While a Phobic Waits: Regional Brain Electrical and Autonomic Activity in Social Phobics during Anticipation of Public Speaking

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Background: *Recent studies have highlighted the role of right-sided anterior temporal and prefrontal activation during anxiety, yet no study has been performed with social phobics that assesses regional brain and autonomic function. This study compared electroencephalograms (EEGs) and autonomic activity in social phobics and controls while they anticipated making a public speech.*

Methods: *Electroencephalograms from 14 scalp locations, heart rate, and blood pressure were recorded while 18 DSM-IV social phobics and 10 controls anticipated making a public speech, as well as immediately after the speech was made. Self-reports of anxiety and affect were also obtained.*

Results: *Phobics showed a significantly greater increase in anxiety and negative affect during the anticipation condition compared with controls. Heart rate was elevated in the phobics relative to the controls in most conditions. Phobics showed a marked increase in right-sided activation in the anterior temporal and lateral prefrontal scalp regions. These heart rate and EEG changes together accounted for $>$ 48% of the variance in the increase in negative affect during the anticipation phase.*

Conclusions: *These findings support the hypothesis of right-sided anterior cortical activation during anxiety and indicate that the combination of EEG and heart rate changes during anticipation account for substantial variance in reported negative affect.* Biol Psychiatry 2000; 47:85–95 © *2000 Society of Biological Psychiatry*

Key Words: Electroencephalogram, autonomic function, social phobia, emotion, regional brain electrical activity

Introduction

The pathophysiology of anxiety has received intensive study over the past decade (e.g., Nutt 1991; Tancer 1993). A number of experiments designed to examine patterns of regional brain function have been conducted with simple phobics, patients with obsessive–compulsive disorder (OCD), and patients with panic disorder (e.g., De Cristofaro et al 1993; Stein and Uhde 1995; Wilson and Mathew 1993). Birbaumer et al (1998) have conducted the only study we know of using measures of regional brain activation in social phobics. They found increased activation of the amygdala with functional magnetic resonance imaging (fMRI) in response to neutral faces in social phobics compared with controls. Both groups showed comparable activation of the amygdala in response to aversive odors.

The primary purpose of the present study was to determine the brain electrical correlates of anticipatory anxiety induced in patients with social phobia. Recent studies examining anticipatory anxiety using positron emission tomography (PET) to measure regional cerebral blood flow have been controversial because of possible muscle artifact confounding the results (Reiman et al 1989). Drevets et al (1992) demonstrated that jaw clenching produced a pattern of regional blood flow change that looked remarkably like that associated with anticipatory anxiety, and claimed on that basis that the previous finding of increased blood flow to the temporal polar region was likely confounded by jaw clenching artifact; however, a subsequent PET study (Rauch et al 1995) found significant increases in right anterior temporal cortex blood flow when simple phobics were exposed to their phobic objects. A teeth clenching control showed that blood flow changes during teeth clenching clearly lay outside the brain and 23 mm anterior to the anterior temporal activation focus found in response to phobic objects. Comparable findings of relative right-sided asymmetry in the anterior temporal and prefrontal regions were reported by Nordahl et al (1990) in a sample of unmedicated patients with panic disorder during the performance of an auditory discrimination task. A recent study by these investigators replicated these findings in a group of imipramine-treated panic disorder patients (Nordahl et al 1998). In contrast, another recent study found the opposite pattern of metabolism, such that patients with panic disorder had increased left parahippocampal metabolism and decreased right

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temporal and right parietal metabolism as compared with normal controls (Bisaga et al 1998). In an analysis of findings across three different anxiety-disordered patient groups (OCD, simple phobia, and posttraumatic stress disorder), Rauch et al (1997) found right-sided activation in various territories of the prefrontal cortex when anxiety symptoms were provoked. Unfortunately, in none of these studies were the appropriate rigorous methods utilized for ascertaining whether a true asymmetric effect was present in the data (see Davidson and Irwin 1999 for discussion).

The present study was designed to test several features of a model of anterior brain asymmetry and emotion. This model is based upon extensive prior data and theory (Davidson 1992, 1998; Davidson et al 1990b) and holds that certain regions within the left prefrontal cortex are part of a circuit that implements approach-related behavior and emotion, whereas other regions within the anterior right hemisphere, including the prefrontal and anterior temporal regions, are part of a circuit that implements withdrawal-related behavior and emotion. These cortical regions are held to interact with several subcortical structures in the elaboration of different components of emotional responding. Whereas literal approach and withdrawal behavior is observed at many levels of phylogeny (Schneirla 1959) and can be easily seen in infants and young children (Davidson and Rickman 1999), it is often not expressed overtly in human adults. Rather, these terms are used to refer to affective processes that generally serve to either decrease the distance between a person and a source of appetitive stimulation or increase the distance between the person and a source of aversive stimulation. The actual distance in many real-life contexts might remain unchanged, but the affective responses occur to facilitate such change.

