

*Original Article***Covert orienting visual attention in full remitted single manic patients**

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Abstract

BACKGROUND: Attentional disturbances in Bipolar I Disorder (BID) have been increasingly reported but the majority of studies have not identified a model emphasizing component operations involved in attentional processes. In this study we sought to assess elementary attentional operations using the Posner paradigm for covert orienting of visuospatial attention, with and without cues, to dissect levels of attentional impairment.

METHODS: The study was carried out with 11 fully remitted BID single manic episode patients and 11 age-matched normal control subjects. The Hamilton Depression Rating Scale (HDRS), Young Mania Rating Scale (YMRS) and Covert Orienting of Visuospatial Attention Task (COVAT) were administered. Reaction Times (RT) on the Posner task were examined with a multivariate approach by an Analysis of Variance (ANOVA) for repeated measures with Group as the between-subject factor and Stimulus Onset Asynchrony (SOA), Cue, and Visual Field as the within subject factors.

RESULTS: The main effects involved Group, Cue, and SOA as well as interactions of Cue by SOA and SOA by Group. There was neither detectable effect of visual field, nor interactions involving visual field. The Group by Cue did not show a main effect. There was no abnormality in the covert orienting in patients (i.e., Group by Cue by SOA by FIELD). RTs in the valid cues were significantly faster than the RTs in the invalid cues in the both groups. Only SOA had a main effect on the reaction time differences between invalid and valid cues.

CONCLUSIONS: The main finding is that BID patients are generally slower compared to controls; however, the slowing is most pronounced at short SOA, suggesting that they are slower to initiate information processing following the cue. Interestingly, BID patients still show a cueing effects (valid RTs < invalid RTs) at short SOAs, suggesting that the RT deficit does not have any relationship with orienting attention, but rather is a deficit in general arousal.

KEY WORDS: Attention, covert orienting, full remission, mania.

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Cognitive dysfunction in distinct phases of Bipolar I Disorder (BID) has been increasingly identified. The pattern of impairment pertains to different cognitive domains such as attention, memory and learning, visuomotor performance, working memory and executive control.¹⁻⁶ Of all the cognitive domains examined in BID patients, investiga-

tion of attention has yielded consistent results, and may provide an important foundation for a clinical understanding of cognitive deficits in BID.⁷ Among the various attentional subdomains, the most consistent findings have been deficits of sustained and selective attention, which usually detected by one of the Continuous Performance Task (CPT) variants.^{5,8-10}

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The main difficulty of studying attention exactly is in that attention itself is invisible. However, attentional tasks based on well developed and theoretically valied models have been at employed to allow better characterization of the component operations involved in attentional processes and provide a better understanding of the link between neurobiological mechanisms and cognitive disturbance. One of the most widely used experimental paradigms in spatial selective visual attention is the task that orients attention with a cue. These experimental paradigms were developed by Posner and his colleagues.^{11,12} In this paradigm, orienting of attention reflects a facilitation or inhibition of the detection of objects, which appear at a certain spatial location depending on the preceding direction of the attention towards or away from this location. The orienting of attention to visual space without eye movements is known as covert orienting.^{13,14} This type of visual attention is typically examined by means of computerized Covert Orienting of Attention Tasks (COVAT). Here, subjects are not allowed to turn their head or eyes towards the source of stimulation; they have to maintain fixation to the centre of the screen and respond as fast as possible to targets, which appear in the periphery of the visual field. A target may appear without a preceding cue, or may follow a generally alerting, but spatially neutral cue, or it may follow a spatial cue, which summons attention to the direction where the target is going to appear (valid cueing) or to the contralateral direction (invalid cueing). Central cues direct attention consciously to one visual field. In contrast, peripheral cues capture visual attention automatically; i.e., without involvement of directed attentional mechanisms. When peripheral cues appear in valid or invalid positions at the same frequency and therefore, they do not predict the subsequent location of the target, Reaction Times (RT) to the target critically depend on stimulus onset asynchrony (SOA) (time from onset of cue to onset of target). With short SOAs (less than 200 ms), invalid cues result in a RT disadvantage over valid trials, which is

