AN ALTERNATIVE TREATMENT FOR DEPRESSION USING EEG BIOFEEDBACK TO ALTER FRONTAL ALPHA ASYMMETRY AND IMPROVE MOOD

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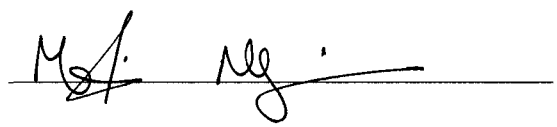
SIGNED: 

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ABSTRACT

The relationship between frontal EEG asymmetry and emotional reactivity is well established in the literature and there is some evidence of a causal link between the two variables (e.g., Allen et al., 2001). EEG biofeedback has been shown to improve depressive symptoms in clinical populations (e.g., Baehr et al., 1997 and Earnest 1999), however concurrent participation in other forms of treatment limits their conclusions. The present study was a double-blind clinical trial of a noninvasive alternative treatment for depression using EEG biofeedback of frontal alpha asymmetry and, of the19 right-handed participants who were randomly assigned to receive contingent or noncontingent biofeedback, only seven completed three sessions per week for 12 weeks. Since only one participant in the noncontingent group completed all 36 sessions, group comparisons were not conducted. Although self-reported depression as determined by HRSD and BDI scores improved over time, this was independent of biofeedback training, because EEG biofeedback did not produce significant changes in frontal alpha asymmetry. In addition, there were no significant within-subjects correlations between asymmetry and BDI score or target value and BDI score.

INTRODUCTION

Major depression was found to be the most common psychiatric disorder in a National Comorbidity Survey, with more than 17% of the respondents reporting a history of a major depressive episode in their lifetime and more than 10% having an episode in the past 12 months (Kessler, McGonagel, Zhao, et al., 1994). The lifetime prevalence of major depression was almost twice in women (21%) as it was in men (12%), and the point prevalence for major depression was approximately 13% for women and 8% for men (Kessler et al., 1994). Given these statistics, it is necessary to continue investigating promising treatments for depression because, although existing treatments for depression are widely available, many individuals are left without lasting relief from depression. While both pharmacological and psychotherapeutic interventions alleviate depression in 50-70% of treatment completers (Elkin et al. 1989), they fail to provide lasting relief for a notable proportion of depressed individuals. Dropout rates are about 32% among patients receiving nonplacebo psychological or pharmacological treatment (Elkin et al., 1989); furthermore, when factoring in those who fail to complete and those who complete but fail to respond to treatment, 47-64% of all patients entering treatment fail to recover. For this relatively large proportion of noncompleters and nonresponders, alternative treatment options are very important.

A recent United-States population survey further documents the importance of alternative treatments for depression. In this survey, depression was one of the ten most frequently reported medical problems and over a third of persons with depression sought alternative treatments often in combination with traditional treatments (Eisenberg,

Kessler, Foster, et al., 1993). The present study therefore involved a small-scale efficacy trial of a noninvasive treatment that, though promising, has not been adequately tested in depression. The aim of this study was to determine whether the efficacy of manipulating frontal brain electroencephalographic (EEG) activity is sufficient to warrant a larger trial.

Previous investigations of EEG have recognized a pattern of asymmetrical frontal brain activity that may be associated with depression and with emotional reactivity related to the risk for depression. Individual differences in baseline resting frontal brain activity appear to be associated to variations in affective reactivity in both infants (e.g., Davidson & Fox, 1989) and adults (e.g., Davidson & Tomarken, 1989). In a recent review of research involving frontal EEG asymmetry Coan and Allen (2003) found that frontal asymmetry reveals considerable trait stability, but that also it is amenable to shifts in affective state. Alterations in frontal EEG asymmetry are observed with changes in emotional states, it is therefore possible that manipulating frontal brain asymmetry may generate changes in emotional state.

Frontal EEG Asymmetry, Emotion, and Depression

Evidence that resting frontal brain activity[1] predicts affective reactivity is substantiated in several studies that highlight the nature of this relationship. In infants, Davidson and Fox (1989) found that 10-month-old infants with reduced left-sided and increased right-sided prefrontal activity were more likely to cry in response to maternal separation. Also, Dawson and colleagues found lower left frontal activity in infants of

[1] Brain activity is assumed to be the inverse of alpha power, which is typically thought to be 8-13 Hz in adults whereas the alpha band is recorded at lower frequencies such as 6-9 Hz in infants (e.g., Dawson, et al., 1992).

depressed mothers, and the pattern of left hypoactivity remained constant while the infants were at rest, as they interacted with their mothers, and as they interacted with other adults (Dawson, Frey, Panagiotides, Yamada, Hessl, & Osterling, 1999). In adults, Wheeler, Davidson, and Tomarken (1993) found that greater left prefrontal activity predicted larger positive affective responses and greater right prefrontal activity predicted larger negative affective responses to emotional film clips. These individual differences in frontal EEG asymmetry have been postulated to reflect a diathesis to respond to emotionally significant events with distinct affective reactivity, which might, in turn, increase the risk for depression and anxiety (Davidson, 1998).

Several studies have established an association between frontal EEG asymmetry (i.e., relatively greater right frontal activity) and depression (e.g., Henriques & Davidson, 1990, 1991), seasonal affective disorder (Allen, Iacono, Depue, & Arbisi, 1993), and panic disorder (Wiedemann, Pauli, Dengler, Lutzenberger, Birbaumer, & Buchkremer, 1999). Left prefrontal hypoactivity in depressed participants has been found to be a traitlike characteristic, which remains relatively stable despite changes in depression severity (Allen, Urry, Hitt, & Coan, 2004, although see Debener, Beauducel, Nessler, Brocke, Heilemann, & Kayser, 2000 and Reid, Duke, & Allen, 1998), and the hypoactivity is present not only during episode (Allen et al., 1993; Gotlib, Ranganath, & Rosenfeld, 1998; Henriques & Davidson, 1991), but also during remission (Allen et al., 1993; Gotlib et al., 1998; Henriques & Davidson, 1990).

