

# Brain ERPs of depressed patients to complex tones in an oddball task: Relation of reduced P3 asymmetry to physical anhedonia

GERARD E. BRUDER,<sup>a</sup> CRAIG E. TENKE,<sup>a</sup> JAMES P. TOWEY,<sup>a</sup> PAUL LEITE,<sup>a</sup> REGAN FONG,<sup>a</sup>  
JONATHAN E. STEWART,<sup>b</sup> PATRICK J. MCGRATH,<sup>b</sup> AND FREDERIC M. QUITKIN<sup>b</sup>

<sup>a</sup>Department of Biopsychology, New York State Psychiatric Institute, New York, NY, USA

<sup>b</sup>Depression Evaluation Service, New York State Psychiatric Institute, New York, NY, USA

## Abstract

Event-related potentials to binaural complex tones were recorded from 40 depressed outpatients and 22 normal control participants at 30 electrode sites. Patients did not differ from control participants in N1 or P3 amplitude but showed greater N2. N2 was greater over right than over the left hemisphere at lateral sites in patients and control participants. A P3 asymmetry was found for control participants and patients with low scores on a physical anhedonia scale, but not for patients with high anhedonia scores. Topographic (local Laplacian) maps corresponding to P3 showed greater radial current flow over right than over left central regions in control participants. Patients with high anhedonia did not show this asymmetry, whereas patients with low anhedonia showed an intermediate asymmetry. These findings support the hypothesis that anhedonic depression is associated with dysfunction of right hemisphere mechanisms mediating the processing of complex pitch information.

**Descriptors:** Depression, P3, Asymmetry, Anhedonia

Studies of event-related brain potentials (ERPs) in depressed persons have generally found reduced amplitude of early potentials such as N1, which might reflect a deficit in sensory processing or arousal level in depression (Burkhart & Thomas, 1993; El Masioui & Lesevre, 1988; Roth, Pfefferbaum, Kelly, Berger, & Koppell, 1981; Shagass, 1981; Yee, Deldin, & Miller, 1992). In contrast, the amplitude of the N2 potential tends to be greater in depressed persons than in normal control individuals (Giese-Davis, Miller, & Knight, 1993; Sandman, Vigor-Zierk, Isenhardt, Wu, & Zetin, 1992; Sara et al., 1994). Giese-Davis et al. found that the enhanced N2 in dysthymic or anhedonic individuals was not due to a difference in mismatch negativity (or N2a) but to greater amplitude of the N2b subcomponent. They suggested that the N2 enhancement may be related to voluntary allocation of conceptual resources. Findings for the P3 potential have been less consistent, with about half of the studies finding a reduction of P3 amplitude in depressed individuals and the other half finding no difference from normal control participants (Roth, Duncan, Pfefferbaum, & Timsit-Berthier,

1986). There is evidence that P3 reduction in depression varies with severity of depressive or psychotic symptoms (Gangadhar, Ancy, Janakiramaiah, & Umopathy, 1993; Santosh, Malhotra, Raghunathan, & Mehra, 1994) and is normalized following clinical recovery (Blackwood et al., 1987). Most studies of ERPs in depressed persons have used relatively simple "oddball" tasks, in which an infrequent target tone occurs in a series of standard tones. In a recent study (Bruder et al., 1995), we measured ERPs of depressed patients to complex tones during a more cognitively challenging dichotic listening test. Normal control participants showed the expected behavioral left ear (right hemisphere) advantage for dichotic pitch discrimination (Siddis, 1980), which was associated with greater P3 amplitude over the right than over the left hemisphere sites. Depressed patients had smaller P3 amplitude than did normal control participants and did not show either the behavioral left ear advantage or the associated hemispheric asymmetry of P3. Our interpretation of these findings was that right hemisphere mechanisms normally involved in mediating complex pitch discrimination (Siddis, 1980; Siddis & Volpe, 1988) were not activated in depressed participants. This interpretation is consistent with other findings for depressed persons using neuropsychological tests (Flor-Henry, 1976; Miller, Fujioka, Chapman, & Chapman, 1995), tests of visual field asymmetries (Heller, Etienne, & Miller, 1995; Jaeger, Borod, & Peselow, 1987; Liotti, Sava, Rizzolatti, & Caffarra, 1991), or dichotic listening tests (Bruder et al., 1989; Johnson & Crockett, 1982; Overby, Harris, & Leek, 1989), which have similarly been interpreted as evidence of right hemisphere dysfunction in depression.

This research was supported by an NIMH grant (MH36295) to G.E.B., and additional support for data processing was provided by a Mental Health Clinical Research Center grant (MH30906).

We thank Deborah Deliyannides, Stephen Donovan, Diane Rizzo and other members of the Depression Evaluation Service, where diagnostic evaluations and treatment of patients were conducted. We also thank Jürgen Kayser for assistance with statistical software.

Address reprint requests to: Dr. Gerard E. Bruder, Department of Biopsychology, New York State Psychiatric Institute, 722 West 168 Street, New York, NY 10032, USA.

Recent studies in healthy adults using auditory and visual “oddball” tasks and sufficiently large numbers of electrodes have found greater P3 amplitude over the right than over the left hemisphere, particularly at frontocentral sites (Alexander et al., 1995, 1996). The main purpose of the present study was to determine whether depressed individuals and normal control participants would show this P3 asymmetry during an oddball task with binaurally presented complex tones. Based on our prior findings for a dichotic complex tone task (Bruder et al., 1995), we hypothesized that depressed participants would show less evidence of P3 asymmetry than normal individuals. Earlier ERP components (N1, N2) were also examined to explore further the stage of information processing responsible for alterations of laterality in depression. Moreover, a larger array of scalp electrodes was used in this study to permit topographic analyses using current source density (CSD) measures. CSD is a “reference-free” representation of patterns of radial (transcranial) scalp current density, which produces topographies with peaks that are more sharply localized than those of scalp potentials (Hjorth, 1980; Nunez, 1981).

An additional purpose of this study was to continue to explore the clinical features of depressed persons who show abnormalities of hemispheric asymmetry. Previous studies have indicated that persons having a melancholic depression with pervasive anhedonia showed no left ear (right hemisphere) advantage on the dichotic complex tone test, whereas individuals having a nonmelancholic depression with preserved mood reactivity and atypical features showed a left ear advantage (Bruder et al., 1989). Anhedonia is not only a defining symptom of melancholic depression but also a feature of schizophrenia (Meehl, 1975) and may be of value for identifying persons “at risk” for psychopathology (Chapman, Kwapil, Eckblad, & Zinser, 1994; Miller & Yee, 1994). In the present study, self-ratings on the Revised Physical Anhedonia Scale (Chapman & Chapman, 1978) were used to evaluate whether or not the symptom of anhedonia is related to abnormalities of P3 asymmetry in depressed individuals. Specifically, it was hypothesized that depressed persons with high physical anhedonia would be particularly likely to show reduced P3 asymmetry.

A methodological issue addressed in this study was the response hand used by participants during the oddball task. Negative movement-related potentials are known to be maximal over frontocentral regions contralateral to the response hand (Kutas & Donchin, 1980; Neshige, Luders, Friedman, & Shibasaki, 1988; Singh et al., 1992). If the movement-related potential overlaps the endogenous ERPs in the oddball task, the increase in negativity at central sites (C3,C4) would increase N2 amplitude and decrease P3 amplitude contralateral to the movement. This activity would result in greater P3 amplitude over the right (C4) than over the left (C3) central site when participants respond with their right hand (Ford et al., 1994). Therefore, the variable of response hand was controlled in this study.

