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EEG Alpha as a Predictor of Response to an SSRI Antidepressant

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Abstract

The present study examined pretreatment differences in regional hemispheric activity among depressed patients who did or did not respond to an SSRI antidepressant and healthy controls. Resting EEG (eyes open and closed; nose reference) was recorded from 28 electrodes (plus eye channels) in 18 depressed patients (13 male; 20-56 years old; 12 treatment responders) when off medication and 18 healthy controls (13 male; 19-56 years old). Clinical response to 12 weeks of fluoxetine treatment was assessed using the CGI-I. Treatment responders had significantly greater alpha power (less activity) when compared to either nonresponders or controls. There was also an overall group by hemisphere interaction, with nonresponders showing greater activity (less alpha) over right than left hemisphere, while responders tended to have the opposite asymmetry. The opposite direction of alpha asymmetry in treatment responders and nonresponders was particularly striking over parietal and occipital sites. Using median values for controls as the cutoff, both alpha asymmetry and amplitude at posterior sites were significantly predictive of clinical response to fluoxetine. The findings replicate our prior study (Bruder et al., 2001) and suggest the potential value of EEG measures of regional hemispheric asymmetry as predictors of therapeutic response to an SSRI antidepressant.

Introduction

In our prior study (Bruder et al., 2001), depressed patients who responded to the SSRI antidepressant fluoxetine (Prozac) differed from treatment nonresponders in pretreatment EEG measures of alpha asymmetry . The present study examined the value of EEG alpha asymmetry and amplitude for predicting clinical response to treatment with fluoxetine.

Participants

N=36	Responders (n = 12)	Nonresponders (n = 6)	Controls (n = 18)
Gender (male/female)	8 / 4	5 / 1	13 / 5
Age (years)	31.2 ± 9.82 (21 – 50)	28.67 ± 13.9 (20 – 56)	31.94 ± 9.8 (19 – 56)
Education (years)	16.2 ± 2.7 (13 – 22)	13.5 ± 1.8 (12 – 16)	15.5 ± 1.85 (12 – 18)
Handedness (EHI)	50.0 ± 73.87 (-80.0 – 100.0)	36.6 ± 87.36 (-81.82 – 100.0)	72.9 ± 19.9 (30 – 100.0)
Hamilton Rating @ Baseline	19.3 ± 3.58 (12 – 26)	22.5 ± 6.47 (12 – 32)	

Methods

***Subjects*:** *N = 18* clinically depressed outpatients were divided into two groups (*n = 12* Responders and *n = 6* Nonresponders) on basis of their treatment outcome after 12 weeks of fluoxetine treatment, as assessed by an independent evaluator using The Clinical Global Impression Improvement Scale (CGI-I). Patients were free of medication for a minimum of one week before the EEG was recorded. A sample of 18 healthy controls was also tested.

Recordings: Resting 30-channel EEG from four 2-minute time periods (order of eyes open/closed counterbalanced as OCCO or COOC across subjects), referenced to nose tip (Grass, 10k gain; 0.1-30Hz band pass; recording using NeuroScan at 200 samples/s); vertical and horizontal EOG recorded differentially.

Signal Processing: Data were segmented into 1.28 s epochs (50% overlap), yielding a frequency resolution of 0.78 Hz; artifactual data eliminated from epoched data under visual guidance (semi-automated procedure).

Spectral Analysis: Hanning window (50%) applied to each EEG epoch; mean Power Spectra computed across epochs for each condition (i.e., eyes open/closed). Alpha power was averaged across 7.8Hz-12.5Hz after verifying the appropriateness of this frequency band for alpha activity in both groups (Responder/Nonresponder) and conditions (eyes open/closed).

Statistics: Effects were evaluated using an ANOVA with Group (Responder/Nonresponder) as a between-subjects factor, and Hemisphere (right/left) and/or electrode Site as within-subjects factors (Greenhouse-Geisser correction where appropriate).