Further evidence of the relationship between depression and left prefrontal function is found in stroke patients. Results from a meta-analytic study conducted by

Narashima, Kosier, and Robinson (2003) illustrated that the severity of depression in left hemisphere stroke patients is inversely correlated with the distance of the lesion from the frontal pole. Davidson (1998) has appropriately inferred that the pattern of reduced activity in the left prefrontal cortex is a neural representation of anhedonia, loss of interest, and a general reduction in goal-directed activity. For example, depressed patients, unlike control participants, responded less to rewards, yet they were as responsive to punishment as normal controls (Henriques, Glowacki, & Davidson, 1994). Davidson (1998) deduced that depression was related to a deficient prefrontal component of the approach system and explained that this system is thought to be related to the positive affect generated as one is close to achieving a goal, prior to the attainment of the goal, as opposed to the happiness following goal accomplishment. The approach-withdrawal notion of asymmetry indicates that relative left frontal activity is related to increased appetitive motivation and heightened interaction with the environment, whereas relative right frontal activity is associated with the predisposition to withdraw from presumably dangerous stimuli (e.g., Henriques & Davidson, 1991).

In addition to the direct relationship of frontal EEG asymmetry to emotion-related psychopathology, differences in affective style have been related to an individual's temperament (Kagan, Reznick, & Snidman, 1988) and personality (Gross, Sutton, & Ketelaar, 1998). Schmidt (1999) found that students who scored high on a measure of shyness exhibited relatively greater right frontal activity, as opposed to those scoring high on a measure of sociability who exhibited relatively greater left frontal activity. Temperament, in turn, has been found to affect emotional reactivity and the development

of psychopathology (e.g., Depue & Iacono, 1989; Fowles, 1987). Researchers have described biobehavioral models considering three essential motivational systems: the behavioral activation system (BAS), the behavioral inhibition system (BIS), and the fight-flight system. A person with a deficiency in any of these systems has been thought to be more prone to psychopathology when given pertinent stimuli (Harmon-Jones & Allen, 1997). For example, individuals exhibiting high levels of BIS are thought to be more likely to develop anxiety disorders, and individuals presenting low levels of BAS are assumed to be predisposed to certain types of depression (Harmon-Jones & Allen, 1997). Among participants administered the BIS/BAS scales (Carver & White, 1994), participants with more left-sided prefrontal activity reported higher BAS levels compared with those demonstrating greater right-sided prefrontal activity (Coan & Allen, 2003; Harmon-Jones & Allen, 1997; Sutton & Davidson, 1997). Based on these findings, Harmon-Jones and Allen (1997) concluded that the anterior EEG asymmetry might tap approach-related motivation that is also indexed by BAS scores.

Frontal EEG asymmetry characterized by reduced left-versus-right activity appears related to a tendency to respond with decreased approach motivation, and may suggest a diathesis toward depression. The correlation between emotion and frontal EEG asymmetry has been observed both in cases where individuals' EEG predicts their affective reactivity and also when individuals' affective reactivity or emotional state has been related to EEG asymmetry. It is therefore possible that alteration of frontal EEG asymmetry may alter how individuals respond emotionally when confronted with emotional provocations. This thus suggests the potential to serve as a treatment for

depression. As mentioned, frontal EEG asymmetry has been observed in depressed individuals during a depressive episode and during remission, however most studies have been correlational and few have attempted to induce change in frontal EEG asymmetry to observe changes in emotional reactivity. An examination of the effects of manipulating frontal asymmetry on depressive symptoms would provide a stronger support for a causal relationship between anterior brain asymmetry and emotional responding. The present study therefore attempted to test this possibility using biofeedback as a tool to alter frontal EEG asymmetry in a depressed community sample.

Biofeedback as a Tool to Alter EEG Asymmetry

Psychophysiologists who studied brain wave activity in the 1960's used biofeedback in an attempt to change human electroencephalographic (EEG) activity, finding that when participants were presented with appropriate auditory information about the alpha rhythm in their EEG, they could be trained to increase or decrease the amount of such activity (e.g., Beatty, 1971, 1972; Kamiya, 1967). On the other hand, Lynch, Paskewitz, and Orne (1974) found that participants receiving contingent feedback and those receiving noncontingent feedback both produced increased levels of alpha in response to visual feedback, compared to resting in the dark. Since there was no effect of biofeedback in participants receiving auditory feedback, Lynch et al. (1974) concluded that increases in alpha density resulted from the experimental situation where participants gradually disinhibited arousal and visual stimulation that normally block alpha activity. Thus, it is essential to hold the experimental environment constant between baseline and biofeedback trials.

Comparatively few studies have investigated biofeedback training of EEG asymmetry per se; i.e., attempting to influence frontal activity such that there is an asymmetrical change. One study examined the effects of biofeedback on asymmetry of frontal slow potentials (Hardman, Gruzelier, Chessman, Jones, Liddiard, Schleichert, & Birbaumer, 1997). Hardman et al. (1997) provided biofeedback training to all participants, and additionally provided half of their participants with emotional strategies, while the other half did not receive any additional guidance. Participants in both groups were trained to increase left frontal activity during some trials and right frontal activity during other trials. Participants in the strategy group did not display a training effect whereas participants in the no strategy group did demonstrate a training effect. The impact of training on emotional reactivity was not assessed.

Baehr, Rosenfeld, and Baehr (1997) conducted a biofeedback treatment study of depression, in conjunction with psychotherapy, by training frontal EEG asymmetry in two patients. MMPI-2 scores indicated a significant reduction in depression and normalization in other factors of the patients' personality structure such as flexibility in thinking and a positive outlook for the future. This study only trained patients to increase relative left frontal activity and not to decrease relative left frontal activity. Similar results were reported by Earnest (1999) who presented a single case study of an adolescent girl receiving biofeedback in conjunction with psychotherapy. Interestingly, the frontal asymmetry scores changed in the direction of relative greater left frontal activity during the last 10 sessions compared to the first 10 sessions of a total of 67 biofeedback sessions. Nevertheless, as Allen, Harmon-Jones, and Cavender (2001)

argued, there remains the possibility that the mere exposure to biofeedback, as opposed to specific effects of the training paradigm on anterior asymmetry, might be the sole influence of the therapeutic effects. Additionally, the biofeedback training was not the only potentially therapeutic activity for these patients, as each was also receiving other treatment aimed at alleviating depression, including psychotherapy and medication.

