DBS of Subthalamic Nucleus and L-DOPA modulate TMS-evoked cortical activity in Parkinson's disease patients

WebPoster

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Background

The effects of deep brain stimulation of the subthalamic nucleus (DBS-STN) and L-DOPA (LD) on cortical activity in Parkinson's disease (PD) are poorly understood. Previous studies suggested that DBS affects specific intracortical circuits, as revealed by motor-evoked potentials (MEPs) **[1,2]**. Here, by combining transcranial magnetic stimulation (TMS) and electroencephalography (EEG) we directly explored the effects of STN-DBS, either alone or in combination with LD, on TMS-evoked cortical activity of implanted PD patients.

Methods

Six advanced PD patients with bilaterally implanted DBS electrodes into the STN were enrolled in the study. All patients were tested in three clinical conditions:

ON/ON condition: L-DOPA-ON/DBS-ON;

OFF/ON condition: L-DOPA-OFF/DBS-ON;

OFF/OFF condition: L-DOPA-OFF/DBS-OFF

Clinical information are reported in **table 1**. TMS pulses were delivered over left M1 while simultaneously acquiring EEG. Eight age-matched healthy volunteers (**HC**) were tested as a control group.

						UPDRS-III			Therapy	DBS-parameters		
n	Age	Sex	Disease Duration (y)	Years since surgery	H &Y	OFF/OFF	OFF/ON	ON/ON	LE/d	Amplitude (V)	Pulse (µs)	Freq (Hz)
1	72	F	8	3	3	43	37	25	800	R:2-L:1.8	R:60-L:90	R:140-L:140
2	77	M	17	10	3	63	51	33	1100	R:2.5-L:2.5	R:60-L:60	R:180-L:180
3	60	M	14	3	3	55	39	18	600	R:3.5-L:3.5	R:90-L:90	R:185-L:185
4	51	M	13	4	3	66	53	33	650	R:3-L:3	R:60-L:60	R:140-L:140
5	57	M	11	6	3	60	44	32	900	R:3.2-L:3.2	R:60-L:60	R:140-L:140
6	66	F	11	3	2	40	29	17	900	R:3.5-L:3.5	R:60-L:60	R:180-L:180

Results

TIME-DOMAIN ANALYSIS

Analysis of global mean field power revealed that STN-DBS (ON/ON and OFF/ON condition) enhanced early GABAa-ergic global TMS-evoked activity, i.e. ~45-80 ms after TMS, compared to OFF/OFF condition (**fig. 1A and 1B**). L-DOPA intake (ON/ON condition) produced a further increase of late GABAb-ergic TMS-evoked activity, i.e. ~80-130 ms after TMS (**fig. 1B and 1C**), that normalized TMS-evoked activity as compared to HC range of values (**fig. 2**).

TIME/FREQUENCY-DOMAIN ANALYSIS

Analysis of the TMS-evoked spectral perturbation showed that the combination of STN-DBS and L-DOPA (ON/ON condition) enhanced α and β TMS-evoked oscillations over central and central-posterior electrodes (**fig. 3**).

