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Processing efficiency and sustained attention in bipolar disorder

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Abstract

We hypothesized that patterns of sustained attention performance in bipolar disorder were consistent with *processing efficiency theory*—a theory of the relationship between central processing capacity and performance. We predicted (1) sustained attention deficits during mania because symptoms interfere with limited-capacity executive control processes resulting in decreased *performance effectiveness*; and (2) decreased *processing efficiency* during euthymia, as indicated by speed/accuracy tradeoffs, consistent with a stable phenotypic abnormality. Twenty-five manic bipolar, 23 euthymic bipolar, and 28 healthy comparison participants were compared on a continuous performance task and administered symptom-rating scales. The manic group was significantly impaired on overall perceptual sensitivity and demonstrated a significant linear decrease in performance over time, consistent with impaired sustained attention. The euthymic group evidenced significantly slower overall hit reaction time (RT), but when RT was controlled they performed similarly to the healthy group over time. Two discriminant functions combined to separate the groups on manic symptom severity and on-task effort/strategy use. These findings are consistent with processing efficiency theory. They suggest that euthymic patients sustain attention through effortful control at the expense of processing efficiency, while acute mania reduces the capacity for control and impairs sustained attention. Problems with processing efficiency are viewed as trait characteristics of bipolar disorder that may be overlooked by traditional error-based assessments. (*JINS*, 2005, *11*, 49–57.)

Keywords: Bipolar disorder, Mania, Processing efficiency theory, Sustained attention, Continuous performance test

INTRODUCTION

The inability to sustain attention over time (impaired vigilance) is an obvious and prevalent behavioral consequence of bipolar disorder (Bearden et al., 2001). Increased error rates and reaction times on tests of sustained attention have been consistently identified in mania (Addington & Addington, 1997; Sax et al., 1995, 1999) and are among the most reliable cognitive indicators of a manic episode (Liu et al., 2002; Nuechterlein et al., 1991). In contrast, researchers have demonstrated in between-subjects studies that, during periods of euthymia (i.e., syndrome-free periods characterized by mild or no mood symptoms), patients show greatly attenuated error rates on tests of sustained attention (Strakowski et al., 2004; Wilder-Willis et al., 2001), although they may continue to exhibit impairment when assessed through RT measures (Wilder-Willis et al., 2001).

The theoretical definition of reaction time (RT) is that it reflects the absolute minimum time in which a given individual can respond with 100% accuracy (Pachella, 1974). However, when accuracy is less than perfect, RT is known to covary with error rate (Pachella, 1974). Because patients, particularly during mania, are not able to perform sustained attention tasks in a completely accurate manner (Addington & Addington, 1997; Bearden et al., 2001; Liu et al., 2002; Nuechterlein et al., 1991; Sax et al., 1995, 1999; Strakowski et al., 2004; Wilder-Willis et al., 2001), RT necessarily covaries with response probabilities. However, previous studies of sustained attention in psychiatric disorders have tended not to report RT (Nuechterlein, 1991). In one study examining the influence of processing speed, RT was used successfully to differentiate specific impair-

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ments of sustained attention during an extended vigilance period in psychotic mania from the general attention deficits in schizophrenia (Fleck et al., 2001).

According to *processing efficiency theory*, heightened internal states (e.g., mania) can cause a reduction in the processing capacity available for concurrent tasks and an increase in on-task effort and strategy use to improve performance (Eysenck & Calvo, 1992). Although extreme moods have been shown to impair performance on tasks with high attentional demands, less severe mood states characteristically impair *efficiency* more than *effectiveness* (e.g., Strakowski et al., 2004; Wilder-Willis et al., 2001). Impaired processing efficiency is characterized by a tendency to sacrifice speed (RT) for accuracy (Eysenck & Calvo, 1992), while performance effectiveness is characterized by standard error-based measures such as performing progressively more poorly over time on tests of sustained attention (Nuechterlein, 1991).

We hypothesized that attention decrements would occur over time in mania, which we expected to interfere with executive control processes. To test this hypothesis, we examined differences in the temporal dynamics and speed/accuracy operating characteristics of bipolar I manic, bipolar I euthymic, and healthy comparison subject groups during a Degraded-Stimulus Continuous Performance Test (CPT-DS; Nuechterlein et al., 1983). We made two directional predictions regarding cognitive performance on the CPT-DS. First, relative to healthy comparison subjects, manic patients would demonstrate impaired performance effectiveness indexed by increasing error rates and/or RTs as attentional demands increase over time (a sustained attention deficit). Second, euthymic patients would demonstrate decreased processing efficiency by trading speed (psychomotor slowing) to perform as effectively (accurately) as healthy comparison subjects.