To illustrate the causal influences of the alteration of anterior EEG asymmetry on responses to emotionally evocative stimuli, Allen et al. (2001) manipulated frontal EEG alpha asymmetry in two directions: increased relative right frontal activity ("RIGHT") and increased relative left activity ("LEFT"). Allen et al. (2001) measured the effects of such training on emotional responding. They found that the direction of biofeedback training appeared to influence subsequent emotional responses, such that participants in the "LEFT" group demonstrated greater positive affect to "happy" films relative to those in the "RIGHT" group. Facial EMG recordings essentially corroborated the self-report data, with participants trained "LEFT" showing a decrease in corrugator activity following training, and with participants trained "RIGHT" showing a decrease in zygomatic activity following training. Results were replicated with a larger effect size on the subsample who responded to the biofeedback manipulations.

A previous study in our laboratory provided biofeedback training based on an asymmetry score corrected for overall activity ([R-L]/[R+L]) in right-handed female participants randomly assigned to receive contingent biofeedback to increase left activity or to receive noncontingent feedback. Each participant in the latter group was presented with the same feedback received by a yoked training participant. Five consecutive days

of biofeedback training provided signals of reward or nonreward depending on whether the difference between right (F4) and left (F3) frontal alpha exceeded a target value or if the pattern across the preceding 3 secs demonstrated consecutive increases toward the target value. Although self-reported affect and facial EMG in response to emotionally evocative film clips showed significant valence-dependent modulation, EEG training effects were largely absent. The failure to obtain changes in asymmetry can possibly be due to one or more of the following procedural alterations: providing multiple reinforcement contingencies may have made learning too complex; correcting R-L for overall power may have made it more difficult to obtain change in asymmetry; or using a yoked group instead of a group trained in the opposite direction may have reduced the between group effect size.

Asymmetrical Manipulation of Frontal Brain Activity in the Treatment of Depression

Further evidence suggesting the promise of asymmetrically manipulating frontal brain activity as a treatment for depression derives from recent studies of the manipulation of brain activity in the frontal cortex using transcranial magnetic stimulation (TMS) (e.g., George, Wasserman, Williams, et al., 1995, 1997; Klein, Kreinin, Chistyakov, et al., 1999). As described by these researchers, TMS produces a localized brief magnetic field in the underlying neural tissue causing depolarization, followed by body movements. Repetitive TMS (rTMS) is a term used to describe TMS pulses that are generated rapidly and repetitively, which generally interfere with information processing in the underlying tissue (George et al., 1999). George et al. (1997) found that high frequency (20 Hz) rTMS over the left prefrontal cortex improved

mood in depressed patients, and Klein et al. (1999) found that low frequency (1 Hz) rTMS over the right prefrontal cortex reduced depressive symptoms in major depression.

The Present Study

The present study involves a small-scale double-blind randomized control trial of asymmetrically manipulating frontal brain activity with biofeedback as a treatment for depression. Although this manipulation holds promise to alter how people respond emotionally, and has been used in several simple unblinded and uncontrolled case studies of depression, no systematic controlled investigation has been conducted. In this controlled trial, participants were randomly assigned to receive biofeedback contingent upon altering their brain activity ("contingent group") or to receive training that was not contingent upon alterations in brain activity, but appeared in all respects identical to the biofeedback training ("noncontingent group"). The only difference between the treatment conditions was the actual manipulation of brain asymmetry; therefore, this design allowed for the assessment of whether manipulating frontal brain asymmetry, per se, produces a therapeutic effect. This design allows for the testing of three specific aims: 1) to determine whether biofeedback training successfully alters frontal brain asymmetry; 2) to determine whether changes in frontal brain asymmetry predict a favorable treatment response, and 3) to examine the within-subjects nature of the relationship between asymmetry and reported mood. As a small scale study, effect sizes were of interest in addition to traditional measures of statistical significance.

METHOD

Participants

Nineteen right-handed individuals from the community participated in the experimental treatment study, of which seven completed the treatment (Handedness scale ranged 36-39; Chapman & Chapman, 1987). Of the individuals who responded to the newspaper advertisement offering treatment for depression, 1144 could be reached and screened over the telephone and they were presented with an option to participate in an experimental treatment study using biofeedback. A total of 138 individuals passed the initial telephone screen, and 67 of them came in for intake assessment whereas the rest did not want to participate due to the three-month commitment and the requirement to attend three training sessions per week. Thirty-one individuals were found to be eligible to participate in the study, however only 19 of them decided to begin biofeedback training and only seven completed all 36 sessions. All participants met DSM-IV criteria for nonchronic Major Depressive Episode without psychotic features, were free of any other Axis I and Axis II mental disorders, and were free of active suicidal potential. Participants obtained a minimum score of 14 and a maximum score of 24 on the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1967). Individuals were excluded if they were pregnant, had heart problems, current cancer, thyroid problems, diabetes, or endocrine problems, or if they were currently receiving any type of treatment for depression, including medication, counseling, or psychotherapy. Individuals were excluded if they had ECT in the last 6 months and if they used cocaine, amphetamines, benzodiazepines, or excessive amounts of alcohol or marijuana. Individuals who had

multiple seizures were excluded, in addition to individuals who had a stroke or a head injury that resulted in a loss of consciousness for more than 10 min.

Procedure and Materials

Following an initial telephone screen, potentially eligible individuals participated in an interview assessing the severity of depression using the HRSD. They were screened for other mental illness using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and SCID-II for Axis II disorders. They were also asked to complete several questionnaires, including the Beck Depression Inventory (BDI; Beck, 1961), the BIS/BAS scales (Carver & White, 1994), the Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, Borkovec, et al., 1990), and the Inventory of Depressive Symptomatology (IDS; Rush et al. 1986). These same assessment procedures were conducted at 3- and 6-month follow up visits, however these follow-up data were not the subject of analysis for this paper.

Symptom Assessment. In addition to the intake assessment, at each subsequent two-week interval, trained clinical raters, blind to the treatment condition, interviewed participants with the 17-item HRSD and the participants completed the PSWQ and the IDS. Inter-rater reliability for the HRSD for studies ongoing in the laboratory over the last few years is very high, as indexed by an intraclass correlation of .96. This figure includes interviews sampled from the present study as well as two other studies over a five-year time interval. At the start of each day of training, participants completed the BDI to assess current mood and suicidal ideation. Adverse events were monitored and tracked continuously.

