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EEG alpha measures predict therapeutic response to an SSRI antidepressant: Pre and post treatment findings

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Abstract

Background—There is growing evidence that individual differences among depressed patients on electrophysiologic (EEG), neuroimaging, and neurocognitive measures are predictive of therapeutic response to antidepressants. This study replicates prior findings of pretreatment differences between SSRI responders and nonresponders in EEG alpha power or asymmetry, and examines whether these differences normalize or are stable following treatment.

Methods—Resting EEG (eyes open and closed) was recorded from 28 electrodes (nose reference) in 18 depressed patients when off medication and at the end of 12 weeks of fluoxetine treatment. Clinical response was assessed by an independent rater using the Clinical Global Improvement scale. EEG data were also obtained for 18 healthy adults matched to patients in gender and age.

Results—Treatment responders had greater alpha power compared to nonresponders and healthy controls, with largest differences at occipital sites where alpha was largest. There were also differences in alpha asymmetry between responders and nonresponders at occipital sites. Responders showed greater alpha (less activity) over right than left hemisphere, whereas nonresponders tended to show the opposite asymmetry. Neither alpha power nor asymmetry changed following treatment and test-retest correlations were high, particularly for alpha power. Alpha power and asymmetry showed reasonable positive predictive value but less negative predictive value.

Discussion—The findings confirm reports of alpha differences between antidepressant responders and nonresponders, and raise hopes for developing EEG tests for selecting effective treatments for patients. The stability of alpha power and asymmetry differences between SSRI responders and nonresponders following treatment suggests that they represent state-independent characteristics.

Clinical Trials—Prozac treatment of major depression: discontinuation study; registration #NCT00447128; and Dichotic listening as a predictor of placebo and medication response in depression; registration #NCT00296725; http://www.clinicaltrials.gov/.

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Keywords

depression; SSRI; EEG; alpha power; hemispheric asymmetry

An abundance of antidepressants with distinct pharmacologic profiles are available for treating depression and yet clinicians have no way of knowing whether a patient will benefit from a specific medication. Studies using neuroimaging (1–4), neurocognitive (5–7), and electrophysiologic (8–12) measures have found that pretreatment differences among depressed patients are related to subsequent clinical response to antidepressants.

The ability of quantitative electroencephalographic (qEEG) measures of "spontaneous" brain electrical activity in a resting state to predict response to a selective serotonin reuptake inhibitor (SSRI) or other antidepressants has been suggested in several studies. Ulrich *et al.* (13) found increased posterior alpha in patients who eventually responded to amitriptyline, suggesting that there may be two subtypes of depression having different pathophysiology and antidepressant response. Prichep *et al.* (14) similarly found evidence for two subgroups of patients having an obsessive-compulsive disorder, one with relative excess of alpha responded well to an SSRI and one with increased relative theta showed little treatment response. Knott *et al.* (15) found that depressed patients who responded to imipramine showed a trend for more alpha, but had significantly less theta compared to nonresponders. Cook *et al.* (16) did not find pretreatment differences between fluoxetine responders and nonresponders in theta, but did find group differences in "cordance", a measure based on a form of surface Laplacian (see Tenke and Kayser [17] for a discussion of methodological limitations). We found a difference in alpha asymmetry between fluoxetine responders and nonresponders (8), which was predicted on the basis of dichotic listening findings (18). Fluoxetine nonresponders showed greater alpha power (less activity) over the left hemisphere than the right, whereas responders tended to have the opposite asymmetry. Two studies have used tomographic (LORETA) analyses to infer theta current density in specific brain regions. Pizzagalli *et al.* (12) localized pretreatment theta increases to rostral anterior cingulate cortex (ACC) in responders to nortriptyline. Similarly, Mulert *et al.* (19) reported that depressed patients responding to either citalopram or reboxetine had increased pretreatment activity localizable to rostral ACC. These findings suggest that pretreatment alpha or theta measures may be of value as predictors of clinical response to SSRI or other antidepressants.

EEG in healthy adults has high test-retest reliability for power in the alpha and theta bands (20), whereas it is somewhat lower for alpha asymmetry (21). Less is known about stability of qEEG in depressed patients during treatment with antidepressants. Studies have reported changes in qEEG following acute administration of antidepressants and suggested that they may be of value for identifying patients who are most likely to benefit from treatment. Knott *et al.* (15) found that depressed patients who responded to 2 weeks of imipramine treatment differed from nonresponders in showing acute increases in theta 3 hours after a test dose, as well as an increase in frontal theta 2 weeks after treatment. In contrast, Cook *et al.* (9) measured qEEG during treatment with fluoxetine or venlafaxine and found no difference between responders and nonresponders in either baseline or acute change in theta power. Patients who responded to 8 weeks of treatment did show an acute decrease in prefrontal "cordance" after 48 hours and one week of treatment. Fewer studies have examined longer-term effects of treatments on qEEG. Knott *et al.* (22) reported that male depressed patients showed a decrease in alpha power and an increase in relative theta/delta after 6 weeks of treatment with the SSRI paroxetine. Deldin and Chiu (23) did not find changes in alpha power or asymmetry in depressed patients following a cognitive intervention to improve mood.

