

Prefrontal Activity Measured by Functional Near Infrared Spectroscopy During Divergent and Convergent Thinking in Bipolar Disorder

Yasemin HOŞGÖREN ALICI¹, Halise DEVRİMCİ ÖZGÜVEN¹, Emre KALE², Isıl YENİHAYAT³, Bora BASKAK³

¹Department of Psychiatry, Gölbaşı Şehit Ahmet Özsoy State Hospital, Ankara, Turkey

²Brain Research Center, Ankara University School of Medicine, Ankara, Turkey

³Department of Psychiatry, Ankara University School of Medicine, Ankara, Turkey

ABSTRACT

Introduction: Biographical research as well as some controlled studies point out to a relationship between bipolar disorder (BD) and creativity. Neurobiological underpinnings of this relationship are unclear. Although there is no consensus on the definition of creativity, Alternative uses Test (AuT) and Remote Association Test (RAT) are frequently used to measure convergent and divergent creativity. We aimed to examine prefrontal cortex (PFC) activity with functional near-infrared spectroscopy (fNIRS) during the RAT and AuT tests in subjects with BD.

Methods: We measured PFC activity in subjects with remitted BD (N=31) and healthy control subjects (N=27) with fNIRS during divergent and convergent thinking tasks (AuT and RAT respectively). We were particularly interested in the antero-posterior dissociation of the activity within the PFC according to the two task domains.

Results: We found that the index subjects displayed lower performance than healthy controls during the AuT and the RAT. AuT and RAT were associated with different activities in the two groups. Anterior PFC (aPFC) activity was higher than posterior PFC (pPFC) activity during the RAT in the index group, and during the AuT in the control group. aPFC activity was negatively correlated with the RAT performance in the index group.

Conclusion: Higher activity in the aPFC may be the functional neuro-anatomical correlate of low convergent creativity performance in BD.

Keywords: Creativity, bipolar disorder, functional near infrared spectroscopy

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INTRODUCTION

Creative thinking refers to utilize an original, useful, and unexpected alternative thinking model in order to overthrow the traditional deep-rooted one, and therefore can be considered as a kind of adaptation (1). Through cognitive perspective, creativity is a highly integrated mental function associated with planning, cognitive flexibility, mentalization, abstract thinking, and executive control (2).

The initial basis to search for a relationship between bipolar disorder (BD) and creativity has been the observations on the over-representation of bipolar subjects within creative artist groups compared to general population (3). Further findings indicated that not only subjects with BD, but their first-degree relatives occupied more creative professions as well, pointing out to a familial association between the disorder and creativity (4). Studies with self-report measures showed that bipolar subjects report themselves as more creative (5). Most (6, 7) but not all (8) studies using validated experimental tasks indicated that bipolar subjects may perform more creative than control subjects. Furthermore, risk for BD as well as hypomania were also associated with creative tendency (9). Relationship of BD and creativity may be mediated by personality traits such as openness to experience and temperament, particularly cyclothymia, but neurobiological underpinnings of the relationship remain unclear (7).

Prefrontal cortex (PFC) has been examined in many studies, and conceptualized as the primary neuroanatomic correlate of creativity (10). Some authors argued for a dorsal vs. ventral dissociation of PFC activity during creativity tasks (2, 10). According to these models a postero-anterior gradient exists. The ventral parts of the PFC are involved in more abstract thinking. Tasks that require controlled memory retrieval, particularly those requiring the selection of a target concept among a set of competing alternatives, activate this area. Dorsal PFC on the other hand is generally involved in tasks that require executive control (10).

Although there is no consensus on the classification of creativity tasks, thought divergence and convergence are considered as two important aspects. While divergence tasks provoke to create many answers to questions, convergence tasks try to catch the one correct answer among many possible alternatives. The classic example of the divergence tasks is the Alternative uses Test (AuT) where the subject is desired to find alternative uses of a common object (i.e., a brick). Here, the subject is stipulated to find rare and original ideas that can be achieved by suppressing ordinary thinking (11). On the other hand, in the Remote Associations Test (RAT) the participant is asked to find the fourth word (i.e., 'cheese') associated with the three given words (i.e., 'rat' - 'blue' - 'cottage') that somehow converge

into that one correct answer. The ‘thing’ that is measured in this test is the “aha!” experience resulted from whether or not there is awareness about the solution of the problem, or the conclusion that does not come to mind instantly while thinking about the problem (12).

Functional near-infrared spectroscopy (fNIRS) is a non-invasive cortical imaging technology capable of measuring relative concentration changes of regional oxyhemoglobin and deoxyhemoglobin as markers of cortical activity in a naturalistic environment. Since fNIRS is relatively insensitive to motion artifacts, subjects can be examined in a natural sitting position, without any surrounding distraction. Ecological validity of this technology makes it a suitable tool to assess cortical activity especially during complicated tasks such as creativity where physical restriction is expected to highly interfere with the task performance. For example, fNIRS has been used in real-world situations such as face-to-face communication and interpersonal cooperation (13).

