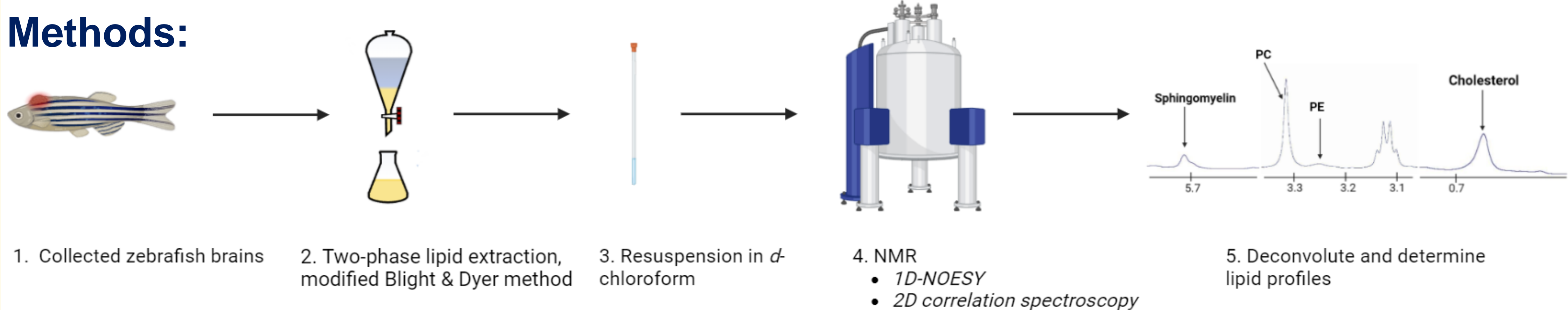


Investigating the lipidome of Parkinson-induced zebrafish brain using NMR and neural network signal deconvolution

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Introduction: Parkinson's disease is a neurodegenerative brain disorder and is characterized by the depletion of dopaminergic neurons in parts of the brain¹. The brain consists of approximately 50% lipids by dry weight. Autosomal, recessive point mutations and deletions in the human DJ-1 gene cause a form of familial Parkinson's disease and are also linked to inflammation, mitochondrial dysfunction, oxidative stress, and altered lipid metabolism². This project aimed to analyze lipid profiles by using NMR in combination with machine learning to deconvolute complex spectra. The lipids were extracted from both wild-type (WT) zebrafish, and from zebrafish where the DJ-/PARK71 gene is deactivated (KO) by using a modified Blight & Dyer method. Zebrafish are used in this experiment due to their high similarity to mammals in molecular mechanisms of development and cellular physiology³.

Methods:



Higher cholesterol in KO than WT

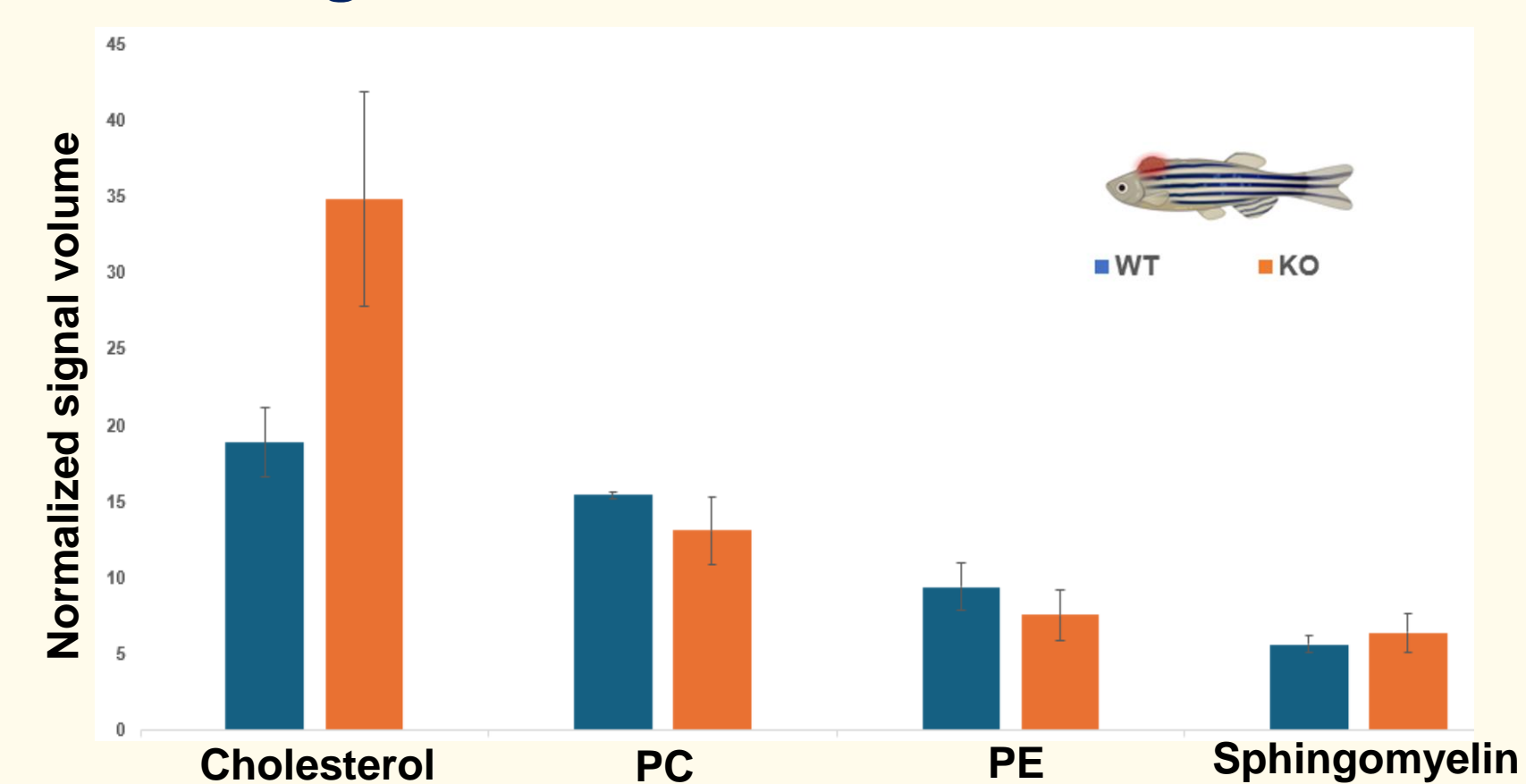


Figure 1: Average signal volume from three WT ZF and three KO ZF of cholesterol, PC (phosphatidylcholines), PE (phosphatidylethanolamine), and sphingomyelin. Error bars represent one standard deviation.