We have experimentally tested aspects of this model by directly manipulating mood in normal control subjects and examining changes in quantitative regional brain electrical activity measures of activation. Using both short film clips (Davidson et al 1990b) and monetary rewards and punishments (Sobotka et al 1992) to manipulate emotion, consistent shifts in the asymmetry of scalp-recorded prefrontal alpha power were observed, with greater right-sided activation produced by negative compared with positive manipulations. In addition, we have demonstrated that these electroencephalogram (EEG) measures of asymmetry are reliable over time and predict differences among subjects in emotional reactivity (Tormarken et al 1992; Wheeler et al 1993). Although quantitative EEG measures are limited in their spatial resolution, they can provide useful information about hemispheric differences in broad regions of the cerebral cortex. Moreover, they are relatively inexpensive, relatively insensitive to head movement, and completely noninvasive. This latter attribute is particularly significant in clinical studies, because patients can be tested on many repeated occasions and the procedures can also be used with infants and children (Davidson and Fox 1982, 1989).

In the present study, we recorded brain electrical activity and autonomic activity while social phobics anticipated making a public speech and then again immediately following the speech. In addition, we obtained self-report measures of anxiety and emotion at different points throughout the procedure. Autonomic activity was measured in addition to brain activity, because some data suggest that social phobics with public speaking phobia are particularly likely to show larger heart rate elevations than controls (Beidel et al 1985; Heimberg et al 1990), although not all studies consistently find such heart rate differences (Hoehn-Saric and McCleod 1993; Hofmann et al 1995; Stein et al 1992, 1994).

We specifically hypothesized that during the anticipation period social phobics would exhibit accentuated activation in right hemisphere prefrontal and anterior temporal regions. We also expected that phobics would show larger heart rate increases during the anticipation period compared with controls. We did not have specific hypotheses about the other conditions.

Methods and Materials

Subjects

Phobic and control subjects were recruited for a treatment study through advertisements in local newspapers. Potential subjects were screened via a telephone interview, and those subjects likely to meet criteria for the study were invited for a diagnostic interview. These subjects were screened with a modified version of the Anxiety Disorders Interview Schedule—Revised (DiNardo et al 1993). Interviews were conducted by one of two laboratory members, both of whom had over 200 hours of experience with structured interviews. Phobic subjects met DSM-IV (American Psychiatric Association 1994) criteria for social phobia and had to have a specific fear of speaking in front of small groups. Phobics had no other axis I diagnosis. The patients were required to be off all benzodiazepines for at least 1 month prior to testing and free of all beta-blockers for a minimum of 3 days prior to testing. Twenty phobic subjects (8 men, 12 women) met all criteria and were invited to participate in the study.

The control subjects were required to have an absence of psychopathology. There were 12 control subjects (5 men, 7 women) who met the criteria. All subjects were right-handed as assessed by the Chapman Handedness Inventory (Chapman and Chapman 1987). Data from 2 phobic subjects and 2 control subjects were lost because they were missing data from one or more regions of interest. This resulted in a final group of 18 social phobia and 10 control subjects. The data from another 4 phobic subjects were incomplete because of excessive artifact in one or more experimental conditions. The two groups did not

differ in age, phobic mean = 25.00 (range 19–40) control mean = 34.90 (range 19–68) [$t(10.1) = -1.78$ $p > .10$], or gender [$p > .50$, Fisher's exact (two-tail)].

Procedure

At the start of the experiment, the subject was provided with an overview of the study and asked to sign a consent form. The subject then filled out the trait form of the Positive and Negative Affect Schedule (PANAS; Watson et al 1988) and the trait form of the State/Trait Anxiety Inventory (STAI; Spielberger et al 1983). Subjects were then fitted with an electrode cap and heart rate (HR) and electrooculogram (EOG) electrodes, after which they completed the state forms of both the PANAS and the STAI. Subjects then sat quietly while four 60-sec baselines were recorded. Baseline EEGs were recorded during both eyes-open and eyes-closed rest periods, the order of which was counterbalanced across subjects. After the resting baselines, systolic and diastolic blood pressure were recorded. The subjects were then informed that they would be expected to give a 5- to 10-min speech to an audience of approximately 24 graduate students and research scientists who "have an interest and expertise in interpersonal behavior." The subjects were told that half of the audience would be in the same room with them, whereas the other 12 would be seated behind a one-way mirror. Subjects were informed that in addition to rating strengths and weaknesses of their speech, these investigators would also be making ratings about the subjects' general personalities. At this time, subjects were not informed of the topic they would be asked to speak on but were told they would have about 1 min to prepare their speech once they had received their topic. During this anticipation period, subjects heard a tape-recorded voice every 30 sec informing them of the time remaining until they would receive their topic. Physiology was recorded throughout this 3-min anticipation period. At the end of this period, subjects filled out state versions of the STAI and the PANAS, and their blood pressure was again measured. The subjects were then told the topic on which they would have to talk and were informed that they would have 2 min to plan their speech. Once again they heard a tape-recorded countdown. Physiology was recorded throughout this 2-min planning condition, and blood pressure was measured at the end of the planning condition. The cables for the electrode cap, the EOG, and HR electrodes were then unplugged and the subject was escorted to a small room where an audience was waiting. Subjects were informed that they were to speak for a full 6 min on the assigned topic. The topic was a current political issue that had been heavily covered in daily news reports.

The raters wore white lab coats and were encouraged to regard the subject critically and enter marks on their rating sheets throughout the entire time the subject was speaking. When the subject finished his or her speech, he or she immediately returned to the laboratory, and blood pressure was recorded. Electrode cables were then reconnected and 2 min of resting physiology were recorded (postspeech condition). At the end of these 2 min, subjects again completed state versions of the STAI and the PANAS. Subjects also filled out a medical history form and a handedness questionnaire (Chapman and Chapman 1987).

