



Università degli Studi di Salerno
Dipartimento di Medicina, Chirurgia ed
Odontoiatria «Scuola Medica Salernitana»
Scuola di Specializzazione in Neurologia



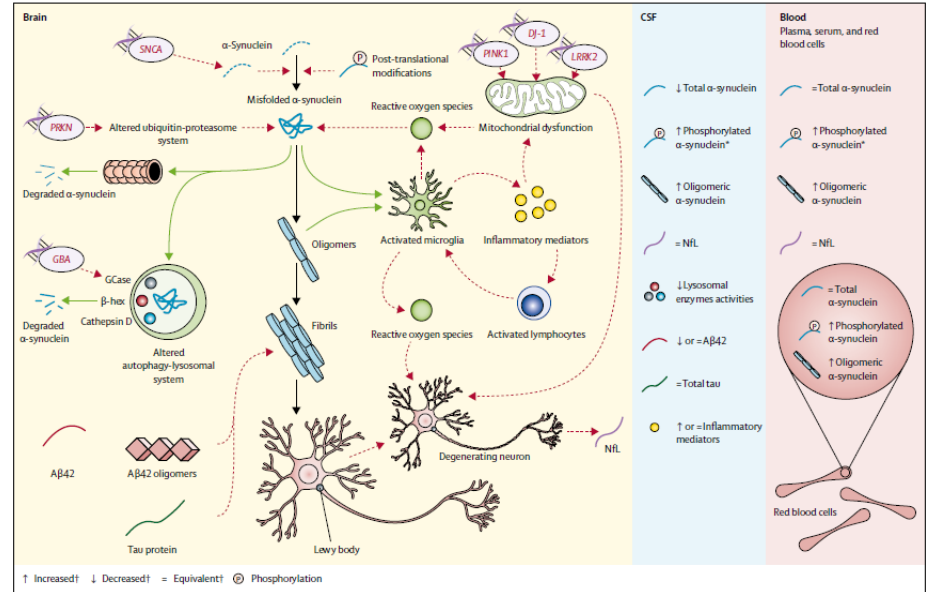
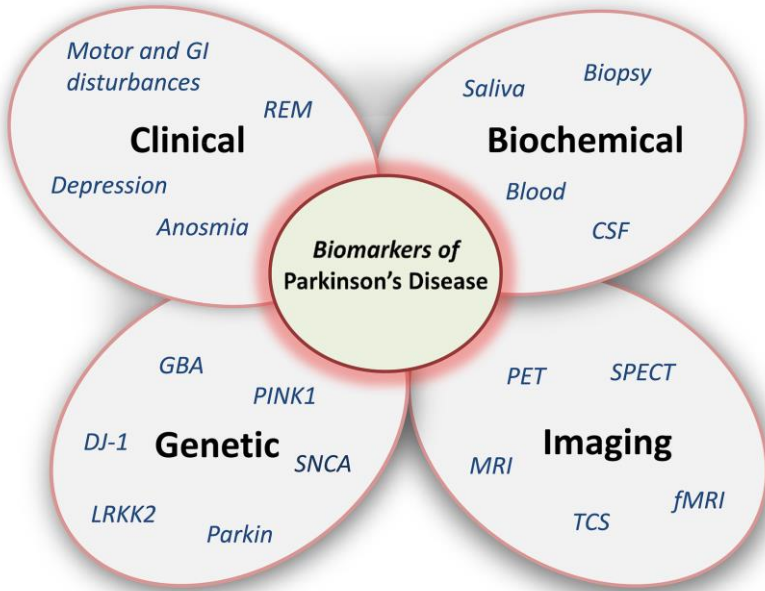
La metabolomica nei parkinsonismi

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Paolo Barone, Marianna Amboni



