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Longitudinal methylome-wide analysis in patients undergoing Electroconvulsive Therapy (ECT)

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ABSTRACT:

Electroconvulsive therapy (ECT) is the treatment of choice for severe and treatment-resistant depression and considered as most effective for this subgroup of patients (Kellner et al, 2020). The molecular mechanisms underlying its effects are largely unknown. As antidepressant treatment has been reported to be associated with epigenetic modifications (Webb et al, 2020); we hypothesized that a strong intervention such as ECT leads to pronounced changes in epigenetic levels. In this study, we analyzed epigenome-wide DNA methylation levels of 34 severely depressed patients before and after ECT treatment using the Illumina Infinium Methylation EPIC BeadChip. Epigenome-wide methylation analysis revealed a significant differential methylated CpG site in *TNKS* to be associated with response to ECT. Two differential methylated regions on chromosomes 8 and 20 were associated with a reduction in depressive symptoms. Pathway analysis yielded no significant pathway related to ECT response. Our findings show that ECT introduces change in DNA methylation levels and could therefore be considered a promising model to study underlying mechanisms in depression and treatment response. To confirm potentially important results larger sample sizes and replication in other cohorts are needed. To this end, we also present a more comprehensive assessment framework for the ongoing phase 2 of the investigation, including additional phenotypic and epigenetic assessments throughout the course of ECT treatment.

1. Kellner CH, Obbels J, Sienaert P. When to consider electroconvulsive therapy (ECT). *Acta Psychiatr Scand.* 2020;141(4):304-315.
2. Webb LM, Phillips KE, Ho MC, Veldic M, Blacker CJ. The Relationship between DNA Methylation and Antidepressant Medications: A Systematic Review. *Int J Mol Sci.* 2020;21(3).

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