Biofeedback training. Contingent biofeedback involved presenting computer generated tones corresponding to the participants' mean alpha asymmetry during the preceding second, where they heard a high reward tone when they exceeded a target value (described below). They heard a low non-reward tone when they did not reach the target value. Contingent biofeedback was thus designed to increase left frontal activity. The tones turned off (i.e., "time-outs") when the participants exhibited excessive eye or muscle movements.

Each control participant receiving noncontingent feedback was yoked to a participant in the training group and presented with the same sequence of tones received by that training participant. Because the yoked control participants received feedback comparable to that received by training participants, the rate of reward, which itself might alter emotion, was therefore comparable for those receiving contingent and noncontingent feedback. However time-outs in the yoked participants were, in fact, calculated on the basis of their own ocular activity in order to provide a realistic training environment for them, but one that did not have the critical contingency for biofeedback.

The study was divided into two phases: the first phase compared contingent to noncontingent treatment (the "treatment effect" phase), as participants were randomly assigned to a treatment condition and received six weeks of contingent or noncontingent biofeedback; the second phase presented all subjects with contingent biofeedback ("contingent only" phase), as all participants received six weeks of contingent biofeedback. This design allowed for all participants to receive the experimental treatment. For a total of 12 weeks, divided into two six-week phases, all participants

received three one-hour training sessions each week. Two of the participants missed one week of biofeedback between weeks 22 and 23 due to vacation, but completed the full 36 sessions of training despite the week interruption. Each session consisted of a five-minute baseline block ("pre-training"), six five-minute blocks of biofeedback training, and another five-minute baseline block ("post-training"), with one-minute breaks between blocks. Three sensors placed on the subjects' heads monitored and recorded EEG activity. Participants were asked to sit still throughout the recording session and were given the following instructions prior to the first biofeedback training session of the day: "We're going to start biofeedback training now. During training, you will attempt to activate the high tone as often as possible and to keep it on for as long as you can. Certain things will cause the tone to turn off altogether. Don't worry if that happens, but try not to make it happen." Participants found this to be vague, especially during the first session, and were presented with the following explanation: "The high tones indicate that your brain activity is changing in the manner we think should help alleviate depression, so pay attention to the tones and try to activate the high-pitched tones."

Participants were never informed that the biofeedback was dependent on frontal alpha asymmetry, they were never provided with possible strategies to activate the high tones, and they were never told that excessive eye or muscle movements caused the tone to turn off. The tones were the only form of feedback the participants received regarding their performance.

EEG Recording and Biofeedback Parameters. Each block of biofeedback training included 300 one-second segments. EEG data were sampled at 256 Hz and

filtered with an elliptical three-pole bandpass filter to extract alpha activity in the 8-13 Hz band with a transition bandwidth of 1 Hz. Filtered EEG data were converted to RMS signals and an alpha asymmetry score (described below) was calculated using the RMS signals for the previous second. Additional bands were monitored for artifactual influences: a delta band (.5-4 Hz) for monitoring ocular artifacts, and an EMG band (70-90 Hz) for monitoring EMG artifacts in scalp leads. EEG signals were recorded from sites F3 and F4 referenced on-line to CZ, using Ag-AgCl electrodes. A ground electrode was placed on the forehead midline. Electrode impedances were less than 10 KOhm, and impedances at sites F3 and F4 were within 1 KOhm of one another. An alpha asymmetry score R-L was computed by comparing the difference in RMS alpha power between right and left sites.

Asymmetry greater than zero indicated relatively greater right frontal alpha activity and presumably relatively greater left frontal activity, since alpha power and activity are inversely related. While the asymmetry score was continuously varying, the mean asymmetry score for each second was computed and compared against the target value established for that trial. The target value for each day was based on each participant's mean and standard deviation of asymmetry score values (R-L) during the post-training block of the previous day, with the exception of the first day where the target value was based on the mean and standard deviation of the asymmetry score values during the pre-training block. The target was defined as the mean asymmetry score plus .85 standard deviations. Assuming a normal distribution of asymmetry scores and no

improvement during the training block, asymmetry scores would exceed this threshold on approximately 20% of trials.

Both the high tones of 1031 Hz and the low tones of 579 Hz were played over the audio speakers. Tones were continuous, such that onset of one tone coincided with the offset of the previous tone. Segments where the integrated RMS value exceeds 35 microvolts in the EOG (0.5–4.0 Hz) frequency or 15 microvolts in EMG (70-90 Hz) frequency resulted in no tone for the following seconds.

RESULTS

Sample Attrition. Nineteen participants began the study, however 12 of them decided to discontinue biofeedback training for the following reasons: "too much of a time commitment," preferring other forms of established (versus experimental) treatment (mainly pharmacological), starting a new job, leaving town for several weeks due to family emergency, given referral for treatment elsewhere due to worsened panic attacks in severity and frequency, and given referral for grief counseling and other treatments after the death of a significant other. The number of sessions completed by the participants who dropped out of the study ranged from one to 12, with a mean of 4.4 sessions. Based on independent sample t-tests, participants who decided to withdraw from the study did not differ significantly in terms of several key measures from those who completed biofeedback training. Table 1 presents the means and standard deviations for the pre-training baseline asymmetry score, $F(1,17)=.005$, *ns*, the initial BDI scores from the intake assessment, $F(1,17)=.323$, *ns*, and the initial HRSD scores from the intake assessment, $F(1,17)=.141$, *ns*. Table 2 presents the percentage of completers and dropouts who were assigned to either condition, as well as demographic information. The internal consistency reliability coefficient for baseline EEG asymmetry as measured by the pre-training block during the first session of all completers was found to be very strong (alpha=.9903), making it a reliable measure of asymmetry.

Table 1

Mean and Standard Deviation of Initial Asymmetry and Depression Scores in Completers and Dropouts

Measure	Completers (N=7)	Dropouts (N=12)
Pre-Training Asymmetry Score	-0.31 (0.28)	-0.15 (0.26)
Intake BDI Score	25.9 (6.2)	23.7 (6.6)
Intake HRSD Score	20.1 (3.4)	20.8 (3.8)

Table 2

Group Assignment and Demographic Information in Completers and Dropouts

Variable		Completers (N=7)	Dropouts (N=12)
Treatment Condition			
	Contingent	86%	92%
	Noncontingent	14%	8%
Age		46.4 (7.7)	41.3 (9)
Gender			
	Female	100%	67%
	Male	0%	33%
Ethnicity			
	Caucasian	72%	58%
	Latino	14%	18%

Asian	0%	8%
Mixed	14%	8%
Unknown	0%	8%

Since participants in the noncontingent group were yoked to those receiving contingent biofeedback, it was important to accrue full sets of data in the contingent group first before assigning participants into the noncontingent group. Among seven participants with completed data, only one received noncontingent biofeedback, therefore group comparisons were not conducted and the following results represent analyses performed within the contingent biofeedback training group. The data from the participant in the noncontingent biofeedback group were not included in the following analyses.

