Effects of pedunculopontine nucleus area stimulation on speech production in Parkinson's disease

S. Pinto [1], A. Maillet [2], A. Ghio [1],
M. Ferraye [2], V. Fraix [2], R. Espesser [1],
S. Chabardès [2], E. Seigneuret [2],
A.L. Benabid [2], B. Debû [2], P. Pollak [2]

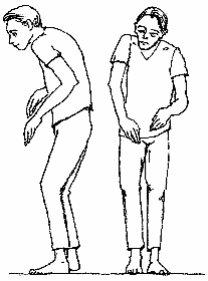
[1] Laboratoire Parole et Langage (LPL), Aix-en-Provence
[2] Grenoble Institut des Neurosciences (GIN), Grenoble

Freezing of gait, Parkinson's disease and PPN

Gait impairment, including freezing (FOG), is frequent in Parkinson disease (PD)
Respond poorly to classical pharmacological and surgical treatments

The PPN is known to modulate locomotor activity
In PD, PPN alteration may be involved in gait and postural impairments

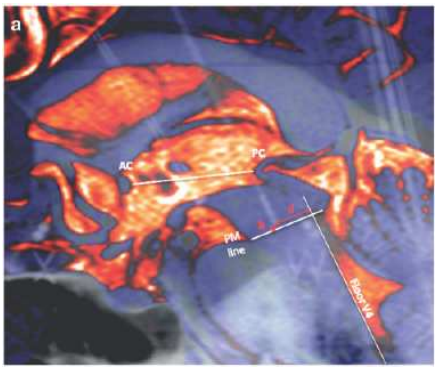
Reports of dramatic improvement of gait disorders following pedunculopontine nucleus stimulation support this idea (Mazzone et al., 2005; Plaha and Gill, 2005; Stefani et al., 2007)



Freezing of gait, dysarthria and PPN

An influence of the PPN area could also be expected in other kinds of motor activities, such as speech

Importance of the periaqueducal gray matter as a convergence zone of orofacial motoneurons (Jurgens, 2002). Periaqueducal grey (PAG) seems to play a role in non-verbal emotional vocal utterances



PAG represents a crucial relay station of the limbic but not the neocortical vocal control pathway (Jurgens and Zwipner, 1996)

PAG is not the site of vocal pattern generation, but rather serves gating functions (Siebert and Jurgens, 2003)

Objective

Since FOG may be improved by PPN area stimulation

BRAIN
A JOURNAL OF NEUROLOGY

Effects of pedunculopontine nucleus area stimulation on gait disorders in Parkinson's disease

M. U. Ferraye,[1,2] B. Debû,[1,2] V. Fraix,[1,2] L. Goetz,[1,2] C. Ardouin,[3] J. Yelnik,[4,5,6] C. Henry-Lagrange,[1,2] E. Seigneuret,[3] B. Piallat,[1,2] P. Krack,[1,2,3] J.-F. Le Bas,[1,2,3] A.-L. Benabid,[1,2,3] S. Chabardès[1,2,3] and P. Pollak[1,2,3]

To evaluate the effect of the PPN area stimulation on temporal speech parameters in PD

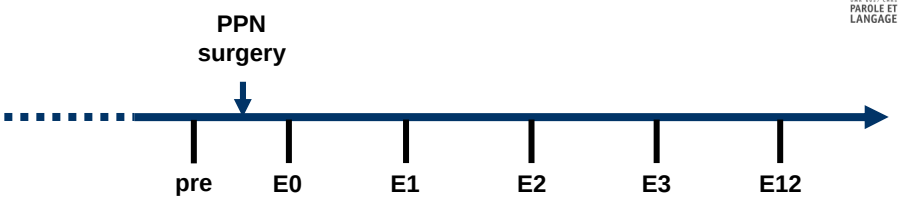
Patients and Methods (1/5) - Patients

7 patients with PD

Severe freezing of gait unresponsive to either L-dopa or bilateral STN stimulation
Bilateral PPN area stimulation