The present study measured resting EEG in a new sample of depressed patients before and after 12 weeks of treatment with the SSRI fluoxetine. The purpose was twofold: (1) to replicate prior findings of pretreatment differences in alpha power and asymmetry between SSRI responders and nonresponders, as well as to examine differences in their theta power. We hypothesized that responders would differ from nonresponders in showing greater alpha power and the opposite alpha asymmetry; (2) to determine whether pretreatment differences between responders and nonresponders normalize during treatment or are stable, state-independent characteristics.

Methods and Materials

Subjects

Outpatients between the ages of 20 and 56 attending a university-affiliated depression research clinic were included. Patients were excluded for any of the following reasons: serious suicide risk, seizure disorder, mental disorders secondary to a general medical condition, substance use disorders (including alcohol abuse) within the last 6 months, psychotic disorders, history of significant head trauma, or other neurologic disorder. All patients signed informed consent forms before participating in the study. All aspects of their diagnostic assessment and treatment were carried out by research psychiatrists.

EEGs were obtained for 18 depressed patients at baseline and again after 12 weeks of open treatment with fluoxetine. All but one patient was treated as part of a clinical trial in which they received 10 mg of fluoxetine during week 1, 20 mg during weeks 2–4, and 40 mg during weeks 5–8, and if still no response, a further increase to 60 mg was permitted during weeks 9–12. Dose increases after week 2 were optional, based on clinical response and tolerability of medication. The end dose of fluoxetine at week 12 was 60mg, except for two patients whose end dose was 40mg (one treatment responder and one nonresponder). The remaining patient was tested before receiving a 6-week single-blind placebo period and, after not responding to placebo, received 12 weeks of fluoxetine treatment beginning at 20 mg and increasing biweekly up to a final dose of 60 mg. A clinician, blind to the patient's EEG data, rated each patient at the end of 12 weeks of treatment using the Clinical Global Impression Improvement scale (CGI-I; 24). Patients who had a CGI-I rating of "much or very much" improved were considered to be responders and all other patients were considered as nonresponders. A 21-item Hamilton Depression scale ($HAM\text{-}D_{21}$; 25) was obtained before and during treatment. EEGs were also obtained for 18 right-handed healthy adults matched to the depressed patients in gender and age. They were screened to exclude those having current or past Axis I psychopathology, substance abuse, history of significant head trauma, and neurological disorders.

Table 1 gives the characteristics of the responders, nonresponders and healthy controls. These groups did not differ significantly in gender or age, but nonresponders had somewhat less education than responders and healthy controls ($p<.05$). Education was not, however, significantly associated with alpha power ($r= .11$, ns) or asymmetry ($r= .32$, ns). Also, group differences in alpha power and asymmetry reported below remained the same when education was included as a covariate. The groups did not differ significantly in handedness, as indicated by their laterality quotient (LQ) on the Edinburgh Inventory (26). Two responders and three nonresponders were left handed and the remaining patients and controls were right handed ($LQ>0$). Handedness LQ scores were not significantly associated with either alpha power ($r= .07$, ns) or asymmetry ($r= -.22$, ns). There was no difference between responders and nonresponders in pretreatment severity of depression on the $HAM\text{-}D_{21}$. Following treatment, responders had markedly lower HAM-D21 scores than nonresponders ($t= 3.57$, $df=16$, $p<.01$) and were essentially in remission (i.e., all had $HAM\text{-}D_{21}$ score ≤ 7 except for one patient who had score of 8). Among responders, 8 met DSM-IV criteria for major depressive disorder

(MDD), 2 for both MDD plus dysthymia, and 1 for dysthymia with past MDD. Among nonresponders, 6 met criteria for MDD and 1 for MDD plus dysthymia. Three responders also met DSM-IV criteria for an anxiety disorder (1 social phobia, 1 panic disorder and 1 obsessive-compulsive disorder). Two nonresponders met criteria for panic disorder.

