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Past, Present and Future Brains
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SIMPOSIO VI
TRAIT IMPULSIVITY, INHIBITORY CONTROL AND IMPULSE DYSCONTROL,
WITH A FOCUS ON PARKINSON'S DISEASE

Neural correlates of inhibitory control and impulse control disorders in Parkinson's Disease

Prof. Gabriella Santangelo,
Dipartimento di Psicologia, Università degli studi della Campania "Luigi Vanvitelli", Caserta

10 Novembre 2023

Dipartimento di Psicologia

Argomenti

1. Controllo inibitorio nella malattia di Parkinson

2. Disturbi del controllo degli impulsi nella malattia di Parkinson

3. Correlati neurali dei deficit del controllo inibitorio e del controllo degli impulsi nella Malattia di Parkinson

1. CONTROLLO INIBITORIO NELLA MALATTIA DI PARKINSON

Il controllo inibitorio

- E’ un processo cognitivo che permette di sospendere le azioni e le decisioni per un tempo sufficiente ad eseguire l’analisi di una situazione in maniera complessa e che garantisce un migliore adattamento al contesto e ai suoi cambiamenti.

- Il controllo inibitorio permette di sopprimere un’informazione che interferisce ed entra in «conflitto» con un’altra.

- L’inibizione consente la risoluzione di questo conflitto tra informazioni tra loro contraddittorie e permette di mantenere una certa coerenza riguardo il comportamento e le intenzioni dell’individuo.

Il controllo inibitorio nella MP

- L’inibizione è stata spesso studiata nella MP in particolare con i test di Stroop e di fluenza verbale (Kudlicka et al., 2011; Martyr & Clare, 2012).

- I pazienti con MP sono spesso significativamente più lente a rispondere a parole di colore incongruente rispetto ai controlli normali nello Stroop test il che indica un controllo inibitorio più scarso (Amieva et al., 2002; Dirnberger & Jahanshahi, 2013; Doninger & Bylsma, 2007; Muslimovic, Post, Speelman, & Schmand, 2005; Pagonabarraga et al., 2007; Sauzeon et al., 2016).

Parkinsonism and Related Disorders 21 (2015) 1219–1226

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Parkinsonism and Related Disorders

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

Mild Cognitive Impairment in newly diagnosed Parkinson's disease: A longitudinal prospective study

Gabriella Santangelo [a, b], Carmine Vitale [b, c], Marina Picillo [d], Marcello Moccia [e], Sofia Cuoco [a], Katia Longo [b], Domenica Pezzella [a], Assunta di Grazia [a], Roberto Erro [f, g], Maria Teresa Pellecchia [d], Marianna Amboni [b], Luigi Trojano [a, **], Paolo Barone [d, *]

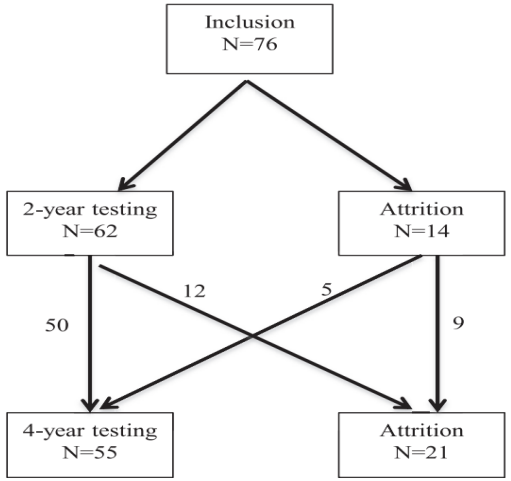

Fig. 1. Patients disposition.

Table 1
Comparison between PD-MCI group and Normal Cognition (PD-CN) group at baseline assessment.