Regionale SIN Campania
Napoli, 13 dicembre 2019

Biomarkers in Degenerative Parkinsonisms



Parnetti et al.2019

Delenclos et al 2015

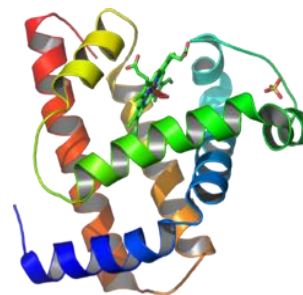
Genomics



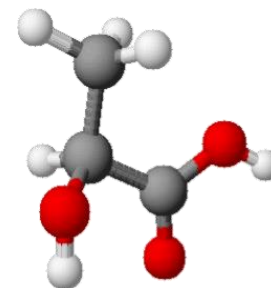
Trascrittomics



Proteomics



Metabolomics



~25.000
GENES

~400.000
TRANSCRIPTS

~1.000.000
PROTEINS

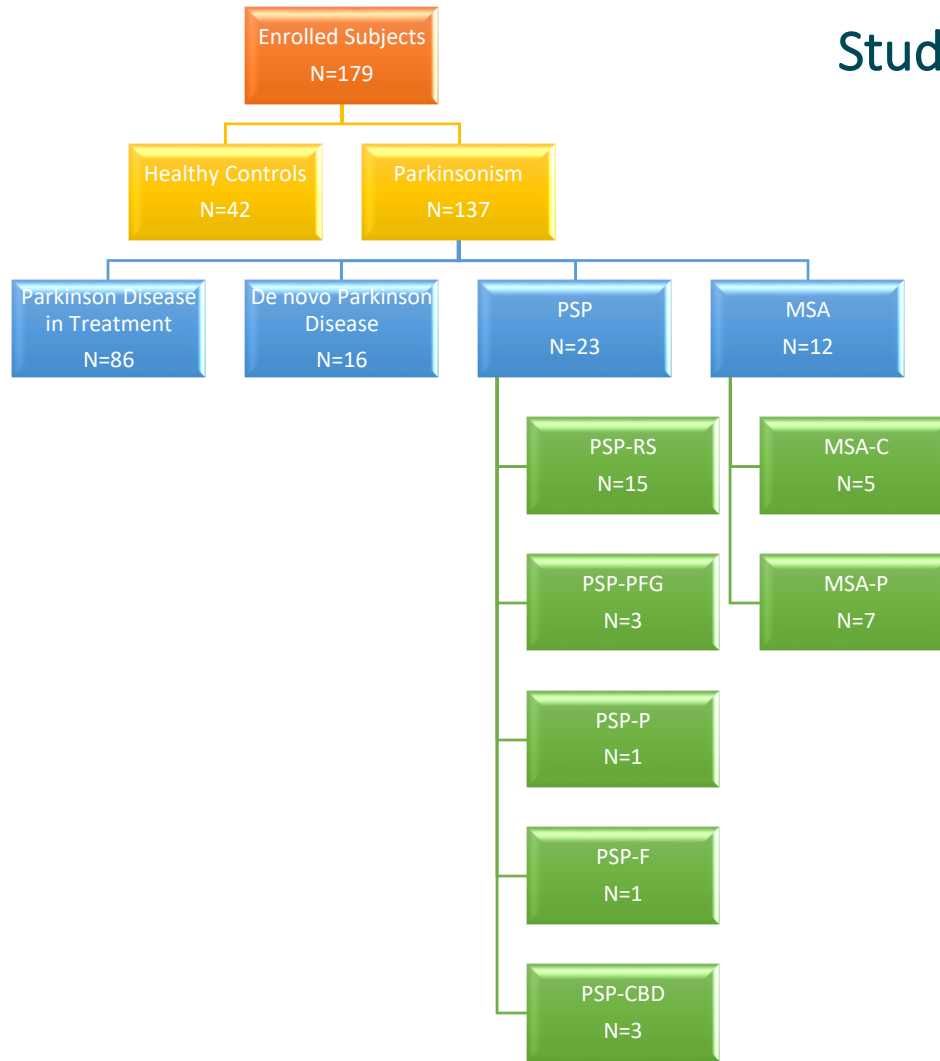
~2500
METABOLITES

ENVIRONMENT

What can be

What is being

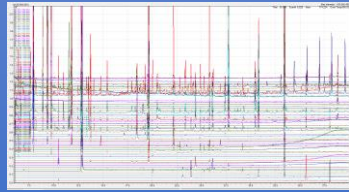
Study design-Samples collection



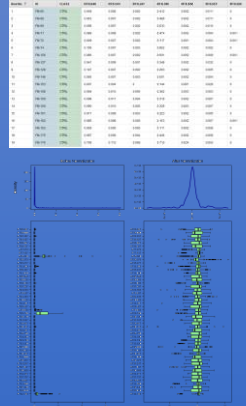
Method Development



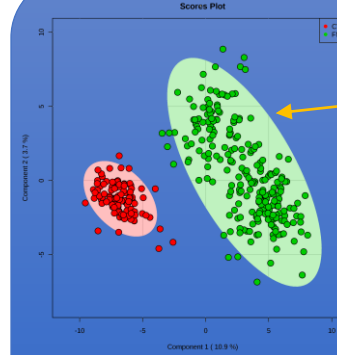
1. Entire blood collection



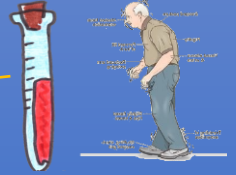
2. Metabolome extraction, purification and analysis



