Pain and Dystonic symptoms

Michele Tinazzi

Department of Neurosciences, Biomedical and Movement Sciences

University of Verona, Italy

Movement Disorders
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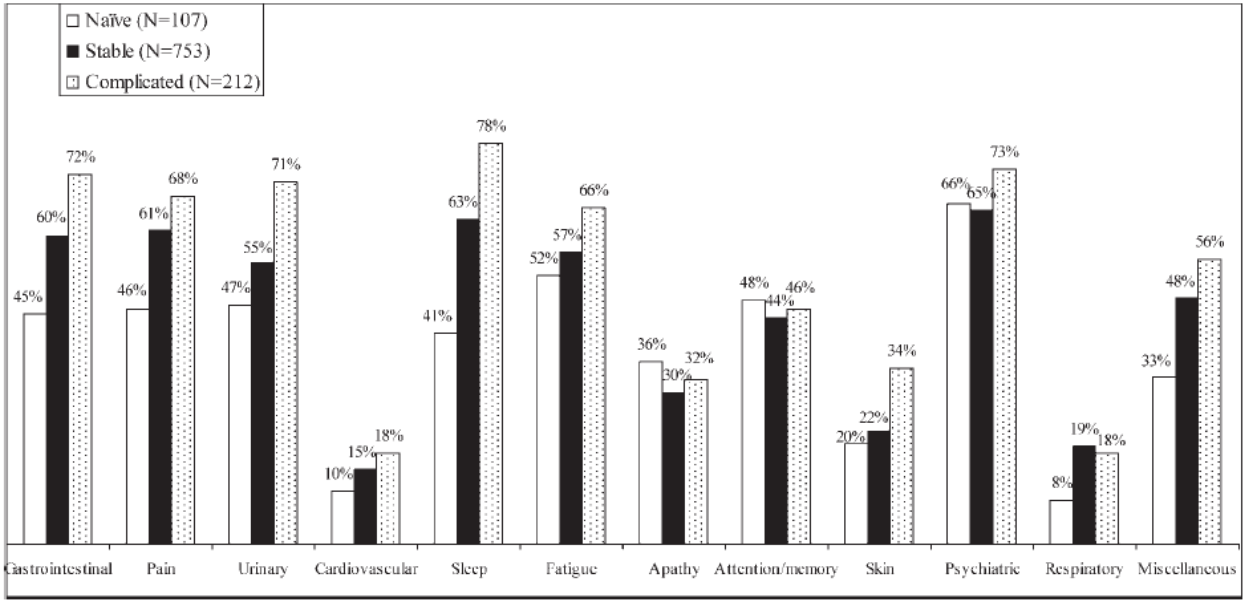
The Priamo Study: A Multicenter Assessment of Nonmotor Symptoms and Their Impact on Quality of Life in Parkinson's Disease

Paolo Barone, MD,[1] Angelo Antonini, MD,[2]* Carlo Colosimo, MD,[3] Roberto Marconi, MD,[4]

et al.

Pain is one of the most frequent (the average prevalence is about 67%) and disabling non motor symptom in PD.
Patients with PD suffer from pain of variable quality and localization, at different stages of disease.



Pain (5)	Undefined pain	223 (20.8)
	Leg Pain	406 (37.9)
	Abdominal pain	61 (5.7)
	Pain related to intake of drugs (e.g., levodopa)	11 (1.0)
	Shoulder pain	205 (19.1)

Classification

International Association for the Study of Pain (IASP)

- **Nociceptive**: chronic pain associated with an ongoing input from real or threatened tissue injury

- **Neuropathic** chronic pain caused by injury or disease affecting the peripheral nervous system or CNS.

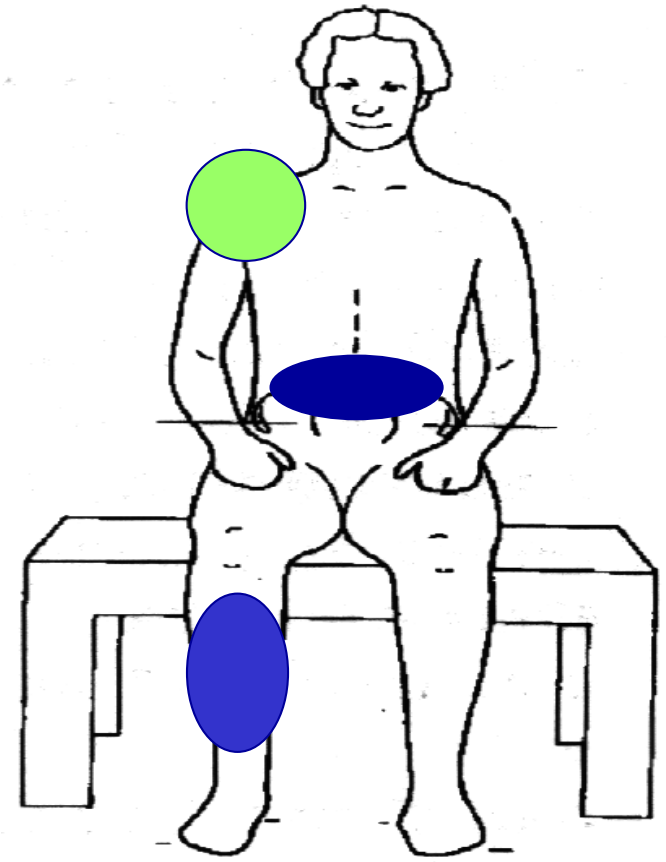
- **Nociplastic** chronic pain states not characterised by obvious activation of nociceptors or neuropathy, “but in whom clinical and psychophysical findings suggest altered nociceptive function”.

Classification

- **Dystonic Pain (associated to visible dystonia):** paroxysmal, variable duration

Ford, Mov Disord 2010

- **Non Dystonic Pain**
  - **Musculoskeletal pain**
    aching, cramping, joint pains
  - **Peripheral neuropathic pain**
    burning, tingling discomfort nerve/root
  - **Central neuropathic pain**
    stabbing, burning, tingling



Unusual pain syndromes: face, head, pharynx, epigastrium, abdomen, pelvis, rectum, and genitalia.

1. Is pain a non motor symptom in PD ?

- Pain is a prevalent symptom in the general population
- Is the frequency of pain greater in PD than in the general population from the same age group?
- Nine controlled studies

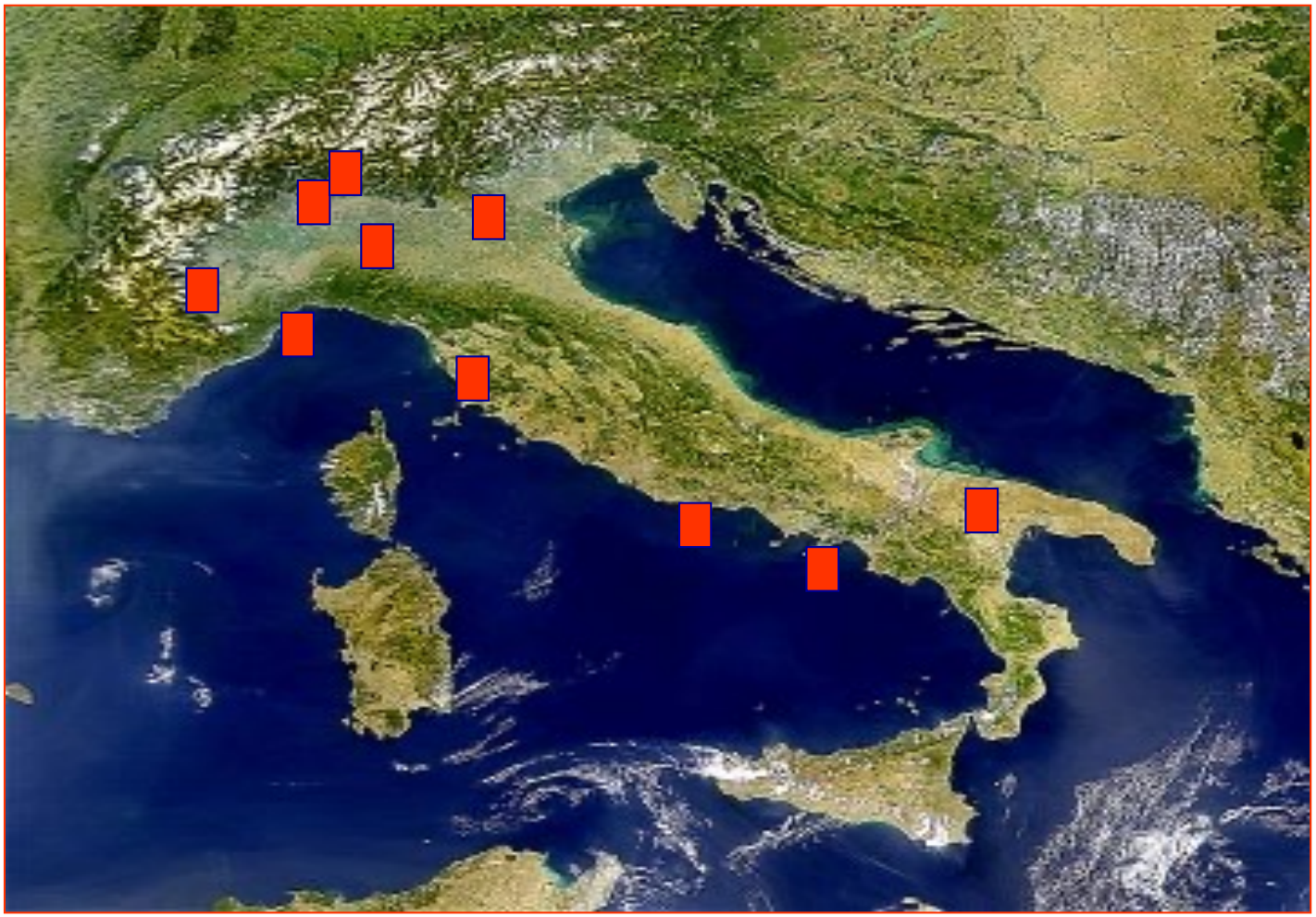
First Author, Journal, year	Pain type	No. PD patients (% pain)	No. control subjects (% pain)	P
Chauduri, Mov Disord 2006	All pains	(27%)	(30%)	0.6
Etchepare, Joint Bone Spine 2006	Back pain	104 (60%)	100 (23%),	<0.001
Broetz, Mov Disord 2007	Back pain	101 (74%)	132 (27%)	<0.001
Negre-Page, Mov Dis 2008	All pains	450 (61%)	98 (58%)	0.74
Defazio, Arch Neurol 2008	All pains	402 (70%)	317 (63%)	0.04
Beiske, Pain 2009	All pains	176 (83%)	Norway people (30%)	<0.001
Ehrt,Am J Geriat Psychiatry2009	All pains	227 (67%)	100 (39%)	<0.001
Brefel-Courbon, Pain 2009	All pains	11.456 (33%)	11.200 (20%)	<0.05
Madden, Mov Disord 2010	Shoulder pain	25 (80%)	25 (40%)	0.006

Pain as a Nonmotor Symptom of Parkinson Disease

Evidence From a Case-Control Study

Giovanni Defazio, MD, PhD; Alfredo Berardelli, MD; Giovanni Fabbrini, MD; Davide Martino, MD; Emiliana Fincati, MD; Antonio Fiaschi, MD; Giuseppe Moretto, MD; Giovanni Abbruzzese, MD; Roberta Marchese, MD; Ubaldo Bonuccelli, MD; Paolo Del Dotto, MD; Paolo Barone, MD; Elisa De Vivo, MD; Alberto Albanese, MD; Angelo Antonini, MD; Margherita Canesi, MD; Leonardo Lopiano, MD; Maurizio Zibetti, MD; Giuseppe Nappi, MD; Emilia Martignoni, MD; Paolo Lamberti, MD; Michele Tinazzi, MD

Arch Neurol. 2008;65(9):1191-1194.



Bari
Genova
Napoli
Milano
Pavia
Pisa
Roma
Torino
Verona

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

Laurence Nègre-Pagès, PhD,[1] Wafa Regragui, MD,[2] Didier Bouhassira, MD,[3] Hélène Grandjean, MD,[4] and Olivier Rascol, MD, PhD,[5,6,7]* on behalf of the DoPaMiP Study Group (Investigators listed at end of report)

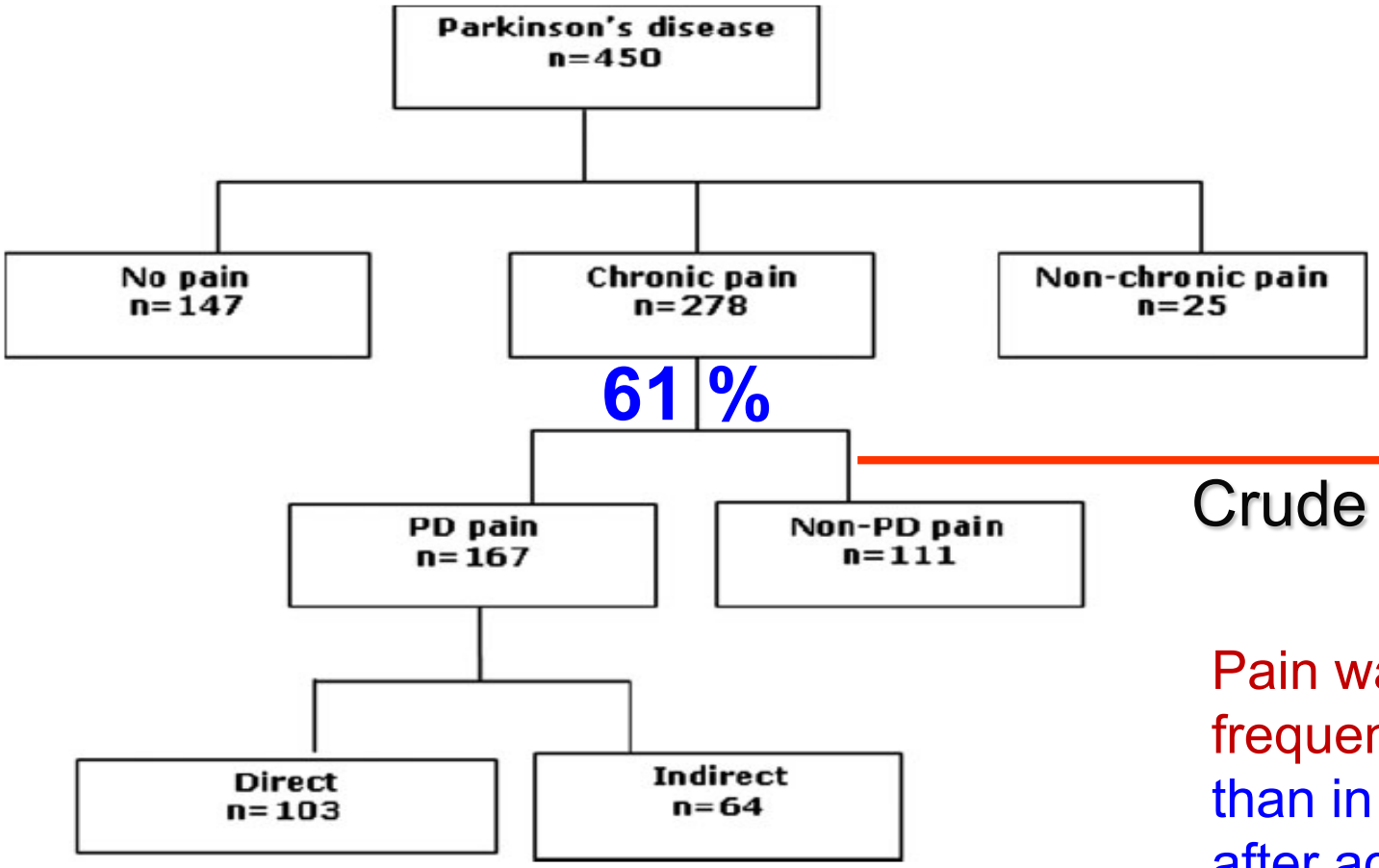


FIG. 1. Types of pain reported by PD patients in the DoPaMiP survey.

CONTROL SUBJECTS
N. 98

CHRONIC PAIN
N. 57

56 %

Crude P = 0.74

Pain was twice more frequent in PD patients than in patients without PD after adjustment for osteo-articular comorbidity, OR = 1.9; 95% CI 1.2–3.2

Classification

Pain can be related to PD in different ways.

- Temporal and topographical relationship with PD (onset and location)
- Influence of motor complications (fluctuations, 'off' dystonia, 'on' dyskinesia)
- Influence of antiparkinson medication
- Patient's opinion about the relationship between pain and PD.

