

# Sensory and Sensorimotor Gating in Bipolar Disorder

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## Abstract

Suppression of the P50 event-related brain potential (ERP) and prepulse inhibition (PPI) are thought to provide operational indices of central system sensory and sensorimotor gating, respectively. Although both have received a great deal of attention in the schizophrenia literature, less is known about potential gating deficits in other patient groups. In the current study, sensory gating was assessed in 35 bipolar patients (21 manic, 11 mixed, and 1 undefined) and 32 healthy controls. The single-channel domain data from the P50 paradigm demonstrated that the bipolar patients had significantly attenuated S1 and S2 amplitudes, and decreased S2 latencies, compared to the controls, with no differences between patient subtypes. No differences in P50 sensory gating ratios were found between bipolar and control groups. Furthermore, a principal components analysis (PCA) performed on both the low (0-20 Hz) and high (20-50 Hz) frequency bands of the P50 component showed that the mixed-episode patients significantly differed from the control patients for the low frequency components at both S1 and S2, but that both manic and mixed-episode subtypes evinced significantly lower levels of power at S1 for the high frequency component. In the PPI paradigm, bipolar patients as a whole significantly reduced amplitudes to the pulse-alone (PA) and pre-pulse (PP) tones and longer response latencies to the PP tones compared to the controls. With respect to subtype differences, significantly attenuated PP amplitudes and increased PP latencies were found in the mixed-episode patients compared to the controls, with manic patients showing comparable results to the latter two groups. However, despite reduced PA and PP amplitudes in the bipolar group, bipolar patients as a whole evinced inhibition (higher PPI ratios;  $p < .05$ ) in comparison to the control

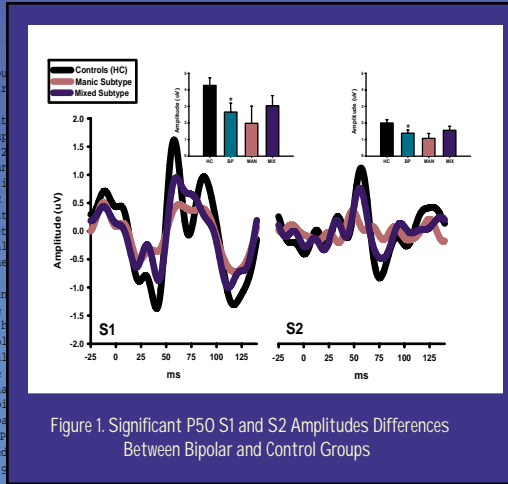


Figure 1. Significant P50 S1 and S2 Amplitudes Differences Between Bipolar and Control Groups

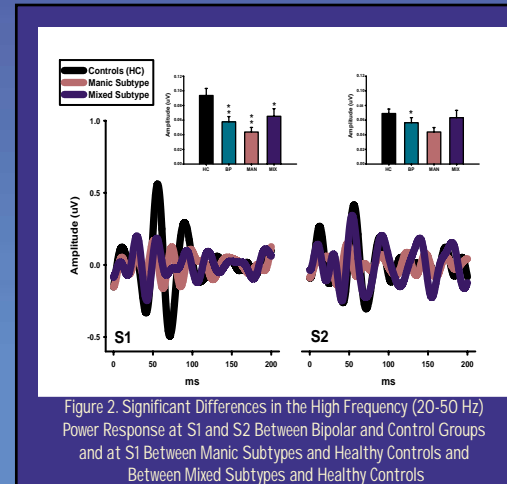


Figure 2. Significant Differences in the High Frequency (20-50 Hz) Power Response at S1 and S2 Between Bipolar and Control Groups and at S1 Between Manic Subtypes and Healthy Controls and Between Mixed Subtypes and Healthy Controls