Procedures

Patients were initially tested during a baseline session after being unmedicated for a minimum of 7 days (6 weeks if receiving fluoxetine), but most patients were drug-free for considerably longer. Four responders and 4 nonresponders were not previously treated with an antidepressant, and 3 responders and 2 nonresponders had not received an antidepressant for over 8 months. All patients were retested at end of the 12^{th} week of fluoxetine treatment using the same procedures as the baseline session. Resting EEG was recorded while subjects sat quietly in a sound-attenuated booth. EEGs were recorded during four 2-min periods, half with eyes open (O) and half with eyes closed (C) in a counterbalanced order (OCCO or COOC). Subjects were instructed to remain still and to avoid blinks or eye movements during the recording period. During the O condition, subjects fixated on a central cross.

Electrophysiologic Recording

Scalp EEG was recorded using a 30 channel electrode cap (Electro Cap International, Eaton, OH) with a nose reference. Ag/AgCl electrodes (Grass, West Warwick, RI) at supra- and infraorbital sites surrounding the right eye were used to monitor eye blinks and vertical eye movements (bipolar), and electrodes at right and left outer canthi monitored horizontal eye movements (bipolar). All electrode impedances were below 5 KΩ. EEGs were recorded through a Grass Neurodata (West Warwick, RI) acquisition system at a gain of 10 K (5 K and 2 K for horizontal and vertical eye channels), with a bandpass of 0.1–30 Hz. A PC-based EEG acquisition system (NeuroScan, Sterling, VA) acquired and digitized the data continuously at 200 samples/sec over each recording period.

Electrophysiologic Analyses

Data were segmented into consecutive 1.28-sec epochs (50% overlap) yielding a frequency resolution of 0.78 Hz. Epochs contaminated by blinks, eye movements, and movement-related artifacts were excluded from analyses by direct visual inspection of the raw data. The DC offset of each epoch was then removed, and the EEG was tapered over the entire 1.28 sec using a Hanning window to suppress spectral side lobes (27). By overlapping epochs by 50% the attenuated data are restored in the adjacent record, preserving data with minimal redundancy. EEG data were subjected to a power spectrum analysis using a Fast-Fourier Transform. At each electrode, alpha power was averaged for artifact-free epochs spanning each recording period for each subject, and subsequently integrated over 7.8 – 12.5 Hz. Common logarithms of alpha power were computed to normalize the data. Secondary analyses also examined group differences in theta power (4–7 Hz). There was a difference among groups in total number of minutes of artifact-free EEG data ($F=3.31$, $df=2,33$, $p<.05$). Normal controls (Mean=3.4±1.1) had fewer minutes of EEG than responders (Mean=4.8±2.1; $p<.05$), but there was no significant difference between responders and nonresponders (Mean=4.3±1.0). However, number of minutes of EEG was not significantly related to either alpha power ($r= .22$, ns) or asymmetry ($r= -.14$, ns).

Statistical Analyses

Analyses focused on alpha because of its inverse relation to cortical activity (28) and prior findings of differences between antidepressant responders and nonresponders. Previous EEG studies have indicated the importance of regional (e.g., anterior vs. posterior) and hemispheric (left vs. right) differences when comparing alpha in depressed and nondepressed subjects. To

examine these regional differences, log alpha power during pretreatment session was computed at medial sites over each hemisphere at frontal (left, F3; right, F4), central (C3; C4), parietal (P3; P4), and occipital (O1;O2) regions. These topographic measures were then used as orthogonal factors in a repeated-measures ANOVA, using three within-subject factors: Hemisphere (left, right), Region (F, C, P, O), and Condition (eyes open, eyes closed), and one between-subjects factor: Group (responder, nonresponder, controls). The sources of significant interactions were further examined by analysis of simple effects. *F* ratios were evaluated using degrees of freedom computed using the Greenhouse–Geisser ε correction (29) where appropriate to counteract heterogeneity of variance– covariance matrices associated with repeated measures. The same ANOVA model was also used to examine theta power. To determine whether pretreatment differences in alpha between responders and nonresponders remained stable or changed following fluoxetine treatment, a repeated-measures ANOVA was performed on log alpha power at occipital sites, where pretreatment differences were maximum. This ANOVA used three within-subject factors: Hemisphere (left, right), Condition (eyes open, eyes closed), and session (pretreatment, fluoxetine), and one between-subjects factor: Group (responder, nonresponder).

