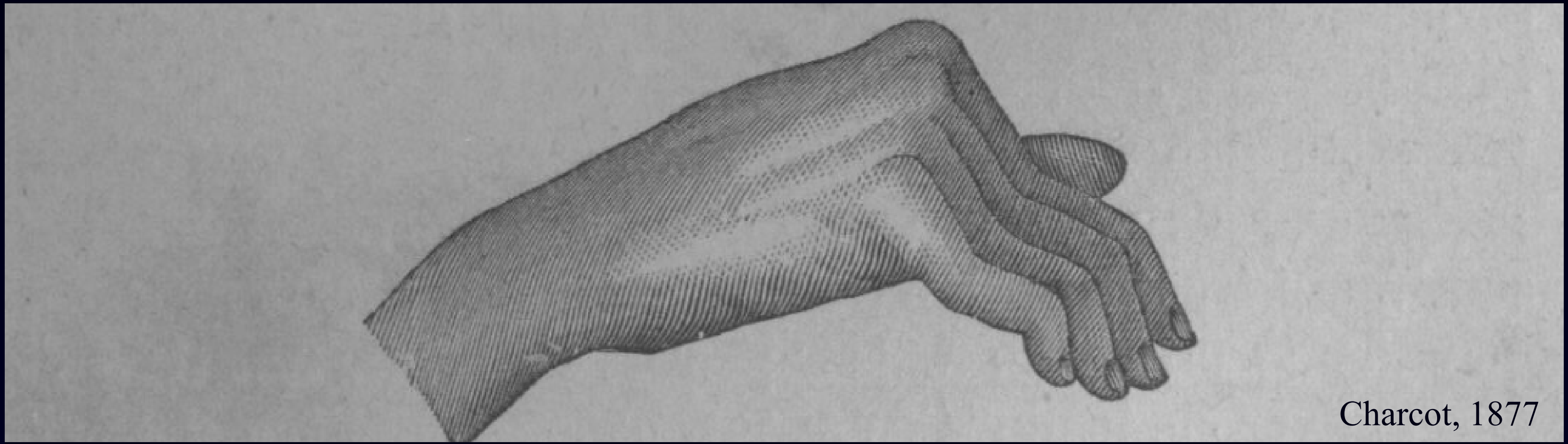
Neurorehabilitation in Parkinson's disease

Guided Self-rehabilitation Contracts to learn *Asymmetric Motor Strengthening*



Jean-Michel Gracies, MD, PhD, Paris

Université Paris-Est Créteil, France

Rehabilitacja w chorobie Parkinsona – co można zrobić?

→ *The quest for Deparkinsonization*

Jean-Michel Gracies, Paryż

Hôpital Albert CHENEVIER – Henri Mondor (Créteil)

Parkinson's Neurorehabilitation treatment

1. There is levodopa, so why rehabilitate? - well, precisely!
2. The parkinsonian acceleropathy
3. From motor strengthening to asymmetric motor strengthening
4. Psychological tool: *Guided Self-rehabilitation Contract*
5. Technical tool: trials on *Asymmetric Motor Strengthening*

Gracies, 2010

Parkinson's Therapeutic (R)evolutions

- **1967**: Chemical treatment = Levodopa
- **1987**: Surgical treatment = Deep Brain Stimulation (>4 yrs post diagnosis)
- **20…**: Physical Treatments?

1. There is levodopa, so why rehabilitate?

- well, precisely!

First aspect of neurorehabilitation in PD?

= decrease dopaminergic treatment
But shh…

Lamont RM, Morris ME, Menz HB, McGinley JL, Brauer SG. Falls in people with Parkinson's disease: A prospective comparison of community and home-based falls. Gait Posture 2017;55:62-67

OBJECTIVE: To compare characteristics of community and home fallers in mild to moderate PD

METHODS: n=196: daily falls diary and telephone hotline to report prospectively occurrence, location and circumstances of falls over 14 months.

RESULTS: 62% fell, with most falling at least once in the community. Compared to people who fell at home, community-only fallers had shorter PD durations (p=0.012), less severe disease (p=0.008) and reported fewer falls in year prior to the study (p=0.003). **Most falls occurred** while people were ambulant, during postural transitions and **when medication was working well**. Community-based falls frequently attributed to environmental factors = challenging terrains (p<0.001), high attention demands (p=0.029), cluttered areas (p<0.001) and tasks requiring speed (p=0.020). Physical loads more in home than community-based falls (p=0.027).

CONCLUSION: **Falls that occur i[illegible]unity typically affect people with earlier PD and less severe disease than h[illegible]sed falls. Individuals experiencing community-based falls may benef[illegible] physiotherapy to manage challenging environments and high attention [illegible]ds.**

?

Chou KL, et al; NINDS NET-PD Investigators. Factors associated with falling in early, treated Parkinson's disease: The NET-PD LS1 cohort. J Neurol Sci. 2017;377:137-143.

OBJECTIVE: To examine frequency of falling and baseline characteristics associated with falling in PD using National Institute of Neurological Disorders and Stroke (NINDS) Exploratory Trials in PD Long-term Study-1 (NET-PD LS-1) dataset.

METHODS: LS-1 database n = 1741 early treated PD subjects (median 4 year FU). Baseline characteristics tested for univariate association with post-baseline falling during the trial. → Significant variables included in a multivariable logistic regression model. A separate analysis using a negative binomial model investigated baseline factors on fall rate.

RESULTS: 728 subjects=42%, fell during the trial, including at baseline. A baseline history of falls was factor most associated with post-baseline falling. Men had lower odds of post-baseline falling compared to women, but for men, the probability of a post-baseline fall increased with age such that after age 70, men and women had similar odds of falling. **Other baseline factors** associated with post-baseline fall and increased fall rate **included** the Unified PD Rating Scale (UPDRS) Activities of Daily Living (ADL) score, total functional capacity (TFC), baseline ambulatory capacity score and **dopamine agonist monotherapy.**

CONCLUSION: **Falls = common in [illegible] PD. The biggest risk factor for falls in PD remains a history of falling. Meas[illegible]tional ability (UPDRS ADL, TFC) and ambulatory capacity are novel clinic[illegible]s needing further study. Age by sex interaction may explain why age has [illegible]onsistent risk factor for falls in PD.**

?!

Sign of the second sleeve:
→ the miracle of levodopa??

PRE
levodopa

POST
levodopa = <u>balance impairment</u> <u>in *late* stages</u>,
↑ reaction times

Rocchi et al, 2002; Beuter et al, 2008
Armand et al, 2009; Hälbig et al, Mov Dis 2011; Dec et al, 2017;
delayed going response: Wylie et al, Neuropsychologia 2018

Graces, 2018

***Guided self-rehabilitation Contract* with *Asymmetric Motor Strengthening 6 weeks*– Stand from ground → altered by levodopa**

04 Apr 2017
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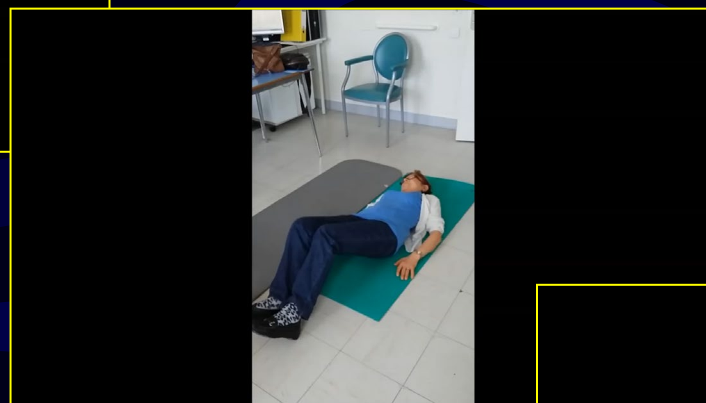
15 sec



17 May 2017
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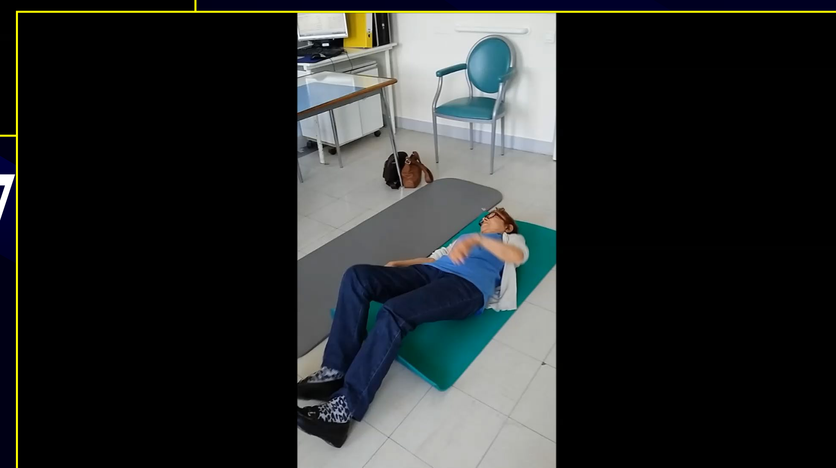


17 May 2017
<u>ON</u> *13.5 sec*

Mov Disord. 2015 September ; 30(10): 1361–1370. doi:10.1002/mds.26269.

Levodopa is a Double-Edged Sword for Balance and Gait in People with Parkinson's Disease

Carolin Curtze, PhD[1], **John G. Nutt, MD**[1], **Patricia Carlson-Kuhta, PhD**[1], **Martina Mancini, PhD**[1], and **Fay B. Horak, PhD**[1,2]

Abstract

Background—The effects of levodopa on balance and gait function in people with Parkinson's disease (PD) is controversial. This study compared the relative responsiveness to levodopa on six domains of balance and gait: postural sway in stance, gait pace, dynamic stability, gait initiation, arm swing, and turning in people with mild and severe PD, with and without dyskinesia.

Methods—We studied 104 subjects with idiopathic PD (Hohen & Yahr II (n=52) and III-IV (n=52)) and 64 age-matched controls. Subjects performed a mobility task in the practical OFF state and ON levodopa: standing quietly for 30 seconds, initiating gait, walking 7 meters, and turning 180 degrees. Thirty-four measures of mobility were computed from inertial sensors. Standardized response means were used to determine the relative responsiveness to levodopa.

Results—The largest improvements with levodopa were found for arm swing and pace-related gait measures. Gait dynamic stability was unaffected by PD and not responsive to levodopa. Levodopa reduced turning duration, but only in subjects with severe PD. In contrast to gait, postural sway in quiet standing increased with levodopa, especially in the more severely affected subjects. The increase in postural sway, as well as decrease in turning duration and exaggerated arm swing with levodopa was observed only for subjects with dyskinesia at the time of testing.

Conclusions—The observed spectrum of levodopa responsiveness in balance and gait measures suggests multiple neural circuits control balance and gait. Many of the negative effects of levodopa may be directly or indirectly caused by dyskinesia.

Parkinson's = 2 stages?

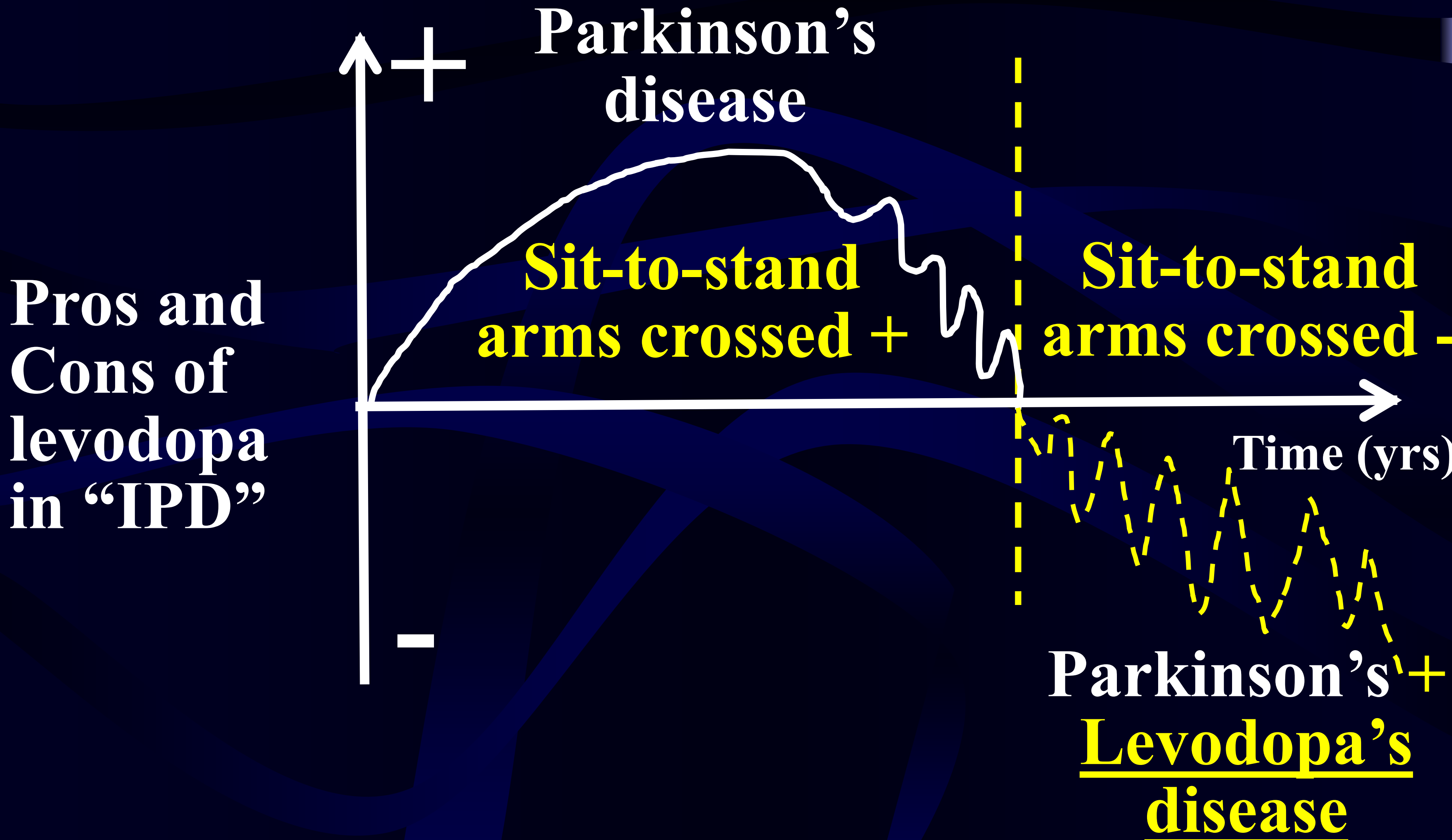
- **Moderate** = **<u>sit-to-stand arms crossed +</u>**
  = preserved independent ambulation,
  cognitive autonomy

- **Advanced** = **<u>sit-to-stand arms crossed -</u>**
  = loss of independent ambulation,
  dysexecutive syndrome

Smulders K, van Nimwegen M, Munneke M, Bloem BR, Kessels RP, Esselink RA. ***Involvement of specific executive functions in mobility in Parkinson's disease.*** *Parkinsonism Relat Disord. 2013;19(1):126-8.*

Gracies, 2010

Dr Levodopa Jekyll then Dr *Levodopa Hyde*
→ How may we convince the prescriber of exogenous dopamine?



Tse et al, JAMDA, 2008; Curtze et al, Mov Dis, 2015

Parkinson's = Two stages, two treatments?

	Sit-to-stand arms crossed+	**Sit-to-stand arms crossed-**
Ambulation	Independent	Dependent
Cognition	Little impaired	Dysexecutive
Chemical treatment	Dopaminergic drugs +	Dopaminergic drugs -
Surgical treatment	+	-
Physical treatment	<u>Teaching the patient</u> Motor strengthening, aerobic, cueing, Goal: improve motor function	<u>Teaching the caregiver</u> compensation strategies Goal: optimize home safety

Gracies 2014

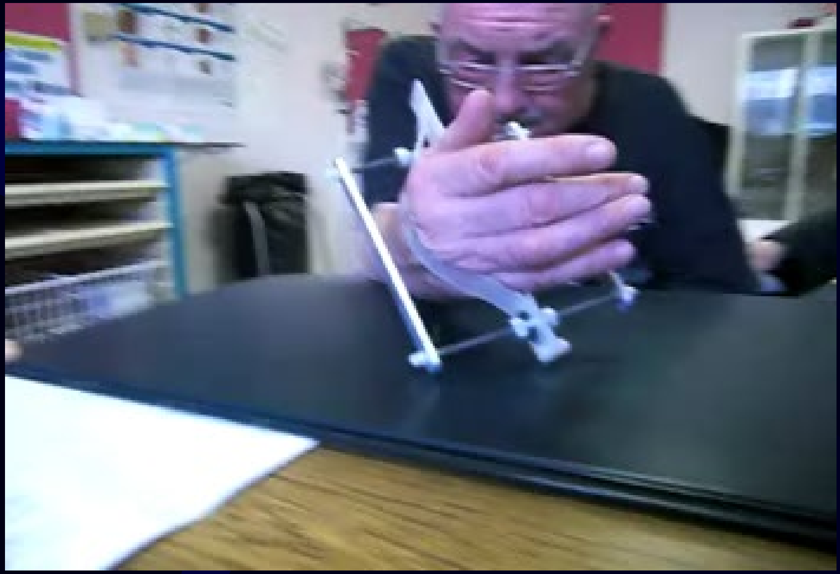
2. The Parkinsonian Acceleropathy

What are the fundamental characteristics of the parkinsonian movement?

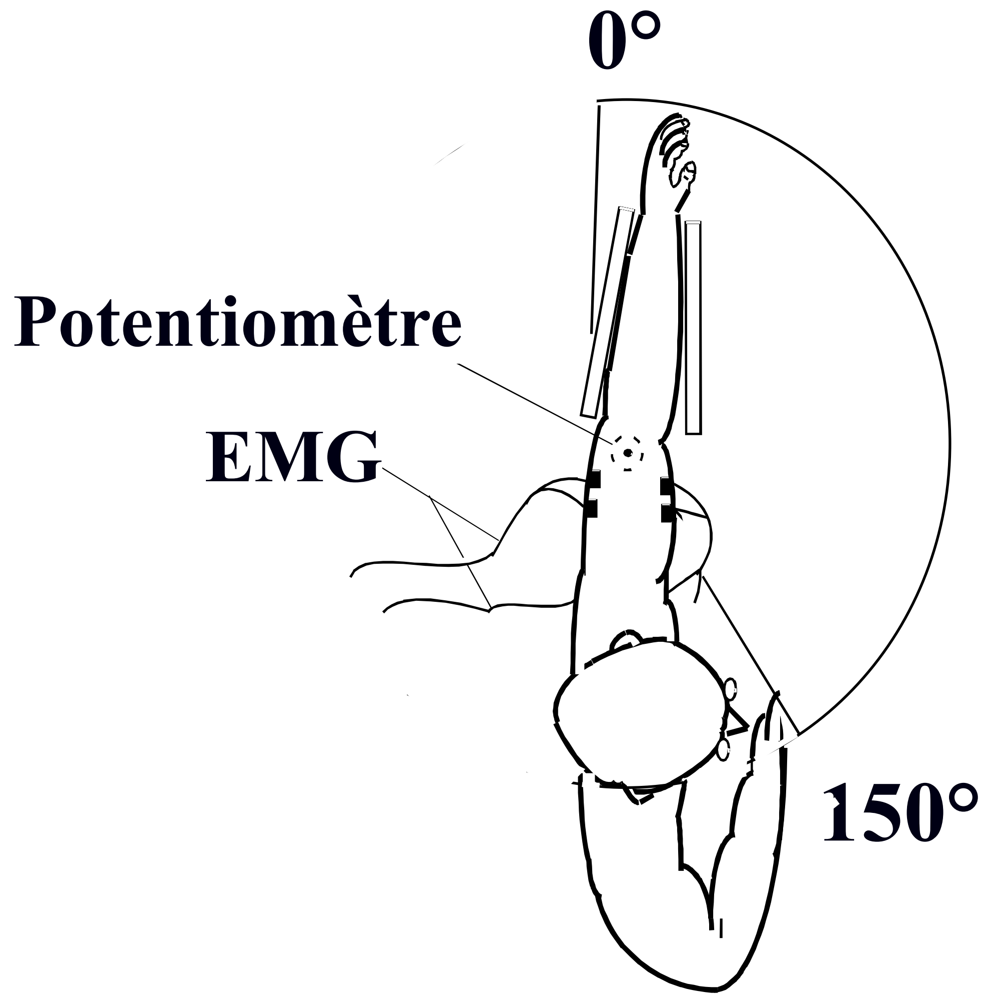
The parkinsonian acceleropathy

Gracies, 2010

Quantification « Bradykinesia »?



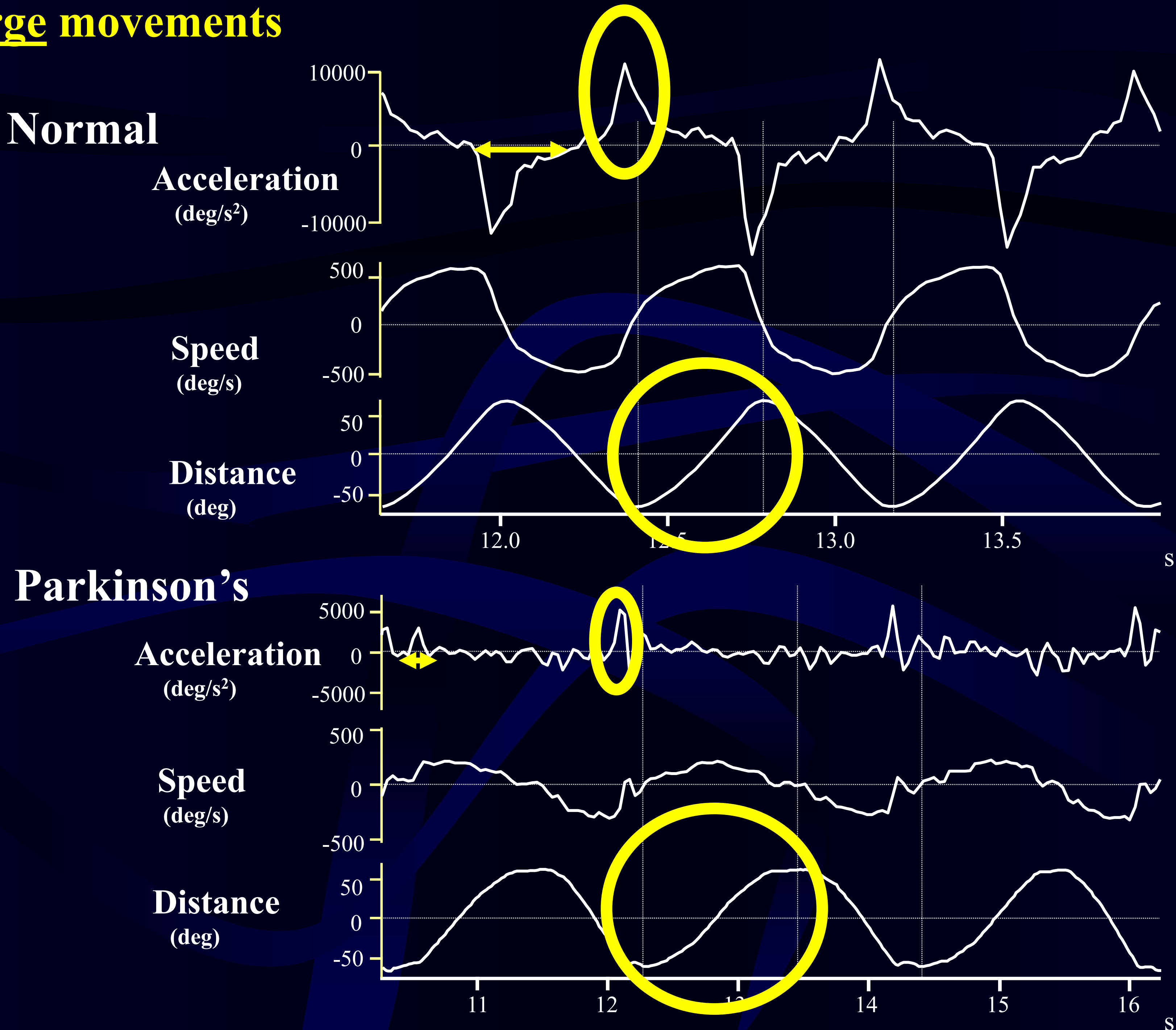
Hypermetria (cereb) **<u>Hypometria! (Park)</u>**



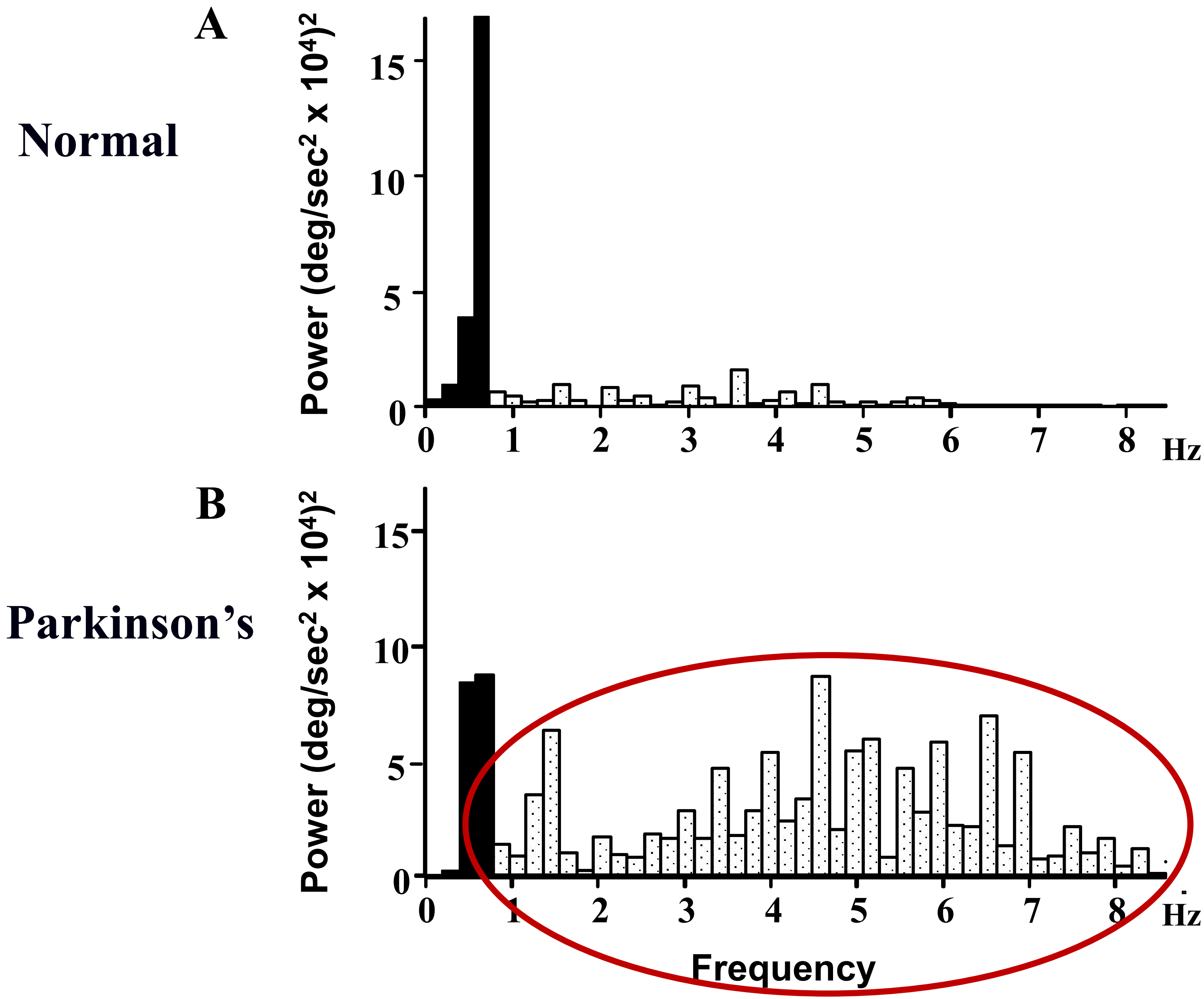
Active large amplitude movements

Gracies, 2003

Large movements



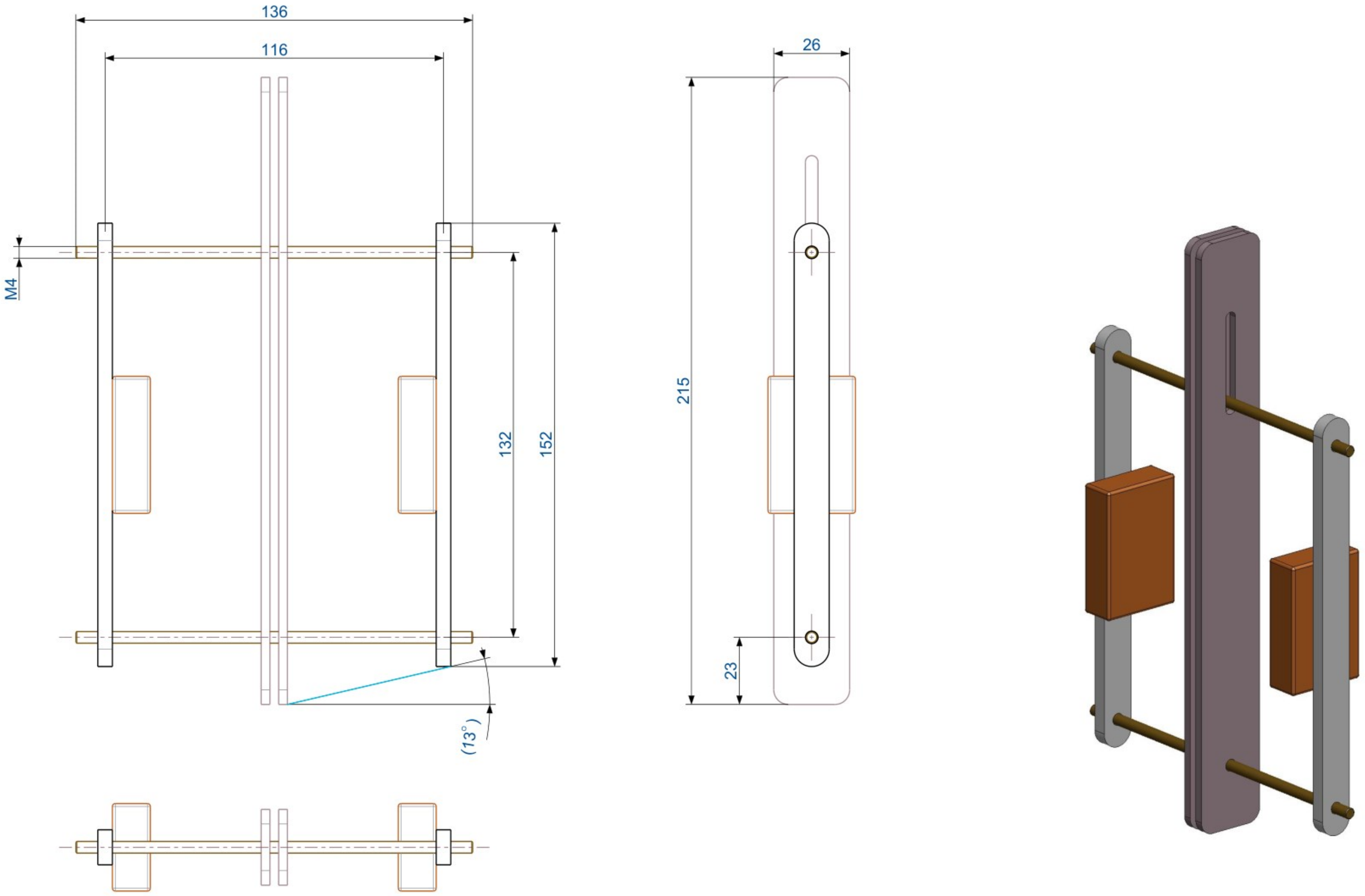
Gracies, 2011


A
Normal
Power (deg/sec2 x 104)2
15
10
5
0
0 1 2 3 4 5 6 7 8 Hz
B
Parkinson's
Power (deg/sec2 x 104)2
15
10
5
0
0 1 2 3 4 5 6 7 8 Hz
Frequency

Parkinsonian acceleropathy
Reduced accelaratory peaks?

