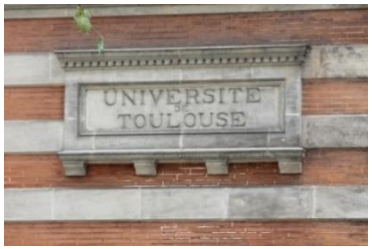
Conduite à tenir devant une douleur chronique chez un patient Parkinsonien

Christine Brefel-Courbon

(Service de Pharmacologie et Service de Neurologie, Inserm U 1214, CHU Toulouse)



Mr D, 62 ans

ATCD :
Maladie de Parkinson depuis 2014 ayant débuté par une akinésie de l'hemicorps gauche.
Stade des fluctuations motrices depuis 2018 (akinésies de fin de dose)

A l'interrogatoire : *« si il n'y avait pas les douleurs, ca irait bien… »*
- Lombalgies +++
- Douleur au niveau du MIG à type de fourmillements, sensation d'étau, douleur profonde

Traitement :
Ropinirole LP 14 mg à 7 H
Stalevo 125 : 1 cp à 7 H, 11h, 15h, 19h

La douleur est un symptôme fréquent de la maladie de Parkinson

Plusieurs études épidémiologiques rapportent que 60% à 80% des malades parkinsoniens se plaignent de douleurs chroniques
(Defazio et al, 2008, Negre-Pages et al, 2008, Beiske et al, 2009)

La douleur est plus fréquente dans la maladie de Parkinson/population générale *(Brefel-Courbon et al, 2009)*

Mr D, 62 ans

A l'interrogatoire :

- **Lombalgie : apparait en charge et lorsqu'il marche longtemps, présente depuis l'âge de 48 ans mais elle s'aggrave depuis le début de la maladie de Parkinson**

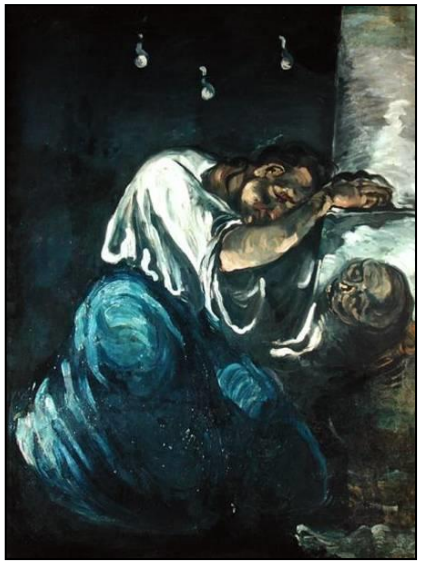
- **Douleur au niveau du MIG (fourmillements, sensation d'étau, douleur profonde) : est apparue 1 ou 2 ans après le début de la maladie. Elle est quasi permanente avec qq paroxysmes (surtout quand il est ralenti)**

Identifier le type de douleur

La douleur est elle liée à la maladie de Parkinson ?

Quel type de douleur?

Quelle physiopathologie ?



Douleur : spécifique /non spécifique

Douleur Spécifique ?

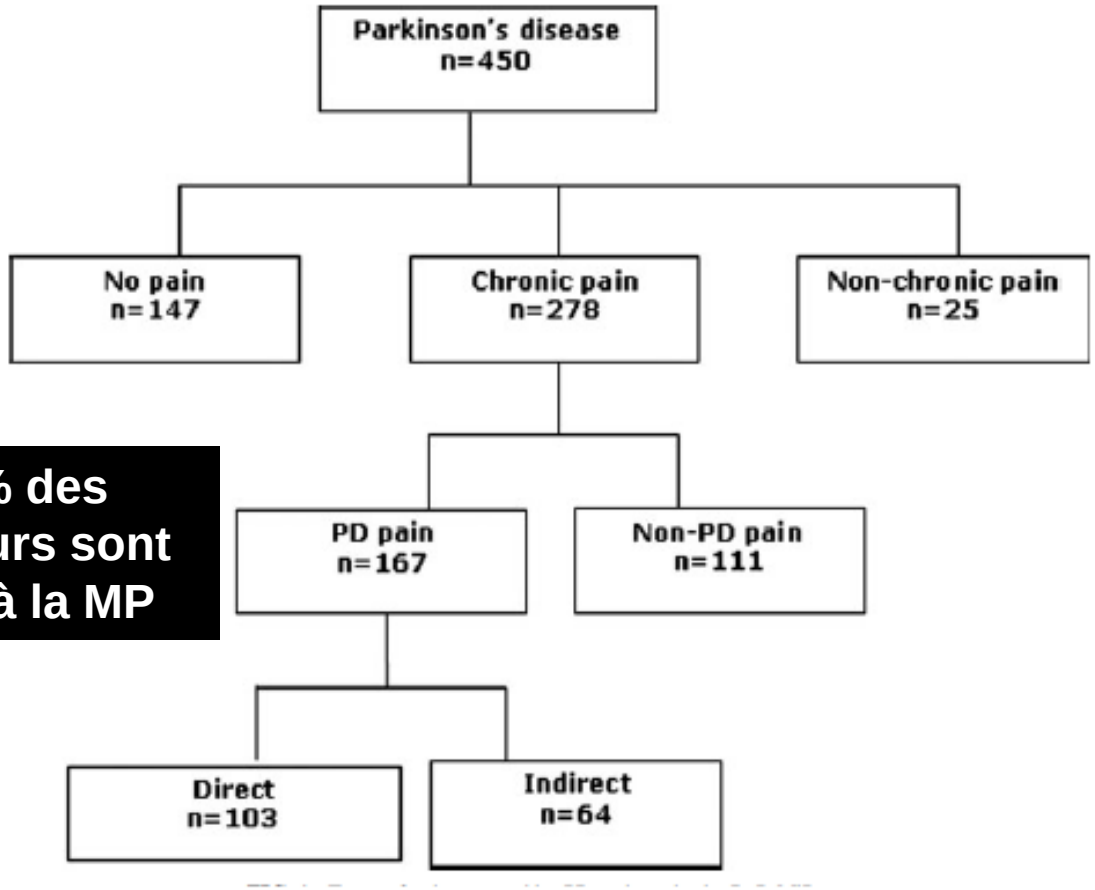
La douleur est elle directement liée à la maladie de Parkinson :?

- **Lien chronologique avec la maladie de Parkinson**
- **Lien topographique (Localisée à l'hemicorps le plus atteint)**
- **S'améliore partiellement avec les medicaments DA**
- **Pas d'étiologie évidente**
- **Le patient établit un lien avec la maladie**

Movement Disorders
Vol. 23, No. 10, 2008, pp. 1361–1369

Chronic Pain in Parkinson's Disease: The Cross-Sectional French DoPaMiP Survey

Negre-pages et al



65% des douleurs sont liées à la MP

Classifier le type de douleur

DIFFERENTS TYPES DE DOULEUR DANS MPI

- Musculoskeletal pain
  - Pain due to parkinsonian rigidity
  - Pain due to rheumatologic disease or skeletal deformity
- Neuropathic-radicular pain
  - Pain due to root lesion, focal or peripheral neuropathy
- Dystonic pain
  - Off-period painful dystonia (includes early morning dystonia)
  - Beginning-of-dose dystonia
  - Peak-dose dystonia
  - End-of-dose dystonia
- Central pain
  - Off-period pain (includes early morning pain)
  - Beginning-of-dose pain
  - Peak-dose pain
  - End-of-dose pain
- Akathisia
  - Off-period ("parkinsonian") akathisia
  - Drug-induced akathisia

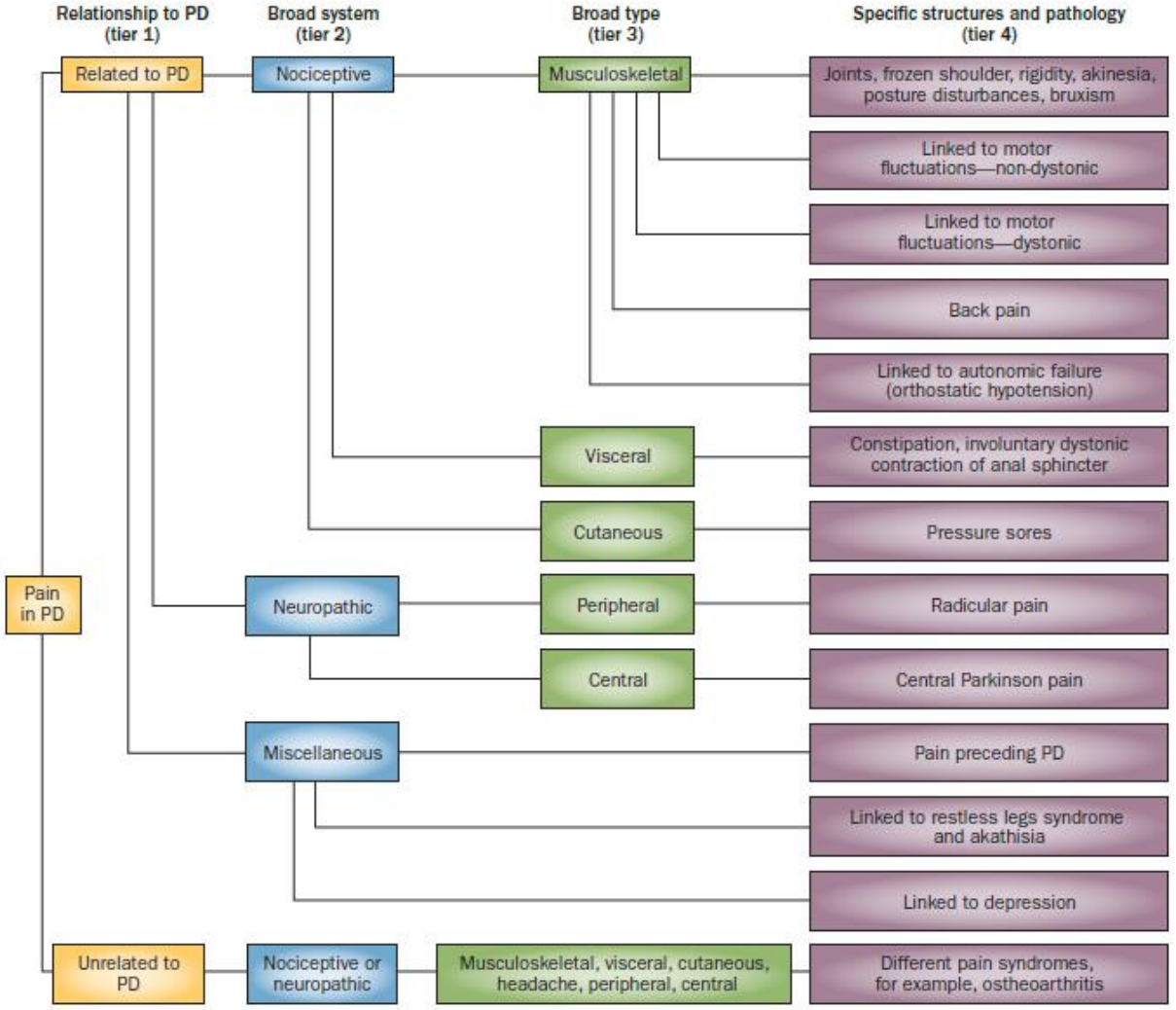
Pain category	Clinical description
Musculoskeletal	Aching, cramping, arthralgic, myalgic sensations Associated findings may include muscle tenderness, arthritic changes, skeletal deformity, limited joint mobility May be exacerbated by parkinsonian rigidity, stiffness, immobility May improve with levodopa May fluctuate with medication dosing May improve with exercise
Radicular-neuropathic	Pain in the territory of a root or nerve, or in a neuropathic distribution Associated with signs of nerve or root damage
Dystonic	Associated with dystonic movements and postures May fluctuate with medication dosing (see Table 3)
Central ("primary") pain	Burning, tingling, formication Relentless, bizarre quality Location not confined to root or nerve territory Not explained by rigidity or dystonia May fluctuate with medication effect
Akathisia	Subjective sense of restlessness or intolerance of remaining still Objective signs of restless behavior May improve with levodopa May fluctuate with medication effect