METHODS

Participants and Materials

Twenty-five inpatients with a current diagnosis of bipolar I disorder, manic or mixed with psychotic features, and 23 outpatients with a current diagnosis of fully remitted bipolar I disorder, most recent episode manic or mixed, were recruited from the inpatient psychiatry units at the University of Cincinnati Medical Center or the Cincinnati First-Episode Mania Study (an ongoing, longitudinal study of outcome following an initial hospitalization for bipolar disorder), respectively. Diagnoses were made with the Structured Clinical Interview for Diagnostic and Statistical Manual–4th Edition (DSM–IV) Axis I Disorders (SCID-I/P; First et al., 1997), by an experienced clinician ($\kappa \geq 0.90$ with S.M.S.). Patients were excluded by a history of major medical, developmental, or neurological disorders as determined by the SCID-I/P and clinical evaluations. Those who met criteria for a substance use disorder were included if they were in sustained full remission (i.e., full criteria for dependence had not been met for a period of 12 months or longer) and had not used substances during the week prior to testing. At the time of testing, seven euthymic and two manic patients were unmedicated while the remainder received some combination of atypical antipsychotic medications, lithium, valproate, carbamazepine, or clonazapam.

Upon hospital admission or a scheduled research appointment, symptom ratings were obtained from patients by administering the Young Mania Rating Scale (YMRS; Young et al., 1978), Hamilton Depression Rating Scale (HDRS; Hamilton, 1960), and the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984). A SAPS total score was determined by summing the global items for each subscale. Euthymia was characterized by HDRS total scores < 10, YMRS total score < 10, and SAPS global scores < 2. All ratings were performed by an experienced rater who had established acceptable interrater reliability (ICC ≥ 0.70 for all YMRS items, HDRS items, and SAPS global scores; Fleck et al., 2001, 2003).

Twenty-eight healthy volunteers were recruited from the same catchment area as the patients (i.e., the Cincinnati Tri-State area including Southwestern Ohio, Southeastern Indiana, and Northern Kentucky). This group was matched with the patient groups on age, years of formal education, sex, and race (see Table 1). Healthy volunteers were excluded by the same criteria used for patients and by a history of psychiatric disorders as determined by the SCID-I/P and initial evaluation. Additionally, both healthy and patient volunteers were excluded by vision that was not corrected to normal. After complete description of the study to the participants, written informed consent was obtained. This study was approved by the University of Cincinnati Institutional Review Board.

Computer Apparatus and Procedures

The computerized Degraded-Stimulus Continuous Performance Task (CPT-DS; Nuechterlein et al., 1983) version 6.02 was administered to patients on an IBM compatible notebook computer within 2 days of symptom assessment. Both patients and healthy volunteers performed the task in a small, quiet room without interruption. The CPT-DS was administered just after a 20-min long test of implicit and explicit memory, the results of which will be reported elsewhere.

The stimuli for the CPT-DS consisted of perceptually degraded (blurred) white numbers between 0 and 9, randomly presented for 35 ms each on a dark background, with an intertrial interval of 1 s. Digit presentation was quasirandom with 41% random pixel reversal for a constant level of visual degradation across all participants. Instructions were read verbatim from the directions provided with the CPT computer program (Nuechterlein & Asarnow, 1993), except that each participant was instructed to "press as quickly *and as accurately* as you can to the zeros," rather than to "press as quickly as you can to

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the zeros," to emphasize both speed and accuracy. Participants, then, responded with a button press on a game-control device as quickly and accurately as possible each time they saw the target number zero (0). The target appeared in 120 (25%) of the 480 trials. No form of error correction signal was provided to participants that would allow them to self-monitor performance.

The experimental trials were divided into three successive blocks to examine sustained attention at early, middle, and late stages of the 8-min vigil. The recorded signal-detection measures included an index of perceptual sensitivity (A′) which measures the ability to discriminate between signal (targets) and noise (non-targets) and an index of response bias (β'') which measures response tendencies (conservative *vs*. liberal responding) and constructs other than sensitivity such as fatigue and motivation. Additionally, hit RT was obtained on correct "go" trials to measure psychomotor processing speed and efficiency. Reaction time may be more consistent with certain psychomotor processing factors that are independent of A′ and β'' in signal-detection theory such as search strategies, decision processes, and response selection and execution components of sustained attention (Fleck et al., 2001).