Symptomatic changes. Changes in self-reported depressive symptoms measured by HRSD that was administered every third week were analyzed in a repeated measures analysis of variance (ANOVA), which did not reveal a significant main effect of Time [(1-7), $F(6, 30)=2.11$, *ns*], even though the pattern demonstrated an overall decrease in scores over time (see Figure 1). A mean BDI score was computed for each two-week period (mean across 6 sessions) and these scores were analyzed in a similar repeated measures ANOVA where a main effect of time (1-6, each consisting of six sessions) was present according to the Greenhouse-Geiser Epsilon correction [$F(5, 25)=6.95$, $p< .05$, $\epsilon=.37$]. Figure 2 presents mean BDI scores over time, beginning with the intake to session 36. To determine the clinical significance of the self-report measures, pre to post

(intake versus session 18) effect sizes was calculated on the BDI scores as well as the HRSD interview scores. As expected, self-reported symptoms of depression declined after an 18-session attendance of biofeedback training as indicated by strong effect sizes on the BDI (0.73) and HRSD (0.66). Similar effect sizes were found when intake scores were compared to scores in session 36 (BDI=0.73, HRSD=0.62).

Training Effects. To examine the effect of biofeedback training on frontal alpha asymmetry, asymmetry scores were analyzed in a Week (1-12) by Session (1-3) by Block (1-6) repeated measures ANOVA, which did not reveal any main effects or interactions (all *ps* >.05). Figure 3 presents the mean asymmetry scores over the first 18 sessions. To assess the possibility that participants learned to alter their frontal EEG asymmetry during training, data were averaged by block across six training sessions, thus each value represented an asymmetry score that included six consecutive training sessions. If participants initially were relatively unable to alter asymmetry but subsequently learned to alter asymmetry, this would be reflected in a block by segment interaction. A repeated measures ANOVA using a Block (1-6) by Segment (1-6, each encompassing six training sessions) did not reveal any significant main effects or interactions (all *ps* > .05).

Within-subject covariation of asymmetry and mood. Although no group level effects of training were apparent, analyses of individual participants were conducted to examine the correspondence between frontal EEG asymmetry and mood. Little evidence was found to support such a correspondence. Within-subject correlations between the mean daily asymmetry score and the BDI score for sessions 1-18 did not reveal any significant relationships (all *ps* > .05; see Table 3). To examine whether the BDI score

could predict subsequent mean asymmetry score or vice versa, lagged correlations were also computed, none of which were significant (all *ps* > .05; see Table 3).

Table 3

Within-Subject Asymmetry and BDI Correlations for the First 18 Sessions

Participant	Asymm. & BDI	Asymm. & Previous BDI	Asymm. & Following BDI
1	-.33	-.19	-.30
2	-.05	-.01	-.02
3	-.10	.02	-.23
4	.24	.38	.21
5	.33	.06	.33
6	.13	.02	-.01

Note. With an N of 18, correlations greater than .47 would be significant at .05 level.

The daily target value that reflects the previous day's performance was thought to be a potentially more reliable and stable estimate of daily EEG asymmetry score, therefore within-subject correlations were computed between the daily target value and the BDI score for sessions 1-18; these did not reveal any significant relationships (all *ps* > .05; see Table 4). To examine whether the BDI score could predict subsequent target value or vice versa, lagged correlations were also computed, none of which were significant (all *ps* > .05; see Table 4). These analyses collectively suggest that factors other than changes in frontal asymmetry contributed to the reductions in reported depressive symptoms.

Table 4

Within-Subject Daily Target Value and BDI Correlations for the First 18 Sessions

Participant	Target & BDI	Target & Previous BDI	Target & Following BDI
1	-.18	-.11	-.13
2	-.05	-.06	-.09
3	.07	.08	.20
4	.13	-.10	-.28
5	.39	.44	.15
6	-.17	-.05	.00

Note. With an N of 18, correlations greater than .47 would be significant at .05 level.

Reinforcement Rate and Artifacts. To confirm that the daily target values produced a reasonable reinforcement rate, the rate of positive reinforcement quantified by the percentage of high beeps (versus low beeps) was examined. Since the target value was titrated each session based on the previous session's mean and standard deviation asymmetry score during the post-training block, no changes were expected across sessions. The rate of positive reinforcement did not increase significantly over the first 18 sessions (all *ps* > .05), however the rate of reinforcement on the first session (8%) increased to a mean of 24% in following 17 sessions. The overall reinforcement rate was 23%±8.2% [mean±s.d] of the trials, suggesting that the daily target value effectively produced the desired reinforcement rate. Previous studies have shown that the rate of artifacts declines over time, however the percentage of daily artifacts (i.e., time outs) over

the first 18 sessions was 0.5%±0.3% [mean±s.d] and there were no noticeable reductions over time. The low rate of artifacts in this sample likely made it difficult to see further reductions.

DISCUSSION

Evidence of the high prevalence of major depression along with the inconsistent and often short-lived effectiveness of traditional treatments compel the need to continue investigating different forms of treatment in search of a more tolerable noninvasive method of reducing depressive symptoms and maintaining longer remission periods. The correlational nature of the relationship between emotional reactivity and frontal EEG asymmetry has been well established in the literature and when Allen et al. (2001) investigated the causal nature of this relationship they found that manipulating frontal alpha asymmetry by using EEG biofeedback influenced subsequent emotional responses in college students. In examining the effects of EEG biofeedback on the treatment of depression, Baehr et al. (1997) and Earnest (1999) found a significant decline in depression, however the participants in those studies were receiving additional treatment, therefore making it difficult to conclude that the biofeedback directly affected depression. However, these encouraging results supported the promise of the present study, which was a controlled noninvasive alternative treatment seeking to determine whether manipulating frontal alpha asymmetry using EEG biofeedback would impact self-reported depression by randomly assigning depressed participants, who did not receive any other treatment for depression, into a contingent or a noncontingent biofeedback group.