Ford et al, 1998

Nat Rev Neurol, 2012

Pains in Parkinson disease—many syndromes under one umbrella

Gunnar Wasner and Günther Deuschl



KING'S PD PAIN SCALE (KPPS) *Chaudhuri et al, 2015*

This scale is designed to define and accurately describe the different types and the pattern of pain that your patient may have experienced during the last month due to his/her Parkinson's disease or related medication.

Each symptom should be scored with respect to

Severity: 0 = None,
1 = Mild (symptoms present but causes little distress or disturbance to patient),
2 = Moderate (some distress or disturbance to patient),
3 = Severe (major source of distress or disturbance to patient).

Frequency 0 = Never
1 = Rarely (< 1/wk),
2 = Often (1/wk),
3 = Frequent (several times per week),
4 = Very Frequent (daily or all the time).

	Severity (0 – 3)	Frequency (0 – 4)	Frequency x Severity
Domain 1: Musculoskeletal Pain			
1. Does the patient experience pain around their joints? (including arthritic pain)	☐	☐	☐
Domain 1 TOTAL SCORE			☐
Domain 2: Chronic Pain			
2. Does the patient experience pain deep within the body? (A generalized constant, dull, aching pain – *central pain*)	☐	☐	☐
3. Does the patient experience pain related to an internal organ? (For example, pain around the liver, stomach or bowel – visceral pain)	☐	☐	☐
Domain 2 TOTAL SCORE			☐
Domain 3: Fluctuation-related Pain			
4. Does the patient experience dyskinetic pain? (pain related to abnormal involuntary movements)	☐	☐	☐
5. Does the patient experience "off" period dystonia in a specific region? (in the area of dystonia)	☐	☐	☐
6. Does the patient experience generalized "off" period pain? (pain in the whole body or areas distant to dystonia)	☐	☐	☐
Domain 3 TOTAL SCORE			☐

	Severity (0 – 3)	Frequency (0 – 4)	Frequency x Severity
Domain 4: Nocturnal Pain			
7. Does the patient experience pain related to jerking leg movements during the night (PLM) or an unpleasant burning sensation in the legs which improves with movement (RLS)	☐	☐	☐
8. Does the patient experience pain related to difficulty turning in bed at night?	☐	☐	☐
Domain 4 TOTAL SCORE			☐
Domain 5: Oro-Facial Pain			
9. Does the patient experience pain when chewing?	☐	☐	☐
10. Does the patient have pain due to grinding their teeth during the night?	☐	☐	☐
11. Does the patient have burning mouth syndrome?	☐	☐	☐
Domain 5 TOTAL SCORE			☐
Domain 6: Discolouration; Oedema/swelling			
12. Does the patient experience a burning pain in their limbs (often associated with swelling or dopaminergic treatment)	☐	☐	☐
13. Does the patients experience generalised lower abdominal pain?	☐	☐	☐
Domain 6 TOTAL SCORE			☐
Domain 7: Radicular Pain			
14. Does the patient experience a shooting pain/ pins and needles down the limbs?	☐	☐	☐
Domain 7 TOTAL SCORE			☐
TOTAL SCORE (all domains) (Somme des scores des 7 domaines)			☐

Comments:

Movement Disorders
CLINICAL PRACTICE
2016
MOVEMENT DISORDERS SOCIETY PAPER

Rating Scales for Pain in Parkinson's Disease: Critique and Recommendations

Santiago Perez-Lloret, MD, PhD,[1,] Daniel Ciampi de Andrade, MD, PhD,[2,3,4] Kelly E. Lyons, PhD,[5] Carmen Rodríguez-Blázquez, PhD,[6] Kallol R. Chaudhuri, MD, FRCP, DSc,[7,8] Guenther Deuschl, MD,[9] Girgio Cruccu, MD,[10] Cristina Sampaio, MD, PhD,[11] Christopher G. Goetz, MD,[12] Anette Schrag, MD,[13] Pablo Martinez-Martin, MD, PhD,[6] Glenn Stebbins, PhD,[12] the Members of the MDS Committee on Rating Scales Development*

TABLE 3 Recommendation for pain rating scales in PD

	Use in PD	Use by Multiple Investigators	Adequate Clinimetric Assessment	Validated in PD	Conclusion
Scales rating pain intensity					
BPI short form	X	X	X	—	Recommended with caution
King's PD Pain Scale	X	X	X	X	Recommended for pain intensity rating
McGill Pain Questionnaire long form	X	X	X	—	Recommended with caution
McGill Pain Questionnaire short form	X	X	X	—	Recommended with caution
NPSI	X	X	X	—	Recommended with caution
NRS	X	X	X	—	Recommended with caution
Pain-O-Meter	X	X	X	—	Recommended with caution
VAS	X	X	X	—	Recommended with caution
Scales for syndromic classification					
DN4	X	X	X	—	Recommended with caution
King's PD Pain Scale	X	X	—	—	Suggested for syndromic aspects
LANSS	X	X	—	—	Suggested
PainDETECT	X	X	—	—	Suggested

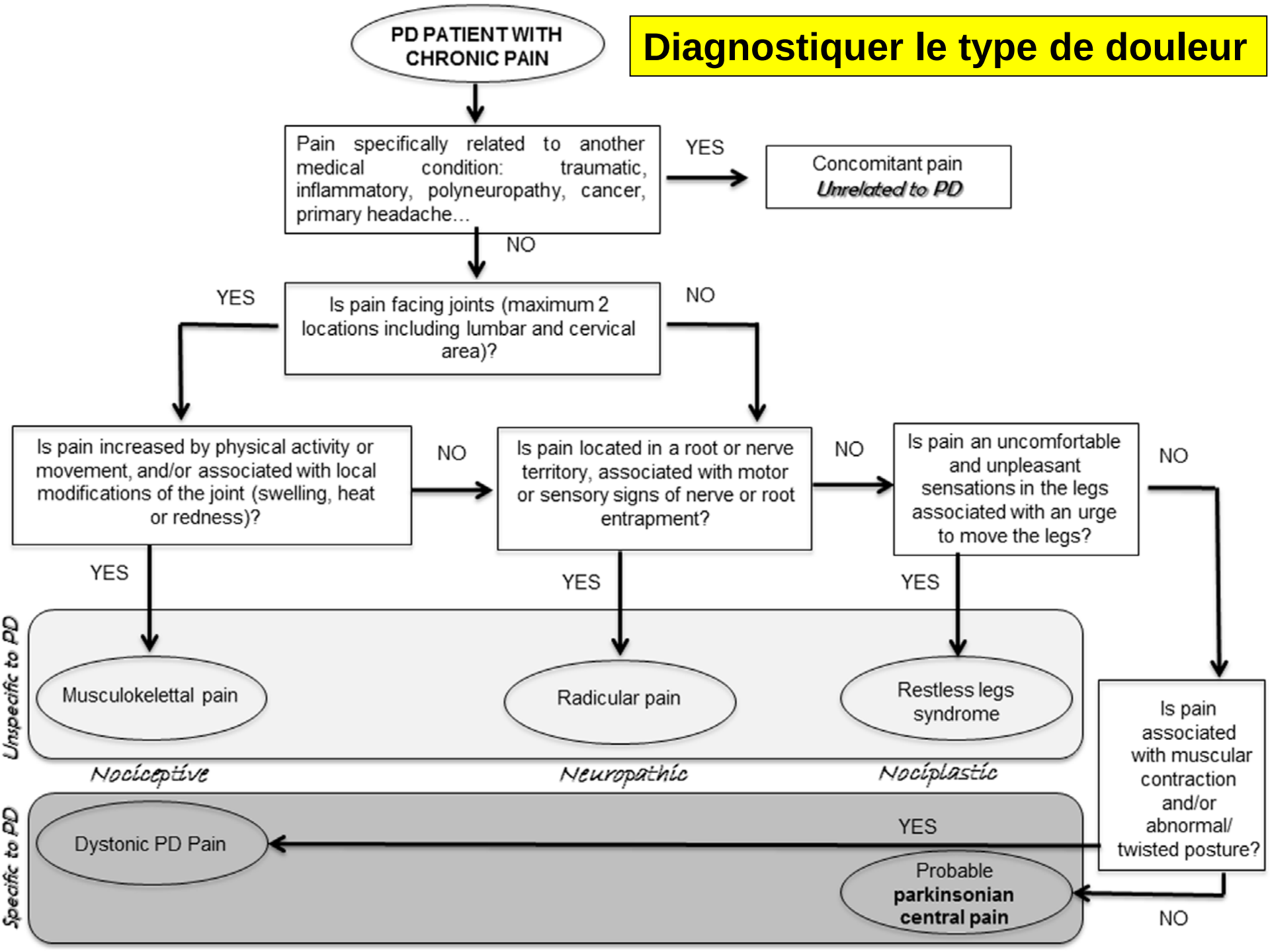
Différents types de douleur dans la maladie de Parkinson

