaneous ongoing pains
- Paroxysmal pains
- Evoked pains
- Paresthesia/Dysesthesia

## Neuropathic Pain Symptom Inventory (NPSI)

Superficial spontaneous pain  
Burning

Deep spontaneous pain  
Squeezing, Pressure

Paroxysmal pain  
Electric Shocks  
Stabbing

Evoked pain  
Brush-evoked  
Cold-evoked  
Pressure-evoked

Paresthesia/dysesthesia  
Tingling  
Pins and Needles

*Bouhassira et al., Pain, 2004*

## Neuropathic Pain Symptom Inventory (NPSI)

### 10 sensory items quantified with NRS

Q1/. Does your pain feel like burning ?

No burning	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Worst burning imaginable
------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

Q2/. Does your pain feel like squeezing ?

No squeezing	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Worst squeezing imaginable
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Q3/. Does your pain feel like pressure ?

No pressure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Worst pressure imaginable
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### 2 items related to the temporal aspect of pain

Q4/. **During the past 24 hours**, your spontaneous pain has been present :

Select the response that best describes your case

- |                        |                          |
|------------------------|--------------------------|
| Permanently            | <input type="checkbox"/> |
| Between 8 and 12 hours | <input type="checkbox"/> |
| Between 4 and 7 hours  | <input type="checkbox"/> |
| Between 1 and 3 hours  | <input type="checkbox"/> |
| Less than 1 hour       | <input type="checkbox"/> |

*Bouhassira et al., Pain, 2004*

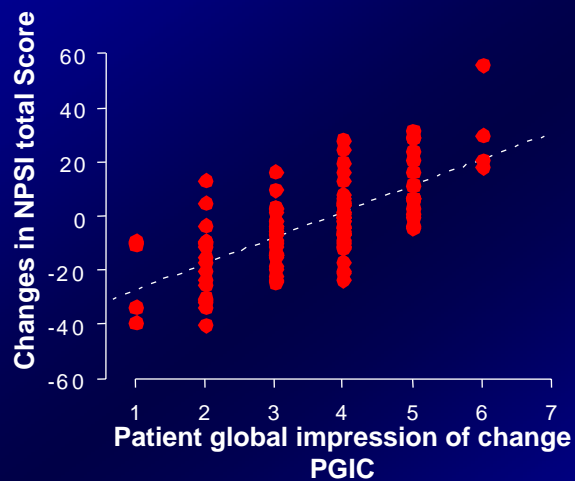
## *NPSI scoring*

Each sensory descriptor is quantified (0-10) NRS

Total score = sum of the 10 items

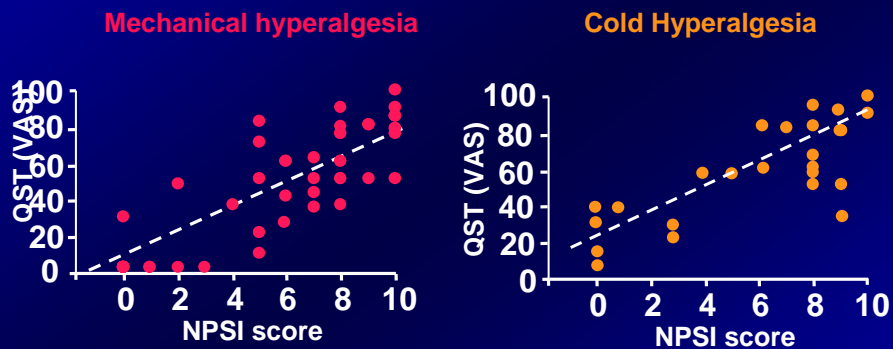
- 5 subscores =
- Burning (superficial pain)
  - Pressure/squeezing (deep pain)
  - Paroxysmal pain
  - Paresthesia/dysesthesia
  - Evoked Pains

## *NPSI Sensitivity to Change*



*Bouhassira et al., Pain, 2004*

## Comparison between NPSI and QST



*Attal et al (submitted)*

## Neuropathic Pain Symptom Inventory (NPSI)

- *The NPSI can be used in large multicenter studies*
- *The NPSI gives information regarding evoked pains similar to QST.*
- *The NPSI should be more sensitive and specific than a simple VAS.*
- *Such an approach should help to identify subgroups of «responders» in pharmacological studies.*

## **Neuropathic Pain Symptom Inventory (NPSI)**

*translations already available:*

English	Greek	Chinese	Tagalog
Spanish	Portugese	Japanese	Hindi
Italian	Russian	Korean	Indonesian
German	Latvian	Thai	Malay
Hungarian	Estonian	Norwegian	Kannada
Afrikaans	Polish	Finish	Punjabi
Croatian	Dutch	Danish	Tamil
Czech	Romanian	Swedish	Urdu



The NPSI is currently being used in more than  
15 international multicenter studies

## **CONCLUSIONS**

- *Identification of neuropathic pain is based only on clinical examination (i.e. no need of lab test).*
- *Diagnosis of the aetiology may necessitate imaging, electrophysiology...*
- *Questionnaires are of interest both for screening and quantification.*
- *Neuropathic pain are frequent in the general population.*