Results

Pretreatment session in responders, nonresponders and controls

There was a difference in overall alpha power among groups (F=3.19, df=2,33, p=.05), with responders having significantly greater alpha when compared to controls (p=.02). The enhanced alpha in responders was most evident at posterior sites where alpha is typically largest (see Figure 1). When separately examined at frontal, central, parietal and occipital regions, the difference in alpha among groups was significant only at occipital sites (F= 3.51, df=2,33, p=.04). Responders had significantly greater alpha when compared to controls (p=.02) at occipital sites and also tended to have greater alpha than nonresponders (p=.06) (see top portion of Figure 2). Although only approaching a conventional level of significance, the alpha difference between responders and nonresponders had a relatively large effect size of 0.98. There was also a trend for the predicted difference in alpha asymmetry among groups at occipital sites (Group by Hemisphere interaction, F=2.68, df=2,33, p=.08). Responders differed significantly from nonresponders in alpha asymmetry (p=.02), with responders showing greater alpha (less activity) over right than left occipital sites and nonresponders tending to show the opposite asymmetry (see bottom of Figure 2). Healthy controls had essentially no alpha asymmetry and did not differ significantly from either patient group.

There was also a difference among the responder, nonresponder and control groups in theta power at occipital sites (F=3.26, df= 2,33, p=.05). Responders had greater theta power (Mean= .29±.22) when compared to controls (Mean= .13±.18; p=.02), whereas nonresponders (Mean= .25±.20) did not differ significantly from the other groups. The difference in theta between responders and controls was also significant at the midline occipital site (p=.02), but not at other midline sites. Although there was a difference in theta across left and right occipital sites (F= 6.88, df=1,33, p=.01), there was no significant group difference in the theta asymmetry.

Pretreatment versus Fluoxetine Treatment Sessions in responders and nonresponders

At occipital sites, where group differences in alpha were most evident, responders tended to have greater alpha power than nonresponders across the pre and post treatment sessions (see Figure 3; F= 3.85, df=1,16, p=.07). There was no significant change in alpha power across sessions and the difference in alpha between responders and nonresponders did not change (i.e., no Group by Session interaction). There was a Group by Hemisphere interaction (F= 6.66, df=1,16, p=.02), with responders showing greater alpha (less activity) over right than left occipital site (F= 5.09, df= 1,16, p=.04) and nonresponders showing a nonsignificant

asymmetry in opposite direction. This group difference in occipital asymmetry did not change across sessions, which is indicated by the lack of a Group by Hemisphere by Session interaction. There was a significant difference in occipital alpha asymmetry in both pretreatment (F=6.16, df=1,16, p= .02) and fluoxetine treatment (F=5.83, df= 1,16, p=.03) sessions. Test-retest correlations confirmed that alpha power was extremely stable across pretreatment and fluoxetine treatment sessions, ranging from r=.92 at frontal to .97 at occipital sites. Test-retest correlations were lower for alpha asymmetry, being .63 at frontal, .56 at central, .73 at parietal, and .86 at occipital sites.

Prediction of Treatment Response

We examined the value of alpha power and asymmetry at occipital sites for predicting treatment response. As in our prior studies, we used the mean asymmetry for healthy controls (Figure 2) as a cutoff to divide patients into those having alpha asymmetry greater than normal (predicted to be responders) or less than normal (predicted to be nonresponders). Similarly, we used mean alpha power for healthy controls as a cutoff for dividing patients into those with greater or less than normal alpha. Indices evaluating predictions of treatment response are given in Table 2. Both alpha power and asymmetry showed reasonable positive predictive value (i.e., response rate of 72.7 % and 77.8 % for patients predicted to be responders), but less negative predictive value (i.e., nonresponse rate of 57.1 % and 55.6 % for patients who were predicted to be nonresponders). Although alpha power and asymmetry were positively correlated (r=.34, p=.04), the small magnitude of this correlation suggests that each provides somewhat independent information for predicting treatment response. We therefore evaluated whether combined use of both would improve the predictive value. In two-thirds of the patients, there was agreement as to the prediction of treatment response across the alpha power and asymmetry measures (i.e., both above vs. below normal). In these cases, using agreement across measures improved the sensitivity and negative predictive value to 83.3 % and 80.0 %.

Right-Handed Responders, Nonresponders and Controls

Although there were too few left-handed patients to allow meaningful conclusions as to the impact of handedness (Figure 2), a comparison was made of the data for only right-handed responders, nonresponders and controls. Overall, all findings reported for the full samples were as strong or stronger for right handers only. Thus, there was a significant difference among groups in alpha power (F=5.50, df= 2,28, p<.01), with responders having greater alpha when compared to both nonresponders (p=.04) and controls (p<.01). Group differences in alpha were present at only occipital sites (Figure 2 top; F= 4.56, df= 2,28, p=.02), where responders had greater alpha than nonresponders (p=.05) and controls (p=.02). At these sites, responders also differed from nonresponders in alpha asymmetry (Figure 2 bottom; F= 5.65, df= 1,11, p=.04). At occipital sites, the same group difference in theta power evident for the full samples was seen for right handers (F=3.54, df= 2,28, p=.04). Responders had greater theta than controls (p=.01), but did not differ significantly from nonresponders.

