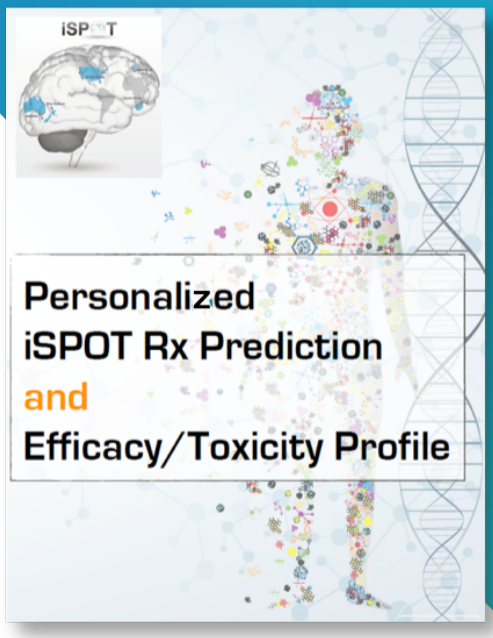
PERSONALIZED TEST FOR TREATMENT PREDICTION IN DEPRESSION



Psychiatry remains without a single personalized test to predict treatment response or remission in Depression.

Major Depressive Disorder is one of the most common psychiatric disorders in the US, with over 15 million people impacted and costing $100 billion annually, of which less than half achieve symptom remission with the first medication tried. The cost associated with a prolonged duration of depressive symptoms is substantial, including lower employment levels and higher risk for a range of other general medical conditions.

Total Brain's aim in undertaking the iSPOT-D study (International Study to Predict Optimized Treatment in Depression) was to develop the first objective Personalized Medicine Test to determine who is more and less likely to respond to three of the most common antidepressant medications.

Across the three antidepressants (n = 1,008 patients), the iSPOT-D Test has an Accuracy of 79-84%, PPV: 70-74%, and NPV of 84-92%

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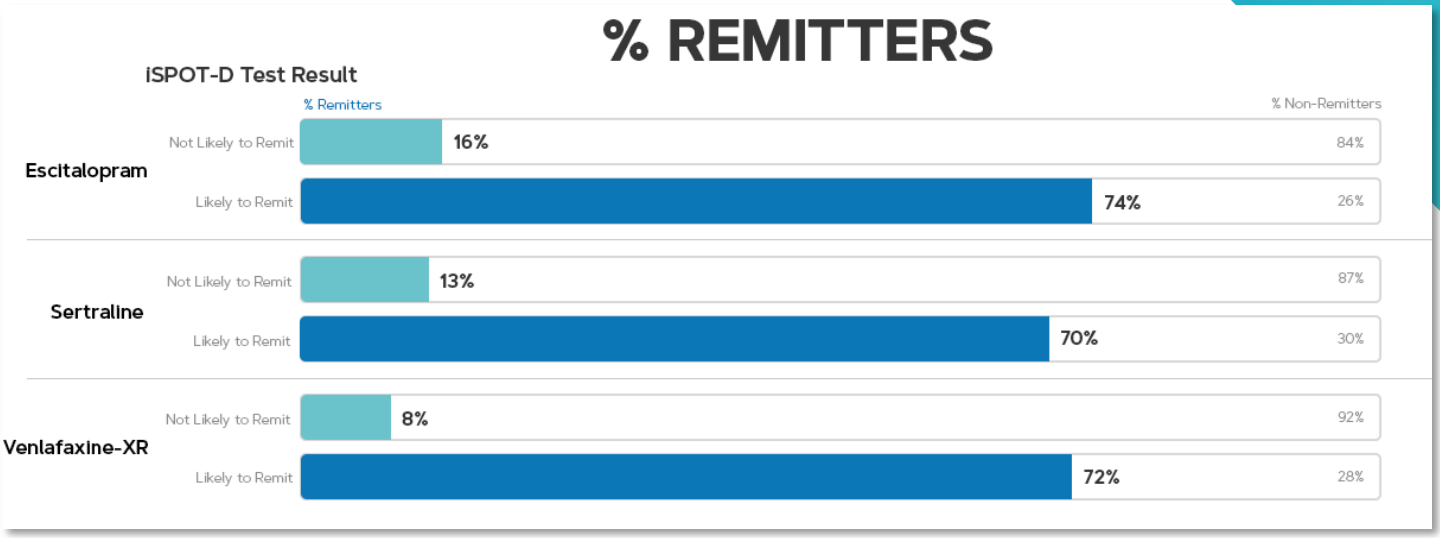
iSPOT-D Study Background

The iSPOT-D test was developed using data from 1,008 patients with Major Depressive Disorder, as part of the iSPOT-D international trial conducted at 20 site locations in five countries (multiple sites in the USA, Australia, New Zealand, The Netherlands, South Africa). Patients were randomized to one of three of the most commonly used antidepressants (escitalopram, sertraline, or venlafaxine-XR), with blood samples collected prior to starting medication and clinical workups before and after 8 weeks of treatment (with 715 patients completing the 8 week follow up session).

Analysis and Results

A multivariate, ensemble analysis approach was used to identify the most significant SNPs to consider for predictive models. This approach was taken, to account for multiple subgroups and treatment outcome definitions, and to increase the robustness of results by reducing the influence of outliers and chance correlations to individual dependent variables. This analysis resulted in an initial set of 200-300 SNPs, which was reduced to a final a set of 21 SNPs by taking those with the highest third quartile p-value.

This final set of SNPs was entered into cross validated k-fold Lasso regression models to create sets of 7 SNPs, which were then entered as predictors as a simple logistic classifier model. The results were highly consistent between males and females, Europeans and non-Europeans, as would be expected with the ensemble approach. Additionally, each set of predictors was run 50 times with 5-fold cross-validation and the seven predictors with the highest absolute standardized beta coefficients were chosen to be carried forward to the next step. Using the seven chosen predictors, 100 iterations of 10-fold cross validation were run to assess model performance.



For escitalopram, 74% of the patients predicted to be likely to remit by the iSPOT-D test actually remitted (compared to 41% remission observed for everyone together), compared to only 16% remission among patients predicted by the iSPOT-D test to be not likely to remit.

For sertraline, 70% remission was achieved in the iSPOT-D test likely to remit group, compared to 13% remission in patients predicted not likely to remit. For venlafaxine-XR, 72% remitted in the iSPOT-D likely to remit group, compared to only 8% remission among the not likely to remit group.

Across the three antidepressants, adding clinical predictors improved predictive models to have an accuracy of 79-84%, Sensitivity of 77-87%, Specificity of 81-83%, PPV: 70-74%, and NPV of 84-92%.

iSPOT shows encouraging training set results to be the first test to predict remission in depression.

Primary Care Physicians (PCPs), Psychiatrists and other clinicians face daily challenges of objective decision making for treatment options in Depression. This test has the potential to greatly benefit these decisions with unprecedented objective information.

The test is now available for partnering and or licensing.

For broader context about the depth of iSPOT data, there are over 30 publications from the iSPOT-D trial on cognition, genomics, EEG, ERP, MRI, DTI, fMRI, and clinical sub-groups. A full list of publications can be found at: https://www.brainresource.com/publications.html