

# Supplementary Material

## Impact of Physical Exercise on Levodopa Therapy Across Parkinson's Disease Stages

**Supplementary Table 1.** Impact of the effort on pharmacokinetic parameters in healthy control (HC) subgroup.

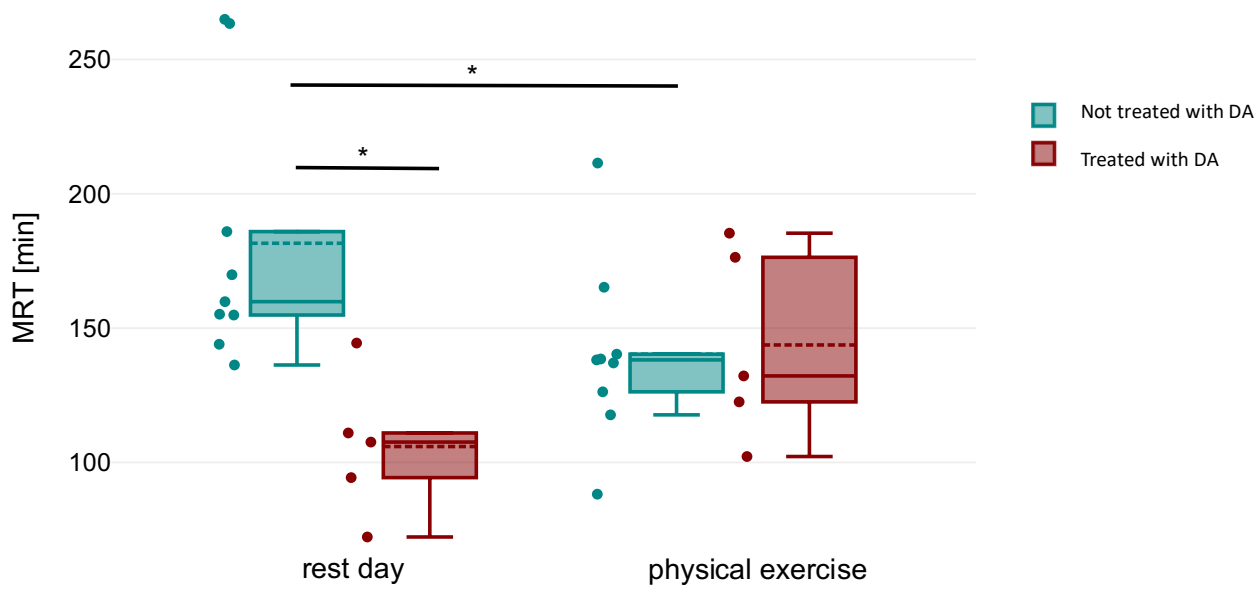
	T-Student test		
	Mean RD (SD)	Mean PE	p
<b>T<sub>max</sub> RD vs. PE [min]</b>	75.7 (29.9)	72.9 (36.8)	0.8
<b>t<sub>1/2</sub> RD vs. PE</b>	59.7 (16.5)	64.4 (22.2)	0.62
<b>C<sub>max</sub> RD vs. PE [µg/ml]</b>	2.5 (1.3)	2.9 (1.4)	0.15
<b>MRT 0-inf RD vs. PE [min]</b>	129.4 (26.3)	132.3 (33.7)	0.78
<b>AUC 0-inf RD vs. PE [mg/ml*min]</b>	0.3 (0.1)	0.32 (0.1)	0.3
<b>V<sub>z</sub> RD vs. PE [l]</b>	69.5 (31.5)	61 (23.7)	0.21
<b>Cl [l/min]</b>	49.5 (22.8)	39.42 (9.1)	0.17

RD, Rest Day; PE, Physical effort day; UPDRS, Unified Parkinson Disease Rating Scale score  
T<sub>max</sub>, Time to peak drug concentration; SD, standard deviation; T<sub>1/2</sub>, half life time; C<sub>max</sub>,  
maximum serum concentration; AUC 0-t, the area under the concentration-time curve from  
dosing (time 0) to time t; MRT 0-t, mean residence time from dosing (time 0) to time t; V<sub>z</sub>/f,  
volume of distribution; Cl/f, clearance; l, liters; min, minutes; mg, miligrams; µg, micrograms;  
ml, milliliters