Heart Rate Recording

Heart rate was recorded from bipolar electrodes positioned on the subject's torso. Heart rate data were passed through an active low pass filter with a cut-off of 99 Hz and a 24 dB/octave roll-off (Dumermuth and Molinari 1987). The electrocardiogram data were digitized online and HR in beats per minute (bpm) was obtained for each sample and then aggregated across condition.

Blood Pressure Measurement

All blood pressure measures were obtained manually with a sphygmomanometer. Both systolic and diastolic pressure were obtained at each reading.

Electroencephalogram Recording

Electroencephalograms were recorded with a Lycra electrode cap (Electro-Cap International, Eaton, OH) from 14 scalp locations: AF1, AF2, F3, F4, F7, F8, T3, T4, P3, P4, C3, C4, Cz, and Fz (International 10/20 system). All placements were referenced to linked ears (A1A2). Electrode impedances were all under 5000 Ω, and the impedances for homologous sites were within 500 Ω of each other. Electrooculogram was recorded from the external canthus and the supra-orbit of one eye to facilitate artifact scoring. Electroencephalograms and EOGs were amplified with a 20-channel Grass (Quincy, MA) Model 12 Neurodata System that had a bandpass of 1–100 Hz and a 60-Hz notch filter. All analog signals were passed through active low pass filters (Rockland [West Nyack, NY] model 424) with a cutoff of 65 Hz and a 24-dB/octave roll-off (Dumermuth and Molinari 1987). The EEGs were digitized online at the rate of 250 samples/sec. The data were then visually edited to remove eye blinks, gross muscle activity and movement artifact. A fast Fourier transform (FFT) was applied to all chunks of artifact-free data that were 2.05 sec in duration, with chunks overlapping by 50%. The FFT output was then converted to power density (μV^2/Hz) in each of eight bands: delta (1–4 Hz), theta (4–8 Hz), alpha-1 (8–10 Hz), alpha-2 (10–13 Hz), beta-1 (13–20 Hz) beta-2 (20–30 Hz), beta-3 (30–40 Hz), and "electromyogram" (EMG) (70–80 Hz), by summing activity across all bins within a band and dividing by the number of 1-Hz bins. Since pilot work showed that the task we used produced considerable muscle tension, power in the 70–80-Hz band was used to statistically correct the EEGs to remove the contributions of muscle activity (see below). Activity in the 70–80-Hz frequency band is presumed to be exclusively myogenic in origin and thus can be used to estimate the contribution of muscle artifact in each lead independent of EEG activity.

Our major hypotheses were tested using power in the alpha-1 band. Analyses of power in all other bands were considered exploratory. We chose to focus on alpha-1 power because a recent factor-analytic study on a large independent sample of normal controls in our laboratory (Goncharova and Davidson 1995) suggests that low- and high-frequency alpha load on two separate factors, and that low-frequency alpha power is more consistently related to affective constructs than high-frequency alpha. It should be noted that the pattern of findings using the

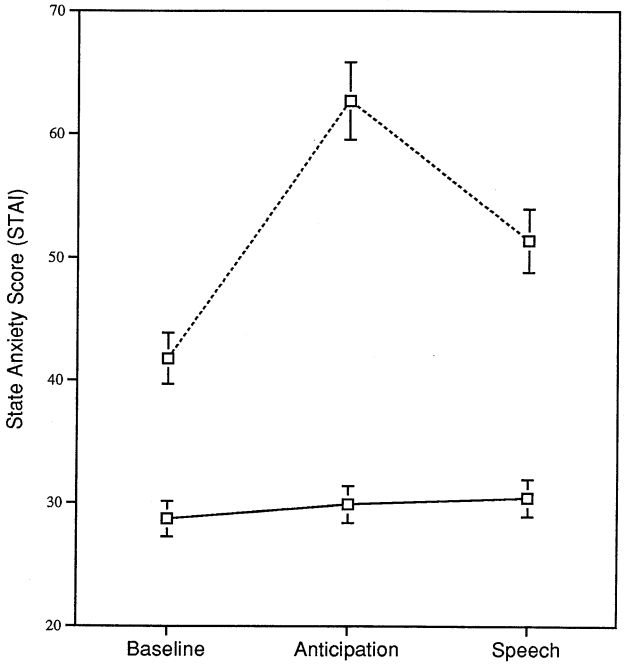

Figure 1. Mean state anxiety scores of phobics (dashed line) and controls (solid line) during baseline, anticipation, and postspeech conditions. Error bars represent standard errors of the mean.

traditional alpha band (8–13 Hz) was identical to that reported here for the more narrow band.

The EEGs were rederived offline to an average reference. An average reference is preferred over other referencing schemes, as it is the least biased by reference location. In addition, test–retest stability for the average reference is superior to other referencing schemes (Larson et al 1997). All power density values were log-transformed to normalize their distribution.

Residualizing the EEGs to Remove the Contributions of Muscle Artifact

To remove any confounding effects of muscle activity in the other frequency bands, within-subject residuals were computed across conditions regressing out variance associated with EMG (Davidson 1988; Ekman and Davidson 1993; Pivik et al 1993). Separate regressions were performed for each subject, electrode site, and band. These regressions yielded residualized values that were used in all subsequent analyses.