## Method

### Participants

ERPs were recorded from 40 depressed outpatients who were attending a university-affiliated depression research clinic at New York State Psychiatric Institute and 22 normal control participants recruited from hospital personnel, local colleges, and a pool of normal volunteers. All aspects of the diagnostic assessment of the depressed individuals were carried out by research psychiatrists in the clinic. All depressed participants had unipolar depressive disorders. Thirty-one patients met DSM-IV criteria for major de-

pressive disorder and the remaining nine met criteria for dysthymic disorder. The depressed participants were tested after a minimum drug-free period of 7–10 days, with most participants being drug-free for a considerably longer period. The normal control participants were screened using a modified version of the Schedule for Affective Disorders and Schizophrenia–Lifetime Version (Spitzer & Endicott, 1975) to exclude those with current or past psychopathology. All participants were screened for hearing loss using a standard audiometric evaluation. Participants had less than a 10-dB difference between ears and a hearing loss no greater than 30 dB at 500, 1000, or 2000 Hz. Individuals were not included in the study if they had a neurological or substance abuse disorder.

Table 1 shows the characteristics of the depressed persons and normal control participants. The depressed participants did not differ significantly from control participants in gender or age. Persons in the depressed group were 22–52 years, and those in the control group were 24–57 years. A small but significant difference was present between groups in mean education,  $t(58) = 3.05$ ,  $p < .01$ , with control participants having more education than those in the depressed group. There was no difference between groups in handedness laterality quotients (LQs) on the Edinburgh Handedness Inventory (Oldfield, 1971). Ten items concerning hand preference for writing, drawing, holding a spoon, and so forth, were used to compute a laterality quotient,  $100(R - L)/(R + L)$ . A score of 100 on this inventory equals complete right-hand preference and  $-100$  equals complete left-hand preference. Four depressed (10%) and two normal control (9%) participants were left handed, whereas the remaining participants were right handed. Response hand was counterbalanced across subjects within each group, with 17 of the 40 depressed participants and 13 of the 22 normal control participants responding with the right hand and the remaining participants responding with the left hand. As would be expected, depressed persons had considerably higher scores on the Beck Depression Inventory (Beck, Ward, Mendelson, & Erbaugh, 1961),  $t(56) = 8.93$ ,  $p < .001$ , and on the Revised Physical

**Table 1.** Participant Characteristics

Variable	Patients	Normal participants
Gender ( <i>n</i> )		
Female	15	10
Male	25	12
Age (years)		
<i>M</i>	37.7	34.1
<i>SD</i>	8.8	9.4
Education (years)		
<i>M</i>	15.0 <sup>a,b</sup>	16.9
<i>SD</i>	2.4	2.2
Handedness (LQ)		
<i>M</i>	69.9	74.9
<i>SD</i>	50.4	44.8
Beck Depression Inventory		
<i>M</i>	20.9 <sup>a</sup>	2.3 <sup>c</sup>
<i>SD</i>	8.6	2.4
Physical Anhedonia Scale		
<i>M</i>	16.5 <sup>a</sup>	12.0 <sup>d</sup>
<i>SD</i>	9.0	5.8

<sup>a</sup>Patients significantly different from normal control participants,  $p < .05$ . <sup>b</sup> $n = 38$ . <sup>c</sup> $n = 18$ . <sup>d</sup> $n = 20$ .

**Table 2.** Characteristics of Anhedonia Subgroups

Variable	Anhedonia	
	High	Low
Gender ( <i>n</i> )		
Female	5	10
Male	15	10
Age (years)		
<i>M</i>	38.5	36.5
<i>SD</i>	9.1	8.7
Education (years)		
<i>M</i>	14.7 <sup>a</sup>	15.3 <sup>a</sup>
<i>SD</i>	2.1	2.1
Handedness (LQ)		
<i>M</i>	73.6	66.2
<i>SD</i>	52.8	49.0
Beck Depression Inventory		
<i>M</i>	22.8	19.0
<i>SD</i>	8.9	8.1
Physical Anhedonia Scale		
<i>M</i>	24.2 <sup>b</sup>	8.8
<i>SD</i>	4.9	3.9

<sup>a</sup>*n* = 19.

<sup>b</sup>Scores for high anhedonia patients were significantly greater than those for low anhedonia patients, *p* < .001.

Anhedonia Scale (Chapman & Chapman, 1978),  $t(58) = 2.32$ ,  $p < .05$ .

The median score of depressed participants on the Revised Physical Anhedonia Scale (*mdn* = 16) was used to divide that group into subgroups with high versus low scores. The characteristics of participants in these subgroups are shown in Table 2. Although there was a somewhat higher percentage of men in the high anhedonia group (75%) than the low anhedonia group (50%), these subgroups did not differ significantly in gender,  $\chi^2(1) = 2.67$ ,  $p > .10$ . Likewise, no significant difference was found in the gender distributions among these subgroups and normal control participants,  $\chi^2(2) = 2.97$ ,  $p > .10$ . No significant difference was found between the high and low anhedonia groups in age, education, or handedness LQs. About an equal number of participants with high (*n* = 9) and low (*n* = 8) anhedonia responded to targets with the right hand. There was also no difference in Beck Depression Inventory scores between these subgroups, and about an equal number of persons in the high (*n* = 15) and low (*n* = 16) anhedonia groups met DSM-IV criteria for major depressive disorder. A marked difference in anhedonia scores was found between groups, with the high anhedonia group having a score more than 2 standard deviations above the mean for normal control participants, and the low anhedonia group having a score essentially the same as the control group.

#### Oddball Task

A series of complex tones of two different fundamental frequencies, separated by an interstimulus interval of 2 s, were presented binaurally in six blocks of 50 trials. Frequent nontarget (80%) and infrequent target (20%) tones in each block had different fundamental frequencies. The complex tones were 250-ms square wave trains, linearly tapered over 10% at each end. The fundamental frequency of each tone corresponded to the major notes in the

octave between middle C (264 Hz) and C5 (528 Hz). The digitally synthesized tones were generated using the STIM portion of the NeuroScan software package and were presented via TDH-49 earphones at 72 dB SPL to each participant seated in a sound-attenuation booth. Each block contained a different pair of fundamental frequencies that were easily discriminable. Participants were instructed to respond as quickly as possible to infrequent target tones by pressing a button on a key pad.

#### Electrophysiological Recording

Scalp EEG was recorded from 13 lateral pairs of electrodes (FP1,2; F3,4; F7,8; FC5,6; FT9,10; C3,4; T7,8; CP5,6; TP9,10; P3,4; P7,8; P9,10; O1,2) and from four midline electrodes (Fz; Cz; Pz; Oz) using an electrode cap (Electro Cap International, Inc.) with a nose reference. Standard Beckman Ag/AgCl electrodes at supra- and infraorbital sites surrounding the right eye were used to monitor eyeblinks and vertical eye movements (bipolar), and electrodes at right and left outer canthi monitored horizontal eye movements (bipolar). All electrode impedances were below 5 Ks. The electroencephalogram (EEG) was recorded through a Grass Neurodata acquisition system at a gain of 10 K (5 K for eye channels), with a bandpass of 0.01–30 Hz. A PC-based EEG acquisition system (NeuroScan) acquired and digitized the data at 100 samples/second.

#### ERP Analyses

Continuous EEG data recorded during the oddball task were segmented for ERPs such that each record extended from 0.2 s before a tone to 1 s afterward. Blinks were corrected on a trial-by-trial basis using a linear regression algorithm (Semlitsch, Anderer, Schuster, & Presslich, 1986). Epochs contaminated by eye movements or other movement-related artifacts were excluded from analyses off-line by using a rejection criterion of  $\pm 100 \mu V$  on any channel. The number of valid trials remaining did not differ between groups. The average number of trials for depressed participants were 44 (range = 10–57) for targets and 170 (range = 45–237) for nontargets. The average number of trials for normal participants were 45 (range = 22–58) for targets and 176 (range = 80–239) for nontargets.

Average ERP waveforms were computed for targets and nontargets at each electrode for each participant, and across participants within each group. ERP amplitudes were measured as average values within the following windows: (a) N1, a negative component between 70 and 150 ms poststimulus; (b) N2, a negative component between 180 and 270 ms; and (c) P3, a late positive component between 280 and 700 ms. For analyses of N2, the difference in amplitude to targets minus nontargets was computed to examine N2 to targets independently from the influence of exogenous components (N1 and P2).