Parameters	PD-MCI (n = 25)	PD-CN (n = 51)	F/U test	P
Age (years)	61.4 ± 8.3	58.9 ± 9.1	1.306	0.257
Education (years)	9.4 ± 4.3	12 ± 3.4	8.344	**0.005**
Age at onset (years)	59.4 ± 8	56.7 ± 8.8	1.519	0.222
UPDRS-motor part	18.4 ± 7.5	12.5 ± 6.2	11.662	**0.001**
H&Y stage	1.9 ± 0.3	1.7 ± 0.5	282.0	0.065
Disease duration (years)	11.2 ± 4.5	13.8 ± 5.8	3.877	0.053
Behavioural variables				
AES-S	38.6 ± 9.9	32.9 ± 5.3	3.792	**0.015**
Memory domain				
Immediate recall	36.3 ± 10.2	41.4 ± 9.2	3.208	**0.030**
Delayed recall	7.2 ± 3.4	8.5 ± 2.6	5.193	**0.003**
Attention domain				
Interference task-Stroop test	8.7 ± 6	17.2 ± 7.5	5.072	**0.003**
TMT-A	75.7 ± 37.2	43.2 ± 21.6	10.463	**<0.001**
TMT-B	242.3 ± 128.8	112.1 ± 54.9	18.161	**<0.001**
Verbal span	3.6 ± 0.6	4.1 ± 0.7	2.878	**0.044**
Corsi's Test	4.9 ± 0.8	5 ± 0.8	2.496	0.069
Frontal functions domain				
Phon-F	24.4 ± 11.4	32.3 ± 9.7	7.839	**<0.001**
CDT	4.5 ± 3.6	8.9 ± 1.8	16.675	**<0.001**
Visuospatial functions domain				
CA	9.9 ± 2.4	12.2 ± 1.7	11.635	**<0.001**
BJLOT	16.2 ± 6.2	22.8 ± 3.6	12.763	**<0.001**
Language				
Nouns denomination task	9.6 ± 0.8	9.9 ± 0.3	1.431	0.243
Verbs denomination task	8.2 ± 1	8.8 ± 0.9	3.678	**0.017**

UPDRS = Unified Parkinson's Disease Rating Scale; H&Y = Hoehn & LEDD = Levodopa Equivalent Daily Dose; TMT-B = Trail Making Test-part B; Phon-F = Phonological Fluency Task; CDT = Clock Drawing Test; CA = Constructional Apraxia test; BJLOT = Benton Judgement Orientation Lines; AES-S = Apathy Evaluation Scale-Self Version. Significant differences are in bold.

3.4. Predictors of conversion to PD-MCI at T2

The logistic regression analysis, with presence/absence of PD-MCI at T2 (0 = presence; 1 = absence) as the dependent variable and clinical and neuropsychological measures as independent variables, showed that reduced score on the interference task of Stroop Test was predictive for development of PD-MCI at T2 (OR = 1.18, beta = 0.17; 95% Confidence interval [CI] = 1.06–1.33; p = 0.004).

Journal of Neuropsychology (2017)

The British Psychological Society

www.wileyonlinelibrary.com

Assessing inhibitory control in early-stage Alzheimer's and Parkinson's disease using the Hayling Sentence Completion Test

Anthony Martyr[1,2], Elina Boycheva[3] and Aleksandra Kudlicka[1,2]*

117 pazienti tra pazienti affetti da MP e pazienti affetti da demenza di Alzheimer sono stati sottoposti all'Hayling Sentence Completion Test.

Table 2. Mean response times, error rate, and overall performance on the Hayling Sentence Completion Test by group

HSCT scores	PwD (n = 30)	PwPD (n = 33)	Controls (n = 54)	ANOVA	p Value	*Post hoc*
HSCT Part 1 (Initiation)						
Raw score (total time)*	35.70 (32.02)	19.39 (11.80)	9.48 (7.05)	$F(2,48.49) = 17.87$	**<.001**	**a,b,c**
Scaled score	3.60 (1.65)	4.42 (1.03)	5.44 (0.90)	$F(2,57.27) = 22.10$	**<.001**	**a,b,c**
HSCT Part 2 (Inhibition)						
Raw score (total time)*	84.57 (46.41)	69.03 (43.61)	51.54 (31.24)	$F(2, 114) = 7.10$	**.001**	**b,c**
Scaled score	3.97 (1.40)	4.49 (1.62)	5.07 (1.23)	$F(2, 114) = 6.33$	**.002**	**b**

Take-home message 1

- Esiste un deficit del controllo inibitorio nei pazienti parkinsoniani

Quali sono i correlati neurali di tali deficit?

Correlati neurali del deficit del controllo inibitorio

- L'incapacità di inibire i comportamenti impulsivi è legata all'iperattività del nucleo subtalamico (StN) (Alegre al. 2013; Schmidt et al., 2013).
-Il nucleo subtalamico è un nodo chiave di un sistema di inibizione cortico-sottocorticale dell'emisfero destro, che comprende anche il giro frontale inferiore (IFG), l'area motoria pre-supplementare (preSMA), la corteccia motoria primaria e i gangli della base [nucleo caudato, substantia nigra (SN)].