3. Dataset building and data pre-treatment



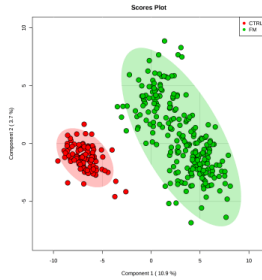
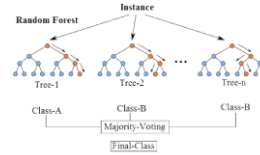
4. Classification models training and ensemble



Diagnostic hypothesis

5. Model testing by means of independent data collection

Ensemble machine learning

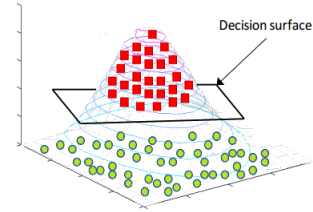


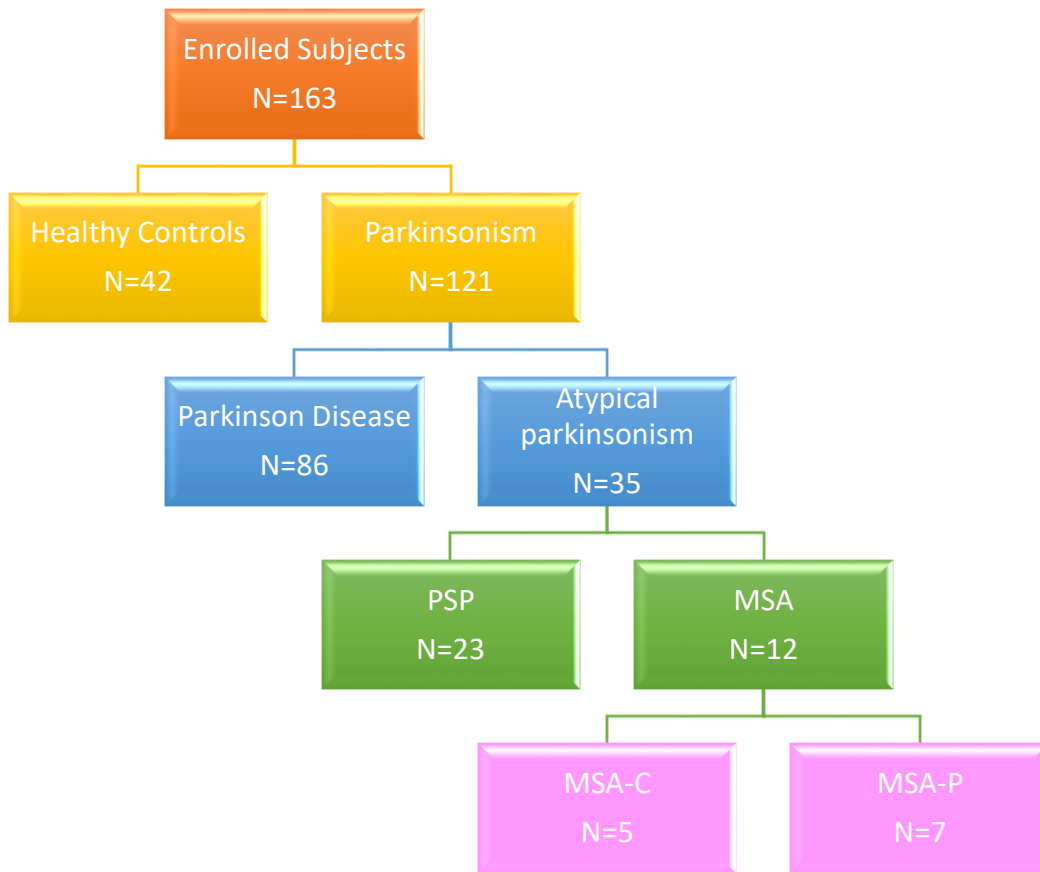
Partial Least
Square
Discriminant
Analysis

Random
Forest

Support
Vector
Machine

Ensemble
Machine
Learning





EML - 1

EML - 2

EML - 3

EML - 4

Model Accuracy	Global accuracy
93,2±5,8%	93,2%
98,6±0,0%	91.8%
83,0±4,0%	76,1%
78,6±17,3%	59.1%

EML - 2

Parameter	Value $\pm$ SE
Sensitivity	0.98 ± 0.02
Specificity	1.00 ± 0.00
Positive Likelihood ratio	ND
Negative Likelihood ratio	0.02
Negative predictive value	0.96 ± 0.03
Positive predictive value	1.00 ± 0.00
Accuracy	0.986 ± 0.000