#### Statistical Methods

Average amplitudes within N1, N2, and P3 windows were subjected to a repeated-measures analysis of variance (ANOVA). To reduce the amount of data in these summary statistical analyses and allow orthogonal groupings of electrodes spanning regions of interest, electrode sites were selected for comparing frontal (F), central (C), and posterior (P) sites at medial and lateral locations over the right and left hemispheres (F = F3,4; F7,8; C = C3,4; T7,8; P = P3,4; P7,8). These regional differences were represented in the ANOVA by variables for frontal-posterior (F,C,P), medial-

lateral, and hemisphere. Stimulus condition (target, nontarget) was also included as an additional repeated measures variable in the ANOVA for N1 and P3. Between-subject variables included group (patient, control) and response hand (right, left). *F* ratios were evaluated using degrees of freedom computed with Greenhouse–Geisser epsilon correction (Jennings & Wood, 1976) where appropriate to counteract heterogeneity of variance–covariance matrices associated with repeated measures. Only findings that reached a .05 significance level are considered in this report. Significant frontal–posterior, medial–lateral, or hemisphere interactions were also evaluated after scaling the amplitudes across electrode sites (McCarthy & Wood, 1985). Higher-order interactions involving response hand, stimulus condition, frontal–posterior, medial–lateral, and hemisphere, which did not have a group interaction and did not bear on the hypotheses of this study, are not dealt with in this report.

Predicted differences in P3 asymmetry between patient subgroups with high versus low anhedonia scores were similarly evaluated in an ANOVA with the variables of group (low anhedonia, high anhedonia, control), response hand, stimulus condition, frontal–posterior, medial–lateral, and hemisphere.

Product-moment correlations were computed to examine the strength of the relationship between ERP measures (amplitudes or asymmetries) and scores on the Beck Depression Inventory and the Revised Physical Anhedonia Scale. Correlations with age and education were also examined. Significant correlations were validated using Spearman rank-order correlations.

### Topographic Analyses

Standard analysis of scalp potentials was supplemented by CSD analyses to localize further the obtained regional differences in P3 asymmetry. A CSD waveform is produced from an estimate of the second spatial derivative (Poisson's equation) of an ERP at each electrode or interpolated point (Nunez, 1981). The CSD preserves localized changes observable in a field potential map, but eliminates activity that varies linearly across the scalp, such as activity volume conducted from other regions. Although the CSD method provides a "reference-free" measure of an ERP topography, the resulting measure is not independent of the specific computational algorithm or the spatial resolution of the recording montage in any region (Tenke, Schroeder, Arezzo & Vaughan, 1993). To maintain the spatial resolution available using our montage, we computed a variant of a local Laplacian at each electrode using the Hjorth algorithm (Hjorth, 1980) with three to five neighboring electrodes. Whenever possible, the four nearest symmetric neighbors were chosen (e.g., for C3 the neighbors were F3, Cz, P3 and T7) to ensure comparability and symmetry of each calculation and to reduce distortion of these computations. Because computing a true second spatial derivative for electrodes at the edges of a montage is impossible, we used a conservative approach by not computing a Hjorth at these locations (i.e., FP1,2; FT9,10; TP9,10; P9,10). Although this method optimized the local Laplacian, the observed P3 asymmetries were also clearly evident using alternative computational approaches, for example, with spherical spline Laplacian interpolation (Tenke et al., in press).

Hemispheric difference maps of the Hjorth values corresponding to P3 asymmetry, illustrating hemispheric differences in radial current flow between homologous pairs of electrodes, were projected onto a map of the lateral view of the right hemisphere. An ANOVA of Hjorth amplitudes within the P3 window was computed for the three medial pairs of electrodes to assess the significance of observed group differences in hemispheric asymmetry.

## Results

### Behavioral Data

Accuracy levels of depressed and nondepressed participants were near perfect and did not differ significantly. The percentage of correct responses to targets was 95.5 ( $SD = 7.3$ ) among depressed participants and 96.5 ( $SD = 4.6$ ) among normal control participants. The percent correct rejection of nontargets was 99.0 ( $SD = 2.7$ ) in depressed participants and 99.6 ( $SD = 0.5$ ) in normal control participants. There was no significant difference among the high and low anhedonia subgroups and the normal control group in either correct responses to targets,  $F(2,59) = 1.39, p > .20$ , or correct rejections,  $F(2,59) = 1.41, p > .20$ .

### ERP Waveforms for Patients and Normals

Figure 1 shows the average ERP waveforms to correctly detected target tones for the depressed and control groups. The N1 component, which is most prominent at frontal and central sites, did not differ between the depressed and control groups. Depressed individuals did show greater N2 amplitude than control participants, a finding that was most evident at central sites. Although some trend was found for depressed participants to have smaller P3 amplitude than normal control participants at central and parietal sites, only the difference in N2 amplitude between groups was confirmed in the statistical analyses presented below.

### N1 Amplitude

ANOVA of the average amplitude in the N1 window indicated that there was no significant difference between the two main groups. There were also no significant interactions involving group.