## Results

- Auditory P50: Single-Channel Time Domain**
- \* P50 S1 and S2 amplitudes were significantly attenuated in the bipolar patients compared to the healthy controls, with no differences between subtypes (see Figure 1).
  - \* P50 S2 response latencies were significantly reduced in the bipolar compared to the healthy controls, with no differences between patient subtypes.
  - \* P50 suppression ratios (S2/S1) did not significantly differ between bipolar patients and the healthy controls, or between the manic and mixed-episode subtypes.
  - \* A significant positive correlation was found between S2 response latencies and scores on the MADRS, with increased latencies associated with greater depressive symptomatology (see Figure 3, panel C).
- Auditory P50: PCA Frequency Analysis**
- \* Mixed-episode patients had significantly reduced power in the low frequency band (0-20 Hz) at both S1 and S2 compared to the healthy controls, with neither group differing significantly from the manic-episode subtypes.
  - \* Both manic and mixed bipolar subtypes showed significant reductions in power in the high frequency band (20-50 Hz) at S1 compared to the control group, with no differences found between the two subtypes (see Figure 2).
  - \* Significantly reduced levels of P50 sensory gating (S2/S1) were found in the bipolar group compared to the control group for the high frequency band as indicated by higher P50 ratios among the bipolar patients.
  - \* A significant correlation was found between S1 high frequency power scores on the general psychopathology scale of the PANSS, where increased power was associated with higher levels of psychopathological symptomatology (see Figure 3, panel A).
  - \* A significant negative relationship was found between positive symptomatology (as measured by the PANSS) and S2 low frequency power, with decreased levels of power associated with greater levels of positive symptomatology (see Figure 3, panel B).
- Acoustic Startle Inhibition and Habituation**
- \* Pulse alone (PA) and pre-pulsed (PP) startle amplitudes were significantly attenuated in the bipolar patients compared to the healthy controls.
  - \* With respect to subtype differences, significantly reduced PA and PP amplitudes were found in the mixed-episode patients compared to the controls, with manic patients showing comparable results to the latter two groups.
  - \* Significantly increased PP response latencies were found in the bipolar patients compared to the healthy controls, with post-hoc analyses indicating significant differences between the mixed-episode patients and the control group (with longer latencies in the patients).
  - \* Bipolar patients as a whole evinced significantly greater PPI (i.e., ratios) in comparison to the control group.
  - \* A habituation effect was obtained for both PA and PP amplitudes across Blocks 1-6, with a significant main effect of diagnosis revealing less habituation in the bipolar group across trial blocks.
  - \* A significant correlation was found between PP latencies and MADRS with increased latencies associated with greater depressive symptomatology (see Figure 3, panel D).

## Background

A diminished ability to filter out, or "gate", irrelevant stimuli has been conceptualized as one of the defining features of schizophrenia; however, much less is known about sensory gating in relation to other disorders. In one of the few auditory P50 event-related potential (ERP) studies conducted with acute manic bipolar patients, it was found that the manic patients showed gating deficits comparable to those observed in schizophrenic patients (Franks et al., 1983). However, in contrast to schizophrenic patients, P50 indices of sensory gating in stable, euthymic bipolar patients were indistinguishable from controls, suggesting a state, versus trait, deficit.

Similarly, sensorimotor gating deficits, as assessed by PPI, have also been found in medicated bipolar patients with acute psychotic mania (Perry et al., 2001). Whereas the bipolar patients did not differ from schizophrenic patients on measures of PPI, the bipolar patients evinced significantly less inhibition than control subjects. Furthermore, both the bipolar and schizophrenic patients showed less startle habituation across trial blocks compared to the controls.

Purpose. The present study was designed to better understand the relationship between sensory and sensorimotor gating and bipolar subtypes by testing manic and mixed-episode patients in both the auditory P50 and PPI paradigms. The Positive and Negative Syndrome Scale (PANSS), the Young Mania Rating Scale (YMRS), and the Montgomery-Asberg Depression Rating Scale (MADRS) were also administered to patients to help

Table 1. Auditory P50 and Acoustic Startle Latencies and Gating Ratios

	Auditory P50					
	Latency (ms)				Suppression Ratios	
	S1		S2		S2/S1 (SORT)	
	M	SD	M	SD	M	SD
Control	58.34	6.70	57.87	4.87	0.72	0.26
Bipolar	56.18	9.51	53.97	7.42	1.18	1.86
Manic	54.10	7.30	52.78	7.58	0.88	0.54
Mixed	57.06	10.35	54.48	7.48	1.31	2.19

	Acoustic Startle					
	Latency (ms)				PPI Ratios	
	PA		PP		100-100(PPPA)	
	M	SD	M	SD	M	SD
Control	64.00	8.57	59.53	8.88	33.77	25.16
Bipolar	67.48	8.11	67.03	11.06	46.76	25.02
Manic	66.38	5.58	64.25	5.57	39.07	25.13
Mixed	67.90	8.97	68.10	12.49	49.68	24.96

## Procedure

The BPRS, YMRS, and MADRS were administered independently to the bipolar patients within 2 days of EEG testing.