- Inthe few hours after a dose de lévodopa, acceleratory peaks (max acceleration) decline first, before max speed or movement duration *(Camarda et al 2005)*

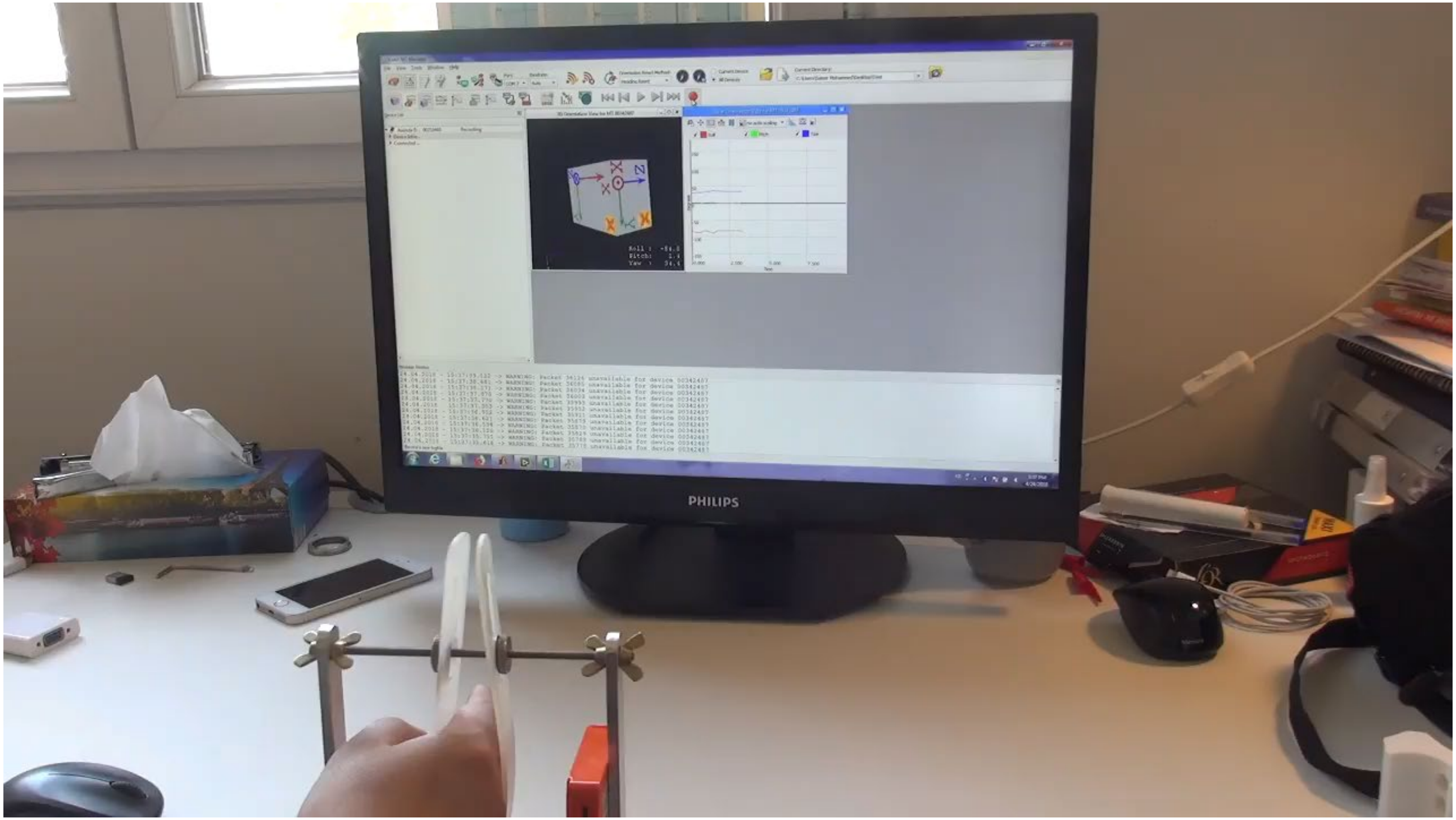
- *Camarda R, Camarda C, Grimaldi S, Camarda LK, Monastero R, Gangitano M. Effects of levodopa oral bolus on the kinematics of the pointing movements in Parkinson's disease patients. J Neurol. 2005;252(9):1074-81.*
- *Bandini A, et al. Markerless Analysis of Articulatory Movements in Patients With Parkinson's Disease. J Voice. 2016 Nov;30(6):766.e1-766.e11*
- *Ishii M, Mashimo H. Accelerometer based analysis of gait initiation failure in advanced juvenile parkinsonism: a single subject study. J Phys Ther Sci. 2016 Nov;28(11):3252-3256*



Alternomètre Portable Connecté

US202117552894 20211216 - EP4014840 (A1)

Alternomètre Portable Connecté
US202117552894 20211216 -
EP4014840 (A1)



Alternomètre Portable Connecté
US202117552894 20211216 -
EP4014840 (A1)

Projet AlternoPark – données préliminaires

Gracies, Legendre, Mohammed

N= 14 sujets sains, âge 67,4±7,4, [52-81]
N=16 sujets parkinsoniens, âge 67,0±7,2, [52-81], délai depuis diagnostic 9,0±1,7, délai depuis début lévodopa 8,6±1,9

Projet AlternoPark

Données préliminaires

Gracies, Legendre, Mohammed

- **N= 14 sujets sains,** âge 67,4±7,4, [52-81]
- **N=16 sujets parkinsoniens,** âge 67,0±7,2, [52-81], **délai depuis diagnostic 9,0±1,7, délai depuis début lévodopa 8,6±1,9**

1. Pouvoir discriminant des paramètres évalués

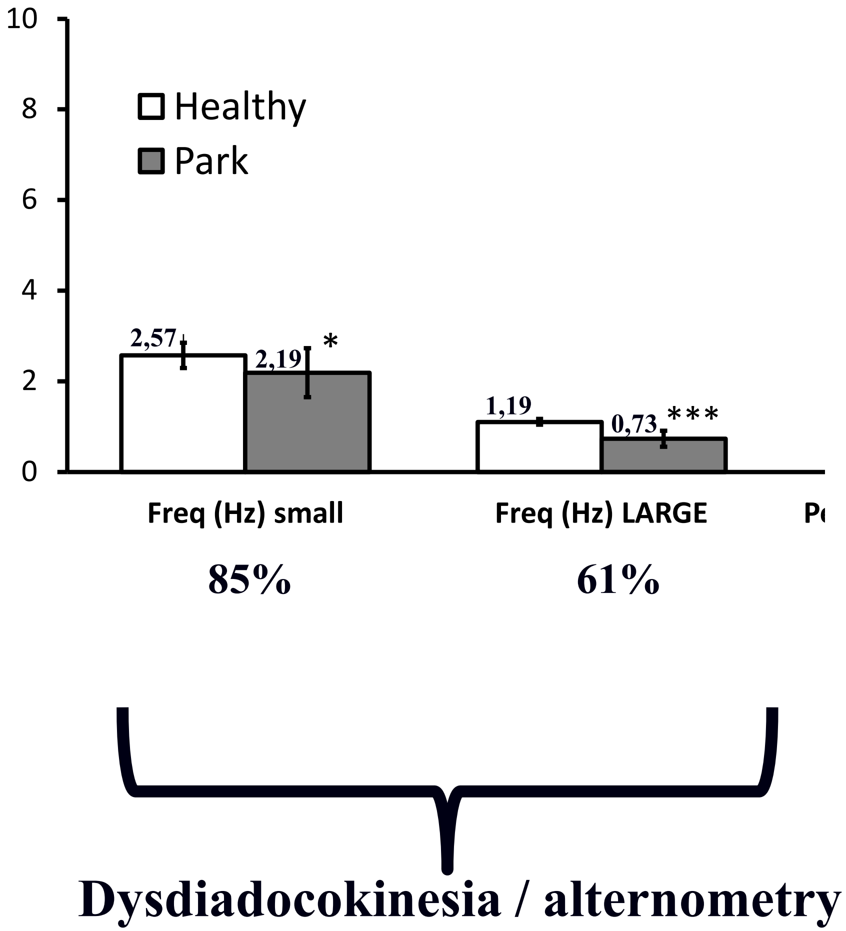
Dans une première comparaison de moyennes, il apparait que ce sont les accélérations maximales en supination qui sont les plus différentes entre échantillons sain et parkinsonien :

Variable	Healthy (15)	Parkinsonian (17	P Value	Test Used
Age (Mean ± SD)	67.40 ± 7.08	66.60 ± 6.80	5.80e-01	T-test
Female (%)	55.17%	54.39%	-	
Years Since Diagnosis (Mean ± SD)	-	9.07 ± 1.72	-	
Years since Treatment (Mean ± SD)	-	8.70 ± 1.86	-	
NoCycles_Large_Dominant	18.60 ± 4.48	12.62 ± 4.44	0,000803277	Mann-Whitney U
NoCycles_Large_Non-Dominant	17.86 ± 4.47	11.67 ± 4.03	0,000242028	Mann-Whitney U
NoCycles_Small_Dominant	53.87 ± 12.96	34.71 ± 9.23	0,000100675	T-test
NoCycles_Small_Non-Dominant	50.21 ± 14.26	34.08 ± 7.67	0,001835634	T-test
freqAvg_Large_Dominant	1.33 ± 0.31	0.91 ± 0.33	0,000468287	Mann-Whitney U
freqAvg_Large_Non-Dominant	1.26 ± 0.31	0.87 ± 0.27	0,000718614	Mann-Whitney U
freqAvg_Small_Dominant	3.92 ± 0.75	2.84 ± 0.71	0,000485934	T-test
freqAvg_Small_Non-Dominant	3.84 ± 1.03	2.72 ± 0.84	0,006408252	T-test
shootAvg_Large_Dominant	10.67 ± 2.33	8.49 ± 2.88	0,028240915	T-test
shootAvg_Large_Non-Dominant	10.80 ± 2.17	7.55 ± 2.87	0,003219733	Mann-Whitney U
shootAvg_Small_Dominant	**37.06 ± 12.25**	**18.76 ± 7.46**	**4,98818E-05**	**T-test**
shootAvg_Small_Non-Dominant	31.76 ± 9.94	20.67 ± 9.61	0,008246459	T-test
AngPronation_Large_Dominant	71.60 ± 15.14	61.18 ± 11.13	0,036430297	T-test
AngPronation_Large_Non-Dominant	66.85 ± 19.68	62.81 ± 23.04	0,617251408	T-test
AngPronation_Small_Dominant	25.32 ± 11.77	23.32 ± 10.98	0,639497849	T-test
AngPronation_Small_Non-Dominant	26.12 ± 17.34	19.83 ± 20.14	0,1896624	Mann-Whitney U
VelPronation_Large_Dominant	1.19e+03 ± 2.48e+02	929.47 ± 303.24	0,012881572	T-test
VelPronation_Large_Non-Dominant	1.23e+03 ± 2.31e+02	951.26 ± 295.73	0,009249315	T-test
VelPronation_Small_Dominant	716.33 ± 253.56	366.72 ± 155.22	0,000137809	T-test
VelPronation_Small_Non-Dominant	699.83 ± 241.19	407.92 ± 182.04	0,00217015	T-test
VelSupination_Large_Dominant	1.16e+03 ± 2.91e+02	935.13 ± 208.75	0,018992061	T-test
VelSupination_Large_Non-Dominant	1.15e+03 ± 2.68e+02	814.66 ± 228.63	0,001298582	T-test
VelSupination_Small_Dominant	639.95 ± 172.26	409.24 ± 199.72	0,002470453	T-test
VelSupination_Small_Non-Dominant	580.83 ± 111.57	399.77 ± 138.79	0,001153735	T-test
AccPronation_Large_Dominant	5.40e+04 ± 1.35e+04	3.65e+04 ± 1.66e+04	0,003269972	T-test
AccPronation_Large_Non-Dominant	5.20e+04 ± 1.42e+04	3.00e+04 ± 1.47e+04	0,001148194	Mann-Whitney U
AccPronation_Small_Dominant	3.34e+04 ± 1.12e+04	1.58e+04 ± 8.22e+03	0,000268184	Mann-Whitney U
AccPronation_Small_Non-Dominant	2.59e+04 ± 8.37e+03	1.38e+04 ± 6.29e+03	0,000287702	Mann-Whitney U
AccSupination_Large_Dominant	**4.42e+04 ± 1.09e+04**	**2.44e+04 ± 9.23e+03**	**6,95698E-06**	**T-test**
AccSupination_Large_Non-Dominant	4.37e+04 ± 1.83e+04	2.44e+04 ± 1.52e+04	0,002419522	Mann-Whitney U
AccSupination_Small_Dominant	**3.80e+04 ± 1.36e+04**	**1.41e+04 ± 5.11e+03**	**1,35436E-06**	**T-test**
AccSupination_Small_Non-Dominant	3.34e+04 ± 1.02e+04	1.67e+04 ± 9.42e+03	0,001090445	Mann-Whitney U
NARJ_Large_Dominant	1.02e+09 ± 3.25e+08	5.43e+08 ± 4.25e+08	0,000403478	Mann-Whitney U
NARJ_Large_Non-Dominant	9.46e+08 ± 3.41e+08	4.48e+08 ± 3.40e+08	0,000375183	Mann-Whitney U
NARJ_Small_Dominant	1.33e+09 ± 8.23e+08	3.64e+08 ± 2.45e+08	0,000250151	T-test
NARJ_Small_Non-Dominant	9.55e+08 ± 5.11e+08	3.84e+08 ± 2.94e+08	0,000625312	Mann-Whitney U
AngSupination_Large_Dominant	67.82 ± 17.86	60.68 ± 19.45	0,296803049	T-test
AngSupination_Large_Non-Dominant	69.93 ± 17.79	68.26 ± 17.27	0,91311608	Mann-Whitney U
AngSupination_Small_Dominant	20.64 ± 12.61	14.36 ± 8.55	0,077133668	Mann-Whitney U
AngSupination_Small_Non-Dominant	20.02 ± 5.44	16.64 ± 9.00	0,250890989	T-test

Table 2 – Comparaison de moyennes mains dominantes et non dominantes entre les deux échantillons

Healthy subjects *vs* Parkinson's

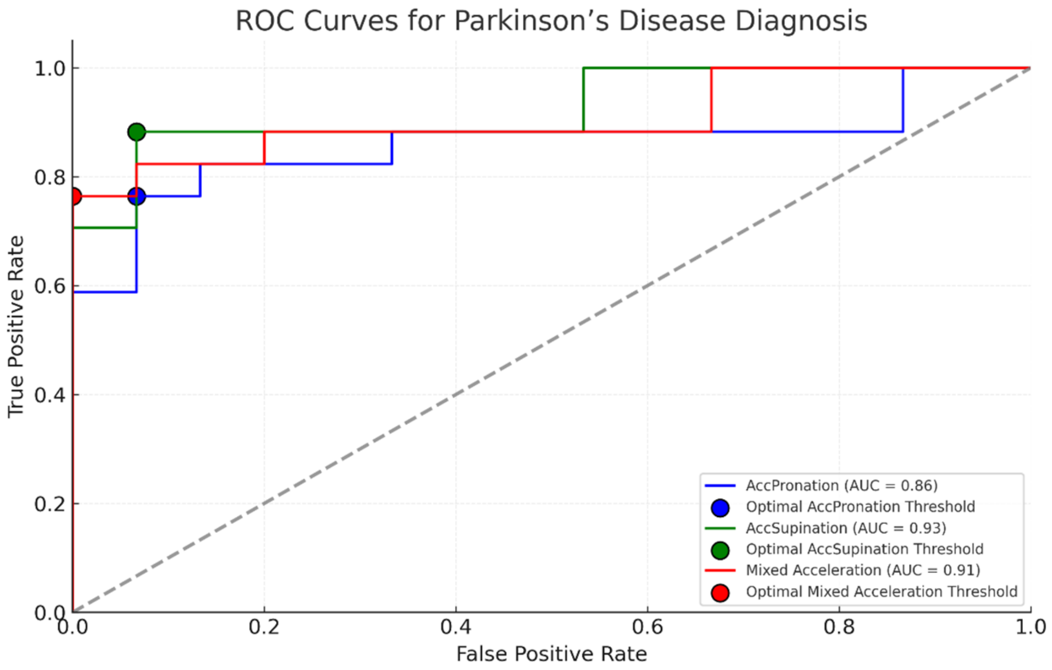
Means (IC 95)



Gracies et al, unpublished

Projet AlternoPark- données préliminaires

Gracies, Legendre, Mohammed



*Meilleures sensibilité et spécificité avec **accélérations en supination sur les mouvements de grande amplitude sur la moyenne des deux mains** :*
Aire max sous courbe 0,93, seuil optimal de 28604,18 m2/s-²
pour lequel sensibilité = 88,2 %, et spécificité = 93,3 %.
Tous autres paramètres (fréquence, amplitudes angulaires, vitesses angulaires, NARJ), bien qu'intéressants, demeurent < en performance diagnostique. Cela confirme la maladie de Parkinson comme un trouble primitif de l'accélération du mouvement.

Parkinson's disease = insufficient agonist EMG Pathophysiology Hypometria/bradykinesia

- **Classic clinical characterization**: slowness over large amplitude imposed (« bradykinésia ») *Flowers, 1975, 1976*

- **EMG Characterization**: underscaled agonist bursts
  - In duration *(Hallett and Khoshbin, 1980; Pfann, 2004, Robichaud, 2002)*
  - In power *(Berardelli et al, 1986; Phillips et al, 1994)*

    → Insufficient Acceleration *(Carboncini, 2001; Broderick, 2009)*

- **Cause** = Alexander's model :
  - Insufficient cortical preparedness = deficit of *internal, induced excitability* of premotor and motor cortices by basal ganglia *Alexander et al, 1990*

Gracies, 2013

Automatized movement

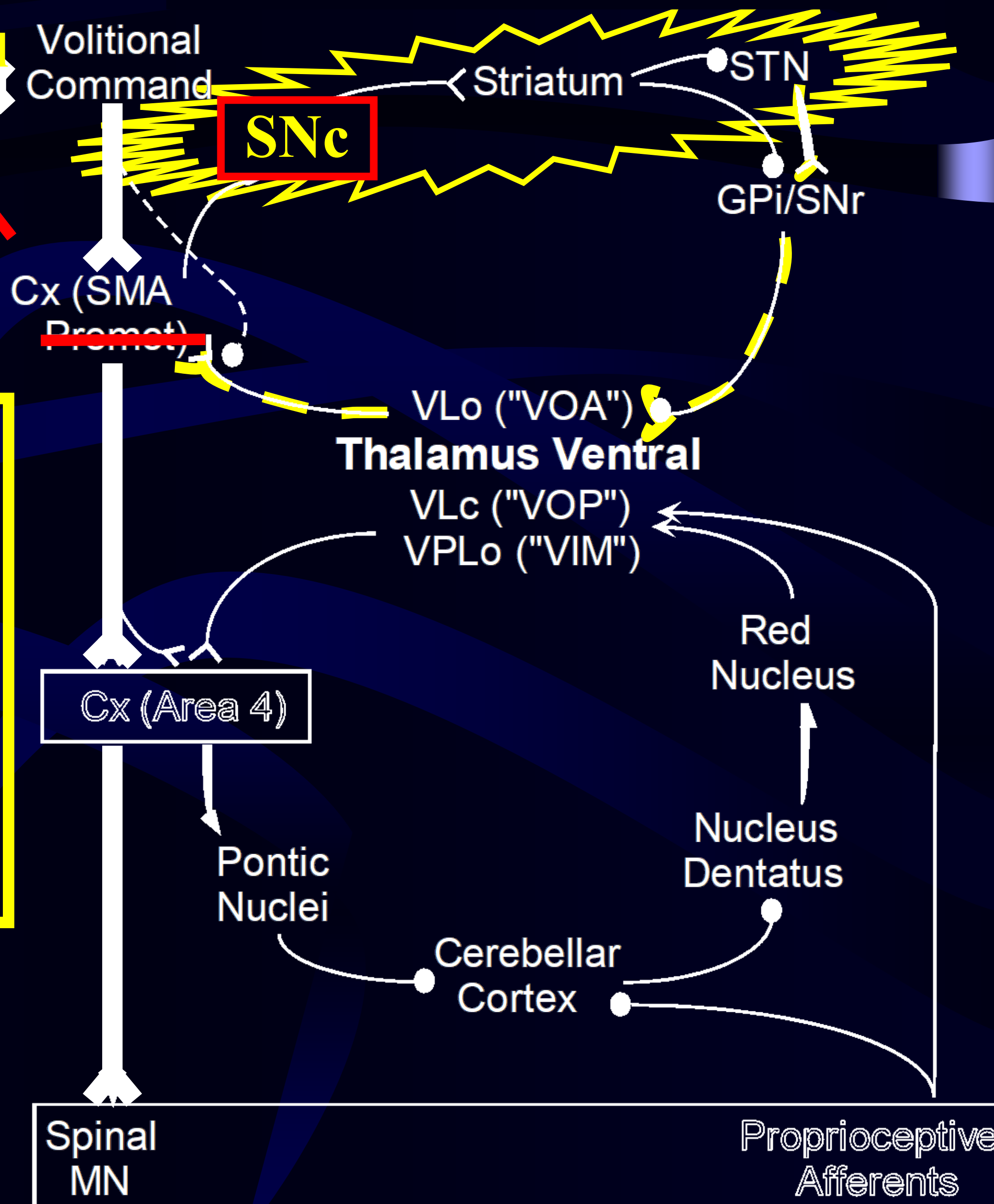
Unusual movement

(external guidance)

→« Cueing »

« Attention »

Cx Préfrontal dorsolat



Loss of cortical motor excitability

Brown et Marsden 1988
Freeman et al 1993;
Georgiou et al 1993;
Kritikos et al 1995

3. To increase motor cortical excitability,
from *motor strengthening*
to *Asymetric Motor Strengthening*

Correlation motor power, balance and parkinsonian symptoms

- Balance impairment
- Slowness in 6-min walking test
- Timed up & go
- Sit-to-stand capacities

= all independently correlated with motor weakness in PD

Clael S et al. Association of Strength and Physical Functions in People with Parkinson's Disease. Neurosci J. 2018;2018:8507018

Toole et al, 1996 ; Schilling et al, 2009; Allen et al, 2010

Gracies, 2010

Mov Disord. Author manuscript; available in PMC 2012 October 15.

Published in final edited form as:
Mov Disord. 2003 February ; 18(2): 157–162. doi:10.1002/mds.10299.

Corrélation force motrice MI et fonction

Leg muscle strength is reduced in PD and relates to the ability to rise from a chair

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[1]Department of Physical Therapy, University of British Columbia, Canada

[2]Rehabilitation Research Laboratory, GF Strong Rehab Centre

[3]Pacific Parkinson's Research Centre, University of BC

Abstract

Individuals with Parkinson's disease (PD) have difficulties rising from a chair; however, factors contributing to this inability have never been investigated. This study compared lower extremity strength between individuals with PD and healthy controls and quantified the relationships between strength and the ability to rise from a chair. Ten males with mild PD and ten male age-matched controls performed maximal concentric, isokinetic knee and hip extensor torque on an isokinetic dynamometer to quantify muscle strength. Subjects also rose from a chair at their comfortable pace without the use of their arms and the duration of this task provided a measure of sit-to-stand (STS) ability. Subjects with PD were tested in an on- and off-medication state on different days. Mean hip and knee extensor torques were less in subjects with PD, with greater deficits found at the hip. Greater hip strength was related to better STS ability in subjects with PD while greater knee strength was related to better STS ability in controls. These results show that individuals with mild PD generate smaller extremity forces compared to controls. Reduced strength, particularly at the hip, may be one factor that contributes to the difficulty of persons with PD to rise from a chair.

Increasing motor cortex excitability by Strengthening

Acute Strength Training Increases Responses to Stimulation of Corticospinal Axons

JAMES L. NUZZO[1,2], BENJAMIN K. BARRY[1,2], SIMON C. GANDEVIA[1,3], and JANET L. TAYLOR[1,2]

[1]*Neuroscience Research Australia, Randwick, NSW, AUSTRALIA;* [2]*School of Medical Sciences, University of New South Wales, Kensington, NSW, AUSTRALIA;* [3]*Prince of Wales Clinical School, University of New South Wales, Kensington, NSW, AUSTRALIA*

Effets médullaires aigus, plus durables 15-25 min?

ABSTRACT

NUZZO, J. L., B. K. BARRY, S. C. GANDEVIA, and J. L. TAYLOR. Acute Strength Training Increases Responses to Stimulation of Corticospinal Axons. *Med. Sci. Sports Exerc.*, Vol. 48, No. 1, pp. 139–150, 2016. **Purpose**: Acute strength training of forearm muscles increases resting twitch forces from motor cortex stimulation. It is unclear if such effects are spinal in origin and if they also occur with training of larger muscles. With the use of subcortical stimulation of corticospinal axons, the current study examined if one session of strength training of the elbow flexor muscles leads to spinal cord changes and if the type of training is important. **Methods**: In experiment 1, 10 subjects completed ballistic isometric training, ballistic concentric training, and no training (control) on separate days. In experiment 2, 13 subjects completed ballistic isometric training and slow-ramp isometric training. Before and after training, transcranial magnetic stimulation over the contralateral motor cortex elicited motor-evoked potentials (MEPs) in the resting biceps brachii, and electrical stimulation of corticospinal tract axons at the cervicomedullary junction elicited cervicomedullary motor–evoked potentials (CMEPs). Motor-evoked potential and CMEP twitch forces were also measured. **Results**: In experiment 1, CMEPs and CMEP twitch forces were significantly facilitated after ballistic isometric training compared to control. In experiment 2, MEPs, MEP twitch forces, CMEPs, and CMEP twitch forces increased for 15 to 25 min after ballistic and slow-ramp isometric training. **Conclusion**: Via processes within the spinal cord, one session of strength training of the elbow flexors increases net output from motoneurons projecting to the trained muscles. Likely mechanisms include increased efficacy of corticospinal-motoneuronal synapses or increased motoneuron excitability. However, the rate of force generation during training is not important for inducing these changes. A concomitant increase in motor cortical excitability is likely. These short-term changes may represent initial neural adaptations to strength training. **Key Words:** BICEPS BRACHII, CERVICOMEDULLARY-EVOKED POTENTIAL, ELBOW FLEXORS, MOTONEURON, PLASTICITY, SPINAL CORD

Nuzzo JL, Barry BK, Gandevia SC, Taylor JL. Acute Strength Training Increases Responses to Stimulation of Corticospinal Axons. Med Sci Sports Exerc. 2016;48(1):139-50

Subacute increase in motor cortical excitability by reinforcement

Healthy subjects: motor strengthening program targeting a given muscle – Glut Max, 6 days - ↑ corticospinal excitability of command to that muscle *(Fisher et al, 2016)*

So does mirror observation of ipsilateral movement. (Garry et al, 2005)

*Fisher BE, Southam AC, Kuo YL, Lee YY, Powers CM (LA). **Evidence of altered corticomotor excitability following targeted activation of gluteus maximus training in healthy individuals**. Neuroreport. 2016*

Garry MI, Loftus A, Summers JJ. Mirror, mirror on the wall: viewing a mirror reflection of unilateral hand movements facilitates ipsilateral M1 excitability. Exp Brain Res. 2005 May;163(1):118-22

Subacute increase in motor cortical excitability by reinforcement

Parkinsonian subjects: eight weeks of high intensity exercises may *normalize corticospinal excitability*, in a way similar to acute effects of a dose of levodopa or apomorphin.

- *Robichaud JA et al. Effect of medication on EMG patterns in individuals with Parkinson's disease. Mov Disord. 2002;17(5):950-60*
- *Fisher, .., Jakowec, Petzinger. The effect of exercise training in improving motor performance and corticomotor excitability in people with early Parkinson's disease. Arch Phys Med Rehabil 2008.*
- *Priori, Berardelli et al. Brain 1994 - Nakashima et al. J Neurol Sci 1995 - Ridding, Inzelberg, Rothwell. Ann Neurol 1995 - Manfredi L et al. Neurophysiol Clin 1998*

Clinical benefits from motor strengthening in elderly and in PD

Lower limb resistance training

High intensity work on quadriceps, hamstrings and plantar flexors:

→ ↓ muscle stiffness in the elderly

Ochala et al, 2007

→ ↓ bradykinesia, rigidity and ↑ walking speed in PD+

→ Improves balance + QOL scores in PD

Hirsch et al., 2003 ; Dibble et al, 2006, 2009 ; Morris et al, 2009

For balance in PD
Motor strenthening > « balance exercises»

- N=32 (resistance training: n = 17, balance training: n = 15; 8 drop-outs) analyzed at W8 following 7-Wk, 2x/wk training.

- **Resistance training group, but not balance training group significantly improved on Fullerton Advanced Balance (FAB) scale** (resistance training: +2.4 points, Cohen's d = -0.46; balance: +0.3 points, d = -0.08)

- Within resistance training group, **improvements FAB scale correlated with improvements of <u>rate of force development</u>** and **stride time variability**.

Schlenstedt C, Paschen S, Kruse A, Raethjen J, Weisser B, Deuschl G. Resistance versus Balance Training to Improve Postural Control in Parkinson's Disease: A Randomized Rater Blinded Controlled Study. PLoS One. 2015;10(10):e0140584

Clinical benefits from motor strengthening in elderly and in PD

Mov Disord. 2013 August ; 28(9): 1230–1240. doi:10.1002/mds.25380.

A Two Year Randomized Controlled Trial of Progressive Resistance Exercise for Parkinson's Disease

Daniel M. Corcos[1,2,3], **Julie A. Robichaud**[1], **Fabian J. David**[1], **Sue E. Leurgans**[3,4], **David E. Vaillancourt**[5], **Cynthia Poon**[1], **Miriam R. Rafferty**[6], **Wendy M. Kohrt**[7], and **Cynthia L. Comella**[3]

Abstract

Background—The effects of progressive resistance exercise (PRE) on the motor signs of Parkinson's disease have not been studied in controlled trials. Our aim was to compare 6, 12, 18, and 24 month outcomes of patients with Parkinson's disease who received PRE to a stretching, balance, and strengthening exercise program.

Mov Disord. 2013 August ; 28(9): 1230–1240. doi:10.1002/mds.25380.

A Two Year Randomized Controlled Trial of Progressive Resistance Exercise for Parkinson's Disease

Daniel M. Corcos[1,2,3], Julie A. Robichaud[1], Fabian J. David[1], Sue E. Leurgans[3,4], David E. Vaillancourt[5], Cynthia Poon[1], Miriam R. Rafferty[6], Wendy M. Kohrt[7], and Cynthia L.

At 24 months, the mFC group had returned to a similar baseline UPDRS-III score (-0·1; SD ±8·7) whereas ***the PRE group score was: -7·4 (±7·4) points lower.***

Gracies, 2010

Motor strengthening improves gait

- Improvement of both groups in gait speed in OFF, cadence OFF or ON, et PF strength OFF.

- PF strength correlated w gait speed and step length at D1 and M24 (not Δ)

Rafferty MR, … Robichaud JA, … Comella CL, Corcos DM. Effects of 2 Years of Exercise on Gait Impairment in People With Parkinson Disease: The PRET-PD Randomized Trial. J Neurol Phys Ther. 2017;41(1):21-30

Gracies, 2010

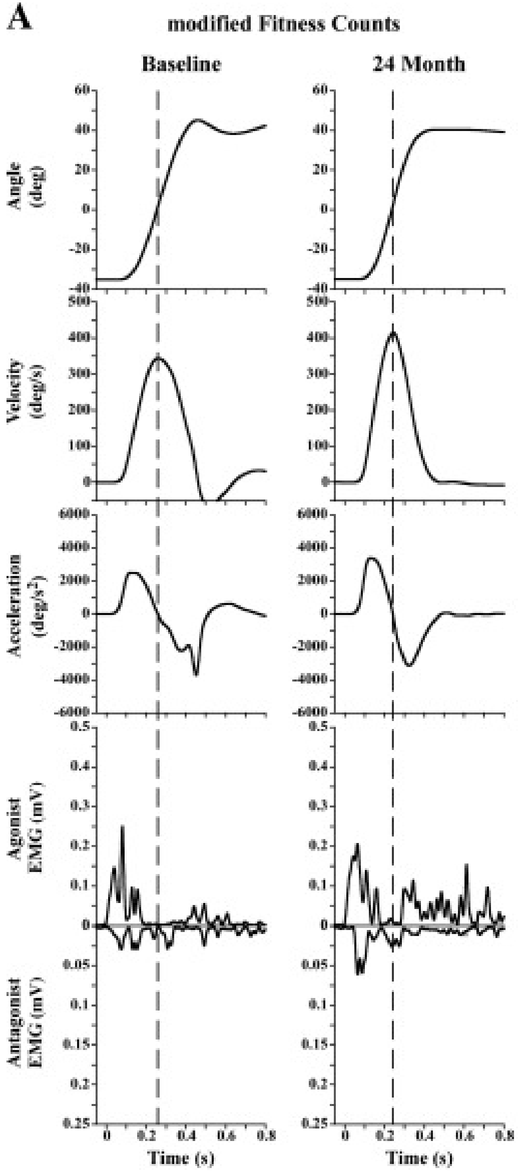
Motor strengthening improves/restores triphasic pattern of ballistic movement EMG

- M 24, PRET *vs* mFC : ↑ movement speed, ↑ ***duration***, ***amplitude***, and amplitude/duration ratio ***of first agonist burst*** + fewer agonist bursts efore peak of speed

- Duration and amplitude of 1st agoist burst and motor strength correcalted with UL bradykinesia

David FJ, Robichaud JA, … Comella CL, Corcos DM.
Progressive resistance exercise restores some properties of the triphasic EMG pattern and improves bradykinesia: the PRET-PD randomized clinical trial.
J Neurophysiol. 2016;116(5):2298-2311

Gracies, 2010



David FJ, Robichaud JA, … Comella CL, Corcos DM.
Progressive resistance exercise restores some properties of the triphasic EMG pattern and improves bradykinesia: the PRET-PD randomized clinical trial.
J Neurophysiol. 2016;116(5):2298-2311

Gracies, 2010

Cognitive effects of motor strengthening in PD

Motor strengthenng - and aerobic - improves attention and working memory

M24:

- Motor strenthening improves digit span (0.5; 0.2, 0.8; p<0.01), Stroop (0.2; −0.1, 0.6; p=0.048), and *Brief Test of Attention* (0.3; 0, 0.8; p=0.048).