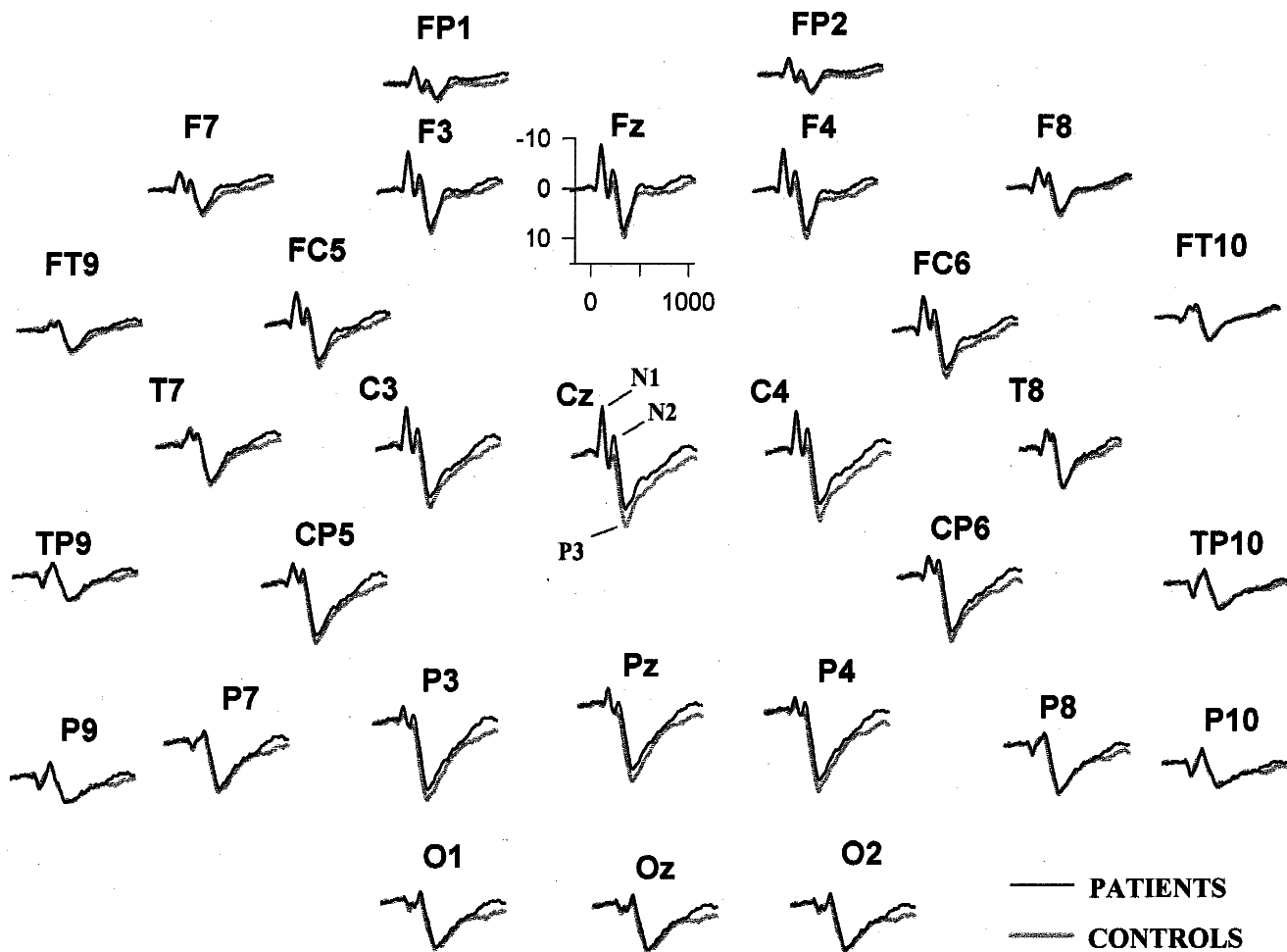
### N2 Amplitude

An ANOVA of average amplitude for target minus nontarget differences confirmed that depressed participants had greater N2 amplitude than did the control participants,  $F(1,58) = 4.03, p < .05$ . As can be seen in Figure 1, the group difference was most evident at medial sites where N2 was largest (e.g., C3, Cz, C4), Group  $\times$  Medial–Lateral interaction,  $F(1,58) = 6.57, p = .01$ . This interaction was also significant after vector scaling the amplitudes across electrode sites,  $F(1,58) = 4.57, p < .05$ . No other significant interactions involving group were found. There was a hemispheric asymmetry of N2, with N2 being greater over the right than over the left hemisphere. This N2 asymmetry was more evident at lateral than at medial electrode sites, as indicated by a Hemisphere  $\times$  Medial–Lateral interaction,  $F(1,58) = 11.61, p = .001$ .

Another question was whether or not larger N2 amplitude was equally present in the low and high anhedonia groups. An ANOVA of the N2 amplitude for the low and high anhedonia subgroups and normal control participants revealed a significant Group  $\times$  Medial–Lateral interaction,  $F(2,56) = 3.75, p < .05$ . At the medial–central electrodes (averaged over C3,4) where N2 was maximal, the N2 of the depressed group ( $M = -6.10, SD = 4.25$ ) was significantly larger than for the normal group participants ( $M = -3.90, SD = 3.44$ ),  $t(60) = 2.21, p < .05$ . There was, however, no difference in the N2 amplitude between the low anhedonia ( $M = -6.35, SD = 4.85$ ) and high anhedonia ( $M = -5.84, SD = 3.65$ ) subgroups, which indicates that the higher N2 amplitude in the depressed participants was not related to physical anhedonia.

### P3 Amplitude

Although the average amplitude in the P3 window tended to be smaller in the depressed group (see Cz and Pz sites in Figure 1), a group difference did not attain significance in the ANOVA. There



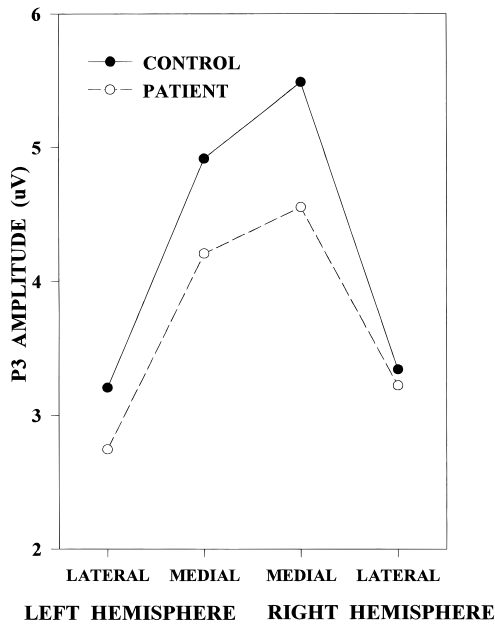
**Figure 1.** Average event-related potential waveforms to targets for depressed patients and normal control participants at 30 electrode sites.

was an overall hemispheric asymmetry of P3, with P3 being generally greater over the right than over the left hemisphere,  $F(1,58) = 13.36, p < .001$ . This P3 asymmetry was greater over medial than over lateral electrode sites in normal control participants but not in depressed participants (see Figure 2), a finding that was reflected in a Group  $\times$  Hemisphere  $\times$  Medial-Lateral interaction,  $F(1,58) = 6.95, p = .01$ . Further analyses confirmed that this three-way interaction was due to the presence of a Hemisphere  $\times$  Medial-Lateral interaction for the control group,  $F(1,20) = 8.50, p < .01$ , but not for depressed participants. This topographic interaction was significant after each topography was scaled by its vector amplitude,  $F(1,58) = 4.94, p < .05$ . There was also a Group  $\times$  Hemisphere  $\times$  Response Hand interaction,  $F(1,58) = 5.41, p < .05$ , but this interaction was not confirmed following vector scaling,  $F(1,58) = 2.33, p > .10$ .

The tendency for depressed persons to show less P3 asymmetry at medial sites than normal participants (Figure 2) was primarily due to the absence of a P3 asymmetry in the high anhedonia subgroup. Figure 3 shows the mean P3 amplitudes at medial and lateral sites over each hemisphere for the low and high anhedonia subgroups and the normal control group. The normal control and low anhedonia groups showed greater P3 amplitude over right than over the left medial sites, whereas the high anhedonia group did

not show this P3 asymmetry. The group difference in P3 asymmetry, which was largest at medial sites to target stimuli, was reflected in an overall ANOVA for low and high anhedonia subgroups and the normal control group as a Group  $\times$  Hemisphere  $\times$  Medial-Lateral  $\times$  Stimulus Condition interaction,  $F(2,56) = 4.51, p < .05$ . This interaction was confirmed after vector scaling of these amplitudes,  $F(2,56) = 3.46, p < .05$ . To clarify this interaction, a separate ANOVA was performed on the P3 amplitudes for each group. The analysis for the normal control group revealed a significant Hemisphere  $\times$  Medial-Lateral  $\times$  Stimulus Condition interaction,  $F(1,20) = 9.59, p < .01$ . As can be seen in Figure 3, normal control participants had the largest P3 asymmetry at medial sites to target stimuli. The ANOVA for the low anhedonia group showed a significant hemisphere effect,  $F(1,18) = 11.10, p < .005$ , with greater P3 amplitude over right than over left hemisphere sites. In contrast, the high anhedonia subgroup showed essentially no P3 asymmetry. The ANOVA for the high anhedonia group did not show either a significant hemisphere effect or a Hemisphere  $\times$  Medial-Lateral  $\times$  Stimulus Condition interaction.