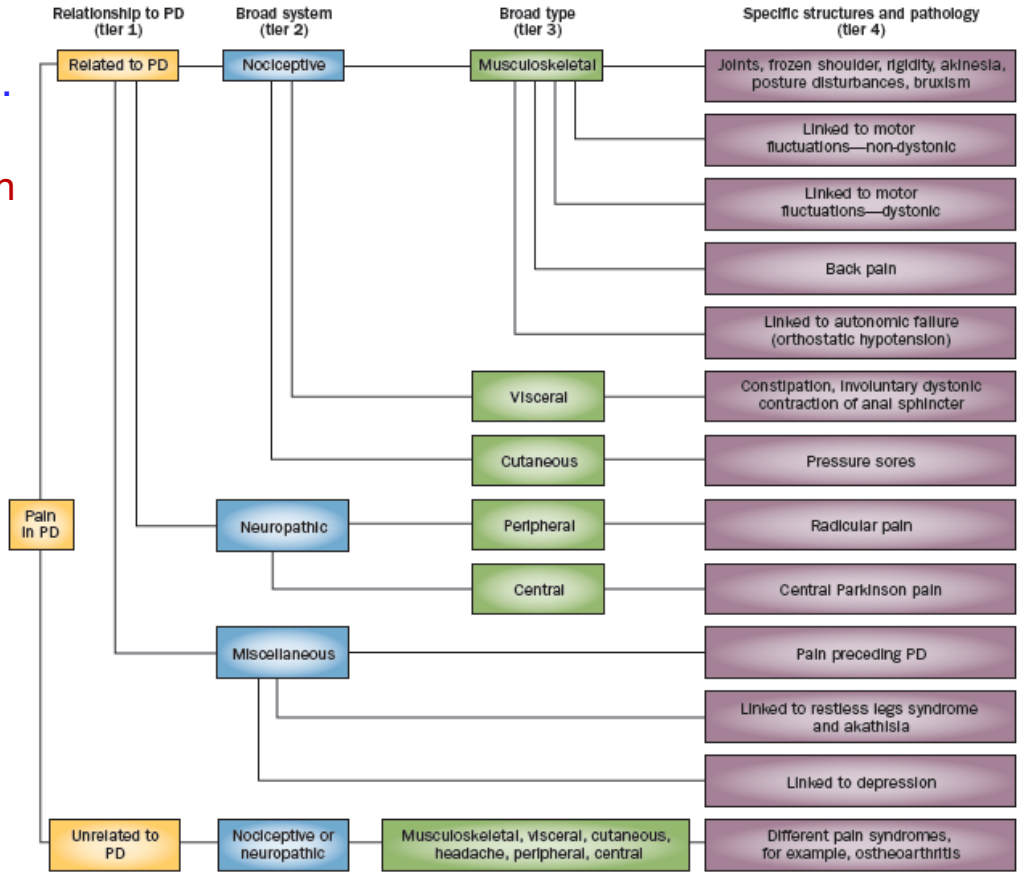


Figure 2 | Taxonomy of pains in PD. Nociceptive pains refer to pains related to an intact nervous system. Neuropathic pains describe pains related to a lesion or disease of the somatosensory system. Miscanelleous pains refer to pains that cannot be clearly assigned as nociceptive or neuropathic. The structure of the table is adopted from a taxonomy of pains in spinal cord injury.[135] Abbreviation: PD, Parkinson disease.

Wasner et al, Nat Rev Neurol 2012

PD – (motor signs) related pain

- In a French study *(Negre-Pages et al. 2008)* PD-related pain was diagnosed in 60% of patients

- In a Norwegian population-based study *(Beiske et al. 2009),* PD-related pain was diagnosed in:

- 51% of patients with dystonic pain
- 43% of patients with musculoskeletal pain
- 34% of patients with peripheral neuropathic pain
- 80% of patients with central neuropathic pain.

PD – (motor signs) related pain?

Several authors proposed to distinguish PD-related pain and PD-unrelated pain *(Lee et al., 2006, Negres-Pages et al., 2008; Wasner and Deuschl, 2012).*

However:

- Diagnosis of PD-related pain is not based on objective criteria
- There is no evidence that pain lacking an apparent relationship with motor symptoms is also related to PD.
- PD neurodegenerative process extends beyond the substantia nigra, and a number of non motor symptoms have been included in the spectrum of PD.

Clinical predictors of pain in PD

- Severity of motor symptoms
- Presence of motor complications
- Younger age at PD onset
- Female gender
- Depressive symptoms
- Medical conditions potentially associated with painful symptoms (i.e., diabetes mellitus, osteoporosis, rheumatic disease, degenerative joint disease, arthritis, disc herniation) *(Goetz et al., 1986; Vela et al., 2002;Tinazzi et al., 2006; Broetz et al., 2007; Defazio et al., 2008; Negre-Page et al., 2008; Ehrt et al., 2009; McNamara et al., 2010; Zambito et al., 2011).*

3. Dopaminergic drugs and Spontaneous Pain

Pain Intensity On and Off Levodopa in Patients with Parkinson's Disease

Angelika Nebe, MD and Georg Ebersbach, MD*

Movement Disorder Clinic, Beelitz-Heilstätten, Germany

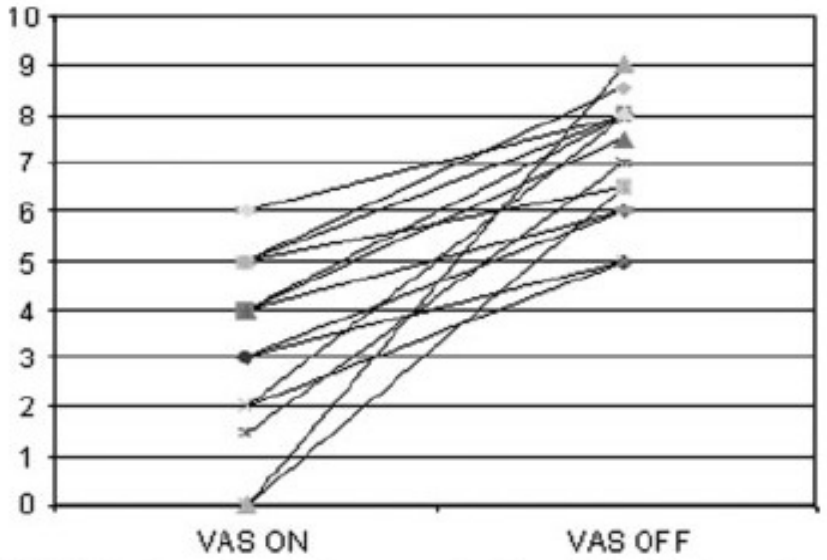


FIG. 1. Ratings of pain for on and off periods (visual analogue scale).

Pain associated with OFF complications may improve during ON periods, at least in some patients

This was observed for muscular pain as well as for pain types for which a relationship with muscular conditions is unlikely (arthralgic, oral and genital pain)

Mixed pain response to dopaminergic drugs

- Pain diminished with L-dopa challenge in 50% of stable responders, 89% of fluctuators, and and 100% of dyskinetic patients (P=0.03) *(Lim et al. 2011).*
- Pain responses are highly susceptible to placebo
- Patients with motor complications may have a high rate of placebo response.

Rotigotine Effects on Early Morning Motor Function and Sleep in Parkinson's Disease: A Double-Blind, Randomized, Placebo-Controlled Study (RECOVER)

Claudia Trenkwalder, MD,[1]* Bryan Kies, FCNeurol (SA),[2] Monika Rudzinska, MD,[3] Jennifer Fine, FCP (SA) Neurology,[4] Janos Nikl, MD,[5] Krystyna Honczarenko, MD,[6] Peter Dioszeghy, MD,[7] Dennis Hill, MD,[8] Tim Anderson, FRACP,[9] Vilho Myllyla, MD,[10] Jan Kassubek, MD,[11] Malcolm Steiger, FRCP,[12] Marco Zucconi, MD,[13] Eduardo Tolosa, MD,[14] Werner Poewe, MD,[15] Erwin Surmann, MSc,[16] John Whitesides, PhD,[17] Babak Boroojerdi, MD,[16] Kallol Ray Chaudhuri, DSc[18] and the RECOVER Study Group

TABLE 2. Mean change from baseline to end of treatment in the secondary outcomes, NADCS and number of nocturias, and the exploratory outcomes, NMS total and individual domain scores, BDI-II, Likert pain scale, PDQ-8, UPDRS Part II (FAS-observed cases)

	Mean (SD) baseline score		Mean (SD) change	
	Placebo	Rotigotine	Placebo	Rotigotine
NADCS	2.7 (2.1) (n = 89)	2.9 (2.2) (n = 178)	−0.7 (2.1) (n = 89)	−1.2 (1.8)[a] (n = 178)
Number of nocturias	2.0 (1.8) (n = 89)	1.9 (1.4) (n = 176)	−0.3 (1.6) (n = 89)	−0.3 (1.3) (n = 176)
NMS total score	41.3 (33.5) (n = 87)	41.1 (34.5) (n = 173)	−3.9 (25.5) (n = 86)	−10.3 (21.2)[a] (n = 172)
Individual NMS domain				
Cardiovascular	1.1 (1.9) (n = 89)	1.0 (1.9) (n = 178)	−0.2 (1.7) (n = 88)	0.0 (1.9) (n = 178)
Sleep/fatigue	9.1 (8.6) (n = 89)	9.5 (9.4) (n = 176)	−1.5 (6.2) (n = 88)	−3.7 (6.8)[b] (n = 176)
Mood/cognition	7.3 (10.0) (n = 89)	7.1 (9.3) (n = 178)	0.2 (11.1) (n = 88)	−3.0 (7.5)[c] (n = 178)
Perception/hallucinations	0.4 (1.4) (n = 89)	0.5 (1.7) (n = 178)	0.0 (1.3) (n = 88)	0.1 (2.4) (n = 178)
Attention/memory	3.9 (5.0) (n = 89)	4.5 (6.4) (n = 178)	0.0 (4.8) (n = 88)	−0.3 (4.6) (n = 178)
Gastrointestinal tract	4.2 (5.7) (n = 89)	3.6 (4.4) (n = 178)	0.0 (3.9) (n = 88)	−0.6 (2.6) (n = 178)
Urinary	6.7 (7.5) (n = 89)	6.6 (7.5) (n = 176)	−0.7 (5.0) (n = 88)	−1.1 (4.9) (n = 176)
Sexual function	3.9 (6.3) (n = 87)	3.7 (5.7) (n = 177)	−0.4 (4.3) (n = 86)	−0.2 (4.9) (n = 177)
Miscellaneous	5.1 (5.6) (n = 89)	4.8 (6.4) (n = 178)	−1.0 (4.2) (n = 88)	−1.3 (3.5) (n = 177)
BDI-II	12.6 (8.8) (n = 89)	12.3 (8.0) (n = 178)	−0.8 (7.6) (n = 89)	−2.7 (5.7)[a] (n = 177)
Likert pain scale	2.6 (2.5) (n = 89)	2.8 (2.4) (n = 178)	−0.1 (2.3) (n = 88)	−0.9 (2.2)[b] (n = 178)
PDQ-8	31.1 (17.0) (n = 89)	30.8 (18.2) (n = 177)	−1.2 (13.7) (n = 89)	−6.9 (11.9)[c] (n = 176)
UPDRS Part II	13.5 (6.3) (n = 89)	12.7 (5.6) (n = 178)	−1.3 (3.4) (n = 89)	−2.6 (3.6)[c] (n = 178)

[a]$P < 0.05$; [b]$P < 0.01$; [c]$P < 0.001$ for rotigotine-placebo treatment difference (ANCOVA; Exploratory Analyses).
BDI-II, Beck depression inventory; PDQ-8, short-form Parkinson's Disease questionnaire; NADCS, Nocturnal Akinesia, Dystonia and Cramps Score; NMS, Parkinson's Disease Nonmotor Symptom Assessment Scale; UPDRS, Unified Parkinson's Disease Rating Scale; FAS, Full Analysis Set.

Rotigotine had the effect to improve early-morning motor symptoms, sleep and pain.

Pain processing in PD

PAIN 2696

Review Article 1996

The role of the basal ganglia in nociception and pain

Eric H. Chudler * and Willie K. Dong

Department of Anesthesiology and Multidisciplinary Pain Center, University of Washington, Seattle, WA 98195 (USA)

(Received 3 December 1993, revision received 29 July 1994, accepted 8 August 1994)

BG are involved not only in motor control but also in non-motor functions, such as the processing of nociceptive inputs.

Multiple parallel pathways connect the BG to a number of structures involved in nociception (intralaminar nuclei of the thalamus, SII, insula, the amygdala, cingulate cortex, prefrontal areas).

European Journal of Neurology 2013, 20: 1517–1523 doi:10.1111/ene.12260

REVIEW ARTICLE

How pain arises in Parkinson's disease?

G. Defazio[a], M. Tinazzi[b] and A. Berardelli[c]

[a]Department of Basic Medical Sciences, Neurosciences and Sense Organs, 'Aldo Moro' University of Bari, Bari; [b]Department of Neurological, Neuropsychological, Morphological and Motor Sciences, University of Verona, Verona; and [c]Department of Neurology and Psychiatry, Sapienza University of Rome and Neuromed Institute, IRCCS, Rome, Italy

1) PD patients WITH pain vs Controls

2) PD patients WITHOUT pain vs Controls

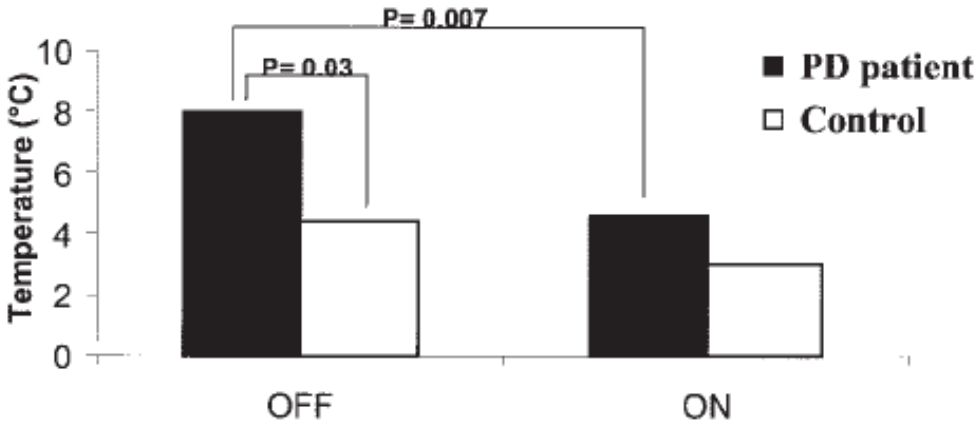
3) PD WITH pain vs PD WITHOUT pain

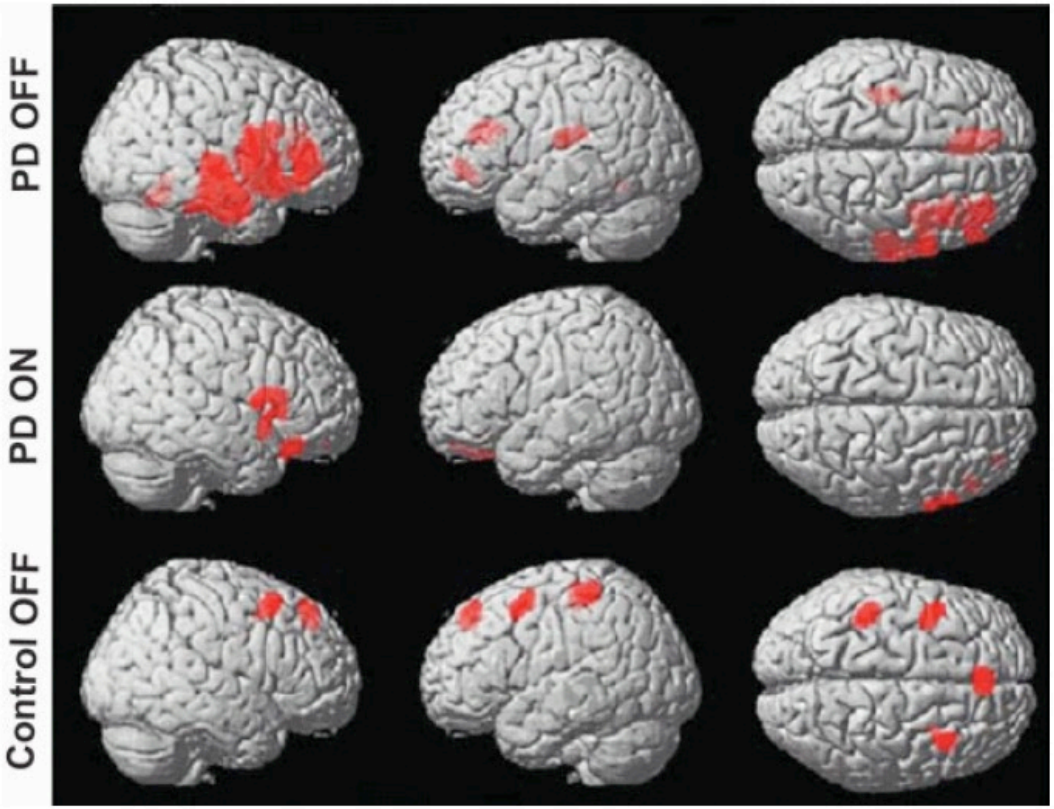
Table 1 Results from studies applying psychophysical and neurophysiological procedures to parkinsonian patients with and without pain under off conditions

Test, first author, year	Parkinsonian patients with pain versus healthy subjects	Pain-free parkinsonian patients versus healthy subjects	Parkinsonian patients with pain versus those without
Pain threshold to electrical stimuli			
Gerdelat-Mas (2007) [27]	Not done	Reduced threshold	Not done
Mylius (2009) [29]	Reduced threshold[b]	Reduced threshold	Similarly reduced threshold[b]
Zambito Marsala (2011) [14]	Reduced threshold[b,c]	Reduced threshold	Similarly reduced threshold[b,c]
Perrotta (2011) [28]	Not done	Reduced threshold	Not done
Pain threshold to cold water			
Brefel-Courbon (2005) [30]	Not done	Reduced threshold	Not done
Brefel-Courbon (2013) [31]	Reduced threshold[a]	Reduced threshold	Similarly reduced threshold[a]
Pain threshold to heat thermode			
Djaldetti (2004) [32]	Reduced threshold[a]	Reduced threshold	Lower threshold in patients with pain[a]
Schestatsky (2007) [33]	Reduced threshold[a]	Reduced threshold	Lower threshold in patients with pain[a]
Mylius (2009) [29]	Normal threshold[b]	Normal threshold	Similar threshold[b]
Pain threshold to laser CO_2			
Schestatsky (2007) [33]	Reduced threshold[a]	Normal threshold	Lower threshold in patients with pain[a]
Tinazzi (2008) [36]	Not done	Reduced threshold	Not done
Tinazzi (2009) [35]	Not done	Reduced threshold	Not done
Tinazzi (2010) [34]	Not done	Reduced threshold	Not done
Pain tolerance to electrical stimuli			
Zambito Marsala (2011) [14]	Reduced threshold[b,c]	Reduced threshold	Similarly reduced threshold[b,c]
NWR threshold			
Gerdelat-Mas (2007) [27]	Not done	Reduced threshold	Not done
Perrotta (2011) [28]	Not done	Reduced threshold	Not done
Mylius (2011) [39]	Reduced threshold[b]	Not done	Not done
Laser evoked potentials			
Tinazzi (2010, 2009, 2008) [34–36]	Reduced N2/P2 amplitude (b)	Reduced N2/P2 amplitude	Lower N2/P2 amplitude in pain patients[b]
Schestatsky (2007) [33]	Increased N2/P2 amplitude[a]	Normal N2/P2 amplitude	Increased N2/P2 amplitude in pain patients[a]

NWR, nociceptive withdrawal reflex.
Pain type: [a]primary central pain; [b]musculoskeletal pain; [c]peripheral neuropathic pain.

