

# EEG Guided Medication Predictions in Treatment Refractory Eating Disorder Patients with Comorbid Depression: Opportunities for Personalized Medicine in Managed Healthcare

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## BACKGROUND

Referenced-EEG (rEEG) is a technology that uses quantitative EEG (QEEG) findings as the independent variable to predict medication response for patients with psychiatric disorders. The rEEG compares a patient's drug-free resting EEG patterns to a database of patients of known response to specific classes, subclasses and individual medications<sup>1</sup>. Based on the known medication responses of similar patients (a phenotype), rEEG provides an objective neurophysiological basis for the consideration of effective psychiatric medications for patients.

Conservative reviews of evidenced based treatments have found few efficacious eating disorder treatments<sup>2</sup>. There are only a few controlled trials available on medication therapies for Anorexia Nervosa (AN) and there are no FDA approved medications for AN. Fluoxetine is the only FDA approved medication for the treatment of Bulimia Nervosa (BN). Many Eating Disorder patients fail to meet all DSM-IV criteria for AN or BN and need to be classified as Eating Disorder Not Otherwise Specified (ED NOS). There is no research to support medication options for these patients. To further complicate treatment, many Eating Disorder patients have multiple comorbid Axis I disorders with estimates for co-morbid depression ranging as high as 88.9%<sup>3</sup>.

## OBJECTIVE

The objective of this long-term cohort study was to explore the use of rEEG to facilitate medication selection for patients with an eating disorder and comorbid depression.

## METHODS

Over a 4 year period, 16 patients, 14 females and 2 males, meeting DSM-IV criteria for both an Eating Disorder and a Mood Disorder completed a rEEG and started medications predicted from the database. Patients or families (for adolescents) voluntarily sought a rEEG because current psychiatric medications were ineffective in controlling Eating Disorder and depressive symptoms. Thirteen patients were followed for 6 months to two years. Two patients (ages 14 and 16) were non-compliant with treatment recommendations. One patient, age 25, dropped out due to distance from the treatment center. The remaining 13 patients were followed for 6 months, had previously failed outpatient treatment and required inpatient or partial hospitalizations (12 inpatients, 1 partial). Average age of patients who completed treatment was 23.6 (range 14.7 to 39.0) years, and average illness duration was 7.6 (range 1.0 to 24.0) years.

Primary outcome measures included the 21-item Hamilton Rating for Depression Scale (HDRS), the Clinical Global Improvement Scale (CGI) and the Clinical Global Severity Scale (CGS). Some of the criteria used to assess improvement in the CGI included: body dissatisfaction, drive for thinness, compulsive exercising, bingeing and purging. These clinical outcomes were assessed and recorded by the treating psychiatrist at baseline, 8-week, 6 month, and 2-years (4 of 11 patients).

## RESULTS

rEEG predicted potential efficacy for medications from the following classes: anticonvulsants, antidepressants and stimulants (Table A). Following rEEG medication recommendations, hospitalization days decreased dramatically. At baseline, HDRS scores averaged 39.8±5.7, indicating all patients suffered from moderate to severe depression symptoms (Figure 1). By week 8, scores decreased to an average of 13.2±6.9; and by 6 months, scores decreased to 8.5±5.2. Paired sample t-tests indicated that these changes were significant at 8 weeks (p<.001; t=12.627; df=12) and at 6 months follow-up (p<.001; t=15.687; df=12). At baseline, average CGS score was 5.54±.66. This score represents a rated illness severity between 'Severely ill' and 'Markedly ill'. By week 8, CGS scores had decreased to an average of 2.85±1.14, representing an illness severity of 'Mildly ill'; CGS scores further decreased to 2.23±.83 at 6 months representing a CGS score between 'Mildly ill' and 'Borderline Mentally ill' (Figure 2). These changes were significant at 8-weeks (p<.001; t=11.355; df=12) and at 6 months (p<.001; t=18.917; df=12). CGI scores improved to an average of 1.77±.72 at 8 weeks reflecting a "much improved" change in symptoms. At 6 months average final CGI was 1.23 ±.44, representing a CGI category between 'much improved' (score of 2) and 'very much improved' (score of 1) (Figure 3).

Table A: rEEG-Guided Medications

Patient and Eating Disorder Diagnosis <sup>a</sup>	Illness Duration (years)	Number of Prior Psychiatric Medication Trials	Number of Days of Hospitalization <sup>b</sup>		Months of Data Post rEEG	rEEG Guided Medications
			24 mo. Prior to rEEG	post-rEEG		
A AN	1.1	1	13	0	24	Lamotrigine, Amphetamine D-amphetamine
B AN	4.7	6	192	5	24	Lamotrigine, Sertraline
C BN	5	6	35	0	6	Oxcarbazepine, Bupropion, Methylphenidate, Metoprolol
D AN	10.5	5	41	0	24	Oxcarbazepine, Duloxetine
E BN	3	3	0 <sup>c</sup>	0	15	Amphetamine D-amphetamine, Lamotrigine
F EDNOS	3.5	4	40	4	21	Lamotrigine, Amphetamine D-amphetamine
G AN	6.3	7	169	66	6	Duloxetine, Divalproex, Bupropion, Aripiprazole <sup>d</sup>
H EDNOS	3.3	10	17	9	24	Oxcarbazepine, Fluoxetine, D-amphetamine
I AN	13	20	68	5	9	Gabapentin, Nortriptyline
J EDNOS	20	14	37	0	11	Gabapentin, Fluoxetine, Bupropion
K BN	3	8	163	39	8	Gabapentin, Bupropion
L AN	1	4	17	0	6	Gabapentin, Methylphenidate
M BN	24	2	7	0	6	Bupropion
<b>Total</b>			<b>789</b>	<b>128</b>		

<sup>a</sup>Combined inpatient and residential hospitalization days. See Table C for more detail. <sup>b</sup>AN = Anorexia Nervosa; BN = Bulimia Nervosa; EDNOS = Eating Disorder Not Otherwise Specified. <sup>c</sup>Aripiprazole not in rEEG database. Used based on clinical judgment only. <sup>d</sup>Patient only in partial hospitalization.