An important question is whether or not the difference in P3 asymmetry among groups could be due to the somewhat higher proportion of men in the high anhedonia subgroup. Although we did not have enough female participants with high anhedonia scores

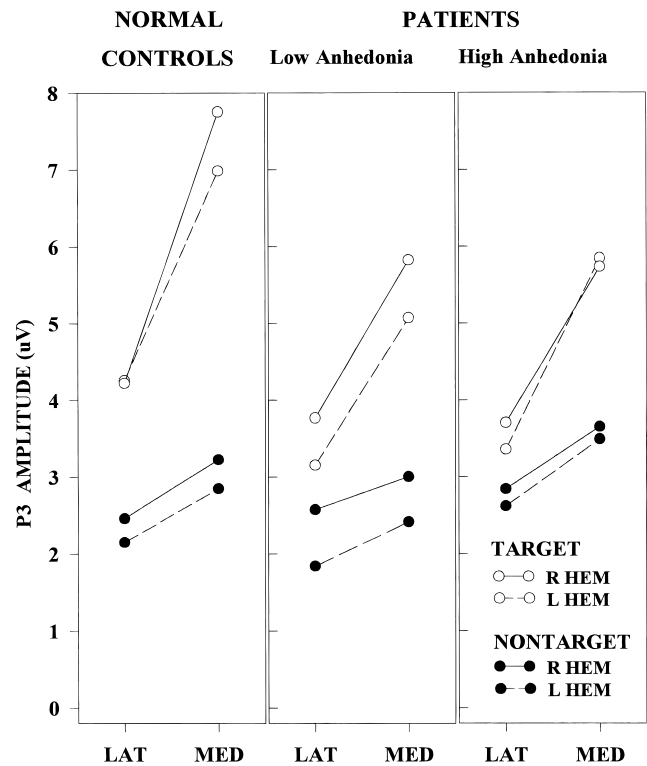


**Figure 2.** Mean P3 amplitude at medial and lateral sites over left and right hemispheres for depressed patients and normal control participants (averaged over targets and nontargets).

to examine the influence of anhedonia separately by gender, we were able to confirm the above group differences in P3 asymmetry when only the data for male participants with high or low anhedonia and normal control participants were entered into an ANOVA. The same difference in P3 asymmetry among groups seen for the full samples at medial sites for target stimuli was evident, and this difference was supported by a significant Group  $\times$  Hemisphere  $\times$  Medial-Lateral  $\times$  Stimulus Condition interaction for men,  $F(2,31) = 3.43, p < .05$ .

**Topographic Analyses**

The topography of regional differences in P3 asymmetry was examined using local Laplacian analyses (Hjorth, 1980). The CSD waveforms to target tones in normal adults showed a major positive peak (source) with a parietal maximum and a latency corresponding to P3 (Tenke et al., in press). This source extended asymmetrically into central regions, with greater amplitude over C4 than over C3. To illustrate the asymmetry of the CSD peak corresponding to the P3 window, the difference between Hjorth estimates for homologous pairs of electrodes over right and left hemispheres were projected onto a map of a lateral view of the right hemisphere (Figure 4). Dark regions indicate sites where radial current flow was greater over the right than over the left hemisphere. As can be seen in Figure 4, the map for the normal control group showed relatively greater current flow over right central regions. Participants with high anhedonia did not show this asymmetry, whereas participants with low anhedonia showed an intermediate asymmetry in the central region. The difference in asymmetry among participants with high and low anhedonia and the normal control group was confirmed in the ANOVA of the CSD for the P3 window. A significant Group  $\times$  Hemisphere interaction was found,  $F(2,56) = 9.69, p < .001$ . A robust Group  $\times$  Hemisphere  $\times$  Stimulus Condition interaction was also found,  $F(2,56) = 7.75, p = .001$ , indicating that the difference in CSD asymmetry across groups was more evident for target than for

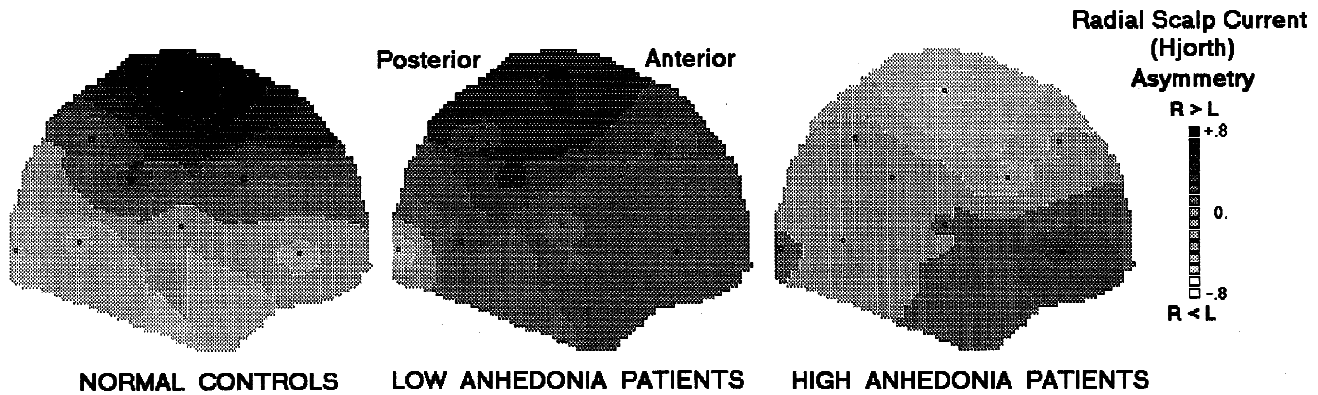


**Figure 3.** Mean P3 amplitude to targets and nontargets for normal control participants and low and high anhedonia patients at medial and lateral sites over each hemisphere.

nontarget stimuli. A one-way ANOVA of the CSD asymmetry scores of each group for target stimuli revealed a significant difference in hemispheric asymmetry among groups,  $F(2,59) = 5.89, p < .005$ . Scheffé multiple comparisons indicated that both the low anhedonia and control groups had significantly greater CSD asymmetry than did the high anhedonia group ( $p < .05$ ), whereas there was no significant difference between the low anhedonia and control groups.

**Correlational Analyses**

Correlations were computed to examine the relation of P3 asymmetry to participant characteristics and to continuous scores on self-rating scales for assessing depression and physical anhedonia. To reduce the number of correlational analyses, only P3 asymmetry to target tones at the central sites (C4 - C3) where P3 asymmetry was largest was entered in these analyses. Also, correlations were computed across all participants to maximize sample size. P3 asymmetry was not significantly correlated with age ( $r = -.01, ns$ ), education level ( $r = .02, ns$ ) or handedness LQ scores ( $r = .09, ns$ ). Significant correlations were found between P3 asymmetry and scores on the Beck Depression Inventory ( $r = -.29, p < .05$ ) and the Revised Physical Anhedonia Scale ( $r = -.38, p < .01$ ). Both correlations were also significant in Spearman analyses ( $r = -.32, p < .05$ , and  $r = -.39, p < .01$ ). Higher depression and physical anhedonia scores were associated with less P3 asymmetry favoring the right central site. Additional analyses were performed to examine the relation between depression or anhedonia scores and amplitude of the N2 and P3 components (mean of amplitude at C3 and C4). No significant correlations were found for these amplitude measures.



**Figure 4.** Differences in radial current flow between homologous pairs of electrodes over right and left hemispheres projected on the lateral view of the right hemisphere for normal control, low and high anhedonia groups.

## Discussion

### ERP Amplitudes in Depression

Depressed participants did not differ from normal control participants in N1 amplitude. This finding agrees with our prior findings for a dichotic complex tone task (Bruder et al., 1995) and indicates that early sensory/attentional processing of complex tones is intact in moderately depressed outpatients. Reduction of N1 amplitude, reported for depressed participants in several studies (Burkhart & Thomas, 1993; El Massioui & Lesevre, 1988; Roth et al., 1981; Yee et al., 1992) is apparently not universal and may be specific to severe depression or a subtype of depressive illness. For instance, Shagass (1981) found reductions of this early ERP component to be more evident in psychotic than neurotic individuals.

The depressed participants did show greater N2 amplitude when compared with normal control participants. This finding is in accord with studies finding enhanced N2 in depressed or dysthymic individuals and "at-risk" participants with high physical anhedonia scores (Giese-Davis et al., 1993; Miller, 1986; Sandman et al., 1992; Sara et al., 1994; Yee et al., 1992). Thus, N2 enhancement appears to be a very robust effect in depressed or anhedonic persons but contrasts sharply with the reduction of N2 amplitude found in schizophrenia (O'Donnell et al., 1993; Salisbury, O'Donnell, McCarley, Shenton, & Benavage, 1994). We did not find a N2 difference between depressed individuals with high versus low physical anhedonia scores, which suggests that anhedonia per se was not responsible for the enhanced N2 in depression. Giese-Davis et al. (1993) reported evidence that N2 enhancement in dysthymic or anhedonic persons is not related to an automatic response to targets, as would be reflected in mismatch negativity (N2a), but rather to a subsequent stage of processing involving initial allocation of conceptual resources (N2b). One possible explanation of the enhanced N2 among depressed participants is, therefore, that they allocate more cognitive resources than would normally be necessary to perform a simple oddball task. The depressed participants in this study and the dysthymic and anhedonic participants in the study by Giese-Davis et al. (1993) showed an enhancement of N2 in the absence of a difference in P3 amplitude. This finding is consistent with the suggestion that N2 and P3 provide independent sources of information (Miller, 1986).