Higher cholesterol in patient than control

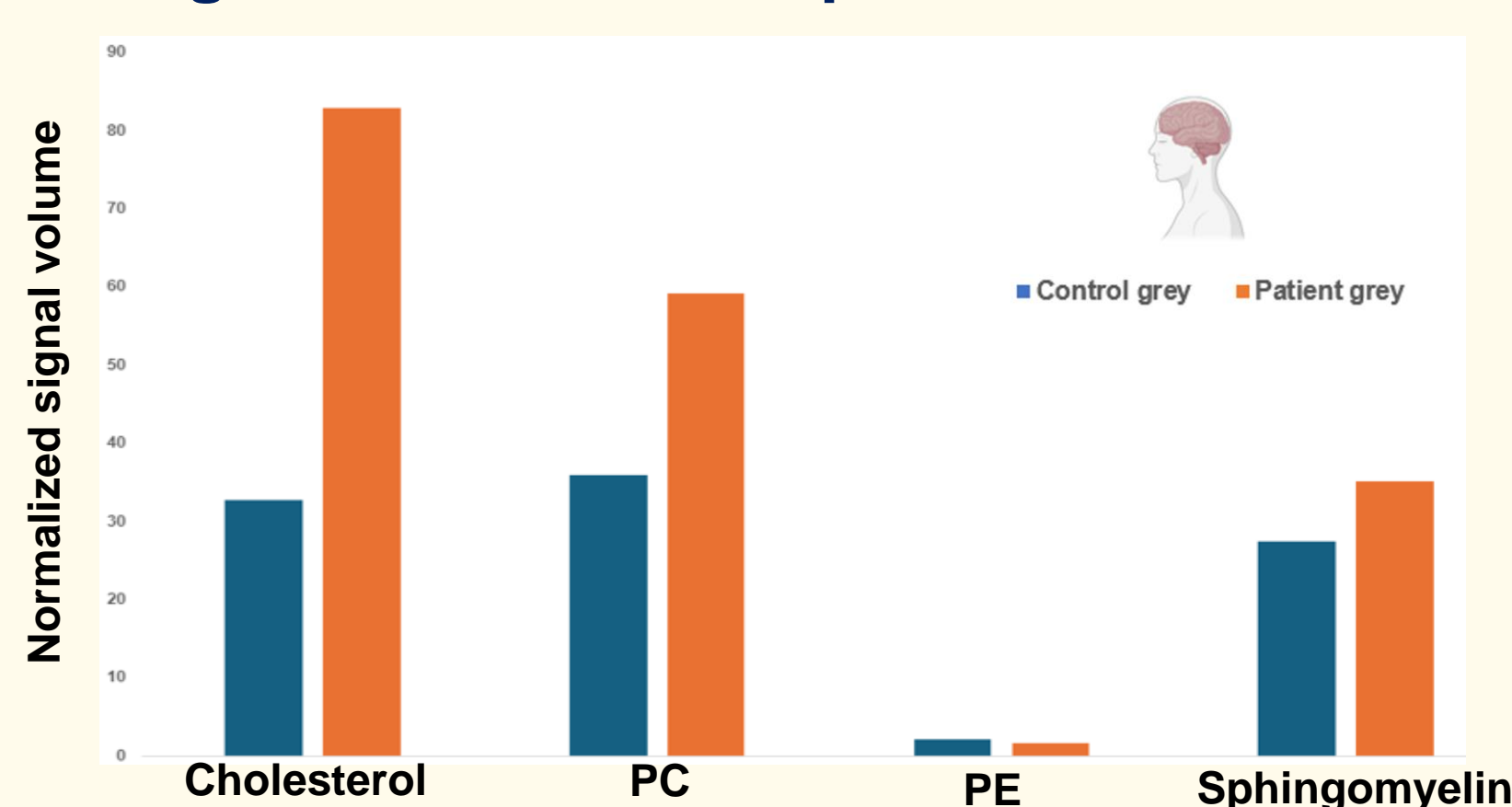


Figure 2: Signal volume from human grey matter of one control and grey matter of one patient of cholesterol, PC (phosphatidylcholines), PE (phosphatidylethanolamine), and sphingomyelin.