Statistical Analyses

All statistical analyses were performed using SPSS Version 11.0.1 (SPSS Inc., Chicago, IL). Diagnostic tests were conducted including Mauchly's Test of sphericity (Mauchly, 1940) and Levene's Test of homogeneity of variance (Levene, 1960). Degrees of freedom were adjusted to correct for violations of sphericity (Huynh & Feldt, 1976) and homogeneity of variance when they occurred in the performance variable analyses. Corrected p values and uncorrected degrees of freedom are reported throughout.

Comparisons among the three groups were made for demographic, clinical, rating scale, and overall performance variables. Chi-square analyses were used to test for differences in the distribution of sex, race, and current medication treatment. Each of the other comparisons was made using a one-way analysis of variance (ANOVA) and followed up with the Tukey honestly significant difference procedure (Tukey HSD) as appropriate.

To examine CPT-DS performance over time, a 3 (Group: control, euthymic, manic) × 3 (Block: early, middle, late) mixed ANOVA was conducted on the A′ measure. For each significant effect or interaction identified by the omnibus test, mean comparisons were made with follow-up t tests using the Bonferroni correction.

Finally, a discriminant function analysis (DFA) was conducted to predict group membership based on the following set of predictors: A′, β'', Hit RT, YMRS, HDRS, and SAPS. This DFA was conducted across the three groups to examine the nature of any reliable dimensions along which the groups differed and the relative importance of each predictor in determining group membership. Additional *post-hoc* analyses were conducted to statistically control for the influence of RT in the CPT-DS analysis and the influence of psychiatric symptoms in the DFA.

RESULTS

Participant Characteristics

As seen in Table 1, the groups were well matched on relevant demographic and clinical characteristics. As expected based on patient inclusion criteria, the manic group received significantly higher mean doses of antipsychotic medication [Chlorpromazine equivalents; $F = 8.34$, $df = 1, 47$, $p < .01$] relative to the euthymic group, and more elevated ratings on scales of mania [YMRS; $F = 211.67$, $df = 2, 75$, $p < .001$], depression [HDRS; $F = 30.78$, $df = 2, 75$, $p < .001$], and positive psychotic symptoms [SAPS; $F = 70.98$, $df = 2, 75$, $p < .001$] relative to both euthymic and healthy comparison groups.

There was *no* departure from homogeneity of variance in any analysis of overall group performance presented in Table 1. The healthy group discriminated between targets and non-targets significantly better than the manic group [A′; $F = 7.34$, $df = 2, 75$, $p < .001$], but no better than the euthymic group. The healthy group also responded 60 ms faster than the euthymic group on average [Hit RT; $F = 5.59$, $df = 2, 75$, $p < .01$], but not significantly faster than the manic group (see Table 1).

Continuous Performance Analysis

The assumptions of sphericity and homogeneity of variance were violated for the A′ ANOVA and corrected appropriately. As depicted in Figure 1a, the group means for A′ indicated different levels and patterns of performance for the groups over time. A repeated-measures ANOVA confirmed this observation, yielding significant main effects of Group [$F = 7.34$, $df = 2, 73$, $p < .001$] and Block [$F = 8.91$, $df = 2, 146$, $p < .001$], that were qualified by a significant Group × Block interaction [$F = 3.18$, $df = 4, 146$, $p < .05$].

Within-group planned comparisons indicated a significant perceptual sensitivity effect over time for the manic group [$F = 6.26$, $df = 2, 48$, $p < .01$] that was linear in nature [$F = 7.88$, $df = 1, 24$, $p < .01$] and characterized by significantly decreased performance at Block 3 relative to Block 1 ($p < .05$). No other group demonstrated a significant within-group Time effect or polynomial trend. Between-group comparisons indicated significantly poorer performance for both manic ($p < .01$) and euthymic groups ($p < .05$) relative to the healthy comparison group at Block 1. At Block 3, only the manic group demonstrated a significant performance deficit relative to the healthy comparison group ($p < .001$).

