HHS Public Access

Author manuscript

*JAMA Psychiatry*. Author manuscript; available in PMC 2023 January 09.

Published in final edited form as:

*JAMA Psychiatry*. 2016 June 01; 73(6): 545–546. doi:10.1001/jamapsychiatry.2016.0348.

# Predicting ECT response with machine learning

**Christopher C. Abbott, MD MS**[1,*], **Dyani Loo, MD**[1], **Jing Sui, PhD**[2,3]

[1.] Department of Psychiatry, University of New Mexico School of Medicine, Albuquerque, NM, USA

[2.] National Laboratory of Pattern Recognition, Institute of Automation, Chinese Academy of Sciences, Beijing, China 100190

[3.] The Mind Research Network, Albuquerque, NM, USA,87106

In this issue of *JAMA Psychiatry,* Redlich *et al* [1] assessed the predictive potential of baseline (pre-ECT) structural neuroimaging with a set of machine-learning-based approaches. In the pre-procedural evaluation and consent process, the ECT clinician must balance the anticipated benefits and risks for an individual patient. Ideally, the ECT clinician would be able to accurately predict a patient's likelihood of response based on demographics, symptom severity, phenomenology, and treatment history. A number of indices were created as early as 1950 based on clinical variables including melancholia, family history, symptom severity, age, gender, presence of psychosis and personality disorders. Unfortunately, a recent meta-analysis of ECT predictors has shown that these clinical predictors are imperfect [2]. Only longer duration of symptoms and antidepressant treatment resistance reliably predict ECT non-responders.

Biological markers (biomarkers) may be informative in identifying depressed patients who will respond to ECT. Specifically, treatment selection biomarkers can be particularly useful for the ECT clinician. Past research has focused on pre-ECT laboratory indices that may be associated with ECT response, including the dexamethasone suppression test and sleep EEG. These tests lacked the sensitivity and specificity needed to augment clinical decision making and subsequently fell out of favor. More recently, neuroimaging treatment selection biomarkers have inconsistently identified regions associated with response. These investigations have identified variations in baseline brain measures that are associated with variations in subsequent outcomes, which could be described more as post-correlation than prediction. Furthermore, the *a priori* regions used in these analyses precluded the identification of new regions or relationships associated with response prediction.

In the current investigation, Redlich *et al* used three groups of study participants: ECT (n = 24), medication (n = 23), and a group of healthy comparison subjects (n = 21). The investigators used clinical judgment to assign patients to ECT or to the antidepressant treatment groups. ECT subjects received structural imaging before and after the ECT series,

[*]Corresponding Author Christopher C. Abbott, Dept. of Psychiatry, University of New Mexico School of Medicine, Albuquerque, NM, USA, 87131, Telephone: (505) 272-2223, Fax: (505) 272-5572, cabbott@salud.unm.edu.

Conflict of Interest Disclosures: None reported.

and the medication and healthy comparison groups received imaging assessments with comparable time frames. Structural changes were assessed with voxel-based morphometry. The investigators used three multivariate analysis methods for the baseline structural imaging: support vector machine (SVM), Gaussian process classifier, and support vector regression. These multivariate methods demonstrated up to 78% accuracy in classifying ECT responders and non-responders and predicted a dimensional measure of treatment response (percent improvement in depression rating). Interestingly, the subgenual cingulate gyrus contributed most to the classification of therapy response. Despite the small sample size, the accuracy demonstrated by Redlich *et al* is close to the 80% threshold necessary to be clinically useful [3].

The current study focused on only region, subgenual cingulate gyrus, for the support vector regression. This region contributed the most to the binary classification. However, the binary classification identified a combination of structural regions, not a single region of interest, that together achieved the final classification. In future prediction works, it is expected that a set of neuroanatomical regions of interest, which interact closely or consist of a particular brain network, could be identified through a nested cross-validation. These brain regions could achieve a more precise prediction on either treatment response, treatment remission or specific individualized symptom score change.

With a larger sample size (n = 45) van Waarde *et al* applied a similar multivariate pattern analysis to resting state fMRI and independent component analysis to predict ECT response [4]. This investigation identified functional networks that predicted ECT response in the the dorsal medial prefrontal cortex (88% accuracy) and the anterior cingulate (80% accuracy). Both van Waarde and Redlich used standard SVM-based prediction models with a leave-one-out cross-validation and only used one imaging measure (grey matter volume or resting-state connectivity). Regardless of methodological issues and limited sample sizes, these investigations identified established dorsal and ventral depression networks predictive of response without *a priori* region feature selection methods.