	1	2	3	4	5	6	7	Mean ± SD
Sex	M	F	M	M	F	M	M	
Age at PD diagnosis	55	50	49	44	31	27	35	42.7 ± 11.2
Age at STN surgery	64	64	65	53	53	47	52	57.7 ± 7.6
Age at PPNa surgery	68	68	72	57	59	56	61	63.3 ± 6.8
Disease duration	13	18	23	13	28	29	26	20.7 ± 7.1
Levodopa equivalent daily dose (mg) (Lozano *et al.*, 1995)	1025	550	800	1170	400	0	890	657
Improvement in the UPDRS motor score under levodopa off STN stimulation (%)	55	23	23	44	46	No levodopa treatment	64	
FOG (off med)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	
Postural instability (off med)	Yes	Yes	Yes	no	Yes	no	no	

Patients and Methods (2/5) – Record timescale



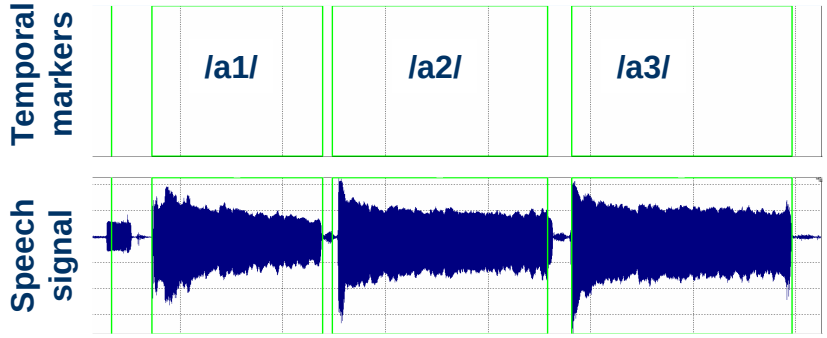
L-dopa	OFF ON		OFF ON		OFF ON		OFF ON		OFF ON		OFF ON	
STN	OFF ON		ON		ON		ON		OFF ON		OFF ON	
PPN	-		OFF	n=7	OFF ON	n=4 n=3	OFF	n=7	OFF ON	n=3 n=4	OFF ON	n=7

Performed with a digital voice recorder (Microtrack, M-Audio) connected with a head-mounted microphone (AKG420)

Analysis performed using the ***Phonedit*** software environment (Laboratoire Parole et Langage, Aix-en-Provence, France)

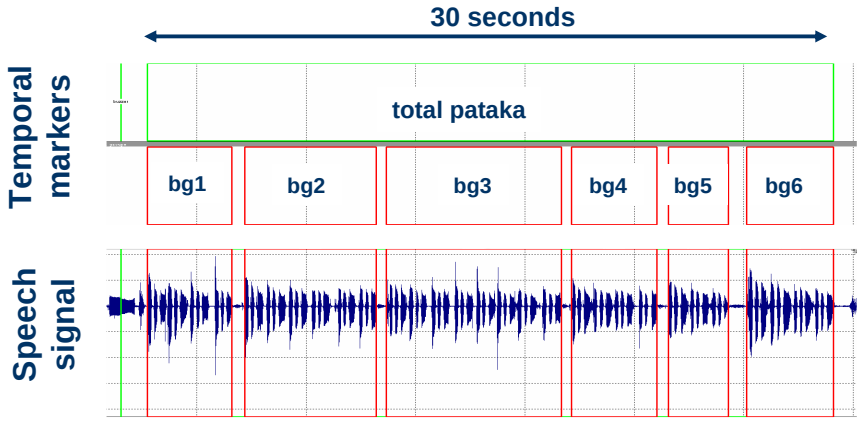
Patients and Methods (3/5) – Speech tasks

Maximal Phonation Time (MPT, in seconds) for the three vowels, averaged



Patients and Methods (4/5) – Speech tasks

Repetition of /pataka/ at a normal speech rate, during 30 seconds
Breath group durations (bg, in seconds)



