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Attention deficits in bipolar disorder: a comparison based on the Continuous Performance Test

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Abstract

Although attentional deficits measured by Continuous Performance Tests (CPTs) have been observed in patients with bipolar disorder, their relationship with clinical state is not well understood. The identical pairs Continuous Performance Test (CPT-IP) shows particular promise as a measure sensitive to trait abnormalities in attentional function. In this study, the CPT-IP was administered to 27 patients with bipolar disorder (22 type I, 5 type II) and 25 demographically matched healthy comparison subjects, in order to assess the presence and nature of attentional deficits as a function of mood symptoms. Results showed significantly impaired CPT performance in bipolar patients compared with healthy subjects. Patients made fewer hits ($p < 0.01$), were slower to respond ($p < 0.007$), and had poorer discrimination ($p < 0.05$) and bias ($p < 0.006$) than comparison subjects. Severity of mania and depression was not correlated with any of the CPT measures. Our findings suggest that attentional dysfunction may be a trait deficit associated with bipolar illness. However, within-subjects longitudinal studies examining fluctuations in performance over time are needed.

Keywords: Continuous Performance Test; Attention; Bipolar disorder; Mood disorders; Trait marker; Neurocognitive impairment

Impaired concentration and distractibility are commonly observed symptoms in bipolar disorder [11], and these symptoms may be accompanied by disturbances in psychomotor speed, learning, memory and executive function [2,14]. Continuous Performance Tests (CPTs) provide a means of quantifying aspects of sustained attention and vigilance in clinical populations [1,4,9,13,15–17]. Studies measuring attentional deficits in bipolar subjects show associations between task performance and the severity of manic symptoms [1,9,11,13,15,18,19]. Bipolar outpatients show less severe attentional impairment compared with inpatients [13]. Bipolar inpatients improve from admission to discharge; but they remain significantly impaired compared with the general population [13]. This pattern suggests certain aspects of attention may be state related in bipolar illness, whereas others represent trait markers, and may be associated with distinct pathophysiological mechanisms [5]. While attentional impairment as a function of acute manic or depressive symptomatology is not surprising, recent investigations demonstrate neuropsychological deficits in bipolar patients in the euthymic state [14]. Euthymic patients demonstrate impairments in attentional performance [6,8], learning executive function, and working memory [8]. Furthermore, differential impairment in target detection, as assessed by a CPT, occurs in euthymic

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bipolar patients compared with healthy controls after controlling for residual affective symptoms [3]. Similarly, stable bipolar patients exhibit impaired performance on the CPT [21], and performance is not associated with residual mood symptoms or medication usage. These findings suggest that attentional dysfunction may represent a trait feature in bipolar disorder.

The present study sought to further characterize the nature of the attentional dysfunction in patients with bipolar disorder with various levels of symptomatology, by utilizing an identical-pairs version of the CPT that is sensitive to genetic liability for schizophrenia [7]. As attentional processing deficits tapped by this test have previously been shown to be heritable, developmentally stable, and independent of clinical state in patients with schizophrenia [7], this measure may also be particularly informative as a trait marker for bipolar disorder.

Twenty-seven patients diagnosed with bipolar disorder (22 type I and 5 type II) were recruited through the inpatient and outpatient research programs at The University of Texas Health Science Center at San Antonio and its affiliated hospitals. Diagnoses were determined by psychiatrists, using the Patient Edition of the Structured Clinical Interview (SCID) [10]. Patients were included if they met DSM-IV criteria for BP-I or BP-II. Exclusion criteria were: (i) any serious medical illness, including neurological disorders; (ii) borderline IQ/mental retardation (IQ less than 80). The patients had an average of illness duration of 15.9 years and the average age of onset was 24.0 years (see Table 1). Thirteen patients met DSM-IV criteria for comorbid generalized anxiety disorder

Table 1
Participants and clinical characteristics

	BP patients	Healthy subjects	Group difference
Demographics			
Age	39.0 (12.3)	35.8 (13.8)	$T = 0.87$, $p = 0.4$
Female	63%	52%	$\chi^2 = 0.64$, $p = 0.4$
Left handed	11%	4%	$\chi^2 = 0.92$, $p = 0.3$
Education Level (yrs)	13.9 (2.1)	15.1 (3.5)	$T = -1.5$, $p = 0.1$
Parental Education (year)	12.7 (2.7)	12.9(3.2)	$T = -0.3$, $p = 0.8$
Verbal IQ	104.6 (9.8)	108.7(10.0)	$T = -1.52$, $p = 0.1$
Full Scale IQ	104.0 (9.7)	109.0(10.1)	$T = -1.68$, $p = 0.1$
Clinical factors			
HAM-D[a]	18.2 (8.3)	N/A	
YMRS[b]	9.9 (6.8)	N/A	
Age at onset	*24.0* (*12.8*)	*N/A*	
Illness duration	*15.9* (*11.4*)	*N/A*	
Depressive episode[c]	7	N/A	
Euthymic[d]	2	N/A	
Manic episode[e]	2	N/A	
Mixed episode[f]	16	N/A	
Family history (*N*)			
Any Psychiatric diagnoses	16	N/A	
Bipolar disorder	6	N/A	
Depression	5	N/A	
Schizophrenia	2	N/A	
Substance abuse	3	N/A	
Comorbidity (*N*)			
Past alcohol	9	N/A	
Current alcohol	7	N/A	
GAD[g]	13	N/A	
PTSD[h]	9	N/A	
Medication use (*N*)			
Atypical antipsychotics	5	N/A	
Other Antidepressants	9	N/A	
SSRI	4	N/A	
Benzodiazepines	6	N/A	
Mood stabilizers	12	N/A	