Although over a thousand people who responded to an advertisement for the treatment of depression were contacted, only 31 were found to be eligible based on the telephone and in-person interviews, and seven of the 19 original participants completed

all 36 sessions. Unfortunately, it is difficult to draw firm conclusions about the results of the study due to the small sample size. The 63% drop out rate is much higher than the average of that reported by other treatment studies, however the present study required a tremendous time commitment from the participants and did not provide any compensation other than the contingent biofeedback for all participants during the second phase of the study. In addition, the experimental nature of the treatment discouraged those who believed established treatments would provide a more immediate relief from their depressive symptoms, especially because they did not want to risk waiting six weeks to receive contingent biofeedback as they did not know to which group they were assigned. Several participants also reported having trouble grasping the concept of biofeedback and often became frustrated in trying to figure out strategies that would activate the high beeps, particularly since the immediate feedback they received was sometimes discouraging (i.e., low beeps). In addition, the present study was more demanding than others in that, not only were participants expected to attend three training sessions per week, but also they were required to actively participate in the effortful task of generating the high beeps when they did were not sure whether or not the feedback was contingent to their own brain activity.

Consistent with previous EEG biofeedback treatment studies of depression (e.g., Baehr et al., 1997 and Earnest, 1999), self-reported depression scores as determined by HRSD and BDI scores generally declined over time. There were significant changes between the pre and post HRSD and BDI scores, however EEG biofeedback training failed to alter frontal alpha asymmetry, therefore the extent to which variations in

asymmetry impact depressive symptoms could not be adequately assessed. In addition, there was no evidence that the participants learned to alter their asymmetry such that their mean asymmetry scores for each of the six blocks within the training sessions did not improve over time, even though the daily target value seemed to reasonably produce positive reinforcement as described by the percentage of high beeps during biofeedback training. The present study differed from previous attempts to alter frontal alpha asymmetry using EEG biofeedback (i.e., Allen et al., 2001 and Hardman et al., 1997) in that those studies were conducted on nondepressed populations over three or five sessions, while the current study recruited depressed individuals from the community, each of whom attended three sessions of biofeedback training for 12 consecutive weeks. In addition, the effect of biofeedback in the Allen et al. (2001) study was more pronounced in the "RIGHT" direction compared to the "LEFT" direction, whereas the present study trained participants only the "LEFT" direction. Mean frontal EEG asymmetry in the present sample showed some minor variation, however these changes were inconsistent and disappeared by the 18^{th} session. It is possible that the asymmetrical changes were not maintained with continued biofeedback training over several weeks and that the alterations observed in previous studies would have also disappeared with continued biofeedback training.

Variables other than the training appeared to produce expected reductions in self-reported depression in the present sample. Although the experimenters were instructed to refrain from engaging in obviously therapeutic conversations with participants (i.e., topics related to daily struggles or to their mood), a generally supportive and reliable

laboratory environment might have had a therapeutic influence. In addition, some participants anecdotally reported feeling relaxed following the biofeedback training sessions, thus their attendance alone could have improved their mood. Unfortunately, since only one participant in the noncontingent biofeedback group completed all 36 sessions, statistical group comparisons in changes in depressive symptoms could not be conducted, but might have provided some explanation in the possible influences of the resulting affective changes. Figure 4 demonstrates the decline of the control participant's BDI scores over time and this pattern of scores is similar to that of the averaged BDI scores in the participants who received contingent biofeedback for 36 sessions. Thus it is apparent that factors other than the contingent EEG biofeedback are likely responsible for the improvement in self-reported depression.

Furthermore, in the absence of group effects, there were no significant within-subjects correlations between daily mean asymmetry score and BDI score or between daily target value and BDI score. It was also evident that BDI scores were not able to predict asymmetry or target value, and vice versa. A participant's change in mood did not necessarily correspond with alteration in frontal asymmetry or daily target value. In addition, reported change in mood did not result in corresponding change in asymmetry during the following session, nor did change in asymmetry result in altered mood during the following session.

Future Directions

It is recommended that future studies try to establish robust training effects with the focus of generating changes in frontal EEG asymmetry in the expected direction by

using biofeedback. It is possible that the biofeedback protocol used in the present study requires modification by using different EEG parameters or by altering the length of training or the number of sessions. It may also be the case that the low rate of reinforcement makes this treatment especially difficult for depressed participants. In order to encourage subjects to increase relative left frontal activity, the threshold needed to be set somewhat above each subject's mean score, resulting in reward tones in fewer than half the trials. Although nondepressed subjects in previous studies may have been able to respond to this feedback schedule, perhaps the preponderance of nonreward tones worked against creating much change in asymmetry in the depressed population.

If better training parameters could be devised, then a follow-up trial might be warranted. In any such trial, it is recommended that patients be informed ahead of time what to expect, with the aim of reducing dropouts and lowering the rate of attrition.

The current data do not suggest great utility for this intervention as a monotherapy. The case reports (Baehr et al., 1997 and Earnest 1999) suggest it may have a role as an adjunct to other forms of therapy, although more consistent training effects and lower dropout rates would need to be established before testing biofeedback as an adjunct to traditional treatment.