A Marques, N Attal, D Bouhassira, X Moisset, N Cantagrel, O Rascol, F Durif, C Brefel-Courbon (Parkinsonism relat Disord 2019)

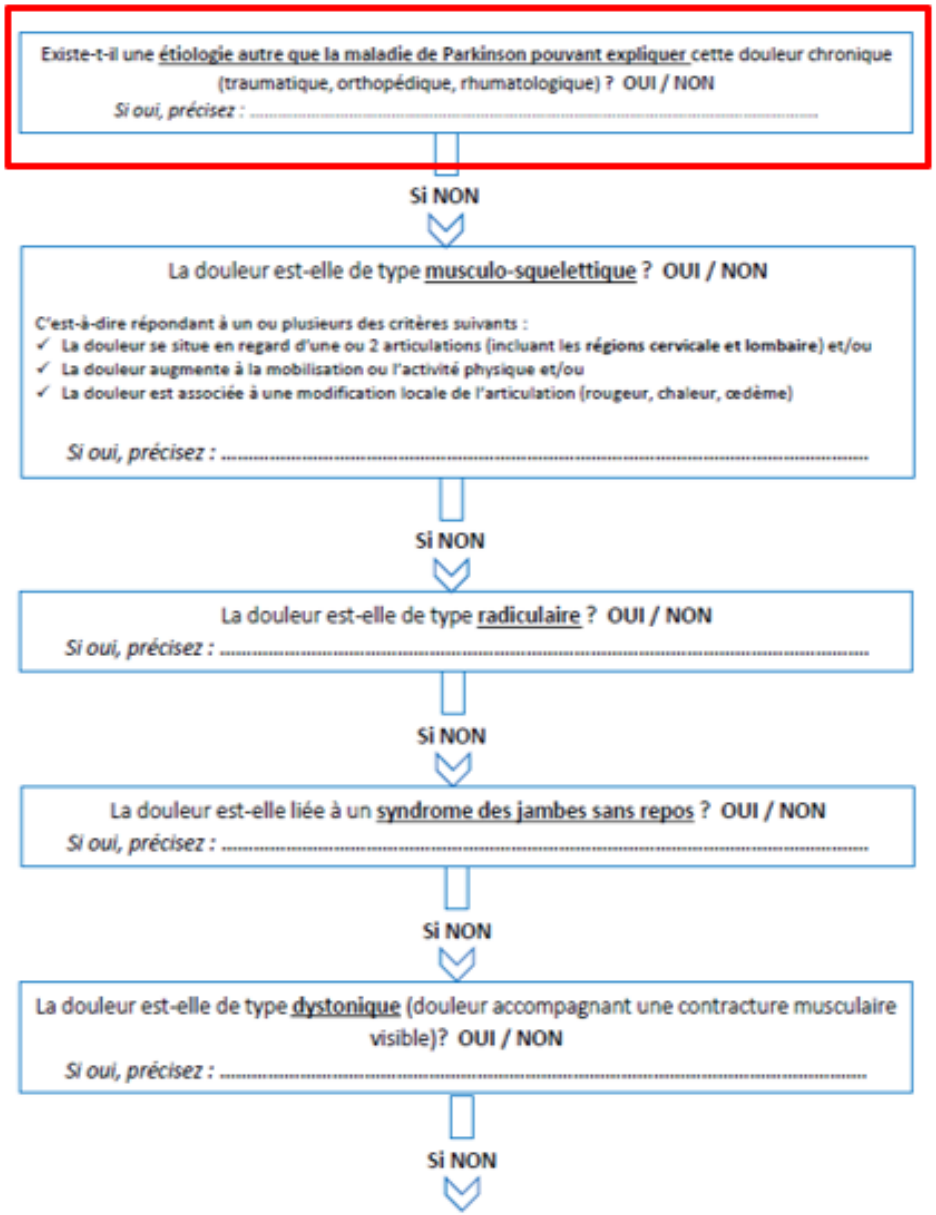
Chronic pain	Nociceptive	Neuropathic	Nociplastic
Unspecific to PD	Musculoskeletal pain	Radicular pain	Restless leg syndrome
Specific to PD	Dystonic pain	_	Central pain

- **La douleur non spécifique peut être aggravée par la maladie de Parkinson**
- **La douleur spécifique : lien chronologique et/ou topographique et pas d'autre cause évidente**

Diagnostiquer le type de douleur



Douleur centrale parkinsonienne : diagnostic d'élimination



Développement d'un auto-questionnaire de diagnostic de la douleur centrale Parkinsonienne (Etude 3 PDO)

Quel type de douleur ?

Mr D, 62 ans
A l'interrogatoire :

- **Lombalgie : apparait en charge et lorsqu'il marche longtemps, présente depuis l'âge de 48 ans mais elle s'aggrave depuis le début de la maladie de Parkinson**

- **Douleur au niveau du MIG (fourmillements, sensation d'étau, douleur profonde) : est apparue 1 ou 2 ans après le début de la maladie. Elle est quasi permanente avec qq paroxysmes (surtout quand il est ralenti)**

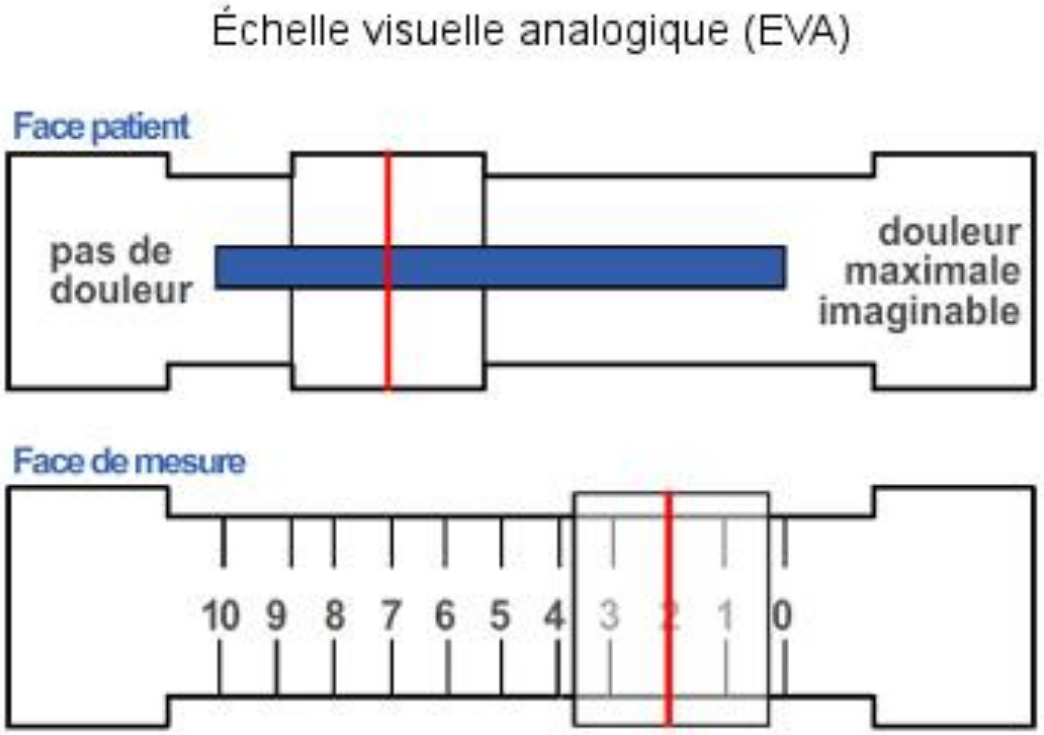
Diagnostic :

Douleur musculosquelettique (lombalgie)
Douleur centrale Parkinsonienne au niveau du MIG

Evaluer l'intensité et le retentissement de la douleur

Evaluation de la douleur ?

Intensité : EVA



Evaluation de la douleur ?

Evaluation fonctionnelle de la douleur

BPI (Brief pain inventory) ou Questionnaire Concis sur les Douleurs

9 – Entourez le chiffre qui décrit le mieux comment, pendant les dernières 24 heures, la douleur a gêné votre

- **Activité générale**

0	1	2	3	4	5	6	7	8	9	10
Aucune Gêne										Gêne complète

- **Humeur**

0	1	2	3	4	5	6	7	8	9	10
Aucune Gêne										Gêne complète

- **Capacité à marcher**

0	1	2	3	4	5	6	7	8	9	10
Aucune Gêne										Gêne complète

- **Travail habituel** (y compris à l'extérieur de la maison et les travaux domestiques)

0	1	2	3	4	5	6	7	8	9	10
Aucune Gêne										Gêne complète

- **Relation avec les autres**

0	1	2	3	4	5	6	7	8	9	10
Aucune Gêne										Gêne complète

- **Sommeil**

0	1	2	3	4	5	6	7	8	9	10
Aucune Gêne										Gêne complète

- **Goût de vivre**

0	1	2	3	4	5	6	7	8	9	10
Aucune Gêne										Gêne complète

Evaluation de la douleur ?

King's PD pain Scale

KING'S PD PAIN SCALE (KPPS)

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Domain 3 TOTAL SCORE			☐

Domain 4: Nocturnal Pain	Severity (0 – 3)	Frequency (0 – 4)	Frequency x Severity
7. Does the patient experience pain related to jerking leg movements during the night (PLM) or an unpleasant burning sensation in the legs which improves with movement (RLS)	☐	☐	☐
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Domain 6 TOTAL SCORE			
Domain 7: Radicular Pain			
14. Does the patient experience a shooting pain/ pins and needles down the limbs?	☐	☐	☐
Domain 7 TOTAL SCORE			☐
TOTAL SCORE (all domains)			☐

Comments:

Traiter la douleur

Mr D, 62 ans

Diagnostic :

Douleur musculosqueletique (lombalgies)
Douleur centrale Parkinsonienne au niveau du MIG

1- Augmentation ou adaptation médicament DA per os
2- Perfusion ss cut apomorphine ou intrajejunale levodopa
3- SCP des NST
4- Antalgique palier 1, 2 ou 3
5- AD imipraminiques ou antiepileptiques