Results

Self-Report Measures

A two-way repeated measures Group (phobic/control) × Condition (baseline/anticipation/postspeech) multivariate analysis of variance (MANOVA; SAS Institute, Cary, NC) was computed on the state anxiety scores, and revealed highly significant main effects for Group [$F(1,25) = 70.16$, $p < .0001$] and Condition [$F(2,24) = 36.64$, $p < .0001$], as well as a highly significant Group × Condition interaction [$F(2,24) = 27.83$, $p < .0001$]. These data are displayed in Figure 1. The phobic subjects report more anxiety in each condition compared with controls. The Condition main effect is carried by the phobics, who show an elevation of reported anxiety during the anticipation condition, whereas controls show virtually no variation in reported anxiety across the three time points.

The PANAS data were analyzed in a three-way repeated measures MANOVA with Group, Condition, and Valence (positive/negative) as variables. This analysis revealed a highly significant three-way interaction [$F(2,24) = 13.20$, $p < .0001$]. These data are presented in Figure 2. As can be seen from this figure, the two groups show no difference in positive affect during the baseline condition, but the phobics show higher negative affect than controls during this period. In response to the anticipation condition, phobics show a large increase in negative affect (67%), whereas controls show an average increase of less than 10%. Just after the speech, positive affect changes little in either group from the anticipation condition; negative affect is somewhat reduced in the phobics, although it is still higher than during the baseline period.

Heart Rate

Heart rate (in bpm) was measured during each of the four conditions of the experiment. A two-way repeated measures MANOVA with Condition and Group as factors was computed on these data. This analysis revealed significant main effects for Condition [$F(3,22) = 15.26$, $p < .0001$] and Group [$F(1,24) = 4.34$, $p < .05$]. The Group × Condition interaction was not significant [$F(3,22) = 2.12$, $p > .10$]. The means for each condition, separately for controls and phobics, are presented in Figure 3. As can be seen from this figure, phobics have higher heart rates throughout all conditions compared with controls. In addition, it can be seen that HR rises for both groups during the anticipation and planning conditions and falls back toward baseline for the postspeech condition.

Blood Pressure

Separate analyses of systolic and diastolic blood pressure (BP) were performed with Group and Condition as factors. These analyses revealed significant main effects for Condition [for systolic: $F(3,22) = 28.43$, $p < .0001$; for diastolic: $F(3,22) = 4.78$, $p = .01$]. The Condition effect was a function of lower BP during the baseline condition compared with the other conditions (see Figure 4). Neither the main effect for Group nor the Group × Condition interaction was significant for either BP measure, though the phobics did show higher systolic and diastolic BP

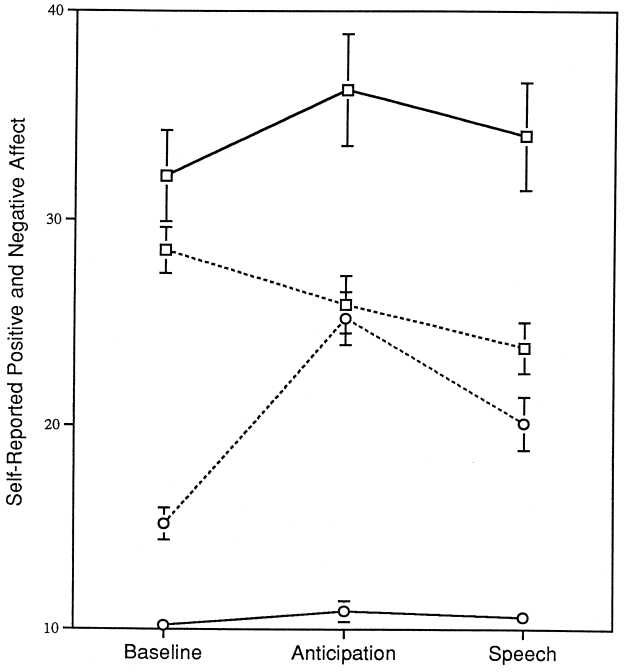

Figure 2. Mean state positive and negative affect (derived from the PANAS; Watson et al 1988) during baseline, anticipation, and postspeech conditions for phobics (phobic-positive, --□--; phobic-negative, --○--) and controls (control-positive, —□—; control-negative, —○—). Error bars represent standard errors of the mean.

during all conditions except baseline compared with controls.

Electrophysiology

ALPHA-1 POWER. The strategy we adopted in the analyses was to first compute overall four-way repeated measures MANOVAs on the residualized log alpha power with Condition, Region (six regions—anterior frontal, midfrontal, lateral frontal, anterior temporal, central, and parietal), and Hemisphere as the within-subjects variables and Group as the between-subjects variable. Our hypotheses called for interactions of Group with Region and Hemisphere. If the change in regional brain electrical asymmetry between the groups was dependent upon condition, then a four-way interaction would be expected. The data revealed a significant four-way interaction [$F(15,8) = 3.84$, $p = .03$].

On the basis of the lack of a main effect for Group or a Group × Hemisphere interaction during the baseline condition, we then calculated baseline minus task change scores for each of the subsequent three conditions (anticipation, planning, and postspeech). Thus, for measures of alpha power, positive numbers indicate less alpha power during the task compared with the baseline. Because decreases in alpha power are interpreted as indicative of increases in activation, positive numbers reflect greater activation during the task compared with baseline. This procedure also has the virtue of reducing variability among subjects in absolute levels of alpha power. All of the remainder of the reported effects are based upon these change scores from baseline.

