Premature Ovarian Insufficiency as a Potential Risk Factor for Parkinson's Disease in Young Women

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Aims:

Recent research has identified mitochondrial dysfunction and inflammaging as common pathogenic mechanisms underlying both Diminished Ovarian Reserve (DOR) and Parkinson's Disease (PD)[1,2]. Building on the hypothesis that premature ovarian aging promotes the senescence of dopaminergic neurons, the objective of this study is to identify an increased risk of developing PD in DOR patients.

Materials and methods:

This was a clinical-diagnostic cohort study that enrolled 30 women with DOR (DOR group) and 30 controls (CNTRL group), between November 2022 and January 2025 at the Infertility Center, "Federico II" Polyclinic, Naples.

Both groups underwent hematochemical analysis, transvaginal ultrasound, neurological examination, and neurodegenerative screening, including: REM Behavior Disorder Screening Questionnaire (RBDSQ); Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Motor Section; Scales for Outcomes in Parkinson's Disease – Autonomic Dysfunction (SCOPA-AUT); Montreal Cognitive Assessment (MoCA), and Smell Identification Test (UPSIT).

		N	Mean	Std. Deviation	Std. Error Mean
MoCA	CNTRL	30	25,30	2,71	0,49
	DOR	30	24,50	2,64	0,48
RBDSQ	CNTRL	30	2,97	1,96	0,36
	DOR	30	4,10	1,83	0,33
SCOPA-AUT	CNTRL	30	11,93	7,32	1,34
	DOR	30	11,60	7,55	1,38
UPDRS	CNTRL	30	0,87	1,33	0,24
	DOR	30	4,47	5,99	1,09
SMELL TEST	CNTRL	30	31,80	2,59	0,47
	DOR	30	30,90	3,04	0,56

Tab. 1 - Descriptive analysis of the DOR and CNTRL populations concerning the results of neurological screening tests used in this study.

		Standardizer[a]	Point Estimate
RBDSQ	Cohen's d	1,892	-0,599
	Hedges' correction	1,917	-0,591
	Glass's delta	1,826	-0,621
UPDRS	Cohen's d	4,337	-0,830
	Hedges' correction	4,394	-0,819
	Glass's delta	5,987	-0,601

Tab. 2 - Independent samples effect sizes indicated a large and medium effect size respectively for the between-group difference in UPDRS and RBDQ.

Results:

MDS-UPDRS and RBDSQ showed higher mean values in the DOR group compared to the CNTRL group (Tab. 1, Tab. 2). A predictive score was established ("Score-Park") that considers the level of impairment detected by the UPDRS and RBDSQ, which graphic distribution shows no overlap in the 95% confidence intervals between the two cohorts (Fig. 1). The results of the regression analysis suggest that there is a statistically significant - although moderate (standardized coefficient Beta = -0.402) - inverse relationship between AFC and UPDRS: as AFC values increase, a tendency towards a decrease in UPDRS scores. The resulting model explains a statistically significant portion of the variance in UPDRS, with a coefficient of determination (R^2) of 0.162 (Adjusted R^2 = 0.146; Tab. 3).

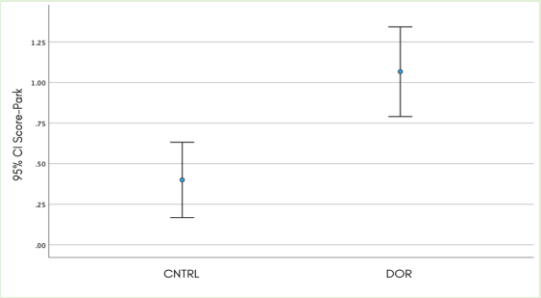

Fig. 1 - predictive score, conventionally termed "Score-Park", that considers the level of impairment detected by the UPDRS and RBDSQ.

Model		Unstandardized Coefficients B	Unstandardized Coefficients Std. Error	Standardized Coefficients Beta	t	Sig.
1	(Constant)	5,504	1,048		5,250	0,000
	AFC	-0,196	0,061	-0,402	-3,226	0,002

a. Dependent Variable: UPDRS

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	,402[a]	0,162	0,146	4,436

a. Predictors: (Constant), AFC

Tab. 3 - The negative sign of the coefficient indicates an inverse relationship between AFC and UPDRS.

Conclusions:

These data confirm that patients in the DOR group have more extrapyramidal signs and REM sleep disorders, often prodromal of Parkinson's Disease. The "Score-Park" indicates a greater risk of developing extrapyramidal diseases in the DOR population compared to the CNTRL group. A statistically significant and moderate inverse relationship was found between AFC (Antral Follicular Count, reduced in the DOR population) and the UPDRS scale, suggesting a higher burden of extrapyramidal motor symptoms in patients with a reduced antral follicular count. Further research with larger samples and longitudinal studies is necessary to clarify the nature and potential clinical relevance of this relationship.

1. Walter A Rocca, Carin Y Smith, Liliana Gazzuola Rocca, Rodolfo Savica, Michelle M Mielke (2022). Association of Premenopausal Bilateral Oophorectomy With Parkinsonism and Parkinson Disease. doi: 10.1001/jamanetworkopen.2022.38663
2. Huang Y, Hu C, Ye H,Luo R, Fu X, Li x; Huang J, Chen W, Zheng Y Inflamm-aging: a new mechanism affecting premature ovarian insufficiency Journal of immunology Research 2019;8069898