The very simplicity of the oddball task and the ability of depressed persons to perform well on this task may also account for why the depressed participants in this study and in about half of studies using an oddball task (Roth et al., 1986) did not show a

reduction of P3 amplitude. Depressed participants in our previous study (Bruder et al., 1995) did show reduced P3 amplitude when performing a more cognitively demanding dichotic complex tone task. Given evidence that P3 reduction in depressed persons is related to severity of illness (Gangadhar et al., 1993; Santosh et al., 1994), it is also possible that the moderately depressed outpatients in this study may not have been disturbed severely enough to show a P3 reduction in an oddball task.

### ERP Asymmetries in Normal Adults

The findings of the present study replicate prior findings for healthy adults showing greater P3 amplitude over right than over left hemisphere in an oddball task (Alexander et al., 1995, 1996). Alexander et al. found this P3 asymmetry at frontocentral sites for target and nontarget stimuli in auditory and visual tasks. In the present study using binaural complex tones, the P3 asymmetry in normal adults was largest at medial and central sites. Topographic analyses using reference-free CSD (local Laplacian) analyses confirmed the presence of a posterior source corresponding to P3. This source extended asymmetrically into central regions, with greater radial current flow over the right than over the left hemisphere. This asymmetry parallels findings of positron emission tomography studies that have found evidence of enhanced activation of right temporal lobe structures during tone discrimination tasks (Holcomb et al., 1996; Mazziotta, Phelps, Carson, & Kuhl, 1982). The involvement of right hemisphere regions in complex pitch discrimination is also suggested by performance asymmetry, P3 asymmetry, and imaging data obtained during dichotic listening tests (Coffey, Bryden, Schroering, Wilson, & Mathew, 1989; Tenke, Bruder, Towey, Leite, & Sidtis, 1993). Although the exact mechanism responsible for greater P3 amplitude over right than over left hemisphere regions remains unknown, the mechanism is likely to reflect asymmetries related to the attentional, working memory, and pitch discrimination processes involved in performing the oddball task.

As in the study by Alexander et al. (1996), the P3 asymmetry to tones in healthy adults was preceded by asymmetry of the N2 component. The amplitude of N2 was greater over right than over left hemisphere sites. However, unlike the P3 asymmetry, N2 asymmetry was largest at lateral sites. Giard, Perrin, Pernier, and Bouchet (1990) found that mismatch negativity in a region 170–240 ms following tone onset was greater over the right than over the left hemisphere. They suggested that this finding may represent an electrophysiological basis of a frontal process, involving predom-

inantly the right hemisphere, associated with an automatic attentional orienting. Rohrbaugh, Newlin, Varner, and Ellingson (1984) found a similar asymmetry of a frontal negative "O-wave," which was also interpreted in terms of a frontal predominance of orienting or attentional processes and right hemisphere dominance for processing tones.

### *ERP Asymmetries in Depression*

Depressed participants also showed asymmetries of N2 and P3 in the oddball task. The P3 asymmetry of depressed participants at medial-central sites tended to be smaller than that seen for normal control participants, primarily because of the lack of a P3 asymmetry in depressed participants with high scores on the Revised Physical Anhedonia scale (Chapman & Chapman, 1981). Topographic (local Laplacian) analyses showed greater radial current over the right than over the left central regions in normal adults, corresponding to the P3 asymmetry. Depressed participants with high anhedonia scores did not show this asymmetry, whereas persons with low anhedonia scores showed an intermediate asymmetry. These findings provide further support for the hypothesis that depressed individuals, in particular those having an anhedonic depression, display right hemisphere dysfunction (Bruder et al., 1989). No difference in N2 asymmetry was found between depressed and normal control participants, strengthening the conclusion that abnormalities of laterality in depression involve late stages of cognitive processing reflected by the P3 component, for example, stimulus evaluation or working memory (Bruder et al., 1995).

Correlational analyses confirmed that higher depression and anhedonia ratings were associated with less P3 asymmetry favoring the right central region. P3 asymmetry was not, however, related to age, education, or handedness scores. Therefore, the difference in education between the depressed and control groups could not explain the difference in P3 asymmetry between these groups. Moreover, there was no difference in education between participants with high versus low anhedonia, but the P3 asymmetry of these subgroups differed in the predicted direction. There was a nonsignificant trend for a higher percentage of males in the high than in the low anhedonia subgroup. Male participants have generally been found to have higher scores than female participants on the Revised Physical Anhedonia Scale (Chmielewski, Fernandes, Yee, & Miller, 1995), which may account for the somewhat greater number of men in the high anhedonia subgroup. It should be noted, however, that no difference in gender was found between the high anhedonia and normal control groups, and, therefore, the absence of P3 asymmetry in the high anhedonia subgroup could not be due to a gender difference. Also, the group differences in P3 asymmetry were unchanged when we examined the data separately for men. However, given the limited number of women in the high anhedonia subgroup, more data will be needed to confirm that the findings generalize to women having an anhedonic depression.

Another unresolved issue is whether or not nonpatient anhedonic individuals, defined on the basis of questionnaire data, might display an absence of P3 asymmetry similar to anhedonic depression. Although studies have found a P3 reduction among anhedonic participants (Miller, 1986; Simons, 1982), this P3 reduction has not been significant in some studies (Giese-Davis et al., 1993) and there are no reports of the reduction being asymmetric. These studies used a limited array of scalp electrodes and were not designed to examine the issue of P3 asymmetry in anhedonia. Further study of the topography of P3 in nonpatient anhedonic individuals is needed to resolve this issue.

### *Influence of Response Hand on ERP Asymmetries*

Asymmetries of N2 and P3 at medial-central sites (C3, C4) have been found to be modulated by response hand, particularly for targets for which a response is required (Tenke et al., in press). Movement-related negative potentials that occur prior to a response would be expected to be maximal over central regions contralateral to the side of the response hand (Neshige et al., 1988; Singh et al., 1992). Because response hand was counterbalanced across participants in each group and was entered as a control factor in analyses, the overall hemispheric asymmetry of P3 and the group difference in P3 asymmetry cannot be due to response-related potentials.

### *Theoretical Model*

Pervasive anhedonia is the cardinal symptom of DSM-IV criteria for major depression with melancholia. Anhedonia was originally hypothesized by Klein (1974) to characterize an "endogenomorphic" subtype of depression with a central nervous system disorder. In the tripartite model of depression and anxiety proposed by Clark and Watson (1991), anhedonia or lack of pleasure is viewed as one of three major symptom subtypes. This model may be helpful in understanding the relationship of anhedonia and other symptom features of depression to abnormalities of regional hemispheric asymmetry. The first subtype includes symptoms of general distress and negative affect that are common to both depression and anxiety. Studies of EEG alpha asymmetries provide evidence that these forms of negative affect and withdrawal behaviors are associated with an abnormal frontal asymmetry characterized by relatively greater right than left frontal activity (Davidson, 1992). The second subtype includes symptoms of anhedonia and absence of positive affect, which are specific to depression. Our prior dichotic listening findings for melancholia (Bruder et al., 1989) and the lack of a P3 asymmetry for complex tones in depressed individuals with high physical anhedonia scores suggest the hypothesis that anhedonic depression is associated with dysfunction of right hemisphere mechanisms mediating complex pitch discrimination. This dysfunction may involve right temporoparietal regions that are implicated not only in pitch discrimination (Coffey et al., 1989; Holcomb et al., 1996; Sidtis, 1985; Sidtis & Volpe, 1988) but also in the generation of the P3 component (Johnson, 1989; Knight, Scabini, Woods, & Clayworth, 1989) and the processing of emotional stimuli (Kayser et al., 1997). Both right frontal activation, in the form of relatively less EEG alpha power, and evidence of right posterior dysfunction on cognitive tests have been reported to occur in depression (Tucker, Stenslie, Roth, & Shearer, 1981). The third subtype includes symptoms of anxious arousal and tension, which are specific to anxiety. Heller et al. (1995) reviewed evidence that somatic manifestations of anxious arousal are associated with hyperactivation of right parietal regions. This evidence is supported by our recent finding of greater activation (less EEG alpha power) over right than over left posterior sites in depressed persons with an anxiety disorder, but not in nonanxious depressed persons (Bruder et al., 1997). Although the present study did not address the issue of comorbidity, it is important to note that an equal number of participants in the high anhedonia ( $n = 7$ ) and low anhedonia ( $n = 7$ ) groups also had an anxiety disorder. The larger P3 asymmetry in the low than in the high anhedonia participants could therefore not be attributed to the presence of anxiety disorders. The three symptom subtypes in the Clark and Watson model, negative affect, anhedonic depression, and anxious arousal, thus may involve different alterations of regional hemispheric function.