Recent investigations have applied a variety of pattern classification approaches to neuroimaging data, aiming to explore neuroanatomical features that are able to predict treatment outcomes or differentiate diagnoses. Future work employing advanced feature selection strategies, such as random forest, improved SVM models, sparse linear or non-linear regression models may improve the individualized prediction accuracy to reach a level that is sufficient to assist pre-treatment clinical decisions. In addition, multimodal brain imaging data fusion is able to provide more facets of brain structure and function and the cross-information for individual subjects [5]. Therefore, combining multimodal information and exploiting the richness of multiple neuroimaging measures can be promising avenues to further improve the sensitivity and specificity of ECT classification.

The secondary objectives of Redlich's investigation were longitudinal analyses to identify longitudinal volumetric changes associated with ECT. The left hippocampus demonstrated a group by time interaction, which was related to increased volume in the ECT group. Post hoc analysis within the ECT group demonstrated increased bilateral medial temporal volumes. ECT-mediated medial temporal lobe neuroplasticity has now been replicated in

several longitudinal neuroimaging investigations. Neuroplasticity appears to be a common mechanism shared by both ECT and chemical antidepressant treatments, but ECT appears to be a more potent stimulator of neuroplasticity consistent with the results of this investigation [6]. Although the underlying mechanism cannot be delineated from structural imaging, animal investigations suggest that possible mechanisms of ECT-mediated neuroplasticity include synaptogenesis, gliogenesis, angiogenesis and neurogenesis [7]. The discrepancy between prediction (subcallosal cingulate gyrus) and anatomic regions associated with volumetric differences (medial temporal lobes) will require additional analysis to understand this complex relationship. Regardless, the reversal of disease-related regional brain atrophy in this patient sample demonstrates neuroplasticity as an antidepressant mechanism. Importantly, the normalization of aberrant medial temporal volumes offers further support for the brain-enabling (and de-stigmatizing) therapeutic components of ECT.

In conclusion, machine learning classification investigations, as demonstrated by Redlich *et al*, will have an impact on precision medicine. ECT, which is the treatment of choice for patients with severe symptom acuity, is the optimal laboratory to investigate and optimize treatment selection biomarkers with machine-learning methods. With further validation at different sites, these classification patterns may inform the ECT clinician about the likelihood of response of an individual patient prior to the ECT series. The ECT clinician will then be able to accurately identify the depressed patient that will respond to ECT and spare the ECT non-responder from the unnecessary risks, time, and costs associated with the procedure.

## Acknowledgements:

Drs. Abbott and Sui receive grant support from Centers of Biomedical Research Excellence (2P20GM103472-01).

## References

1. Redlich R, Opel N, Grotegerd D, et al. The prediction of individual response to electroconvulsive therapy by structural MRI. JAMA psychiatry. 2016.
2. Haq AU, Sitzmann AF, Goldman ML, Maixner DF, Mickey BJ. Response of depression to electroconvulsive therapy: a meta-analysis of clinical predictors. The Journal of clinical psychiatry. 2015;76(10):1374–1384. [PubMed: 26528644]
3. American Psychiatric Association. Consensus report of the APA Work Group on Neuroimaging Markers of Psychiatric Disorders2012, Arlington, VA, USA.
4. van Waarde JA, Scholte HS, van Oudheusden LJ, Verwey B, Denys D, van Wingen GA. A functional MRI marker may predict the outcome of electroconvulsive therapy in severe and treatment-resistant depression. Molecular psychiatry. 2014.
5. Calhoun VD, Sui J. Multimodal Fusion of Brain Imaging Data: A Key to Finding the Missing Link(s) in Complex Mental Illness. Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2016;In press.
6. Malberg JE, Eisch AJ, Nestler EJ, Duman RS. Chronic antidepressant treatment increases neurogenesis in adult rat hippocampus. J Neurosci. 2000;20(24):9104–9110. [PubMed: 11124987]
7. Bouckaert F, Sienaert P, Obbels J, et al. ECT: Its Brain Enabling Effects: A Review of Electroconvulsive Therapy-Induced Structural Brain Plasticity. J ECT. 2014;30(2):143–151. [PubMed: 24810772]