



Biomarkers for Rapid Identification of Treatment Effectiveness (BRITE): Testing Symptoms and Biomarkers as Predictors of Response and Remission in MDD

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ABSTRACT*

Objective: To evaluate predictive accuracy of frontal quantitative electroencephalography (fqEEG) for response and remission in MDD relative to symptom measures and genetic biomarkers.

Method: 73 subjects (age: 43 ± 13; 66% female) meeting DSM-IV criteria for MDD entered treatment with escitalopram (ESC 10 mg/day) for 7 weeks in one limb of a study (www.BRITE-MD.org). At each visit we assessed severity of depression with the Hamilton Depression Rating Scale (HAM-D-17), and we recorded 4-channel fqEEG (At1-Fpz, At2-Fpz, A1-Fpz, A2-Fpz). A composite EEG index (Antidepressant Treatment Response (ATR)) was developed to predict clinical response assessed at baseline and week 1. Clinicians predicted likelihood of response or remission based on clinical impression at the week 1 visit, and genetic polymorphisms associated with antidepressant treatment response as well as serum drug levels were examined. Response to treatment was defined as a reduction of baseline HAM-D at week 7 of ≥ 50%, and remission as HAM-D ≤ 7 at week 7. **Results:** 38 (52%) subjects responded and 28 (38%) remitted. ATR correlated with % change in HAM-D from baseline to week 7 (R=-0.433, p<0.001). ATR was higher in responders than non-responders (59 ± 10 vs. 50 ± 8, p<0.001) and remitters than non-remitters (59 ± 11 vs. 52 ± 9, p=0.002). Clinician prediction of response and remission was not statistically significant, and there was no significant association between genetic biomarkers or serum drug levels and response. Logistic regression showed that ATR was the single strongest predictor of remission (p=0.002). **Discussion:** EEG response to initial dosing predicted clinical response and remission and was superior to clinical predictors as well as putative genetic biomarkers.

Conclusions: This prospective evaluation confirms that an EEG biomarker can be used to predict treatment efficacy after one week of ESC. Future studies should evaluate the utility of this EEG predictor in guiding treatment decisions.

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INTRODUCTION

- ◆ Prior work demonstrated that frontal EEG activity predicted response to antidepressant treatment [1][2]
- ◆ This work evaluated a simple-to-use frontal quantitative EEG (fqEEG) biomarker of efficacy of antidepressant treatment response (ATR)

METHODS

- ◆ MDD subjects (DSM-IV criteria; baseline IDS-C ≥ 12) entered a longitudinal, 7-week prospective treatment study with escitalopram (10mg/day)
- ◆ Clinical response was defined as a ≥ 50% reduction in HAM-D-17 from baseline to week 7
- ◆ At each study visit (baseline, 48hrs, week 1, 2 and 7), 4-channel fqEEGs were recorded (At1-Fpz, At2-Fpz, A1-Fpz, A2-Fpz) and HAM-D-17 was assessed
- ◆ Power spectra of the EEG were estimated for each consecutive 2-sec EEG epoch collected during a resting period with closed eyes
- ◆ ATR (rev 4.1), a composite index previously derived to predict clinical response from EEG features, was tested using fqEEG assessed at baseline and week1
 - ATR ranges from 0 (low probability of response) to 100 (high probability of response)

RESULTS

- ◆ 73 subjects (66% female, age 43 ± 13 y.o.) completed 7 weeks of treatment and had fqEEG and clinical data available for this final analysis
- ◆ 52% and 38% were antidepressant treatment responders and remitters, respectively
- ◆ At week1:
 - ◆ ATR was significantly higher in treatment responders than in non-responders (59 ± 10 vs. 50 ± 8, p<0.001) and higher in remitters than non-remitters (59 ± 11 vs. 52 ± 9, p=0.002)
 - ◆ ATR correlated with % change in HAM-D-17 from baseline to week 7 (R=-0.433, p<0.001).
 - ◆ ATR prediction of response and remission (74% accuracy each) were numerically better than clinician prediction of response (51% accuracy) and remission (57% accuracy)
- ◆ Age, race, gender and baseline HAM-D-17, HR, SBP, DBP, 5HT2a polymorphisms and plasma drug levels did not predict response or remission
- ◆ Logistic regression identified ATR (p=0.001) and the percentage change in HAM-D-17 within the first week (p=0.034) as elements of response-prediction model
 - ◆ Logistic regression identified ATR (p=0.002) as the single best predictor of remission

RESULTS (Continued)

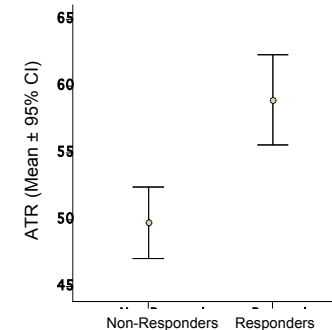


Figure 1. Distribution of ATR values (mean ± 95% CI) for Responders (right) and Non-Responders (left). ATR was higher in Responders than Non-Responders (59 ± 10 vs. 50 ± 8, p<0.001)

CONCLUSIONS

- ◆ Antidepressant Treatment Response (ATR) Index measured after 1 week of medication predicts clinical response at 7 weeks to fixed-dosed treatment with escitalopram (10mg/day) in MDD in an ongoing study (www.brite-md.org)
- ◆ Clinical implication: Early identification of positive or negative EEG response to treatment may aid in decisions regarding medication adjustments, potentially leading to improved compliance and efficacy of antidepressant therapy

REFERENCES

- [1] Cook IA, Leuchter AF, Witte EA, Stubbeman WF, Abrams M, Rosenberg S. **Early Changes in Prefrontal Activity Characterize Clinical Responders to Antidepressants.** *Neuropsychopharmacology* 2002; 27:130-131.
- [2] Iosifescu D, Greenwald S, Smith C, Devlin P, Alpert J, Hamill S, Fava M. **Frontal EEG at 1 Week Predicts Clinical Response to SSRI Treatment in Major Depressive Disorder.** Presented at the 2006 Annual Meeting of the American Psychiatric Association, Toronto, CA (#231).