Altered Functional Interactions of Inhibition Regions in Cognitively Normal Parkinson's Disease

Deborah L. Harrington[1,2], Qian Shen[1,3], Rebecca J. Theilmann[2], Gabriel N. Castillo[1,2], Irene Litvan[3], J. Vincent Filoteo[4,5], Mingxiong Huang[2,6] and Roland R. Lee[2,6]*

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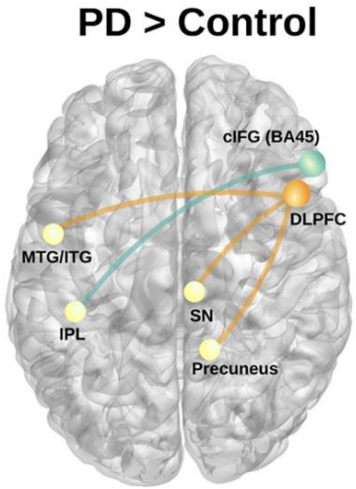


Risultati:
-connettività rafforzata tra IFG con la corteccia parietale (lobulo parietale inferiore, rete dorsale della attenzione controllata) e connettività rafforzata tra corteccia prefrontale dorsolaterale e giro temporale medio-inferiore, precuneo e substantia nigra.
Pertanto, gli elementi chiave della rete di inibizione hanno mostrato interazioni rafforzate con le reti dell'attenzione controllata e dell'attenzione guidata dallo stimolo

2. DISTURBI DEL CONTROLLO DEGLI IMPULSI NELLA MALATTIA DI PARKINSON

I disturbi del controllo degli impulsi (ICD) nella MP

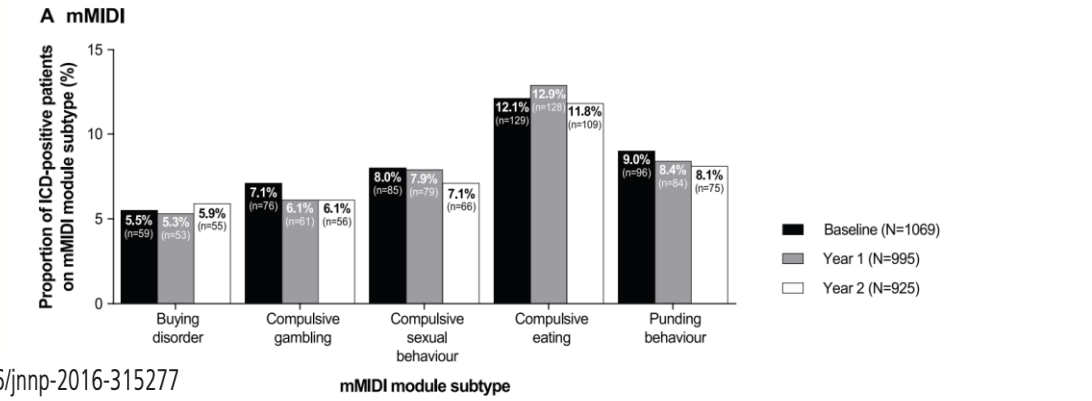
- Gli ICD sono disturbi neuropsichiatrici caratterizzati dalla presenza di azioni o gesti incontrollabili
- La prevalenza degli ICD nella MP è pari fino al 40%