[a] Hamilton Depression Scale.
[b] Young Mania Rating Scale.
[c] Depressed mood state was defined as HAM-D >8 and YMRS <8.
[d] Euthymic mood state was defined as HAM-D <8 and YMRS <8.
[e] Manic state was defined as HAM-D <8 and YMRS >8.
[f] Mixed state as HAM-D >8 and YMRS >8.
[g] Generalized anxiety disorder diagnosed by SCID.
[h] Post-traumatic stress disorder diagnosed by SCID.

(GAD) and nine met criteria for current post-traumatic stress disorder (PTSD). Seven patients have been diagnosed with alcohol abuse/dependence but none with drug abuse.

Nine subjects were not taking any psychotropic medications. Eighteen of the patients were under treatment, 13 of them were taking antidepressants (4 SSRI's, and 9 other antidepressants), 12 were taking mood stabilizers (lithium, carbamazepine, oxcarbazepine, valproic acid, topiramate, lamotrigine, and gabapentine), six were prescribed benzodiazepines and five were taking atypical antipsichotics. All patients were stable outpatients at the time of assessment, and had been on maintenance therapy with the currently prescribed medications for 2 years at most.

Twenty-five comparison subjects were recruited through radio and newspaper advertisements. Exclusion criteria were the same as used for patients except for a history of psychiatric disorders as determined by the SCID, and the additional requirement that they could not have any first degree relative with history of mood or psychotic disorder. In order to confirm eligibility for the study and exclude medical problems, participants underwent a thorough and detailed medical history, physical examination, and laboratory testing. After an explanation of the study, informed consent was obtained. Clinical mood states were defined according to the Hamilton Rating Scale (HAM-D 21-item) and the Young Mania Rating Scale (YMRS) [12,22], as follows: depressed as HAM-D >8 and YMRS <8, mixed as HAM-D >8 and YMRS >8, manic as HAM-D <8 and YMRS >8, and euthymic as HAM-D <8 and YMRS <8 (see Table 1). All subjects were administered a 6-min version of an identical pairs Continuous Performance Test (CPT-IP), previously shown to be sensitive to attentional impairment in patients with schizophrenia and their relatives (see Fig. 1) [4]. Visual stimuli were generated on a computer monitor. An array of 4 degraded numbers was presented, and the participant's task was to press the space bar whenever the same array of digits appeared twice in a row. Outcome measures included (1) the number of correct responses or "hits," (2) hit reaction time (RT), in milliseconds, (3) a non-parametric discriminability index (a') that measures the ability to discriminate between targets and non-targets, and (4) an index of response bias (β) that represents the likelihood of saying yes across all targets and foils [20].

Patients and healthy comparison subjects were well matched on age, gender, handedness, educational attainment, education, and ethnic background (see Table 1). Ethnic background was similar across samples, ($\chi^2 = 5.5$, $p = 0.2$) and reflected the community from which study participants were recruited (South Texas: 34% Hispanic, 4% African American, 53% non-Hispanic White, 9% other). Based on Wechsler Test of Adult Reading (WTAR) performance, full scale and verbal IQ did not differ between groups (see Table 1).

ANOVA indicated that bipolar patients overall performed significantly worse on the CPT than healthy subjects. Patients yielded fewer hits than control subjects (39.7 ± 7.3 versus 44.9 ± 6.9, respectively; $F(1,51) = 6.78$, $p < 0.01$) (see Table 2). Moreover, hit reaction time (*RT*) was significantly slower in bipolar patients (493 ± 53 ms versus 453 ± 49 ms; $F(1,51) = 7.78$, $p < 0.007$). Target discrimination was also impaired in patients (0.94 ± 0.04 versus 0.97 ± 0.05; $F(1,51) = 3.92$, $p < 0.05$). Furthermore, bias response was *higher* in bipolar patients than in controls, indicating increased *rate of false* responding (0.84 ± 0.21 versus 0.49 ± 0.59; $F(1,51) = 8.09$, $p < 0.006$). Repeating the statistical analysis (ANOVA) after excluding patients with comorbid alcohol abuse, patients with bipolar II disorder, and patients who were on antipsychotic medication did not alter the pattern of results (see Table 2). Finally, no significant correlation between the performance measures and symptom severity (as measured by depressive and manic symptoms on HAM-D and YMRS, respectively) was found within the bipolar group (see Table 3).