due to the necessity to disengage attention from the previously cued and redirect it to the target location. In contrast, with longer SOAs, valid cues result in longer RTs to the subsequent target.¹² This latter phenomenon is thought to reflect an automatic, inhibitory mechanism protecting the organism from redirecting attention to previously scanned, insignificant locations, and is called Inhibition of Return (IOR).¹² Dysfunction in right parietal regions should demonstrate asymmetries in the orienting of attention.^{15,16} Therefore, this paradigm has inherent sensitivity to detect right hemisphere abnormalities in this application. While electrophysiological studies in BID have revealed relative functional deficits in the non-dominant (usually right) hemisphere in both phases of mania and depression,^{17,18} functional neuroimaging findings of hemispheric asymmetry in BID patients have varied.¹⁹⁻²² If BID is associated with right cerebral hemisphere dysfunction, specific attentional abnormalities will be predicted during COVAT performance. According to our search, there has been no published study investigating the Posner paradigm focused in BID patients yet. We have studied the Posner paradigm as a reliable measure of covert orienting of attention process in young and middle-aged patients with BID, single manic episode, in full remission to predict presence of right parietal dysfunction.

Methods

Participants and design

The study was ethically and scientifically discussed and approved by the Department of Research of Isfahan University of Medical Sciences, Isfahan, Iran. All patients admitted to Noor university hospital (affiliated to Isfahan University of Medical Sciences) from March 2006 to June 2007 who had a DSM-IV based diagnosis of BID single manic episode were identified using our computerized database registry and considered for participation in this study.²³ We identified 36 suitable subjects, 27 of whom agreed to participate in the study. The subjects were then screened for inclusion

and exclusion criteria. The inclusion criteria were right-handedness, at least secondary high school education, and age between 18 and 45 years. The exclusion criteria included relapse or recurrence of mood episode and co-morbid major psychiatric or medical disorder such as alcoholism, drug abuse, head trauma, or epilepsy. Eleven (5 men) patients met all criteria and entered the study. All 11 patients were receiving valproate sodium and three were also taking lithium. Control subjects were matched for handedness, age, gender, and education and were screened for psychiatric disorders using the Persian version of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I).²⁴ Participants in both groups were assessed with Persian versions of Young Mania Rating Scale (YMRS)²⁵ and Hamilton Depression Rating Scale (HDRS-24)²⁶ by the same interviewer. Cut off scores of current symptoms to define euthymia (YMRS<6 and HDRS<7) were similar to previous studies.^{5,27} Informed written consent was obtained from all subjects.

Posner test

Patients and controls were instructed to maintain fixation on a cross of 1° in the centre of the screen. Ocular movements were ruled out by direct observation of the patient's eyes by a trained person. In each trial, two squares of 3° of visual angle were displayed on the screen at about 7° to the left and to the right of the fixation point. Overall, the task consisted of 96 trials preceded by 15 practice trials. The experimental design was composed of 64 "valid" trials (cue and target appeared in the same side of the visual field: 32 in the left visual field and 32 in the right visual field), 16 "invalid" trials (cue and target were in opposite sides of the visual field: 8 in the left visual field and 8 in the right visual field), and "neutral" trials (cue appeared on the central fixation point: 8 in the left visual field and 8 in the right visual field). After 500 ms an arrow (cue) appeared on the top of one of the two squares or on the fixation point, and after a random variable stimulus onset asynchrony (SOA) of 200 or 800 ms, a filled white square (target stimulus) appeared

randomly inside one of the two peripheral squares. The peripheral cue was used to guide automatic covert orienting of attention. Inter-trial interval was of 2 seconds. Mean reaction times in the valid, invalid and neutral trials for the two SOAs were recorded. Comparison of the Validity Effect (i.e., reaction time difference between invalid and valid cue conditions) at SOA 200 and SOA 800 ms was used as a reliable measure of covert orienting of attention process.^{28,29}

Statistical analysis

Statistical analyses were performed using the SPSS for Windows, Release 13 (SPSS Inc., Chicago, IL). Reaction times were examined with a multivariate approach by an Analysis of Variance (ANOVA) for repeated measures with Group (control subjects versus euthymic BID patients) as the between-subject factor and SOA (800 ms, 200ms), Cue (valid, invalid), and Visual Field (left, right) as the within subject factors.