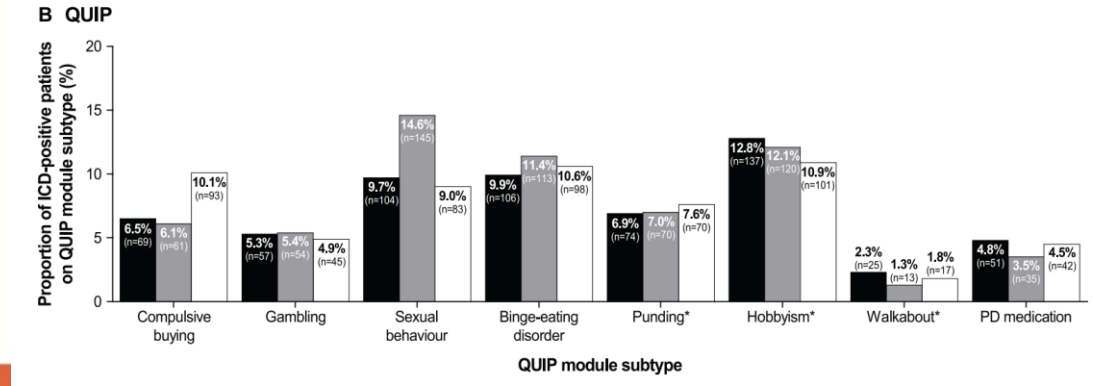
RESEARCH PAPER

ICARUS study: prevalence and clinical features of impulse control disorders in Parkinson's disease

Angelo Antonini,[1] Paolo Barone,[2] Ubaldo Bonuccelli,[3] Karin Annoni,[4] Mahnaz Asgharnejad,[5] Paolo Stanzione[6]

Antonini A, *et al*. *J Neurol Neurosurg Psychiatry* 2017;**88**:317–324. doi:10.1136/jnnp-2016-315277





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Neuroscience and Biobehavioral Reviews

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

Meta-analysis

The relationship between Impulse Control Disorders and cognitive dysfunctions in Parkinson's Disease: A meta-analysis☆

Gabriella Santangelo[a,*], Simona Raimo[a], Paolo Barone[b]

[a] Department of Psychology, University of Campania Luigi Vanvitelli, Caserta, Italy
[b] Department of Medicine, Center for Neurodegenerative Diseases (CEMAND), University of Salerno, Italy

Table 3
Summary of meta-analytic results.

Domains/Outcomes	K	N	ICD+	ICD−	Pooled effect size Hedges'g (P value)	(95% Confidence Intervals)		Homogeneity statistics			Egger's t test for publication bias	Trim and fill
						LL	UL	Q (df)	P	I^2		
Abstraction ability*	8	459	212	247	−0.40 **(0.002)**	−0.65	-0.15	10.82 (7)	0.146	35.33	−0.58	0
EF- Fluid Reasoning	7	345	152	193	−0.23 (0.136)	−0.52	0.07	10.58 (6)	0.102	43.31	−3.64 **(p = 0.015)**	0
EF- Generativity-Fluency for letters	14	870	382	488	0.01 (0.937)	−0.23	0.25	35.92 (13)	0.001	63.81	−0.87	0
EF- Generativity-Fluency for categories	10	646	283	363	−0.08 (0.638)	−0.08	-0.24	32.56 (9)	<0.001	72.36	−1.49	0
EF-Inhibition	13	758	357	401	−0.10 (0.448)	−0.36	0.16	32.38 (12)	0.001	62.94	−0.5	0
EF-Set-shifting (TMT:B)	5	259	137	122	−0.59 **(<0.001)**	−0.84	-0.34	1.30 (4)	0.861	0	1	0
EF-Set-shifting (TMT:B-A)	7	421	224	197	−0.46 (0.043)	−0.091	-0.01	27.86 (6)	<0.001	78.47	−0.45	0
EF- Updating	7	309	146	163	0.26 (0.034)	0.02	0.5	6.53 (6)	0.367	8.09	0.38	0
EF-global	11	679	229	450	−0.08 (0.615)	−0.38	0.22	30.46 (10)	0.001	67.17	−0.02	2 (−0.19 [−0.49–0.10])
Language	6	341	151	190	−0.24 (0.066)	−0.49	0.02	6.25 (5)	0.283	19.99	0.59	0
Processing speed, Attention, Working Memory	17	890	433	457	−0.10 (0.406)	−0.32	0.16	42.88 (16)	<0.001	62.69	−2.31 **(p = 0.035)**	0
Spatial Long term Memory	5	405	173	232	−0.33 (0.071)	−0.68	0.03	10.55 (4)	0.032	62.07	−1.4	0
Verbal Long Term Memory	12	732	343	389	−0.07 (0.633)	−0.38	0.23	40.15 (11)	<0.001	72.6	−1.26	1 (−0.12 [−0.42–0.18])
Verbal Short Term Memory	10	514	240	274	−0.15 (0.324)	−0.45	0.15	23.91 (9)	0.004	62.36	0.37	1 (−0.23 [−0.53–0.08])
Visuospatial/Constructional abilities	9	556	266	290	**−0.42 (0.005)**	−0.71	-0.13	19.32 (8)	0.013	58.59	−1.84	0
Decision making	10	352	171	181	**0.54 (0.001)**	0.23	0.85	18.56 (9)	0.029	51.51	1.31	0
Spatial short term memory	7	404	199	205	−0.10 (0.511)	−0.41	0.2	13.44 (6)	0.037	55.35	−0.98	0
Global Cognition	28	2492	960	1532	0.02 (0.781)	−0.11	0.15	49.48 (27)	0.005	45.43	−2.49 **(p = 0.020)**	0