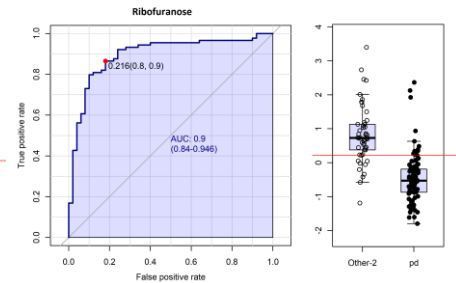
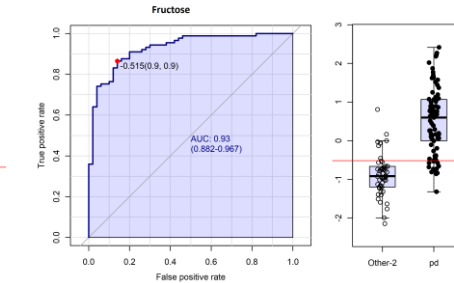
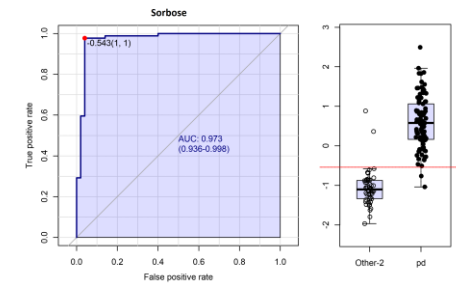
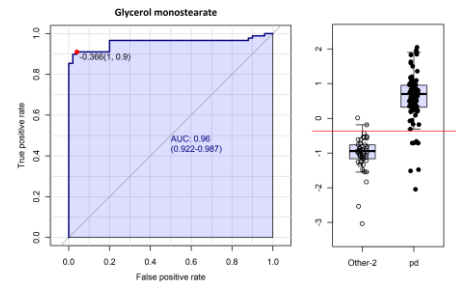
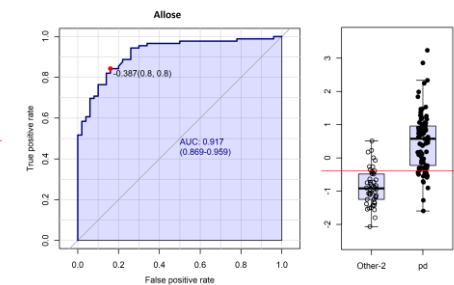
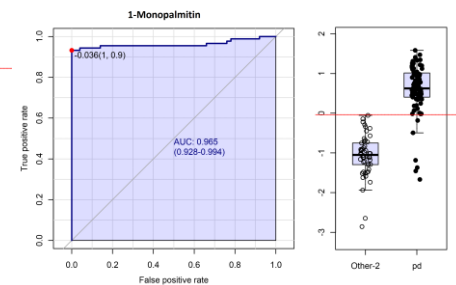
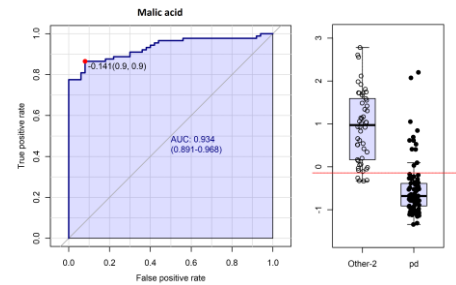
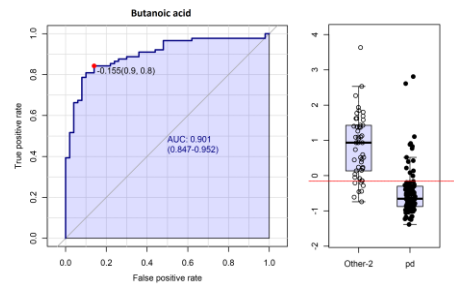
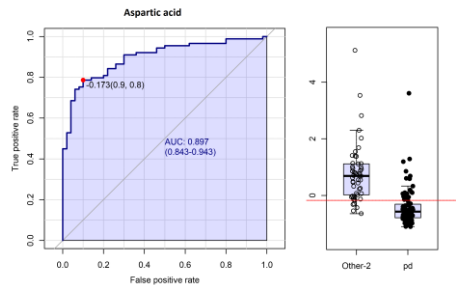
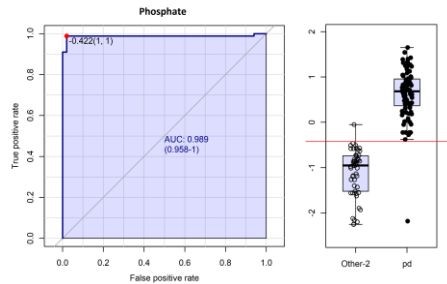
EML - 3

Parameter	Value $\pm$ SE
Sensitivity	0.78 ± 0.07
Specificity	0.94 ± 0.06
Positive Likelihood ratio	12.54
Negative Likelihood ratio	0.23
Negative predictive value	0.65 ± 0.10
Positive predictive value	0.97 ± 0.03
Accuracy	0.830 ± 0.04