- « modified Fitness Counts » ↗ digit span (0.7; 0.3, 1.7; p<0.01) and Stroop (0.3; 0.1, 0.5; p=0.03).

David FJ, Robichaud JA, Leurgans SE, … Comella CL, Vaillancourt DE, Corcos DM. Exercise improves cognition in Parkinson's disease:The PRET-PD randomized, clinical trial. Mov Disord. 2015;30(12):1657-63

Psychological effects of motor strengthening in general

Acute anxiolytic and antidepressant effect of motor strengthening

Affective benefits associated with aerobic exercise = well documented.

→ Individuals enrolled in weight training class (n = 104) randomly assigned 1 of 5 exercise conditions: control, low-long, low-short, high-long, and high-short, varying intensities, and rest time. Anxiety and positive and negative affect measurements collected *immediately* following exercise workouts.

Low-long group reported higher <u>positive affect</u> than control group, at 5-minute postexercise.

Effect for time on **<u>anxiety</u>** ($p = 0.003$): highest anxiety detected at 5-minute postexercise, and **<u>significant reductions in anxiety at both 20-minute and 40-minute postexercise</u>**.

Bibeau WS, Moore JB, Mitchell NG, Vargas-Tonsing T, Bartholomew JB (Maryland). Effects of acute resistance training of different intensities and rest periods on anxiety and affect. J Strength Cond Res. 2010 Aug;24(8):2184-91

Gracies, 2010

Parkinsonism: agonist - antagonist imbalance

Handwriting: larger accelerations in wrist flexion-ulnar deviation movements than in extension – radial deviation movements *Teulings et al, 1997*

Rapid alternating movements in pronation/supination and in elbow flexion/extension *Gracies et al, 2001*

Motor power: relative weakness of extensors / flexors *Robichaud et al, 2004*

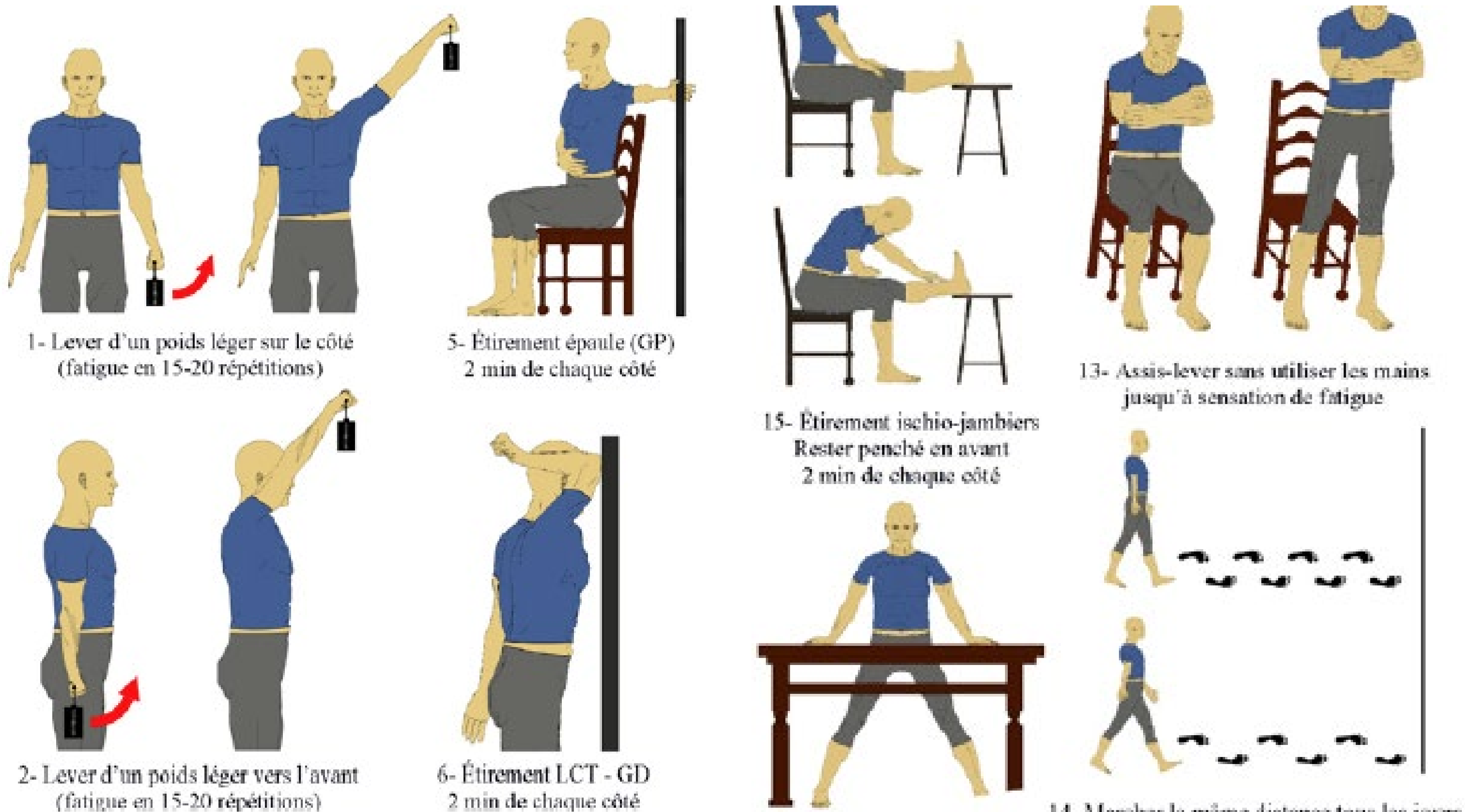
Posture… : extensor hypoactivity

Spiralography : agonist-antagonist asymmetry contributes to particular shape of spirals « shell-like» in advanced disease *Chen et Gracies, 2005*

Gracies, 2010

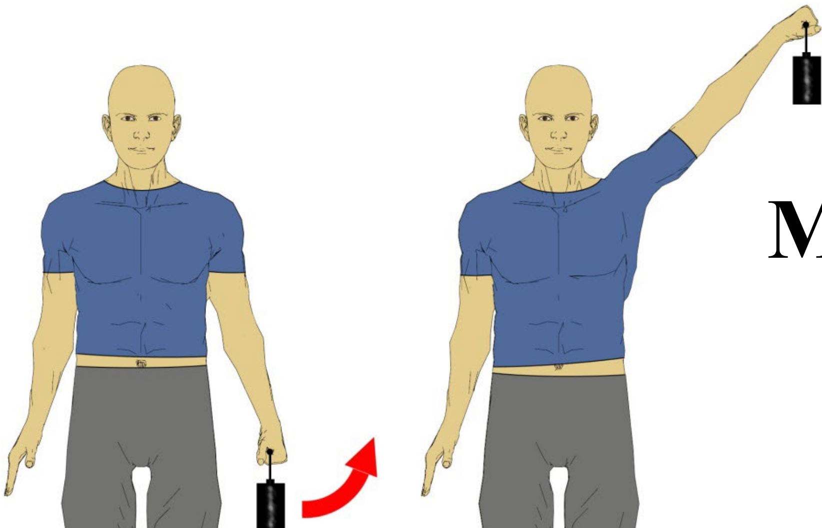
Asymetric Motor Strengthening

- Increase excitability of command to « opening » agonists (Classen 2008): extensors, abductors, supinators, etc.
- Stretch « closing » antagonists: flexors, pronators, adductors etc..

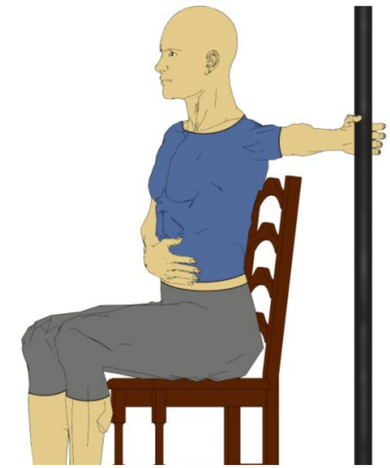


Asymmetric motor strengthening

Mild to moderate stages (I)



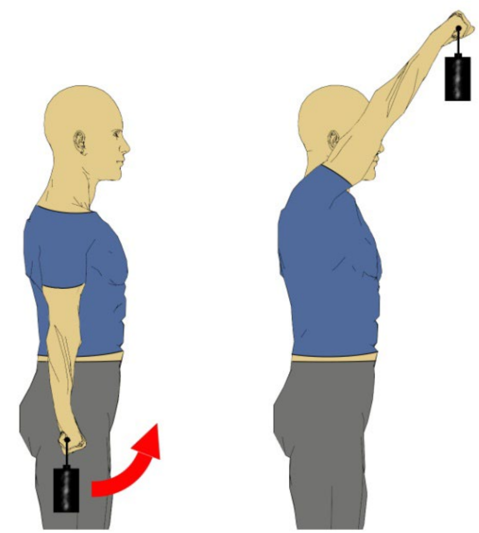
1- Light weight lift to the side
→ <u>Fatigue</u> after 15-20 repeats



2 - PM stretch
2 minutes each side

Recruitment of spinal extensors
(Moseley et al, 2002; Khouw et Herbert, 1998)

4- Stretch LHT-LD
2 mn each side

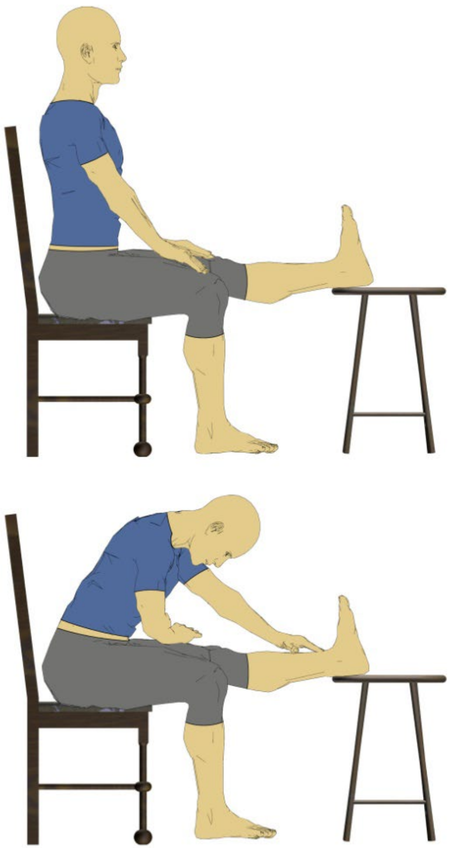


3- Light weight lift to the front
→ <u>Fatigue</u> after 15-20 repeats

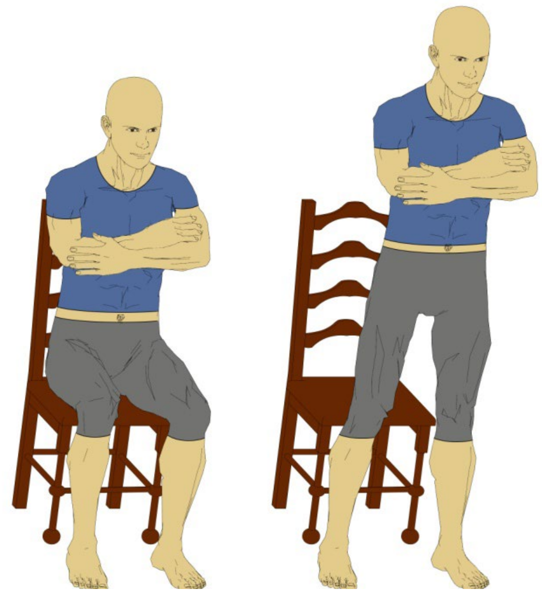
→ ***Clear feeling of physical fatigue*** *(Rooney et al, 1994)*

Gracies, 2010

Asymmetric motor strengthening



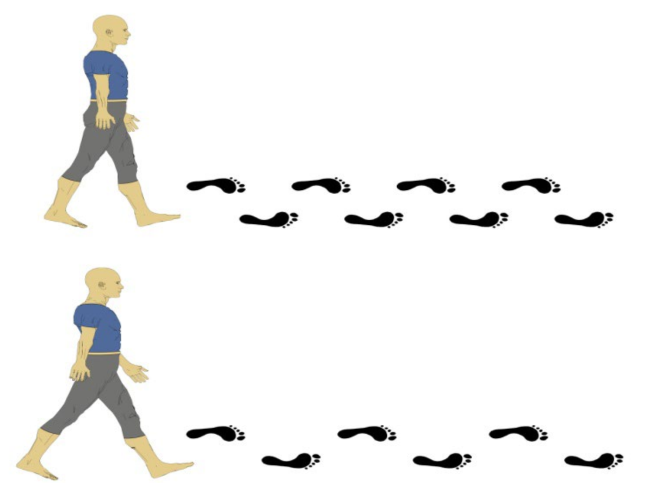
6 – Hamstrings stretch
Bend forward
2 mn each side



5- Sit-to-stand w/o hands
until fatigue

7 - Adductor stretch
2 mn /day

Mild to moderate stages (2)



8 – Walk same distance every day
With as few steps as possible

Gracies, 2010

3. Guided Self-rehabilitation Contracts to learn *Asymetric Motor Strengthening*

Guided Self-rehabilitation Contracts in Parkinsonism

Psychologically = diary-based

Technically = agonist-based

Gracies JM. Guided Self-rehabilitation Contract in Spastic Paresis. Springer Int Publ, Switzerland, 2016; ISBN 978-3-319-29107-9; ISBN 978-3-319-29108-6 (eBook);118p.

GSC
Psychological aspect
=
<u>diary-based</u> rehabilitation

How to get a person with parkinsonism to self-rehabilitate, over the long term?

Rehabilitation of parkinsonism is confronted with at least a double problem with motivation.

1. Chronicity of the required work
2. Information received on "progression"..

How to enhance motivation?

Guided Self-rehab = Contract

Self-monitoring!

Psychiatry: Continuous, daily holding of a diary may have antidepressant properties *per se*. **At least holding a diary may provide positive reinforcement by itself**

Ackerman AM & Shapiro ES. J Appl Behav Anal. 1984;17(3):403–407;
Hanel F & Martin G. Int J Rehabil Res. 1980;3(4):505–517;
Lenderking WR et al. Contemp Clin Trials. 2008;29(6):867–877.

Guided Self-rehab = Contract

Self-monitoring!

Addictology: Self-monitoring diary + moral contract between patient and therapist = components of a *physical inactivity-cessation programme* (akin to smoking cessation programmes)

Burkhart PV et al. J Nurs Scholarsh. 2007;39(2):133-40;
Kilmann PR et al. J Clin Psychol. 1977;33(3):912–914;
Strecher VJ. Public Health Rep. 1983;98(5):497–502.

International Randomized Clinical Trial, Stroke Inpatient Rehabilitation With Reinforcement of Walking Speed (SIRROWS), Improves Outcomes

Bruce H. Dobkin, MD[1], **Prudence Plummer-D'Amato, PhD**[2], **Robert Elashoff, PhD**[1], **Jihey Lee, PhD**[1], and **the SIRROWS Group**

[1]Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, USA

[2]Northeastern University, Boston, Massachusetts, USA

Abstract

Background—Feedback about performance may optimize motor relearning after stroke.

Objectives—Develop an international collaboration to rapidly test the potential efficacy of daily verbal feedback about walking speed during inpatient rehabilitation after stroke, using a protocol that requires no research funds.

Methods—This phase 2, single-blinded, multicenter trial randomized inpatients to either feedback about self-selected fast walking speed (daily reinforcement of speed, DRS) immediately after a single, daily 10-m walk or to no reinforcement of speed (NRS) after the walk, performed within the context of routine physical therapy. The primary outcome was velocity for a 15.2-m (50-foot) timed walk at discharge. Secondary outcomes were walking distance in 3 minutes, length of stay (LOS), and level of independence (Functional Ambulation Classification, FAC).

Dobkin BH et al. *Neurorehabil Neural Repair.* 2010;24:235–242.

International Randomized Clinical Trial, Stroke Inpatient Rehabilitation With Reinforcement of Walking Speed (SIRROWS), Improves Outcomes

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[1]Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, USA

[2]Northeastern University, Boston, Massachusetts, USA

age, gender, time from onset of stroke to entry, initial velocity, and level of walking-related disability. The walking speed at discharge for DRS (0.91 m/s) was greater (P = .01) than that for NRS (0.72 m/s). No difference was found for LOS. LOS for both DRS and NRS was significantly shorter, however, for those who had mean walking speeds >0.4 m/s at entry. The DRS group did not have a higher proportion of FAC independent walkers (P = .1) and did not walk longer distances (P = .09).

Conclusions—An Internet-based collaboration of 18 centers found that feedback about performance once a day produced gains in walking speed large enough to permit unlimited, slow community ambulation at discharge from inpatient rehabilitation.

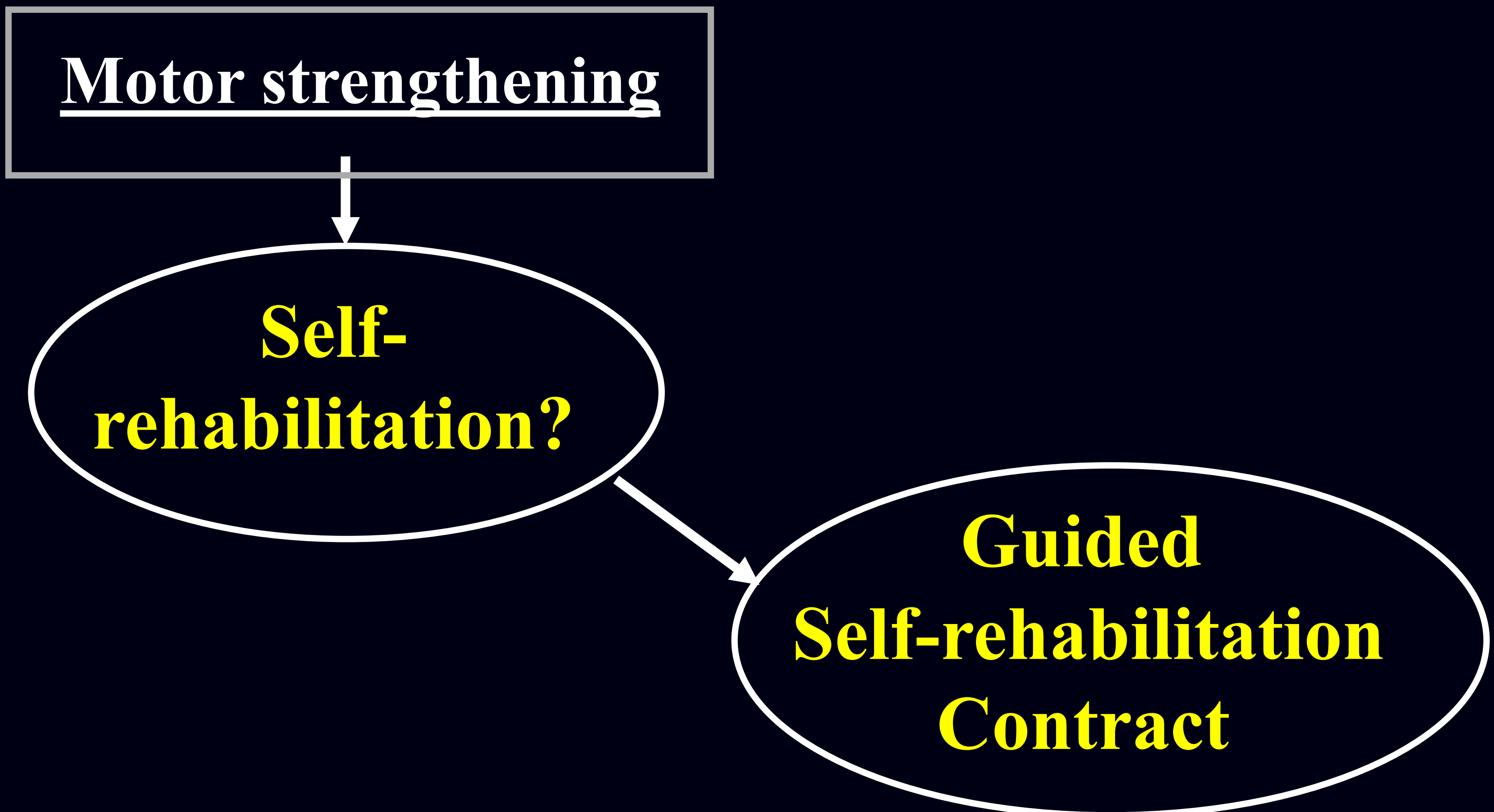
Dobkin BH et al. *Neurorehabil Neural Repair.* 2010;24:235–242.

Generating motivation = mandating a Diary

Name Cecilia — 1 minute (stretch before and after)

Dates	8/06	8/07	8/08	8/09	8/10	8/11	8/12	8/13	8/14	8/15	8/16	8/17	8/18	8/19	8/20	8/21	8/22	8/23
Shoulder Flexions (hip to target)	26	25		26	25	25	24		26	25	24	25	25	25	24	24	23	24
Shoulder Abductions (hip to target)	25	24		27	26	24	27		25	26	24	24	25	25	24	25	24	24
Shoulder External Rotations (stomach to wall)	25	27		26	26	26	26		26	27	26	25	25	27	27	25	26	25
Elbow Extensions (nose to target)	23	24		24	23	25	24		24	23	23	24	23	24	24	23	23	23
Elbow supinations (hand tapper)	20	23		26	23	23	23		26	25	25	23	24	23	25	25	24	23
Wrist extensions (hand flaps)	24	24		30	23	26	25		28	26	31	25	25	27	27	27	29	26
Thumb abductions	4	4		4	5	5	5		6	5	5	5	6	4	4	4	5	6
Thumb extensions	31	30		40	41	43	40		39	40	45	40	44	45	45	47	42	38
II extensions	30	30		22	23	22	21		30	32	24	22	21	20	24	22	25	25
III extensions	23	23		22	25	24	24		26	30	25	23	24	24	23	23	25	25
IV extensions	8	6		7	9	8	11		11	11	12	10	9	11	10	12	18	18
V extensions	70	67		68	68	70	69		73	71	72	69	67	69	70	71	66	68
Hip Flexions (floor to hand)	41	40		40	40	42	42		43	42	41	44	43	43	40	42	41	41
Steps (10 up and 10 down)	58	58		57	57	56	56		57	57	58	56	58	58	58	58	59	58
2 minute walking																		

Motor strengthening
Key factors = fatigue and repetition



Guided Self-rehab = Contract

Role of the therapist

1. The physical therapist does not <u>practice</u> the therapy, e.g. 25 mn 3x/week ...

→ 2. The physical therapist <u>prescribes</u> and <u>coaches</u> the therapy, e.g. 90 mn, 2x/month

Gracies JM. Guided Self-rehabilitation Contract in Spastic Paresis. Springer Int Publ, Switzerland, 2016; ISBN 978-3-319-29107-9; ISBN 978-3-319-29108-6 (eBook);118p.

Guided Self-rehab = Contract

Role of the patient

1. The patient practices the therapy, e.g. 60 mn, 6 or 7d/7

2. The patient documents the therapy, in writing, in a diary

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Guided Self-rehab Contract =

1. Patient works and documents
2. Therapist teaches and coaches

→ For each important <u>agonist</u>!!

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Guided Self-rehab Contract =

1. Patient works and documents
2. Therapist teaches and coaches

Accept

"long-term" perspective!

Gracies JM. Guided Self-rehabilitation Contract in Spastic Paresis. Springer Int Publ, Switzerland, 2016; ISBN 978-3-319-29107-9; ISBN 978-3-319-29108-6 (eBook);118p.

Increasing motor cortex excitability

Gracies, 2010

Increasing motor cortex excitability for body openers

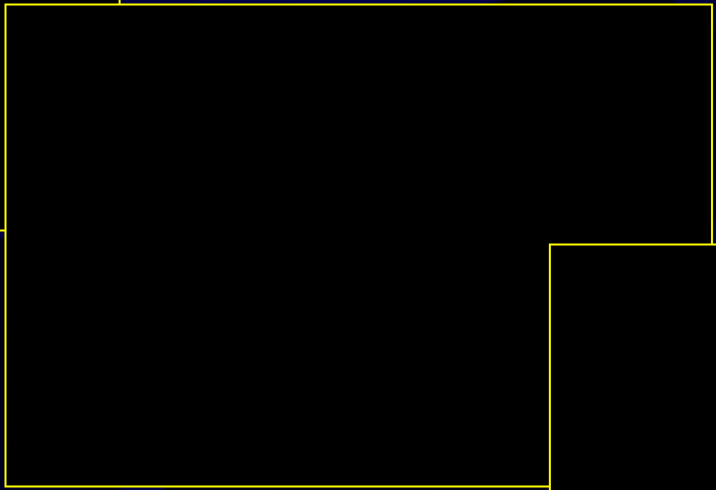
Gracies, 2010

Increasing motor cortex excitability for body openers

Gracies, 2010

Eight weeks of asymmetric motor strengthening 60 min x 3/ week Supine-to-Stand

D1



M2

M5

Gracies, 2013

Eight weeks of asymmetric motor strengthening 60 min x 3/ week Supine-to-Stand

D1

M2

M5

Gracies, 2013

Asymmetric motor strengthening GSC - 6 months – Sit-to-stand - power

Nov 14

May 15

GSC Asymmetric motor strengthening
6 months – Gait
Step length regulation at fast speed

Nov 14

May 15

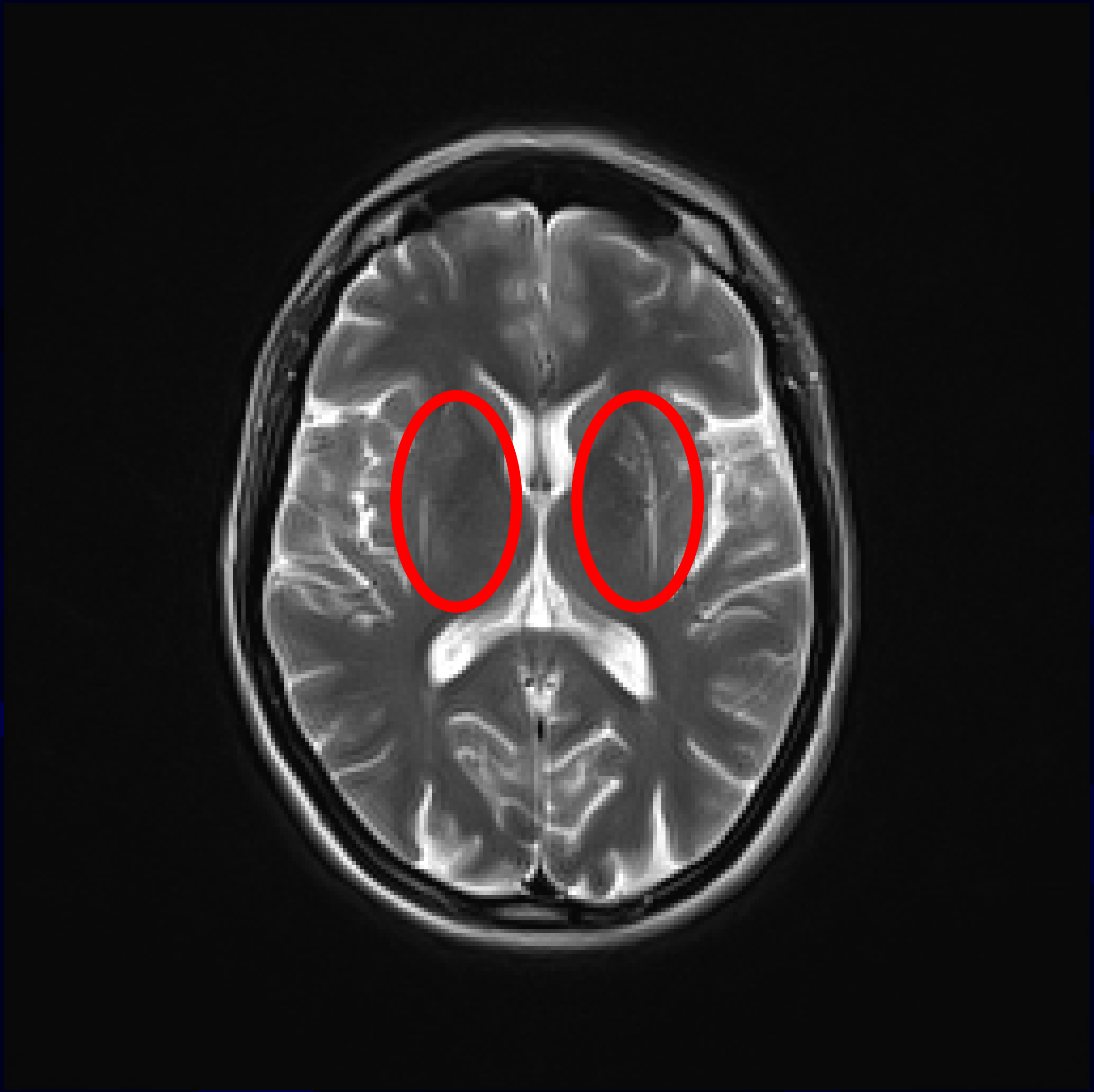
Gracies, 2014

Asymmetric motor strengthening 6 months – Stand from ground

Nov 14

Feb 15

May 15



AMS (2010)

Józef Julian Franciszek Feliks Babiński
«De l'asynergie cérébelleuse», in: *Rev Neurol*, 7 (1899): 806-816.