Discussion

Patients who responded to fluoxentine had greater EEG alpha when compared to healthy controls, whereas nonresponders did not differ from controls. An excess of alpha has previously been reported for patients having an obsessive-compulsive disorder who responded to an SSRI (14) and in affectively-disordered patients who responded to treatment with an antidepressant or secondary treatment with an anticonvulsant or lithium (13,30). Early studies of resting EEG reported finding greater alpha with eyes closed in depressed patients when compared to controls (31,32). Given the inverse relation of alpha power and cortical activity, increased alpha was viewed as evidence of reduced activity in depressed patients. Our findings indicate that this reduced cortical activity is evident in a subgroup of depressed patients who respond to an SSRI

and is a predictor of those who most benefit from this treatment. This may not, however, be specific to SSRI antidepressants, in that depressed patients who responded to tricyclic antidepressants also showed increased alpha (13,15). In contrast, decreased alpha has been found to be predictive of improvement in mood following cognitive restructuring (23). The increase in occipital power in fluoxetine responders was also found in the theta band, which suggests that this qEEG difference is not specific to alpha, but includes somewhat lower frequencies as well. It is noteworthy that a distinct spectral component with a peak that spans both the alpha and theta bands is identifiable in the resting EEG using a reference-free approach (17).

SSRI responders also differed from nonresponders in their alpha asymmetry, which is in accord with our prior findings (8). At occipital sites, where alpha is largest, responders showed an asymmetry indicative of greater activity over left than right hemisphere, whereas nonresponders had the opposite direction of asymmetry. The favoring of left over right hemisphere activity in responders is the asymmetry seen for patients having a “pure” MDD in EEG studies (33,34) and SSRI responders in dichotic listening studies (5). Although the specificity of the posterior alpha asymmetry to SSRI responders is unknown, alpha asymmetry at frontal but not posterior sites predicted mood improvement following cognitive restructuring (23). In the present study, frontal alpha asymmetry did not differ between fluoxetine responders and nonresponders.

Neither alpha power nor asymmetry changed following 12 weeks of treatment with fluoxetine. The extremely high test-retest correlations for alpha power in depressed patients ($r \geq .90$) are comparable to those previously reported for healthy adults for retest periods over one year, and twin studies indicate that alpha power is a stable, heritable trait (20). Elevated alpha power has been found in recovered depressed patients in a euthymic state, which led Pollock and Schneider (35) to hypothesize that it reflects a trait difference in a subgroup of depressed patients. Our findings suggest that this trait is present in patients who respond favorably to an SSRI.

Although there was no significant change in alpha asymmetry after 12 weeks of treatment, test-retest correlations were lower than seen for alpha amplitude, but were still moderately high ($r = .56$ to $.86$), particularly at occipital sites. Test-retest correlations in healthy adults are also lower for alpha asymmetry than alpha power, with about 60% of the variance of alpha asymmetry attributed to a temporally stable trait (21). The alpha asymmetry in SSRI responders at occipital sites has been found in depressed adolescents and adults (33,34,36,37), in remitted depressed patients (38), and in offspring of parents concordant for MDD who have increased risk for developing a depressive disorder (39). This alpha asymmetry may therefore be a trait marker of vulnerability to a familial form of depression that responds to an SSRI.

It is known that serotonergic activity is closely related to arousal. In an awake state, serotoneric cells in raphé nuclei display a constant pattern of discharge that decreases in firing rate as arousal decreases to a sleep state (40). We hypothesize that increased alpha in depressed patients who respond to an SSRI reflects low arousal associated with low serotonergic activity. Evidence for the role of right temporoparietal and subcortical regions in mediating arousal (41,42) suggests a possible mechanism that could account not only for increased alpha in SSRI responders, but also their alpha asymmetry. Heller *et al.* (42) presented a model suggesting that depression is related to dysfunction of right temporoparietal mechanisms mediating emotional arousal. Thus, low serotonergic activity, presumably related to reduced activity of mesencephalic raphé nuclei and cortical afferents, could play a role in both the increased alpha and alpha asymmetry in SSRI responders.

A question remains as to why clinical improvement in SSRI responders did not normalize their alpha. Although a common serotonergic mechanism may underlie both depression and EEG abnormalities in responders, they need not have the same pharmacological properties. A preclinical study (44) found that spontaneous firing of serotonin neurons in dorsal raphé of rats was not altered after two weeks of escitalopram administration, whereas combined treatment with this SSRI plus bupropion resulted in a marked increase in firing rates. Moreover, persistence of alpha abnormalities in treatment responders is compatible with their being an endophenotyic marker of vulnerability to MDD (39).