**Auditory P50 Paradigm.** Auditory paired clicks (S1 and S2) with an interstimulus interval of 500 ms were presented every 7-11 s to create a total of 130 trials. To help maintain attention, participants were asked to press a button in response to "rare" pairs of clicks that were randomly presented throughout the paradigm to comprise 20 of the 130 trials.

In addition to characterizing the P50 ERP in the time domain at a single electrode site (FCZ), power analyses were performed by decomposing the P50 waveform with a principal components analysis (PCA) method into both low (0-20 Hz) and high (20-50 Hz) frequency bands in an attempt to better characterize the sensory registration (20-50 Hz) and information processing (0-20 Hz) stages that are captured in the P50 component.

**PPI Paradigm.** The prepulse and startle stimuli were organized into six blocks, with each block containing a randomly ordered series of three startle stimuli presented alone and three startle stimuli that were preceded by the prepulse tone. A 120 ms interstimulus interval separated the prepulse and startle stimuli, and trials were presented every 16-20 s.

## Subjects

32 healthy controls and 35 bipolar patients (23 mixed, 11 manic, and 1 undefined) were recruited from ongoing pharmacokinetic studies in which they were enrolled independent of the present sensory gating protocol. At the time of testing, 9 of the bipolar patients were unmedicated (1 manic, 7 mixed, and 1 undefined), 15 were on psychotropic medications (5 manic and 10 mixed), 4 were on antipsychotic medications (1 manic and 3 mixed), and the medication status of 7 patients could not be determined due to previous randomization into double-blind pharmacokinetic studies.

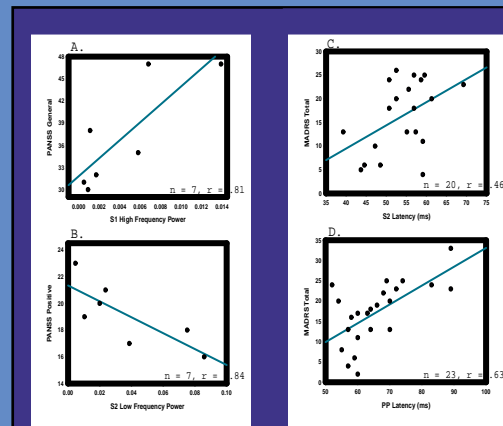


Figure 3. Scatterplots of Bipolar Symptom Rating Scales vs. P50 and PPI Response Characteristics

## Conclusions

The present study aimed to help clarify the relationship between sensory and sensorimotor gating deficits and bipolar symptomatology. The results from the single-channel P50 data fail to support previous findings of comparable S1 and S2 magnitudes, but disrupted P50 suppression, between bipolar patients and controls (Franks et al., 1983). Furthermore, our previous reports suggest that bipolar patients in the acute manic phase disrupted PPI (Perry et al., 2001), the present findings found no differences between patient subtypes, but did find that bipolar patients as a whole showed increased PPI compared to the control participants. Although attenuated response amplitudes in the bipolar patients compared to the control group were found in both the P50 and PPI paradigms, the divergent results between P50 suppression in the time domain and PPI highlight the need to differentiate sensory and sensorimotor gating when characterizing inhibitory deficits in patient populations.

The analysis of the P50 component in the frequency domain extended the use of an analysis technique that was originally developed for the study of schizophrenia (Clementz et al., 2001) to the bipolar population. In contrast to the present findings, schizophrenic patients differed from controls in the low frequency band at S1 (Clementz et al., 2001), which suggests that both manic and mixed-episode subtypes may evince perceptual anomalies than schizophrenic patients, a line of research

## References

- Clementz, BA & Blumenfeld, LD (2001). Multi-channel EEG assessment of auditory evoked response suppression in schizophrenia. *Experimental Brain Research* (in press).
- Franks, RD, Adler, LE, Waldo, MC, Albert, J, & Freedman, R (1983). Neurophysiological studies of sensory gating in mania: Comparison of manic bipolar patients and controls. *Biological Psychiatry*, 18 (9), 989-1005.
- Perry, W, Minassian, A, Peifel, D, & Braff, DL (2001). Sensorimotor gating deficits in bipolar disorder patients with acute psychotic mania. *Biological Psychiatry*, 50, 418-424.