Etude DOLORES : Rotigotine

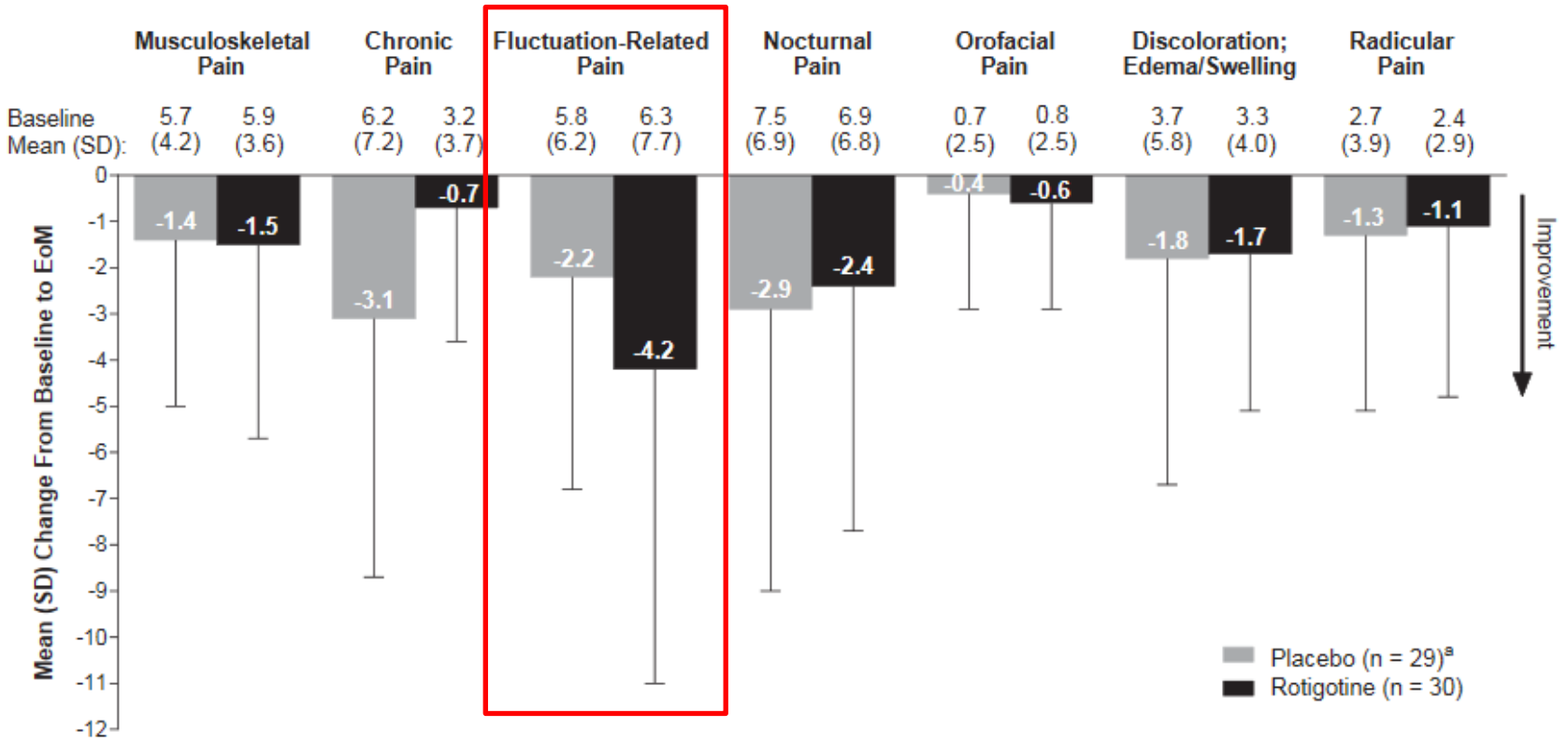


Figure 3. Secondary efficacy variable: change from baseline to EoM in the 7 domains of the King's PD Pain Scale (full analysis set, last observation carried forward). [a]One patient without postbaseline values. EoM, end of maintenance.

Perfusion ss cut apomorphine

Acta Neurol Scand. 1999 Sep;100(3):163-7.

Nocturnal subcutaneous apomorphine infusion in Parkinson's disease and restless legs syndrome.

Reuter I, Ellis CM, Ray Chaudhuri K.

6 Parkinsoniens : amélioration de la douleur nocturne dystonique

Mov Disord. 2000 Jan;15(1):167-9.

Subcutaneous apomorphine injections as a treatment for intractable pain in Parkinson's disease.

Factor SA, Brown DL, Molho ES.

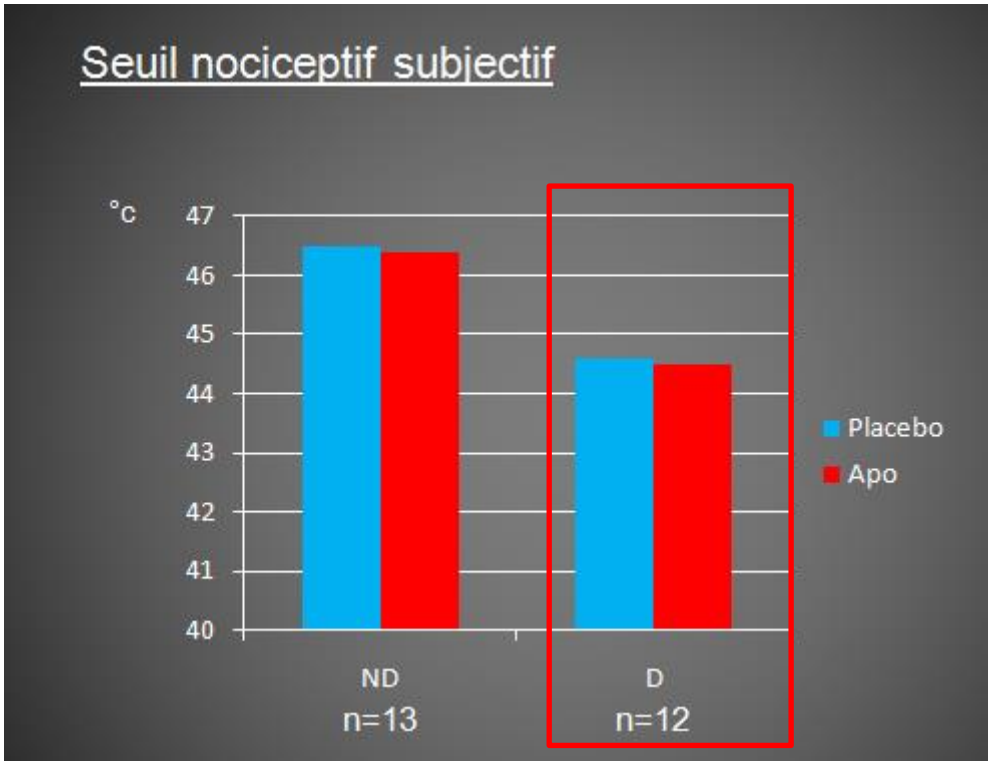
Case report : Parkinsonienne de 75 ans avec « OFF period pain »

Donc amélioration des douleurs dystoniques MAIS….

Apomorphine Effect on Pain Threshold in Parkinson's Disease: A Clinical and Positron Emission Tomography Study

Dellapina et al, 2011, Mov Disord

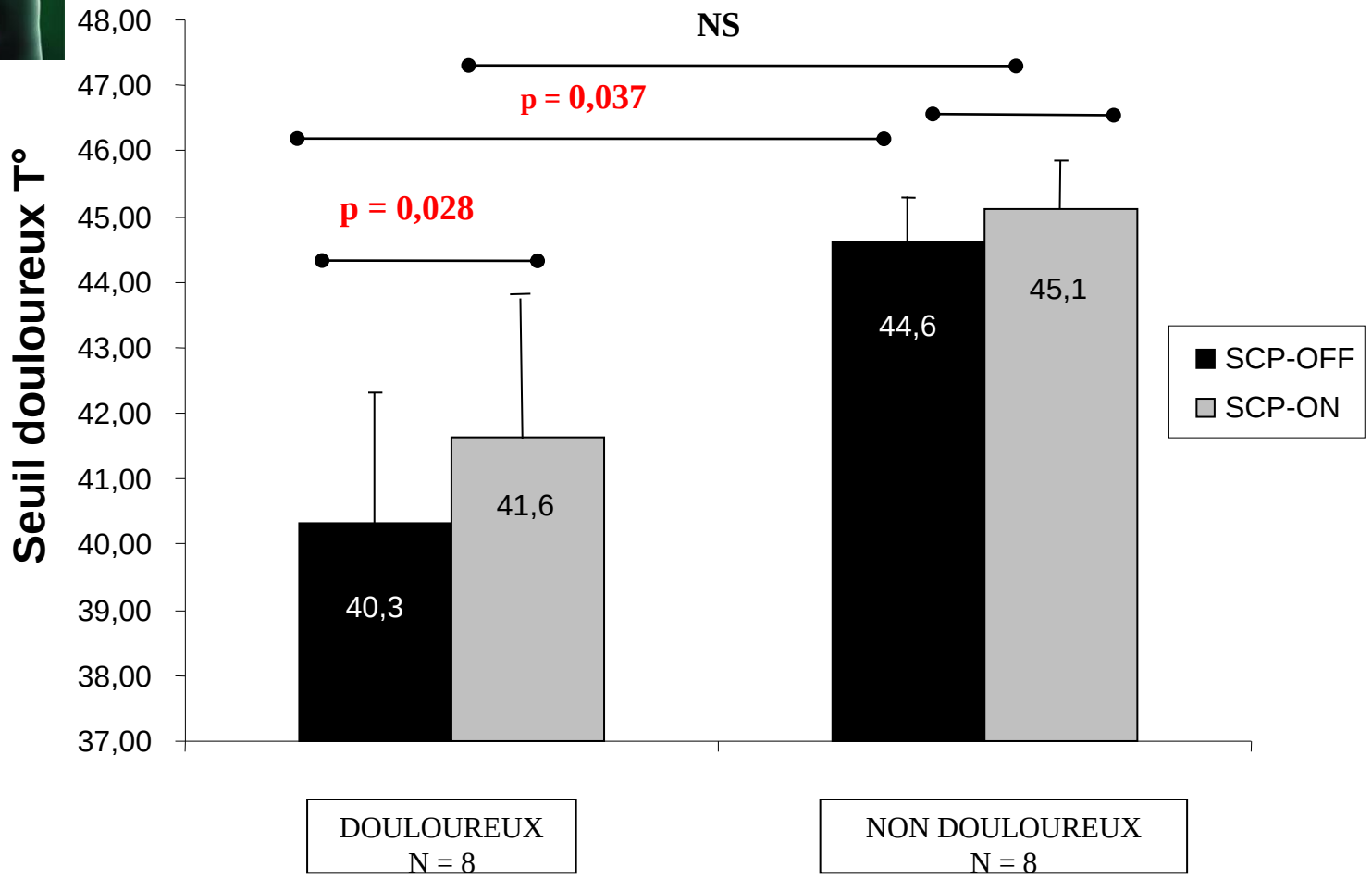
Etude comparative apomorphine vs placebo, rando, DA chez 12 Parkinsoniens avec douleur centrale



Pain, 2012

Effect of subthalamic deep brain stimulation on pain in Parkinson's disease

Estelle Dellapina [a,b,*], Fabienne Ory-Magne [c], Wafa Regragui [c], Claire Thalamas [d], Yves Lazorthes [e], Olivier Rascol [a,b,d,f], Pierre Payoux [a,b], Christine Brefel-Courbon [a,b,c,f]



La SCP du NST élève le seuil nociceptif chez les Parkinsoniens douloureux.