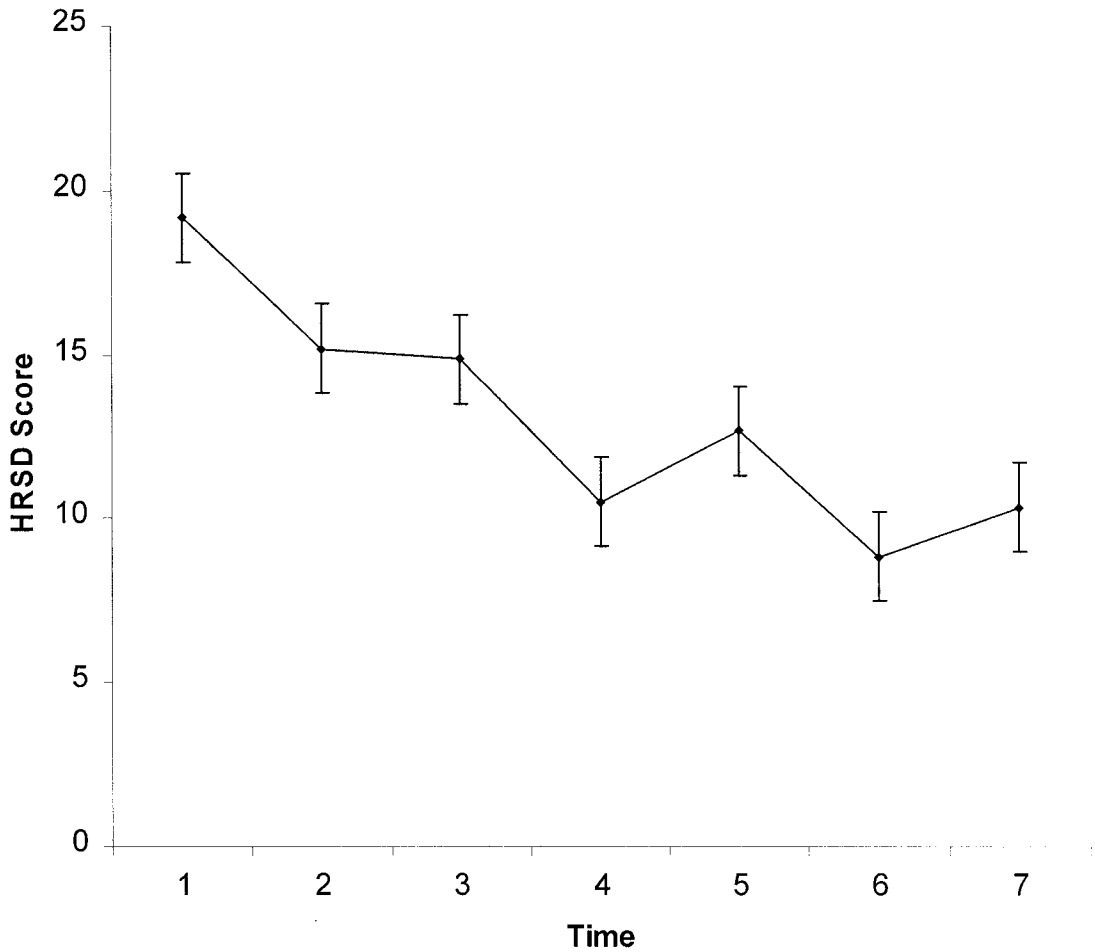
APPENDIX: FIGURES

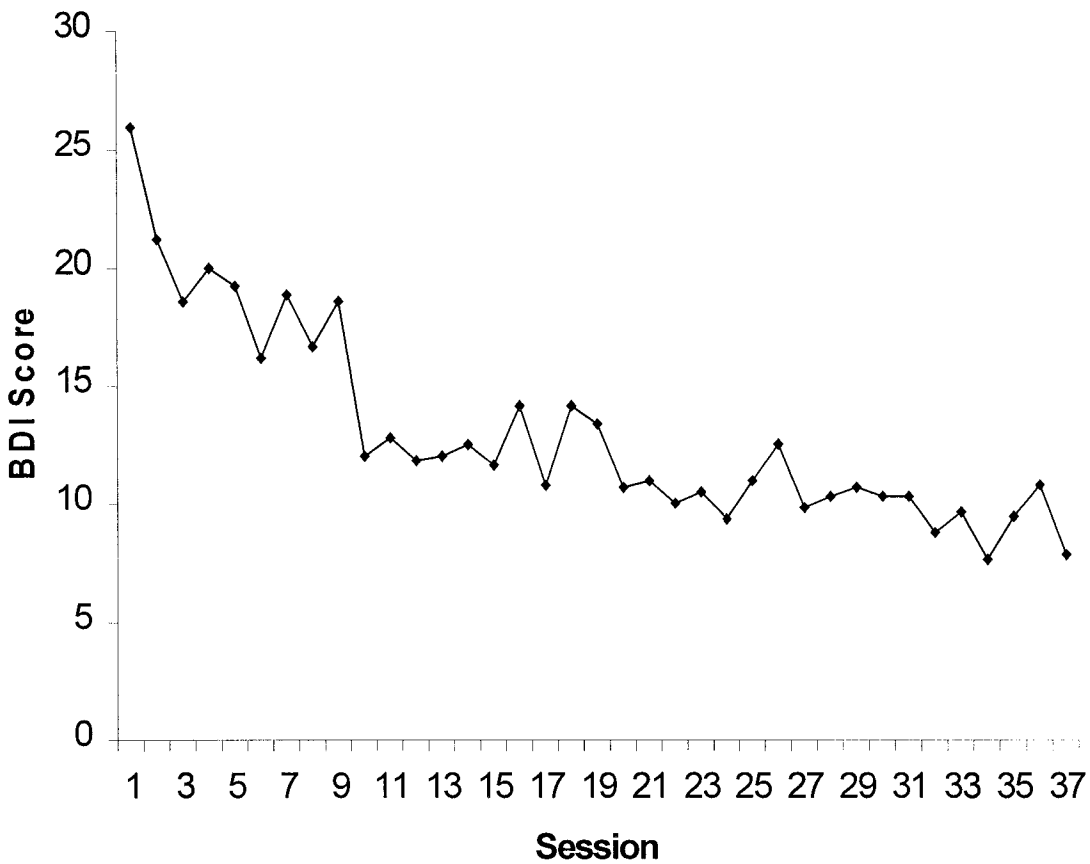
Figure1. Although not statistically significant, this figure demonstrates a decreasing pattern of HRSD scores over time, beginning with the intake and through session 36.