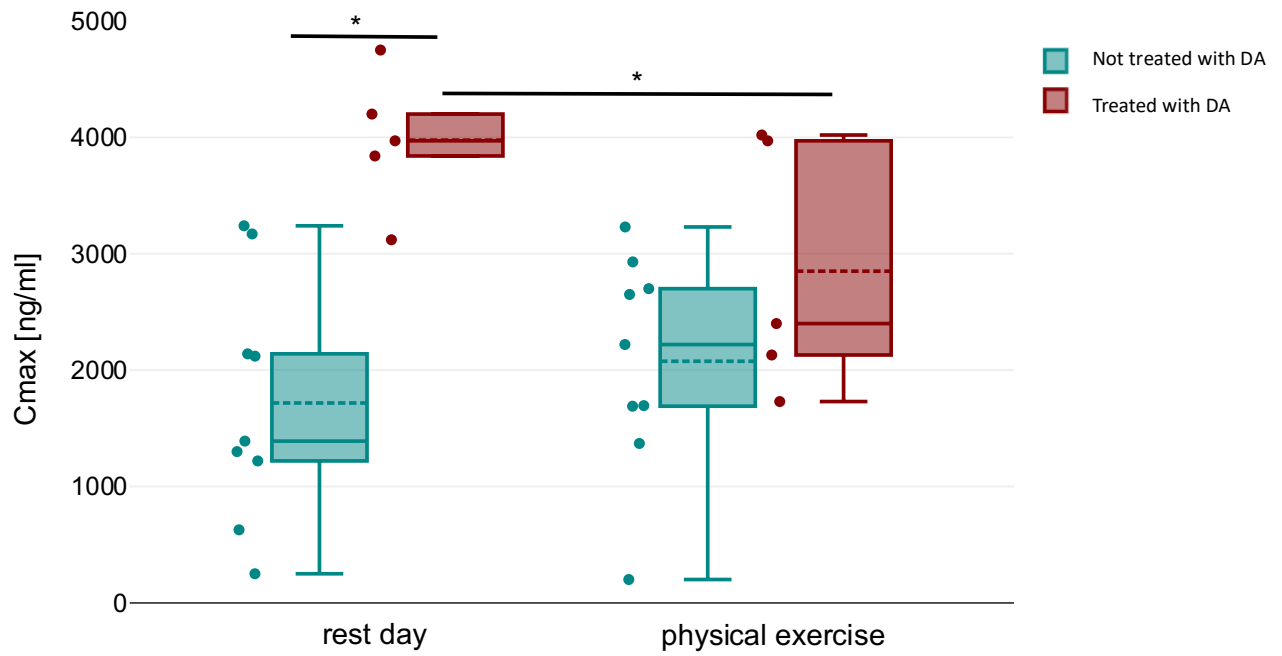
**Supplementary Table 2.** Effect of dopamine agonist (DA) treatment on bioavailability parameters of levodopa in rest and after physical effort

	<b>T-Student test</b>					
	DA-treated group			Group untreated with DA		
	Mean RD (SD)	Mean PE (SD)	p	Mean RD (SD)	Mean PE (SD)	p
<b>T<sub>max</sub> [min]</b>	48 (10.9)	66 (37.2)	0.42	100 (33.5)	85.6 (35.7)	0.35
<b>C<sub>max</sub> [µg/ml]</b>	4 (0.6)	2.8 (1.1)	0.02*	1.7 (1.04)	2.08 (0.9)	0.11
<b>t<sub>1/2</sub> [min]</b>	62.4 (18.9)	69.5 (30.4)	0.7	88.4 (34.6)	63.1 (19.9)	0.06
<b>MRT 0-inf [min]</b>	105.9 (26.4)	143.7 (35.7)	0.15	181.6 (48.9)	140.3 (33.8)	0.02*
<b>AUC 0-inf [mg/ml*min]</b>	0.4 (0.2)	0.4 (0.1)	0.43	0.3 (0.1)	0.3(0.1)	0.74
<b>V<sub>z</sub> RD vs. PE [l]</b>	44.2 (7.6)	54.9 (27.7)	0.35	15 (16.7)	13.1 (20.6)	0.41
<b>Cl RD vs. PE [l/min]</b>	32 (12.4)	32.2 (5)	0.96	<i>38.9 (34.6-61.5)</i>	<i>41.8 (34.6-59.1)</i>	0.77