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Average Alpha Power Spectra

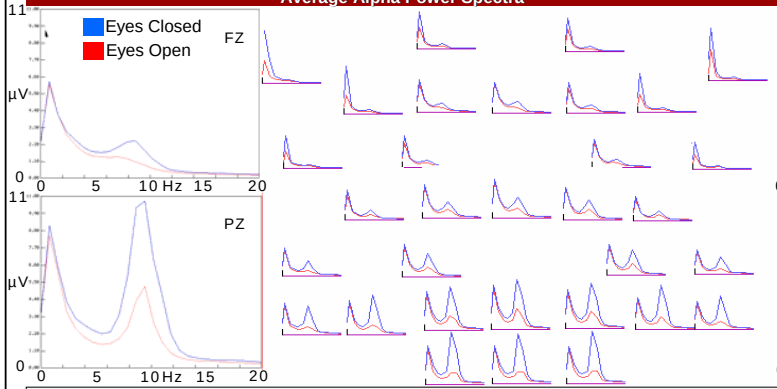

Fig 1. Resting EEG power spectra for eyes open and closed conditions across response groups. The topographic and spectral specificity is characteristic of condition-dependent alpha. (Peak in alpha band greatest for eyes closed; posterior topography.)

Average Alpha Power Spectra

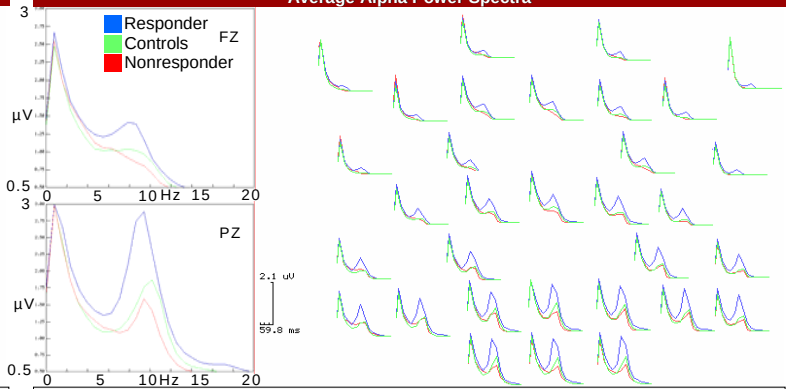

Fig 2.. Alpha levels differed significantly among groups with Responders having the largest alpha amplitude and Nonresponders the smallest.

Differences in Log Alpha Power

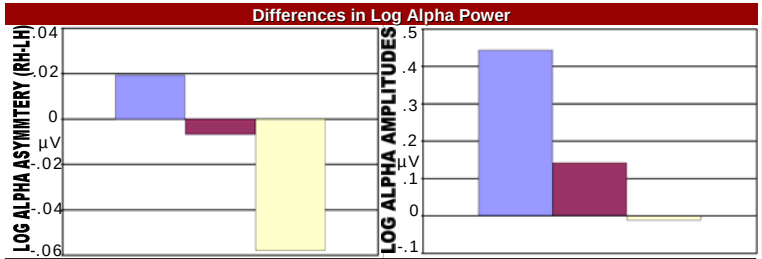

Fig 3. Log alpha asymmetries at medial sites differed significantly for responders, controls, and nonresponders.

Fig 4. Log alpha amplitudes at medial sites differed significantly for responders, controls, and nonresponders.

Average Alpha Amplitude Spectra Topographic Maps

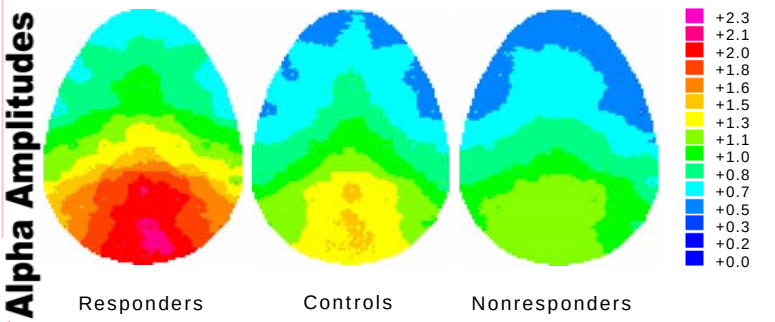

Fig. 6. Alpha levels between groups differed significantly with Responders showing the largest alpha levels and nonresponders with the smallest amount of alpha.