Reduced cold water Pth in pain-free PD





Using the cold water test, a PET study in pain-free PD patients documented a reduced pain threshold associated with an increased activation of brain structures involved in the processing of nociceptive stimuli, such as insula, prefrontal cortex, ACC that were normalized after acute L-dopa administration *(Brefel-Courbon et al. 2005)*

Reduced LEPs in pain–free PD

Pain 136 (2008) 117–124

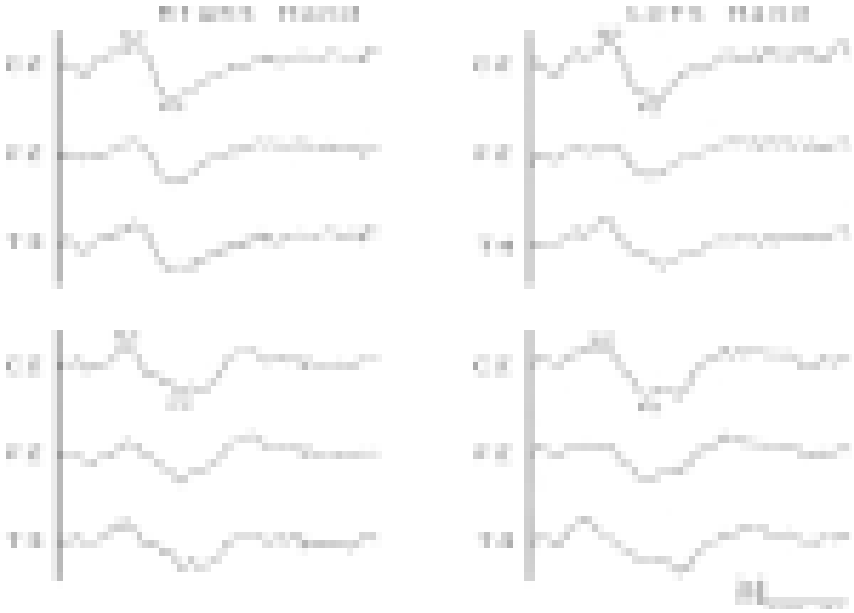
PAIN

www.elsevier.com/locate/pain

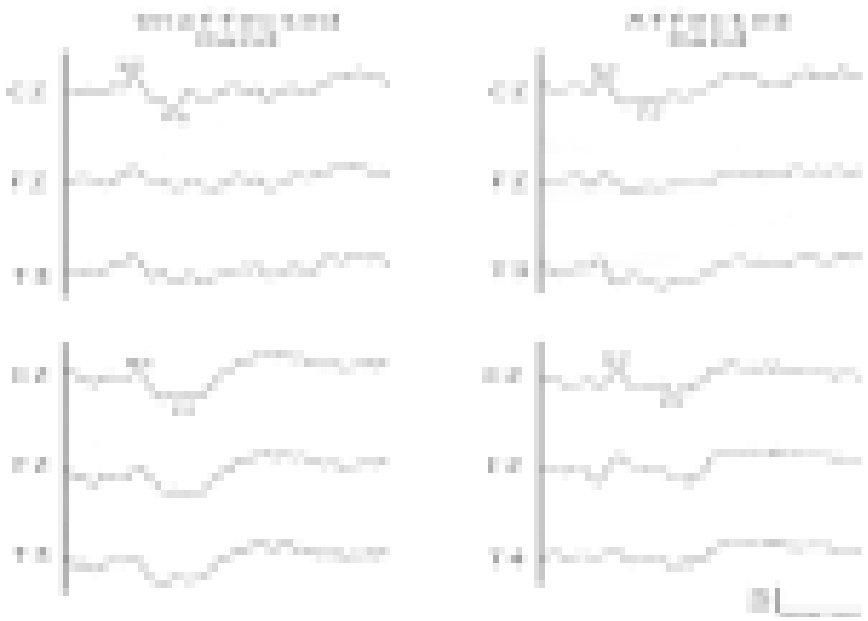
Abnormal processing of the nociceptive input in Parkinson's disease:
A study with CO_2 laser evoked potentials

Michele Tinazzi [a,b,*,1], Claudia Del Vesco [a,1], Giovanni Defazio [c],
Emiliana Fincati [b], Nicola Smania [a], Giuseppe Moretto [b], Antonio Fiaschi [a],
Domenica Le Pera [d], Massimiliano Valeriani [e]

LEPs from the hand in 2 Normal subjects

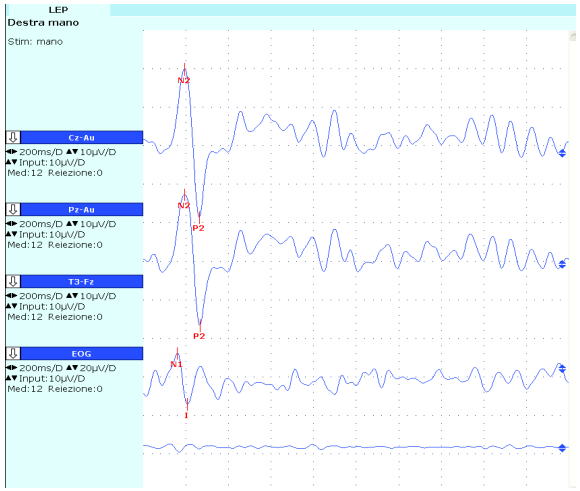


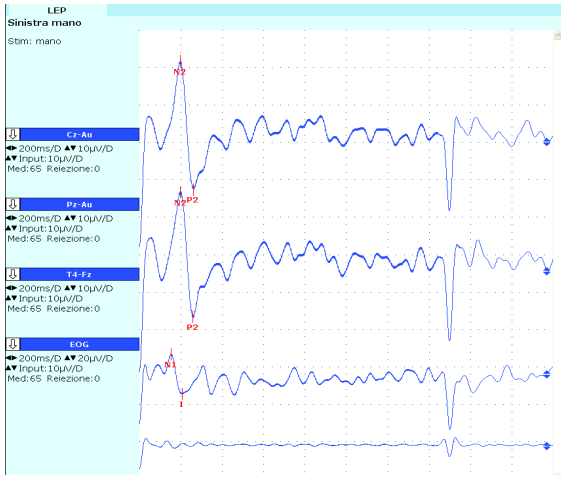
LEPs from the hand in 2 pain-free PD patients



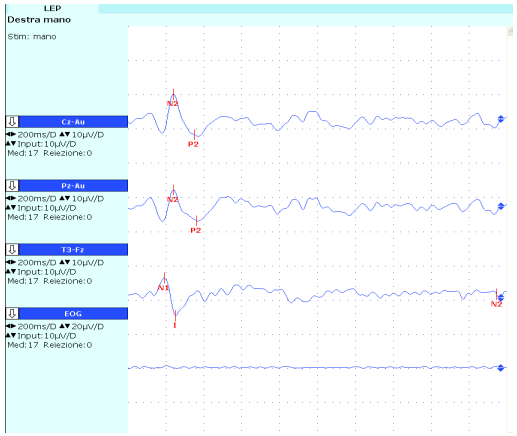
The N2/P2 amplitude was significantly lower in pain-free emiparkinsonian patients (regardless of the affected body side) than in controls. *(Tinazzi et al. 2008)*

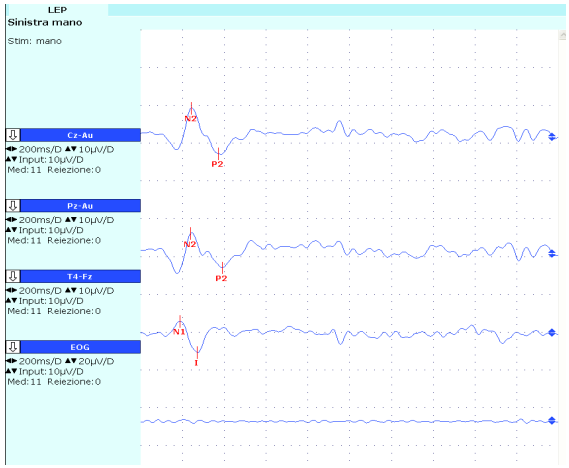
Normal



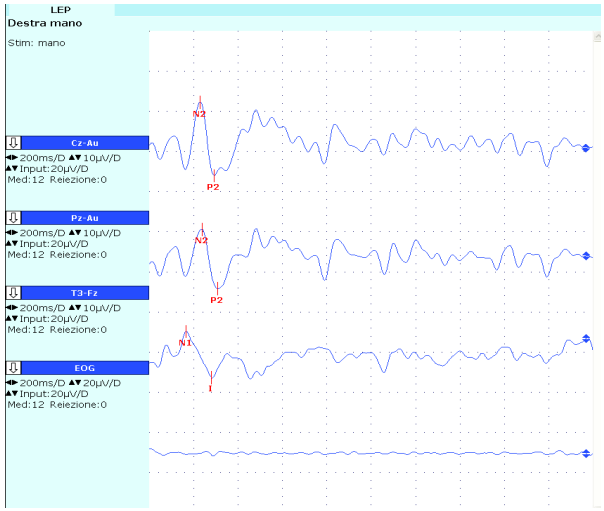


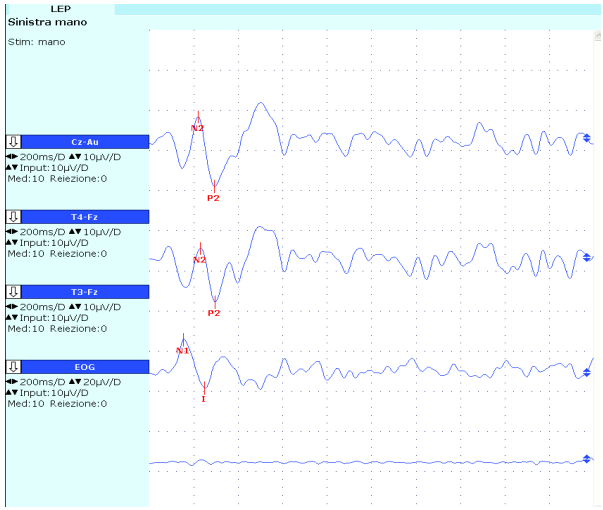
PD





PD





In both PD patients (13) and control subjects (12), laser stimulation (**YAP**) gave rise to a main negative N2/P2 complex at the vertex (which originates from the cingulate gyrus and insula) preceded by a lateralized N1/P1 response (originating from the opercolar cortex/SII).

N2/P2 peak-to-peak amplitude was significantly lower in PD patients (regardless of the clinically affected body side) than in controls.

The N1/P1 amplitude was not significant different between PD patients and control subjects.

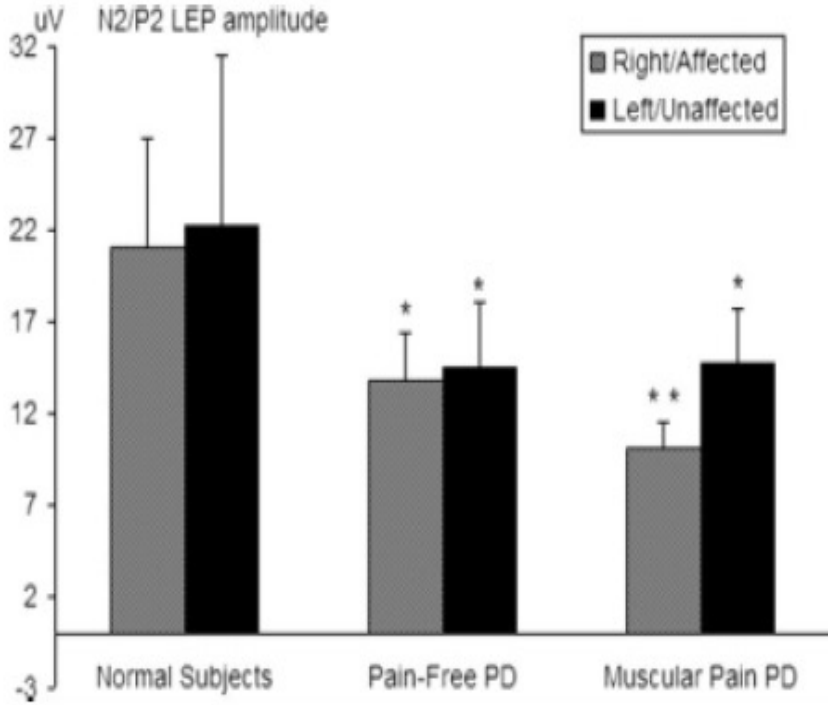
Tinazzi et al. 2017

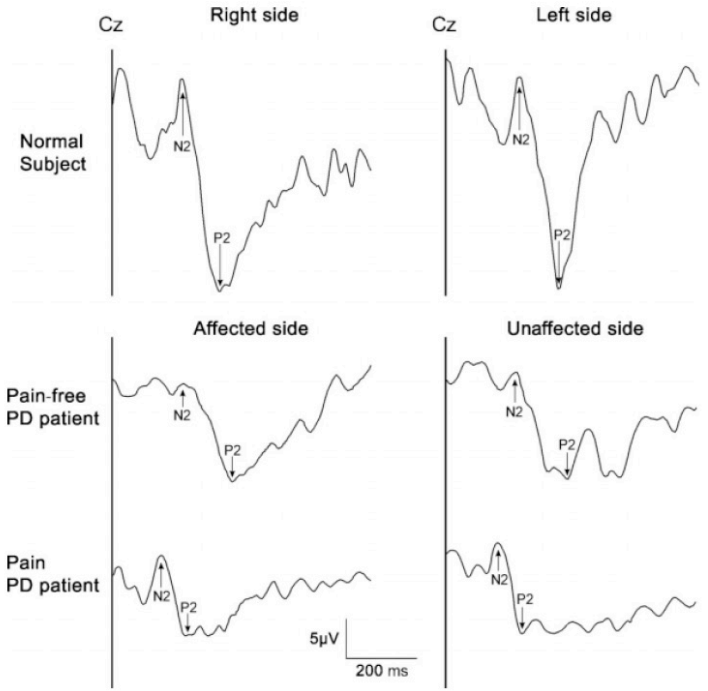
Movement Disorders
Vol. 25, No. 2, 2010, pp. 213–220

Muscular Pain in Parkinson's Disease and Nociceptive Processing Assessed With CO_2 Laser-Evoked Potentials

Michele Tinazzi, MD, PhD,[1,2] Serena Recchia, MD,[1*] Sara Simonetto, MD,[1]
Stefano Tamburin, MD, PhD,[1] Giovanni Defazio, MD, PhD,[3] Antonio Fiaschi, MD, PhD,[1]
Giuseppe Moretto, MD,[2] and Massimiliano Valeriani, MD[4]

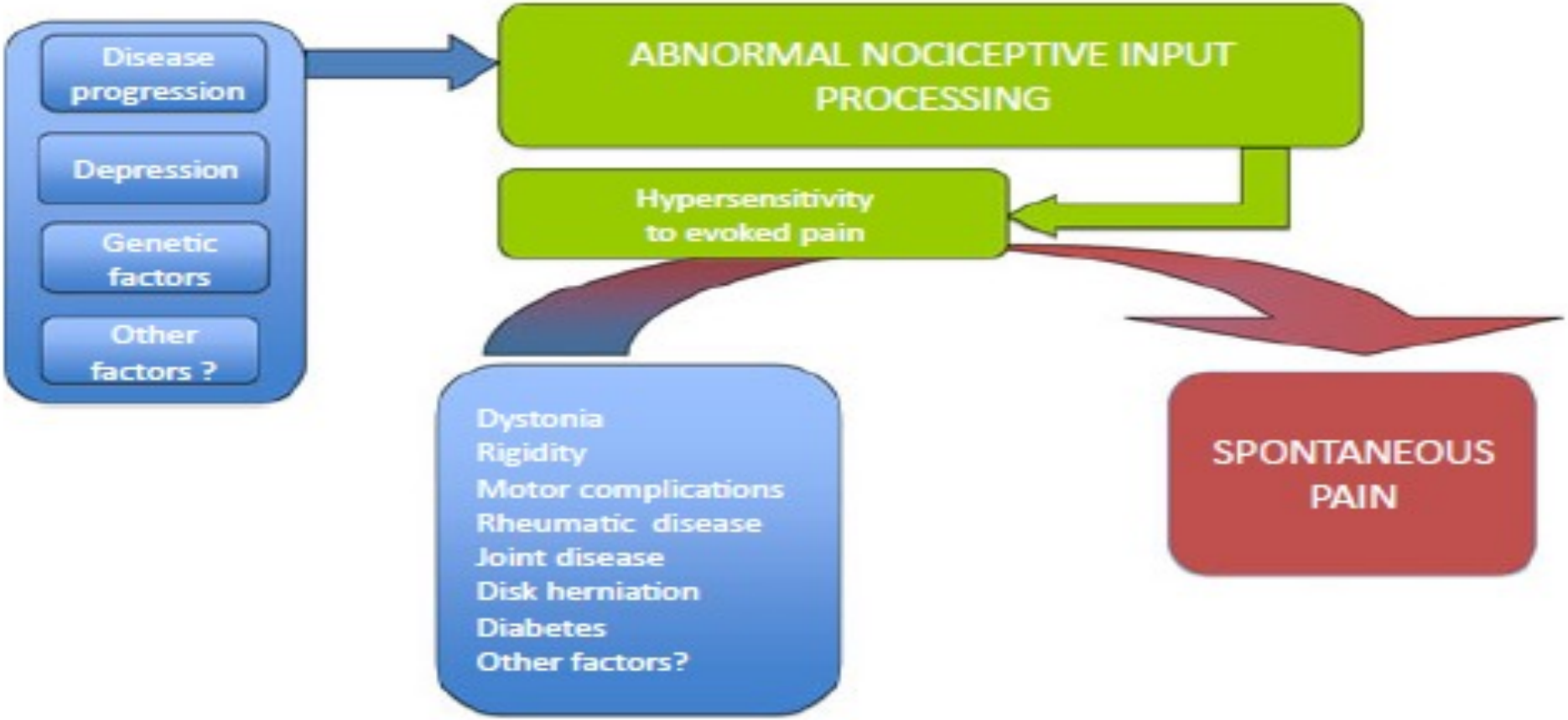
Reduced LEPs in PD with muscular pain





In both groups of PD (with and without pain), the mean N2/P2 amplitude was significantly reduced when compared with controls on both the affected and unaffected side.