*Abstraction ability/concept formation; EF, Executive Function; TMT, Trail Making Test; K = number of studies; N = total number of participants; ICD+ = number of PD patients with ICD; ICD− = number of PD patients without ICD; LL = Lower Limit; UP = Upper Limit; Q and I^2 = heterogeneity statistics; df = degrees of freedom: EF = Executive Functions; statistically significant values are reported in bold.

Comparative Neuropsychological Profile of Pathological Gambling, Hypersexuality, and Compulsive Eating in Parkinson's Disease

Carmine Vitale, MD, PhD,[1,2,3] Gabriella Santangelo, PhD,[2,3,4] Luigi Trojano, MD,[4] Francesca Verde,[4] Mariangela Rocco, MD,[2] Dario Grossi, MD,[4] and Paolo Barone, MD, PhD[2,3]*

Movement Disorders, Vol. 26, No. 5, 2011

TABLE 2. Cognitive comparisons among patients with hypersexuality (HS), with compulsive eating (CE), with pathological gambling (PG), with multiple impulse control disorders (mICDs), and without ICDs (controls)

	HS (n = 13)	CE (n = 12)	PG (n = 14)	Multiple ICDs (n = 10)	Controls (n = 14)	*P*
Neuropsychological parameters						
MMSE	27.4 ± 2.2	26 ± 1.9	27.4 ± 2.2	26.5 ± 2.6	28.2 ± 1.4	.100
a) Frontal Functions						
1) Cognitive flexibility WCST—global score	109 ± 21	104.7 ± 29.1	105.1 ± 15.9	96.2 ± 20	76.3 ± 37.6	.009
2) Spatial planning ROCF—copy task	21.4 ± 7.1[a]	23.7 ± 10.8[a]	23.5 ± 7.2[a]	21.1 ± 6[a]	30.7 ± 4.1	.003
3) Set shifting TMT: B-A	143 ± 73.5[a]	112.8 ± 80.5[a]	138.8 ± 57.9[a]	137.1 ± 91.6[a]	66.1 ± 23.3	.001
4) Selective attention Attentive matrices	41.8 ± 10.9	44.4 ± 9.8	47.9 ± 7	43 ± 16	52.1 ± 5.7	.061
5) Inhibitory control Stroop Test—interference task	6.8 ± 4.3[a,b]	12.1 ± 8.2	13.6 ± 7.4	8.3 ± 5.4[a,b]	15.1 ± 6	.004
b) Memory						
1) Immediate recall	28 ± 7.2[a,b,c]	36.5 ± 10.1[a,b]	41.4 ± 11	31.6 ± 6.7[a,b]	49.1 ± 9.9	<.001
2) Delayed recall	6 ± 2[a,b]	6 ± 3[a]	8.4 ± 2.8	6.7 ± 1.5[a,b]	10.2 ± 3.2	.002
Neuropsychiatric parameters						
HAMD-17 score	8.6 ± 5.4	14 ± 8.8	11.3 ± 5.7	14.3 ± 6.5	10.6 ± 8.5	.217
HADS total score	13 ± 9	18.1 ± 6.8	17.7 ± 8.1	17.4 ± 7.1	12.7 ± 7.6	.296
HADS-A score	5.4 ± 4.1	9.4 ± 4.2	8.8 ± 4.5	8.1 ± 4.8	6.6 ± 4.2	.099
HADS-D score	7.6 ± 6.3	8.7 ± 3.7	8.9 ± 4.6	9.3 ± 3.7	6.1 ± 4.1	.435
Anxiety disorders (DSM-IV criteria)	0	0	0	0	0	—

HS, hypersexuality, CE, compulsive eating; PG, pathological gambling; MMSE, Mini Mental State Examination; WCST, Wisconsin Card Sorting Test; ROCF, Rey-Osterrieth Complex Figure Test; TMT, Trail Making Test; HAMD-17, Hamilton Depression Rating Scale; HADS, Hospital Anxiety and Depression Scale; HADS-A, Hospital Anxiety and Depression Scale–Anxiety; HADS-D, Hospital Anxiety and Depression Scale–Depression.
[a]Significantly different from controls (PD patients without ICDs); [b]significantly different from PD with PG; [c]significantly different from PD with CE.

