Increased cerebrospinal fluid lactate levels in Parkison's Disease: is it a proof of mitochondrial inefficiency?

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OBJECTIVE

Human and animal models studies revealed that in Parkinson's Disease (PD) mitochondrial dysfunction might be a defect that occurs early in its pathogenesis. Moreover, mitochondrial inefficiency may appear to be a widespread feature in both sporadic and monogenic forms of PD. Cerebrospinal-fluid (CSF) lactate levels may represent a valid biomarker to measure in vivo cerebral mitochondrial function and glucose metabolism. On these basis, the aim of the present study is to evaluate in PD patients CSF lactate levels, and to correlate its concentrations to other CSF biomarkers (tau proteins and beta-amyloid). Furthermore, we also investigate whether CSF lactate levels correlate with motor impairment, disease duration and/or clinical phenotype.

METHODS

We enrolled a population of non-demented PD patients who underwent neurological examination and CSF biomarkers analysis for the assessment of lactate, tau proteins and beta-amyloid levels. We also evaluate CSF biomarkers differences dividing PD patients in subgroups on the basis of the disease motor impairment. Moreover, correlation between CSF biomarkers were investigated. Finally, PD patients were compared to a population of healthy controls.

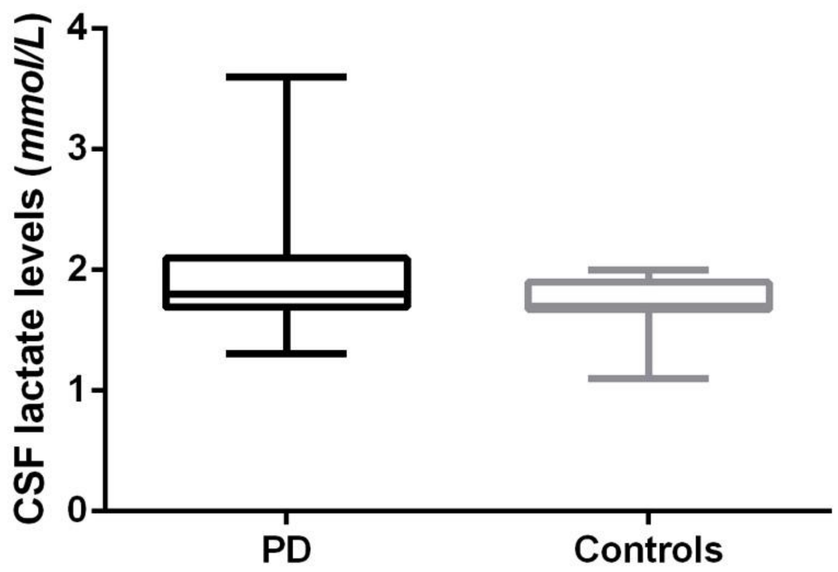
RESULTS

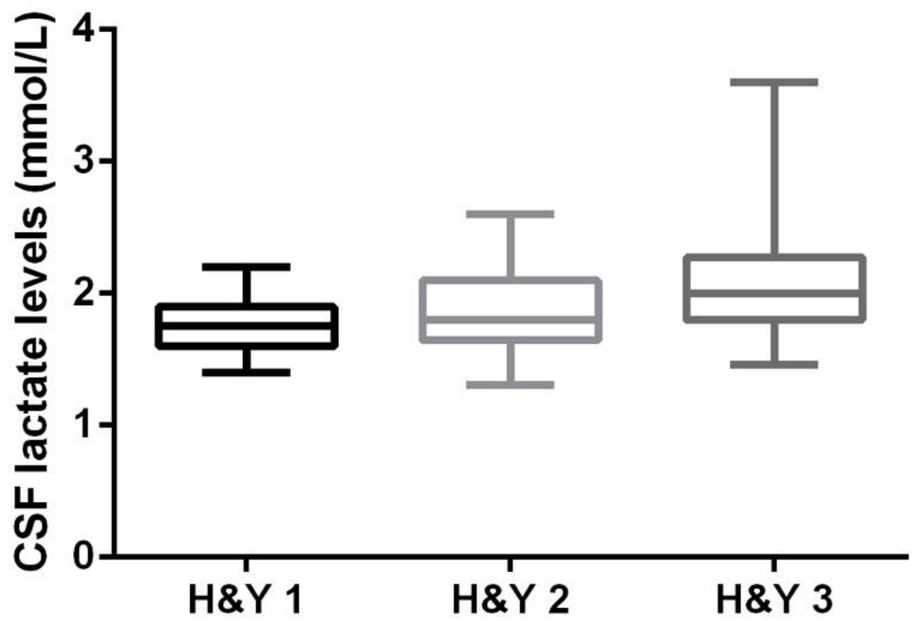
CSF Data	PD patients (n=91)	Controls (n=60)	P VALUE
Glucose	63.60±10.05	61.06±7.21	NS
Lactate	***1.91±0.37***	1.72±0.19	<0.05
Proteins	55.23±23.35	37.99±9.15	<0.01
Albumin	34.72±19.63	20.62±6.79	<0.001
BBB	7.95±4.10	4.98±1.81	NS
IgG	3.95±2.29	2.45±0.94	NS
T-tau	238.39±213.32	204.92±94.14	NS
P-tau	38.70±20.76	41.48±14.44	NS
$A\beta_{42}$	***594.57±286.45***	836.51±232.71	<0.0001