Results

The baseline characteristics of participants were shown in table 1. Reaction times less than 100 ms (anticipations errors) and trials with eye movement were excluded from the results. These errors were not significantly different between euthymic bipolar patients and control groups (4.8% vs. 3.5%, respectively). The main effects involved Cue, [F (2, 20) = 8.4, P = 0.001], SOA [F (1, 20) = 160.5, P < 0.001], as well as an interaction of Cue and SOA [F (2, 20) = 4.4, P = 0.031]. Another noteworthy result was the interaction of SOA and Group [F (1, 20) = 14.1, P = 0.001]. There was also a main effect of Group [F (1, 20) = 6.5, P = 0.019]. There was neither detectable effect of visual field, nor interaction involving visual field (e.g., Group by Field; Group by Field by Cue; etc). The Group by Cue interaction was not significant [F (2, 20) = 8.5, P = 0.1]. In particular, there was no evidence for an abnormality in the covert orienting of attention in euthymic bipolar patients (i.e., Group by Cue by SOA by Field) [F (2, 20) = 0.3, P = 0.55]. The euthymic bipolar patients,

Table 1. Demographic and Clinical Characteristics of Subjects.

Characteristics	All		Euthymic BID Patients		Control	
	Mean	SD	Mean	SD	Mean	SD
Number of subjects	22		11		11	
Sex						
Male (%)	10(45.5)		5 (45.5)		5 (45.5)	
Female (%)	12 (54.5)		6 (54.5)		6 (54.5)	
Age (year)	25.0	4.3	25.2	4.6	24.9	4.3
Education	12.3	1.4	12.1	1.1	12.7	1.6
IQ	96.3	6.5	96.8	7.8	95.5	5.3
YMRS	2.6	1.5	3.2	0.6	2.1	1.1
HDRS	3.4	1.6	3.3	1.6	3.4	1.2
Duration of Eutymia(month)	-	-	7.4	3.2	-	-

IQ= Intelligence Quotient; YMRS= Young Mania Rating Scale; HDRS=Hamilton Depression Rating Scale

like normal controls, understood and used the cue information since the reaction time in the valid cue condition was significantly faster than the reaction time in the invalid cue condition [$F(1, 20) = 40.5, P < 0.001$]. The ANOVA of the validity effects (i.e., reaction time difference between invalid and valid cue conditions) revealed a significant main effect of SOA 200 [$F(1, 20) = 17.5, P < 0.001$]. Neither Group nor Field had main effect. There was no interaction of SOA by Group by Field. There were no differences between patients and controls for all validity effects at SOA 800 ms.

Discussion

The identification of the Posner (faster RTs in valid condition) and SOA effects (faster RTs for longer SOA) established the adequacy of the experimental model both in controls and patients (figure 1). The main finding is that BID patients are generally slower compared to controls; however, the slowing is most pronounced at short SOA (figure 2), suggesting that they are slower to initiate information processing following the cue. The interesting aspect of this is that they still show a cueing effects (valid RTs < invalid RTs) at short SOAs, suggesting that the RT deficit does not have any relationship with orienting attention, but rather is a deficit in general arousal. In other words, they carry out the same attentional operations; it just takes them longer to process the sensory information and execute a response. This finding was in contrast to previ-

ous electrophysiological reports of deficits in right hemisphere function in BID patients,^{17,18} but potentially in accordance with the absence of asymmetry in a study of covert visuospatial orienting of attention in unipolar depression.³⁰ Given the effect of mood stabilizers on overall slowing in arousal, there are at least three possibilities: (I) sensory processing is slowed, (II) response selection is slowed, or (III) response execution is slowed. In the simple detection task used here, option II seems unlikely since there is only a single response (which effectively removes the 'response selection' component of the task). Therefore, we would suggest that the slowing is due to either factor I or factor III. To dissociate these factors, degrading the quality of the sensory stimulus might be considered in a future study (using an integrated noise mask for example). If degrading the stimulus exacerbates the slowing observed in BID patients (compared to controls), this would implicate impaired sensory processing in these patients as the source of the RT slowing. For both groups, with short SOA, valid cues resulted in RT advantage over invalid trials (figure 2), which was due to a reflexive attention shift towards the source of stimulation. On the other hand, with longer SOA, valid cues result in longer RTs to the next target. Intact inhibition of return effect (IOR) in euthymic BID patient, according to the COVAT theory,^{11,31} donates euthymic BID the ability to complete the "disengage, engage, and move" operations when there is sufficient time