Pazienti con ipersessualità presentarono prestazioni significativamente deficitarie sullo Stroop test rispetto ai pazienti con gioco d'azzardo patologico.

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Neuroscience and Biobehavioral Reviews 107 (2019) 672–685

Neural bases of impulse control disorders in Parkinson's disease: A systematic review and an ALE meta-analysis

Gabriella Santangelo[a,*], Simona Raimo[a,b,c], Maria Cropano[a], Carmine Vitale[d], Paolo Barone[e], Luigi Trojano[a]

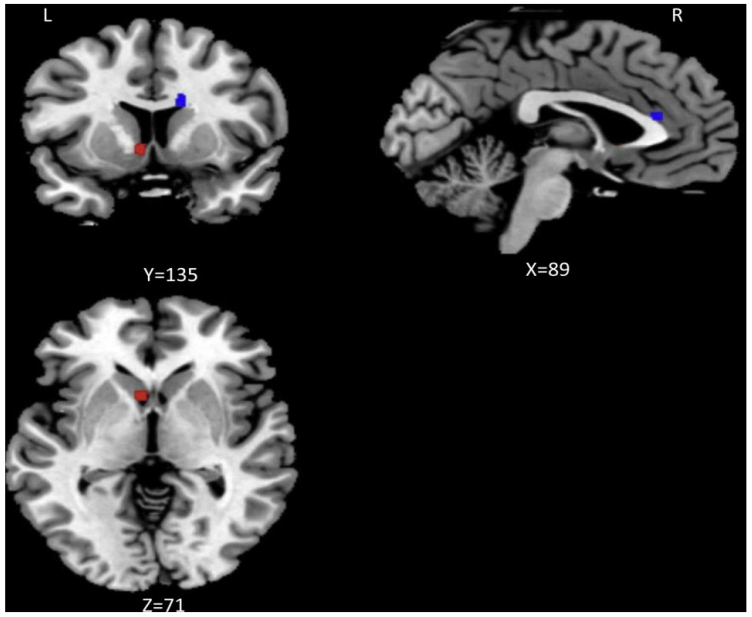

Table 3
ALE Meta-analysis of 14 whole brain activity studies investigating ICD in PD.

Region	BA	H	Volume	MNI Coordinates
PD + ICD < PD-ICD				
Anterior cingulate cortex	24	R	2256	12 36 8
PD + ICD > PD-ICD				
Ventral Striatum		L	832	−20 10 -10

H, Hemisphere; R, Right; L, Left; BA, Brodmann areas; MNI, Montreal Neurological Institute; PD, Parkinson's disease; ICD, impulse control disorder; PD + ICD, Parkinson's disease patients with impulse control disorder; PD-ICD, Parkinson's disease patients without impulse control disorder.

Fig. 2. Meta-analytic findings: significant brain activation increases in L ventral striatum cluster and significant brain activation decrease in R anterior cingulate cortex cluster. L = left, R = right.

3. CORRELATI NEURALI CONDIVISI TRA DEFICIT DEL CONTROLLO INIBITORIO E DEL CONTROLLO DEGLI IMPULSI NELLA MALATTIA DI PARKINSON?

doi:10.1093/brain/awaa318 BRAIN 2020: 143; 3734–3747 | 3734
BRAIN
A JOURNAL OF NEUROLOGY

Inhibitory control dysfunction in parkinsonian impulse control disorders

Garance M. Meyer,[1,2,3,4,†] Charlotte Spay,[1,2,3,4,†] Alina Beliakova,[1,2,3,4] Gabriel Gaugain,[1,2,3,4] Gianni Pezzoli,[5,§] Bénédicte Ballanger,[1,2,3,4] Philippe Boulinguez[1,2,3,4,‡] and Roberto Cilia[6,‡,§]