Asymmetries at Medial Electrode Pairs

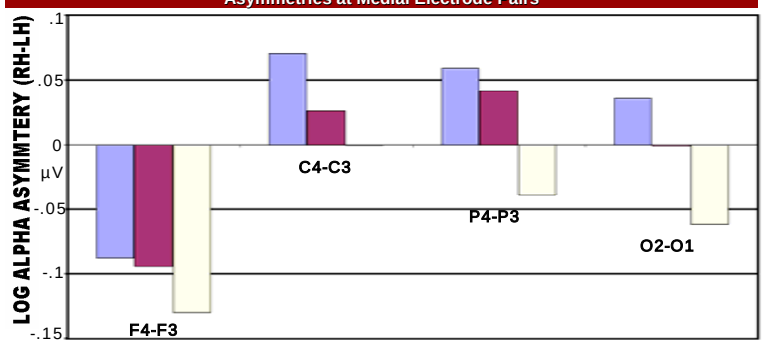

Fig 5. Log alpha asymmetries at medial electrode sites for responders, controls, and nonresponders. Alpha asymmetry differed significantly among groups at posterior sites (P4-P3, O2-O1).

Responder and NonResponder Chi Square Split By Median Control

	Frontal RH-LH		Central RH-LH		Parietal RH-LH		Occipital RH-LH	
	RESP	NONRES	RESP	NONRES	RESP	NONRES	RESP	NONRES
>Median	5	2	10	2	9	1	8	1
<Median	7	4	2	4	3	5	4	5
Value	.117	NS	4.500	p<.05*	5.513	p<.05*	4.000	p<.05*
	Frontal Amplitude		Central Amplitude		Parietal Amplitude		Occipital Amplitude	
	RESP	NONRES	RESP	NONRES	RESP	NONRES	RESP	NONRES
>Median	10	3	8	2	9	3	8	1
<Median	2	3	4	4	3	3	4	5
Value	2.215	NS	1.800	NS	1.125	NS	4.000	p<.05*

Fig 7. Chi Square split by median control demonstrates prediction of treatment outcome by significant hemispheric differences at Central, Parietal, and Occipital medial electrode sites. In addition a Chi Square of responders and nonresponders split by median control demonstrates similar levels of treatment prediction for occipital amplitude differences.

Results

1) **Alpha power differed significantly across groups** (group F(1,33)=5.54 p<.01). There was also an overall **group by hemisphere interaction** between responders, nonresponders, and controls (group F(2,33)=3.55 p=<.05.

2) **Responders had greater overall alpha power** compared to controls (Fig. 4, group F(1,28)=7.48 p=.01) and nonresponders (group F(1,16)=6.76 p=.02). There was no significant difference between controls and responders.

3)There was a **group by hemisphere interaction**, with nonresponders showing overall greater activity (less alpha) over right than left hemisphere while responders do not (Fig.3, F(1,16)=8.95 p<.01).

4) **At posterior sites** (where alpha is well-defined) responders showed less activity (greater alpha) over right than left hemisphere sites, whereas **nonresponders showed the opposite asymmetry** (Fig. 5, Simple effects for parietal: Group x Hemisphere F(1,16)=15.57 p<.01; Occipital: Group x Hemisphere F(1,16)=13 p<.01).

5) All groups showed **greater activity (less alpha) over right than left frontal sites** (Fig. 5, Simple effects for Frontal: Hemisphere F(1,33)=12.84 p<.01; no group interaction).

Conclusion

1) Patients who responded to fluoxetine showed greater alpha power when compared to controls and nonresponders.
2) As in our prior study (Bruder et al. 2001), nonresponders showed an alpha asymmetry indicative of overall greater activity over the right than left hemisphere, whereas responders tended to show the opposite asymmetry particularly at posterior sites.
3) When patients were classified according to control medians for alpha amplitude and asymmetry, both measures of posterior alpha were predictive of clinical response.

Acknowledgements

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