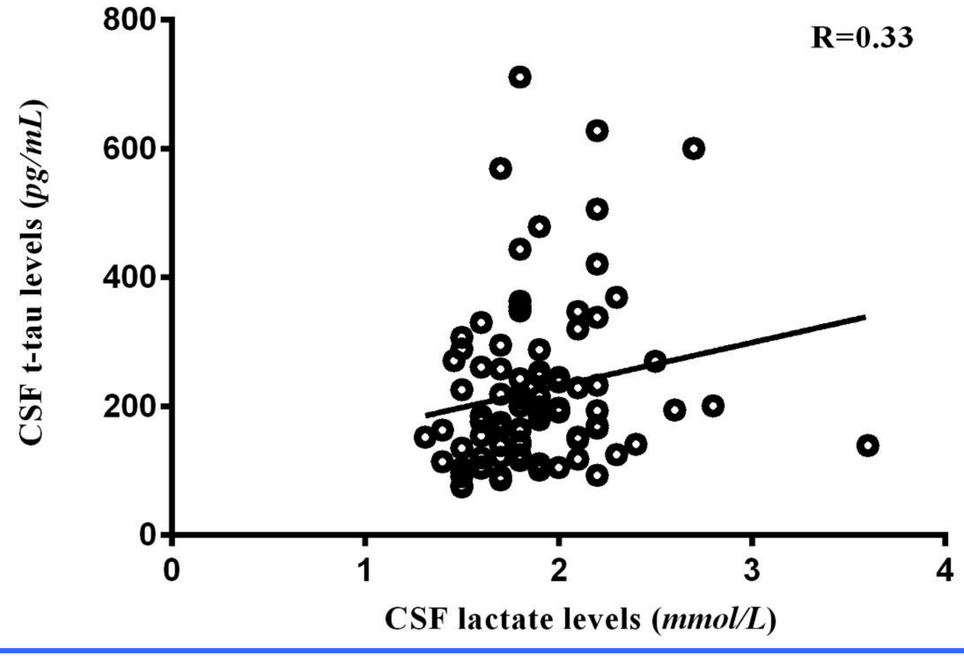
Demographic and Clinical Data	PD Patients (n=91)	Controls (n=60)	P VALUE
Age	63.96±9.88	68.06±7.63	NS
Sex	35 F 56 M	23 F 37 M	NS
UPDRS	23.83±12.63	*NA*	NA
MMSE	26.83±2.66	28.88±0.95	NS

Clinical Data	H&Y 1 (n=32)	H&Y 2 (n=41)	H&Y 3 (n=18)
Glucose	60.40±7.46	65.07±12.25	65.94±7.10
Lactate	1.75±0.19	***1.91±0.40****	***2.12±0.50***$^{+,\circ}$
Proteins	51.19±19.86	57.01±20.57	57.96±35.48
Albumin	31.13±16.84	37.00±18.20	35.73±27.65
BBB	7.42±3.74	8.21±3.56	8.33±6.16
T-tau	176.06±69.68	***245.39±248.25****	***333.27±264.70***$^{+,\circ}$
P-tau	34.96±13.57	40±25.75	41.27±18.98
$A\beta_{42}$	610.78±229.85	624.05±315.73	497.44±310.94

$^{+}$ H&Y3 vs H&Y1, p<0.01, * H&Y2 vs H&Y1, p<0.05, ° H&Y3 vs H&Y2, p<0.05







CONCLUSIONS

In this study, we verified in PD patients the occurrence of mitochondria impairment, as documented by the finding that PD patients show high CSF lactate levels. Moreover, since we found that CSF lactate levels increased from the mild to the advanced stages of the disease, we hypothesize that mitochondrial dysfunction may be deteriorate in PD patients. Finally, the correlation between CSF lactate and tau proteins levels may suggest that tau-mediated neurodegeneration may concur in mitochondria impairment.

On this basis, we propose the clinical potential of assessing CSF lactate levels in PD patients to better define the neuronal brain metabolism damage and mitochondrial inefficiency.