Two mechanisms underlying pain in PD?



Defazio G, Tinazzi M, Berardelli A. Eur J Neurol, 2013

Targeting pain in Parkinson's disease

Angelo Antonini, Michele Tinazzi

Pain assessment

Curr Neurol Neurosci Rep (2016) 16:28
DOI 10.1007/s11910-016-0628-7

MOVEMENT DISORDERS (S FOX, SECTION EDITOR)

Integrated Approach for Pain Management in Parkinson Disease

Christian Geroin[1] · Marialuisa Gandolfi[1,2] · Veronica Bruno[3] · Nicola Smania[1,2] · Michele Tinazzi[4]

Clinical assessment of pain focuses on pain diagnosis and/or the assessment of specific clinical features (pain intensity, quality, and disability) to plan specific treatments.

No standardized, specific clinical assessments have been developed yet for the evaluation of pain in PD patients. Many clinical and instrumental measures were used in several observational/interventional studies involving patients with different types and qualities of pain both on and off medication.

Rotigotine Effects on Early Morning Motor Function and Sleep in Parkinson's Disease: A Double-Blind, Randomized, Placebo-Controlled Study (RECOVER)

Claudia Trenkwalder, MD,[1]* Bryan Kies, FCNeurol (SA),[2] Monika Rudzinska, MD,[3] Jennifer Fine, FCP (SA) Neurology,[4] Janos Nikl, MD,[5] Krystyna Honczarenko, MD,[6] Peter Dioszeghy, MD,[7] Dennis Hill, MD,[8] Tim Anderson, FRACP,[9] Vilho Myllyla, MD,[10] Jan Kassubek, MD,[11] Malcolm Steiger, FRCP,[12] Marco Zucconi, MD,[13] Eduardo Tolosa, MD,[14] Werner Poewe, MD,[15] Erwin Surmann, MSc,[16] John Whitesides, PhD,[17] Babak Boroojerdi, MD,[16] Kallol Ray Chaudhuri, DSc[18] and the RECOVER Study Group

TABLE 2. Mean change from baseline to end of treatment in the secondary outcomes, NADCS and number of nocturias, and the exploratory outcomes, NMS total and individual domain scores, BDI-II, Likert pain scale, PDQ-8, UPDRS Part II (FAS-observed cases)

	Mean (SD) baseline score		Mean (SD) change	
	Placebo	Rotigotine	Placebo	Rotigotine
NADCS	2.7 (2.1) (n = 89)	2.9 (2.2) (n = 178)	−0.7 (2.1) (n = 89)	−1.2 (1.8)[a] (n = 178)
Number of nocturias	2.0 (1.8) (n = 89)	1.9 (1.4) (n = 176)	−0.3 (1.6) (n = 89)	−0.3 (1.3) (n = 176)
NMS total score	41.3 (33.5) (n = 87)	41.1 (34.5) (n = 173)	−3.9 (25.5) (n = 86)	−10.3 (21.2)[a] (n = 172)
Individual NMS domain				
Cardiovascular	1.1 (1.9) (n = 89)	1.0 (1.9) (n = 178)	−0.2 (1.7) (n = 88)	0.0 (1.9) (n = 178)
Sleep/fatigue	9.1 (8.6) (n = 89)	9.5 (9.4) (n = 176)	−1.5 (6.2) (n = 88)	−3.7 (6.8)[b] (n = 176)
Mood/cognition	7.3 (10.0) (n = 89)	7.1 (9.3) (n = 178)	0.2 (11.1) (n = 88)	−3.0 (7.5)[c] (n = 178)
Perception/hallucinations	0.4 (1.4) (n = 89)	0.5 (1.7) (n = 178)	0.0 (1.3) (n = 88)	0.1 (2.4) (n = 178)
Attention/memory	3.9 (5.0) (n = 89)	4.5 (6.4) (n = 178)	0.0 (4.8) (n = 88)	−0.3 (4.6) (n = 178)
Gastrointestinal tract	4.2 (5.7) (n = 89)	3.6 (4.4) (n = 178)	0.0 (3.9) (n = 88)	−0.6 (2.6) (n = 178)
Urinary	6.7 (7.5) (n = 89)	6.6 (7.5) (n = 176)	−0.7 (5.0) (n = 88)	−1.1 (4.9) (n = 176)
Sexual function	3.9 (6.3) (n = 87)	3.7 (5.7) (n = 177)	−0.4 (4.3) (n = 86)	−0.2 (4.9) (n = 177)
Miscellaneous	5.1 (5.6) (n = 89)	4.8 (6.4) (n = 178)	−1.0 (4.2) (n = 88)	−1.3 (3.5) (n = 177)
BDI-II	12.6 (8.8) (n = 89)	12.3 (8.0) (n = 178)	−0.8 (7.6) (n = 89)	−2.7 (5.7)[a] (n = 177)
Likert pain scale	2.6 (2.5) (n = 89)	2.8 (2.4) (n = 178)	−0.1 (2.3) (n = 88)	−0.9 (2.2)[b] (n = 178)
PDQ-8	31.1 (17.0) (n = 89)	30.8 (18.2) (n = 177)	−1.2 (13.7) (n = 89)	−6.9 (11.9)[c] (n = 176)
UPDRS Part II	13.5 (6.3) (n = 89)	12.7 (5.6) (n = 178)	−1.3 (3.4) (n = 89)	−2.6 (3.6)[c] (n = 178)

[a]$P < 0.05$; [b]$P < 0.01$; [c]$P < 0.001$ for rotigotine-placebo treatment difference (ANCOVA; Exploratory Analyses).
BDI-II, Beck depression inventory; PDQ-8, short-form Parkinson's Disease questionnaire; NADCS, Nocturnal Akinesia, Dystonia and Cramps Score; NMS, Parkinson's Disease Nonmotor Symptom Assessment Scale; UPDRS, Unified Parkinson's Disease Rating Scale; FAS, Full Analysis Set.

Rotigotine had the effect to improve early-morning motor symptoms, sleep and pain.

RESEARCH ARTICLE

Movement Disorders, Vol. 30, No. 12, 2015

King's Parkinson's Disease Pain Scale, The First Scale for Pain in PD: An International Validation

K. Ray Chaudhuri, MD, DSc,[1,2,3] A. Rizos, MSc,[1*] C. Trenkwalder, MD, PhD,[4] O. Rascol, MD, PhD,[5] S. Pal, MD,[6] D. Martino, MD,[7] C. Carroll, MD,[8] D. Paviour, MD,[9] C. Falup-Pecurariu, MD,[10] B. Kessel, MD,[11] M. Silverdale, MD,[12] A. Todorova, MD,[1] A. Sauerbier, MD,[1] P. Odin, MD, PhD,[13,14] A. Antonini, MD, PhD,[15] and P. Martinez-Martin, MD, PhD,[16] on behalf of EUROPAR and the IPMDS Non Motor PD Study Group

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

Lancet Neurol 2015; 14: 1161–70

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*

We included patients aged 25 years or older, who had Hoehn and Yahr Stage II–IV Parkinson's disease, an average 24-h pain score of 6 or more on an 11-point numerical rating scale[29] over the 7 days before randomisation, severe pain in at least one subsection of the Chaudhuri and Schapira pain classification system (now known as the King's Parkinson's Disease Pain Scale),[30,31] and who were considered likely to benefit from

Clin Neuropharmacol. 2007 Jul-Aug;30(4):201-5.

The effect of duloxetine on primary pain symptoms in Parkinson disease.

Djaldetti R, Yust-Katz S, Kolianov V, Melamed E, Dabby R.

13 out of 20 patients improved

Journal of Neural Transmission
https://doi.org/10.1007/s00702-020-02218-7

NEUROLOGY AND PRECLINICAL NEUROLOGICAL STUDIES - ORIGINAL ARTICLE

Effects of safinamide on pain in Parkinson's disease with motor fluctuations: an exploratory study

Christian Geroin[1] · Ilaria A. Di Vico[1] · Giovanna Squintani[2] · Alessia Segatti[2] · Tommaso Bovi[2] · Michele Tinazzi[1]

Received: 13 April 2020 / Accepted: 12 June 2020

After 12 weeks of add-on safinamide therapy, a significant improvement was noted in the primary (KPPS, BPI Intensity and interference, and NRS) and the secondary outcomes (UPDRS III, IV, CGI, and PDQ39).

Safinamide has mainly a direct effect on pain in PD and only partially improves pain with an indirect effect secondary to the improvement in motor complications.

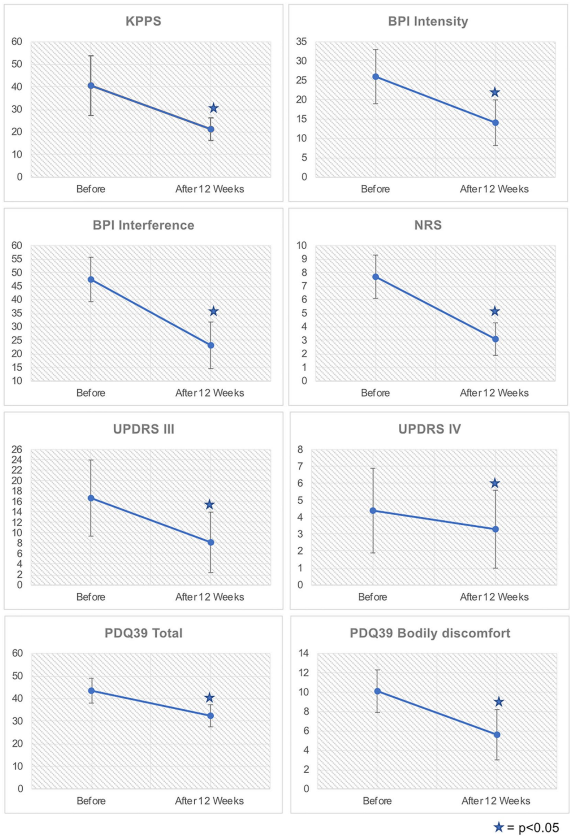


Fig. 1 Changes on the Kings Parkinson's Pain Scale (KPPS), the Brief Pain Inventory (BPI) intensity and interference, the 11-point Numeric Rating Scale (NRS), the Unified Parkinson's Disease Rating Scale (UPDRS parts III and IV), and the Parkinson's disease quality of life (PDQ39) total and subitem bodily discomfort before and after safinamide treatment. Plus–minus values are the mean ± standard deviation

Pain Treatment in PD

Pain treatment should target the:

1) mechanisms underlying the abnormal nociceptive input processing in the CNS

2) locoregional factors possibly triggering spontaneous pain in predisposed patients

REVIEW ARTICLE

European Journal of Neurology 2018, 25: 917–924, e67–e69

Pain in Parkinson's disease: facts and uncertainties

A. Antonini[a], M. Tinazzi[b], G. Abbruzzese[c], A. Berardelli[d,e], K. R. Chaudhuri[f], G. Defazio[g], J. Ferreira[h], P. Martinez-Martin[i], C. Trenkwalder[j] and O. Rascol[k]

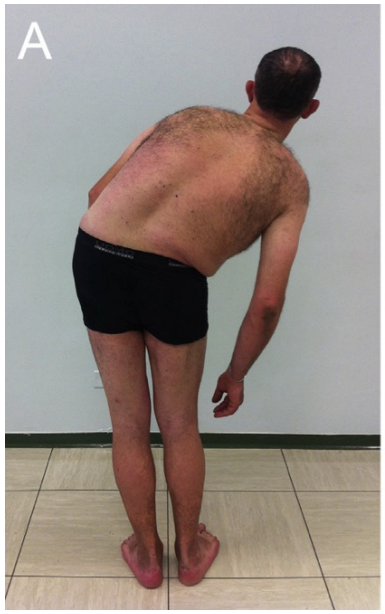
Pain Treatment in PD

Dopaminergic medication may relieve pain, particularly in patients with motor complications, by:
-normalizing pain processing abnormalities
-improving rigidity or bradykinesia.

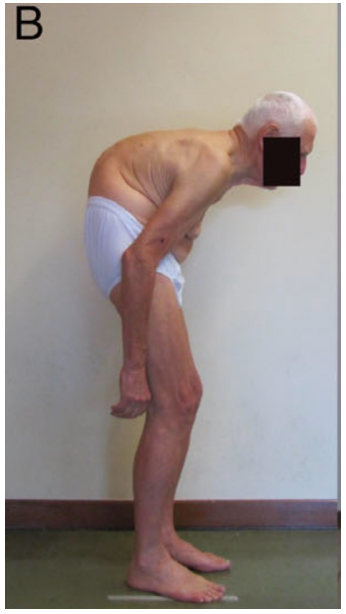
Drugs acting on non dopaminergic neurotransmitter systems known to contribute to pain processing mechanisms (i.e. glutammate, norepinephrine,) might be useful in managing pain in PD.

Axial postural abnormalities in Parkinsonism

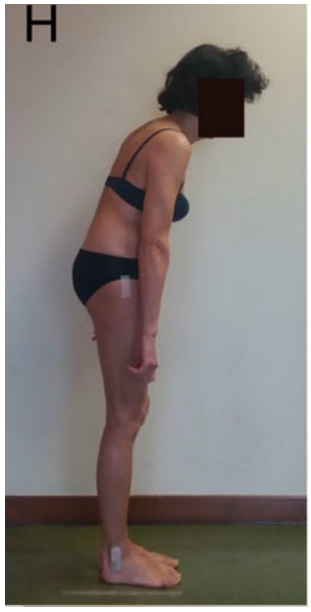
Pisa syndrome (PS)



Camptocormia (CC)

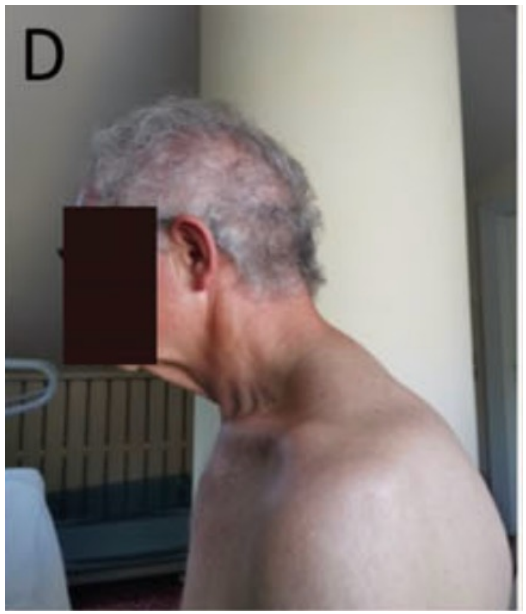


Thoracic fulcrum

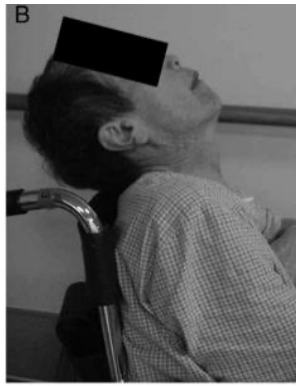


Lumbar fulcrum

Antecollis (AC)



Retrocollis



- Axial postural abnormalities are frequent and disabling manifestations complicating the clinical picture of patients with parkinsonism, appearing while sitting or standing, worsened during walking, and usually resolved in the lying position or during passive mobilization of the trunk (mobile deformity),
- Early detection and treatment of PA may **prevent** back pain, falls, and **fixed, unreversible deformities,** thereby avoiding complications that may arise from such conditions.

Doherty et al Lancet Neurol. 2011
Tinazzi et al Mov Disord 2016

Etiology and Time Course

Camptocormia/Antecollis

Box 1 Possible aetiologies of camptocormia

- Neurodegenerative diseases
  - Parkinson's disease[8–11]
  - Multiple system atrophy[12–14]
  - Dementia with Lewy bodies[15]
  - Alzheimer's disease[16]
- Dystonias
  - Dopa-responsive dystonia[17 18]
  - Segmental dystonia[19]
  - Generalised dystonia[19]
- Amyotrophic lateral sclerosis[20 21]
- Inherited myopathies
  - Facioscapulohumeral muscular dystrophy[22–24]
  - Myotonic dystrophy[25]
  - Duchenne muscular dystrophy[26]
  - Nemaline myopathy[27]
  - Myofibrillary myopathy[28]
  - Mitochondrial myopathy[29 30]
- Acquired myopathies
  - Polymyositis[31]
  - Hypothyroidism[32]
  - Inclusion body myositis[33 34]
- Myasthenia gravis[35 36]
- Chronic inflammatory demyelinating polyradiculoneuropathy[37]
- Medication-induced
  - Sodium valproate[38]
  - Clozapine[39]
  - Olanzapine[39 40]
  - Pramipexole[41]
  - Ropinirole[42]
- Lumbar disc herniation[43]
- Lentricular lesion due to stroke[44]
- Hiatal hernia[45]
- Radiotherapy-induced[46 47]
- Paraneoplastic process[48]
- Familial cerebellar hypoplasia[49]

Srivanitchapoom P, *et al*. *J Neurol Neurosurg Psychiatry* 2016;**87**:75–85.