Réduction significative des paramètres cliniques douloureux à 12 mois

Deep brain stimulation of the subthalamic nucleus improves pain in Parkinson's disease

2014

Jean Pellaprat [a,b,*], Fabienne Ory-Magne [c], Cindy Canivet [c], Marion Simonetta-Moreau [a,b,c], Jean-Albert Lotterie [a,b,d], Fatai Radji [c], Christophe Arbus [a,b,e], Angélique Gerdelat [a,b,c], Patrick Chaynes [f], Christine Brefel-Courbon [a,b,c,g]

Demographic characteristics and clinical values before and 12 months after STN-DBS.

	Baseline	12 months	*p*
Sex (M/F)	37/21		n.a.
Age (years)	60.3 ± 7.8		n.a.
Duration of PD (years)	12.3 ± 3.8		n.a.
LEDD (mg/d)	1272.4 ± 480	553.3 ± 318	<0.0001
UPDRS III scores			
- OFF	37.4 ± 14.8	–	n.a.
- ON	15.7 ± 9.9	–	n.a.
- OFF drug and OFF DBS	–	31.7 ± 13.4	n.a.
- OFF drug and ON DBS	–	15.8 ± 9.3	n.a.
MADRS/60	8.9 ± 6.9	9.2 ± 7.3	0.85
MPQ-QDSA			
- Total/60	13.8 ± 11.3	7.6 ± 6.9	<0.0001
- Sensory/32	6.5 ± 5.9	4.6 ± 3.7	0.03
- Affective/28	7.3 ± 6.8	3.0 ± 4.1	<0.0001
Pain location			
- Head + neck	58.0%	27.1%	0.001
- Upper limbs	60.0%	54.2%	0.61
- Lower limbs	74.0%	43.8%	0.02
- Trunk	54.0%	33.3%	0.15
PDQ-39 Bodily discomfort subscore/100	50.3 ± 19.2	40.2 ± 20.3	<0.001
UPDRS II item 17/4	1.2 ± 1.2	0.8 ± 1.1	0.03
UPDRS IV item 35 (presence of early morning dystonia)	60.7%	20.0%	<0.0001

Effects of deep brain stimulation on pain and other nonmotor symptoms in Parkinson disease

2014

Rubens G. Cury, MD
Ricardo Galhardoni
Erich T. Fonoff, MD, PhD
Maria G. dos Santos Ghilardi, MD
Fernanda Fonoff
Debora Arnaut
Martin L. Myczkowski
Marco A. Marcolin, MD
Edson Bor-Seng-Shu, MD, PhD
Egberto R. Barbosa, MD PhD
Manoel J. Teixeira, MD, PhD
Daniel Ciampi de Andrade, MD, PhD

Correspondence to Prof. Ciampi de Andrade: ciampi@usp.br

Table 2 Effects of STN-DBS on pain in Parkinson disease

Data	Baseline	STN-DBS 12 mo	*p* Value
Pain prevalence, patients	29/41 (70.7)	9/41 (21.9)	<0.001[a]
Pain subtype			
Musculoskeletal	26/29 (89.7)	5/9 (55.5)	<0.001[a]
Dystonic	14/29 (48.3)	1/9 (11.1)	<0.001[a]
Central	2/29 (6.9)	1/9 (11.1)	NS
Radicular/neuropathic	2/29 (6.9)	2/9 (22.2)	NS
Pain worsened during off-medication periods	20/29 (69)	1/9 (11.1)	<0.001[a]
VAS	60.31 ± 20.50	10.61 ± 20.44	<0.001[a]
BPI, pain severity	6.50 ± 2.76	1.93 ± 3.06	<0.001[a]
BPI, pain interference daily activity	4.75 ± 2.87	1.40 ± 2.46	<0.001[a]
McGill sensitive	12.16 ± 9.47	3.23 ± 5.85	<0.001[a]
McGill affective	6.17 ± 4.75	1.92 ± 3.68	<0.001[a]
Neuropathic Pain Symptom Inventory	30.87 ± 16.09	23.62 ± 25.62	0.327
Pain Catastrophizing Scale	28.13 ± 14.83	19.00 ± 18.42	0.068

An 8-Year Follow-up on the Effect of Subthalamic Nucleus Deep Brain Stimulation on Pain in Parkinson Disease

2015

Yu Jin Jung, MD; Han-Joon Kim, MD, PhD; Beom S. Jeon, MD, PhD; Hyeyoung Park, MD; Woong-Woo Lee, MD; Sun Ha Paek, MD, PhD

Antalgique palier 1, 2 ,3

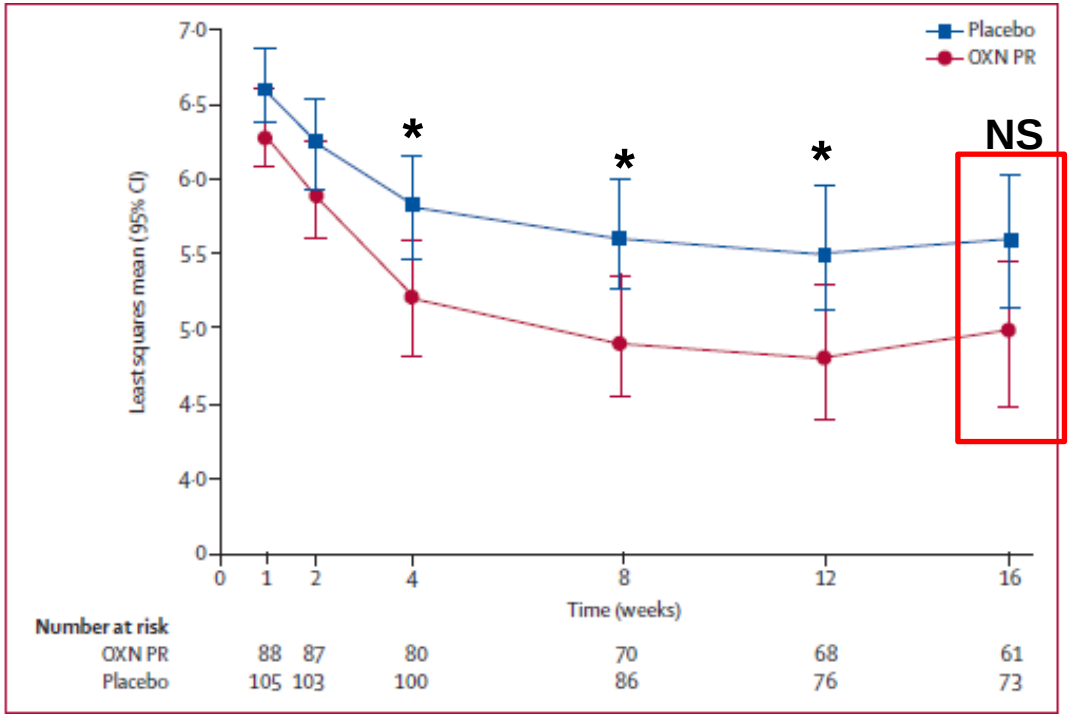
Aucune évaluation concernant les médicaments non opioïdes

Prolonged-release oxycodone–naloxone for treatment of severe pain in patients with Parkinson's disease (PANDA): a double-blind, randomised, placebo-controlled trial

2015

*Claudia Trenkwalder, K Ray Chaudhuri, Pablo Martinez-Martin, Olivier Rascol, Reinhard Ehret, Martin Vališ, Maria Sátori, Anna Krygowska-Wajs, Maria J Marti, Karen Reimer, Alexander Oksche, Mark Lomax, Julia DeCesare, Michael Hopp, for the PANDA study group**

	OXN PR group (n=88)	Placebo group (n=106)
Mean age (SD; years)	66·7 (8·9)	67·5 (8·1)
Men	43 (49%)	57 (54%)
Women	45 (51%)	49 (46%)
Mean MMSE score (SD)	28·6 (1·5)	28·6 (1·5)
Mean UPDRS score (SD)		
Part III	30·9 (14)	30·7 (12)
Part IV	5·1 (3·6)	4·9 (3·8)
Hoehn and Yahr classification		
Stage 2	20 (23%)	33 (31%)
Stage 2·5	27 (31%)	33 (31%)
Stage 3	35 (40%)	28 (26%)
Stage 4	6 (7%)	12 (11%)
Mean duration of Parkinson's disease (SD; years)	6·9 (5·2)	6·7 (4·2)
Mean duration of Parkinson's disease-related pain (SD; years)	3·4 (3·0)	3·4 (2·8)
Current Parkinson's disease medication use		
Patients taking one or more Parkinson's disease medication	83 (94%)	99 (93%)
Dopaminergic drugs	82 (93%)	97 (92%)
Parkinson's disease-related pain characteristics		
Mean 24-h pain score (SD)*	7·3 (1·0)	7·3 (0·9)
Severe types of Parkinson's disease-related pain†		
Musculoskeletal pain	67 (76%)	77 (73%)
Parkinson's disease-related chronic pain	19 (22%)	27 (26%)
Fluctuation-related pain	26 (30%)	34 (32%)
Nocturnal pain	26 (30%)	37 (35%)
Orofacial pain	2 (2%)	6 (6%)
Pain in limbs with discolouration	17 (19%)	20 (19%)



tous types de douleurs !