Scores plot

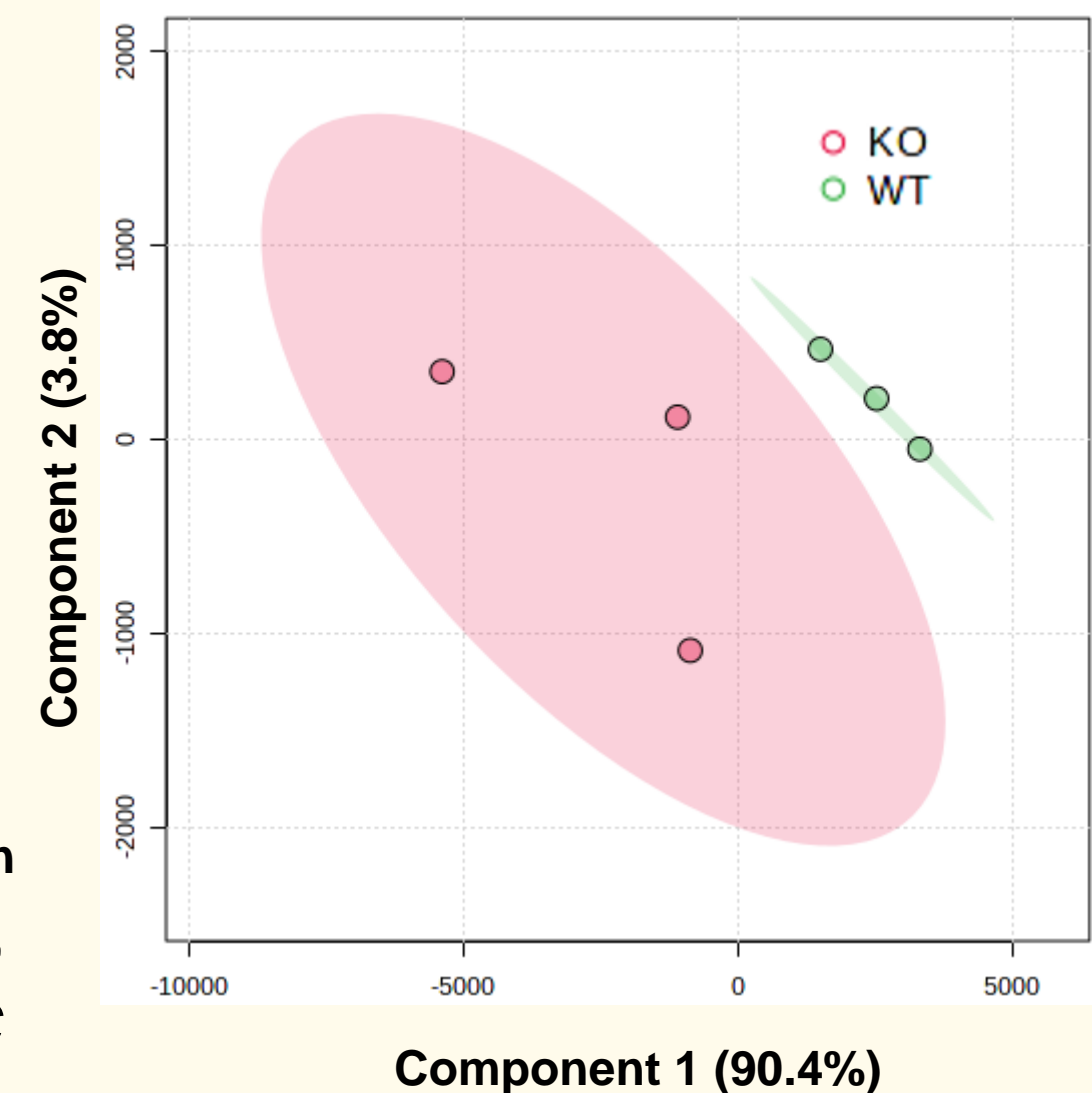


Figure 3: PLS-DA score plot

Volcano plot: cholesterol is above the threshold

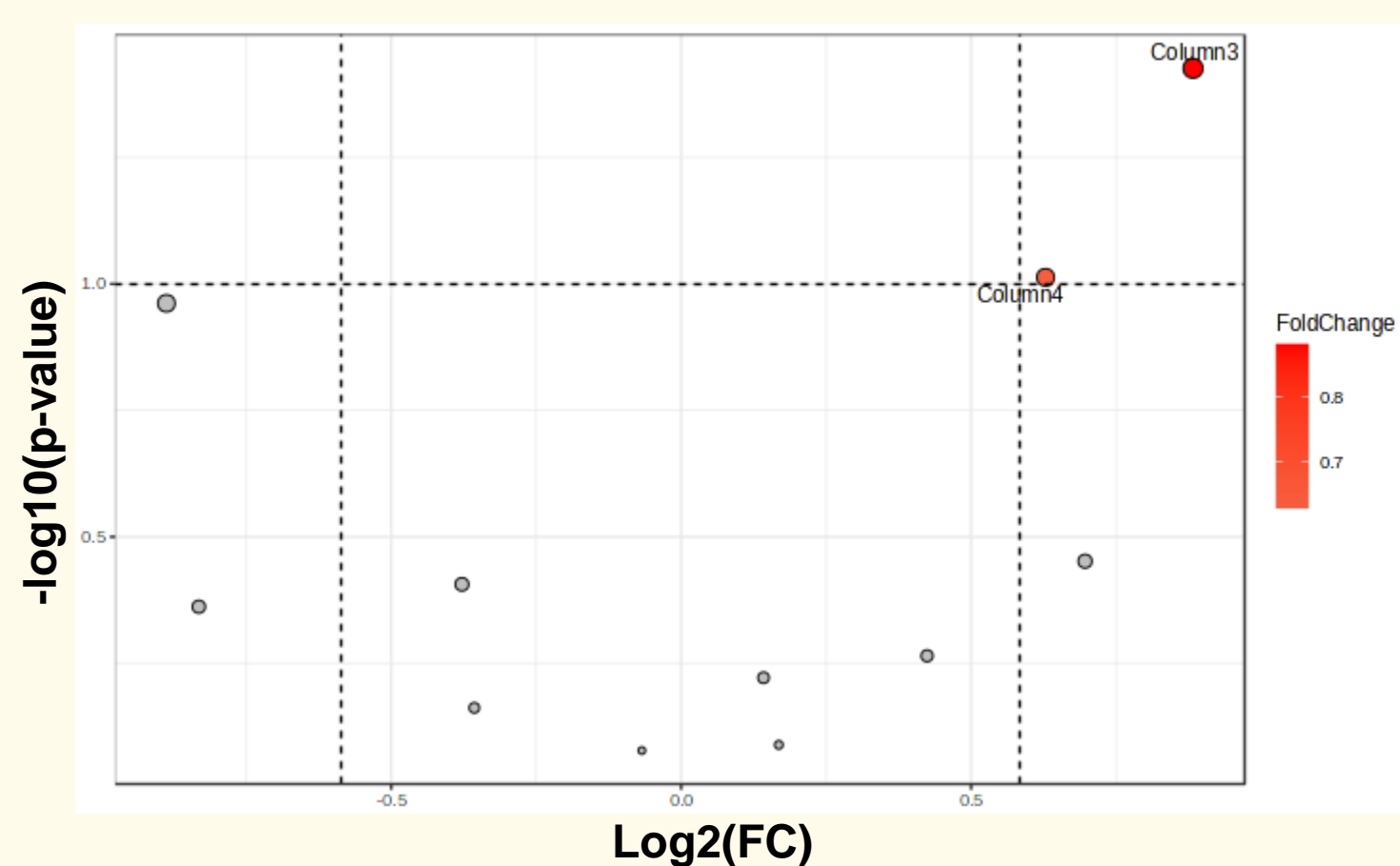


Figure 4: Features selected by volcano plot with fold change threshold 1.5x and t-test threshold 0.05. The red circles represent features above the threshold (cholesterol).

Discussion: The results from this experiment show significant (p-value: 0.03) differences in the signal volume from cholesterol in WT ZF and KO ZF. These differences are also shown in the grey matter from human samples. The control patient has a higher signal volume from cholesterol. These results are based on one human sample. For future projects, it's important to understand whether high levels of cholesterol in the brain cause Parkinson's or if Parkinson's leads to higher levels of cholesterol.

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