Table B: rEEG Guided Medications: 6 classes / 14 agents

Antidepressants (n)	Anticonvulsants (n)	Stimulants (n)	MAOI's (n)
Bupropion (4)	Lamotrigine (3)	Amphetamine (2)	Selegiline (1)
Duloxetine (2)	Oxcarbazepine (3)	D-Amphetamine (2)	Antipsychotics
Nortriptyline (1)	Gabapentin (5)	Methylphenidate (2)	Aripiprazole (1)
Fluoxetine (1)	Divalproex (1)		<b>Beta Blockers</b>
			Metoprolol (1)

<sup>n</sup> is equal to the number of patients out of 13 who were prescribed this medication based on rEEG Recommendations.

Table C: Estimated Cost of Hospitalizations Before and After rEEG

	Pre rEEG	Estimated Cost of Care	Post rEEG	Estimated Cost of Care
Total Hospitalizations	53		7	
Inpatient & Residential	789	\$1,578,000.00	114	\$228,000.00
Partial Hospital Days	210	\$168,000.00	15	\$12,000.00
Total Cost of Care:		\$1,746,000.00		\$240,000.00

<sup>a</sup>Cost of Care assumes \$2000 per day in inpatient hospitalization and \$800 per day per in partial hospitalization. Numbers for cost estimates taken from Crow and Nymann, 2004<sup>5</sup>.

## CONCLUSIONS

Medication trials have provided limited insight and guidance in the pharmacological management of Eating Disorders. rEEG guided medication predictions resulted in improvements with depression and eating disorder symptoms in treatment refractory patients that had required either partial, residential, or inpatient level of care as determined by managed behavioral health care reviewers.

Improvements in both HDRS and CGI scores were evident at 8-weeks, 6-months, and 2 years (for 4 patients). The medications selected from rEEG correlations involved combinations from different classes of medications. The diversity of medications successfully utilized in treatment of this dually diagnosed cohort extended beyond the available literature and our own clinical experience. It is one of the key findings of this study. Without objective physiologic guidance, implementing such a broad based strategy would be extremely difficult. Based on rEEG correlations, stimulant medications were used in the treatment of five patients, only one of which experienced weight loss. These results may support recent findings that ADHD can predict eating disorder pathology in adolescent girls<sup>6</sup>. The decrease in HDRS for these thirteen patients is striking. In addition to decreasing symptoms, the decrease in hospitalizations and cost of inpatient care for these patients (approximately 1.5 million dollars) should be investigated further. The durability of response to rEEG guided medications and the broader options of medication combinations portends well for advancing treatment for Eating Disorder patients.

Anorexia Nervosa is a potentially fatal illness. Improved pharmacotherapy could decrease the high morbidity and mortality in patients with disordered eating. Further research is needed to determine the full utility and limitations of rEEG in the treatment of eating disorder patients.

## REFERENCES

- Suffin SC, Emory WH, Gutierrez N, et al. A QEEG Method for Predicting Pharmacotherapeutic Outcome in Refractory Major Depressive Disorder. *J of Physicians and Surgeons* 2007; 12:104-108.
- Treasure J, Schmidt U. Anorexia nervosa. *Clin Evid* 2004; 11:1192-203.
- Godart NT, Perdereau F, Rein Z, Berthoz S, Wallier J, Jeammet Ph, Flament MF. Comorbidity studies of eating disorders and mood disorders. *Critical review of the literature. J Affect Disord* 2007; 97:37-49.
- Mikami, Hinshaw, Patterson, & Lee: Eating pathology among adolescent girls with Attention-Deficit/Hyperactivity Disorder. *J of Abnormal Psychology* 2008, 117, 225-235.
- Crow SJ, Nymann JA. The Cost-Effectiveness of Anorexia Nervosa Treatment. *Int J Eat Disord* 2004; 35: 155-160.

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Figure 1 – Hamilton Depression Scores, Baseline to 2 years

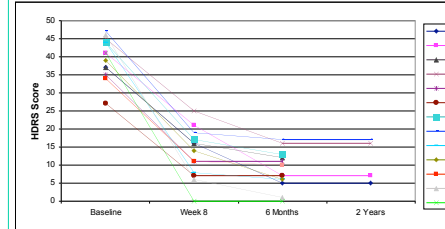
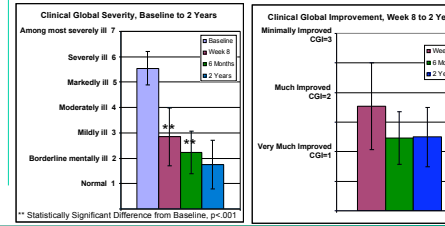


Figure 2 & 3 – Clinical Global Severity and Clinical Global Improvement



\*\* Statistically Significant Difference from Baseline, p<.001