Due to the speed/accuracy tradeoffs identified for the patient groups in the initial comparisons (i.e., the manic group was more error prone but as rapid as the healthy group while the euthymic group was slower but as accurate

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Table 1. Demographic, clinical, symptom and performance characteristics across three groups

Characteristics	Group 0 Healthy ($n = 28$)	Group 1 Euthymic ($n = 23$)	Group 2 Manic ($n = 25$)	F/χ^2	p	Tukey[a]
Demographic						
Age, years (*SD*)	28 (9)	28 (7)	28 (7)	.05	.95	ns
Education, years (*SD*)	14 (1)	13 (2)	14 (2)	.27	.77	ns
Sex, female, *n* (%)	17 (61)	10 (44)	9 (36)	3.44	.18	—
Race, white, *n* (%)	23 (82)	15 (65)	20 (80)	2.28	.32	—
Clinical						
Chlorpromazine equivalents, mg (*SD*)[b]		124 (194)	311 (249)	8.34	.01	—
On medication, *n* (%)		16 (70)	23 (92)	2.62	.11	—
Onset age, years (*SD*)[c]		23 (6)	24 (8)	.19	.67	—
Hospitalizations, *n* (*SD*)		2 (1)	3 (3)	1.56	.22	—
Symptom rating scale[d]						
YMRS score (*SD*)	.2 (1)	2 (2)	25 (8)	148.97	.001	0, 1 < 2
HDRS score (*SD*)	.4 (1)	2 (2)	11 (8)	27.74	.001	0, 1 < 2
SAPS score (*SD*)	0 (0)	.1 (.3)	6 (3)	21.83	.001	0, 1 < 2
Performance[e]						
A′ (*SD*)	.96 (.02)	.93 (.05)	.91 (.08)	30.11	.001	0 > 2
β'' (*SD*)	.52 (.20)	.49 (.22)	.40 (.28)	1.86	.16	ns
Hit RT, ms (*SD*)	499 (49)	559 (69)	521 (73)	5.59	.01	0 < 1

[a]ns indicates no two groups are significantly different; — indicates no comparison due to a chi-square, Fisher exact, or two group omnibus test; otherwise Tukey's Honestly Significant Difference, $p < .05$.
[b]Each patient's average daily dose of antipsychotic medication in the 48 hr prior to testing was converted to an approximate mg equivalent of 100 mg of chlorpromazine based on Pies (1998) and current recommended dosing for newer compounds.
[c]Defined as the age at which the first affective episode began (ICC > .90).
[d]YMRS indicates Young Mania Rating Scale; HDRS indicates Hamilton Depression Rating Scale; SAPS indicates Scale for the Assessment of Positive Symptoms.
[e]A′ indicates CPT-DS perceptual sensitivity; β'' indicates CPT-DS response bias; Hit RT indicates CPT-DS hit reaction time.

as the healthy group; see Table 1), we conducted a *post-hoc*, repeated-measures ANCOVA with Hit RT at Blocks 1, 2, and 3 as covariates to estimate accuracy while controlling for RT. We speculated that RT slowing by the euthymic group (i.e., high hit RT) and impulsivity by the manic group (i.e., relatively low hit RT in context of low β''), might represent cognitive control strategies that influenced perceptual sensitivity. The assumptions of sphericity and homogeneity of variance were again violated for this ANOVA and corrected. As depicted in Figure 1b, the adjusted group means for A′ indicated different levels and patterns of performance for the groups over blocks of time. A repeated-measures ANOVA confirmed this observation, yielding significant main effects of Group [$F = 6.20$, $df = 2, 70$, $p < .01$] and Block [$F = 6.37$, $df = 2, 140$, $p < .01$], that were qualified by a significant Group × Block interaction [$F = 3.52$, $df = 4, 140$, $p < .05$].

Within-group mean comparisons yielded no significant mean effects of time or polynomial trends for the healthy volunteer, euthymic, or manic groups. Between-group comparisons indicated significantly poorer performance for the manic group relative to the healthy comparison group at Block 1 ($p < .01$). At Block 3, the manic group demonstrated a significant performance deficit relative to both the healthy comparison and euthymic groups ($p < .01$).

To examine further the influence of medications, *post-hoc* Kolmogorov-Smirnov Tests were conducted between those patients receiving medications ($n = 39$) and those who were not ($n = 9$). No significant differences were identified on any performance variables as a function of medication status. Additionally, no statistically significant relationships were identified between chlorpromazine equivalents and any of the performance variables.

Discriminant Function Analysis

Incorporating the three groups in a DFA with A′, β'', Hit RT, YMRS, HDRS, and SAPS as predictors, two discriminant functions were identified that combined to separate the groups significantly [$\chi^2 = 208.84$, $df = 12$, $p < .001$]. As depicted in Figure 2, the first function separated the manic patient group from the euthymic and healthy groups while the second separated the healthy from the euthymic group. The manic group's scatter plot for the second function encompassed that of the other two groups despite having a group centroid falling in between. With the first function removed, there was still significant separation between groups [$\chi^2 = 12.56$, $df = 5$, $p < .05$]. The two functions accounted for 98.7% and 1.3% of the variance between groups, respectively.