This study has limitations. First, the sample of SSRI nonresponders was small (n=7). It was, however, larger in our prior study (8) and the difference in alpha asymmetry between fluoxetine responders (n=34) and nonresponders (n=19) was the same as the present study. Also, heightened alpha in responders (n=11) was seen not only when compared to nonresponders, but also compared to healthy controls (n=18). The stability of differences between responders and nonresponders across pre and post treatment sessions also increases confidence in the findings. A second limitation is that patients in this study were predominately men, which may raise a question as to whether findings generalize to women. The number of women was larger in our prior studies (5,8) and the difference in hemispheric asymmetry between responders and nonresponders was even stronger among women than men. Third, the EEG findings were obtained during open-label treatment and placebo effects are unknown. In a study in which a placebo control group was included (43), we found no difference between placebo responders and nonresponders in hemispheric asymmetry for dichotic listening. Lastly, although differences between responders and nonresponders in alpha power and asymmetry appear to represent stable, state-independent traits, their biological basis is unknown. An ongoing study is using a high-density electrode array and current source density measures (17) to provide spatial resolution to more adequately address the neuroanatomical origin of these differences. Studies are also needed to determine their relation to genetic and neurochemical mechanisms that may underlie responsiveness to antidepressants. The findings do raise hopes for developing qEEG tests for selecting effective treatments for depressed patients.

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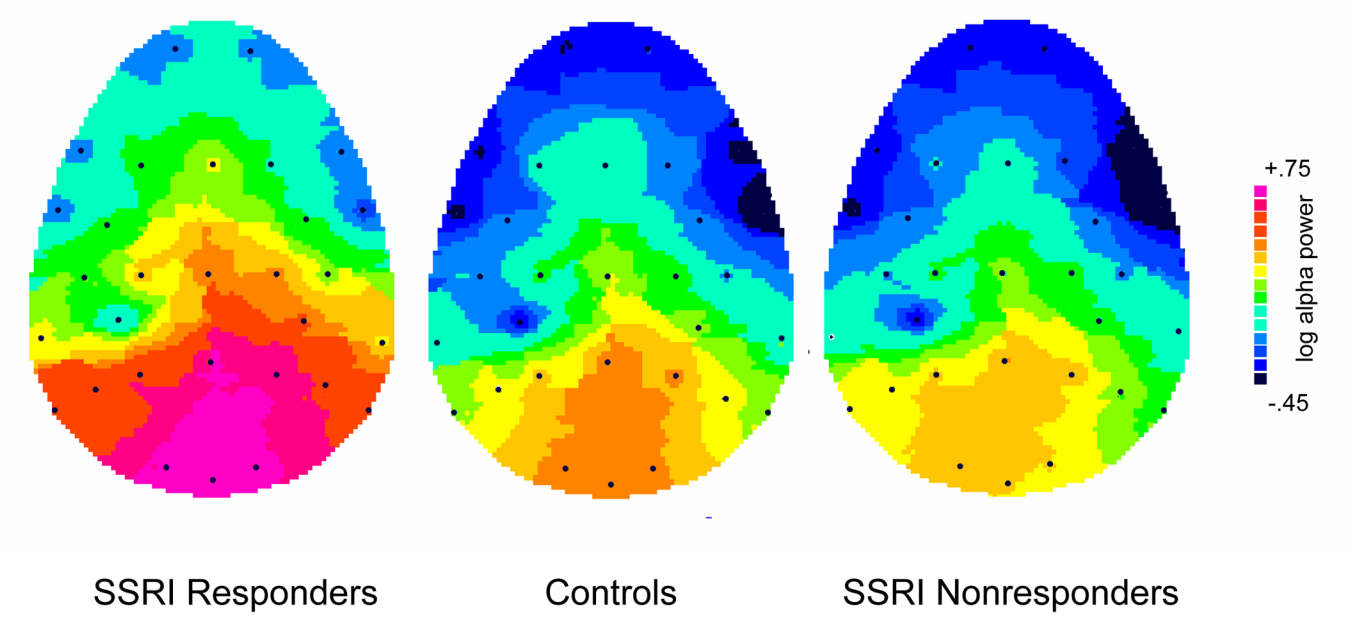

Figure 1.
Topography of pretreatment alpha power for responders, nonresponders, and healthy controls, illustrating that group differences in alpha are most evident over posterior sites (bottom portion of maps).