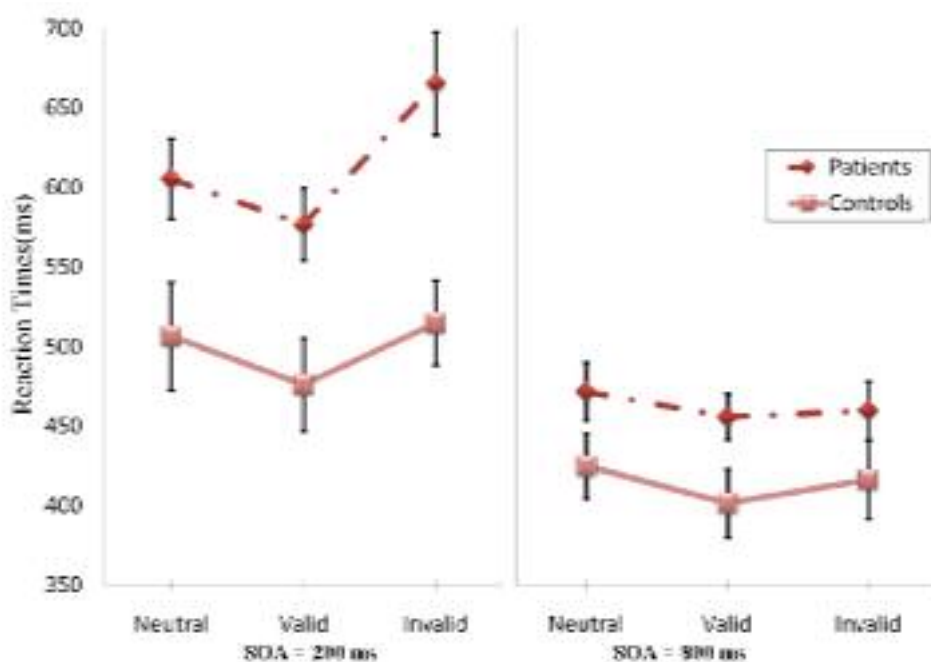


Figure 1. Mean reaction times for each trial type for patients and controls.

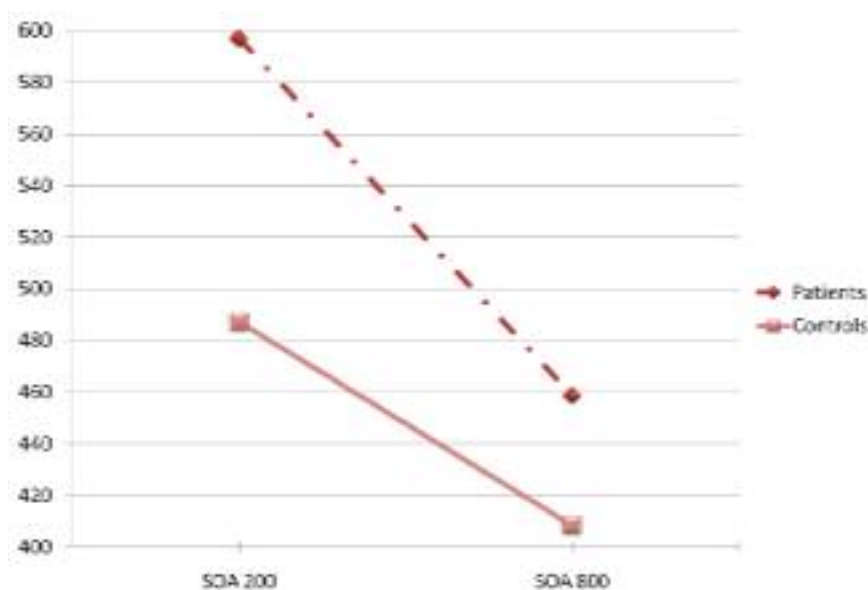


Figure 2. Mean reaction times for each SOA for patients and control.

between presentation of the cue and the target. This study had several advantages as follows: 1) might be the first investigation of COVAT in BID, 2) patients were examined after the first mood episode to reduce the effect of recurrent

episodes on cognitive abilities, 3) patients were in full remission to omit the effect of acute mental illness, 4) subjects were young and middle aged, 5) both short and long SOAs were used, 6) matched controls and patients in

age, sex, and education, 7) handedness was considered. The limitations of our work were small sample size and treatment with drugs that might affect cognition. Well-designed fol-

low up studies might try specifically to determine which aspect of information processing is impaired in this disorder.

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