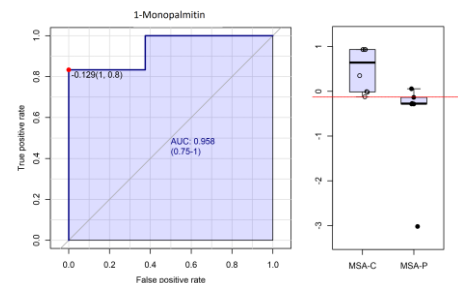
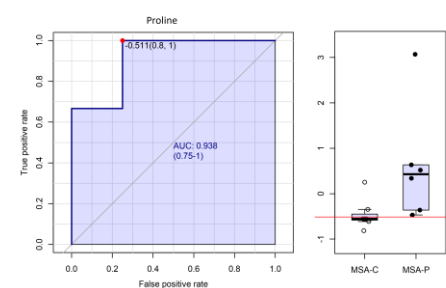
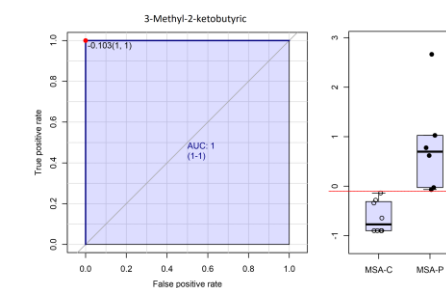
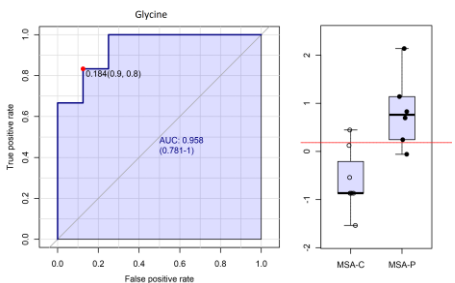
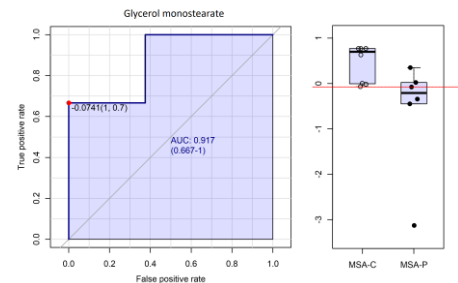
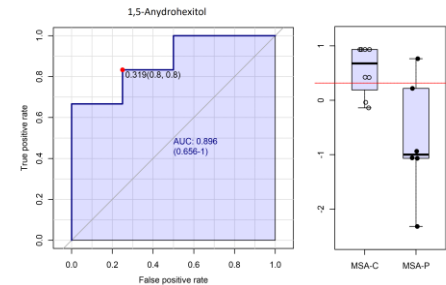
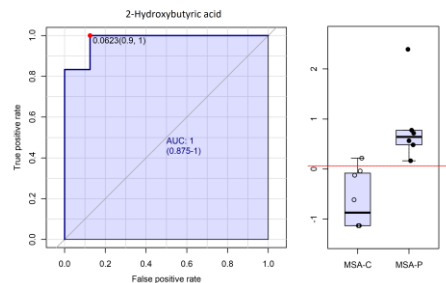
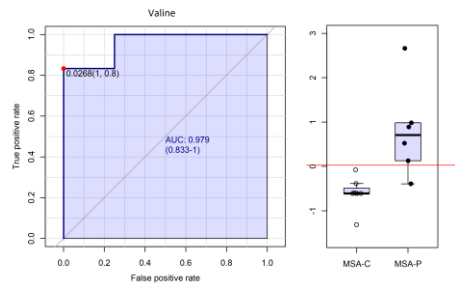
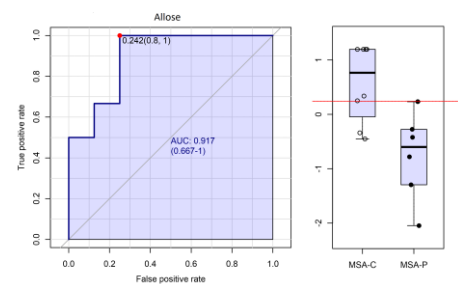
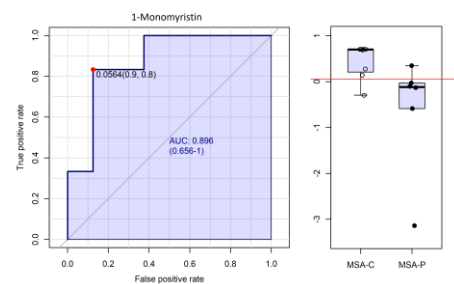
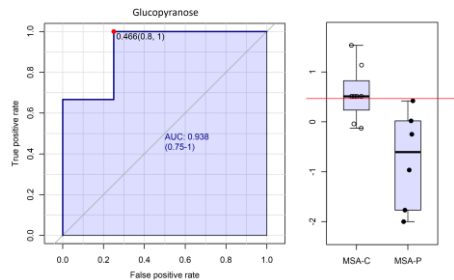
EML - 4