Anticipation Condition. For the anticipation condition, there was a significant Hemisphere × Group interaction [$F(1,26) = 6.00$, $p < .03$] and a nonsignificant Region × Hemisphere × Group interaction [$F(5,22) = 2.16$, $p < .10$]. Because we had specific a priori hypotheses for the anterior scalp regions, we performed separate MANOVAs by region. Significant or marginally significant Group × Hemisphere interactions were obtained for the anterior temporal (T3/4) [$F(1,26) = 12.01$, $p < .002$] and the lateral frontal (F7/8) regions [$F(1,26) = 3.68$, $p < .06$] (see Figure 5). These interactions were a result of phobics showing greater activation in the right- compared with the left-sided region relative to controls, who in most cases showed the opposite pattern. There was also a trend for the phobics to show greater relative right-sided activation in the parietal region [$F(1,22) = 3.26$, $p = .08$]. There were no main effects for Group.

The overall patterning of data is illustrated in Figure 6, which displays a topographic *t* map of the magnitude of activation (i.e., decrease in alpha power) during the anticipation condition compared with baseline.

Planning Condition. For the planning condition, the Hemisphere × Group interaction was significant [$F(1,22) = 5.80$, $p < .03$]. No other interactions with Group were

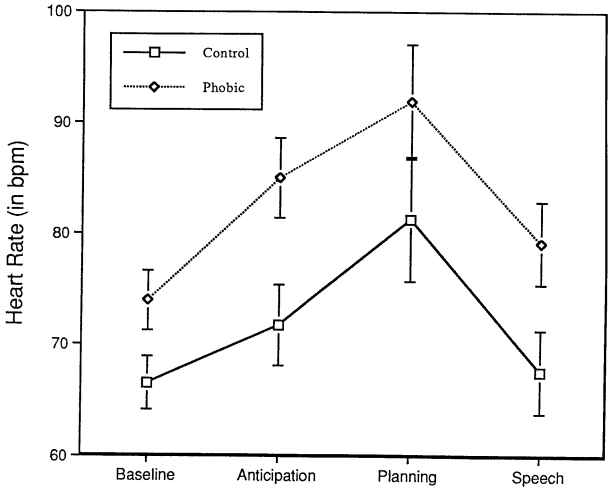

Figure 3. Mean heart rate during baseline, anticipation, planning, and postspeech conditions for phobics and controls. Error bars represent standard errors of the mean.

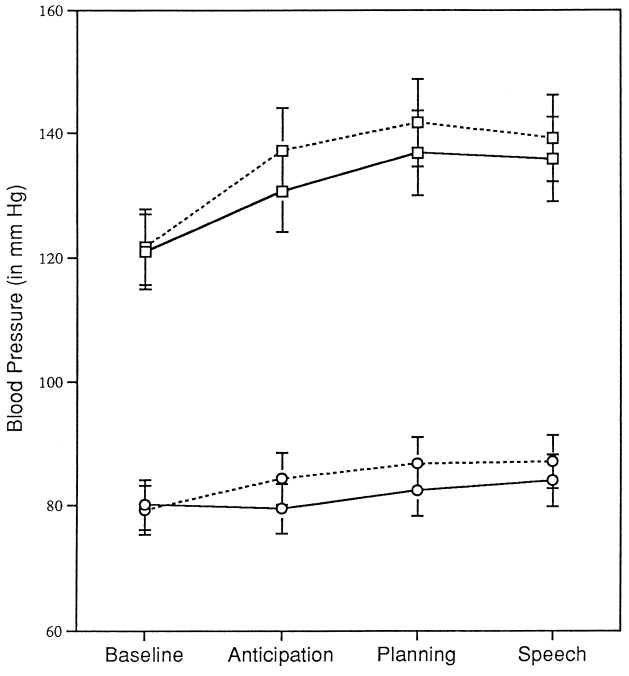

Figure 4. Mean systolic and diastolic blood pressure during baseline, anticipation, planning, and postspeech conditions for phobics (phobic-systolic, --□--; phobic-diastolic, --○--) and controls (control-systolic, —□—; control-diastolic, —○—). Error bars represent standard errors of the mean.

significant. As in the anticipation condition, the pattern of results was the same, with the phobics showing relatively more right versus left-sided activation during this condition compared with controls. Also as in the anticipation condition, there were no main effects for Group.

Postspeech Condition. For the postspeech condition, none of the interactions with Group were significant (all Fs < 2.0).

OTHER BANDS. We computed overall MANOVAs with Condition, Region, and Hemisphere as repeated factors and Group as a between-groups factor for data in each of the other bands. There were six additional bands that we tested (alpha-2, delta, theta, beta-1, beta-2, and beta-3). We used a Bonferonni-corrected alpha level of .05/6 ($p < .008$), since we did not have a priori predictions for effects in these other bands.

Analyses of the alpha-2 band yielded no significant interactions with Group or main effect for Group (all ps $>$ .25). In the delta band, no significant effects with Group were present (all ps $> .08$). In the theta band, there were no significant effects with Group, but the Hemisphere $\times$ Group interaction was marginally significant [$F(1,22) = 5.30$, $p < .04$]. The direction of this interaction parallels the effects described above for the alpha-1 band. All other ps were $>.08$ for power in the theta band.