Médicament opioïde et douleur centrale dans la maladie de Parkinson

EVALUATION DES EFFETS ANTALGIQUES DE L'OXYCODONE LP ET DE LA L-DOPA, VERSUS PLACEBO, DANS LES DOULEURS NEUROPATHIQUES CENTRALES DU PATIENT PARKINSONIEN

Essai **OXYDOPA**

N° 14 7440 01

PHRC National 2014

Promoteur : CHU de Toulouse

Investigateur coordonnateur : Dr. Christine Brefel-Courbon

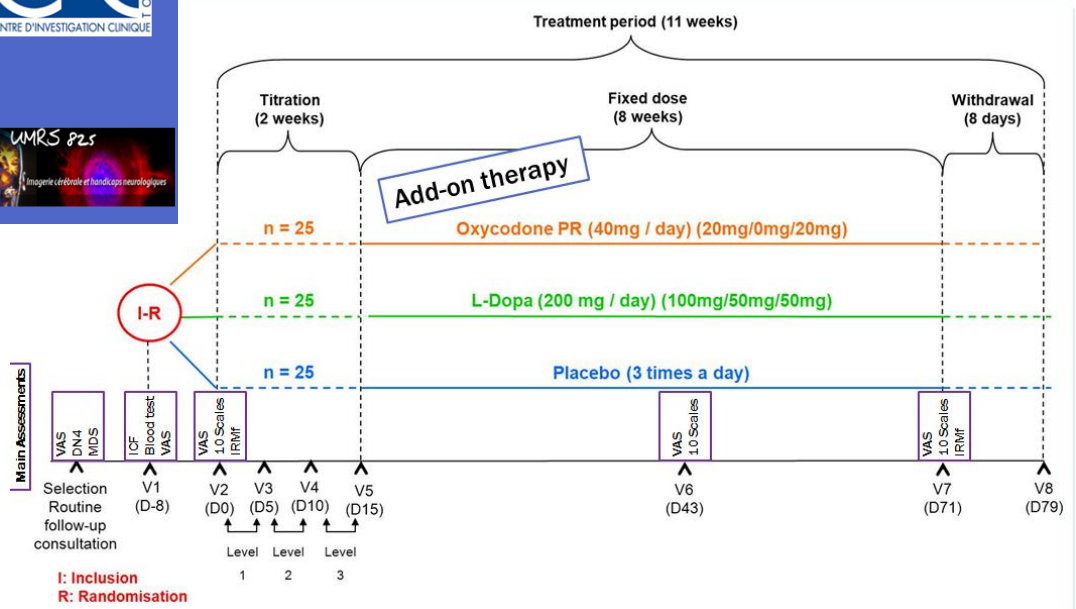
Hôpitaux de Toulouse

nspark
RÉSEAU LABELLISÉ FCRIN

CIC TOULOUSE
CENTRE D'INVESTIGATION CLINIQUE

UMR S 825
Imagerie cérébrale et handicaps neurologiques

DESIGN DE L'ÉTUDE



AD imipraminiques ou antiepileptiques ? Duloxetine ?

The effect of duloxetine on primary pain symptoms in Parkinson disease
Djaldetti et al, 2007

Twenty-three patients with PD with painful phenomena were treated with duloxetine for 6 weeks in an open-label design.

TABLE 1. Pain Assessment Before and After Treatment With Duloxetine

	Before Treatment	After Treatment	*P*
BDI	5.8 ± 4.0	4.9 ± 3.6	>0.1
PDQ-39	59.6 ± 32.7	54.1 ± 30.0	<0.07
BPI	66.2 ± 21.5	43.6 ± 28.5	<0.0009
SF-MPQ	15.1 ± 5.9	9.4 ± 6.7	<0.003
VAS	7.6 ± 3.2	4.2 ± 2.6	<0.0001

All scores are mean ± SD.
PDQ-39 indicates Parkinson Disease Quality of Life Questionnaire–39-item version; VAS, Visual Analog Scale; BDI, Beck Depression Inventory; BPI, Brief Pain Inventory.

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A double-blind, randomized controlled trial of duloxetine for pain in Parkinson's disease

Hirotaka Iwaki[a,b,c], Rina Ando[a], Satoshi Tada[a], Noriko Nishikawa[d], Tomoaki Tsujii[a], Yuki Yamanishi[a], Noriyuki Miyaue[a,e], Hayato Yabe[a,e], Masahiro Nagai[a], Masahiro Nomoto[a,f,*]

[a] Department of Neurology and Clinical Pharmacology, Ehime University, Ehime, Japan
[b] Laboratory of Neurogenetics, National Institute on Aging, National Institute of Health, MD, USA
[c] Data Tecnica International, MD, USA
[d] Department of Neurology, National Center Hospital of Neurology and Psychiatry, Tokyo, Japan
[e] Department of Neurology, Saiseikai Matsuyama Hospital, Ehime, Japan
[f] Department of Neurology, Saiseikai Imabari Hospital, Ehime, Japan

ARTICLE INFO

Keywords:
Parkinson's disease
Pain
Duloxetine hydrochloride
Randomized controlled trial

ABSTRACT

Background: Duloxetine proved effective for treating pain in people with Parkinson's disease in a single-arm, open-label study.
Objective: To evaluate the efficacy of duloxetine in a double-blind, randomized, placebo-controlled trial.
Methods: We randomly assigned 46 patients with Parkinson's disease with pain to either the duloxetine 40 mg/day arm or the placebo arm. After 10 weeks, we tested the change from baseline in 24-hour average pain severity measured by a visual analogue scale.
Results: We could not confirm the effect of duloxetine on pain. Exploratory analyses indicated that treatment with duloxetine was associated with improved scores on the Unified Parkinson's Disease Rating Scale Part III and 3 domains of the Parkinson's Disease Questionnaire – 39.
Conclusions: The study failed to provide evidence for the use of duloxetine for treating pain in people with Parkinson's disease.

Table 2
Estimated effect of duloxetine in change from Baseline to Week 10.

	Baseline mean (SD)		Mean change (SE) from Baseline to Week10		Mean difference (SE) in change (Duloxetine - Placebo)	
Outcome	Duloxetin	Placebo	Duloxetine	Placebo	Difference	[95% C.I.]
VAS, mm	47.87 (24.74)	47.83 (23.61)	−0.83 (4.79)	−1.91 (4.24)	1.09 (6.39)	[−11.44, 13.62]
Timed Up and Go, seconds	11.36 (5.02)	9.08 (2.88)	−0.43 (0.37)	0.29 (0.27)	−0.72 (0.45)	[−1.61, 0.17]
Beck's Depression Inventory	13.48 (6.86)	13.70 (8.56)	−1.22 (1.22)	−0.43 (1.38)	−0.78 (1.84)	[−4.38, 2.82]
SF-MPQ PRI total	10.74 (6.72)	9.09 (8.34)	−0.87 (1.37)	−0.43 (1.52)	−0.43 (2.05)	[−4.45, 3.58]
UPDRS Part III	25.61 (7.45)	22.91 (7.04)	−1.61 (0.43)**	−0.43 (0.39)	−1.17 (0.57)*	[−2.30, −0.05]
Parkinson's Diseaese Questionnaire - 39						
Mobility, %	45.00 (25.26)	31.63 (28.77)	−6.96 (3.78)	−1.20 (3.85)	−5.76 (5.39)	[−16.33, 4.81]
Activities of daily living, %	33.51 (24.67)*	18.48 (16.89)	−4.35 (4.10)	5.25 (2.32)*	−9.60 (4.71)*	[−18.82, −0.38]
Emotional welll-being, %	29.53 (20.60)	22.83 (18.46)	−10.51 (2.70)***	2.54 (2.90)	−13.04 (3.96)**	[−20.81, −5.28]
Stigma, %	14.67 (16.71)	18.48 (16.80)	−2.72 (3.79)	−1.63 (2.12)	−1.09 (3.34)	[−9.60, 7.42]
Social support, %	9.06 (18.79)	11.59 (13.47)	−4.71 (3.91)	−3.99 (2.51)	−0.72 (4.65)	[−9.83, 8.38]
Cognition, %	49.28 (38.76)	30.80 (21.97)	−6.88 (5.92)	0.36 (2.31)	−7.25 (6.35)	[−19.70, 5.21]
Communication, %	16.67 (17.04)	11.59 (13.23)	−6.52 (2.82)*	0.72 (2.09)	−7.25 (3.51)*	[−14.12, −0.37]
Bodily discomfort, %	39.86 (21.90)	28.99 (16.06)	1.09 (4.61)	2.90 (4.15)	−1.81 (6.20)	[−13.96, 10.33]

* $P < .05$, ** $P < .01$, *** $P < .001$ for the baseline differences between the two arms, for the changes from baseline to Week 10 within each arm, and for the differences in change between the two arm (t-test). SF-MPQ, short-form McGill Pain Questionnaire; PRI, pain rating index; UPDRS, Unified Parkinson's Disease Rating Scale.

Dose trop faible (40 mg/j) ?

tous types de douleurs !

Traitement non médicamenteux de la douleur ?

Effectiveness of aquatic therapy for the control of pain and increased functionality in people with Parkinson's disease: a randomized clinical trial

Sagrario PÉREZ de la CRUZ *

Department of Nursing, Physiotherapy and Medicine, University of Almería, Almería, Spain

*Corresponding author: Sagrario Pérez de la Cruz, Department of Nursing, Physiotherapy and Medicine, University of Almería, Carretera de Sacramento s/n, 04120, La Cañada de San Urbano (Almería), Spain. E-mail: spd205@ual.es

2017

ABSTRACT

BACKGROUND: Gait, balance disorders and pain associated with Parkinson's disease represent important therapeutic challenges, as they are related with an increased risk of falls, together with disability and physical decline.
AIM: To compare the effects of an aquatic ai chi training program on the perception of pain, the maintenance of balance and the functional independence of patients with Parkinson's disease.
DESIGN: A single-blind randomized controlled trial.
SETTING: Parkinson's associations and municipal pools.
POPULATION: Thirty individuals from two Parkinson's associations in Spain participated in the study. Inclusion criteria: individuals diagnosed with Parkinson's disease in stages 1 to 3 (Hoehn and Yahr Scale), older than 40 years, in the off phase (not medicated) and with a score greater or equal to 24 on the Mini-Mental State Examination Scale, without any medical contraindications and who accepted the study norms.
METHODS: The experimental group (N.=15 patients) participated in a program of aquatic ai chi. The control group (N.=15) received therapy on dry land. The intervention lasted 10 weeks with sessions held twice weekly. The pain VAS, Tinetti, Berg, Test Get Up and Go, Five Times Test and Unified Parkinson's Disease Rating Scale were used.
RESULTS: Significant differences were found between the baseline and one-month follow up assessments in pain perception values (F=26.89, P<0.001), and the Tinetti Test (F=21.57, P<0.001) in the experimental group compared to the control group (P<0.05) with the exception of the FTSTS (P=0.006). In the control group, improvements were only seen on the VAS Pain Scale (F=8.3, P=0.004) and these were less significant than the changes found in the experimental group. Regarding the scores obtained on the UPDRS scale in the experimental group, there were significant differences in activities of daily living and motor examination, with the exception of mentation, behavior and mood.
CONCLUSIONS: An aquatic ai chi program appears to be a valid treatment option for patients diagnosed with mild to moderate Parkinson's disease for the treatment of pain, balance and functional capacity.
CLINICAL REHABILITATION IMPACT: Physical exercise performed in water has positive effects on some of the necessary elements that contribute towards improved biomechanical gait patterns in our patients with Parkinson's disease.