Parameter	Value $\pm$ SE
Sensitivity	0.83 ± 0.15
Specificity	0.75 ± 0.15
Positive Likelihood ratio	3.33
Negative Likelihood ratio	0.22
Negative predictive value	0.86 ± 0.13
Positive predictive value	0.71 ± 0.17
Accuracy	0.786 ± 0.173

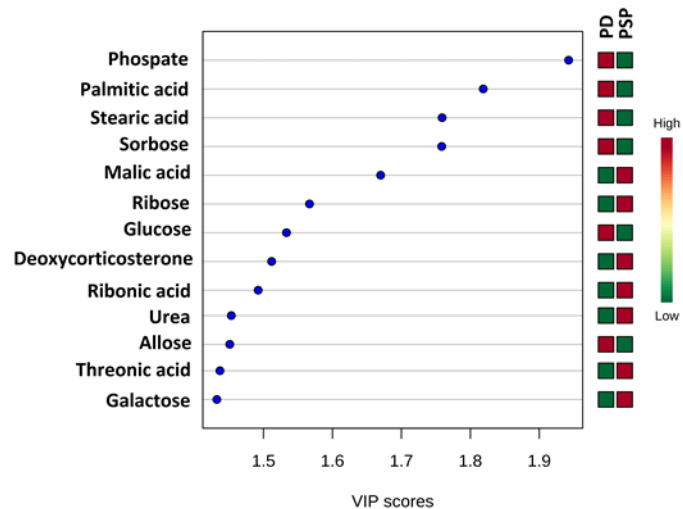
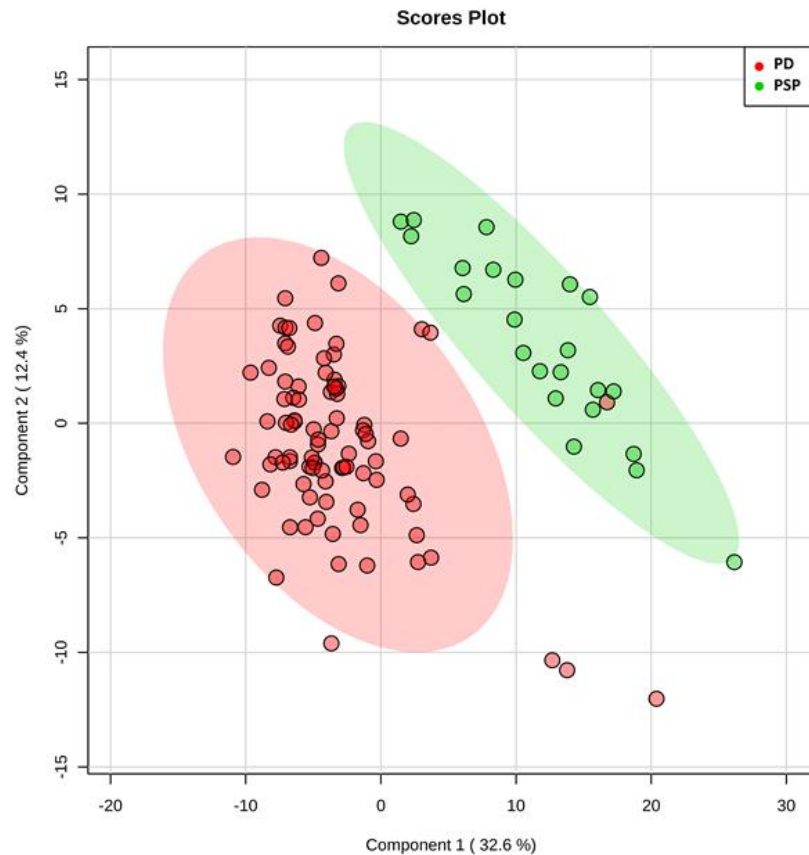
EML - 2