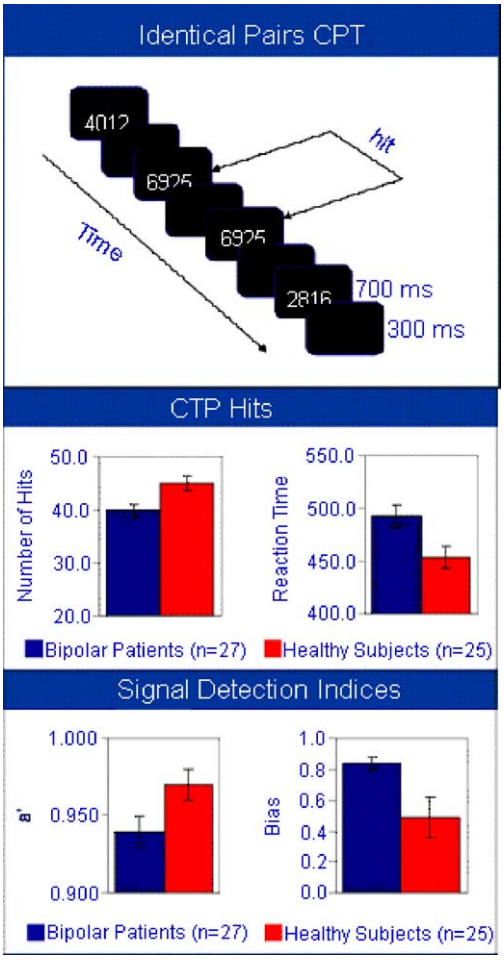

Fig. 1. Bipolar patients were impaired compared with healthy subjects on the CPT: patients made fewer hits, were slower to respond, had poorer discrimination, and increased bias as compared to matched comparison subjects.

Our results show impaired attentional functioning, as measured by the identical pairs CPT, in bipolar patients with various levels of symptomatology. No relationship was observed between CPT performance and severity of manic or depressive symptoms. These data confirm previous findings [3,21] and suggest that attentional dysfunction may be a trait deficit

Table 2
ANOVA analysis

CPT measure	Full sample ($N = 27$)	BP type I only ($n = 22$)	Without alcoholism ($n = 20$)	Without antipsychotic ($n = 22$)	Without PTSD ($n = 19$)
Hits	6.78[a], $p = 0.01$[b]	6.25, $p = 0.02$	5.16, $p = 0.03$	8.39, $p = 0.01$	8.49, $p = 0.01$
Hits RT	7.78, $p = 0.01$	6.84, $p = 0.1$	8.01, $p = 0.01$	6.69, $p = 0.01$	5.02, $p = 0.03$
Descriminability (a')	3.92, $p = 0.05$	3.34, $p = 0.07$	2.75, $p = 0.1$	5.13, $p = 0.03$	5.32, $p = 0.03$
Bias (β)	8.09, $p = 0.01$	7.39, $p = 0.01$	6.68, $p = 0.01$	6.69, $p = 0.01$	4.91, $p = 0.03$

ANOVA analysis between (1) the complete sample of 27 BP patients and 25 healthy subjects; (2) excluding patients with BP type II ($n = 5$); (3) excluding patients with current alcohol dependence/abuse ($n = 7$); (4) excluding patients with antipsychotic medications ($n = 5$); (5) excluding patients with comorbid PTSD ($n = 8$).

[a] F statistic.

[b] p-value.

Table 3
Spearman correlation coefficients between symptom ratings and CPT performance

CPT measure	HAMD	YMRS	Illness duration
Hits[a]	−0.117, $p = 0.56$	−0.346, $p = 0.08$	0.116, $p = 0.82$
Hits RT[b]	0.088, $p = 0.66$	0.245, $p = 0.22$	−0.203, $p = 0.70$
Descriminability (a')[c]	−0.068, $p = 0.74$	−0.296, $p = 0.13$	0.145, $p = 0.78$
Bias (β)[d]	−0.091, $p = 0.65$	−0.078, $p = 0.70$	0.221, $p = 0.67$

[a] Number of correct responses.

[b] Hits reaction time.

[c] Non-parametric discriminability index, which measures the ability to discriminate between targets and non-targets [20].

[d] Index of response bias that measures constructs other than sensitivity such as fatigue and motivation [20].

in patients with bipolar disorder [5]. Although two studies reported improved CPT performance in bipolar patients following symptom remission [13,18], patients remained impaired in terms of target detection compared with the general population [13], suggesting that sustained attention deficit may be a trait marker that is exacerbated in times of acute illness (i.e., state-modulated, but not state-dependent). Given the paucity of within-subjects' designs in bipolar research, this issue warrants further attention.

In conclusion, our findings suggest that impaired CPT performance could represent a trait abnormality in bipolar disorder that may be associated with structural or neurochemical brain abnormalities [3]. Nonetheless, longitudinal studies examining different aspects of attentional performance in unmedicated first-episode bipolar patients are warranted. Attentional impairment as measured by the CPT may provide a useful marker for genetic vulnerability to bipolar disorder, as well as schizophrenia, which should be further examined in future studies.

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