Patients and Methods (5/5) – Statistical analysis

A **linear mixed model** was used (**R software**) for group analyses with
- ***patient*** as a ***random term***
- ***treatment nature*** (L-dopa, STN stimulation, PPN stimulation) and ***state*** (off, on) as ***fixed effects***

p-values < 0.05

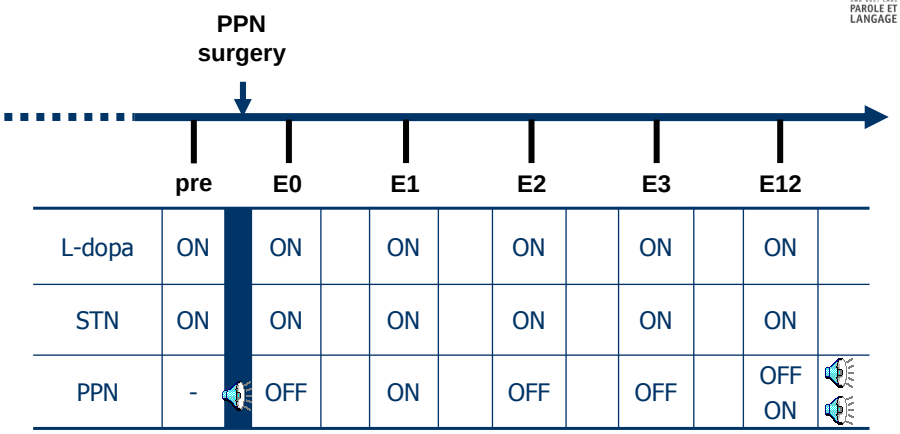
3 approaches :

1/ Postoperative PPN stimulation main effect
(E1, E2, E3, E12) PPN_off *vs.* (E1, E2, E3, E12) PPN_on
L-dopa_off/on
STN_on

2/ Modification of PPN effect along time

3/ Pre- *vs.* postoperative data comparison
(E0) vs. (E12) PPN_off/on
L-dopa_off/on
STN_off/on

Results (1/5) – Perceptive data



Clinical evaluation of dysarthric speech
French version adapted from the Frenchay (Auzou *et al*., 2002)

34 raters, each of them listening to part of the data
Each file listened by 3 different raters
Under analysis

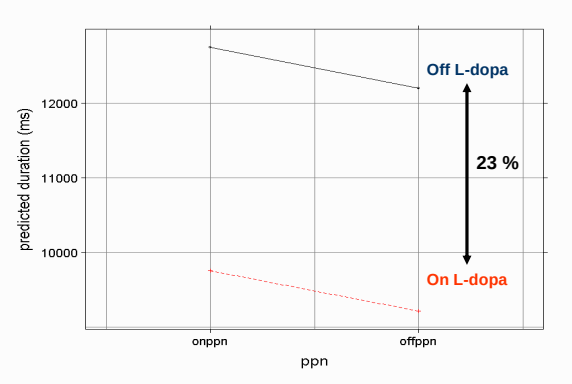
Results (2/5) – PPN main effect – *Maximum Phonation Time*

off vs. on PPN stimulation (STN on, off/on dopa)

- ✓ No effect of PPN stimulation, nor any interaction between L-dopa and PPN stimulation (p=0.3)
- ✓ No modification of PPN stimulation effects from the first to the last postoperative evaluations (p=0.3)

off vs. on L-dopa

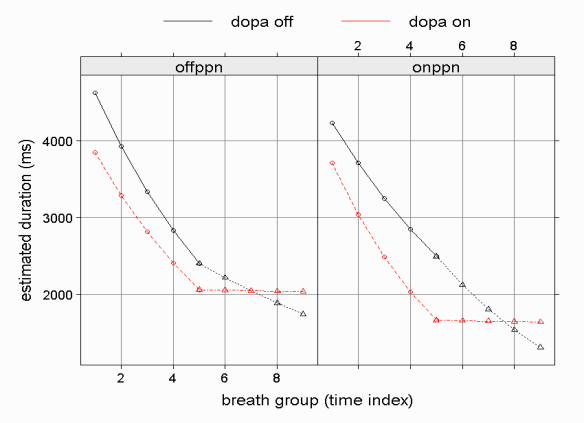
- ✓ Significant L-dopa deleterious effect (p<0.001), reducing the MPT up to 23%