There were no effects that approached significance in the beta-1 band (all ps $> .35$). In the beta-2 band, the Condition $\times$ Hemisphere $\times$ Group interaction approached significance [$F(2,21) = 5.25$, $p < .02$]. This interaction was a function of the phobics having more beta-2 power in the right compared with left hemisphere during the planning task, whereas the controls tended to show more power in this band in the left than right hemisphere. All other effects with Group for the beta-2 band had ps $> .15$. There were no effects with Group that approached significance in the beta-3 band (all ps $> .4$).

HIERARCHICAL REGRESSIONS EXAMINING EEG AND HR AS PREDICTORS OF TASK-INDUCED EMOTIONAL CHANGES. Because there was evidence for both HR and EEG asymmetry differences accompanying changes in anxiety and mood, we examined the extent to which each physiologic system accounted for overlapping or unique portions of the variance in these self-report measures. In light of the fact that the anticipation condition yielded the most consistent group differences, we restricted our analyses to change scores from baseline for this condition. We computed two groups of regressions across Group. We entered in the first step the two anterior EEG asymmetry variables that we found to most reliably differentiate between groups: anterior temporal and lateral frontal asymmetry. For the anticipation condition, increases in right-sided activation in the anterior temporal and lateral frontal regions accounted for 29.1% of the variance in the increase in state anxiety in response to this condition [$F(2,22) = 4.52$, $p = .02$]. The increase in HR accounted for an additional 13.2% of the unique variance in state anxiety (after accounting for the effects of the EEG variables) [$F(1,23) = 4.82$, $p < .04$ for the increment in r^2]. Thus, the EEG and HR variables together account for 42.3% of the variance in the increase in state anxiety in response to the anticipation condition [$F(3,21) = 5.14$, $p < .01$ for the model].

Reversing the order of entry of variables into the regression equation indicates that when the HR change score is entered first, it accounts for 20.3% of the variance in the increase in state anxiety during the anticipation condition [$F(1,23) = 5.89$, $p = .02$]. The anterior asymmetry variables next accounted for an additional 22.0% of the variance [$F(2, 22) = 5.58$, $p = .01$].

When the identical form of hierarchical regression was performed on the PANAS-negative affect change scores in response to the anticipation condition, an identical, though even more robust, pattern emerged. The two anterior EEG asymmetry variables entered as Step 1 in the regression accounted for 28.8% of the variance in the increase in

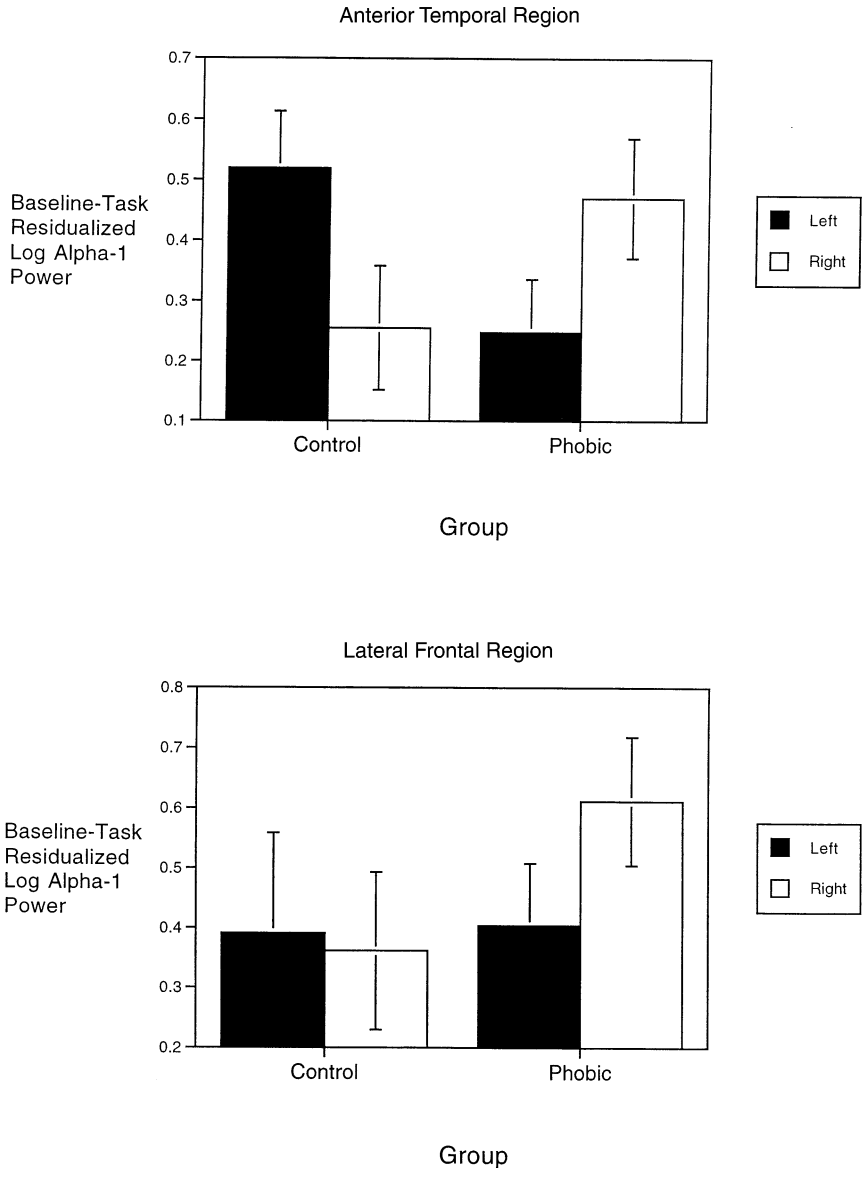

Figure 5. Baseline minus anticipation condition residualized EEG for alpha-1 (8–10 Hz) power density for average-reference data for the left and right anterior temporal (T3/T4) and lateral frontal (F7/F8) scalp sites for phobics and controls. Because the data are expressed as change scores from baseline, higher numbers denote increased activation during the anticipation condition relative to baseline. Error bars represent standard errors of the mean.

