

Lipidomics in patients receiving ECT

– Preliminary findings

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Introduction

- Major depressive disorder (MDD) is a highly prevalent and debilitating mental illness¹.
- Altered clinical lipid parameters in MDD have been assessed in several studies with inconsistent results².
- Lipidomics research supports an altered lipid metabolism in MDD³.
- Electroconvulsive therapy (ECT) is the most effective acute treatment of MDD⁴.
- The mechanisms of action of ECT are not fully understood.
- Previous studies have found altered serum lipid profiles after ECT⁵⁻⁷.
- Lipidomics approaches have not been applied in ECT research.
- The present study assessed changes in serum lipid metabolite concentrations in MDD patients undergoing ECT, in an attempt to elucidate the role of lipids in MDD pathology and ECT effect.

Method

- The study is part of a multidisciplinary trial investigating the mechanisms of ECT⁸.
- Serum lipid levels were measured in 16 patients suffering from treatment resistant MDD using a non-targeted lipidomics approach.
- Blood samples were obtained before first treatment and approximately one week after the completed treatment series.
- Ultrahigh performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) technology was used to detect lipid metabolites.
- A matched pairs t-test was used to compare pre and post-treatment samples, and false positives were corrected by a false discovery rate (q-value) calculation.

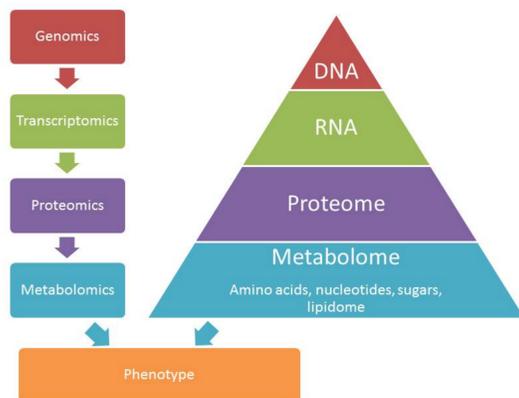


Figure 1: Illustration of the relationship between DNA and the phenotype expressed, via the metabolome. Metabolomics technology, including lipidomics, can be utilized to better understand phenotype expression (e.g. MDD.)

Table 1: Demographics and clinical features of 16 MDD patients.

Characteristic	Mean ± SE (min-max)
Age in years	47.3 ± 3.7 (25-78)
Sex (F/M), n	10/6
MADRS pre ECT	33.4 ± 1.7 (18-44)
MADRS post ECT	13.4 ± 2.3 (0-29)
Number of ECT sessions	10.1 ± 1.0 (4-20)

MADRS: Montgomery-Aasberg Depression Rating Scale, SE: Standard error of the mean.

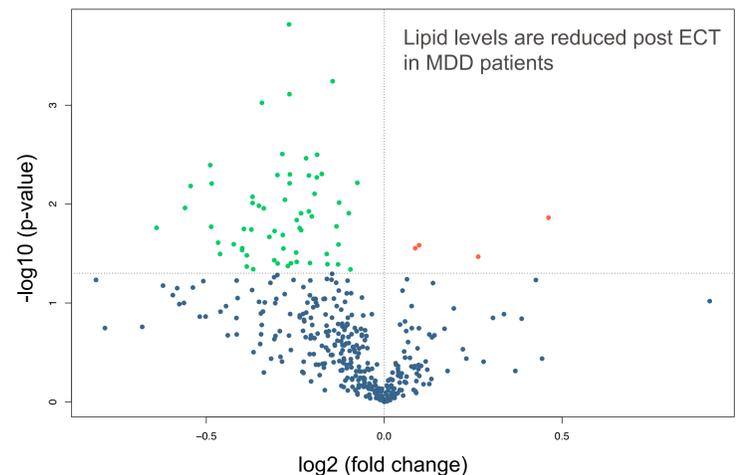


Figure 2: Volcano plot of the relationship between significance (p-value) and fold change in paired samples pre and post ECT. Green and red colored dots represent lipid metabolites reduced and increased, respectively, post ECT with $p < 0.05$.

Results

- In total, 401 lipid metabolite compounds were investigated, of which 69 were significantly altered after ECT.
- Post-treatment samples showed reduction of serum concentration in several classes of lipid metabolites, especially free fatty acids (FFAs) – saturated, monounsaturated and polyunsaturated.
- Significant decreases were found in:
 - Nearly all of the detected monoacylglycerol species
 - Several diacylglycerol species
 - Several lysolipids and other phospholipid breakdown products
 - A number of fatty acid dicarboxylates

Discussion

The observed changes in lipid levels can be mediated by different processes, including changes in biosynthesis and breakdown rates of FFAs. This can be related to altered levels of exercise, distribution and storage of lipids or dietary changes, which could reflect lifestyle changes made during treatment and recovery. More investigations are needed to explore the contributions of these processes and possible relation to MDD and ECT.

Interestingly, several of the observed lipid alterations were opposite to previous lipidomics findings in MDD³, perhaps suggesting a reversal of a pathological state.

Conclusion

Concentrations of several lipid metabolites were reduced in MDD patients after ECT. This study supports previous findings on ECT's effect on lipid metabolism. Further investigations in larger samples should be performed to confirm these results and evaluate the clinical significance of the findings.

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