Pisa syndrome

TABLE 1. Conditions associated with Pisa syndrome and proposed pathogenetic classification in Parkinson's disease

Category	Reference
Idiopathic (no underlying disease or exposure to medication)	8
Associated with medications	
Atypical antipsychotics (ie, sertindole, olanzapine clozapine)	3
Typical antipsychotics (ie, zotepine, chlorpromazine, haloperidol)	
Tricyclic antidepressants	
Selective serotonin reuptake inhibitors	
Cholinesterase inhibitors (ie, rivastigmine, donepezil)	
Antiemetic drugs	
Lithium carbonate	
Benzodiazepines	
Tiapride	
Associated with disorders of PNS	
Myasthenia gravis[b]	9
Associated with psychiatric diseases	
Schizophrenia[a] (exposed to antipsychotic drugs)	10,11
Associated with structural and other acquired disorders of CNS	
Postencephalitic parkinsonism[b]	12
Subacute sclerosing panencephalitis	13
Subdural haematoma[b]	14
Hashimoto's encephalopathy[a]	15
Associated with neurodegenerative diseases	
Multiple system atrophy[a]	5
Amyotrophic lateral sclerosis[a]	16
Dementia with Lewy bodies[a]	17
Presenile dementia[a]	1
Progressive supranuclear palsy[a,b]	18,19
Alzheimer's disease[a]	2,7,20-23
Huntington's disease[a]	24
Parkinson's disease	
Without apparent trigger	
Dystonic and/or myopathic mechanism and muscle atrophy	25-29
Impaired integration of vestibular and/or other sensory modalities	30-33
Scoliosis	34,35
Adverse effect of medication/surgery	
Dopaminergic therapy	36-42
Nondopaminergic therapies	21,43,44
Surgery (subthalamotomy, pallidotomy)	45-47

Tinazzi et. al *Movement* Disorders, Vol. 31, No. 12, 2016

Acute < 1 month: drug-induced, dystonias, lenticular vascular lesion

Subchronic ≥ 1 month < 3 months: myopathies, myasthenia gravis

Chronic ≥ 3 months: neurodegenerative diseases, myopathies

Epidemiology

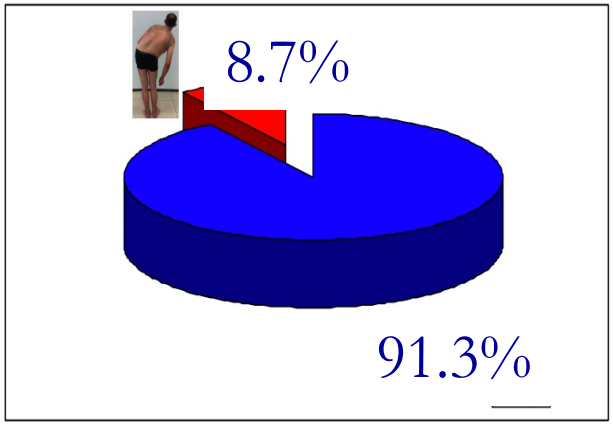
	Country	Number of patients with PD	Prevalence (%)	Diagnostic criteria
Camptocormia				
Abe et al[8]	Japan	153	18%	45° TL flexion
Tiple et al[6]	Italy	275	7%	45°TL flexion
Lepoutre et al[9]	France	700	3%	TL flexion
Ashour and Jankovic[1]	USA	164	12%	45° TL flexion
Antecollis				
Ashour and Jankovic[1]	USA	164	6%	>45° neck flexion
Yamada et al[10]	Japan	126	6%	NA
Kashihara et al[11]	Japan	252	6%	Neck flexion
Fujimoto[12]	Japan	131	5%	NA
Pisa syndrome				
Bonanni et al[13]	Italy	1400	2%	>15° lateral flexion
Tinazzi et al	Italy	1631	8.7%	≥ 10° lateral flexion

Doherty et al. Lancet Neurol 2011 Modified

Pisa syndrome in Parkinson disease

An observational multicenter Italian study

Michele Tinazzi, MD, PhD*
Alfonso Fasano, MD, PhD*
Christian Geroin, PT
Francesca Morgante, MD, PhD
Roberto Ceravolo, MD
Simone Rossi, MD, PhD
Astrid Thomas, MD, PhD
Giovanni Fabbrini, MD
Annarita Bentivoglio, MD, PhD
Filippo Tamma, MD
Giovanni Cossu, MD
Nicola Modugno, MD, PhD
Mario Zappia, MD
Maria Antonietta Volontè, MD
Carlo Dallocchio, MD
Giovanni Abbruzzese, MD
Claudio Pacchetti, MD
Roberto Marconi, MD
Giovanni Defazio, MD, PhD
Margherita Canesi, MD
Antonino Cannas, MD
Antonio Pisani, MD, PhD
Rina Mirandola, STAT MSc
Paolo Barone, MD, PhD
Carmine Vitale, MD, PhD*
On behalf of the Italian Pisa Syndrome Study Group



143/1631

Measurements of axial postural abnormalities

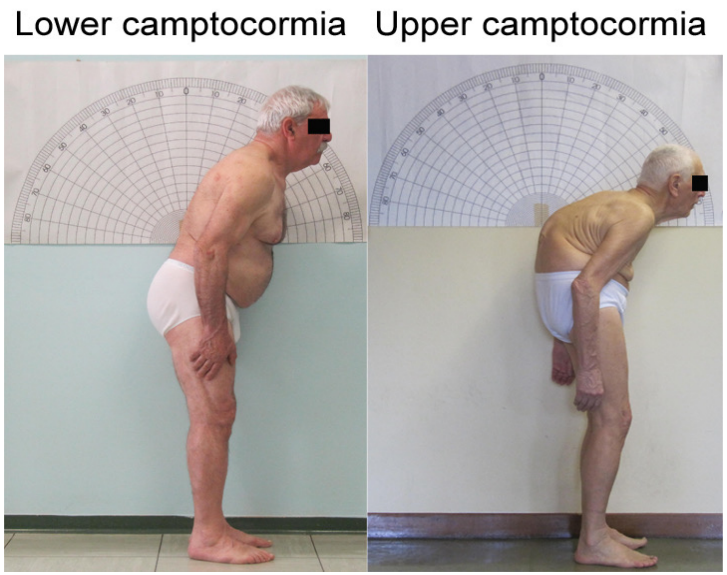
Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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

Diagnostic criteria for camptocormia in Parkinson's disease: A consensus-based proposal

Alfonso Fasano[a,b,*], Christian Geroin[c], Alfredo Berardelli[d], Bastiaan R. Bloem[e], Alberto J. Espay[f], Mark Hallett[g], Anthony E. Lang[a,b], Michele Tinazzi[h]



Experts reached consensus on camptocormia defined as:

- **lower (L1-Sacrum, hip flexion)** forward bending **angle ≥30°**
- **upper (C7 to T12-L1)** bending **angle ≥45°**

Parkinsonism and Related Disorders 53 (2018) 53–57

Parkinsonism and Related Disorders 52 (2018) 1–5

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

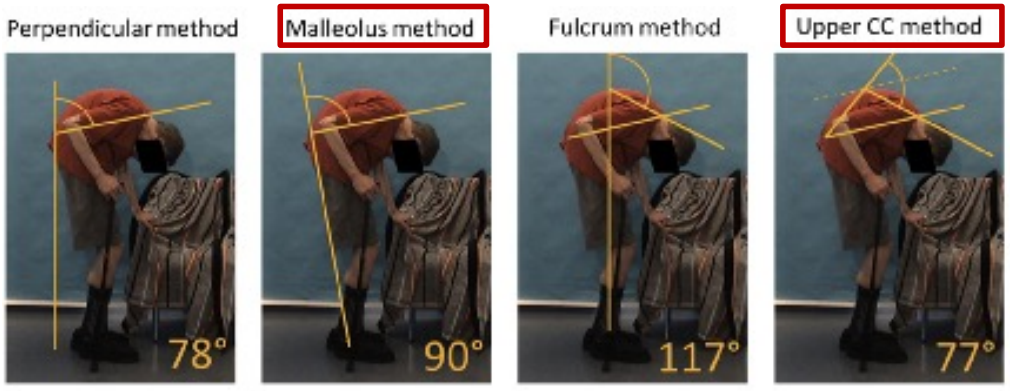
journal homepage: www.elsevier.com/locate/parkreldis

2018

Short communication

Consensus for the measurement of the camptocormia angle in the standing patient

Nils G. Margraf[a], Robin Wolke[a], Oliver Granert[a], Alfredo Berardelli[b], Bastian R. Bloem[c], Ruth Djaldetti[d], Alberto J. Espay[e], Alfonso Fasano[f,g,h], Yoshihiko Furusawa[i], Nir Giladi[j], Mark Hallett[k], Joseph Jankovic[l], Miho Murata[i], Michele Tinazzi[m], Jens Volkmann[n], Daniela Berg[a], Günther Deuschl[a,*]



Two expert raters analyzed the photographs of 39 PD patients with camptocormia while standing. They used **four different software-based methods** to determine the camptocormia angle. An **International Consensus Group** reviewed the results and drafted recommendations.

Lower Camptocormia: Malleolus Method

Upper Camptocormia: Upper CC Method

An **app** is provided on the web for these measurements (http://www.neurologie.uni-kiel.de/de/axial-posturale- stoerungen/camptoapp).

CENTERS

University of Verona
University of Pisa
University of Ancona
University of Chieti-Pescara
University of Trieste
University and Institute for Research and Medical Care IRCCS San Raffaele, Roma
University of Torino

Overall, the WG underestimated measurements, especially in lower FTF with an average of -8.66 ° (90% of cases).

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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

2019

Validity of the wall goniometer as a screening tool to detect postural abnormalities in Parkinson's disease

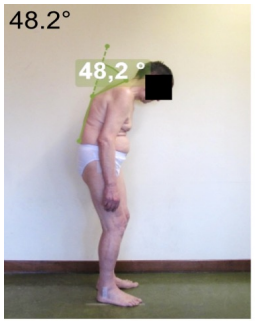
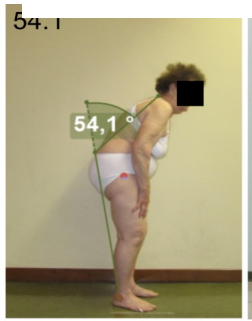
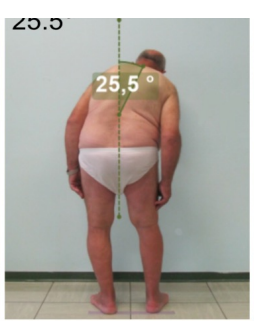
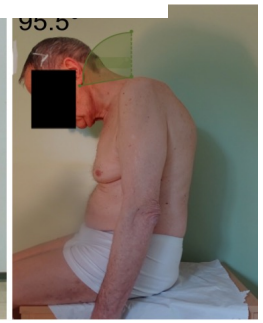
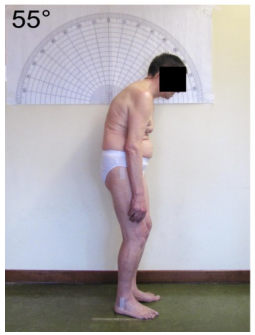
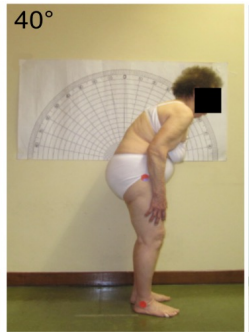
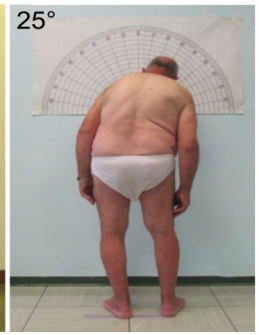
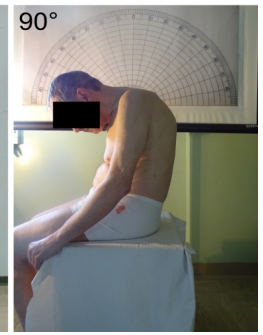
Michele Tinazzi[a], Marialuisa Gandolfi[b,c], Carlo Alberto Artusi[d], Ruggero Lanzafame[a], Elisabetta Zanolin[e], Roberto Ceravolo[f], Marianna Capecci[g], Elisa Andrenelli[g], Maria Gabriella Ceravolo[g], Laura Bonanni[h], Marco Onofrj[h], Roberta Telese[h], Claudio Bertolotti[i], Paola Polverino[i], Paolo Manganotti[i], Sonia Mazzucchi[f], Sara Giannoni[f], Laura Vacca[j], Fabrizio Stocchi[j], Miriam Casali[j], Maurizio Zibetti[d], Leonardo Lopiano[d], Alfonso Fasano[k,l], Christian Geroin[a,*]

Software-based measurements (Gold Standard)

Sensitivity (%) IC 95%

283 PTS

Wall goniometer measurements

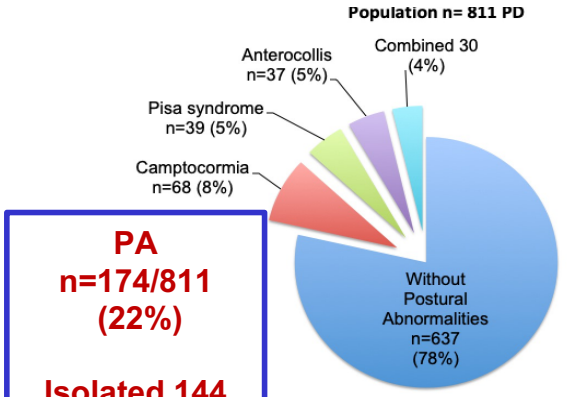
u-ATF	l-ATF	Lat-TF	ANF
			
76.67 (66.57; 84.94)	63.64 (40.66; 82.80)	100 (91.40; 100)	95.74 (85.46; 99.48)
			
n=188	n=40	n=88	n=61

Movement Disorders
CLINICAL PRACTICE
RESEARCH ARTICLE 2019

Postural Abnormalities in Parkinson's Disease: An Epidemiological and Clinical Multicenter Study

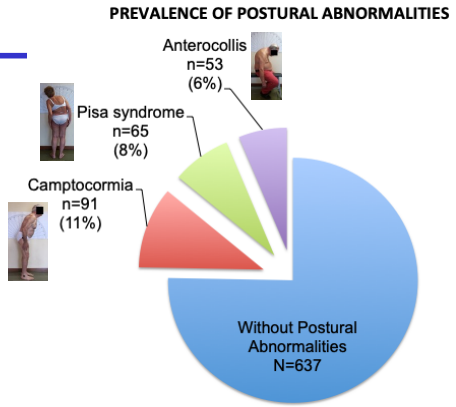
Michele Tinazzi, MD, PhD,[1] Marialuisa Gandolfi, MD, PhD,[2,3] Roberto Ceravolo, MD,[4] Marianna Capecci, MD, PhD,[5] Elisa Andrenelli, MD,[5] Maria Gabriella Ceravolo, MD, PhD,[5] Laura Bonanni, MD, PhD,[6] Marco Onofrj, MD,[6] Michela Vitale, MD,[6] Mauro Catalan, MD,[7] Paola Polverino, MD,[7] Claudio Bertolotti, MD,[7] Sonia Mazzucchi, MD,[4] Sara Giannoni, MD,[4] Nicola Smania, MD,[2,3] Stefano Tamburin, MD, PhD,[1] Laura Vacca, MD, PhD,[8] Fabrizio Stocchi, MD, PhD,[8] Fabiana G. Radicati, PhD,[8] Carlo Alberto Artusi, MD,[9] Maurizio Zibetti, MD, PhD,[9] Leonardo Lopiano, MD, PhD,[9] Alfonso Fasano, MD, PhD,[10,11] and Christian Geroin, PhD[1]*

CENTERS
University of Verona
University of Pisa
University of Ancona
University of Chieti-Pescara
University of Trieste
University and Institute for Research and Medical Care IRCCS San Raffaele, Roma
University of Torino



PA n=174/811 (22%)

Isolated 144
Combined 30



Diagnostic Criteria of PA

- u-CC ≥ 45°
- l-CC ≥ 30°
- PS ≥ 10°
- AC ≥ 45°

MULTIVARIATE ANALYSIS Predictors:

- Male gender
- Older age
- H&Y stage

International Parkinson and Movement Disorder Society

Task Force on Postural Abnormalities in Parkinsonism

December 2020- December 2022

International Parkinson and
Movement Disorder Society

International Parkinson and Movement Disorder Society

Advance.
Improve.
Educate.
Collaborate.