PANAS-negative affect in response to the anticipation condition [$F(2,22) = 4.45$, $p = .02$]. The increase in HR accounted for an additional 19.9% of the unique variance in PANAS-negative affect [$F(1,23) = 8.16$, $p < .01$]. Thus, the EEG and HR variables together accounted for 48.7% of the variance in the increase in PANAS-negative affect in response to the anticipation condition [$F(3,21) = 6.65$, $p < .005$ for the model].

Again, the order of entry of the variables was reversed. When HR was entered first, it accounted for 27.9% of the variance in the increase in PANAS-negative affect during the anticipation condition [$F(1,23) = 8.88$, $p < .01$]. The two anterior EEG asymmetry variables entered as Step 2 accounted for an additional 20.8% of the variance in the increase in PANAS-negative affect [$F(2,22) = 8.65$, $p < .002$].

Discussion

Our findings represent the first study in which quantitative EEG and autonomic measures have been jointly recorded from social phobics during the provocation of anxiety. We specifically predicted that while phobics anticipated making a public speech, they would exhibit increased right-sided anterior activation and would show elevations in HR compared with controls. In line with our predictions, we found significant elevations in self-reported anxiety and negative affect in anticipation of speaking among phobics,

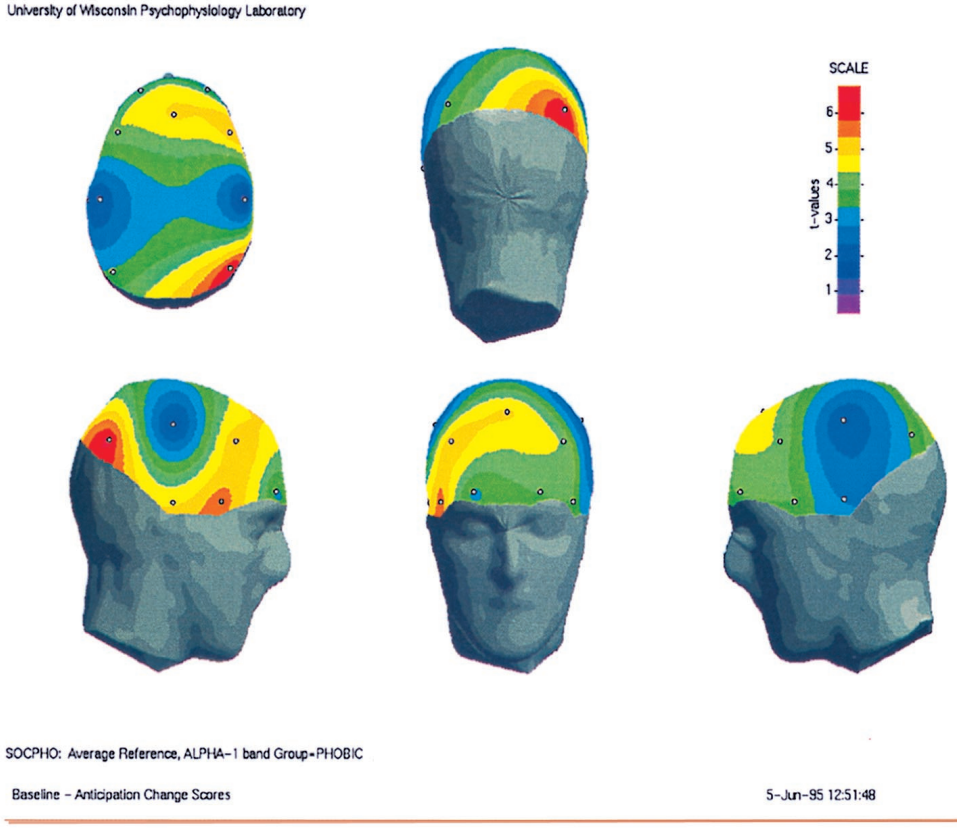

Figure 6. Topographic map of the baseline minus anticipation residualized alpha power density change score *t* values derived from average-reference data. Maps were created by calculating the relevant *t* score for each site and then using a spline interpolation to map the resulting *t* scores onto a normative head model. Higher *t* values are reflected in the red end of the color scale and denote increased activation in the anticipation condition compared with baseline. The top portion of the figure displays the *t* map for the phobics and the bottom portion displays the *t* map for the controls. We present summary topographic maps to illustrate the regional patterning of brain electrical activity across the scalp; however, our inferential statistics are not based upon interpolated pixel values but rather upon actual measured power at actual electrode sites.

but not among controls, illustrating the differential effects of this manipulation. Heart rate was elevated for the phobics relative to the control subjects during all but the planning condition. In response to the anticipation condition, pronounced differences in regional EEG were present in the phobics compared with the controls. Phobics showed increased right-sided activation in the anterior temporal and lateral prefrontal regions compared with controls. In addition, there was a trend toward increased right-sided parietal activation as well. This general pattern of increased right-sided activation was present during both the anticipation condition and the planning condition. These EEG changes were specific to the alpha-1 band. Regression analyses indicated that both the HR increase and the increase in right-sided prefrontal and anterior temporal activation from baseline to anticipation accounted for significant independent variance in the increase in both state anxiety and state negative affect during the latter condition. Together, the anterior EEG asymmetry measures and HR accounted for 48.7% of the variance in the change in state negative affect during the anticipation condition relative to baseline. We chose to conduct the regression analyses across Group so that we would have an adequate sample size for this analysis; however, it must be noted that since there were large group differences in anxiety and negative affect, the findings we observed should not be taken as an estimate of the variance that would be accounted for by the EEG and HR measures in an unselected sample.