(*Cite this article as:* Pérez de la Cruz S. Effectiveness of aquatic therapy for the control of pain and increased functionality in people with Parkinson's disease: a randomized clinical trial. Eur J Phys Rehabil Med 2017;53:825-32. DOI: 10.23736/S1973-9087.17.04647-0)

Key words: Postural balance - Parkinson disease - Pain - Rehabilitation - Exercise.

2 groupes de 15 Park
2 fois/sem pendant 10 sem

Research Article

Effects of a Flexibility and Relaxation Programme, Walking, and Nordic Walking on Parkinson's Disease

I. Reuter,[1,2] S. Mehnert,[1] P. Leone,[2] M. Kaps,[1] M. Oechsner,[3] and M. Engelhardt[4]

[1] *Department of Neurology, Justus Liebig University, Am Steg 14, 35392 Giessen, Germany*
[2] *Soemmerring Institute, Bad Nauheim, Germany*
[3] *Parkinsonklinik Bad Nauheim, Germany*
[4] *Department of Orthopedics and Trauma surgery, Klinikum Osnabrück, 49076 Osnabrück, Germany*

Correspondence should be addressed to I. Reuter, iris.reuter@neuro.med.uni-giessen.de

Received 1 October 2010; Revised 4 January 2011; Accepted 28 January 2011

Academic Editor: Ben Hurley

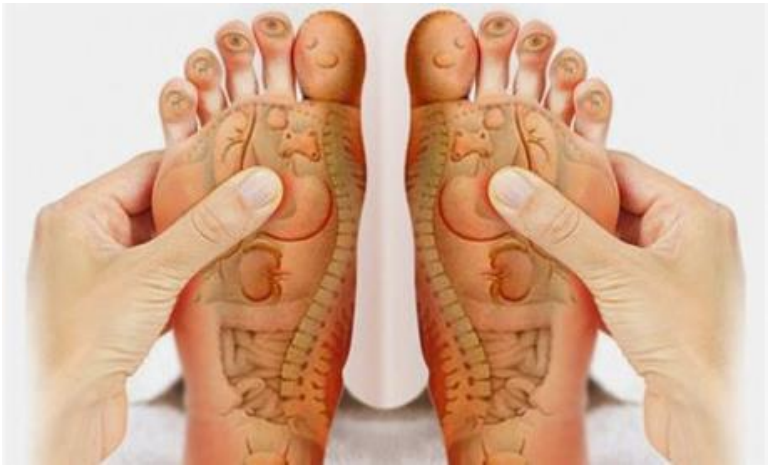
Symptoms of Parkinson's disease (PD) progress despite optimized medical treatment. The present study investigated the effects of a flexibility and relaxation programme, walking, and Nordic walking (NW) on walking speed, stride length, stride length variability, Parkinson-specific disability (UPDRS), and health-related quality of life (PDQ 39). 90 PD patients were randomly allocated to the 3 treatment groups. Patients participated in a 6-month study with 3 exercise sessions per week, each lasting 70 min. Assessment after completion of the training showed that pain was reduced in all groups, and balance and health-related quality of life were improved. Furthermore, walking, and Nordic walking improved stride length, gait variability, maximal walking speed, exercise capacity at submaximal level, and PD disease-specific disability on the UPDRS in addition. Nordic walking was superior to the flexibility and relaxation programme and walking in improving postural stability, stride length, gait pattern and gait variability. No significant injuries occurred during the training. All patients of the Nordic walking group continued Nordic walking after completing the study.

Étude comparative randomisée
3 groupes : relaxation/marche/marche nordique
30 Park/groupes : 3 fois/sem pendant 6 mois

Traitement non médicamenteux de la douleur ?

Hypnose ?

Réflexologie plantaire?



Quelques questions…

- ✓ **A quel moment survient la douleur ?**
- ✓ **A quel âge ?**
- ✓ **Est elle associée aux fluctuations motrices ?**
- ✓ **Quelle est la prévalence des différentes douleurs ?**
- ✓ **Quels mécanismes physiopathologiques sous jacents**

A quel moment survient la douleur ?

Nonmotor Symptoms as Presenting Complaints in Parkinson's Disease: A Clinicopathological Study

2008

Sean S. O'Sullivan, MRCPI,[1] David R. Williams, PhD,[1,2] David A. Gallagher, MRCP,[3] Luke A. Massey, MRCP,[1] Laura Silveira-Moriyama, MD,[1] and Andrew J. Lees, FRCP[1]

	Total cases (N = 433)
Male:female (%)	274:159 (63:37%)
Number of patients with a documented family history of PD (%)	31 (7%)
Age of PD onset mean ± SD	60.9 ± 10.4 years
Interval between symptom onset and diagnosis of PD; median, interquartile range (years)	1.1 (0.9–2.4)
Duration of PD before death; mean ± SD (years)	14.9 ± 6.9
Age of death; mean ± SD	75.8 ± 7.4
First symptoms including tremor	196 (45.3%)
First symptoms including bradykinesia	136 (31.4%)
First symptoms including rigidity	44 (10.2%)
First symptoms including unspecified gait disturbance	51 (11.8%)
First symptoms including pain	65 (15%)
First symptoms including urinary dysfunction	17 (3.9%)
First symptoms including depression or anxiety	11 (2.5%)
Other symptoms	59 (13.6%)

15 à 20 % des patients ont une douleur au moment du diagnostic (1er symptôme)

European Journal of Neurology 2013, **20:** 1398–1404 doi:10.1111/ene.12197

Preceding pain symptoms and Parkinson's disease: a nationwide population-based cohort study

2 cohortes Nationales (Taiwan)

33 388 sujets : 32 cas incidents de maladie de Parkinson sur 3 ans

Sujets avec douleur modérée à sévère ont une incidence plus élevée de MP : Hazard ratio : 2,88 (95%CI : 1,05-7,86, p=0,04)

Conclusions: These findings support the hypothesis that pain is associated with PD in the pre-motor stage of the disease. Further research is needed to clarify the role of sensory system involvement in the pre-motor phase of PD.

La douleur survient préférentiellement chez les Parkinsoniens jeunes

TABLE 2. *Demographic and clinical characteristics of parkinsonian patients with no pain, chronic pain related to PD (PD-pain) or chronic pain unrelated to PD (non-PD-pain)* **Nègre-Pages et al, 2008**

	No pain (n = 147)	PD-pain (n = 167)	Non-PD-pain (n = 111)	*P* value
Pain intensity (VAS)	–	6.5 ± 2.0 [6.2–6.8]	6.0 ± 2.2 [5.6–6.4]	0.03
SF-McGill score	–	16 ± 9.4 [14.4–17.5]	12.3 ± 8.3 [10.8–13.9]	0.002
Sensory score	–	6.9 ± 4.1 [6.3–7.6]	6.3 ± 4.3 [5.5–7.1]	0.25
Emotional score	–	9.1 ± 6.8 [8–10.1]	6.2 ± 5.1 [5.2–7.2]	0.0003
Sex (% male)	61.2% [53–69]	53.9% [46–61]	51.4% [42–61]	0.24
Age (years)	69.7 ± 10.4 [68–71.4]	66.4 ± 9.8 [64.9–67.9]	71.7 ± 7.7 [70.3–73.1]	<0.0001‡‡,◇◇◇
MMSE score	28.0 ± 2.2 [27.6–28.3]	27.9 ± 2.6 [27.5–28.3]	28.0 ± 1.8 [27.6–28.3]	0.98

Facteur prédictif de douleur *(Silverdale et al, 2018)*

Multiple linear regression for pain severity - Short form McGill Pain Questionnaire (SFMPQ).

	R^2	Beta	t	95% Confidence intervals		sig
				lower	upper	
	0.21					
MDS-UPDRS-III		0.003	0.185	−0.031	0.038	0.853
MDS-UPDRS-IV		0.213	2.121	0.016	0.411	**0.034**
SCOPA		0.224	6.031	0.151	0.297	**< 0.001**
LADS		0.224	5.347	0.142	0.307	**< 0.001**
MoCA		−0.005	−0.076	−0.135	0.125	0.940
Age		−0.072	−2.801	−0.123	−0.022	**0.005**
Disease Duration		0.071	0.676	−0.136	0.278	0.394
Gender (Female)		1.619	3.450	0.698	2.540	**0.001**

Age plus jeune lors du diagnostic

TABLE 4. *Logistic regression model of factors significantly associated with PD-pain, with parkinsonian patients with no pain used as the control group*

	OR [95% CI]	Adjusted OR [95% CI]*
Age at PD onset		
≤65 years	3 [1.9–4.8]	3 [1.7–5.4]
>65 years	1	1
Motor fluctuations		
Presence	3.5 [2.1–5.8]	2.8 [1.5–5.1]
Absence	1	1
Depressive symptoms (HADS-D > 7)		
Yes	2.1 [1.3–3.4]	2 [1.1–3.6]
No	1	1

Adjusted *R*-square value 0.23.
Goodness of fit, Hosmer and Lemeshow[19] – Pr > Chi^2: 0.8039.
*OR adjusted for age at onset, PD duration, motor fluctuations, dyskinesia, UPDRS II+III, dopatherapy duration, HADS-A and HADS-D.

Nègre-Pages et al, 2008

La douleur souvent associée aux fluctuations motrices

Facteur prédictif de douleur *(Silverdale et al, 2018)*

Multiple linear regression for pain severity - Short form McGill Pain Questionnaire (SFMPQ).

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Nègre-Pages et al, 2008

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*OR adjusted for age at onset, PD duration, motor fluctuations, dyskinesia, UPDRS II+III, dopatherapy duration, HADS-A and HADS-D.