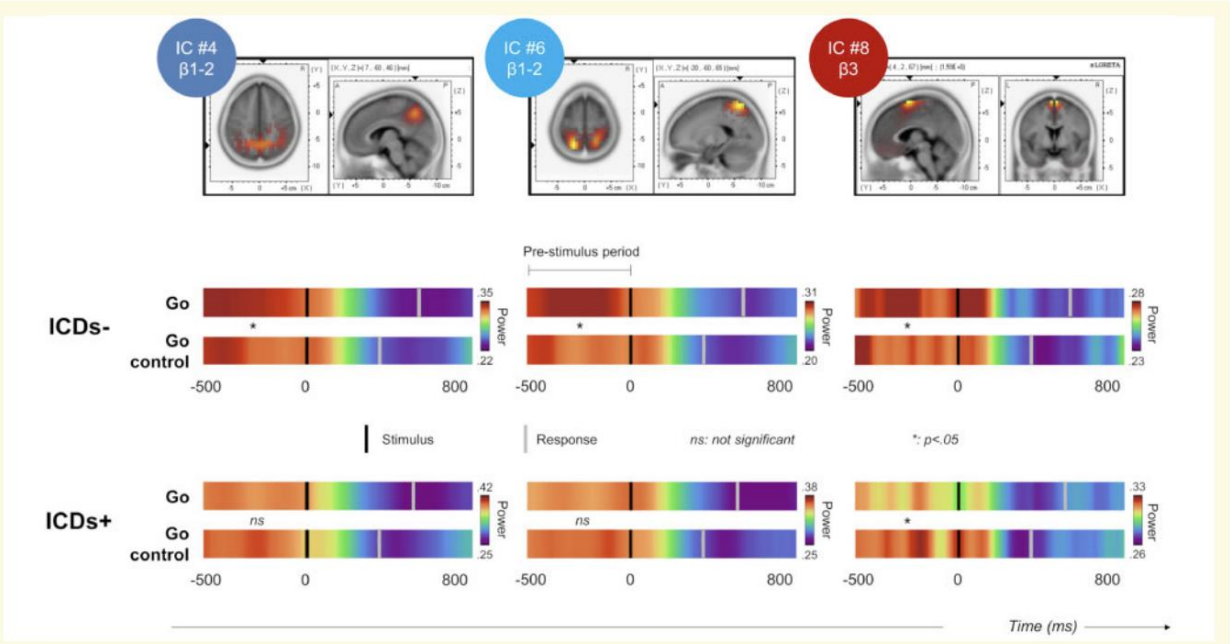

Figure 4 Neural correlates of motor impulsivity in patients with Parkinson's disease with ICDs (ICD+) with respect to patients with Parkinson's disease without ICDs (ICD–). Precuneus (ICs 4 and 6) and SMA (IC 8) beta activity (absolute power data averaged across subjects) is abnormal in ICD + patients. While ICD– patients show a pattern of prestimulus activity suggesting increased proactive inhibitory control when action restraint is required (increased power in Go trials) with respect to the control condition (Go_control trials), ICD + patients do not show similar activation. This dysfunction is associated with more commission errors and shorter reaction time in ICD + patients with respect to ICD– patients.

Patients with Parkinson's disease with ICDs proved to be more impulsive than those without ICDs. This was associated with decreased beta activity in the precuneus and in a region of the medial frontal cortex centred on the supplementary motor area.

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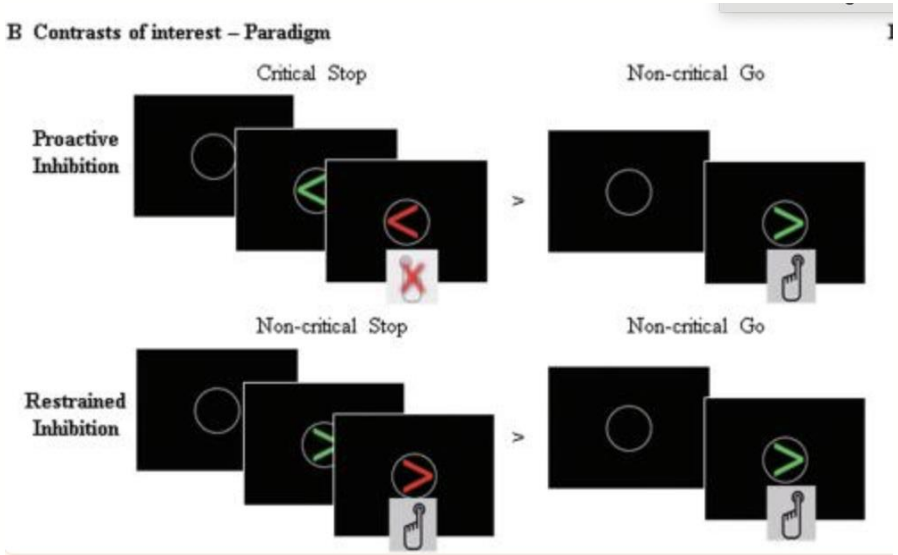
NeuroImage: Clinical 32 (2021) 102822