The pattern of increased right-sided activation in the temporal and frontal regions among social phobics is consistent with the patterns of cerebral activation observed in other anxiety disorders (Nordahl et al 1998; Rauch et al 1995, 1997) and in depressed patients who have a comorbid anxiety disorder (Bruder et al 1997). Furthermore, the results suggest that it is the elicitation of anxiety that accounts for the increase in right anterior activation. Social phobics, like individuals with panic disorders or simple phobias, show increased right anterior activation when they are in an anxious state. We did not observe differences between the two groups in cerebral activation during the resting baselines. The trend toward increased right-sided parietal activation among the phobics during the anticipation condition is consistent with proposals that assign a special role to this brain region in the regulation of arousal (Heller and Nitschke 1997; see Davidson et al 1999 for review).

These findings indicate the utility of using measures of brain electrical activity to predict the increase in anxiety in response to provocative challenge and underscore the fact that changes in HR are at least partially independent of changes in cortical activation in response to this challenge. The increase in right-sided anterior activation is likely associated with the increased vigilance and attention associated with anxiety (MacLeod and Mathews 1988). Regions of the prefrontal cortex and structures with which it is interconnected (e.g., the anterior cingulate) have been implicated in various attentional processes (Posner 1995). The HR changes are likely produced by activity in subcortical structures such as the amygdala (LeDoux 1987) and hypothalamus (Smith et al 1990). Though these subcortical structures are part of a circuit that includes the prefrontal cortex, it is likely that the territories of prefrontal cortex with which the amygdala and other subcortical structures are most directly connected are sufficiently ventral and medial (Amaral et al 1992) to be unreflected in the scalp EEG.

Several features of our methodology for the recording and analysis of the electrophysiologic data warrant emphasis. First, the EEG was rederived to an average reference, which yields estimates of scalp distribution that are least biased by reference location. Second, we examined power in all frequency bands and found the effects to be restricted to the alpha band, similar to our previous research in both normal (Davidson et al 1990a) and depressed (Henriques and Davidson 1991) subjects. Third, we sampled the EEG at a relatively fast sampling rate (250 Hz) to permit the extraction of a high-frequency "EMG" band (70–80 Hz). Power in this latter band was used to residualize the EEG in the traditional frequency bands and statistically remove the variance contributed by muscle activity. As we have advocated in the past (Davidson 1988; Ekman and Davidson 1993; Henriques and Davidson 1990; Larson et al 1997), we regard this step as particularly critical in studies in which anxiety is elicited, because the production of anxiety is often accompanied by significant elevations in muscle tension, which will intrude into the traditional EEG frequency bands and cause artifactual changes in EEG power, even in the alpha band (Pivik et al 1993). This procedure eliminated any possible confounding from scalp and facial muscle tension and jaw clenching.

There were group differences in self-reported affect and in HR during the baseline condition, with the phobics reporting more negative affect and displaying higher HR during this period compared with the controls; however, no significant Group $\times$ Hemisphere interaction was observed for EEG measures during the baseline period. On the basis of the lack of a significant group difference at baseline, we computed change scores from baseline. The fact that phobics did show elevations compared with controls in negative affect and HR during the period indicates that the former group was indeed somewhat more anxious than the controls even prior to the imposition of the speech challenge. This is understandable in light of the fact that subjects were aware that a speech

challenge would be required during the session, as indicated by their informed consent. We observed group differences in brain electrical activity in response to the speech stress after subtracting out baseline activity, during which no significant group differences were observed. The fact that phobics were clearly in a more anxious state during baseline compared with the controls works against our finding significant group differences in the change from the baseline to the anticipation condition.

Despite the utility of scalp-recorded electrophysiology that we have demonstrated here, there are significant limitations that must not go unmentioned. Chief among these is the relatively poor spatial resolution afforded by these methods. Although techniques are on the horizon for very high-density electrode arrays that improve spatial resolution (Nunez 1995), such techniques ultimately must be used in conjunction with other neuroimaging modalities that provide better spatial resolution (e.g., fMRI), and most importantly, enable the detection of activity in subcortical structures (see Davidson and Irwin 1999 for review).

This study highlights the utility of combining quantitative electrophysiology with autonomic recording in the study of the central and peripheral physiologic changes associated with anxiety. When recorded and analyzed in the manner featured in this article, these methods, along with self-report, provide a unique window to examine the multiple response systems implicated in anxiety. The findings strongly confirm the major hypotheses that this study was designed to test and specifically indicate that when anxiety is provoked in social phobics while they wait to make a public speech, significant increases in right-sided anterior temporal and lateral prefrontal activation occur.

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