Increasing excitability of motor cortices → standing up from ground

MSA Year 7 +++
7 weeks of GSC
weekly sessions
motor
strengthening

Gracies, 2010

Increasing excitability of motor cortices → doing *Géant* Glacier

14 years from symptom onset to death++

Consort Diagram

Included n=38

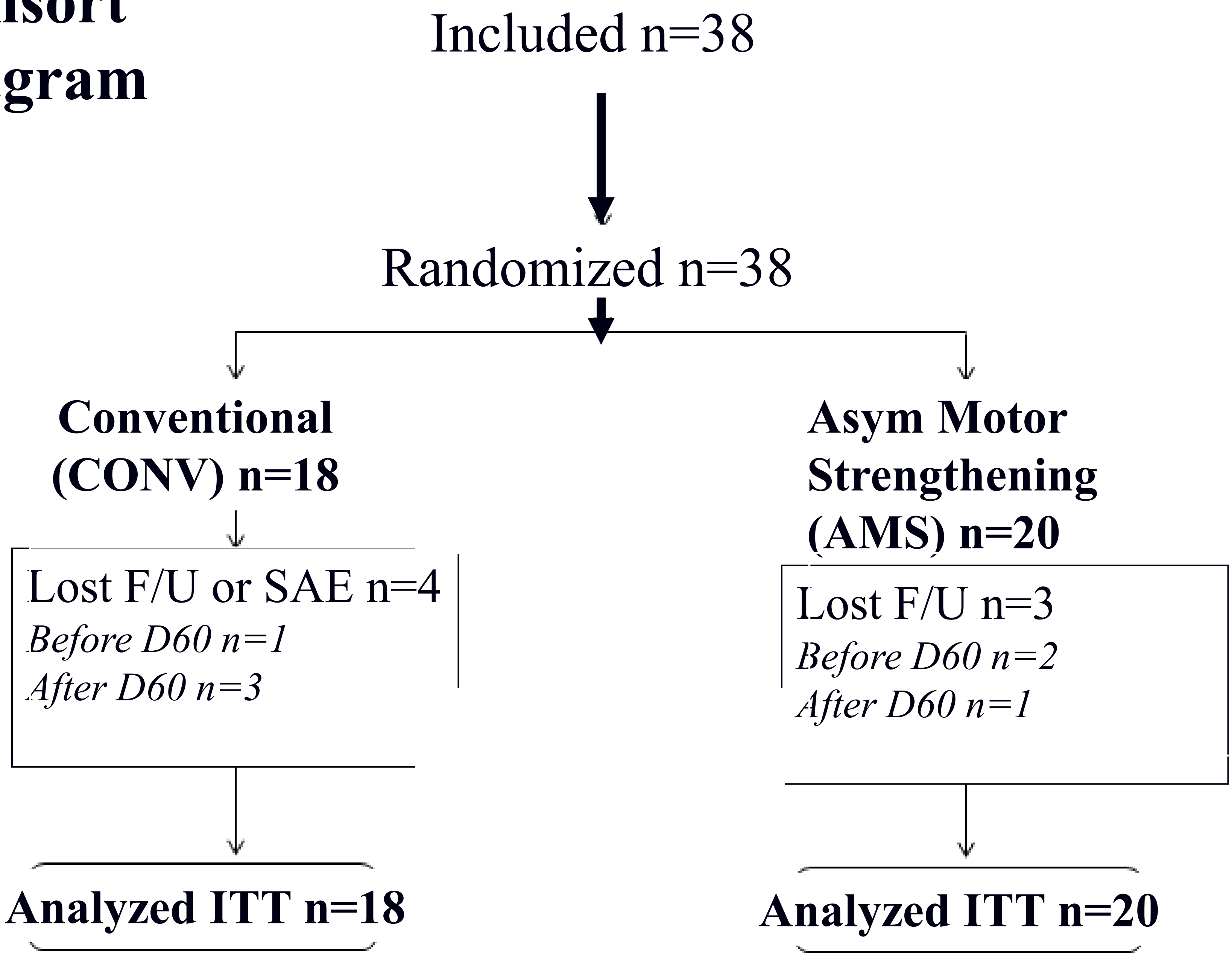
Randomized n=38

Analyzed ITT n=18

Analyzed ITT n=20

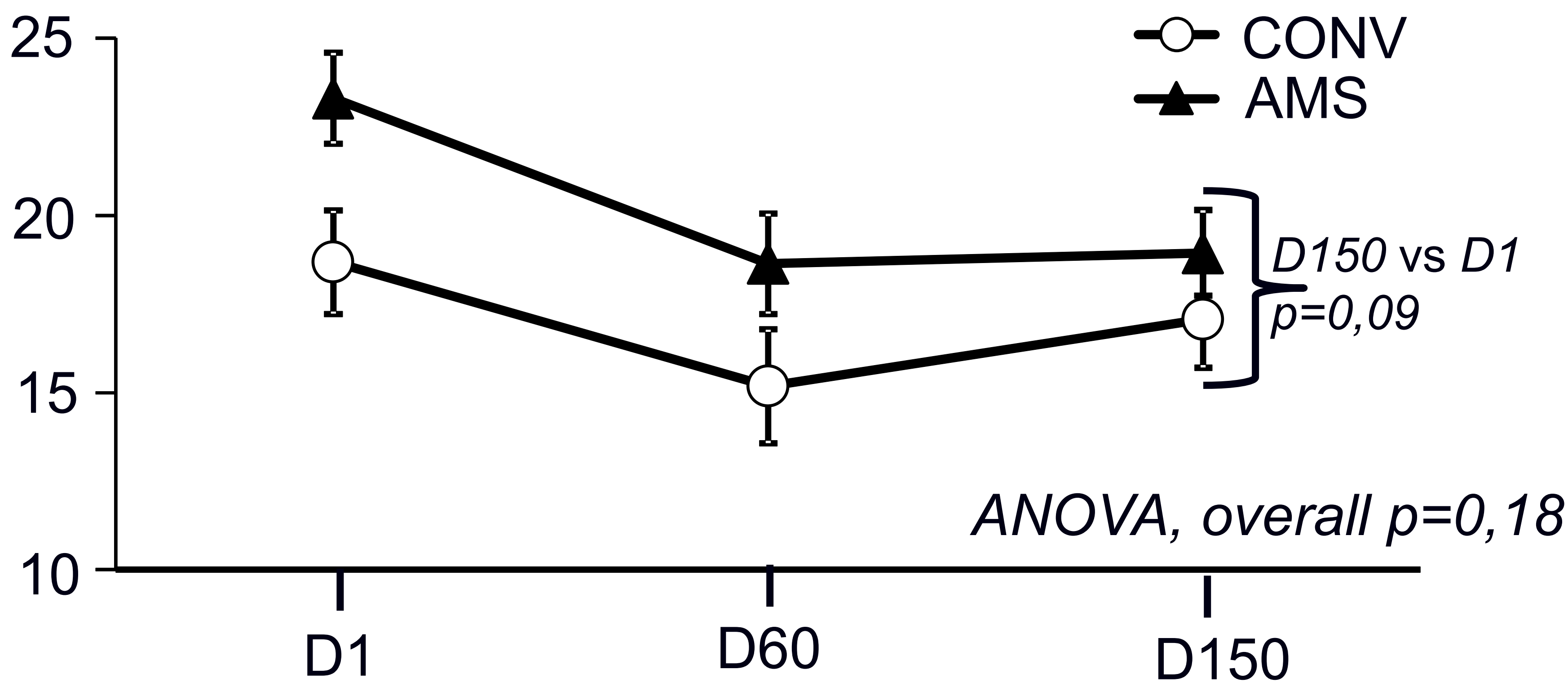
PHRC Asymot, Gracies, Bayle, Hutin, Baude unpublished

Consort Diagram



PHRC Asymot, Gracies, Bayle, Hutin, Baude unpublished

UPDRS III OFF
D1-D60-D150



PHRC Asymot, Gracies, Bayle, Hutin, Baude unpublished

Secondary outcome measures

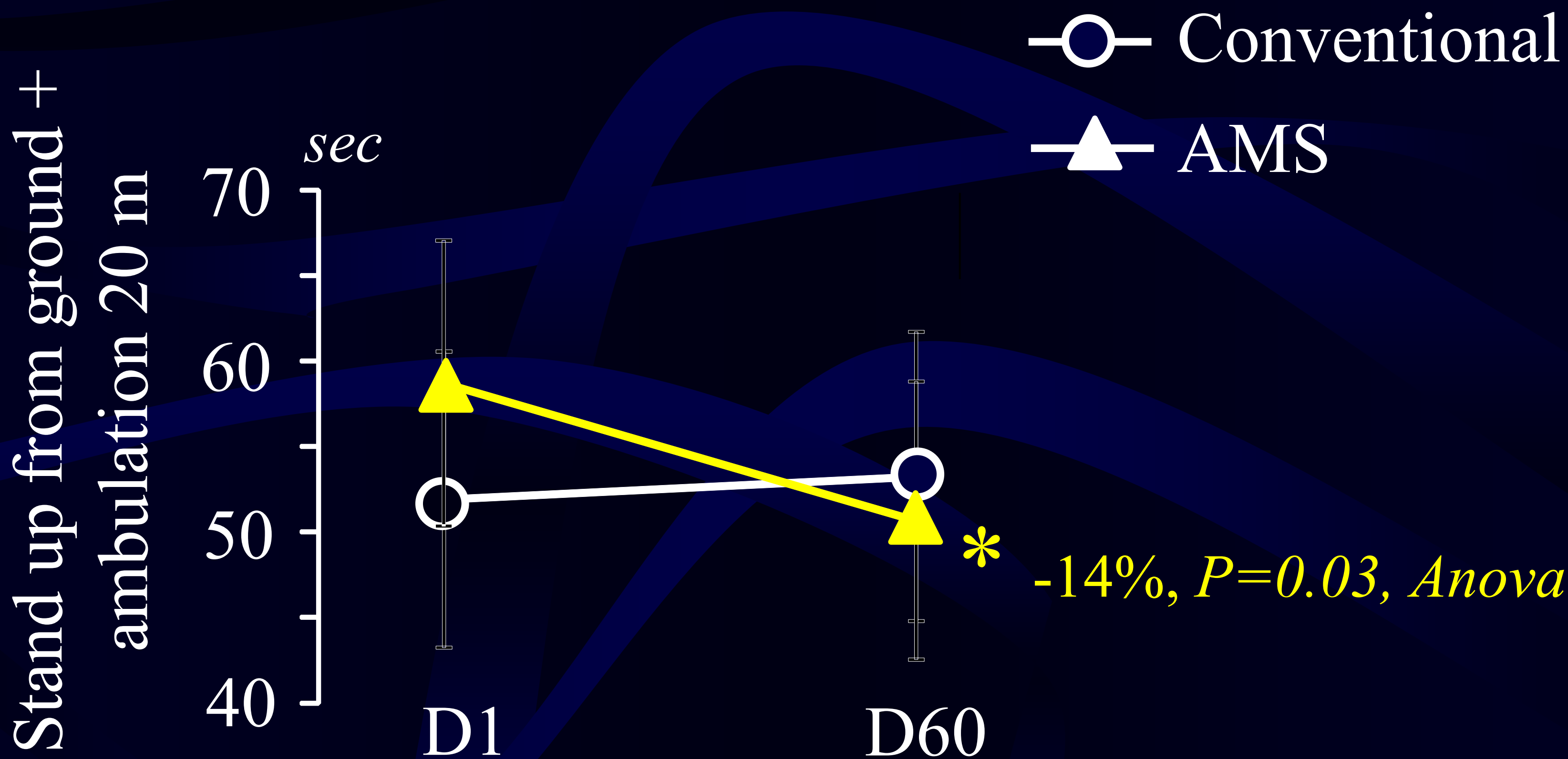
Post hoc GMT+ = ***Time to stand up + time to walk 20 m***

GMT (sec) + Comfortable AT20 (sec)

PHRC Asymot, Gracies, Bayle, Hutin, Baude unpublished

Subacute study 8 weeks -'GMT+' *(post hoc)*

Time to stand up from ground + 20m walk



PHRC Asymot, Gracies, Bayle, Hutin, Baude unpublished

Thèse de Charles Bertin

Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Contrat d’auto-rééducation guidée dans la maladie de Parkinson pendant 3 ans : L’utilisation d’un registre influence-t-elle la prescription de lévodopa et l’évolution motrice?

Charles Bertin

et

Maud Pradines, PT, PhD, Damien Motavasseli, MD, Marjolaine Baude, MD, Caroline Gault-Colas, MD, Tymothée Poitou, MD, Etienne Savard, MD, Nicolas Bayle, MD, Jean-Michel Gracies, MD, PhD

Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Introduction

Maladie de Parkinson (1) :

- 2ème cause de handicap moteur après l'AVC
- Diagnostiquée souvent à partir de l'âge de 55 ans
- Causes possibles multiples : toxiques, traumatiques, infectieuses, vasculaires, génétiques

(1) Ascherio A, Schwarzschild MA. The epidemiology of Parkinson's disease: risk factors and prevention. Lancet Neurol. 2016;15(12):1257-1272

Historique des traitements - chimiques et chirurgicaux

1817 : Soutien personnel + nursing
1890 : Anticholinergiques naturels (Atropa belladonna, Charcot)
1910 : Chirurgies lésionnelles / tractus pyramidal
1940 : Chirurgies lésionnelles / noyaux gris centraux
1940 : Anticholinergiques synthétiques
1967 : Lévodopa
1970 : Agonistes dopaminergiques (bromocriptine)
1991 : Stimulation cérébrale profonde
1998 : Inhibiteurs COMT (tolcapone, entacapone)
Années 2000 : pompes (apomorphine, jénunales lévodopa)…
2023 : Place des traitements physiques???

Introduction

- Traitements physiques sous-utilisés par rapport aux traitements chimiques dopaminergiques et chirurgicaux *(1)*.
- Incapacité des traitements dopaminergiques à contrôler l'aggravation du <u>handicap fonctionnel moteur</u> après quelques années *(1)*.
- Multiples effets secondaires des traitements chimiques *(2)* et chirurgicaux *(3)*.

(1) Gracies JM. Neurorééducation des syndromes parkinsoniens. Rev Neurol (Paris). 2010;166(2):196-212.

(2) Lang AE, Lozano AM. Parkinson's disease. Second of two parts. N Engl J Med. 199815;339(16):1130-43.

(3) Olanow CW, Watts RL, Koller WC. An algorithm (decision tree) for the management of Parkinson's disease (2001): treatment guidelines. Neurology. 2001;56(11 Suppl 5):S1-S88.

Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Introduction

- Choix des stratégies de rééducation : guidé par stade d'évolution *(1)*
- Stades modérés : intérêt de l'enseignement d'exercices simples au patient avec contrat d'auto-rééducation guidée *(2)*
- Technique physique démontrée à moyen-long terme (2 ans) : *renforcement moteur +++ (Corcos et al, 2013)* > exercices aérobies à haute intensité, stratégies attentionnelles (indiçage)
- Effets à plus long terme *dans la pratique* +++ ?

(1) Gracies JM. Neurorééducation des syndromes parkinsoniens Rev Neurol (Paris). 2010;166(2):196-212.

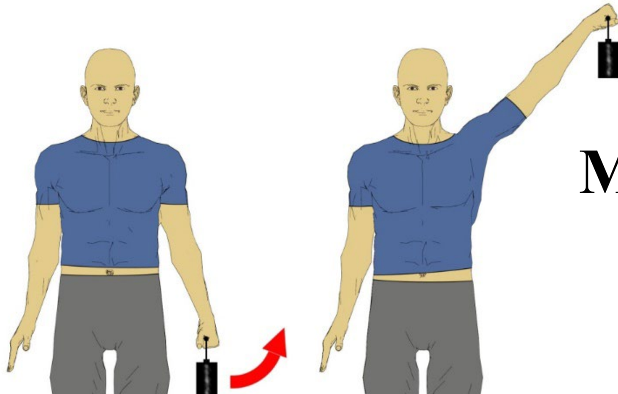
(2) Gracies JM. Guided Self-rehabilitation Contract in spastic paresis. Springer International Publishing, Switzerland, 2016; ISBN 978-3-319-29107-9; ISBN 978-3-319-29108-6 (eBook); DOI 10.1007/978-3-319-29108-6; 118p.

(3) Corcos DM, Comella CL. A two-year randomized controlled trial of progressive resistance exercise for Parkinson's disease. Mov Disord. 2013;28(9):1230-40

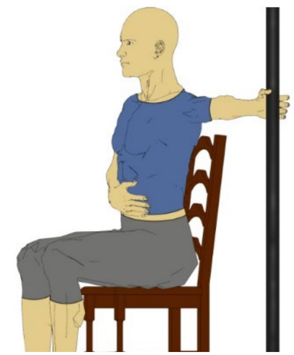
Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Asymmetric motor strengthening

Mild to moderate stages (I)



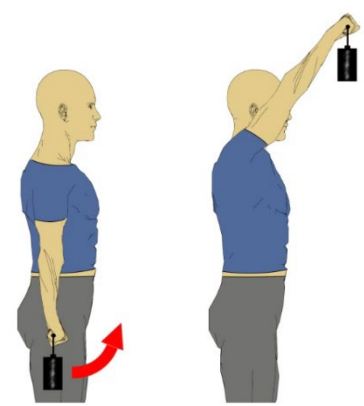
1- Light weight lift to the side
→ <u>Fatigue</u> after 15-20 repeats



2 - PM stretch
2 minutes each side

Recruitment of spinal extensors
(Moseley et al, 2002; Khouw et Herbert, 1998)

4- Stretch LHT-LD
2 mn each side



3- Light weight lift to the front
→ <u>Fatigue</u> after 15-20 repeats

Gracies, 2010

→ ***Clear feeling of physical fatigue*** ***(Rooney et al, 1994)***

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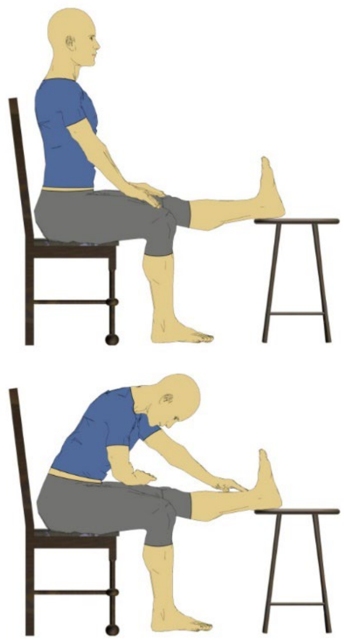
Asymmetric motor strengthening

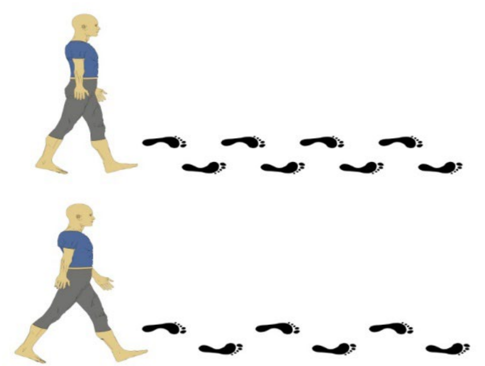


6 – Hamstrings stretch
Bend forward
2 mn each side

5- Sit-to-stand w/o hands
until fatigue

7 - Adductor stretch
2 mn /day

Mild to moderate stages (2)



8 – Walk same distance every day
With as few steps as possible

Gracies, 2010

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S'étirer pendant une minute, avant et après la série de renforcement moteur

Date	15/11	16/11	17/11	18/11	19/11	20/11	21/11	22/11	23/11
Flexion d'épaule	25	24	25	22	26	24	25	25	26
Abduction d'épaule	22	23	24	25	25	25	23	23	25
Extension de coude	25	25	25	24	24	23	25	25	25
Supination de poignet	25	24	25	22	26	24	25	25	26
Extension de poignet	22	23	24	25	25	25	23	23	25
Flexion de hanche	25	25	25	24	24	23	25	25	25
2 minutes de marche	2	2	2	2	2	2	2	2	2

Exemple de registre du travail physique rempli par le patient

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Objectif principal

→ L'utilisation d'un *registre* du travail physique, outil psychologique de renforcement positif (2) (3), au sein d'un Contrat d'Auto-rééducation Guidée influence-t-elle l'évolution motrice et la prescription de lévodopa sur le long terme (3 ans) ?

(1) Pothakos, 2009

(2) Ackerman AM & Shapiro ES. J Appl Behav Anal. 1984

(3) Hanel F & Martin G. Int J Rehabil Res. 1980Lenderking WR et al. Contemp Clin Trials. 2008

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Hypothèse principale

→ L’utilisation d’un *registre* du travail physique, outil psychologique de renforcement positif (2,3), au sein d’un Contrat d’Auto-rééducation Guidée sur le long terme (3 ans) diminue le besoin en lévodopa et améliore l’évolution motrice, sur des tâches de motricité <u>spontanée</u> (non indicée, ex déambulation à vitesse confortable).

(1) Pothakos, 2009

(2) Ackerman AM & Shapiro ES. J Appl Behav Anal. 1984

(3) Hanel F & Martin G. Int J Rehabil Res. 1980Lenderking WR et al. Contemp Clin Trials. 2008

Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Méthodes

- Étude rétrospective
- Multicentrique
- Critères inclusion dossiers :
    1. Patients présentant une maladie de Parkinson idiopathique
    2. Age > 18 ans
    3. Score UPDRS III (OFF ou ON) < 40 à la première visite
    4. Délai depuis le diagnostic <15 ans à la première visite
    5. Délai depuis les premiers symptômes moteurs ≤ 16 ans à la première visite
    6. <u>Suivi ≥36 mois</u> en neurorééducation ou en neurologie aux HU Henri Mondor

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Méthodes

- Critères de non-inclusion dossiers :
  - Autres affections neurologiques ou orthopédiques en dehors de la maladie de Parkinson, susceptibles de perturber les évaluations

- Deux groupes de patients seront définis :
  1. Suivis en contrat d'autorééducation guidée avec registre : CAR
  2. Suivis en contrat d'autorééducation guidée sans registre : CSR

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Méthodes

Critère d'évaluation primaire : Différence de changement de la posologie prescrite d'équivalents-lévodopa (1) entre le groupe CAR et le groupe CSR

- Stat: *RANK Anova* à deux facteurs, groupe et visite et une variable dépendante: LED/vitesse d'écriture/vitesse de déambulation (AT20)

(1) Jost et al, Mov Dis, 2023

Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Méthodes

Critères d'évaluation secondaires (en OFF) :

1. UPDRS III (CS *vs* CAR ou CSR)
2. Posologie en équivalents-lévodopa (CS vs CAR ou CSR)
3. Vitesse de déambulation et longueur des pas à allure confortable, allure rapide, et en marche à grands pas *(AT 20 ; Hutin et al, 2023)*
4. Moyennes des vitesses d'écriture sur trois phrases consécutives *(Tchaikovski et al 2016; Thèse de médecine)*
5. Paramètre exploratoire : VitGP/VitR *(Behrman et al, 2018)*
6. Exploration corrélation entre paramètres qui caractérisent patients : UPDRS III, vitesse d'écriture, vitesse et LP en condition confortable et LED

- *Hutin E, Ghédira M, Mardale V, Boutou M, Santiago T, Joudoux S, Gault-Colas C, Gracies JM, Bayle N. Test-Retest and Inter-Rater Reliability of the 20-Meter Ambulation Test in Patients with Parkinson's Disease. J Rehabil Med. 2023 Mar 21;55*
- *Tchaikovski V, Gracies JM, Hutin E, Bayle N, Radot C. Characteristics of Parkinson's disease in pen and paper handwriting and correlation with ambulation parameters. Ann Phys Rehabil Med. 2016;59S:e65-e66*
- *Behrman AL, Teitelbaum P, Cauraugh JH. Verbal instructional sets to normalise the temporal and spatial gait variables in Parkinson's disease. J Neurol Neurosurg Psychiatry. 1998 Oct;65(4):580-2*

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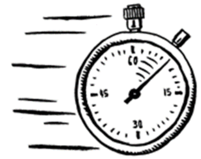
Méthodes



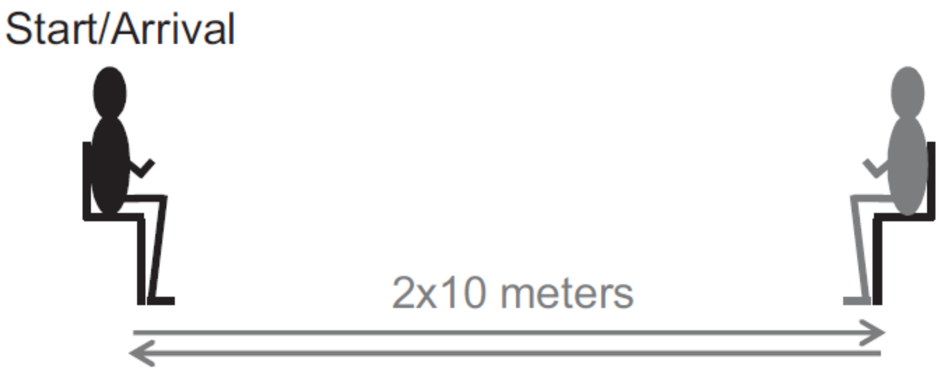
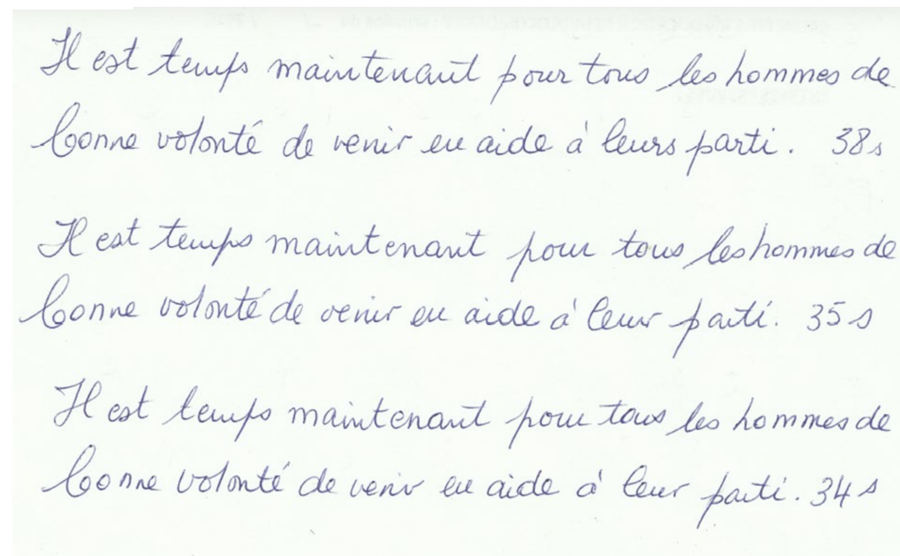


Fig. 1. The 20-m ambulation test (AT20). The AT20 evaluates walking over a 20 m total distance back and forth between 2 chairs, 10 m apart, starting and ending in a seated position.



AT20

Vitesse écriture

- Hutin E, Ghédira M, Mardale V, Boutou M, Santiago T, Joudoux S, Gault-Colas C, Gracies JM, Bayle N. Test-Retest and Inter-Rater Reliability of the 20-Meter Ambulation Test in Patients with Parkinson's Disease. J Rehabil Med. 2023 Mar 21;55

- Tchaikovski V, Gracies JM, Hutin E, Bayle N, Radot C. Characteristics of Parkinson's disease in pen and paper handwriting and correlation with ambulation parameters. Ann Phys Rehabil Med. 2016;59S:e65-e66

Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Méthodes

- Stat: *RANK Anova univariée* à deux facteurs, groupe et visite et une variable dépendante : LED / vitesse d'écriture / vitesse de déambulation / longueur de pas (AT20)
- Exploration corrélations (paramétriques puis Spearman) entre différents param moteurs, UPDRS *vs* Vit Ecriture *vs* LED *vs* paramètres de marche en vitesse confortable

(1) Jost et al, Mov Dis, 2023

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Caractéristiques des groupes à la 1ère consultation en neurorééducation (n = 22)	Avec registre (n = 11)	Sans registre (n = 11)
	Médianes, Q1, Q3	
Âge (ans)	67 [61;72]	72 [66;73]
Sexe	4F/7H	4H/7F
Délai depuis premiers symptômes (années)	5 [3;9]	5 [4;8]
Délai depuis diagnostic (années)	3 [2;4]	4 [1;5]
Hoehn & Yahr	2,5 [2;3]	1 [1;2]
UPDRS III OFF	16 [9,5;19,0]	12 [9,5;17]
LED (mg/j)	350,5 [129;425]	300 [175;565]
Rigidité (n,%)	8 (73%)	2 (18,2%)
Tremblement de repos (n,%)	6 (55%)	9 (81,2%)
Troubles de l'équilibre (n,%)	5 (46%)	1 (9%)
Vitesse de marche confortable (m/s)	0,83 [0,74;0,93]	1,04 [0,96;1,12]
Moyenne des vitesses d'écriture V1 à V3 (mm/s)	7,51 [5,44;11,41]	9,23 [6,06;9,90]

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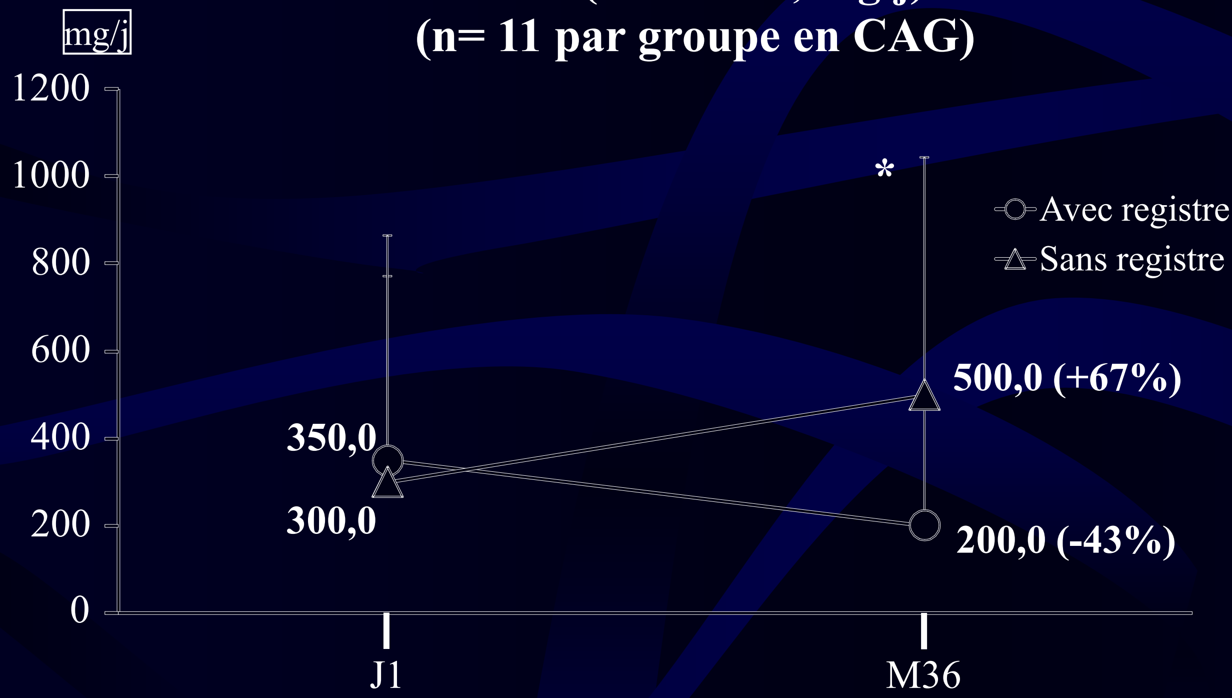
Résultats : critère d'évaluation primaire

LED (médianes; mg/j)
(n= 11 par groupe en CAG)



Evolution de la prescription de LED	Avec registre (CAR)	Sans registre (CSR)
Test de Rank-ANOVA	2^{E}-04	
Test de Mann-Whitney	0,003	

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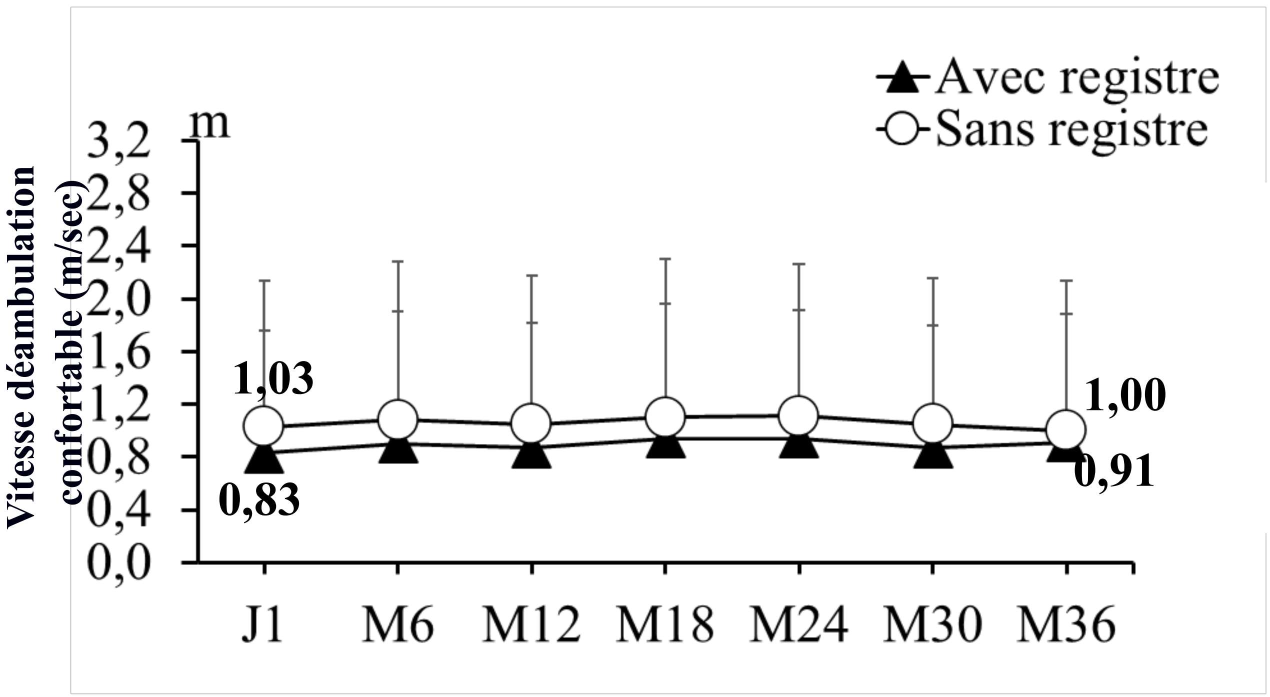
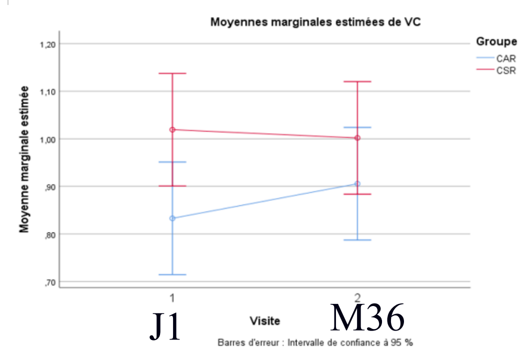
Critère secondaire :