The loading matrix between predictors and discriminant functions revealed that YMRS (.62) was the best predictor of the first function. The best predictors of the second function were A′ (−.91) and Hit RT (.87). Predictors with a

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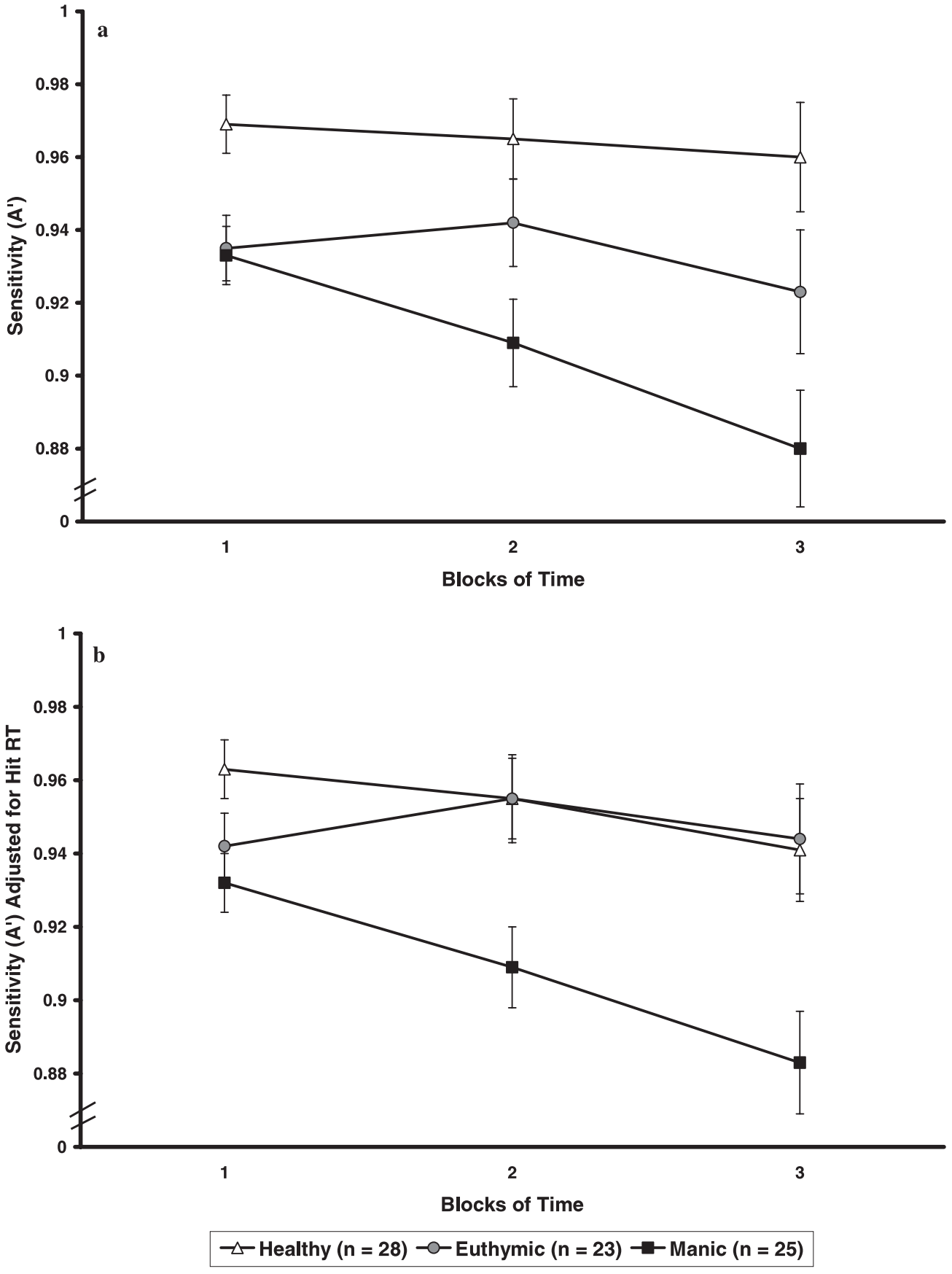

Fig. 1. Group comparison of mean CPT-DS perceptual sensitivity (A′) across three successive blocks of time in ANOVA (a) and ANCOVA with Hit RT at block 1, 2, and 3 as the covariates (b).