Results (3/5) – PPN main effect – *Diadochokinesis breath groups*

✓ Similar results were found for the /pataka/ task, regarding the main effect of PPN stimulation

✓Fatigue at the end of the performance ➔ convergence of L-dopa off and on lines



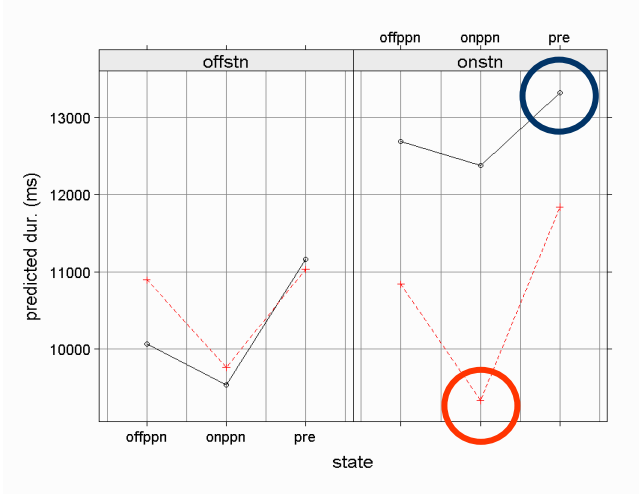
Results (4/5) – Pre vs. postoperative data – *MPT*

PAROLE ET LANGAGE

✓ Negative synergestic effect of treatments

✓ **Worst** MPT were found **on dopa / on STN / on PPN** (p<0.001)

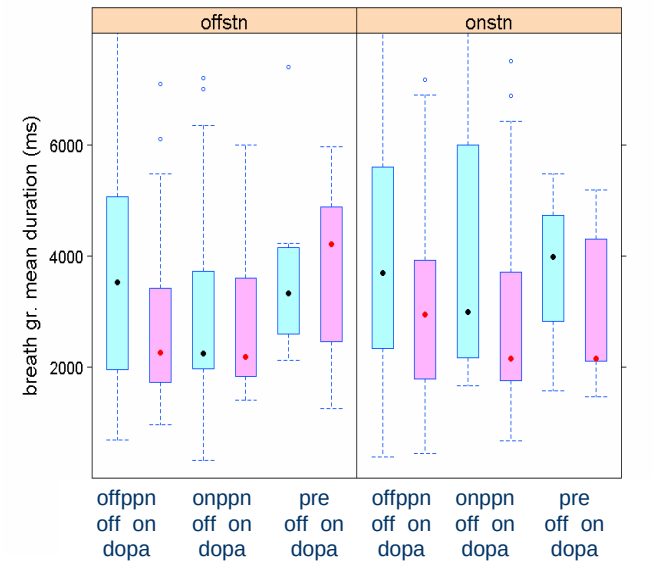
✓ **Best** situation was **off dopa / on STN / pre-PPN surgery**



Results (5/5) – Pre vs. postoperative data – *breath groups*

PAROLE ET LANGAGE

✓ Less clear
✓ Similar trends



Conclusions and perspectives

PAROLE ET LANGAGE

From a PPN area stimulation point of view

✓ **Speech is not influenced by PPN area stimulation in patients with PD and STN stimulation**
✓ **However, L-dopa does worsen speech and this worsening is increased under PPN stimulation**
PPN area is not involved in speech voluntary produced

From a speech task point of view

✓ **Temporal speech parametres are not influenced by PPN area stimulation in patients with PD and STN stimulation**
✓ **However, L-dopa does worsen these speech parametres and this worsening is increased under PPN stimulation**
Information on speech intensity, frequency and articulatory rates are still needed to conclude precisely

Acknowledgments – This work was supported by grants from Michael J. Fox Foundation, Fondation de France and Medtronic. Support from the Grenoble University Hospital has to be mentioned as regards to the study promotion