Task Force on Postural Abnormalities in Parkinsonism

Chairs

Michele Tinazzi MD, PhD

Roongroj Bhidayasiri, MD, PhD

Definitions and diagnostic criteria of axial postural abnormalities

Movement Disorders
CLINICAL PRACTICE
RESEARCH ARTICLE

Task Force Consensus on Nosology and Cut-Off Values for Axial Postural Abnormalities in Parkinsonism

MDS Podcast

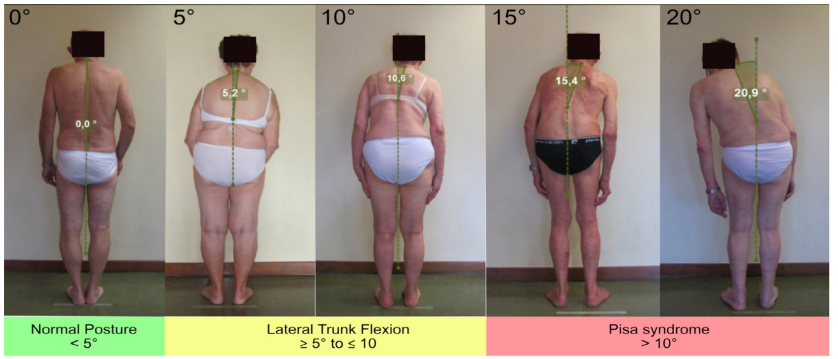
Michele Tinazzi, MD, PhD,[1,*] Christian Geroin, PhD,[1,*] Roongroj Bhidayasiri, MD, FRCP,[2,3] Bastiaan R. Bloem, MD, PhD,[4] Tamine Capato, PhD,[4,5] Ruth Djaldetti, MD,[6] Karen Doherty, MRCP,[7,8] Alfonso Fasano, MD, PhD,[9,10,11] Houyam Tibar, MD,[12] Leonardo Lopiano, MD, PhD,[13,14] Nils G. Margraf, MD, PhD,[15] Marcelo Merello, MD, PhD,[16] Caroline Moreau, MD, PhD,[17] Yoshikazu Ugawa, MD, PhD,[18] and Carlo Alberto Artusi, MD,[13,14] on behalf of the International Parkinson and Movement Disorders Society Task Force on Postural Abnormalities

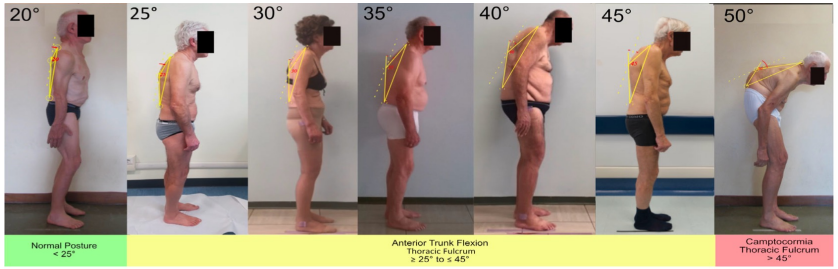
TABLE 1 *Questionnaire on Survey 1: nosology*

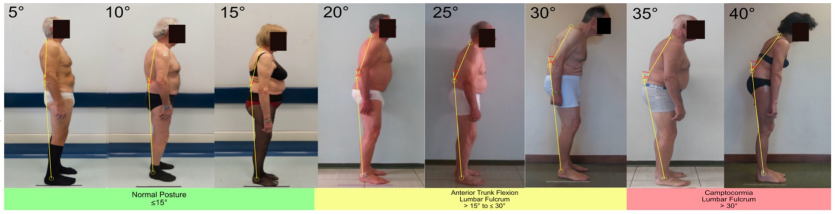
Abnormal postures, postural abnormalities, postural deviations, postural deformities, trunk asymmetry, trunk posture disturbances, trunk deformities, trunk flexion, bent spine, other (free enter)	
Side leaning, lateral bending, lateral flexion, lateral trunk deviation, lateral trunk bending, lateral trunk flexion, frontal plane trunk deformity, frontal plane trunk flexion, mild Pisa syndrome, early Pisa syndrome, pre Pisa syndrome, other (free enter)	
Forward bending, anterior trunk deviation, anterior trunk bending, anterior trunk flexion, sagittal plane trunk deformity, sagittal plane trunk flexion, stooped posture, mild camptocormia, early camptocormia, pre camptocormia, other (free enter)	
Anterior neck flexion, anterior neck bending, anterior neck deviation, mild antecollis/anterocollis, pre anterocollis/antecollis, other (free enter)	

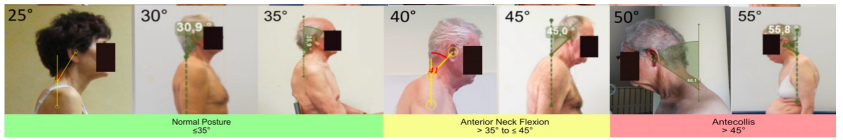
Cut-off values	
Coronal plane postural abnormalities	
<5°	Normal posture
≥5° to ≤10°	Lateral trunk flexion
>10°	Pisa syndrome
Sagittal plane postural abnormalities	
Thoracic	
<25°	Normal posture
≥25° to ≤45°	Anterior trunk flexion thoracic fulcrum (C7-T12 vertebrae)
>45°	Camptocormia thoracic fulcrum (C7-T12 vertebrae)
Lumbar	
≤15°	Normal posture
>15° to ≤30°	Anterior trunk flexion lumbar fulcrum (L1–L5 vertebrae, hip flexion)
>30°	Camptocormia lumbar fulcrum (L1–L5 vertebrae, hip flexion)
Cervical	
≤35°	Normal neck posture
>35° to ≤45°	Anterior neck flexion
>45°	Antecollis

MOVEMENT DISORDERS CLINICAL PRACTICE 2022. doi: 10.1002/mdc3.13460









Mild forms included

u- ATF ≥ 25°
l- ATF > 15°
Lat TF ≥ 5°
ANF > 35°

u-CC > 45°
l-CC > 30°
PS > 10°
AC > 45°

Measurements of axial postural abnormalities

Movement Disorders
CLINICAL PRACTICE

RESEARCH ARTICLE

Assessment of Axial Postural Abnormalities in Parkinsonism: Automatic Picture Analysis Software

Carlo Alberto Artusi, MD, PhD,[1,2] Christian Geroin, PhD,[3] Gabriele Imbalzano, MD,[1,2] Serena Camozzi, PT,[3] Stefano Aldegheri, PhD,[4] Leonardo Lopiano, MD, PhD,[1,2] Michele Tinazzi, MD, PhD,[3,] and Nicola Bombieri, PhD[4]*

MOVEMENT DISORDERS CLINICAL PRACTICE 2023. doi: 10.1002/mdc3.13692

sensors

MDPI

Article

Camera- and Viewpoint-Agnostic Evaluation of Axial Postural Abnormalities in People with Parkinson's Disease through Augmented Human Pose Estimation

Stefano Aldegheri [1], Carlo Alberto Artusi [2,3], Serena Camozzi [4], Roberto Di Marco [1,*], Christian Geroin [4], Gabriele Imbalzano [2,3], Leonardo Lopiano [2,3], Michele Tinazzi [4] and Nicola Bombieri [1]

Software-based measurements **(freeware NeuroPostureApp)** of axial PA in parkinsonism are the gold standard but may be time-consuming and not always feasible in clinical practice.

We developed and validated a new software based (AutoPosturePD (APP) to **perform automatic measures of axial PA.**

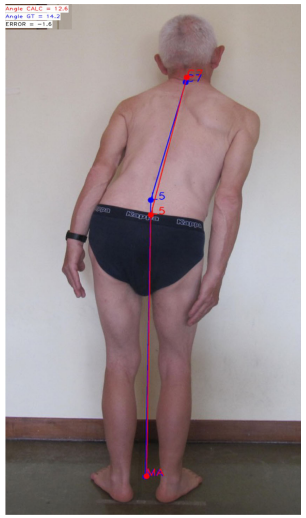


FIG. 2. Example of the angles calculated by the APP throughout the automatic identification of the patient's reference bones. APP, AutoPosturePD.

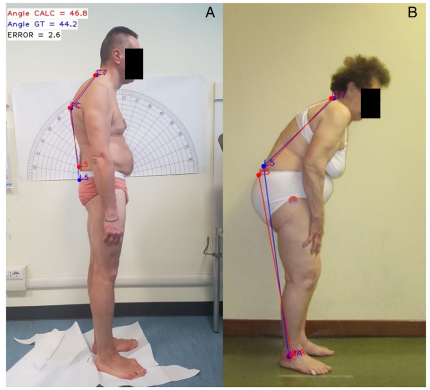


FIG. 4. An example of the angles calculated through the reference bones C7, L5, MA and C7, FC, and L5. The figure on the top left side reports the error of measurement between the angle calculated by the APP and through the key-points identified manually by the clinician. APP, AutoPosturePD. (A) Anterior trunk flexion - thoracic fulcrum. (B) Anterior trunk flexion - lumbar fulcrum.

Automatic video-analysis for measuring PA in dynamic conditions

Research questions

1. Does **posture change** in Parkinson's disease (PD) during **dynamic conditions** (e.g., standing, walking, performing dual tasks)?

2. Can we **reliably measure PA in dynamic conditions** and capturing PA changes by an automatic video-analysis?

Aims

1. **To systematically quantify changes of PA in parkinsonism during dynamic conditions**

2. **To validate an automatic video-analysis for measuring PA in patients with PD vs. the current gold standard**

Scoping Review

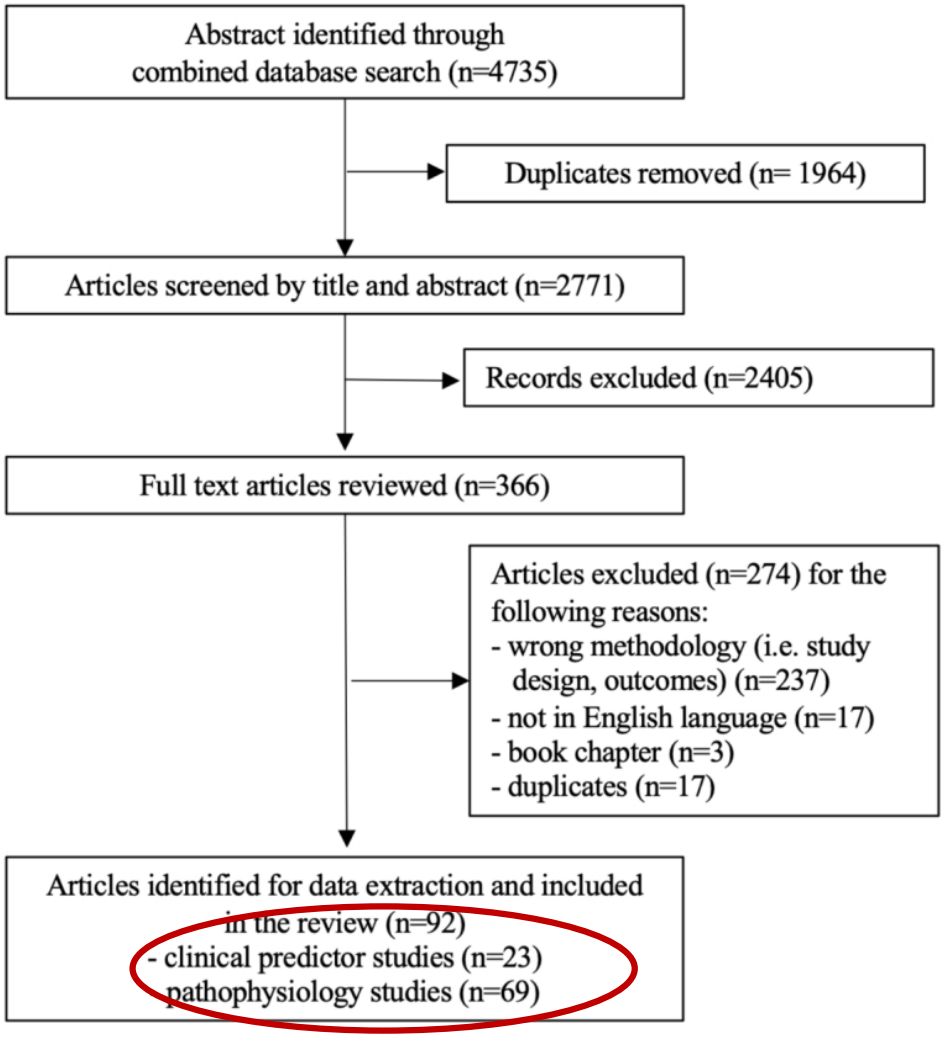


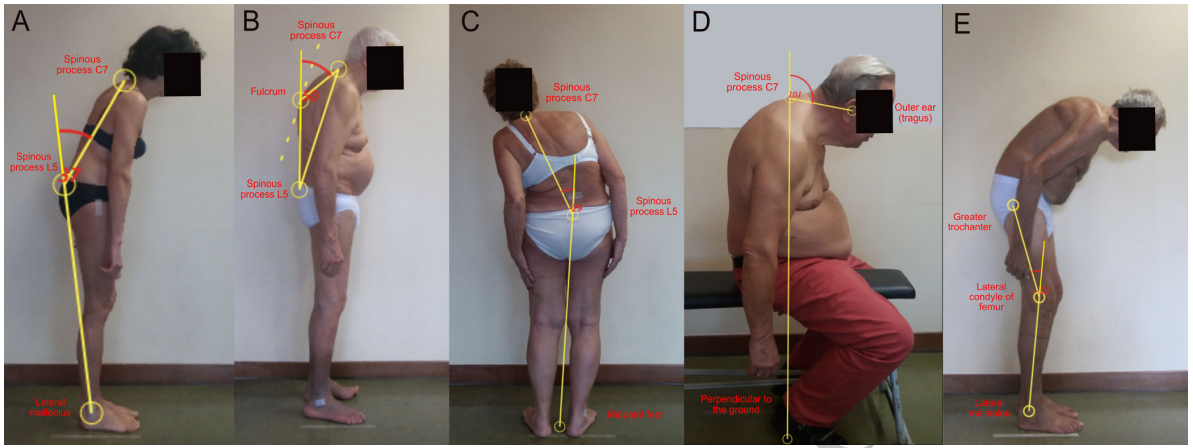
Fig. 1. Study flow chart: phases of the scoping review.

Artusi, Geroin,….and Tinazzi submitted to MDCP

2023

Axial Postural Abnormalities in Parkinsonism: Gaps in Predictors, Pathophysiology, and Management

Christian Geroin, PhD,[1*] Carlo Alberto Artusi, MD, PhD,[2] Jorik Nonnekes, MD, PhD,[3] Camila Aquino, MD, PhD,[4] Divyani Garg, MD, DM, DNB, MNAMS,[5,6] Marian L. Dale, MD, MRC,[7] Darbe Schlosser,[8] Yijie Lai, MD,[9] Mohammad Al-Wardat, PT, PhD,[10] Mehri Salari, MD, PhD,[11] Robin Wolke, MD,[12] Valery Tsinda Labou, PhD,[13] Gabriele Imbalzano, MD,[2] Serena Camozzi, PT,[1] Marcelo Merello, MD, PhD,[14] Bastiaan R. Bloem, MD, PhD,[15] Tamine Capato, PhD,[15,16] Ruth Djaldetti, MD,[17] Karen Doherty, MD, FRCP,[18,19] Alfonso Fasano, MD, PhD,[20,21,22] Houyam Tibar, MD,[23] Leonardo Lopiano, MD, PhD,[2,24] Nils G. Margraf, MD, PhD,[12] Caroline Moreau, MD, PhD,[25] Yoshikazu Ugawa, MD, PhD,[26] Roongroj Bhidayasiri, MD, FRCP,[27,28] Michele Tinazzi, MD, PhD,[1*] and on behalf of the International Parkinson and Movement Disorders Society Task Force on Postural Abnormalities,



Pathophysiology of axial postural abnormalities

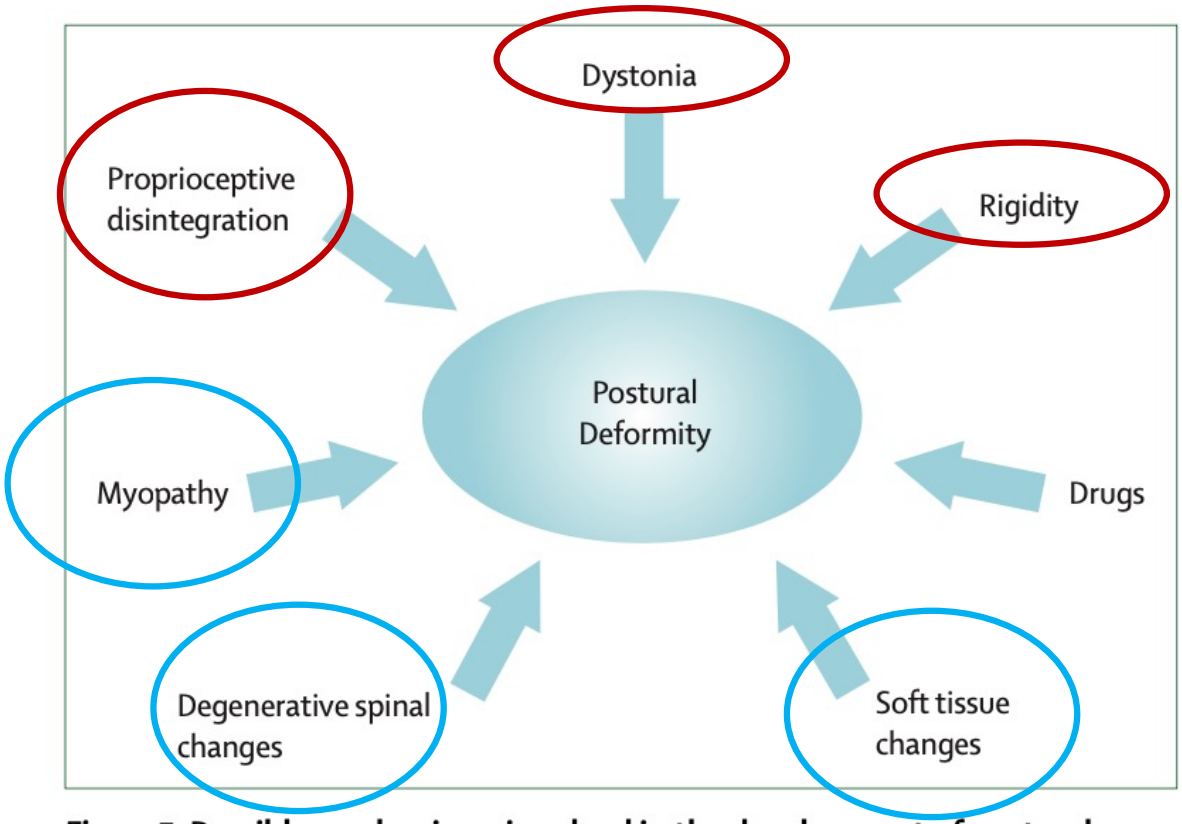


***Figure 5*: Possible mechanisms involved in the development of postural deformity in Parkinson's disease**

The pathophysiology of axial postural abnormalities in PD is not well understood, but a number of different causes have been proposed:

- **Central mechanisms**: dystonia, rigidity, and proprioceptive disintegration
- **Peripheral mechanisms**: myopathy, soft and skeletal tissue changes