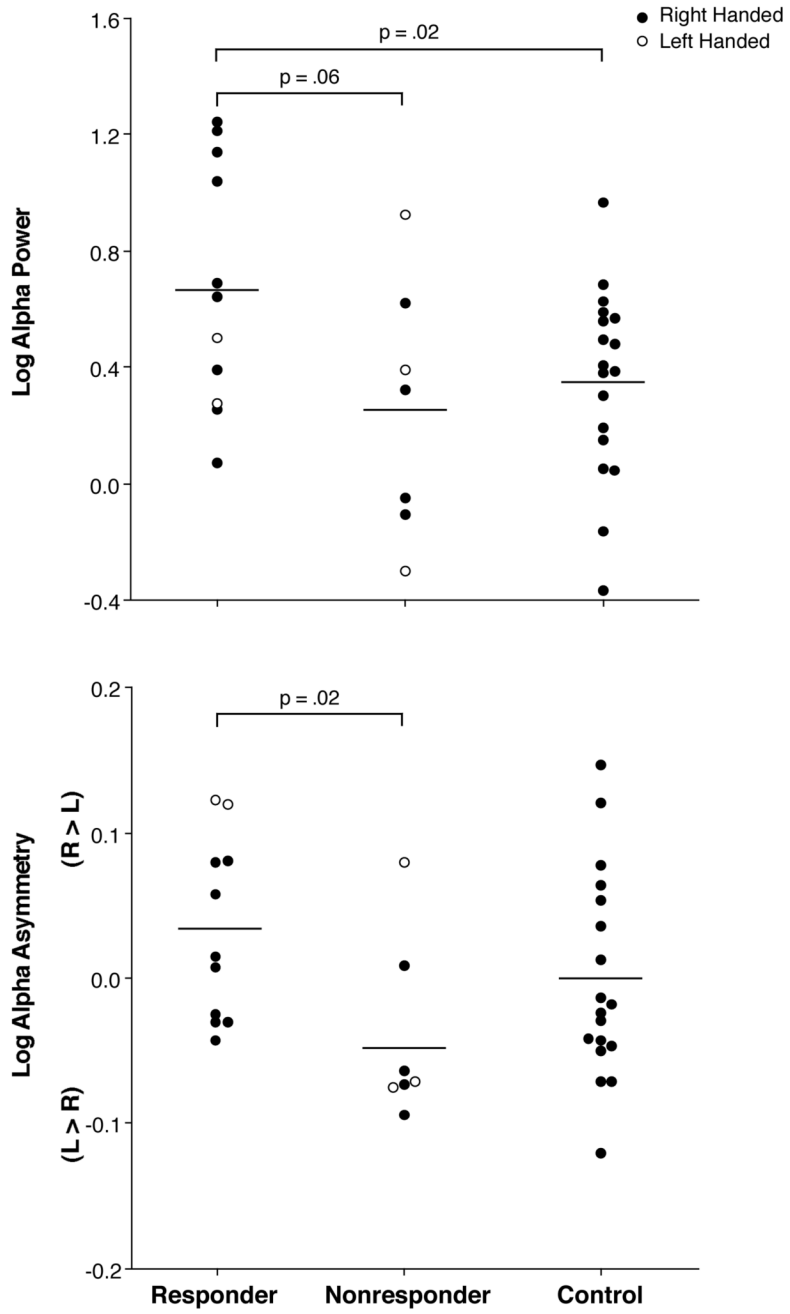

Figure 2.
Log alpha power and asymmetry for the responders, nonresponders and healthy controls.