Functional correlates of response inhibition in impulse control disorders in Parkinson's disease

Teresa Esteban-Peñalba [a,1], Pedro M. Paz-Alonso [a,b,1], Irene Navalpotro-Gómez [c], María C. Rodríguez-Oroz [d,e,*]



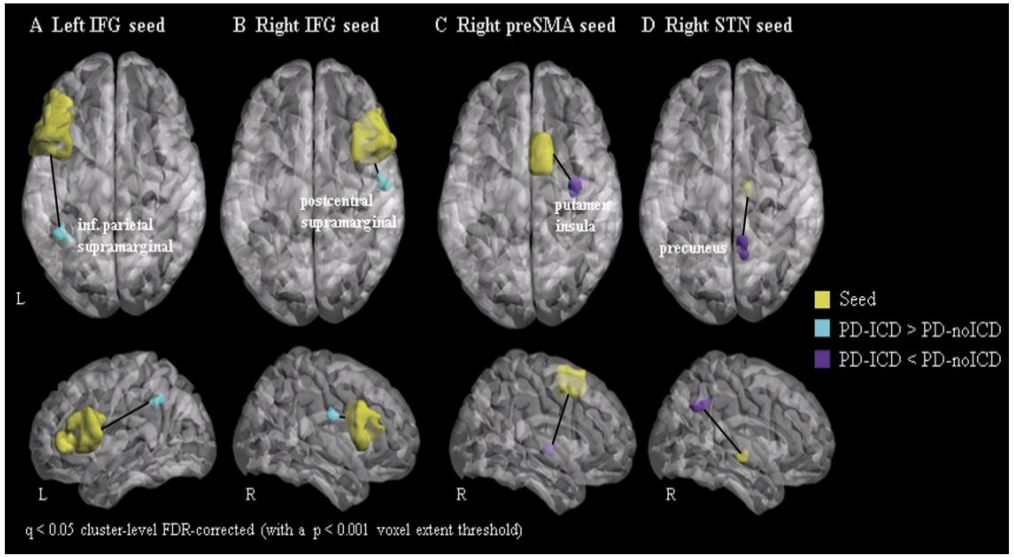


Fig. 4. Functional whole-brain connectivity during Restrained Inhibition. Compared to PD-noICD participants, PD-ICD patients showed increased functional coupling of the left IFG (A) and right IFG (B) with parietal regions, plus decreased functional co-activation of the right preSMA (C) with putamen/insula and right STN (D) with precuneus.

Durante l'inibizione proattiva, pazienti con ICD mostrano iperattivazione di un network di inibizione bilaterale rispetto ai pazienti senza ICD. Durante l'inibizione trattenuta

Si verificava una iperattivazione del giro frontale inferiore sinistro (connessa al monitoraggio) e cambiamenti nella co-attivazione funzionale tra regioni inibitorie e la corteccia parietale inferiore e il giro soprammarginale destro.

Take-home message 2

- Nei pazienti con ICD si verificano deficit del controllo inibitorio, pertanto sia impulsività che deficit del controllo inibitorio posso essere considerate come epifenomeni di alterata connessione funzionale tra:

rete inibitoria (motoria) e **rete attentiva volontaria**

Giro frontale inferiore,
Nucleo subtalamico,
area motoria supplementare,
corteccia motoria primaria
Gangli della base
Substantia nigra

Corteccia pre-frontale laterale e anteriore,
Corteccia prefrontale dorso laterale,
corteccia prefrontale mediale
giro del cingolo,
corteccia parietale inferiore e superiore;

THANK YOU FOR YOUR ATTENTION