Doherty et al. Lancet Neurol 2011
Tinazzi et al. Mov Disord 2016

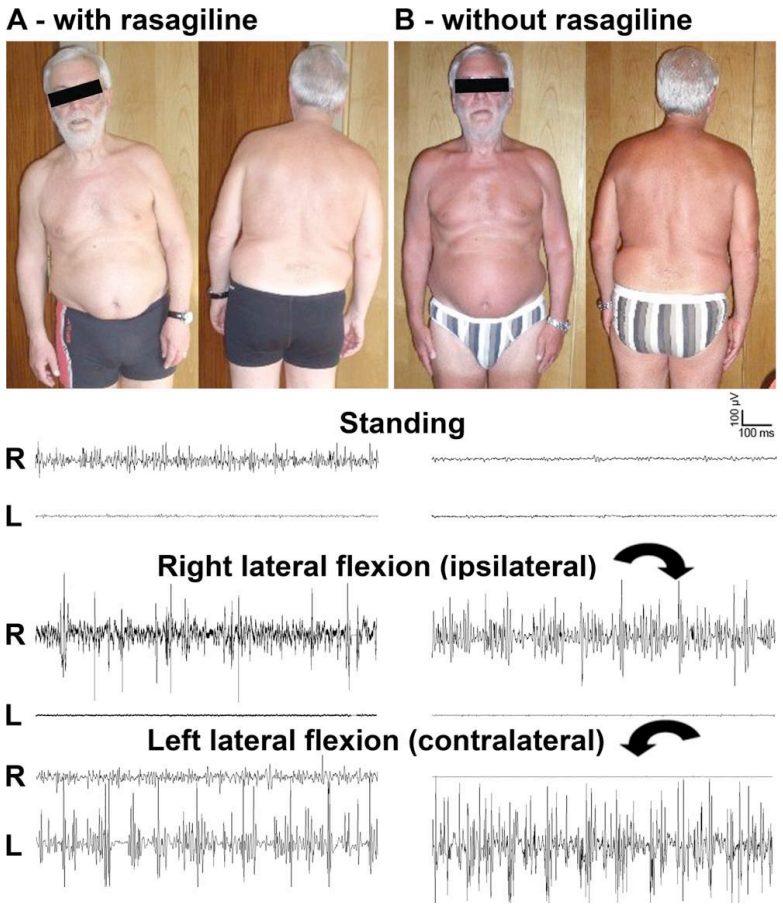
Pathophysiology of Pisa syndrome

LETTERS: NEW OBSERVATIONS

Reversible Pisa Syndrome in Patients with Parkinson's Disease on Rasagiline Therapy

Alfonso Fasano, MD, PhD[1,2*] Alessandro Di Matteo, MD,[3]
Carmine Vitale, MD, PhD,[4,5,6] Giovanna Squintani, MD,[3]
Laura Ferigo, MD,[3] Federica Bombieri, MD[3]
Gabriella Santangelo, PhD[6,7], Marianna Amboni, MD[4,5,6]
Paolo Barone, MD, PhD[5,6] and Michele Tinazzi, MD, PhD[3]

ID[a]	Sex	Age (y)	Disease duration (y)	Involved side at onset	PS direction	Bending degrees[b]
1	M	64	5	L	R	12°
2	M	73	5	L	L	11°
3	M	72	7	L	R	21°
4	F	67	5	L	R	23°



Rasagiline Therapy (1 mg)

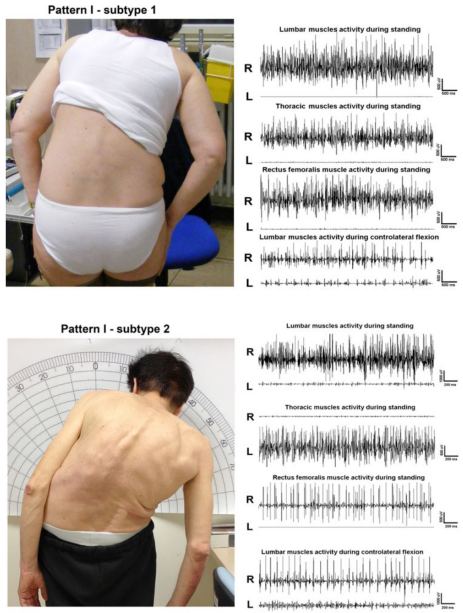
Pathophysiology of Pisa syndrome

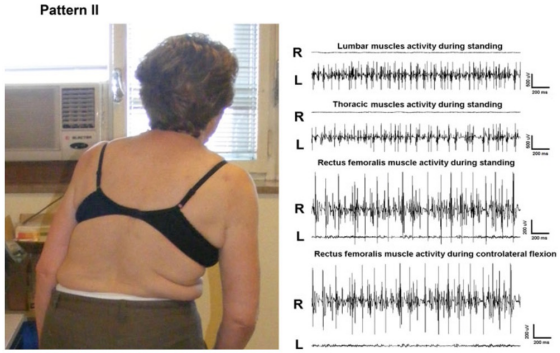
J Neurol (2013) 260:2138–2148
DOI 10.1007/s00415-013-6945-8

ORIGINAL COMMUNICATION

Pisa syndrome in Parkinson's disease: an electrophysiological and imaging study

Michele Tinazzi · Ina Juergenson · Giovanna Squintani · Gaetano Vattemi · Stefania Montemezzi · Daniela Censi · Paolo Barone · Tommaso Bovi · Alfonso Fasano





Two different electromyographical patterns:

- **1) hyperactivity of paraspinals (lumbar and thoracic) ipsilateral** to the trunk lateral flexion (30% of cases)
- **2) hyperactivity** of **non-paraspinal muscles** (e.g., external oblique muscles, rectus femoris, iliopsoas) **ipsilateral** to the trunk lateral flexion (70% of cases)

- **hyperactivity** of paraspinal muscles contralateral to the side of flexion may have a compensatory action to further limit trunk bending.

MUSCLE ATROPHY (probably caused by secondary mechanisms)

- **Ipsilateral bending side: muscle disuse**
- **Contralateral bending side: muscle stretching stress**

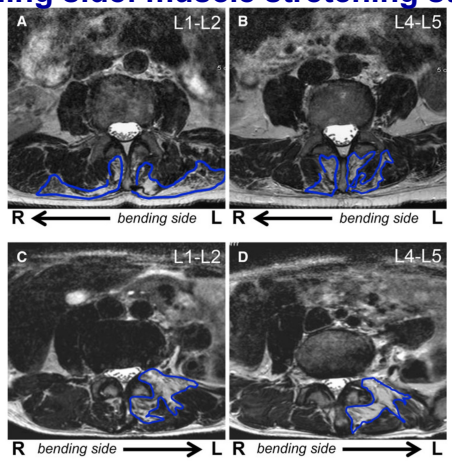


Fig. 5 Axial TSE T2-weighted MRI images at lumbar level showing atrophic involution of paraspinal muscles in two representative patients with different EMG patterns; atrophy is highlighted by *blue contours*. A–B) Case 1 (Pattern I-subtype 1): atrophic involution can be observed on both sides, even though a slight difference can be seen; fat involution is more evident on the *left side* (moderate atrophy—between 30 and 50 %) than on the right side (mild atrophy—less than 30 %). C–D) Case 11 (Pattern II): severe atrophy (more than 50 %) and fat involution are demonstrated on the *left side*

Pathophysiology of Camptocormia

Parkinsonism and Related Disorders 71 (2020) 28–34

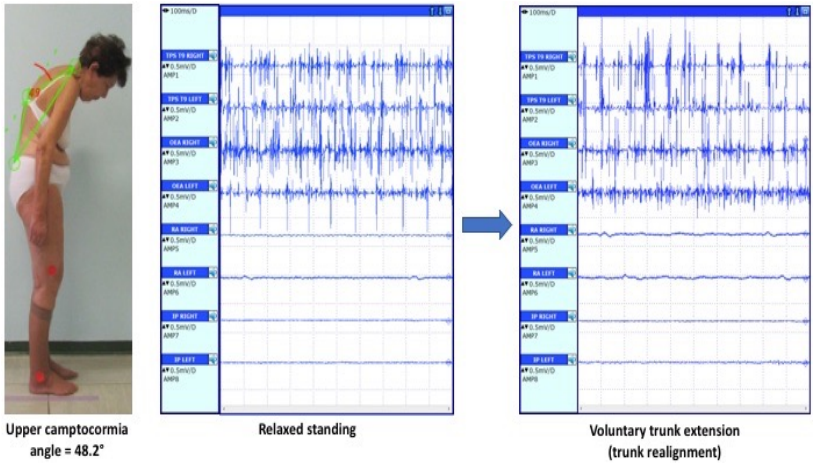
Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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

Upper camptocormia in Parkinson's disease: Neurophysiological and imaging findings of both central and peripheral pathophysiological mechanisms

Francesca Magrinelli[a,*], Christian Geroin[a], Giovanna Squintani[b], Marialuisa Gandolfi[c], Giulio Rizzo[d], Marco Barillari[d], Gaetano Vattemi[a], Francesca Morgante[e,f], Michele Tinazzi[a]



Thoracic paraspinal muscles (T9 level)		UCC (*n* = 10)	PD (*n* = 10)	*p* Value
EMG (relaxed standing)	%MVC (%)	24.7 ± 18.6	16.8 ± 15.4	0.280
Multi-MUP analysis	Mean duration (ms)	8.5 ± 0.7	9.5 ± 0.6	**0.005***
	Mean amplitude (μV)	1214.3 ± 274.8	1604.3 ± 239.3	**0.004***
	Polyphasic MUPs (%)	7.9 ± 5.0	9.8 ± 6.9	0.579
MRI	Area (mm^2)	3455.3 ± 1303.0	3621.2 ± 1301.5	0.579
	Fat fraction (%)	17.5 ± 17.2	10.8 ± 8.1	0.684

Hyperactivity of OEA might sustain UCC in PD.

Concurrent **mild myopathic changes** in **TPS muscles** in PD with UCC may be secondary to muscle disuse

Impaired proprioception

Hindawi
Parkinson's Disease
Volume 2019, Article ID 9026890, 7 pages
https://doi.org/10.1155/2019/9026890

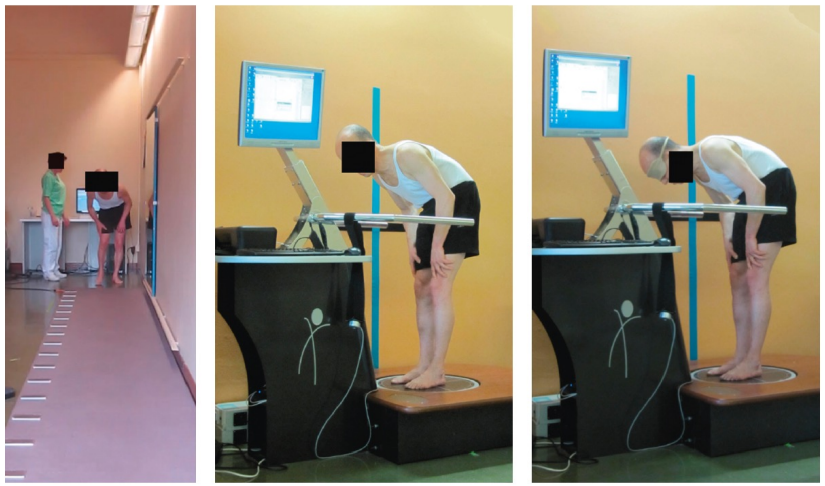
Research Article

Do Upper and Lower Camptocormias Affect Gait and Postural Control in Patients with Parkinson's Disease? An Observational Cross-Sectional Study

Christian Geroin,[1,2] Marialuisa Gandolfi,[2,3] Isacco Maddalena,[3] Nicola Smania,[2,3] and Michele Tinazzi[1,2]

PD Patients: **16 Upper CC, 14 Lower CC, 16 without CC.**

Conclusions: patients with **Lower CC** were associated with **more severe gait and postural control impairment** than patients with Upper CC or without CC.



(a) (b) (c)

Figure 1: A patient with lower CC during the gait (a) and posturographic assessment with eyes open (b) and eyes closed condition (c).

Pharmacological and non-pharmacological treatment

- Optimization of PD therapy (remove the prescribed dopaminergic therapy potentially associated with subacute onset of axial PA)
- Withdrawal of non-PD therapies (in suspected drug-induced PA)
- Lidocaine injection
- **Botulinum toxin injection**
- Rehabilitation
- Pallidotomy and DBS targeting the STN and Gpi
- Orthopedic surgical correction

Optimization of PD therapy

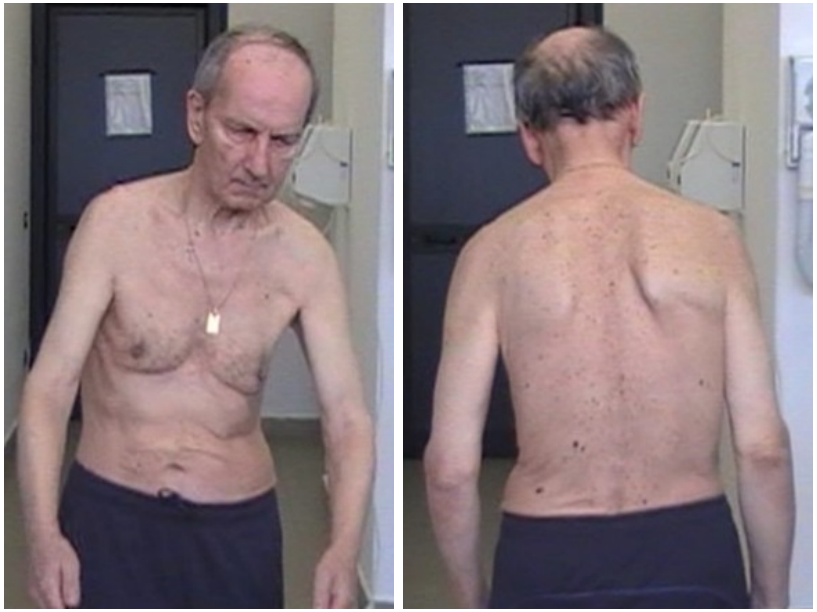
Reversible Pisa Syndrome in Patients with Parkinson's Disease on Rasagiline Therapy

Alfonso Fasano, MD, PhD[1,2*] Alessandro Di Matteo, MD,[3]
Carmine Vitale, MD, PhD,[4,5,6] Giovanna Squintani, MD,[3]
Laura Ferigo, MD,[3] Federica Bombieri, MD[3]
Gabriella Santangelo, PhD[6,7], Marianna Amboni, MD[4,5,6]
Paolo Barone, MD, PhD[5,6] and Michele Tinazzi, MD, PhD[3]

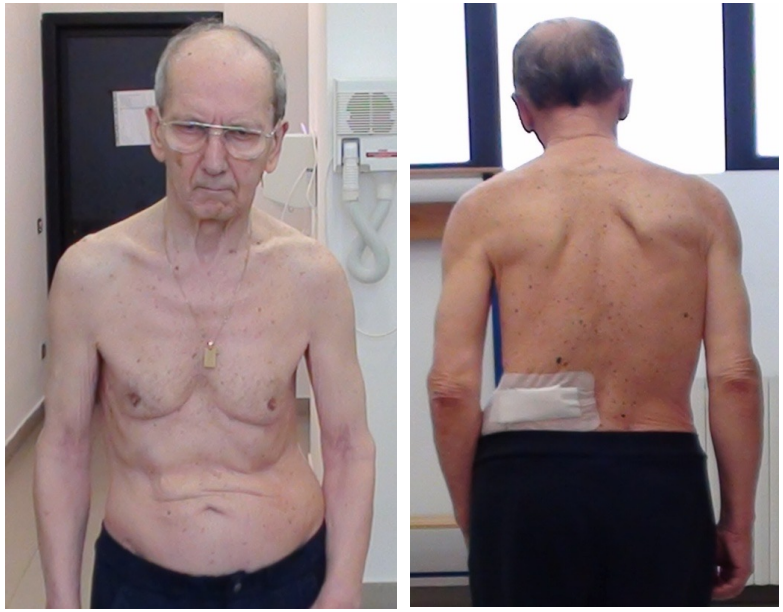
Rasagiline

ID[a]	Sex	Age (y)	Disease duration (y)	Involved side at onset	PS direction	Bending degrees[b]
1	M	64	5	L	R	12°
2	M	73	5	L	L	11°
3	M	72	7	L	R	21°
4	F	67	5	L	R	23°

A – with rasagiline



B – without rasagiline



Lidocaine injection

Parkinsonism and Related Disorders 19 (2013) 350–354

Contents lists available at SciVerse ScienceDirect

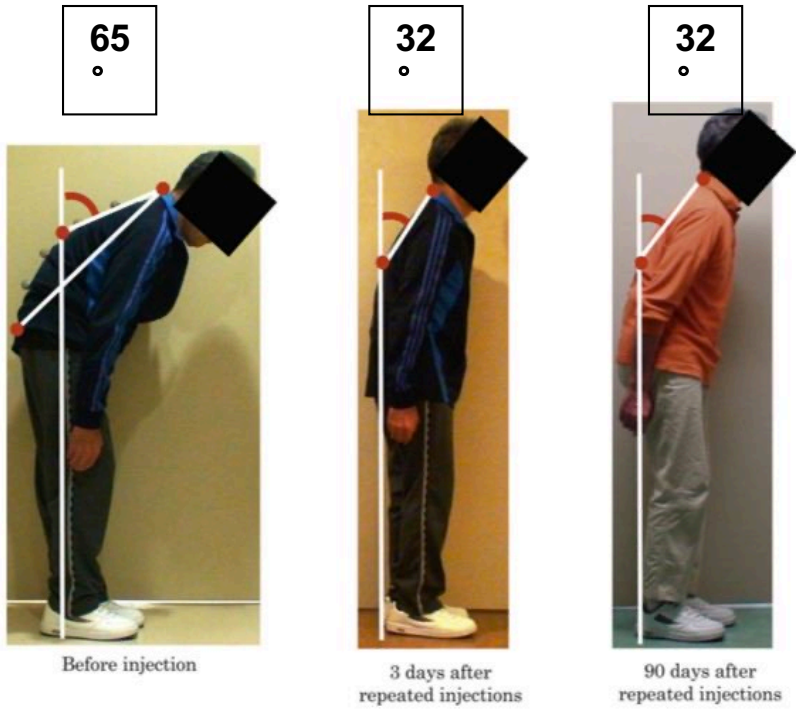
Parkinsonism and Related Disorders

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

Short communication

Long-term effect of repeated lidocaine injections into the external oblique for upper camptocormia in Parkinson's disease

Yoshihiko Furusawa [a,d,*], Yohei Mukai [a], Tomoya Kawazoe [a], Terunori Sano [a], Harumasa Nakamura [a], Chikako Sakamoto [b], Yasuyuki Iwata [b], Mizuki Wakita [b], Yasuhiro Nakata [c], Kohei Kamiya [c], Yoko Kobayashi [b], Takashi Sakamoto [a], Yoshihisa Takiyama [d], Miho Murata [a]



Repeated lidocaine injections into the **external oblique of 12 PD patients for 4-5 days** and **evaluated** the effects of such treatment for up to **90 days**.