Vitesse déambulation confortable





Rank Anova P=0,007

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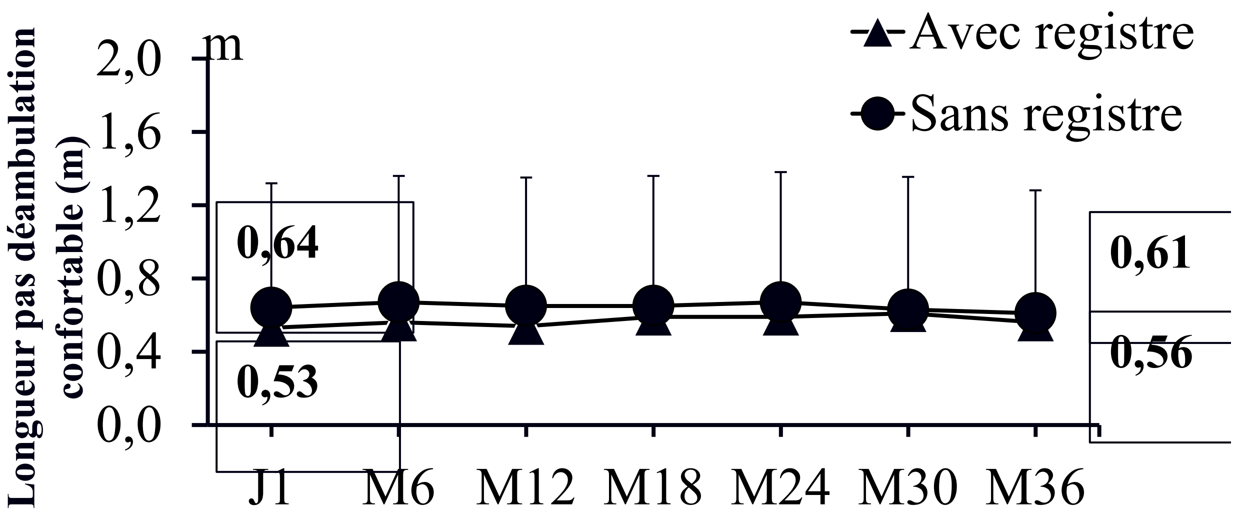
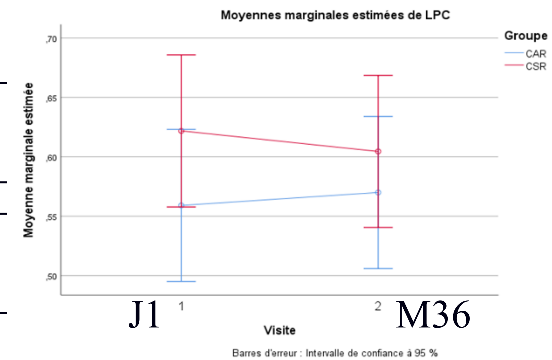
Critère secondaire : longueur pas déambulation confortable





Rank Anova P=0,038

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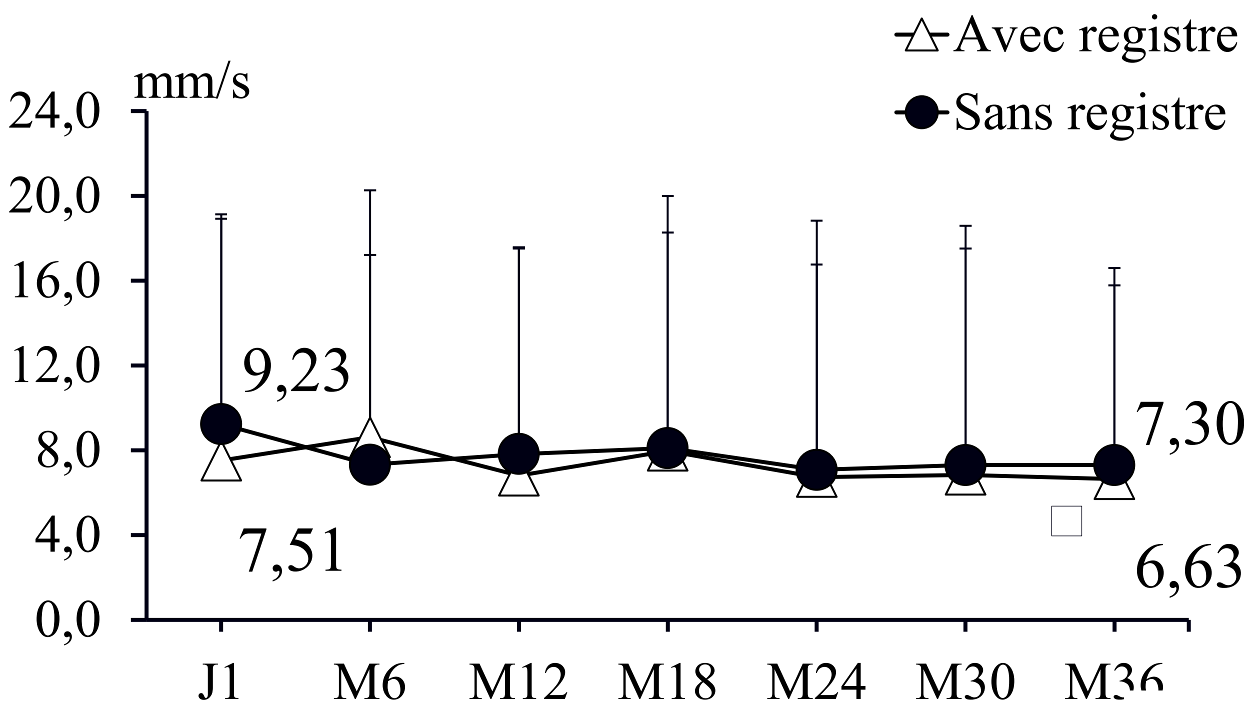
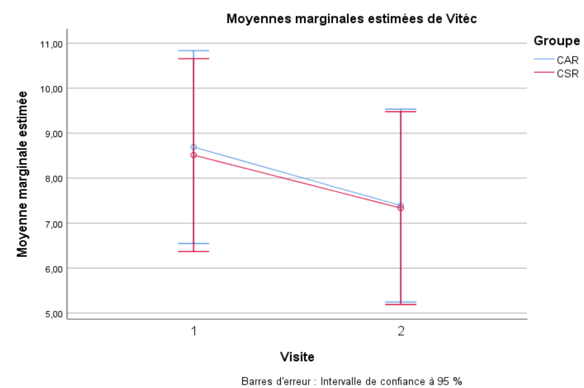
Critère secondaire : vitesse d'écriture





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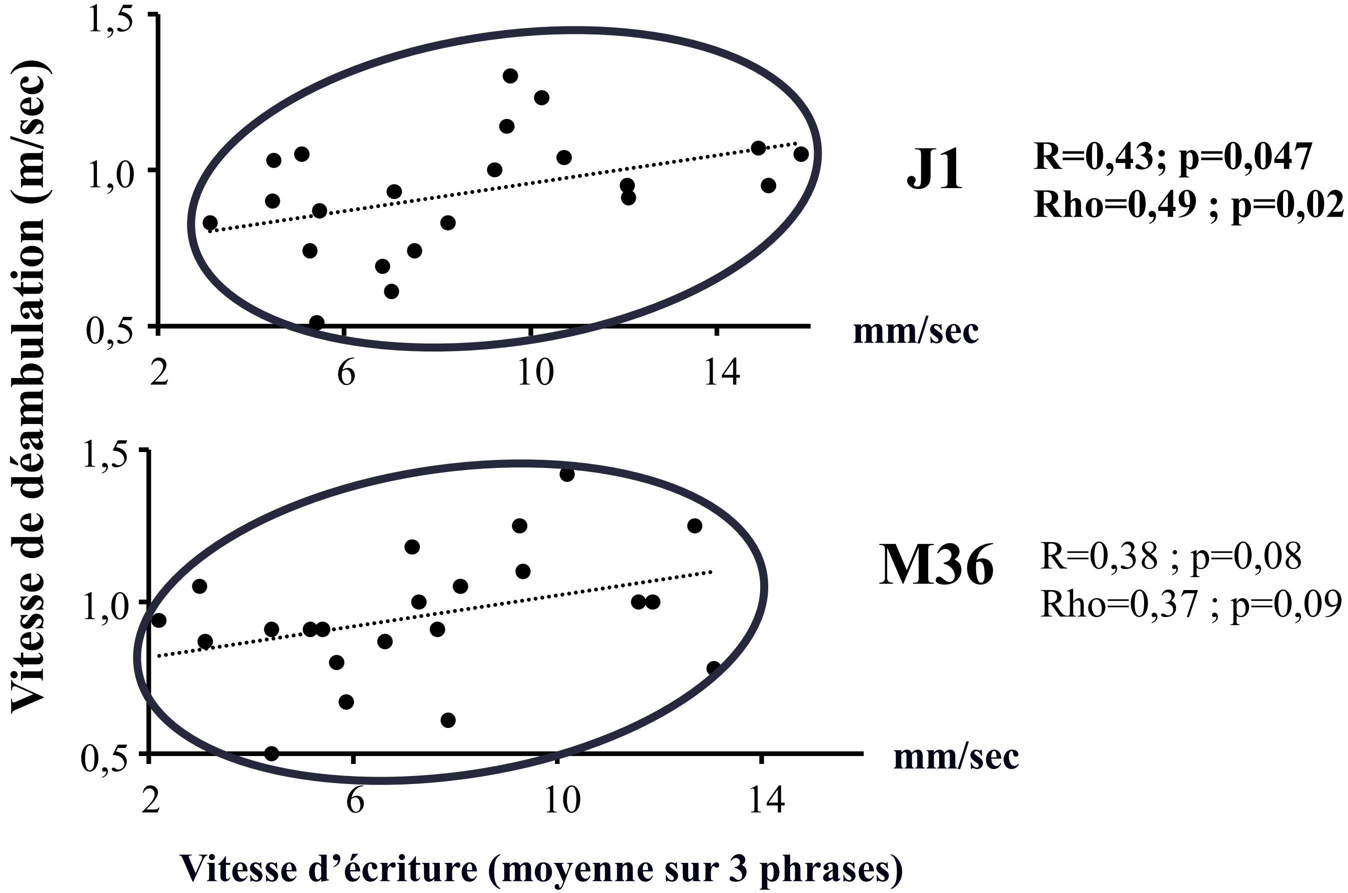
Critère secondaire : corrélation vitesse d'écriture - marche confortable



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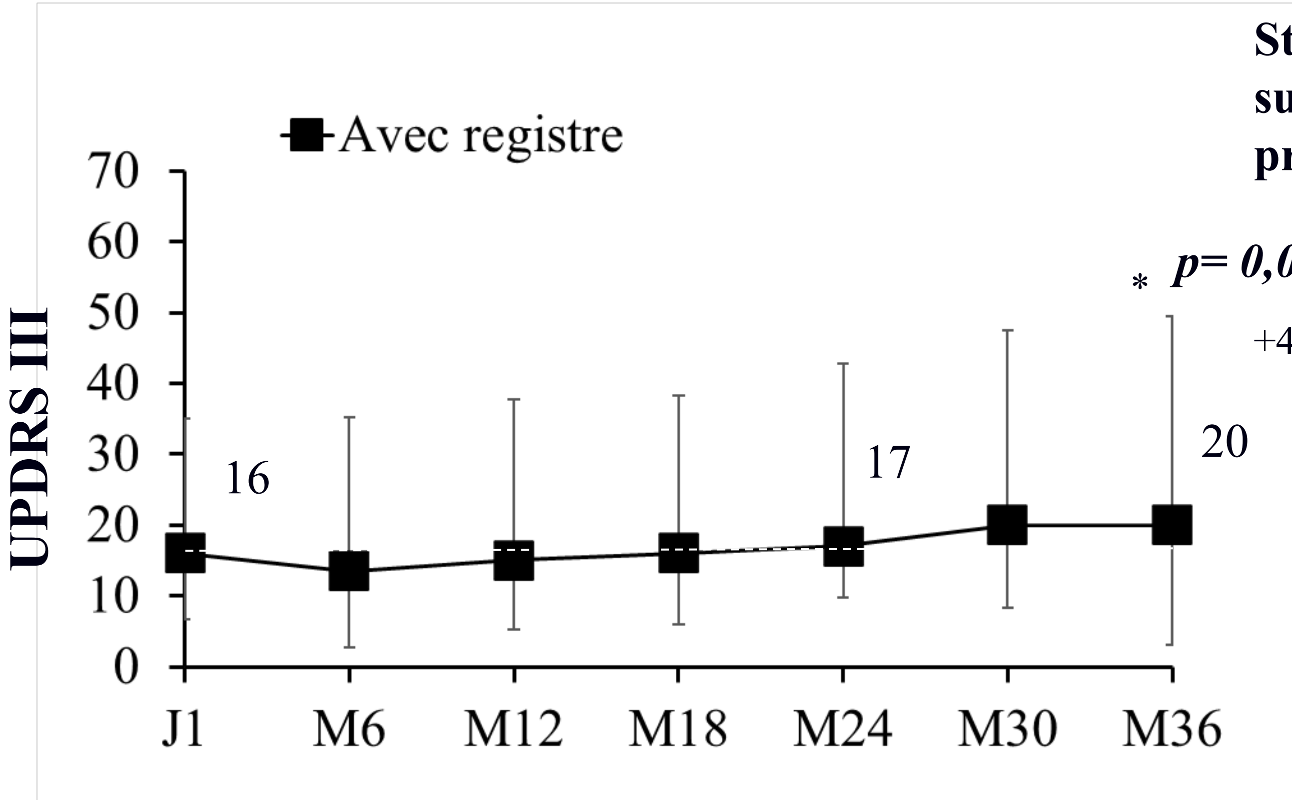
Critère secondaire : UPDRS III *(groupe CAR)*



Stabilité relative sur les 2 premières années

p= 0,02*

+4 points sur 3 ans

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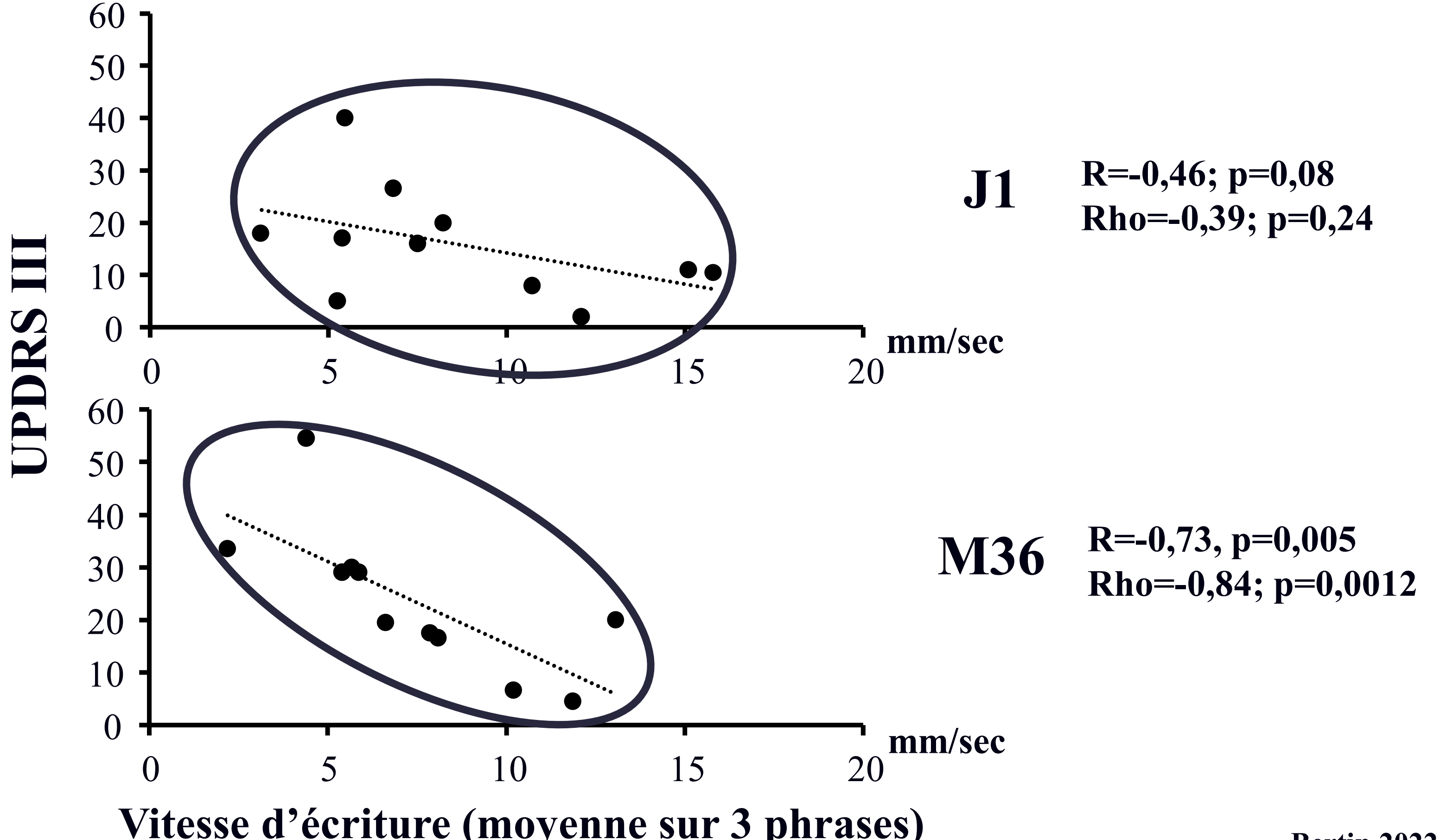
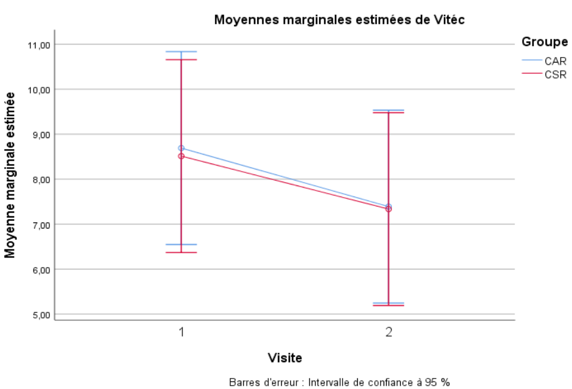
Critère secondaire : corrélation vitesse d'écriture – UPDRS III

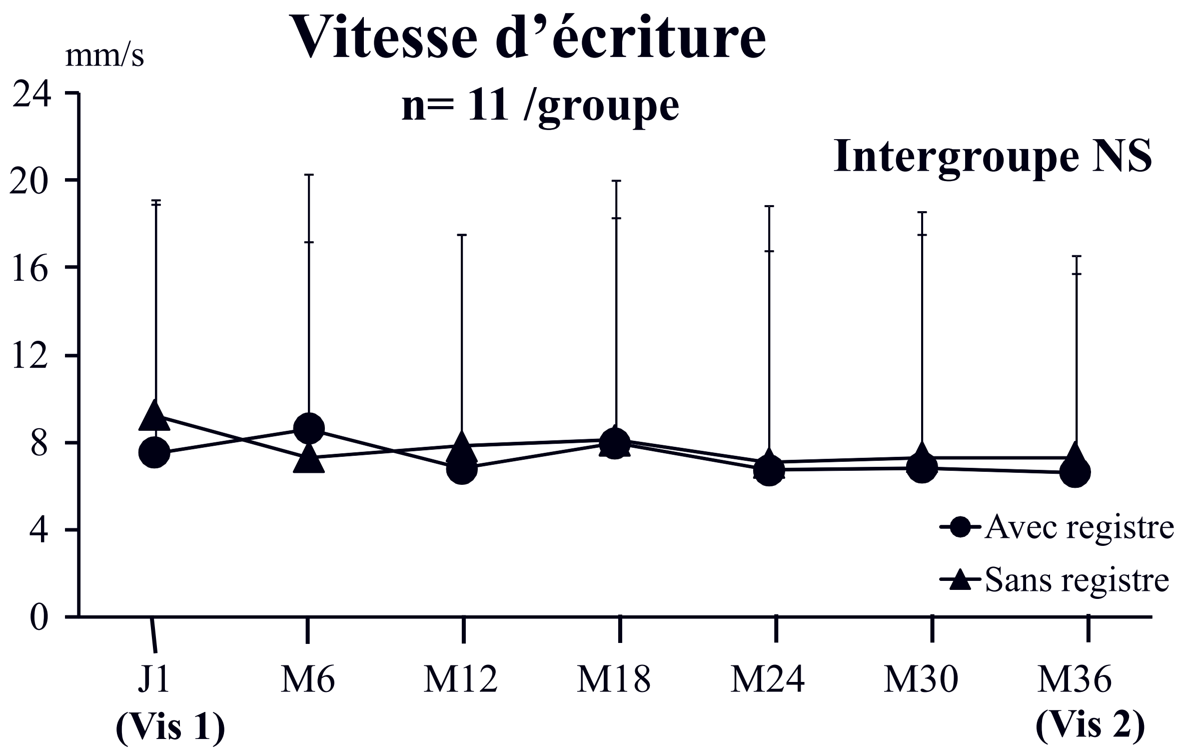


Bertin 2022

Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Résultats : évolution critères secondaires





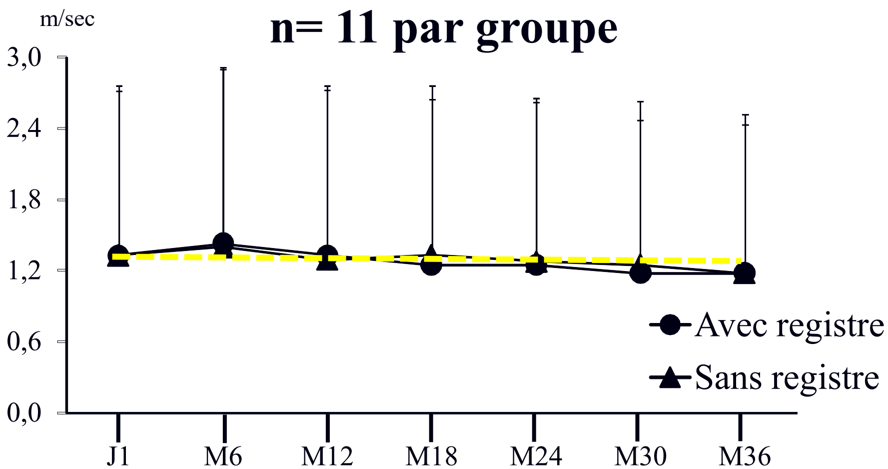
Bertin 2023

Bertin et al (ISPRM Lisbonne 2022), Long-term stabilization of motor capacities using Guided Self-rehabilitation Contracts (GSC) in parkinsonism. J Int Soc Phys Rehabil Med 2022;5, Suppl S2 :119-411

Résultats : évolution paramètres moteurs indicés

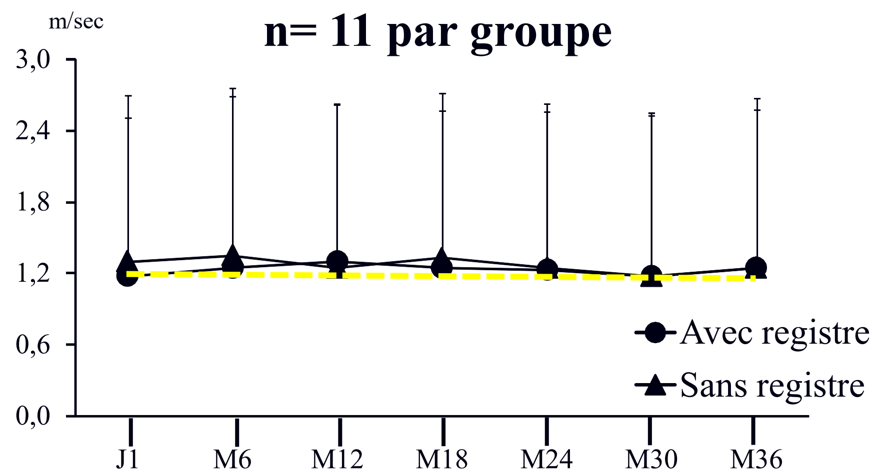
Vit déambulation marche rapide

n= 11 par groupe



Vit déambulation grands pas

n= 11 par groupe



Bertin 2023

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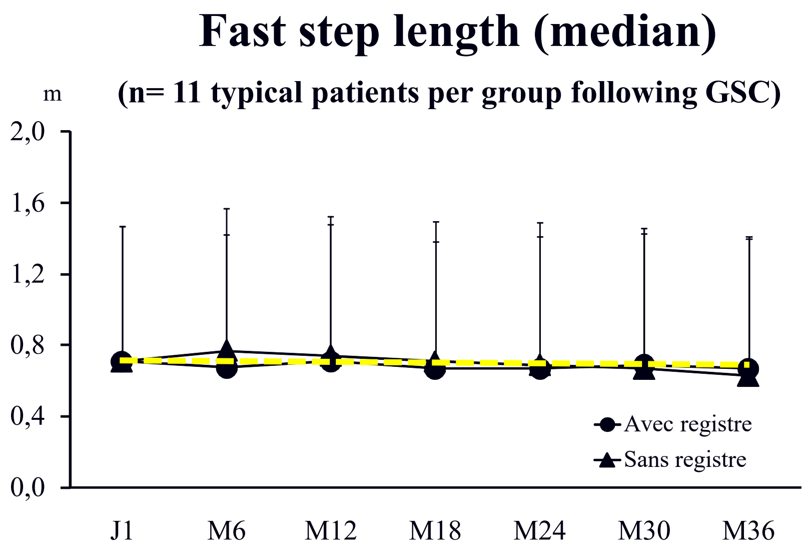
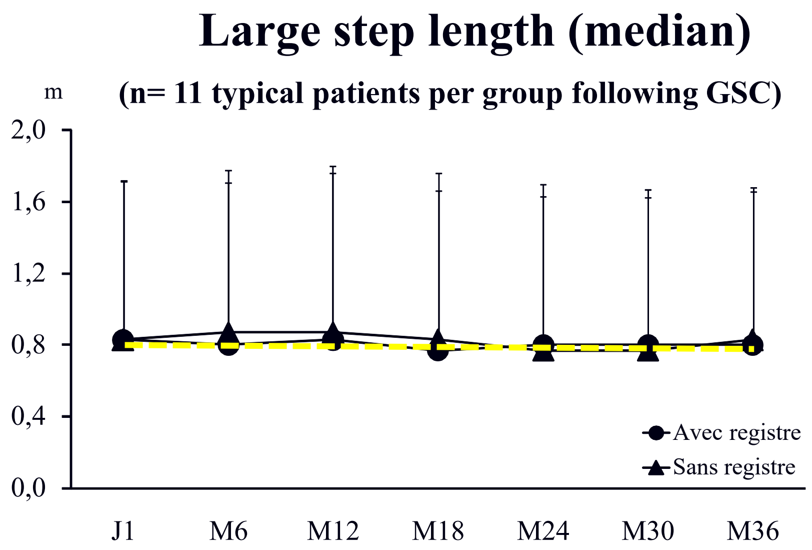
Résultats : critère dévaluation secondaire





Bertin 2023

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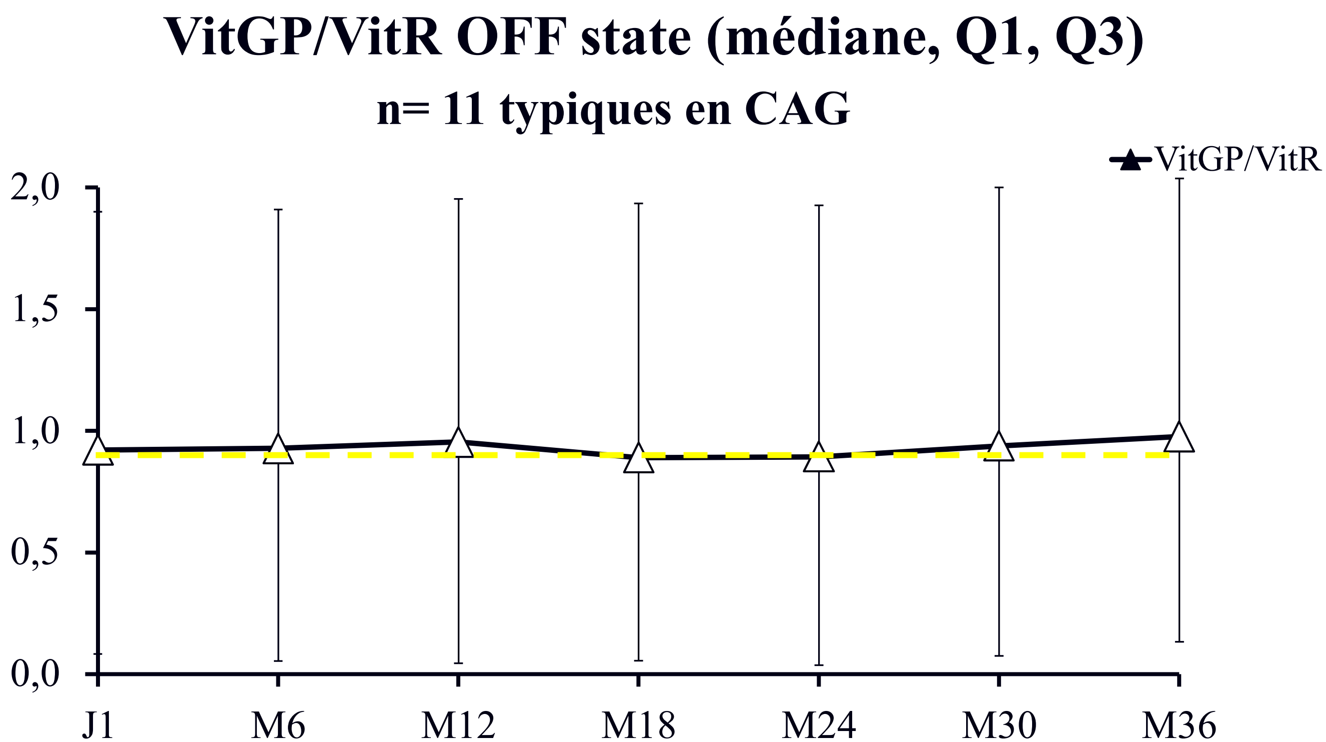
Résultats



Bertin 2022

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Discussion (1) – Intérêt du registre

L'utilisation d'un registre au sein d'un contrat d'autorééducation guidée sur 3 ans de suivi a été associée à :

1.Diminution de la dose prescrite en équivalents-lévodopa *vs* augmentation de 200 mg/j sur 3 ans dans le groupe sans registre.

2.Petite augmentation vitesse et longueur de pas en déambulation confortable *vs* modeste diminution de ces paramètres dans le groupe sans registre.