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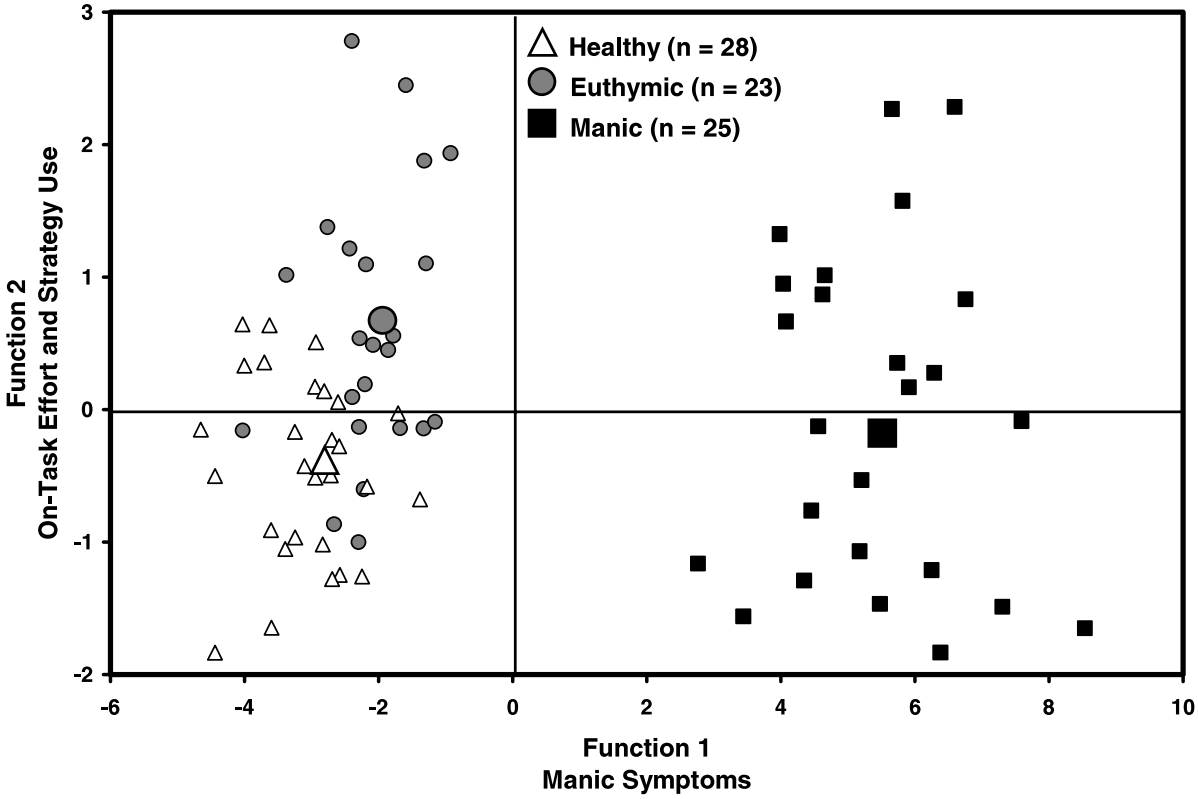

Fig. 2. Scatter plot demonstrating the covariance between psychiatric symptoms and performance. Displayed are the group centroids on two discriminant functions derived from three performance variables (A′, β'', and Hit RT) and three symptom rating scale variables (YMRS, HDRS, and SAPS total scores).

loading $< .50$ were not interpreted (Tabachnick & Fidell, 2001). Pooled correlation among the performance measures and symptom-rating scales revealed no statistically significant relationships ($r = -.09$ to $.19$, $p > .05$). A significant negative relationships between Hit RT and A′ [$r = -.96$, $p < .05$] indicated that RT increased as perceptual sensitivity diminished.

Classification results were based on Fisher's linear discriminant functions. Of the total sample, 91% were correctly classified, compared to 33.3% that would be classified correctly by chance alone. One-hundred percent of the manic patients were correctly classified, followed by 93% of the healthy volunteer group and 78% of the patients in the euthymic group. Euthymic patients were more likely to be misclassified to the healthy group than to the manic group (22% *vs*. 0%) and healthy subjects were more likely to be misclassified to the euthymic group than to the manic group (7% vs. 0%).