↓

Repeated injections produced long-term improvement in **9 out of 12** patients (**from 62.1° ± 13.4° to 49.0° ±18.5) (75%)**, which **was maintained during the 90-day observation period in 8** of these patients.

↓

Repeated lidocaine injections into the external oblique muscle have therapeutic effect on upper camptocormia

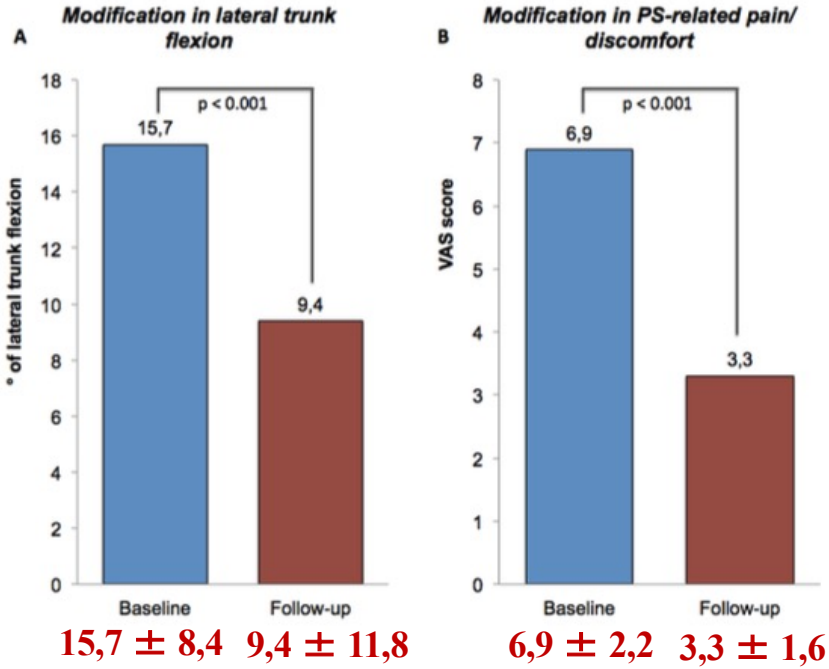
Botulinum toxin injection

Parkinsonism and Related Disorders 62 (2019) 231–235

Botulinum toxin for Pisa syndrome: An MRI-, ultrasound- and electromyography-guided pilot study

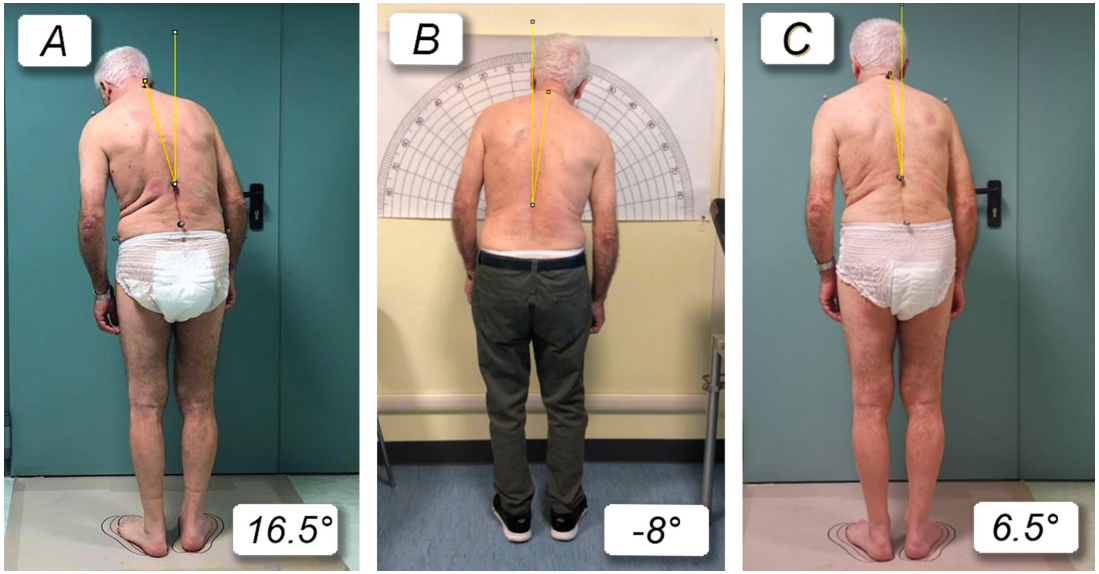
Carlo Alberto Artusi[a,1], Sara Bortolani[a,1], Aristide Merola[b], Maurizio Zibetti[a], Marco Busso[c], Stefania De Mercanti[d], Paolo Arnoffi[c], Simone Martinetto[c], Elena Gaidolfi[e], Andrea Veltri[c], Pierangelo Barbero[d], Leonardo Lopiano[a,*]

13 PD patients



15,7 ± 8,4 9,4 ± 11,8 6,9 ± 2,2 3,3 ± 1,6

A: before BoNT **B: 10 days after BoNT** **C: 1 month after BoNT**



Rehabilitation + Botulinum toxin injection

Parkinsonism and Related Disorders 20 (2014) 1140–1144

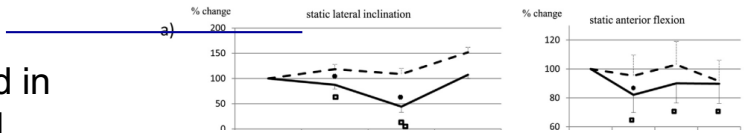
Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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

Botulinum toxin type A potentiates the effect of neuromotor rehabilitation of Pisa syndrome in Parkinson disease: A placebo controlled study

C. Tassorelli [a, d, *], R. De Icco [a, d], E. Alfonsi [b], M. Bartolo [e], M. Serrao [f], M. Avenali [a, d], I. De Paoli [a, d], C. Conte [g], N.G. Pozzi [c], P. Bramanti [h], G. Nappi [a, b, c], G. Sandrini [a, d]

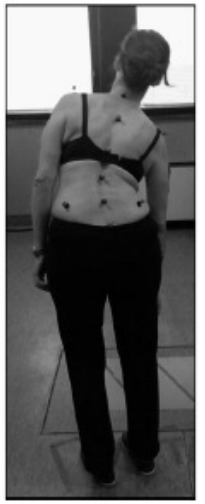


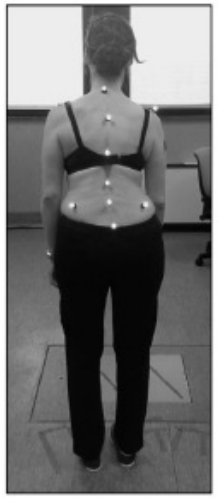
26 PD+PS patients were enrolled in a randomized placebo-controlled trial.

group A was treated with iBTA before undergoing CT (a 4-week intensive programme)
group B received **saline** before the 4-week CT treatment.

Patients were evaluated at baseline, **1, 3 and 6 months** with kinematic analysis of movement, UPDRS, and VAS for pain.

At the end of the rehabilitation period, group A showed a significantly more marked reduction in pain score as compared with group B and a more prolonged efficacy on several clinical and kinematic variables.





Rehabilitation

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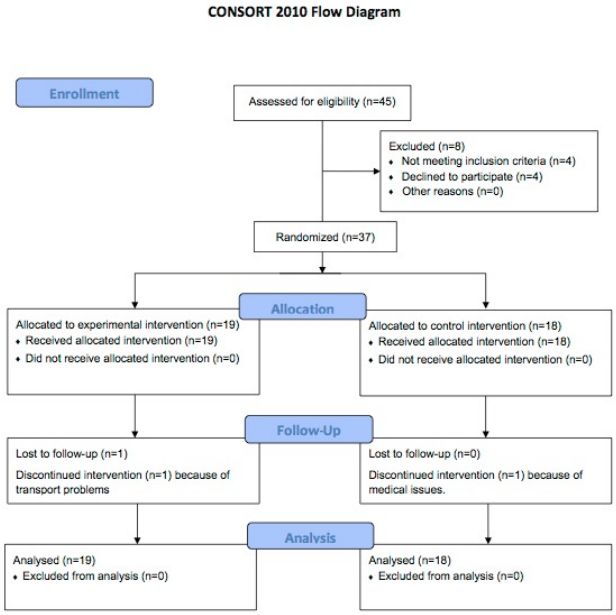
Four-week trunk-specific exercise program decreases forward trunk flexion in Parkinson's disease: A single-blinded, randomized controlled trial

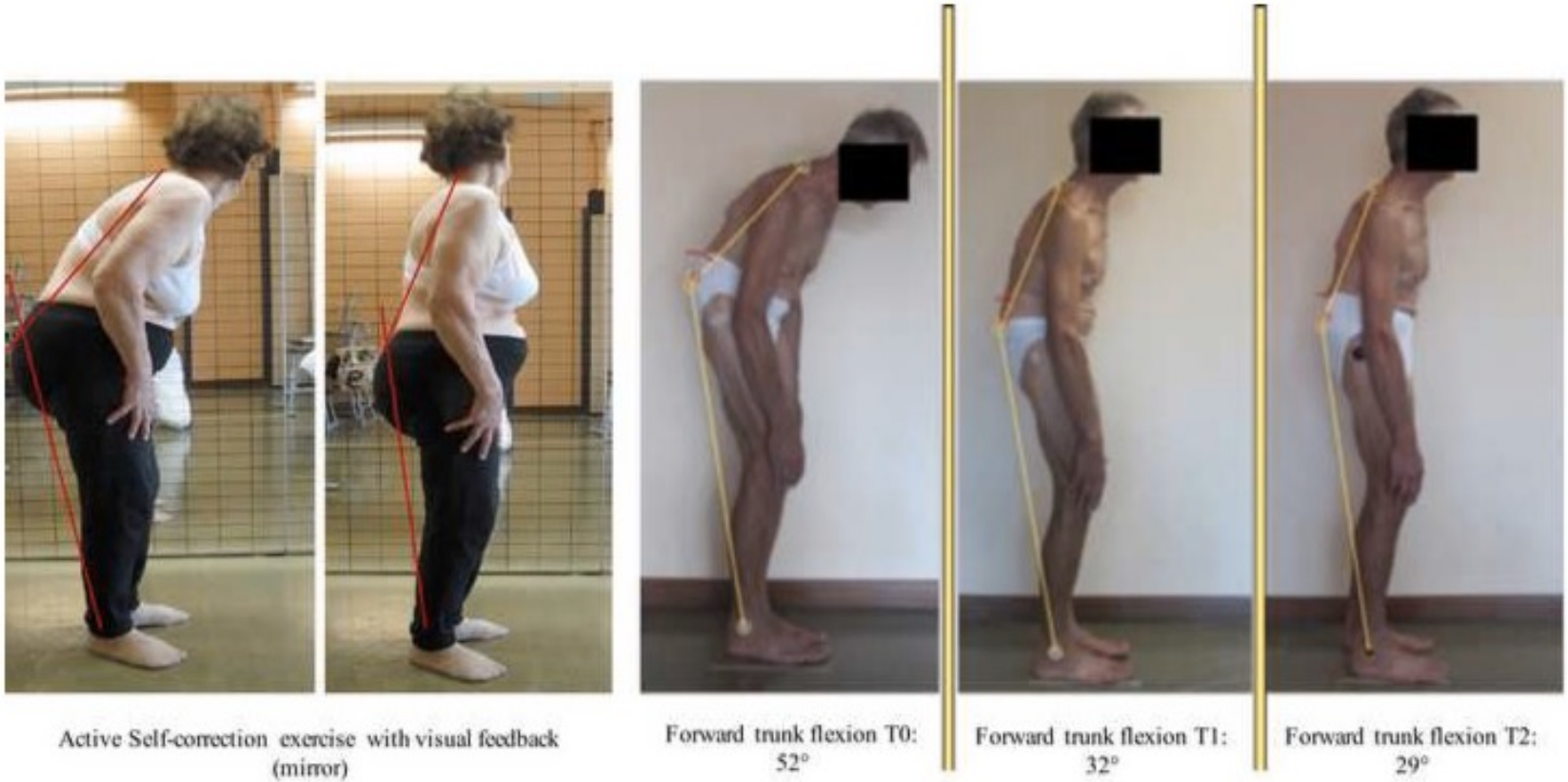
Marialuisa Gandolfi[a,b,*,1], Michele Tinazzi[a,**,1], Francesca Magrinelli[a], Giulia Busselli[a,b], Eleonora Dimitrova[a,b], Niccolò Polo[a], Paolo Manganotti[c], Alfonso Fasano[d,e], Nicola Smania[a,b,2], Christian Geroin[a,2]

37 patients with PD (H&Y 1-4) and anterior trunk flexion were randomised in the **experimental (n=19) or a control group (n=18).**

The former consisted of active **self-correction exercises with visual and proprioceptive feedback,** 10 passive and active trunk stabilization exercises and functional tasks.

The latter consisted of **joint mobilization,** muscle strengthening and stretching, gait and balance exercises. Protocols lasted 4 weeks (60 min/day, 5 day/week). (T1 and T2 immediately after and one month after last session of physiotherapy)





Active Self-correction exercise with visual feedback (mirror)

Forward trunk flexion T0: 52°

Forward trunk flexion T1: 32°

Forward trunk flexion T2: 29°

The four-week trunk-specific rehabilitation training decreased the forward trunk flexion severity and increased postural control in patients.

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Water-based therapeutic exercise

Treatment 60-min sessions (5 x week) over a period of 8 weeks

Article

CLINICAL REHABILITATION

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Water-based vs. non-water-based physiotherapy for rehabilitation of postural deformities in Parkinson's disease: a randomized controlled pilot study

Daniele Volpe[1], Maria Giulia Giantin[1], Pilleri Manuela[1], Consuelo Filippetto[2,3], Elisa Pelosin[4], Giovanni Abbruzzese[4] and Angelo Antonini[2]

Table 2. Statistical analysis of primary and secondary outcomes.

	Water-based group (mean ± SD)			Non-water-based group (mean ± SD)		
	Baseline	8 weeks	16 weeks	Baseline	8 weeks	16 weeks
Postural parameters						
BAK-cervical (mm)	231.5 ± 93.9	166.3 ± 56[a]	196 ± 83.1[b]	177.1 ± 71.7	178.8 ± 54.8	184.1 ± 52.7
BAK-dorsal (mm)	46.6 ± 28.3	24.1 ± 22.2[a]	34.2 ± 30	38.7 ± 22.6	32.2 ± 26.3	33.7 ± 25.8
Shoulder symmetry (°)	6.8 ± 2.5	4.5 ± 1.7[a]	7 ± 3	5.8 ± 3.6	5.5 ± 3.1	6.1 ± 4
Pelvic symmetry (°)	3.6 ± 2.5	3.3 ± 3.1[a]	3 ± 2.4	4.2 ± 3.9	3.5 ± 3.1	3.3 ± 4.6
Motor performance tests						
UPDRS-III (score)	40.9 ± 6.7	34.8 ± 5.6	37.2 ± 6.1	40.2 ± 11.1	33 ± 12.8	35.2 ± 11.3
BBS (score)	46.7 ± 6.6	50.2 ± 4.6	48.8 ± 5.1	42.3 ± 8.5	49.2 ± 5.1	44.6 ± 6.9
ABC (%)	62 ± 18.4	70.1 ± 19.7	68 ± 19.3	71.1 ± 18.7	73.5 ± 20.4	69.3 ± 25.4
TUG (sec)	12.9 ± 2.1	11.5 ± 2	12 ± 2.4	14.8 ± 8.4	11.6 ± 2.3	12 ± 2.4
FES (score)	8.3 ± 5.5	6 ± 4.6	7.6 ± 6.5	11 ± 7.5	9.7 ± 7.6	11.4 ± 8.1
Quality of life and pain						
PDQ-39 (score)	49.1 ± 20.3	39.5 ± 18.9[a]	38.1 ± 20.7[b]	50.8 ± 20.8	46.6 ± 20.7[a]	61 ± 19.6[b]
Likert (score)	5.7 ± 2.5	3.8 ± 2.2	5.3 ± 2.9	5.7 ± 3	3 ± 2.7	4.5 ± 2.7

Conclusion: Our results show that water-based physiotherapy was effective for improving postural deformities in patients with Parkinson's disease.

Clinical messages

- Water-based physiotherapy was effective in improving postural deformities (in the sagittal or coronal planes) in patients with Parkinson's disease. Similar improvement could not be achieved in patients submitted to non-water-based training exercises.
- The improvement of postural abnormalities after water-based exercises might be related to a compensation of defective proprioceptive mechanism in Parkinson's disease.
- Water-based intervention might represent a useful approach to postural deformities in Parkinson's disease, but its effectiveness needs to be supported with large randomized controlled trial studies.

Future Research

- To develop **a clinical rating scale for Axial Postural Abnormalities** in parkinsonism which takes into account of both of the level and degrees of bending (**rated by the neurologist: done**) and the functional limitations in everyday life (**rated by the patient: to do**)

- To conduct prospective**, observational, long-term** studies with large samples of PD patients to explore the **potential risk (causal) factors and pathophysiology** involved in their development.

- **To perform RCT** to compare the **efficacy of different pharmacological and non pharmacological interventions and their combined effect** (ie, botulinum toxin injections + physiotherapy). Such controlled studies could also focus on the merits of dopaminergic therapy withdrawal when these are suspected to have played a role in causing axial postural abnormalities.

- To assess **the effectiveness** of proper **physical exercises** (i.e. streghtening of thoracic and lumbar paraspinal muscles) in PD patients with MILD forms to prevent severe Axial Postural Abnormalities

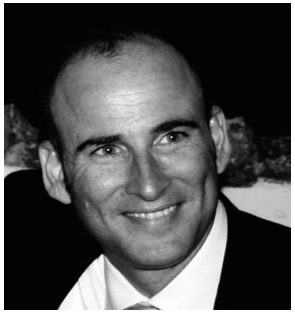
Ta nalities in Parkinsonism

Dr. Christian Geroin

Prof. Marialuisa Gandolfi

Dr. Carloalberto Artusi

Dr. Stefano Aldegheri



Prof. Nicola Bombieri

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