Mais : étude non prospective, autres raisons possibles que le registre, y compris effets possibles des cliniciens (MPR, neuro) impliqués

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Discussion (2) – valeur suggérée du CAG

1. **Stabilité paramètres déambulation, notamment indicés ++ sur 3 ans**
2. **Stabilité relative UPDRS-III / littérature** ***(+3,2 pts et +5,6 pts en 6 mois dans Schenkman 2018 et van der Kolk 2019; +7,8 pts sur 3,5 ans dans Fahn 2004)***
3. **Faible augmentation posologie prescrite lévodopa / littérature, même dans groupe sans registre** ***(3 ; +200 mg en 3 ans dans CSR vs +246 mg/j en 2 ans dans groupe médical d'Earlystim; Schuepbach 2013)***
4. **Paramètres se dégradant : vit écrit, ratio VitGP/VitR et UPDRS III**
5. **Intérêt vitesse écriture comme reflet UPDRS III et déambulation i.e. parkinsonisme général?**
6. **Effet relativement faibles doses utilisées?**
7. **Futur : continuer sur 5 ans**

(1) Fahn S et al; Parkinson Study Group. Levodopa and the progression of Parkinson's disease. N Engl J Med. 2004;351(24):2498-508

(2) Schenkman M, …Corcos DM. Effect of High-Intensity Treadmill Exercise on Motor Symptoms in Patients With De Novo Parkinson Disease: A Phase 2 Randomized Clinical Trial. JAMA Neurol. 2018;75(2):219-226

(3) van der Kolk NM, …Bloem BR. Effectiveness of home-based and remotely supervised aerobic exercise in Parkinson's disease: a double-blind, randomised controlled trial. Lancet Neurol. 2019;18(11):998-1008

(4) Schuepbach WM, et al EARLYSTIM Study Group. Neurostimulation for Parkinson's disease with early motor complications. N Engl J Med. 2013 Feb 14;368(7):610-22

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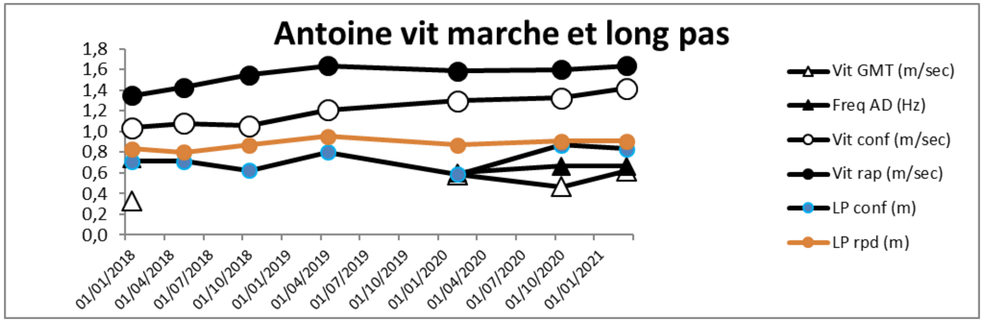
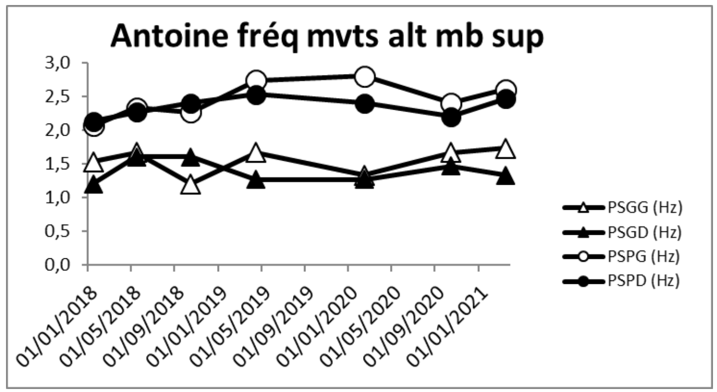
Exemples individuels

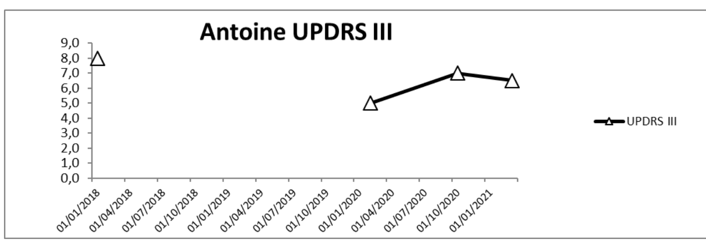
Exemple individuel d'amélioration sur 3 ans

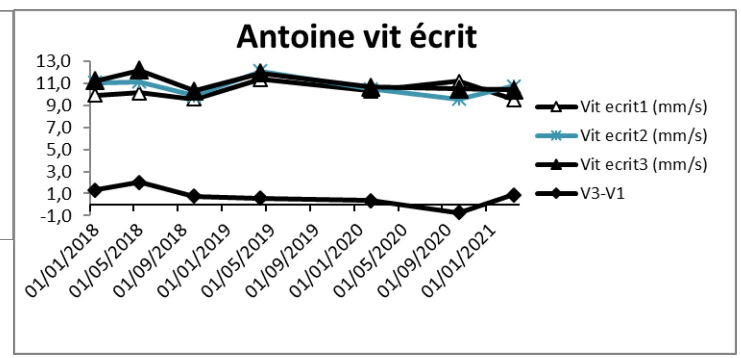


Renforcement moteur et travail aérobie intenses - ~ 1h/ jour

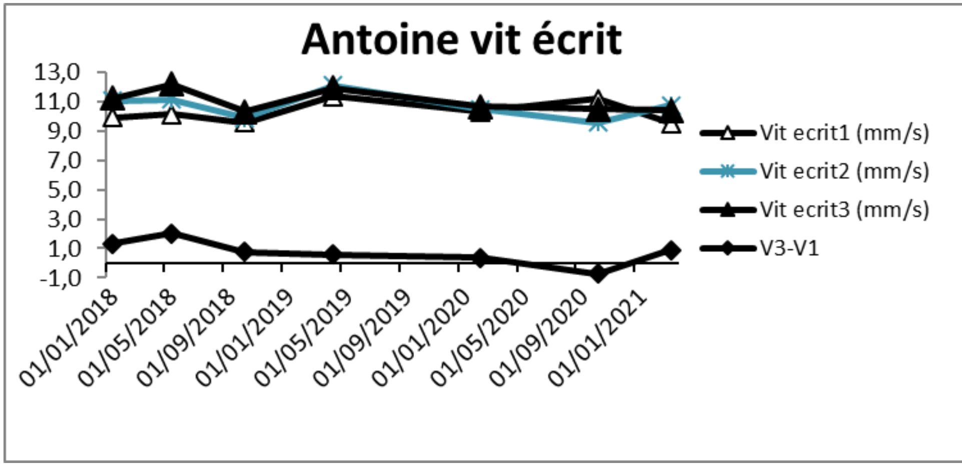
Homme 59 ans
Début sympt 2015
"contracture » av-bras droit - Diag Park 2016 - début lévodopa 2018 - 187,5 mg/j – doses stables

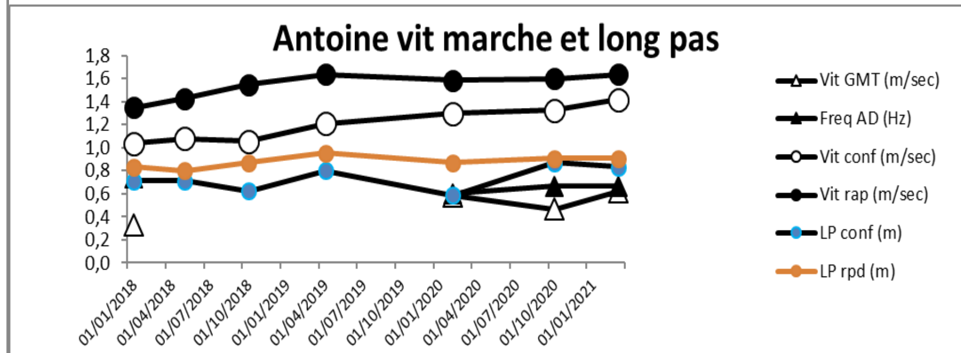






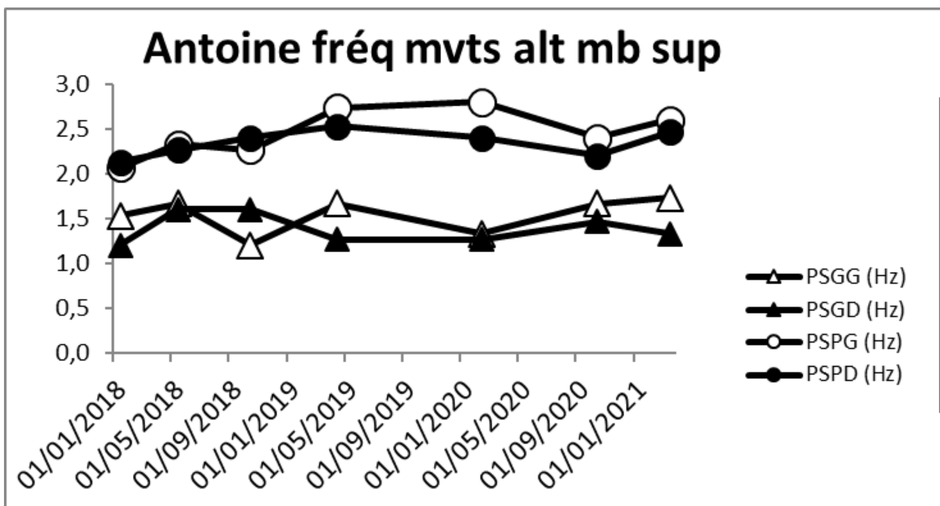
TR - Suivi = 3 ans

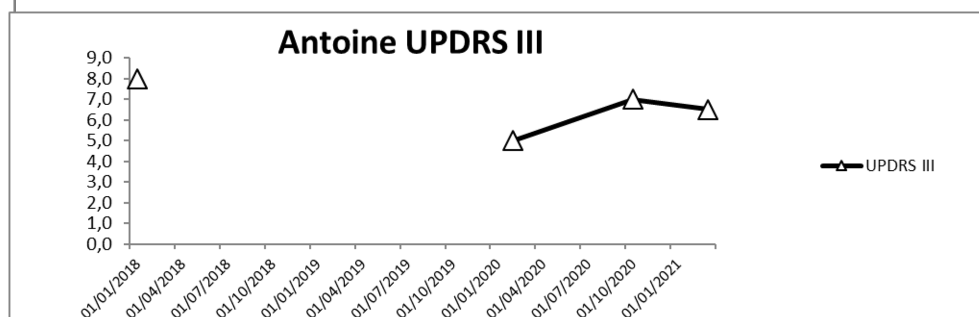




Mvts automatisés mbs sup **Mvts automatisés mbs inf**

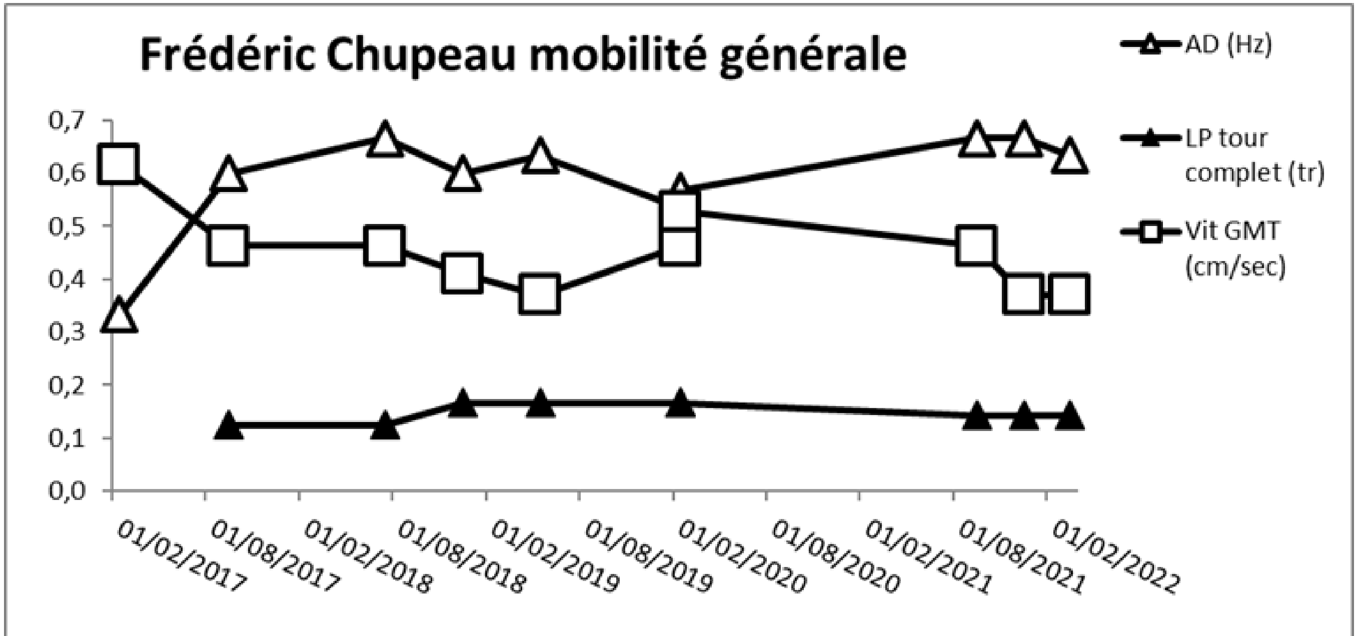
Début sympt 2015 "contracture » av-bras droit - Diag Park 2016 - début lévodopa 2018 187,5 mg/j

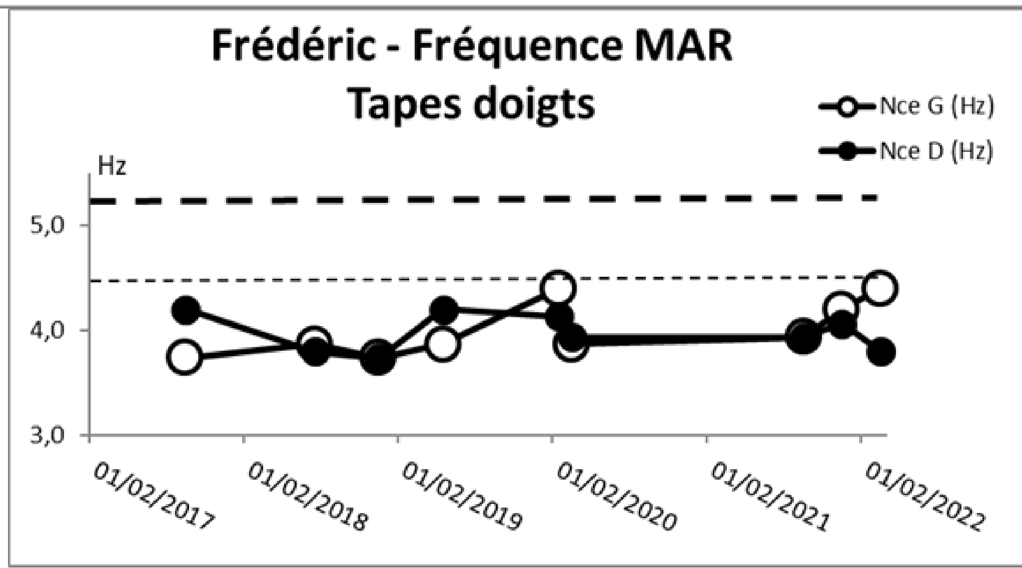




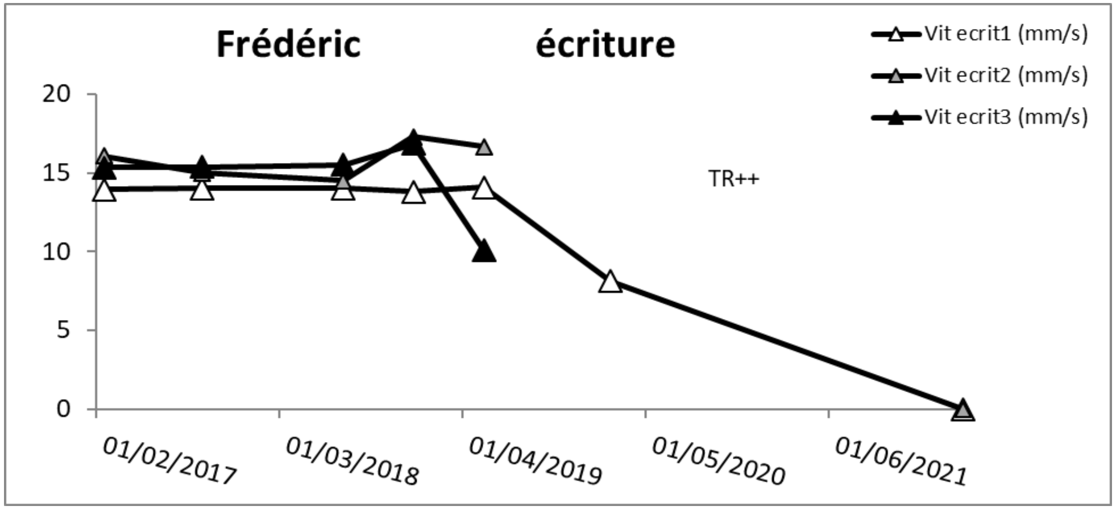
Mvts inhabituels mbs sup

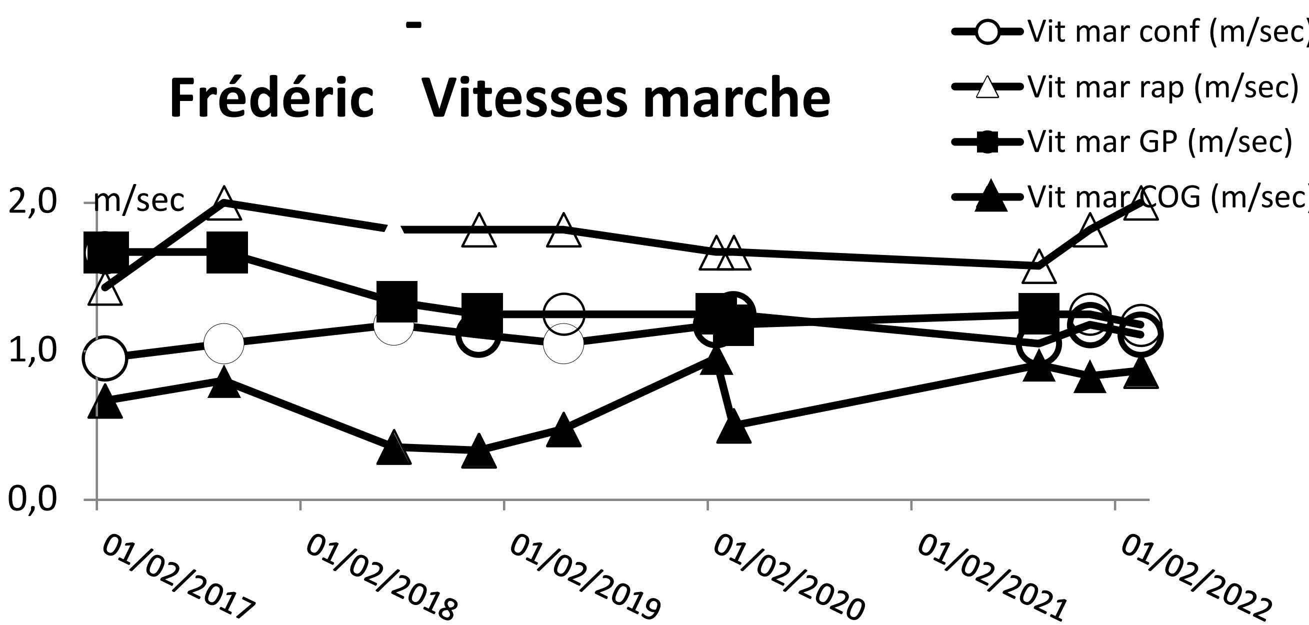
Stabilisation performances avec le renforcement moteur – 5 ans





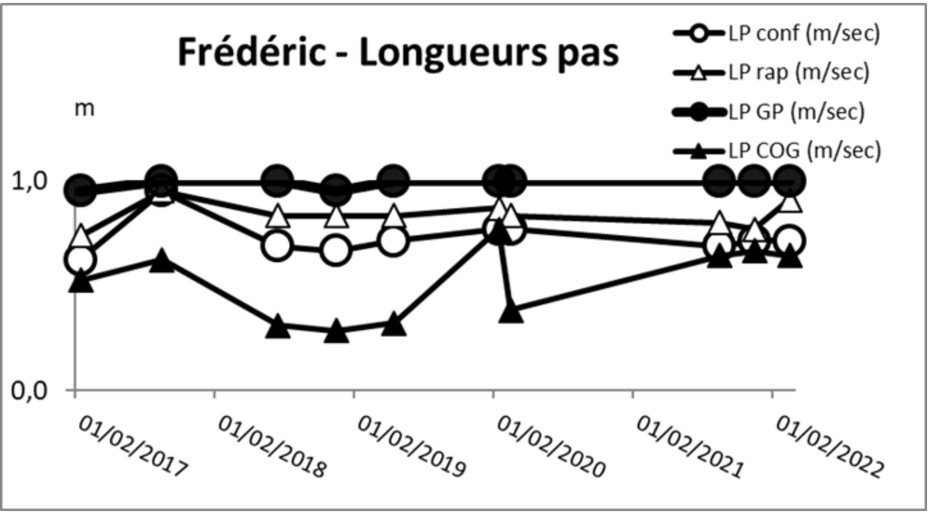
Stabilisation performances avec le renforcement moteur – 5 ans

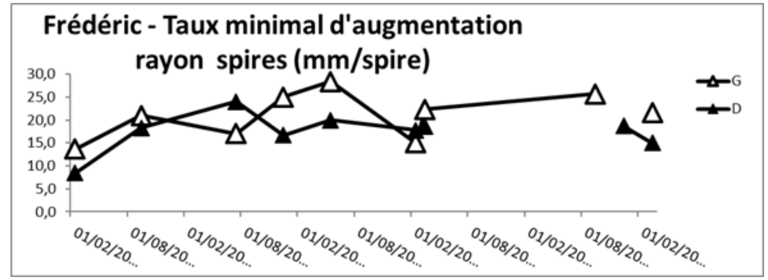


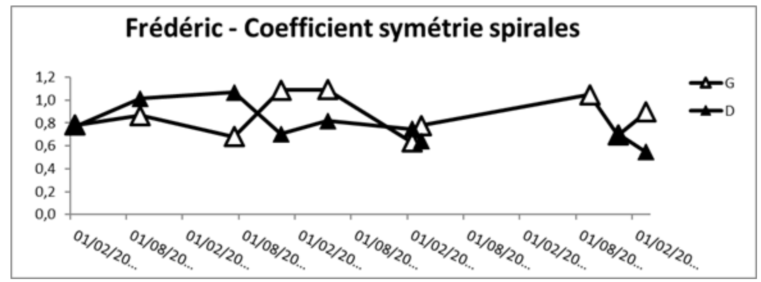


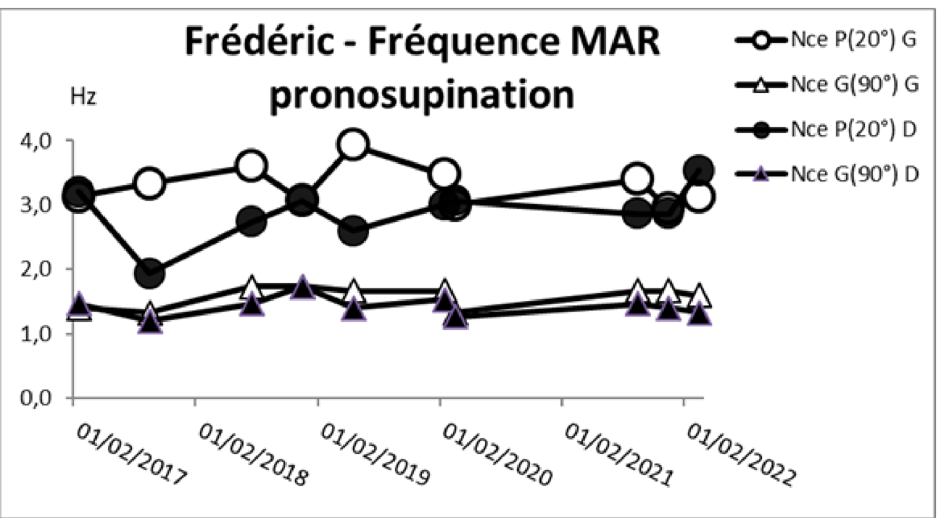
Gracies, 2022

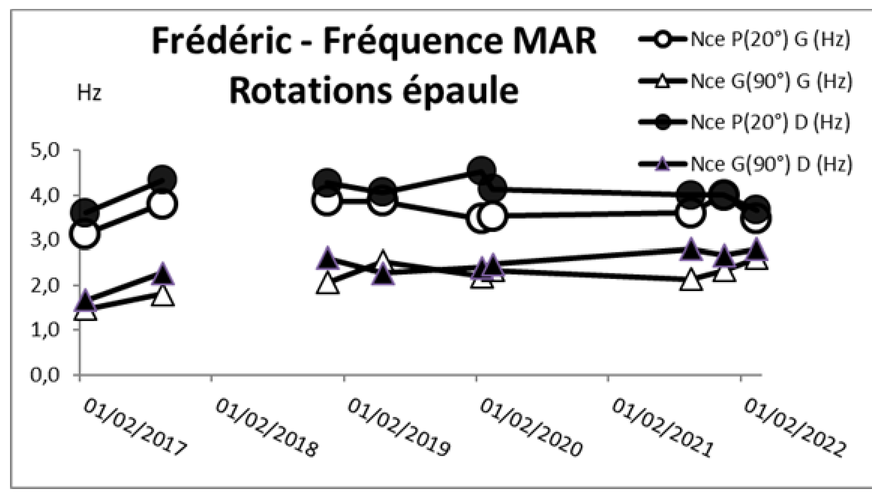
Stabilisation performances avec le renforcement moteur – 5 ans



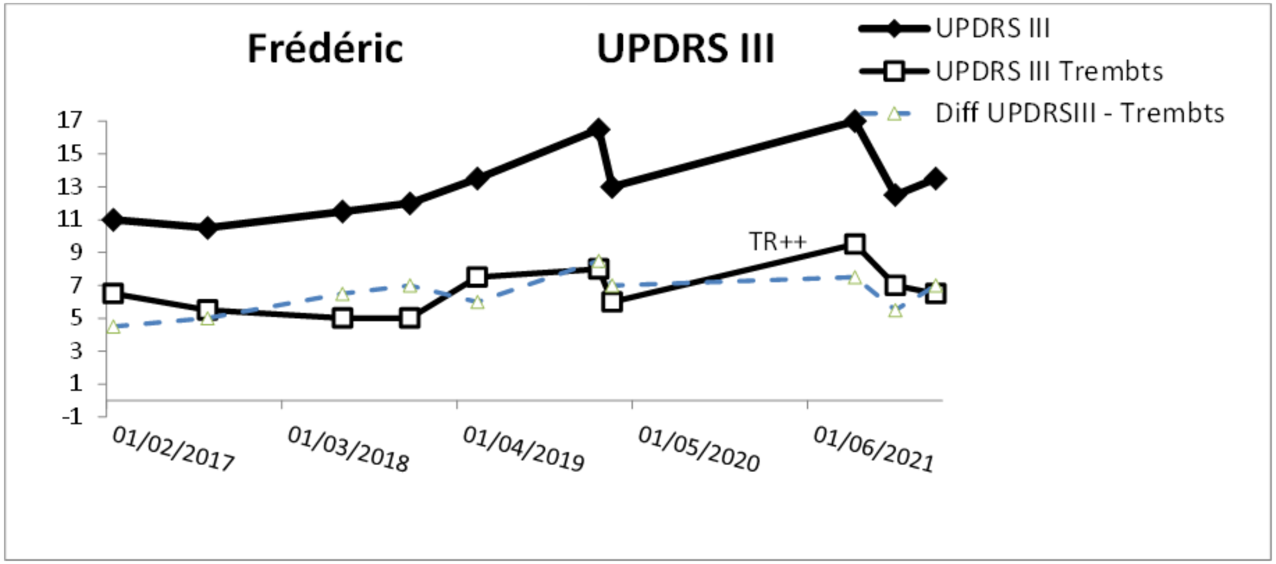


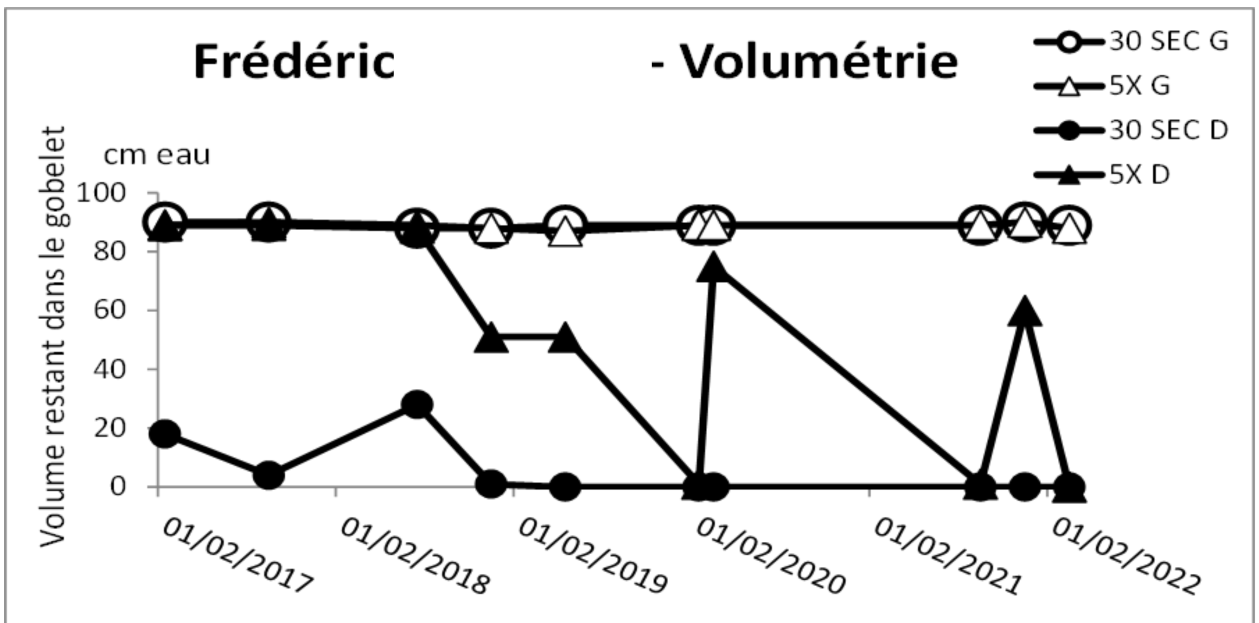






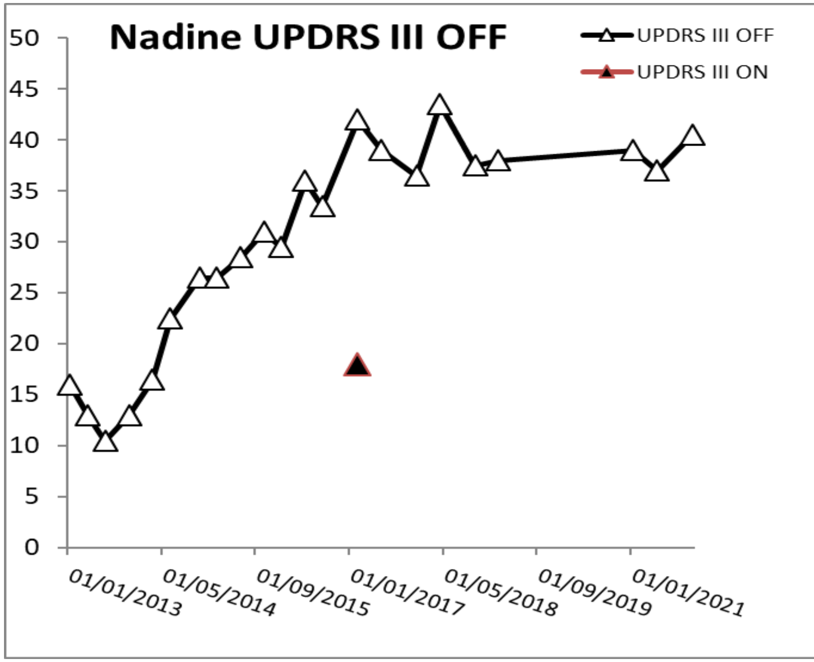
Stabilisation performances avec le renforcement moteur – 5 ans