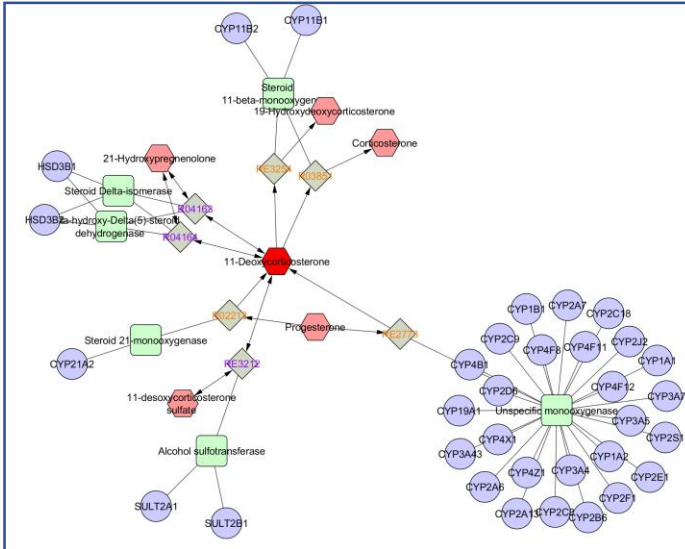
EML - 4



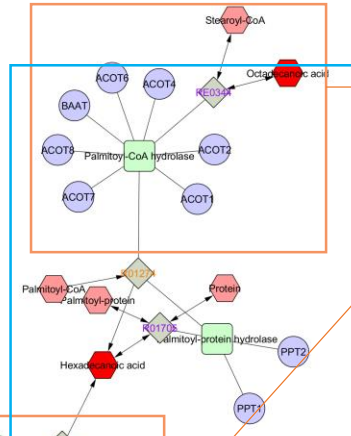
Separation between PD and PSP patients



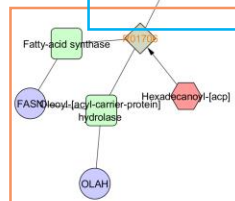
C21-steroid hormone biosynthesis and metabolism