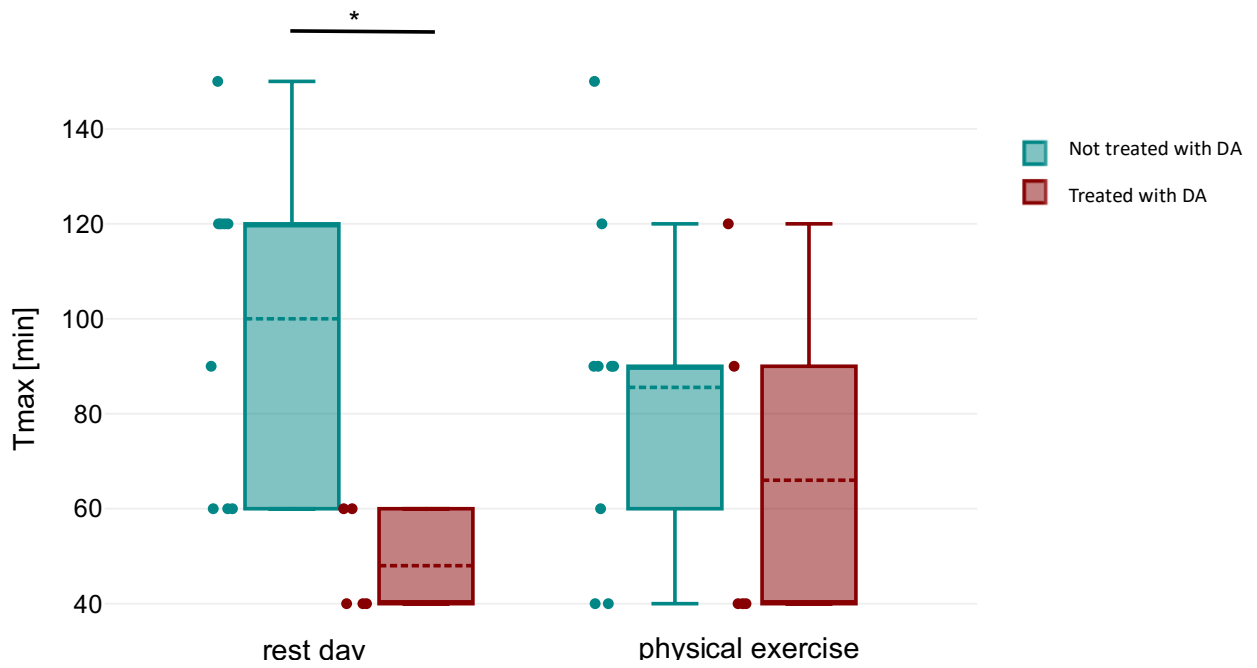
RD, Rest Day; PE, Physical effort day; UPDRS, Unified Parkinson Disease Rating Scale score; T<sub>max</sub>, Time to peak drug concentration; T<sub>1/2</sub>, half life time; C<sub>max</sub>, maximum serum concentration; AUC 0-inf, the area under the concentration-time curve from dosing (time 0) to infinity; MRT 0-inf, mean residence time from dosing (time 0) to infinity; V<sub>z</sub>, volume of distribution; Cl, clearance. Significant differences are marked with\*. *Italics*, non parametric values, presented as median and interquartile range; l, liters; min, minutes; mg, miligrams; µg, micrograms; ml, milliliters



**Supplementary Figure 1.** Mean Residence Time (MRT) of levodopa during rest day and physical exercise day compared between patients treated with dopamine agonist (DA) - red, and untreated with DA - blue. Lines with \* indicate significant differences between the groups.  $p < 0.05$  was considered statistically significant. min, minutes.



**Supplementary Figure 2.** Maximum serum concentration (Cmax) of levodopa during rest day and physical exercise day compared between patients treated with dopamine agonist (DA) - red, and untreated with DA - blue. Lines with \* indicate significant differences between the groups.  $p < 0.05$  was considered statistically significant. ng, nanograms; ml, milliliters



**Supplementary Figure 3.** Time to peak drug concentration ( $T_{max}$ ) of levodopa during rest day and physical exercise day compared between patients treated with dopamine agonist (DA) - red, and untreated with DA - blue. Lines with \*indicate significant differences between the groups.  $p < 0.05$  was considered statistically significant. Min, minutes.