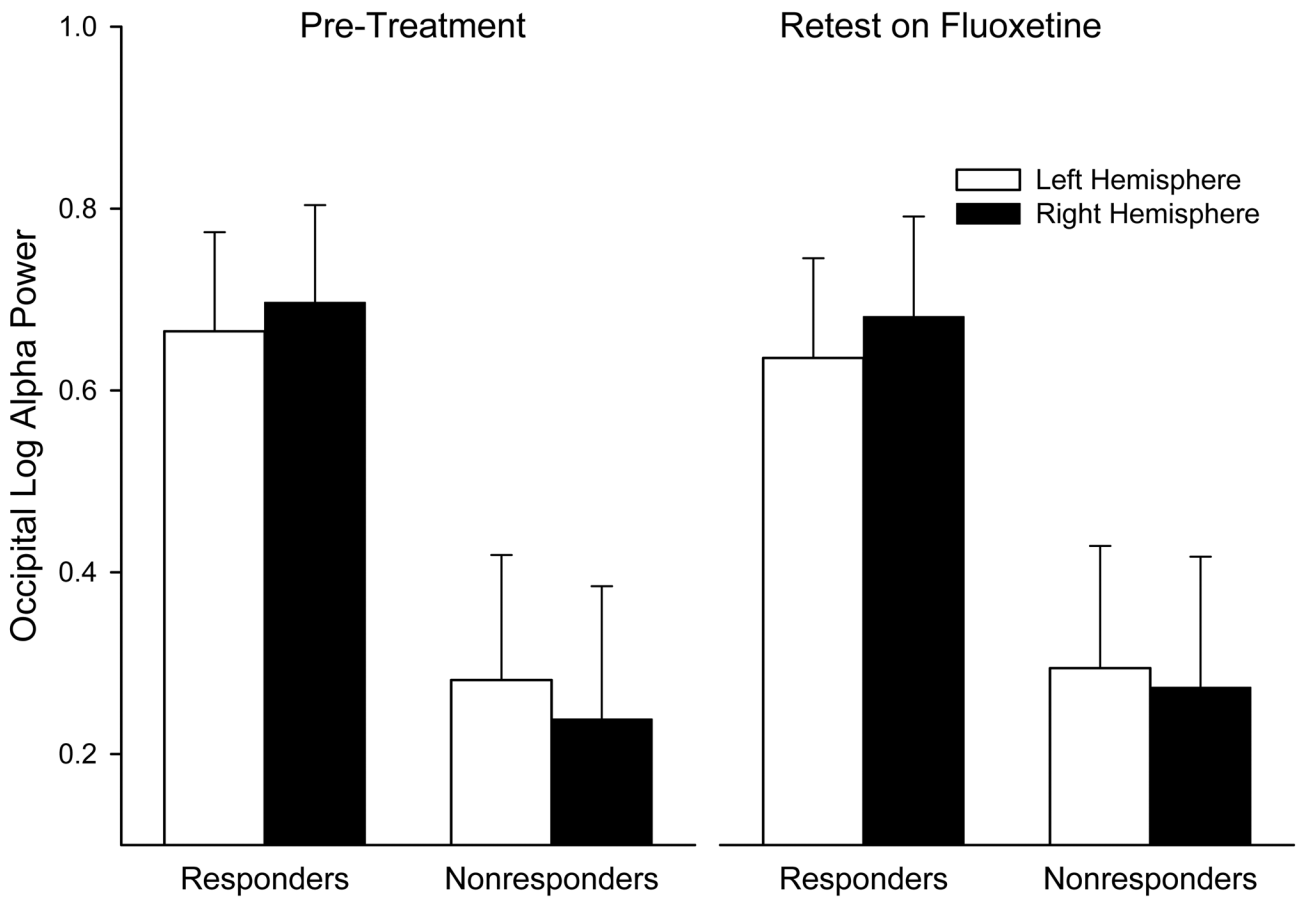

Figure 3.
Mean log alpha power over right and left hemisphere for responders and nonresponders before treatment and after 12 weeks on fluoxetine (bars= standard errors).

Table 1

Characteristics of Treatment Responders, Nonresponders and Healthy Controls

	Responders	Nonresponders	Controls
Gender			
M/F	7/4	6/1	13/5
Age (years)			
M	38.0	33.7	31.7
SD	9.4	9.7	7.6
Education (years)[a]			
M	16.5	13.4	15.5
SD	2.6	1.6	1.8
Handedness (Laterality Quotient)			
M	61.8	19.7	72.9
SD	64.5	91.1	19.9
Pretreatment HAM-D			
M	19.0	19.7	
SD	2.1	6.6	
Post-Treatment HAM-D[b]			
M	5.4	15.4	
SD	2.5	8.6	

[a] N = 10 for responders. Significant difference among groups in education ($F = 4.27$, $df = 2, 32$, $p < .05$). Newman-Keuls post-hoc test, nonresponders < responders = controls.

[b] Responders differ significantly from nonresponders in post-treatment HAM-D ($t = 3.57$, $df = 16$, $p < .01$).

Table 2

Indices Evaluating Predictions of Response Using Log Alpha Power and Log Alpha Asymmetry at Occipital Sites

	Alpha Power	Alpha Asymmetry	Combined
Sensitivity [a]	72.7	63.6	83.3
Specificity [b]	57.5	71.4	67.7
Positive predictive value [c]	72.7	77.8	71.4
Negative predictive value [d]	57.1	55.6	80.0

[a] Sensitivity = percentage of responders who were predicted to be responders.

[b] Specificity = percentage of nonresponders who were predicted to be nonresponders.

[c] Positive predictive value = response rate for patients who were predicted to be responders.

[d] Negative predictive value = nonresponse rate for patients who were predicted to be nonresponders.