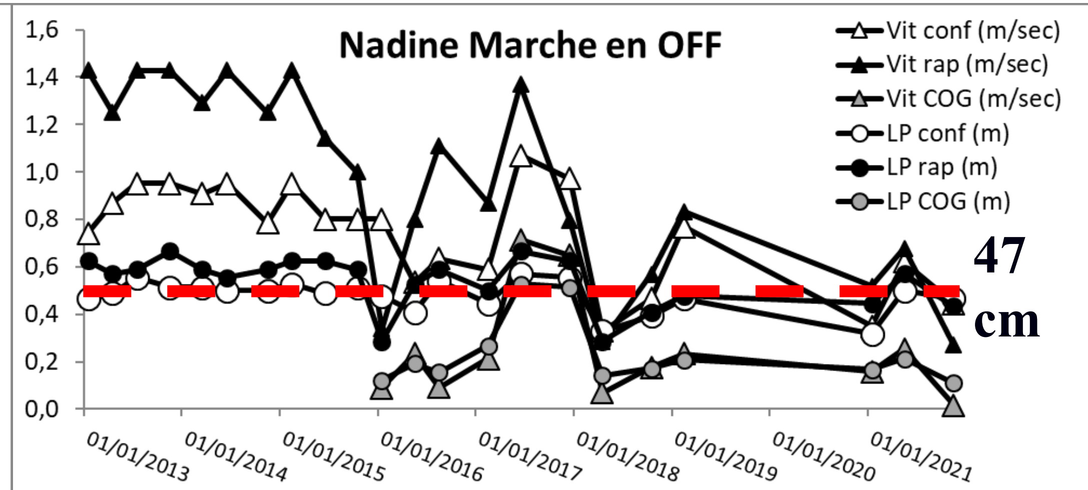




Gracies, 2010

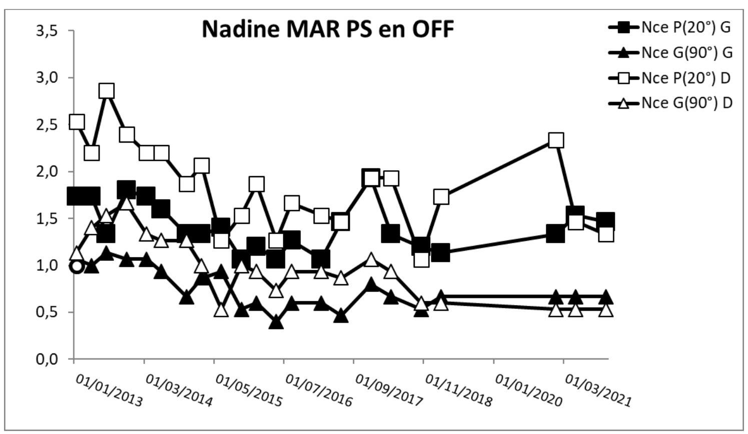
TR - Suivi = 8 ans



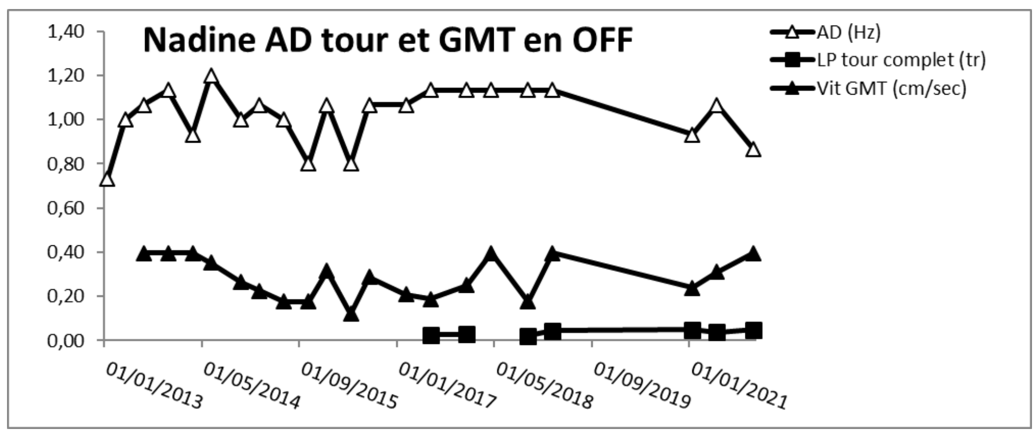


Mvts automatisés mbs inf

MPI 2010 début modopar juin 2016

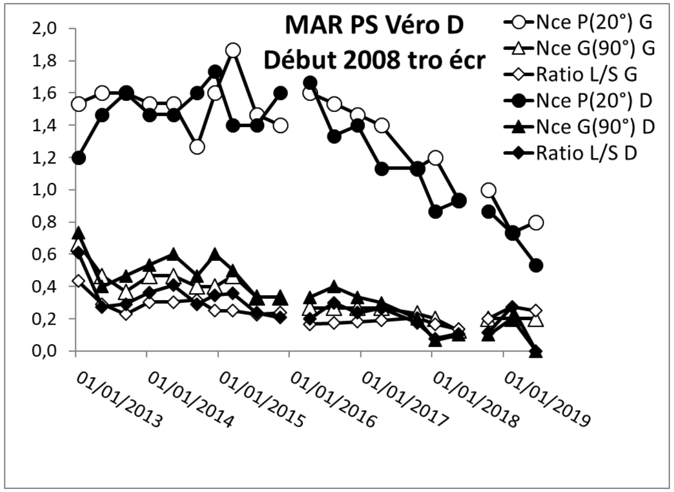


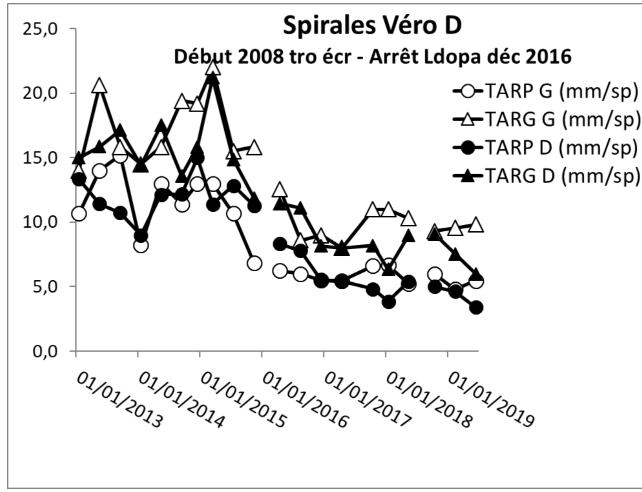
Mvts inhabituels mbs sup

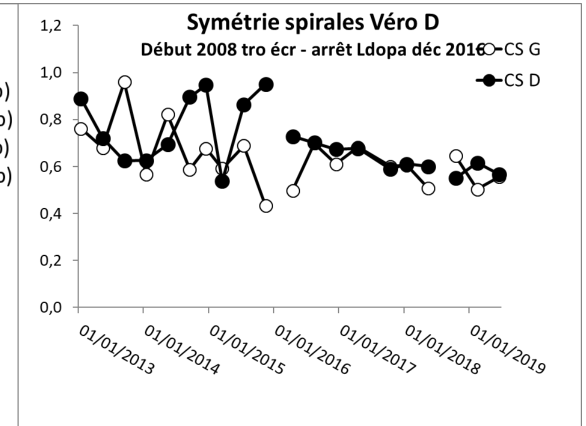


Mvts inhabituels mbs inf

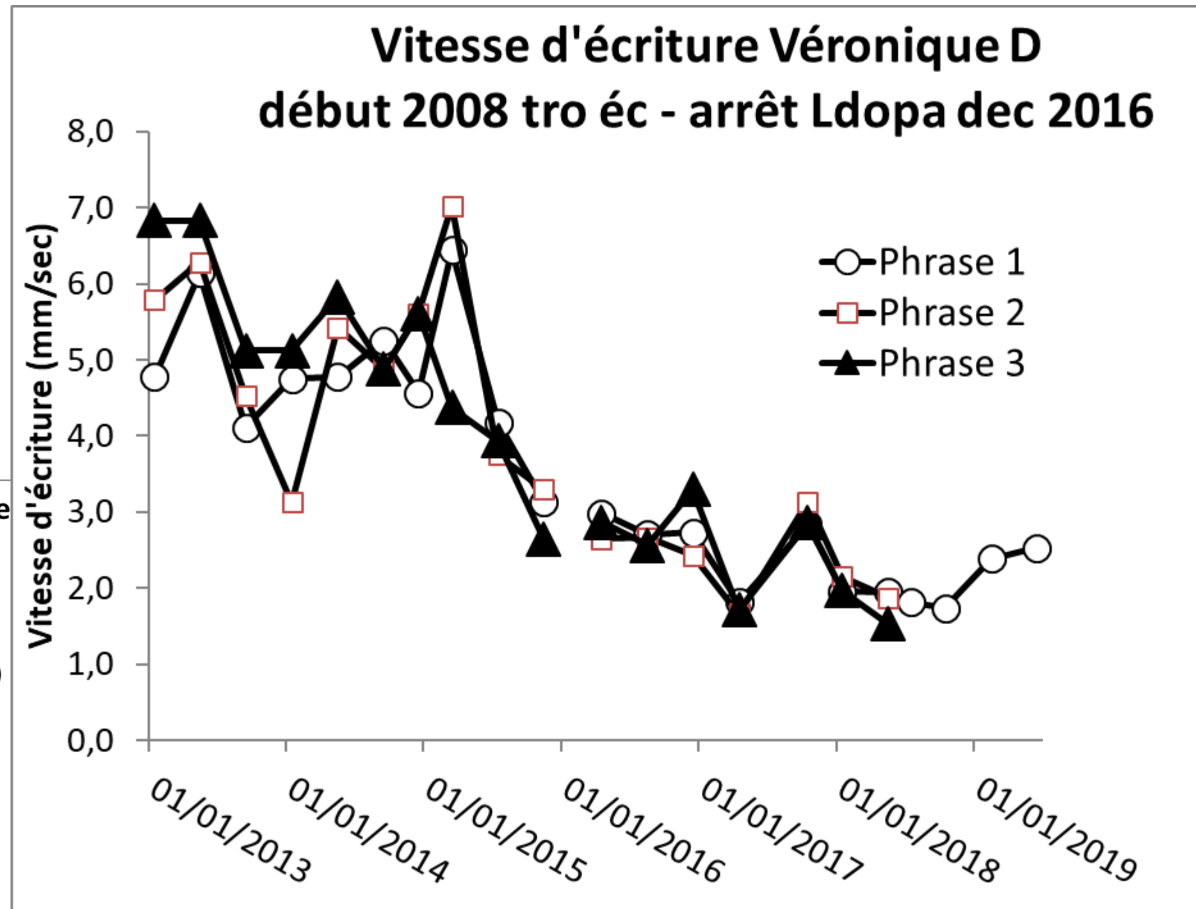
AMS - 6 ans

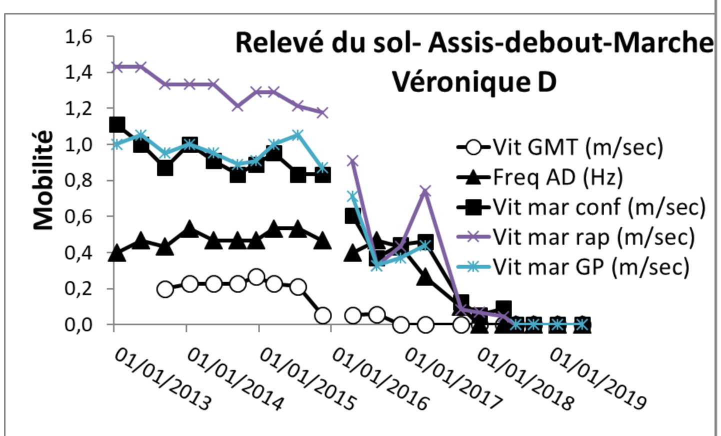






Début sympt 2008 tro écrit, dlr bras dt - Diag "Park" 2010--> puis AMS





Stabilisation performances with AMS/GSC - 5 years

07/02/17

26/09/17

Début 2014 (58 a) TR main D – Dg 2015 – Début dopa 2016

29/03/22

Remerciements

<u>Mondor-Chenevier, Créteil</u>

Maud PRADINES, PT, PhD
Émilie HUTIN, PhD
Nicolas BAYLE, MD
Thara SANTIAGO, PT
Mouna GHEDIRA, PT, PhD
Mina BOUTOU, MSc
Marjolaine BAUDE, MD
Caroline COLAS, MD
Damien MOTAVASSELI, MD
Tymothée POITOU, MD
Etienne SAVARD, MD
…

<u>www.neuroloco.org</u>

Grazie

Physical Treatment of PD :

Ingredients ?

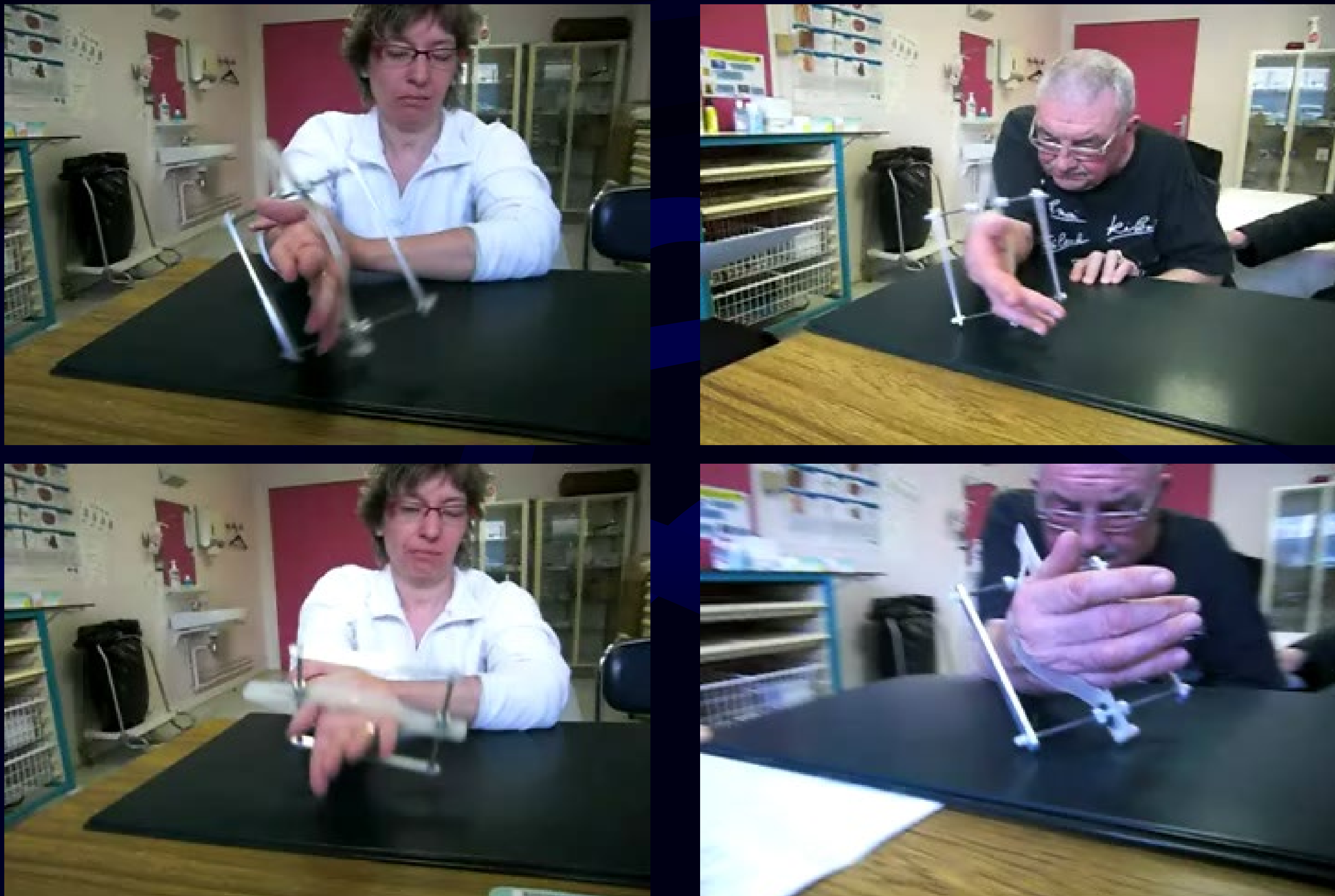
1. **Pathophysiology: in man**
2. **Results of programs of physical work: in phenotypic animal models ++**

Physical Treatment of PD :
Ingredients ?

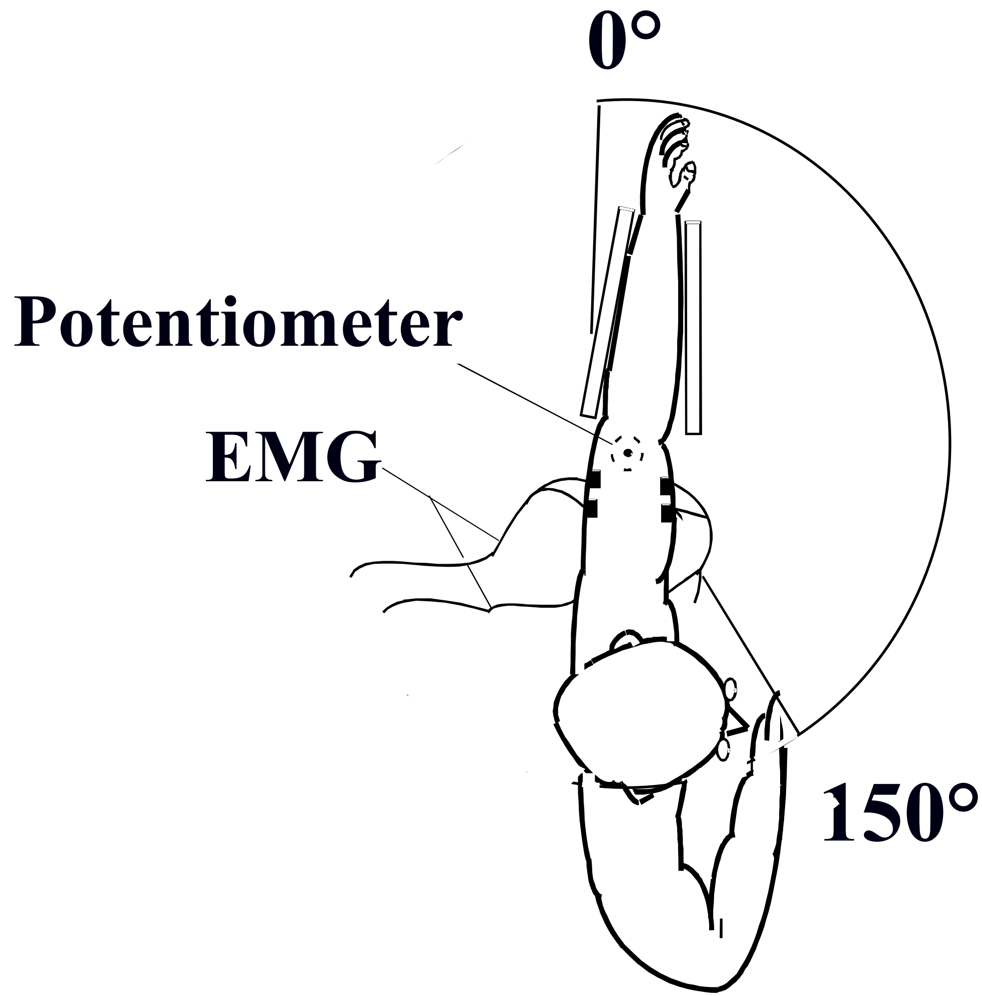
1. **Pathophysiology – in man**

What are the fundamental characteristics of parkinsonian movements?

« Bradykinesia »??

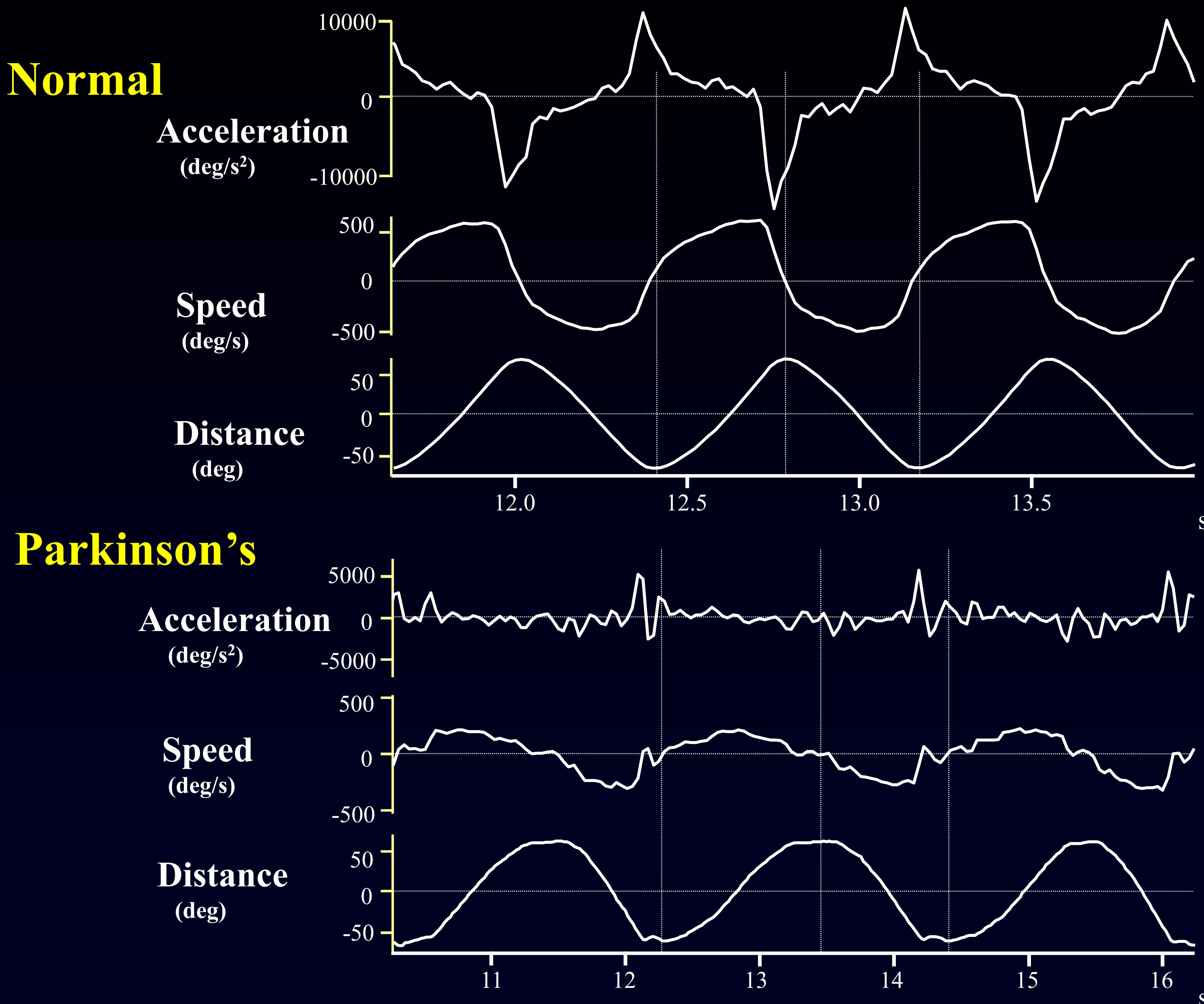


Hypermetria **Hypometria!**



Active Movements

Gracies, 2003



Gracies, 2011

Pathophysiology Parkinson's Hypometria/bradykinesia

- Classic **clinical** characterization: slowness over imposed large amplitude (« bradykinesia ») *(Flowers, 1975, 1976)*

- **EMG characterization**, underscaled agonist bursts:
  - Duration *(Hallett and Khoshbin, 1980)*
  - Power *(Berardelli et al, 1986; Phillips et al, 1994)*

  → Insufficient acceleration *(Broderick et al, 2009)*

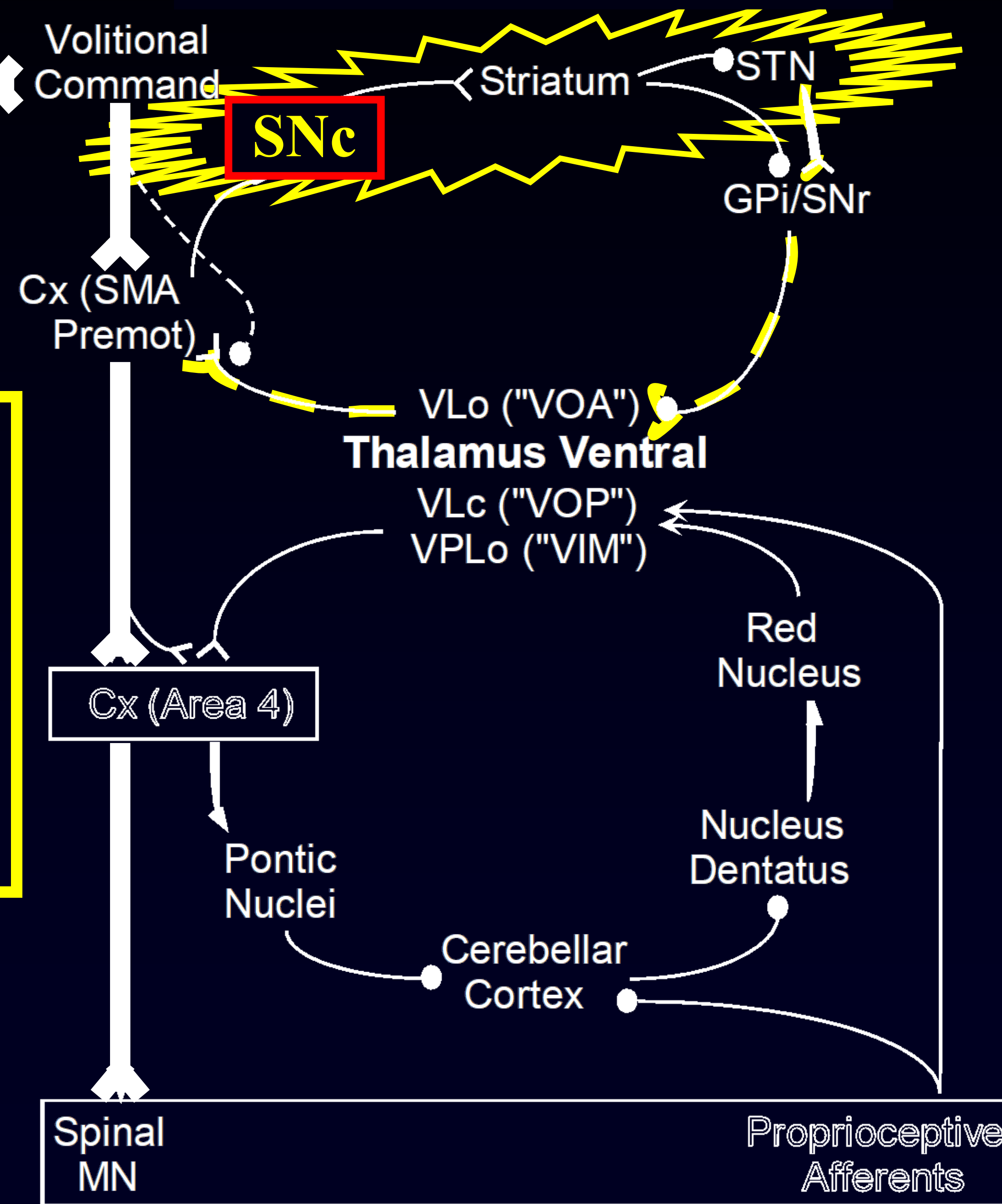
- **Cause** = Alexander's model :
  - Insufficient cortical preparation = lack of « internal excitation »/« induced excitability » of motor and premotor cortices by basal ganglia *(Alexander et al, 1990)*

Increasing motor cortex excitability

by Dehabituation

Unusual Movement (external guidance - attention)

Automatic Movement



Lack of Motor Cortical Self-activation

Brown et Marsden 1988
Freeman et al 1993;
Georgiou et al 1993;
Kritikos et al 1995

Gracies, 2010

How to increase excitability of motor cortices?

1. **Attentional strategies**

=> De-habituation

=> Cueing *(Meg Morris..)*

AN

ESSAY

ON THE

SHAKING PALSY.

BY

JAMES PARKINSON,

MEMBER OF THE ROYAL COLLEGE OF SURGEONS.

LONDON:

PRINTED BY WHITTINGHAM AND ROWLAND,
Goswell Street,

FOR SHERWOOD, NEELY, AND JONES,
PATERNOSTER ROW.

1817.

Gracies, 2010

Natural History (cont)

> 3 yrs post onset = emergence of functional difficulties

- Risk of falls (forward) : walking requires attention , on tiptoes ; faster and shorter steps
- Loss of finger dexterity (writing, buttons..)
- Intensification of tremor *(later « reemergence »)*
- Posture gradually stooped
- Sleep disturbances, frequent nights awakenings
- Sphincter disturbances : pollakiuria, constipation

Gracies, 2010

Dehabituation + *Cues* increase attention!

→ Attentional Strategies

→ Cueing - Verbal Instructions

(Meg Morris++)

Extreme sensitivity motor performance to attention given = characteristic of movement preparation impairment (parkinsonian hypometria)

Not to that extent in other central movement disorders, from conception (apraxia) to execution (spastic paresis). *(Muller et al, 1997; Gracies, 2010)*

Cognitive cueing = dehabituation: <u>unusual</u> walking Concentration on step length

« Normal » Walking

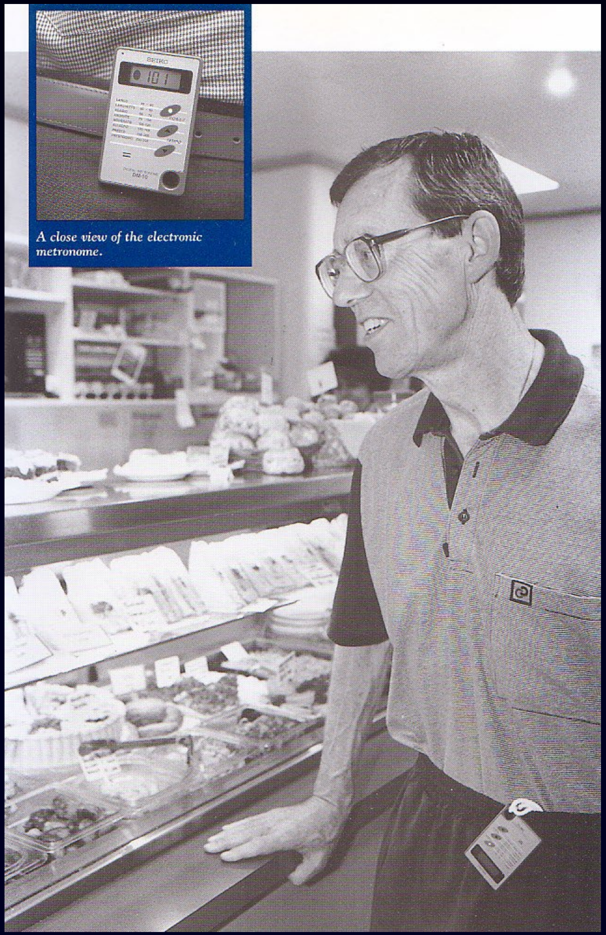
Fast Walking

« Big step » Walking

Do big steps!