FIG.1 GMFP

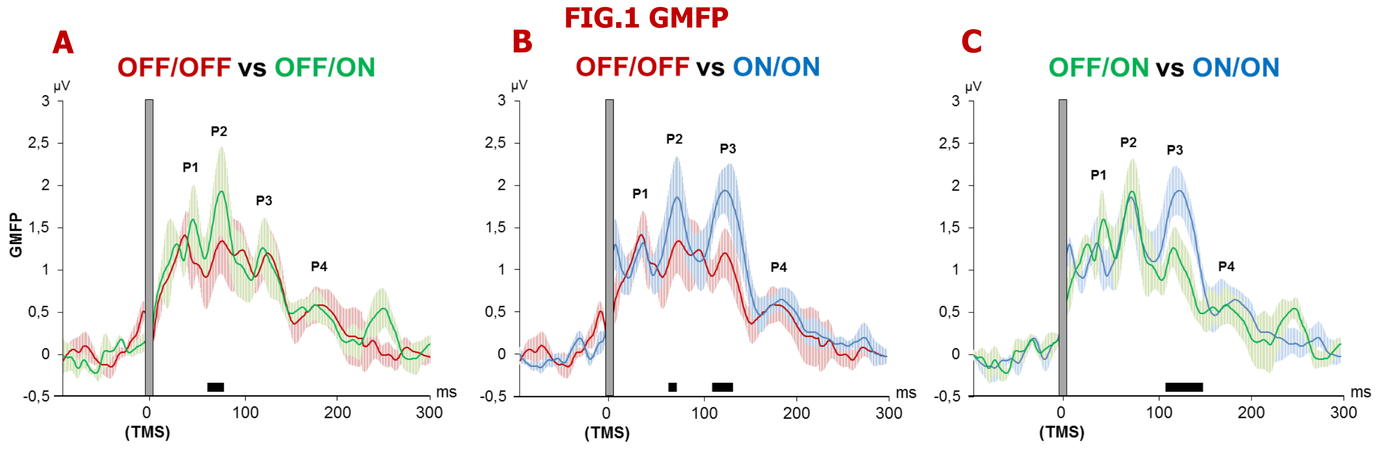


FIG.2 TMS-EVOKED MEAN ACTIVITY

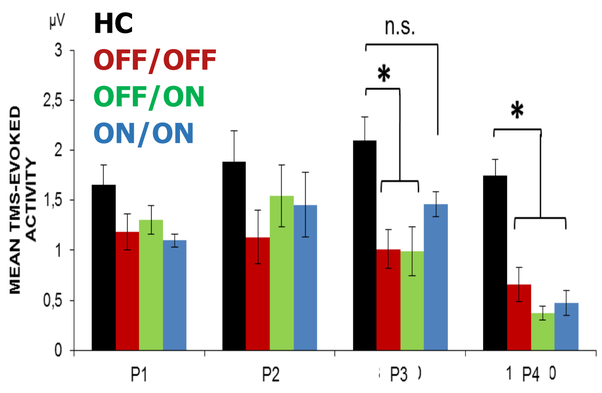
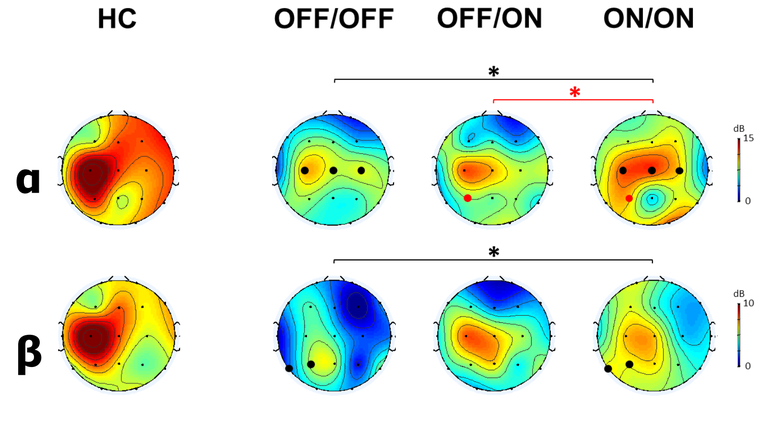


FIG.3 TRSP



Conclusions

The present data show that STN-DBS, either alone or in association with L-DOPA, induces a remarkable modulation of TMS-evoked cortical activity over M1 in specific time intervals. In agreement with previous studies **[1,2]**, when STN-DBS is applied alone it prompts a selective modulation of early TMS-evoked activity, presumably GABAa-mediated **[3]**. The association with L-DOPA results in additional distinct modulation of later TMS-evoked activity, presumably GABAb-mediated **[4]**, whose amplitude was brought to normal range of values (i.e. no difference with HC), and to an enhancement of natural frequencies of M1 (i.e. α and β). These findings demonstrate that the two therapies have synergistic effects on M1 activity.

[1] Cunic et al. (2002) *Neurology.* 58:1665–1672.; **[2]** Däuper et al. (2002) *Neurology.* 59:700–706; **[3]** Premoli et al. (2014) *J of Neurosci.* 34:5603-5612; **[4]** Casula et al. (2014) *Neuroimage*. 98:225-232