Given that patient volunteers were assigned to groups based on YMRS scores, creating a possible confound, we conducted a *post-hoc* DFA incorporating performance variables only (A′ β'', Hit RT). This run yielded two functions that combined to separated the groups [$\chi^2 = 172.54$, $df = 6$, $p < .001$]. With the first function removed there was still significant separation [$\chi^2 = 10.27$, $df = 2$, $p < .01$]. The only interpretable loadings were Hit RT (1.0) and A′ ($-.96$) on the second function. The classification results indicated that 88% of the participants in each group were correctly classified.

DISCUSSION

The present study examined sustained attention over an 8-min vigil in manic inpatients, euthymic outpatients, and healthy comparison subjects. Healthy subjects demonstrated significantly better perceptual sensitivity (A′) than did manic patients. Furthermore, healthy subjects evidenced significantly faster hit RTs than did euthymic patients. These initial comparisons suggested that an overall sensitivity deficit was most severe during mania (i.e., the manic group traded accuracy for speed), while overall hit RT slowing was most severe during euthymia (i.e., the euthymic group traded speed for accuracy). It should also be noted that the manic group was slower on average than the healthy comparison group, although not significantly so. There were no significant differences in response bias (β'') that would influence these behavioral tendencies.

In the analysis of continuous performance over time, perceptual sensitivity showed significant Group by Block interactions. When RT was left to covary with sensitivity

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(see Figure 1a), healthy subjects outperformed both patient groups at the beginning of the vigil. By the end of the vigil, the healthy group only outperformed the manic group, which demonstrated a linear performance decrement across the vigil, consistent with the performance of subjects with sustained attention deficits (Corkum & Siegel, 1993; Nuechterlein, 1991) and with our first hypothesis (impaired performance effectiveness in mania—significantly higher error rates as attentional demands increase over time). When RT was removed from the model (see Figure 1b) based on the initial finding of speed/accuracy tradeoffs in the patient groups, the sensitivity function for the euthymic group changed considerably, although the other group functions changed little. The euthymic group function became statistically indistinguishable from that of the healthy comparison group, suggesting that euthymic patients, in particular, engaged in a speed/accuracy tradeoff as predicted in hypothesis two (processing inefficiency in euthymia—normal accuracy at the expense of significantly slower RT). Euthymic patients may have adopted a compensatory cognitive control strategy to maintain sustained attention performance by increasing accuracy at the expense of speed.

The DFA yielded a model of symptomatology and sustained attention performance that discriminated the groups on two dimensions. The first dimension accounted for the majority of variability, separating manic patients from euthymic patients and healthy volunteers. This dimension was related to manic symptoms, as would be expected based on the group assignments. The second dimension, although significant, accounted for little additional variance, and would have little diagnostic value in separating these groups beyond symptoms alone. However, the theoretical significance of the second dimension is important for an understanding of information processing in mania, as highlighted by the results of the *post-hoc* DFA. It can be viewed as a spectrum of on-line effort and strategy use required to maintain attention. Healthy subjects required little effort to perform the CPT-DS relative to both patient groups, but especially less than the euthymic group. Euthymic subjects required greater effort to sustain attention for 8 min, and may have responded more slowly as a compensatory strategy to maintain sensitivity at a relatively high level. Behaviorally, individual levels of cognitive processing effort required to sustain attention were predicted by both Hit RT and A′. The healthy group responded both quickly and with high sensitivity indicating that little processing effort was required to sustain attention. The euthymic group traded speed for accuracy, indicating that some additional processing resources or effort was required to maintain attention. Finally, the manic patients responded in a variable fashion, as might be expected of acutely ill patients who encompassed the entire spectrum of cognitive resource utilization.

Taken together, these results are consistent with *processing efficiency* theory (Eysenck & Calvo, 1992). The ability to sustain attention in bipolar disorder may involve compensatory control processes that result in psychomotor slowing and increase attentional capacity. This type of compensatory process would be expected to spare *attentional effectiveness* at the expense of *processing efficiency*. The theory would predict that severe symptoms reduce processing capacity during manic episodes to such a great extent that compensatory cognitive processes can no longer support effective sustained attention. These compensatory processes may represent a phenotypic abnormality involving executive resources that are disrupted by acute mania (Ackenheil, 2001). However, due to the cyclical course of bipolar disorder, it is difficult to determine how stable compensatory control processes should be, or how large speed/accuracy tradeoffs should be, to be considered phenotypic characteristics.