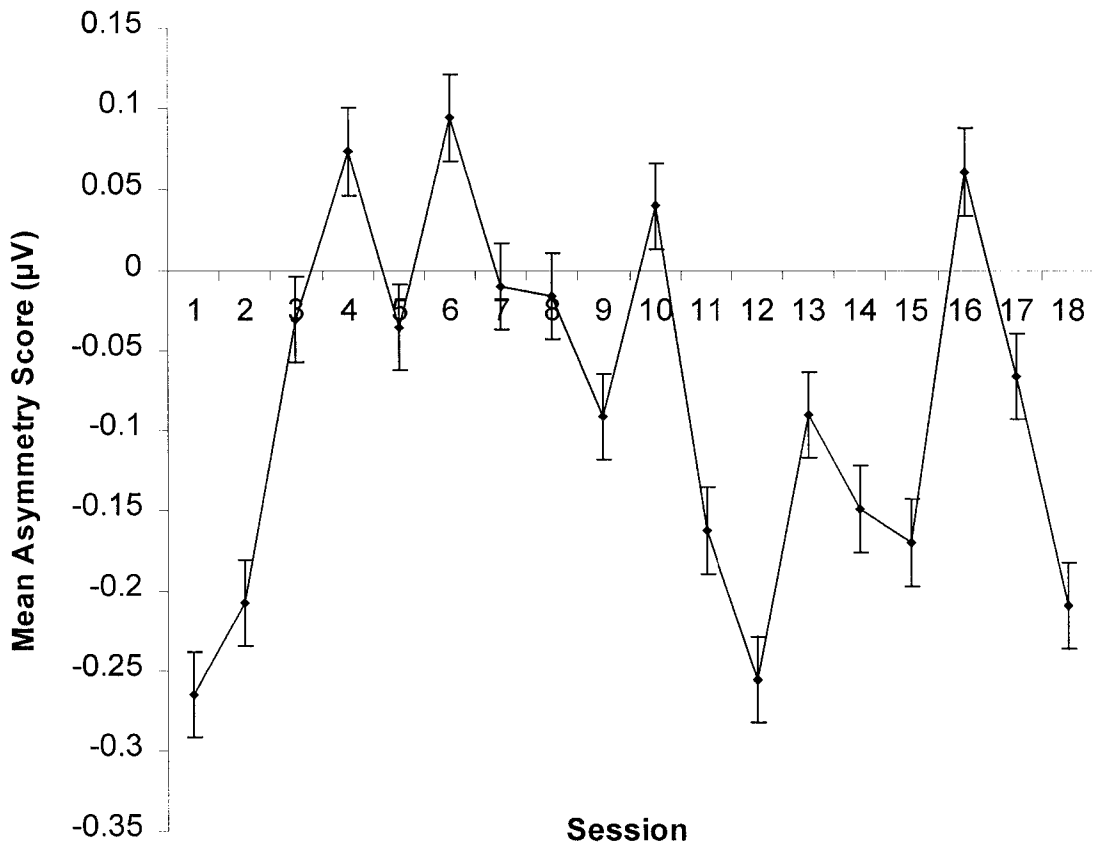
Figure 2. Self-reported depressive symptoms measured by the administration of BDI at every session are decreased over time ($p < .05$).

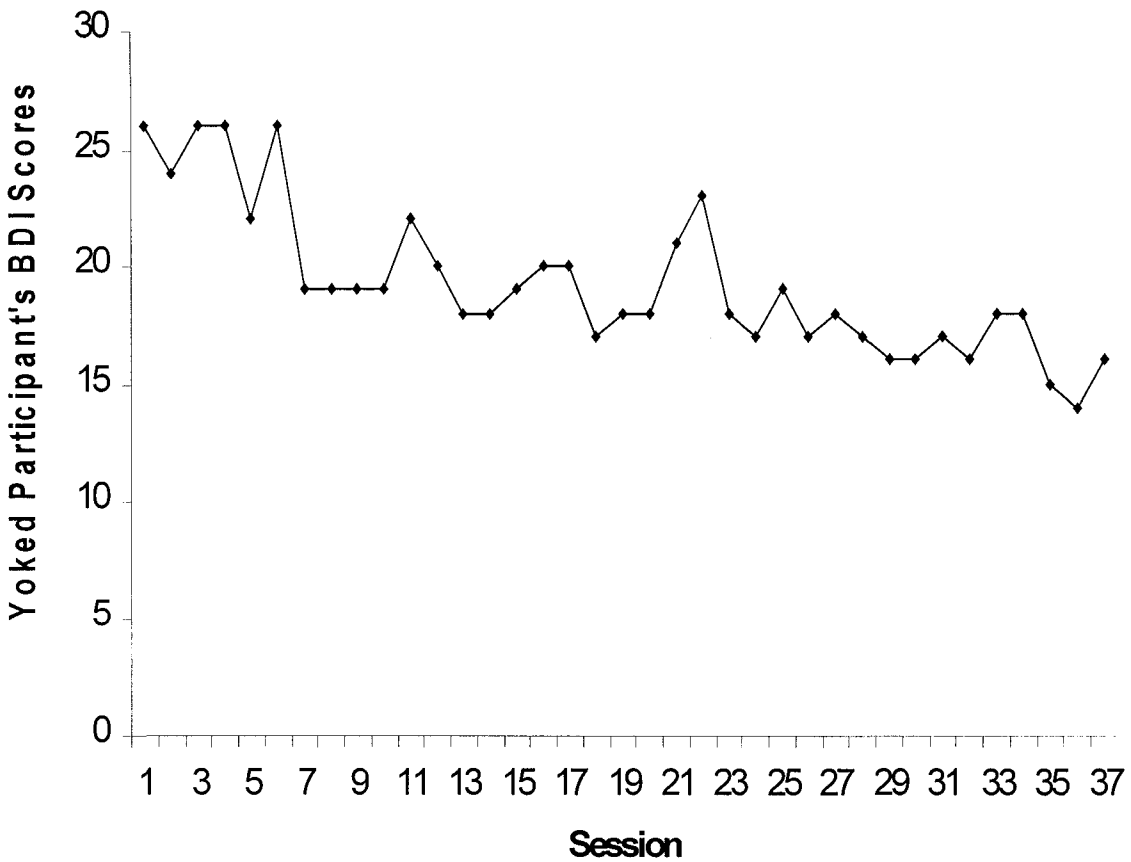
Figure 3. There were no significant changes in mean frontal EEG asymmetry score across biofeedback training sessions. The figure demonstrates minor fluctuations, however the mean asymmetry score on session 18 is very similar to that of the first session.

Figure 4. Yoked participant's BDI scores show a pattern of change over time similar to that seen in the participants in the contingent group.


25
20
15
10
5
0
HRSD Score
1
2
3
4
5
6
7
Time


30
25
20
15
10
5
0
BDI Score
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37
Session


0.15
0.1
0.05
0
-0.05
-0.1
-0.15
-0.2
-0.25
-0.3
-0.35
Mean Asymmetry Score (µV)
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
Session


Yoked Participant's BDI Scores
30
25
20
15
10
5
0
1 3 5 7 9 11 13 15 17 19 21 23 25 27 29 31 33 35 37
Session

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