Further study of the relationship of physical anhedonia to regional hemispheric activation is needed to confirm the findings of this study and to test the above model. The present study was limited by reliance on a self-report measure of anhedonia. Electrophysiological measures (e.g., skin conductance) or observer ratings of participant responses to pleasant or unpleasant stimuli could

be used to provide more direct measures of anhedonia. Moreover, ERP measures could be obtained using emotional stimuli to determine whether blunted affective responses to these stimuli in depressed persons are associated with reduced P3 asymmetry, which would be consistent with a hypothesis of right temporoparietal dysfunction in anhedonic depression.

## REFERENCES

- Alexander, J. E., Bauer, L. O., Kuperman, S., Morzorati, S., O'Connor, S. J., Rohrbaugh, J., Porjesz, B., Begleiter, H., & Polich, J. (1996). Hemispheric differences for P300 amplitude from an auditory oddball task. *International Journal of Psychophysiology*, *21*, 189–196.
- Alexander, J. E., Porjesz, B., Bauer, L. O., Kuperman, S., Morzorati, S., O'Connor, S. J., Rohrbaugh, J., Begleiter, H., & Polich, J. (1995). P300 hemispheric asymmetries from a visual oddball task. *Psychophysiology*, *32*, 467–475.
- Beck, A. T., Ward, C. H., Mendelson, M., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, *4*, 561–571.
- Blackwood, D. H. R., Whakly, L. J., Christie, J. E., Blackburn, I. M., St. Clair, D. M., & McInnes, A. (1987). Changes in auditory P3 event-related potentials in schizophrenia and depression. *British Journal of Psychiatry*, *150*, 154–160.
- Bruder, G. E., Fong, R., Tenke, C. E., Leite, P., Towey, J. P., Stewart, J. E., McGrath, P. J., & Quitkin, F. M. (1997). Regional brain asymmetries in major depression with or without an anxiety disorder: A quantitative electroencephalographic study. *Biological Psychiatry*, *41*, 939–948.
- Bruder, G. E., Quitkin, F. M., Stewart, J. W., Martin, C., Voglmaier, M., & Harrison, W. M. (1989). Cerebral laterality and depression: Differences in perceptual asymmetry among diagnostic subtypes. *Journal of Abnormal Psychology*, *98*, 177–186.
- Bruder, G. E., Tenke, C. E., Stewart, J. W., Towey, J. P., Leite, P., Voglmaier, M., & Quitkin, F. M. (1995). Brain event-related potentials to complex tones in depressed patients: Relations to perceptual asymmetry and clinical features. *Psychophysiology*, *32*, 373–381.
- Burkhardt, M. A., & Thomas, D. G. (1993). Event-related potential measures of attention in moderately depressed subjects. *Electroencephalography and Clinical Neurophysiology*, *88*, 42–50.
- Chapman, L. J., & Chapman, J. P. (1978). *Revised Physical Anhedonia Scale*. (Available from L. J. Chapman, Department of Psychology, 1202 West Johnson Street, University of Wisconsin, Madison, WI 53706, USA).
- Chapman, L. J., Chapman, J. P., Kwapil, T. R., Eckblad, M., & Zinser, M. C. (1994). Putatively psychosis-prone subjects 10 years later. *Journal of Abnormal Psychology*, *103*, 171–183.
- Chmielewski, P. M., Fernandes, L. O. L., Yee, C. M., & Miller, G. A. (1995). Ethnicity and gender in scales of psychosis proneness and mood disorders. *Journal of Abnormal Psychology*, *104*, 464–470.
- Clark, L. A., & Watson, D. (1991). Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology*, *100*, 316–336.
- Coffey, C. E., Bryden, M. P., Schroering, E. S., Wilson, W. H., & Mathew, R. J. (1989). Regional cerebral blood flow correlates of a dichotic listening task. *Journal of Neuropsychiatry*, *1*, 46–52.
- Davidson, R. (1992). Anterior cerebral asymmetry and the nature of emotion. *Brain and Cognition*, *20*, 125–151.
- El Massioui, F., & Lesevre, N. (1988). Attention impairment and psychomotor retardation in depressed patients: An event-related potential study. *Electroencephalography and Clinical Neurophysiology*, *70*, 46–55.
- Flor-Henry, P. (1976). Lateralized temporal-limbic dysfunction and psychopathology. *Annals of the New York Academy of Sciences*, *280*, 777–795.
- Ford, J. M., White, P. M., Csernansky, J. G., Faustman, W. O., Roth, W. T., & Pfefferbaum, A. (1994). ERPs in schizophrenia: Effects of antipsychotic medication. *Biological Psychiatry*, *36*, 153–170.
- Gangadhar, B. N., Ancy, J., Janakiramiah N., & Umopathy, C. (1993). P300 amplitude in non-bipolar, melancholic depression. *Journal of Affective Disorders*, *28*, 57–60.
- Giard, M. H., Perrin, F., Pernier, J., & Bouchet, P. (1990). Brain generators implicated in the processing of auditory stimulus deviance: A topographic event-related potential study. *Psychophysiology*, *27*, 627–640.
- Giese-Davis, J. E., Miller, G. A., & Knight, R. A. (1993). Memory template comparison processes in anhedonia and dysthymia. *Psychophysiology*, *30*, 646–656.
- Heller, W., Etienne, M. A., & Miller, G. A. (1995). Patterns of perceptual asymmetry in depression and anxiety: Implications for neuropsychological models of emotion and psychopathology. *Journal of Abnormal Psychology*, *104*, 327–333.
- Hjorth, B. (1980). Source derivation simplifies topographical EEG interpretation. *American Journal of EEG Technology*, *20*, 121–132.
- Holcomb, H. H., Gordon, B., Loats, H. L., Gastineau, E., Zhao, Z., Medoff, D., Dannals, R. F., Woods, R., & Tamminga, C. A. (1996). Brain metabolism patterns are sensitive to attentional effort associated with a tone recognition task. *Biological Psychiatry*, *39*, 1013–1022.
- Jaeger, J., Borod, J. C., & Peselow, E. (1987). Depressed patients have atypical hemispace biases in the perception of emotional chimeric faces. *Journal of Abnormal Psychology*, *96*, 321–324.
- Jennings, J. R., & Wood, C. C. (1976). The E-adjustment procedure for repeated-measures analyses of variance. *Psychophysiology*, *13*, 277–278.
- Johnson, O., & Crockett, D. (1982). Changes in perceptual asymmetries with clinical improvement of depression and schizophrenia. *Journal of Abnormal Psychology*, *91*, 45–54.
- Johnson, R., Jr. (1989). Auditory and visual P300s in temporal lobectomy patients: Evidence for modality dependent generators. *Psychophysiology*, *26*, 633–650.
- Kayser, J., Tenke, C., Nordby, H., Hammerborg, D., Hugdahl, K., & Erdmann, G. (1997). Event-related potential (ERP) asymmetries to emotional stimuli in a visual half-field paradigm. *Psychophysiology*, *34*, 414–426.
- Klein, D. F. (1974). Endogenomorphic depression: A conceptual and terminal revision. *Archives of General Psychiatry*, *31*, 447–454.
- Knight, R. T., Scabini, D., Woods, D. L., & Clayworth, C. C. (1989). Contribution of temporal-parietal junction to the human auditory P3. *Brain Research*, *502*, 109–116.
- Kutas, M., & Donchin, E. (1980). Preparation to respond as manifested by movement-related potentials. *Brain Research*, *202*, 95–115.
- Liotti, M., Sava, D., Rizzolatti, G., & Caffarra, P. (1991). Differential hemispheric asymmetries in depression and anxiety: A reaction-time study. *Biological Psychiatry*, *29*, 887–899.
- Mazziotta, J. C., Phelps, M. E., Carson, R. E., & Kuhl, D. E. (1982). Tomographic mapping of human cerebral metabolism: Auditory stimulation. *Neurology*, *32*, 921–937.
- McCarthy, G., & Wood, C. C. (1985). Scalp distributions of event-related potentials: An ambiguity associated with analysis of variance models. *Electroencephalography and Clinical Neurophysiology*, *62*, 203–208.
- Meehl, P. E. (1975). Hedonic capacity: Some conjectures. *Bulletin of the Menninger Clinic*, *39*, 295–307.
- Miller, E. N., Fujioka, T. A. T., Chapman, L. J., & Chapman, J. P. (1995). Hemispheric asymmetries of function in patients with major affective disorders. *Journal of Psychiatric Research*, *29*, 173–183.
- Miller, G. A. (1986). Information processing deficits in anhedonia and perceptual aberration: A psychophysiological analysis. *Biological Psychiatry*, *21*, 100–115.
- Miller, G. A., & Yee, C. M. (1994). Risk for severe psychopathology: Psychometric screening and psychophysiological assessment. In J. R. Jennings, P. K. Ackles, & M. G. H. Coles (Eds.), *Advances in psychophysiology* (Vol. 5, pp. 1–54). London: Jessica Kingsley.
- Neshige, R., Luders, H., Friedman, L., & Shibasaki, H. (1988). Recording of movement-related potentials from the human cortex. *Brain*, *24*, 439–445.
- Nunez, P. L. (1981). *Electric fields of the brain: The neurophysics of EEG*. New York: Oxford University Press.
- O'Donnell, B. F., Shenton, M. E., McMarley, R. W., Faux, S. F., Smith, R. S., Salisbury, D. F., Pollak, S. D., Kikinis, R., & Jolesz, F. A. (1993). The auditory N2 component in schizophrenia: Relationship to MRI temporal lobe gray matter and to other ERP abnormalities. *Biological Psychiatry*, *34*, 26–40.

- Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. *Neuropsychologia*, *9*, 97–113.
- Overby, L. A., III, Harris, A. E., & Leek, M. R. (1989). Perceptual asymmetry in schizophrenia and affective disorder: Implications from a right hemisphere task. *Neuropsychologia*, *27*, 861–870.
- Rohrbaugh, J. W., Newlin, D. B., Varner, J. L., & Ellingson, R. J. (1984). Bilateral distribution of the O wave. In R. Karrer, J. Cohen, & P. Tueting (Eds.), *Brain and information: Event-related potentials. Annals of the New York Academy of Sciences*, *425*, 267–270.
- Roth, W. T., Duncan, C. C., Pfefferbaum, A., & Timsit-Berthier, M. (1986). Applications of cognitive ERPs in psychiatric patients. In W. C. McCallum, R. Zappoli, & F. Denoth (Eds.), *Cerebral psychophysiology: Studies in event-related potential* (EEG Suppl. 38, pp. 419–438). Amsterdam: Elsevier.
- Roth, W. T., Pfefferbaum, A., Kelly, A. F., Berger, P. A., & Kopell, B. S. (1981). Auditory event-related potentials in schizophrenia and depression. *Psychiatry Research*, *4*, 199–212.
- Salisbury, D. F., O'Donnell, B. F., McCarley, R. W., Shenton, M. E., & Benavage, A. (1994). The N2 event-related potential reflects attention deficit in schizophrenia. *Biological Psychology*, *39*, 1–13.
- Sandman, C. A., Vigor-Zierk, C. S., Isenhardt, R., Wu, J., & Zetin, M. (1992). Cardiovascular phase relationships to the cortical event-related potential of schizophrenic, depressed and normal subjects. *Biological Psychiatry*, *32*, 778–789.
- Santosh, P. J., Malhotra, S., Raghunathan, M., & Mehra, Y. N. (1994). A study of P300 in melancholic depression—correlation with psychotic features. *Biological Psychiatry*, *35*, 474–479.
- Sara, G., Gordon, E., Kraiuhin, C., Coyle, S., Howson, A., & Meares, R. (1994). The P300 ERP component: An index of cognitive dysfunction in depression? *Journal of Affective Disorders*, *31*, 29–38.
- Semlitsch, H. V., Anderer, P., Schuster, P., & Presslich, O. (1986). A solution for reliable and valid reduction of ocular artifacts, applied to P300 ERP. *Psychophysiology*, *23*, 695–703.
- Shagass, C. (1981). Neurophysiological evidence for different types of depression. *Journal of Behavior Therapy and Experimental Psychiatry*, *12*, 99–111.
- Sidtis, J. J. (1980). On the nature of the cortical function underlying right hemisphere auditory perception. *Neuropsychologia*, *18*, 321–330.
- Sidtis, J. J. (1981). The complex tone test: Implications for the assessment of auditory laterality effects. *Neuropsychologia*, *19*, 103–112.
- Sidtis, J. J., & Volpe, B. T. (1988). Selective loss of complex-pitch or speech discrimination after unilateral cerebral lesion. *Brain and Language*, *34*, 235–245.
- Simons, R. F. (1982). Physical anhedonia and future psychopathology: An electrocortical continuity? *Psychophysiology*, *19*, 433–441.
- Singh, J., Knight, R. T., Rosenlicht, N., Kotun, J. M., Beckley, D. J., & Woods, D. L. (1992). Abnormal premovement brain potentials in schizophrenia. *Schizophrenia Research*, *8*, 31–41.
- Spitzer, R. L., & Endicott, J. (1975). *Schedule for affective disorders and schizophrenia: Lifetime version*. New York: Biometrics Research Division, New York State Psychiatric Institute.
- Tenke, C. E., Bruder, G. E., Towey, J. P., Leite, P., & Sidtis, J. J. (1993). Correspondence between brain ERP and behavioral asymmetries in a dichotic complex tone test. *Psychophysiology*, *30*, 62–70.
- Tenke, C. E., Kayser, J., Fong, R., Leite, P., Towey, J. P., & Bruder, G. E. (in press). Response- and stimulus-related ERP asymmetries in a tonal oddball task: A Laplacian analysis. *Brain Topography*.
- Tenke, C. E., Schroeder, C. E., Arezzo, J. C., & Vaughan, H. G., Jr. (1993). Interpretation of high-resolution current source density profiles: A simulation of sublaminal contributions to the visual evoked potential. *Experimental Brain Research*, *94*, 183–192.
- Tucker, D. M., Stenslie, C. E., Roth, R. S., & Shearer, S. L. (1981). Right frontal lobe activation and right hemisphere performance: Decrement during a depressed mood. *Archives of General Psychiatry*, *38*, 169–174.
- Yee, C. M., Deldin, P. J., & Miller, G. A. (1992). Stimulus intensity effects in dysthymia and anhedonia. *Journal of Abnormal Psychology*, *101*, 230–233.

(RECEIVED September 18, 1996; ACCEPTED May 14, 1997)