Physical treatment - early stages
Cueing as training technique

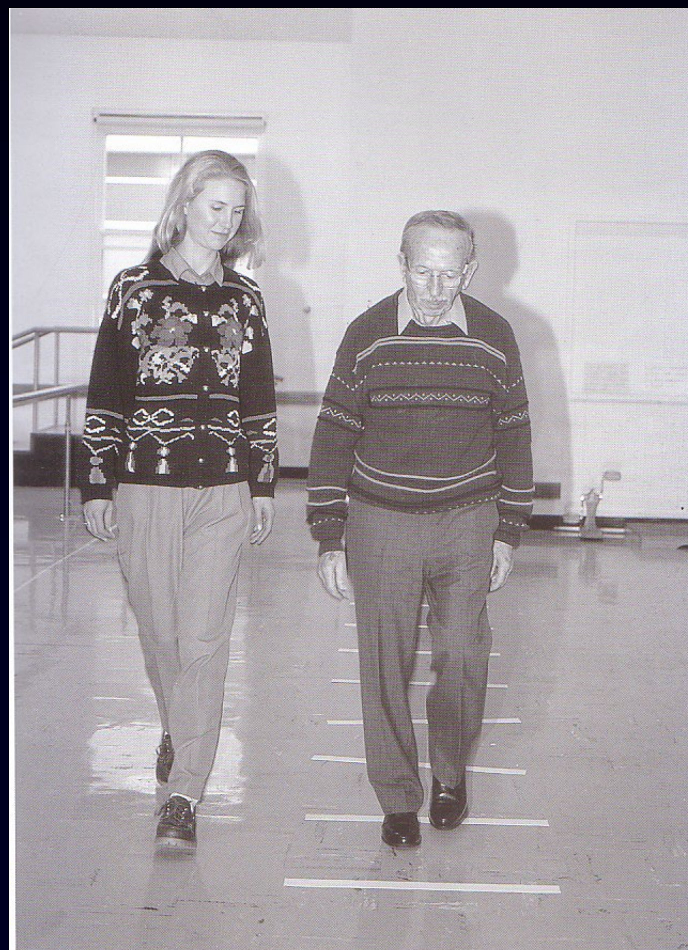
Acoustic Cues

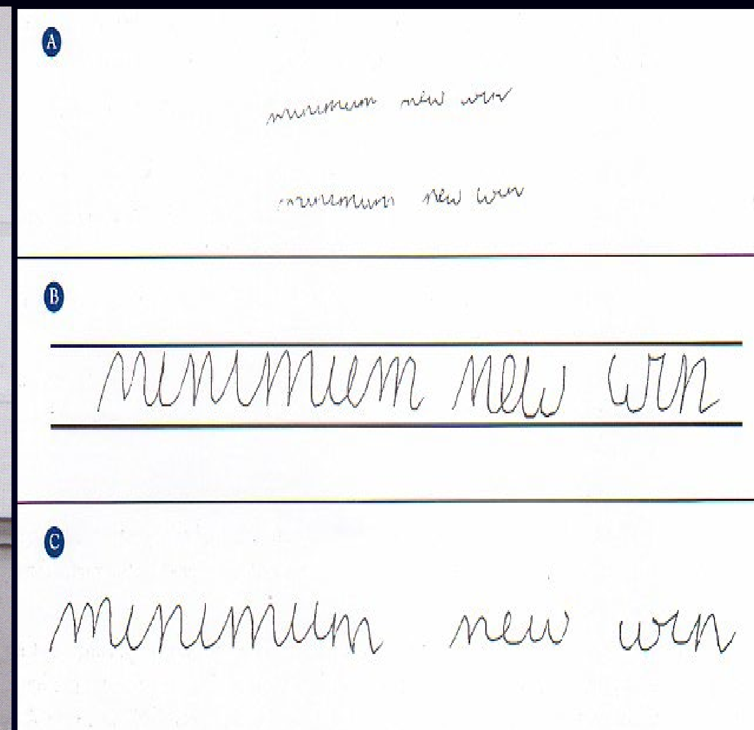


Morris et al, 1995; Enzensberger et al., 1997

Physical treatment - early stages
Cueing as training technique

Visual cues





Morris et al, 1995

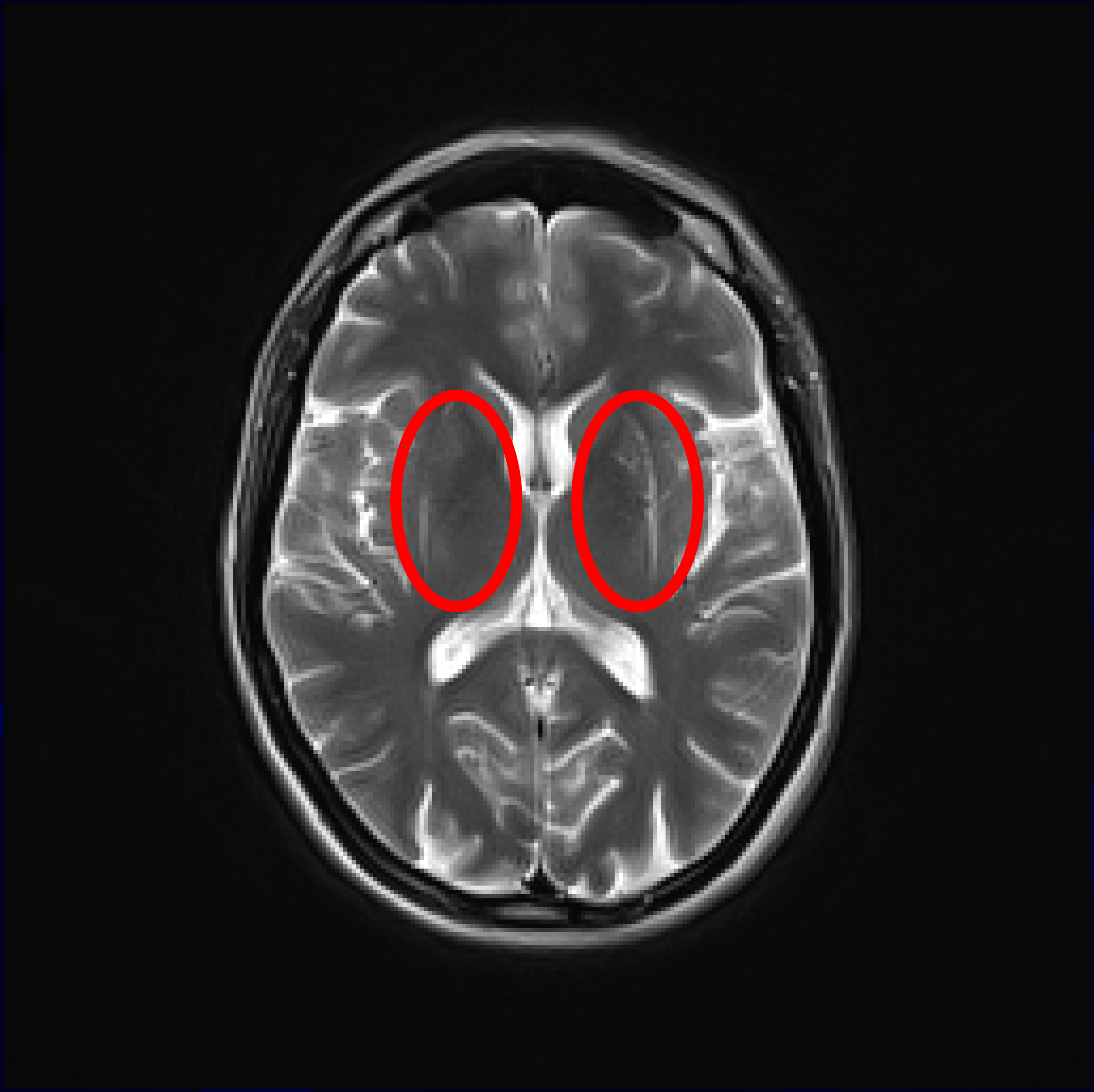
Advanced Stages
Cueing as Compensation

Visual cues

Increasing motor cortex excitability




Gracies, 2010



AMS (2010)

Józef Julian Franciszek Feliks Babiński
«De l'asynergie cérébelleuse», in: *Rev Neurol*, 7 (1899): 806-816.

Increasing excitability of motor cortices → standing up from ground

MSA Year 7 +++
7 weeks of weekly motor strengthening

Gracies, 2010

Increasing excitability of motor cortices → doing *Géant* Glacier

14 years from symptom onset to death++

Asymmetric motor strengthening 6 months – Sit-to-stand - power

Nov 14

May 15

Gracies, 2014

Asymmetric motor strengthening 6 months – Gait

Step length regulation at fast speed

Nov 14 **May 15**

Gracies, 2014

Asymmetric motor strengthening 6 months – Stand from ground

Nov 14

Feb 15

May 15

Asymmetric motor strengthening 6 weeks– Stand up from ground

04 Apr 17 OFF

15 sec

17 May 17 OFF

10 sec

17 May 17 ON

13.5 sec

Gracies, 2014

ASYMOT Study

Bayle, Hutin, Santiago, Joudoux, Canoui-Poitrine, Gracies, Baude, *unpublished*

Parkinsonism: agonist - antagonist imbalance

<u>Handwriting</u>: larger accelerations in wrist flexion-ulnar deviation movements than in extension – radial deviation movements *Teulings et al, 1997*

<u>Rapid alternating movements</u> in pronation/supination and in elbow flexion/extension *Gracies et al, 2001*

<u>Motor power</u>: relative weakness of extensors / flexors *Robichaud et al, 2004)*

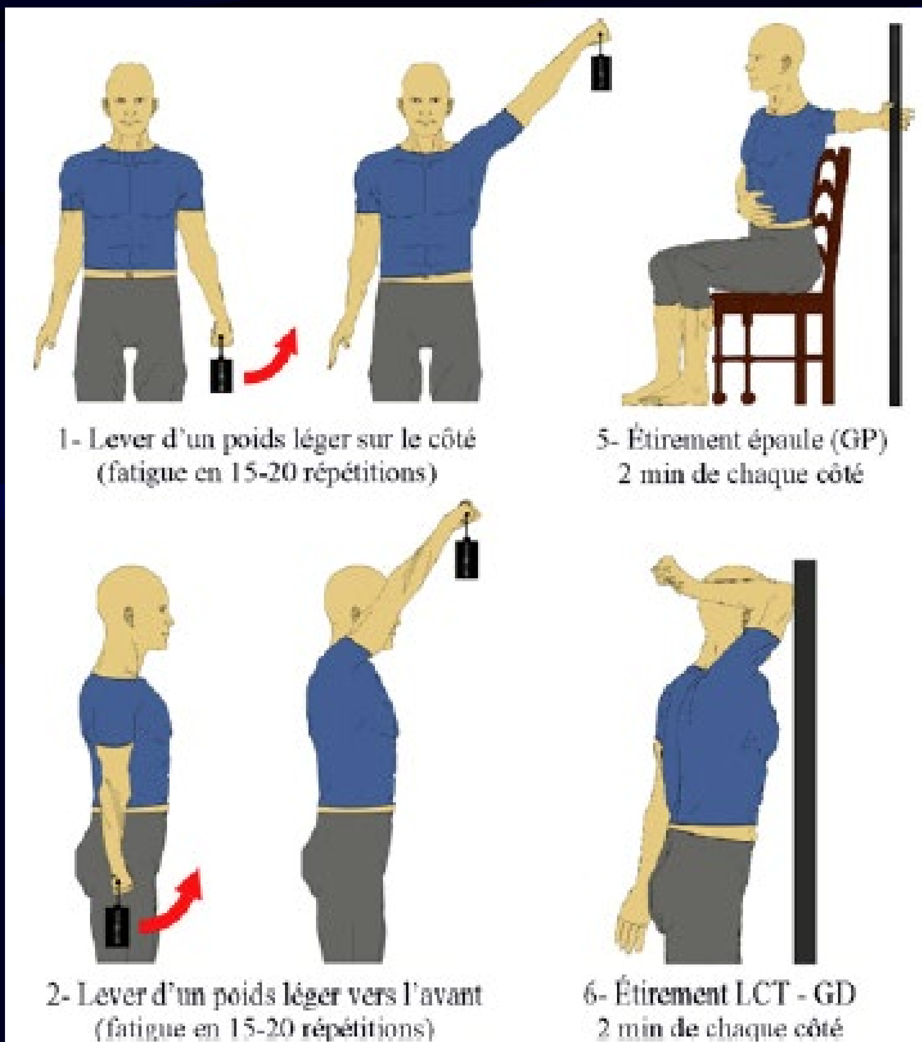
<u>Posture…</u> : extensor hypoactivity

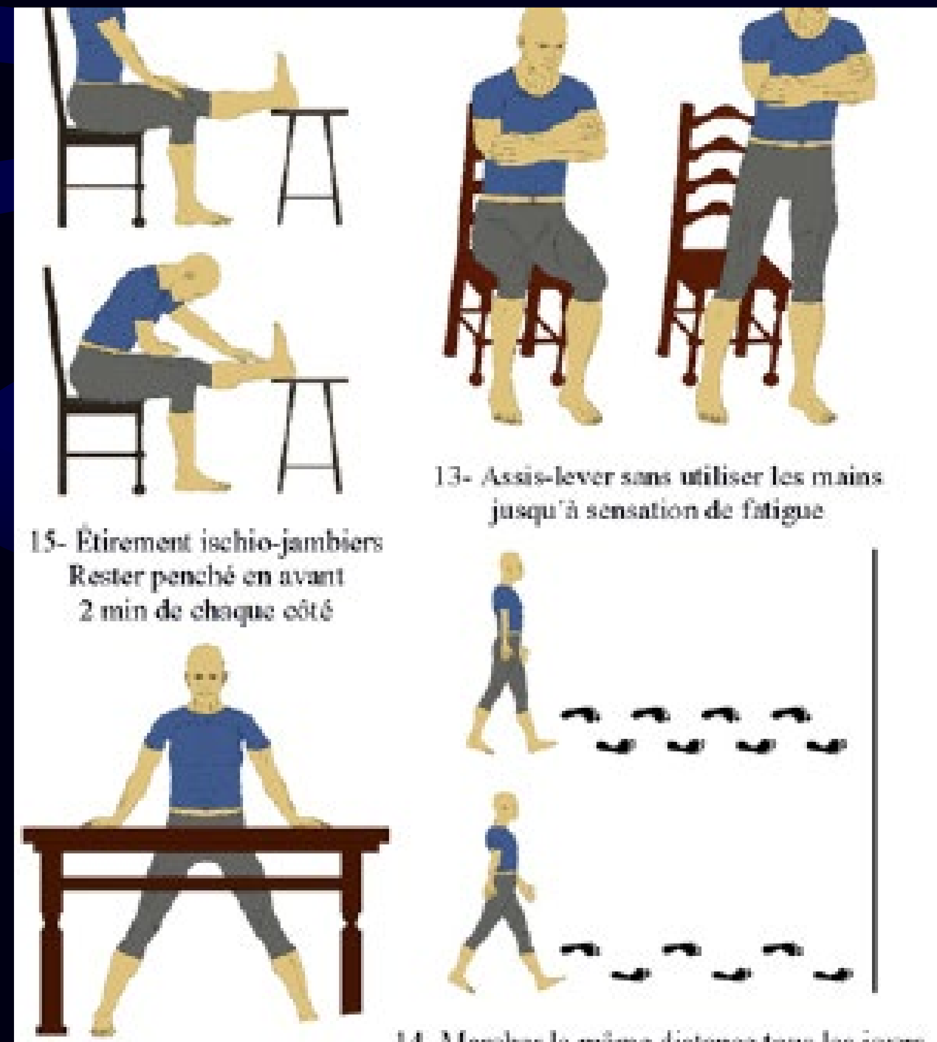
<u>Spiralography</u> : agonist-antagonist asymmetry contributes to particular shape of spirals « shell-like» in advanced disease *Chen et Gracies, 2005*

Gracies, 2010

Asymetric Motor Strengthening

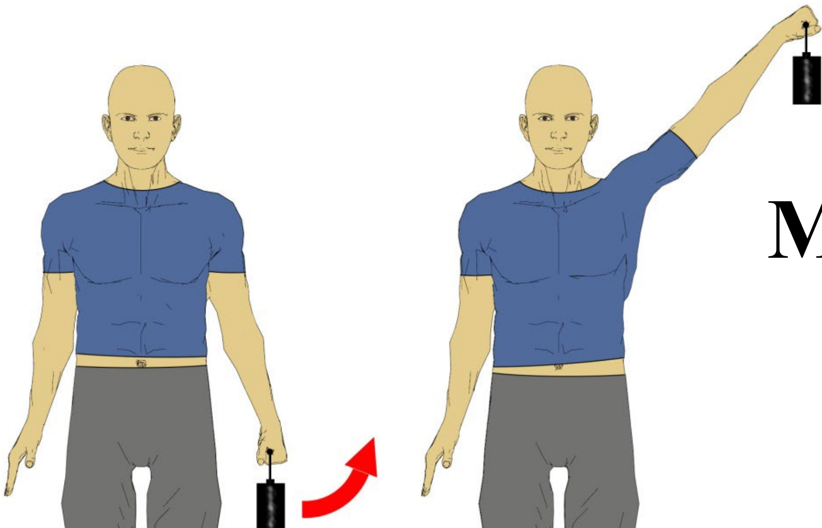
- Increase excitability of command to « opening » agonists (Classen 2008): extensors, abductors, supinators, etc.
- Stretch « closing » antagonists: flexors, pronators, adductors etc..



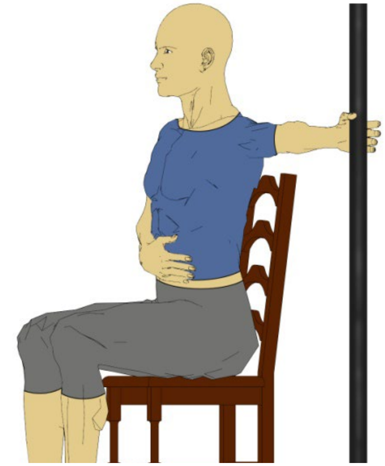


Asymmetric motor strengthening

Mild to moderate stages (I)



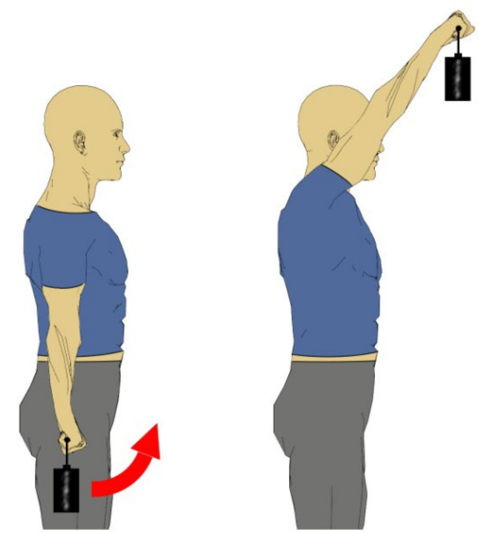
1- Light weight lift to the side
→ <u>Fatigue</u> after 15-20 repeats



2 - PM stretch
2 minutes each side

Recruitment of spinal extensors
(Moseley et al, 2002; Khouw et Herbert, 1998)

4- Stretch LHT-LD
2 mn each side

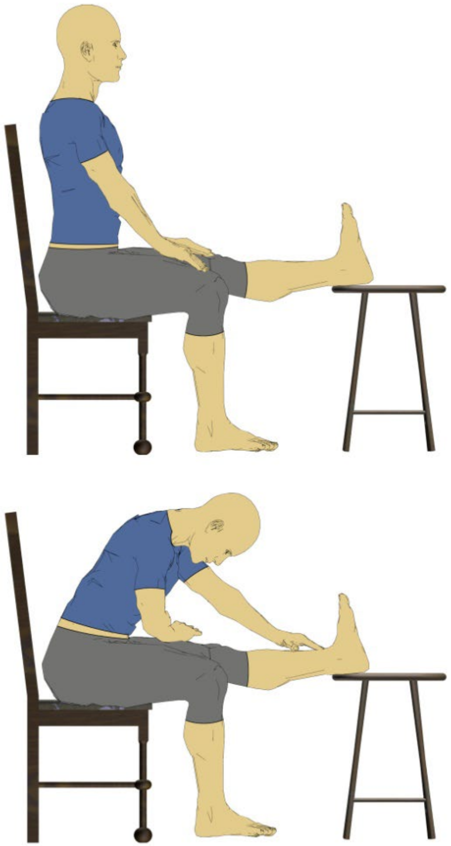


3- Light weight lift to the front
→ <u>Fatigue</u> after 15-20 repeats

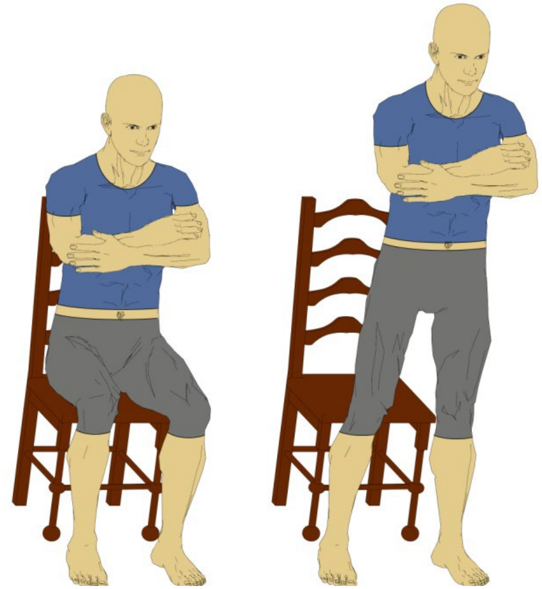
→ ***Clear feeling of physical fatigue*** *(Rooney et al, 1994)*

Gracies, 2010

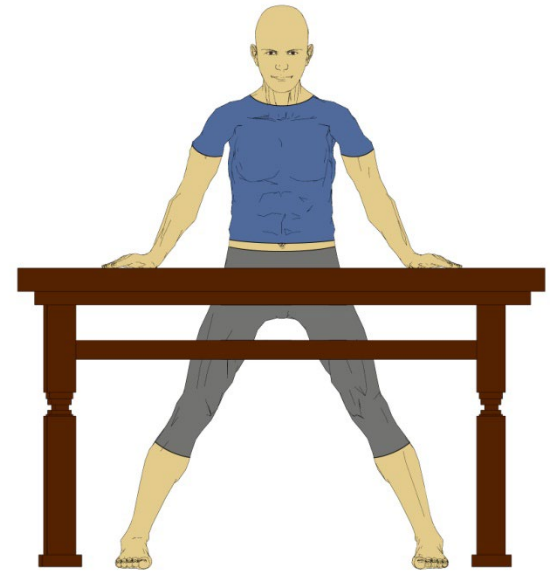
Asymmetric motor strengthening



6 – Hamstrings stretch
Bend forward
2 mn each side

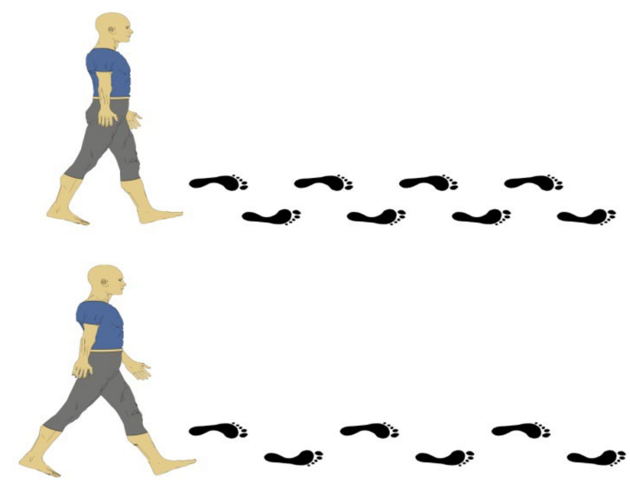


5- Sit-to-stand w/o hands
until fatigue



7 - Adductor stretch
2 mn /day

Mild to moderate stages (2)



8 – Walk same distance every day
With as few steps as possible

Gracies, 2010

Asymmetric Motor Strengthening

Increasing motor cortex excitability for body openers

Gracies, 2010

Increasing motor cortex excitability for body openers

Gracies, 2010

Increasing motor cortex excitability for body openers

Gracies, 2010

Increasing motor cortex excitability for body openers

Gracies, 2010

Training of standing up from ground

Gracies, 2010

Population

Inclusion criteria

- Diagnosis of IPD – UKPDSBB criteria
- Hoehn et Yahr 2, 3 - OFF
- Age ≥ 18

Exclusion criteria

- Intercurrent disease with threat to functional or vital prognosis
- Major cognitive dysfunction
- Participation in another research protocol
- Non-affiliation to social security/medicare

Comparing two programs

Objective: comparison 3 x/week, 1-hour home visits:

« Global » program

= « Conventional » rehabilitation

Techniques:

- **Passive and active joint mobilization**
- **Balance and gait training**
- **Proprioceptive training**
- **Cardio-respiratory training**
- **Relaxation techniques**

vs

Asymmetric Motor Strengthening

Principle = ↑ agonist activity in body openers: extensors, supinators, abductors, external rotators

(because more paretic than antagonist body closers: flexors, pronators, adductors and internal rotators)

= Balance restoration between forces

Techniques:

- **Motor training of opening agonists**
- **Stretch of closing antagonists**

Asymmetric Motor Strengthening: focused on extensor training

Principle : alternate fatiguing series of active exercises – weight adjusted to evoke fatigue in 15-25 repeats, ~ 1 min with bouts of sub max passive stretch ~ 2 min, each side

1. Series of active shoulder abductions	L+R	2 mn	--------- 1 mn rest
2. Stretch of horizontal shoulder adductors	L+R	4 mn	
3. Series of active shoulder flexions	L+R	2 mn	---------- 1 mn repos
(= associated w paravertebral muscle recruitment (*Moseley et al, 2002, 2003*))			
4. Stretch of vertical shoulder adductors	L+R	4 mn	
5. Series of push ups (= work of spinal and elbow extensors)		2 mn	--------- 1 mn repos
6. Stretch of shoulder internal rotators	L+R	4 mn	
7. Series of active supinations against resistance :			
Elbow to body using avec Flexbar (Theraband)	L+R	2 mn	---------- 1 mn repos
8. Stretch of elbow flexors and pronators	L+R	4 mn	
9. Series of actives hip abductions, knee straight, standing	L+R	2 mn	--------- 1 mn repos
10. Stretch of finger and wrist flexors	L+R	4 mn	
11. Series of active hip extensions, knee straight, standing	L+R	2 mn	--------- 1 mn repos
12. Stretch of hamstrings (seated with foot laid on chair)	L+R	4 mn	
13. Series of standing on tiptoes, standing (plantar flexors)		2 mn	-------- 1 mn repos
14. Stretch of hip adductos (standing, with support on bar or furniture)		4 mn	
15. Series of sit-to-stand, arms crossed		2 mn	--------- 1 mn repos
16. Stretch of rectus femoris (patient lying on side, grabbing ankle et with ipsilateral hand bring hip into extension while knee in maximal flexion)	L+R	4 mn	

17. Walk on specific distance, focusing on step length and counting steps. At each session the patient tries to beat the recors of the smallest number of steps required. When record no longer beaten, distance doubled and start again. 2 mn

ASYMOT - design

Double randomization:

- of rehabilitation program
- of therapist involved (out of two study therapists)

ASYMOT time course

- Asymmetric motor strengthening *vs* conventional rehabilitation program during 2 months
- Changes at D60 and at D150

ASYMOT – Outcomes

Primary: Δscore UPDRS III OFF, btw D1 and D60

Secondary:

1. UPDRS III OFF and ON at D1, D60, D150

+ OFF D1, D60, D150:

2. Time to stand up from floor (GMT)

3. Max ambulatory speed and step lengh over 20m btw 2 chairs (modified UP and GO)

4. Post hoc : '*GMT+*' = Time to stand up from floor plus ambulate 20 meters

5. Frequency small and large rapid alternating movements

6. Spiralography - 7. Handwriting parameters

8. Spine posture (Spinal Mouse™)

9. MSPIR: upper limb function

Global Mobility Task

Supine

Turn over (sec)

Dog position (sec)

Kneeling(sec)

One knee up (sec)

Stand up (sec)

Peppe A et al Acta Neurol Scand. 2007; Pauwels. Ann Phys Rehabil Med 2013

Consort Diagram

Included n=38

↓

Randomized n=38

Secondary outcome measures

Post hoc GMT+ = *Time to stand up + time to walk 20 m*

GMT (sec) + Comfortable AT20 (sec)

Gracies, 2014

Eight weeks of home therapy
60 min x 3/ week
Supine-to-Stand

D1

M2

M5

Gracies, 2013

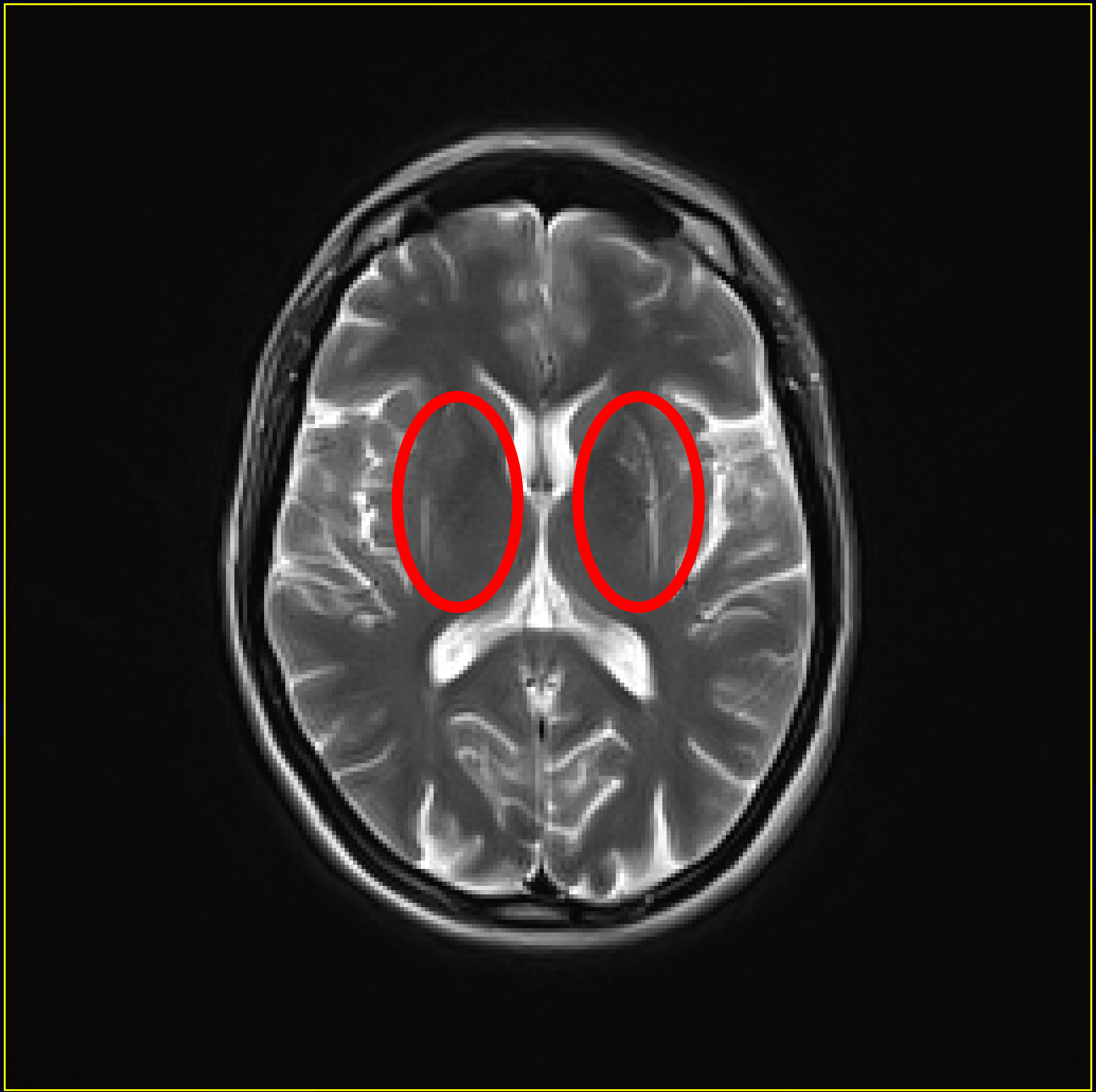
Eight weeks of home therapy
60 min x 3/ week
Supine-to-Stand

D1

M2

M5

Gracies, 2013



AMS (2010)

Józef Julian Franciszek Feliks Babiński
«De l’asynergie cérébelleuse», in: *Rev Neurol*, 7 (1899): 806-816.

Asymmetric motor strengthening 7 weeks – Stand from ground

MSA Year 7 +++

Gracies, 2010

Conclusions I: Asymetric Motor Strengthening

I. ***Exam at rest:*** Eight weeks of AMS failed to bring extra-benefits on UPDRS III in OFF (physician's subjectivity, exam mostly at rest) at D60 compared with conventional therapy → negative on primary

II. ***Exam of motor activities,*** post hoc: eight weeks of AMS produced benefit compared with conventional therapy on global mobility: **Get up from ground and ambulation**.

Conclusions II: pooled data

I. Some improvements magnified at D150
 → **One has trained patients to self-train**

II. Improved markers of parkinsonism:
- Contribution of step length increase to acceleration
- Frequency of large movements + L/S ratio increased in more hypometric hand
- Coefficient of symmetry of spirals increased in more hypometric hand

→ **“Deparkinsonization”? Affinity to more affected side?**