It is interesting to note that perceptual sensitivity scores increased after statistically controlling processing speed, which made the euthymic group appear more like the healthy group. Moreover, unlike the manic group, the euthymic group *did not* display a monotonically decreasing sensitivity function consistent with impaired sustained attention (Corkum & Siegel, 1993; Nuechterlein, 1991). Thus, although executive control invokes and regulates the automatic modulatory effects of attention at the expense of processing efficiency, it does not necessarily increase the processing effectiveness of sustained attention in bipolar disorder. This finding has important clinical and physiological implications. Control processes are open to conscious awareness, making them more responsive to cognitive-behavioral remediation than are automatic processes (Burgess & Robertson, 2002). Cognitive reorganization may place bipolar patients in a unique position to either learn or, in the case of RT slowing during sustained attention, unlearn compensatory strategies in support of more efficient information processing and better functional recovery.

These results are also consistent with physiological models of attention and emotion (e.g., Lichter & Cummings, 2001; Riccio et al., 2002). In healthy adults, increased activation in areas of prefrontal cortex and anterior cingulate has been implicated in the ability to sustain attention (Adler et al., 2001; Hager et al., 1998). Yamasaki et al. (2002) demonstrated a possible intersection between anterior limbic brain circuits of emotion and attention within the anterior cingulate gyrus. They suggested that strong activation of emotional networks by experimental means can produce strong emotional states that disrupt functions of attention (Yamasaki et al., 2002). Consequently, dysregulation of the anterior limbic network during mania might be expected to disrupt brain regions required for attention as well.

Unmedicated euthymic patients with bipolar disorder show an ability to sustain attention as effectively as healthy subjects, but only by overactivating areas of ventrolateral prefrontal cortex and limbic/paralimbic areas (Strakowski et al., 2004). The authors of these findings suggested the hypothesis that euthymic patients rely on executive control processes of prefrontal cortex to sustain attention over time (Strakowski et al., 2004). Cortically mediated executive processes may be capable of maintaining attentional

abilities otherwise subserved by altered subcortical structures until emotional homeostasis is disrupted in bipolar disorder. Based on the current findings, we would predict that ventrolateral prefrontal cortex is "recruited" to maintain attention during euthymia (Strakowski et al., 2004) due to subcortical brain abnormalities within the anterior limbic brain network (Altshuler et al., 1995; Aylward et al., 1994; Strakowski et al., 1993a, 1993b, 1999, 2002a, 2002b; Swayze et al., 1990). An alternative hypothesis is that the ability to self-monitor attention over time is ameliorated by disruption of the frontal-thalamic gating system (Stuss & Benson, 1984, 1986) rather than the subcortical structures *per se*. If mania disrupts frontal-thalamic gating, then we might also expect sustained attention deficits. Functional neuroimaging research comparing manic and euthymic patients with bipolar disorder will be needed to test these neuroanatomic speculations.

Several limitations must be considered when assessing these interpretations. First, the patient groups had different medication exposure. Although medication effects were allowed to vary in the present study, treated (antipsychotics + mood stabilizers) and untreated patients did not perform differently and chlorpromazine equivalents were unrelated to performance. Therefore, although both antipsychotic and mood-stabilizing agents may increase RT (Strauss et al., 1987; Tellegen, 1965), the RT effects in the present sample of patients are not likely due to the direct influence of psychotropic medications. Second, a longitudinal design assessing the same individuals in both euthymic and manic mood states would provide a better test of the stated hypotheses. Third, the scope of the study was restricted to sustained attention. The extent to which these findings can be extended to other cognitive domains will need to be determined. Fourth, co-occurring Axis I disorders, with the exception of past substance-use disorders, were a cause for exclusion from this study. This practice may limit the ability to generalize these findings to the broader population. Finally, unlike repeated-measures analyses, DFA may be unstable (Tabachnick & Fidell, 2001) and these results should be considered preliminary until replicated in another sample. With respect to the DFA including symptom measures, the circularity of including YMRS scores when they were also essential defining features of group membership must be considered.

The present finding of adequate sustained attention but decreased processing efficiency in euthymic patients with bipolar disorder supports the contention that cognitive reorganization may allow disrupted automatic processes to be performed through effortful control. A future study might manipulate the speed/accuracy operating characteristics of subjects on the CPT-DS by stressing speed in one experimental condition and accuracy in another to test and extend a processing efficiency model of bipolar disorder. We would predict better performance in a condition emphasizing speed. It would also be interesting to assess whether speed/accuracy tradeoffs are intentional strategies or automatic control processes.

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