La prévalence des différentes douleurs

PLOS ONE | 2015

100 Parkinsoniens

RESEARCH ARTICLE

Pain in Parkinson´s Disease: A Cross-Sectional Study of Its Prevalence, Types, and Relationship to Depression and Quality of Life

Peter Valkovic[1,2☯*], Michal Minar[1☯*], Helena Singliarova[1,3], Jan Harsany[1], Marta Hanakova[1], Jana Martinkova[1], Jan Benetin[4]

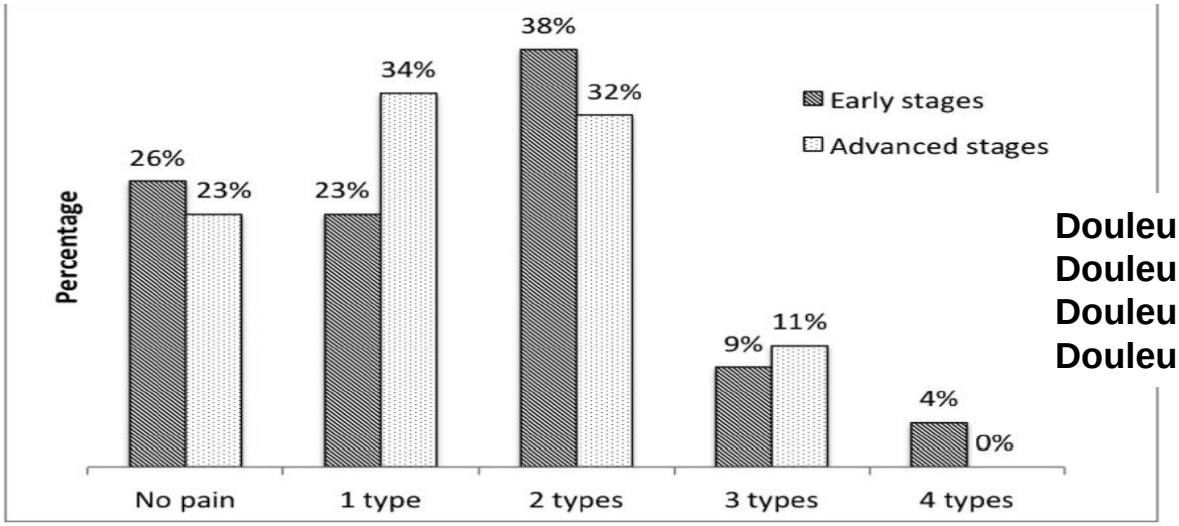
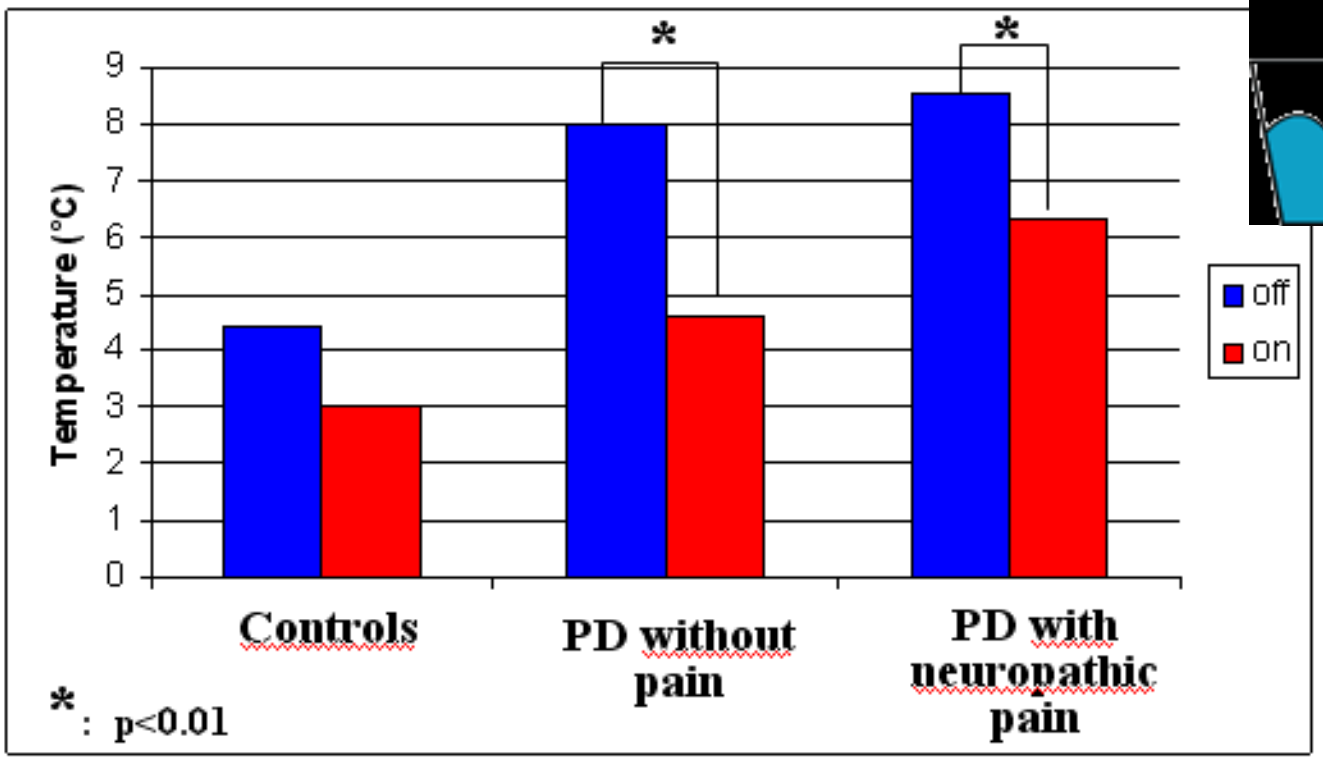


Fig 2. Types of pain in PD patients.

Douleurs musculosquelettiques : 41%
Douleurs dystoniques : 17%
Douleurs radiculaires : 27%
Douleurs centrales : 22%

Il existe un abaissement du seuil de la douleur dans la maladie de Parkinson



Brefel-Courbon et al, 2005; 2013

In OFF condition, pain thresholds in the two groups of PD patients were significantly lower than controls (p=0.03).

L-Dopa significantly raised pain threshold in PD patients with and without pain but not in controls.

Contents lists available at ScienceDirect

Ageing Research Reviews

2017

journal homepage: www.elsevier.com/locate/arr

Pain perception in Parkinson's disease: A systematic review and meta-analysis of experimental studies

Trevor Thompson[a,*], Katy Gallop[b], Christoph U. Correll[c,d], Andre F. Carvalho[e], Nicola Veronese[f], Ellen Wright[g], Brendon Stubbs[h,i]

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

2018

journal homepage: www.elsevier.com/locate/parkreldis

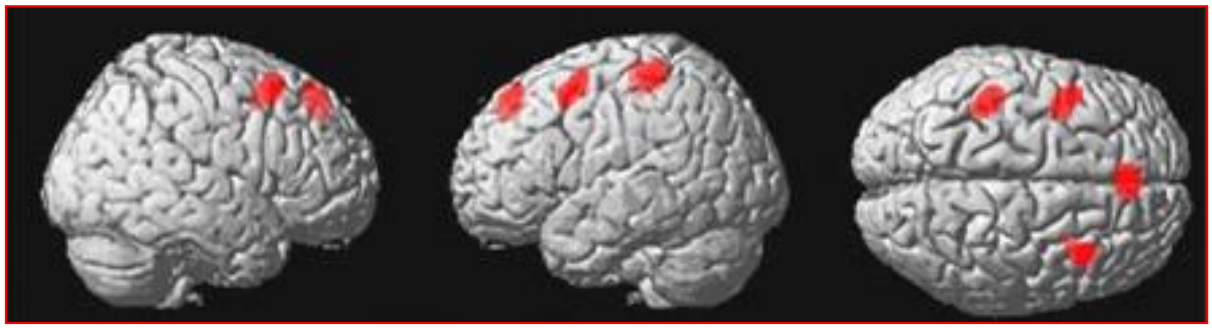
Review article

Pain sensitivity in Parkinson's disease: Systematic review and meta-analysis

Simon Sung[a, b, *], Nirosen Vijiaratnam[b], Daniela Wan Chi Chan[c], Michael Farrell[d], Andrew H. Evans[a]

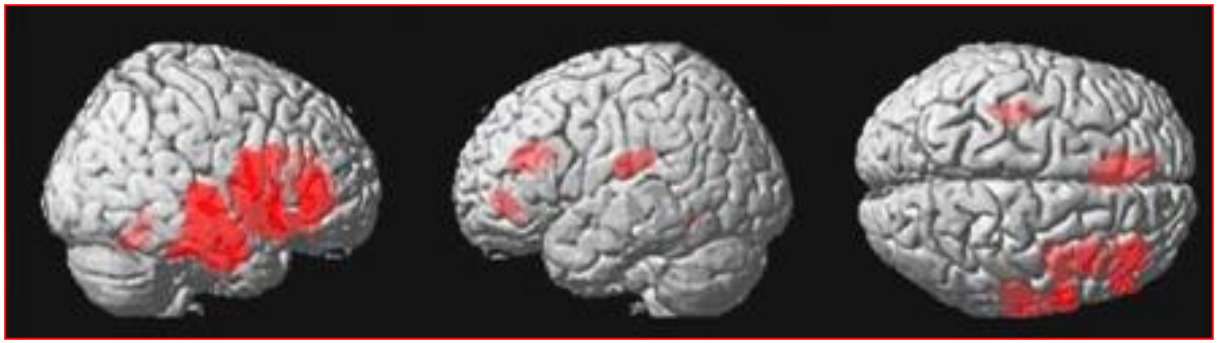
Processus d'intégration nociceptive anormal au niveau du SN central

Stimulation expérimentale douloureuse



condition OFF

Témoin



Parkinson

➡ Hyperactivation du circuit de la douleur dans la maladie de Parkinson

Brefel-Courbon, 2005; 2013

Conclusion

La douleur dans la maladie de Parkinson

Abaissement du seuil nociceptif

↑ **des douleurs non spécifiques**

Apparition de douleurs spécifiques

- **Nociceptives (dystoniques)**
- **Nociplastiques (central pain)**

- **Dysfonctionnement cérébral des aires nociceptives**
- **partiellement modulé par la lévodopa**

Classification physiopathologique et traitement médicamenteux des douleurs chroniques dans la maladie de Parkinson

CHRONIC PAIN	Nociceptive	Neuropathic	Nociplastic
Unspecific to PD ↑ Med DA (L-Dopa)	Musculoskeletal pain AINS, paracetamol….	Radicular pain AD antiépileptiques	Restless leg syndrome Gabapentine, pregabaline
Specific to PD	Dystonic pain ↑ Med DA	_	Central pain ↑ Med DA Opioïde ? AD ? Antiépileptiques ?

Traitement de la douleur en fonction de sa physiopathologie