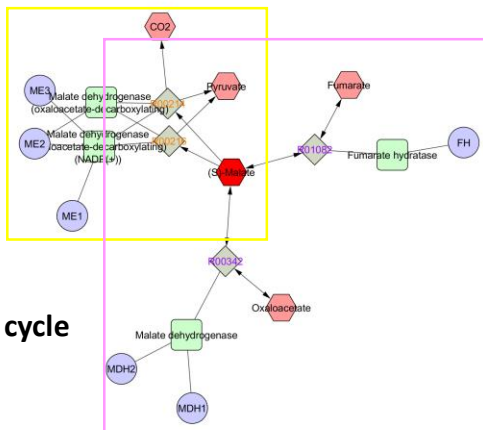
De novo fatty acid biosynthesis



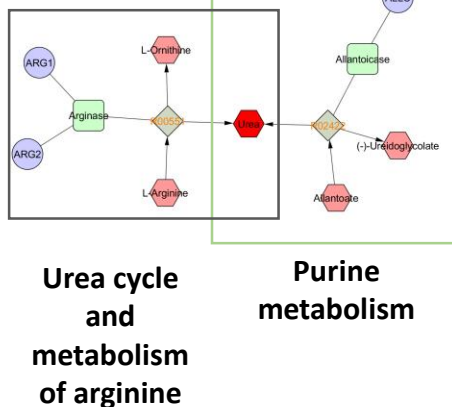
Saturated fatty acids beta oxidation



Glycolysis and gluconeogenesis

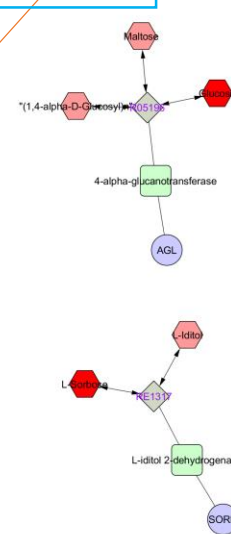


TCA cycle

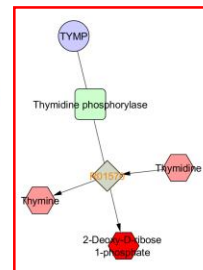


Urea cycle and metabolism of arginine

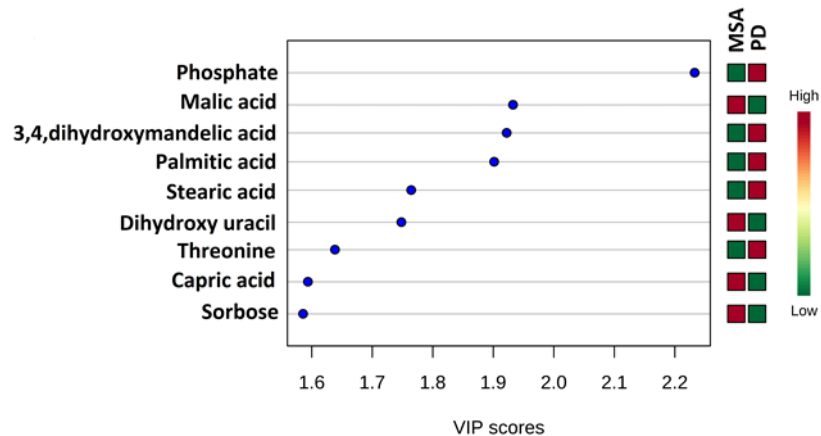
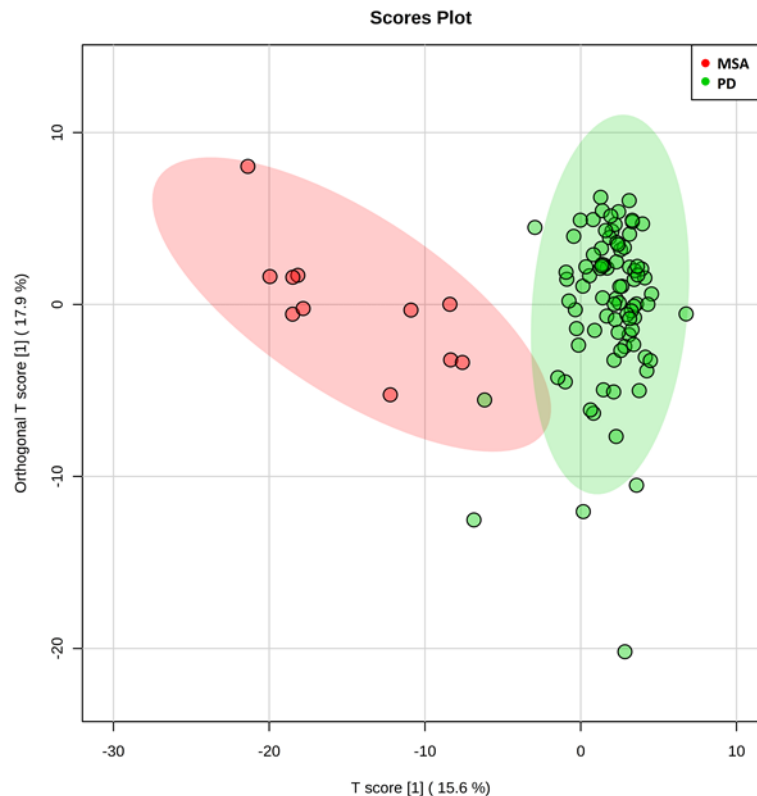
Purine metabolism



Pyrimidine metabolism



Separation between PD and MSA patients



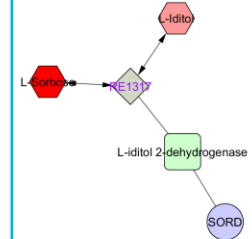
Saturated fatty acids beta-oxidation

[illegible][illegible]

The diagram illustrates the TCA cycle and its connections to other metabolic pathways. The TCA cycle is highlighted in a pink box, showing intermediates like Malate, Oxaloacetate, Pyruvate, and CO2. Other pathways include gluconeogenesis (MDH1, MDH2, Malate dehydrogenase), glyoxylate shunt (ME1, ME2, ME3, Fumarate hydratase), and glycolysis/gluconeogenesis (K01083, K00124).

Tyrosine metabolism

The diagram illustrates a metabolic pathway. At the top left, a purple circle labeled "DPYD" is connected by a grey arrow to a green hexagon labeled "Dihydropyrimidine dehydrogenase (NADP(+))". From this enzyme, a grey arrow points to a purple diamond labeled "K00009". From "K00009", a grey arrow points to a red hexagon labeled "Uracil". Another grey arrow points from "K00009" to a red hexagon labeled "5,6-Dihydrouracil". From "5,6-Dihydrouracil", a grey arrow points to a purple diamond labeled "K02209". From "K02209", a grey arrow points to a red hexagon labeled "3-Ureidopropionate". A grey arrow also points from "K02209" to a green hexagon labeled "Dihydropyrimidine", which is then connected by a grey arrow to a purple circle labeled "DPYS" at the bottom left.

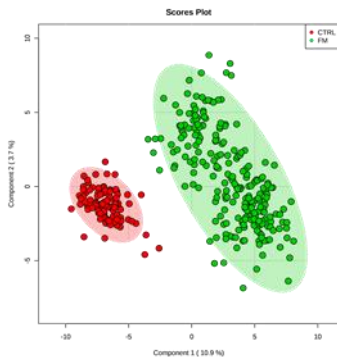
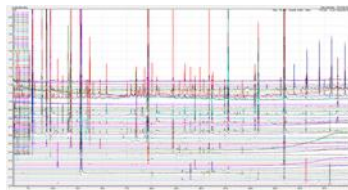


Conclusions

Metabolomics can be an useful tool to train a decisional algorithm

This decisional algorithm can support the clinical diagnoses of neurodegenerative parkinsonisms

Final diagnosis cannot prescind clinical evaluation and follow up





Thank you