In the present study, we aimed to examine PFC activity during divergent and convergent creative thinking in bipolar subjects. We were especially interested in the antero-posterior dissociation of the activity according to the two task domains. We hypothesized that the antero-posterior gradient deviates from normal during the convergent vs. divergent idea generation in subjects with remitted BD.

MATERIALS AND METHODS

The Groups

In a cross-sectional design, we compared BD patients with healthy control subjects in two tasks of creativity and measured PFC activity with fNIRS during these tasks.

The index group comprised 31 subjects with DSM-IV (*Diagnostic and Statistical Manual of Mental Disorders, 4th ed.*) BD followed at a university hospital compared to 27 healthy control subjects. The BD subjects were in clinical remission as ascertained by a Young Mania Rating Scale (YMRS) score lower than 7, Hamilton Depression Scale (HDS) score lower than 7 and Clinical Global Impressions Scale (CGI) illness severity rating lower than 5. Hand preference was evaluated by Turkish version of Chapman and Chapman's Hand Preference Questionnaire. All subjects were right-handed. The groups were similar in terms of age, gender, level of education and overall IQ (Table 1). The control subjects were evaluated by two experienced psychiatrists in order to rule out the existence of a psychiatric disorder or a history of any psychiatric treatment. The study was approved

by the Ankara University Ethics Committee and the participants were enrolled after having signed the written informed consent. All participants were physically healthy at the time of recruitment, and none had a history of head trauma, serious medical illness, or alcohol/substance use. Since working memory performance may interfere with creativity and may be differentially represented among the two groups, Auditory Consonant Trigrams Test (ACT) was employed to control this interference.

Assessment of Creativity

Creativity assessment included two tests. Divergent thinking was assessed by the Alternate Uses Test (AuT) (11) and thought convergence was assessed by the Remote Associates Test (RAT) (12).

In the adopted AuT the subjects are stipulated to think of as many uses as possible for three simple objects; (i) a paperbox, (ii) a piece of coal, and (iii) half glass of water in three minutes per each object. The behavioral data output was obtained in line with Silvia and colleagues' method (14, 15). We adjusted this method. The performance was audio-recorded, and the recordings were later evaluated by a blind clinical psychologist in terms of fluency and divergence. First, total number of created ideas were counted (AuT-Id) for all objects representing the idea fluency score (AuT-If). The divergence scores (AuT-Dv) consisted of (i) originality, (ii) rarity, and (iii) utility (cleverness) of each idea. The evaluations were made on a 5 point Likert scale (from not original/rare/useful at all, to very original/rare/useful). Then, the AuT scores were obtained for each object separately and were calculated by dividing the sum of originality, rarity, and utility scores of each object by the number of created ideas. Total AuT score was the sum of AuT scores calculated for the three objects.

During the RAT the subjects were presented three words and asked to find the ‘target word’ that is associated with all of the presented words in 30 runs (i.e., the target word ‘-long’ is associated with each of the three stimuli words; -time, -hair and -stretch). The ‘run’s were stratified into three layers (difficult, normal, and easy) according to remoteness of the target word to the stimuli words. There were two behavioral outputs; total number of correct responses (NCR) and the RAT score that is the sum score of the difficulty points of each correct response (correct responses corresponded to 1 point for easy, 2 points for normal, and 3 points for difficult questions). A previous study indicated that the Turkish version of the RAT may differentiate Bipolar Subjects from healthy control subjects (16).

Functional Near Infrared Spectroscopy

We used the fNIRS device (ETG-4000; Hitachi Medical Co., Tokyo, Japan) located at Ankara University Brain Research Center fNIRS Laboratory to measure cortical activity during the modified AuT and RAT. The fNIRS instrument measures relative changes in oxygenated ($\Delta\text{Oxy-Hb}$) and deoxygenated hemoglobin ($\Delta\text{deoxy-Hb}$) through optodes (emitters and detectors) of 2 wavelengths (695 and 830 nm) of infrared light (indicated as mM/L) on the basis of the Beer-Lambert law. As a result, it is possible to noninvasively probe the human cerebral cortex using near-infrared light and monitor the cerebral concentration of hemoglobin, which is the dominant near-infrared absorbing species in the brain (13).

The distance between emitter/detector pairs was set at 3.0 cm, and the channels were defined as the area between these pairs. The 3 cm space between the optodes allows the device to measure $\Delta\text{Oxy-Hb}$ and $\Delta\text{deoxy-Hb}$ at 2–3 cm depth from the scalp that corresponds to the surface of the cerebral cortex (17). The optodes were fixed to scalp via two thermoplastic 3×3 shells, with the lowest optodes positioned along the Fp1-Fp2 line according to the international 10–20 system used in electroencephalography (Fig. 1) (18–22).

Table 1. Socio-demographic and clinical characteristics of the groups

	IG (N=31)	CG (N=27)	
Gender (F/M)	21/10	18/9	$\chi^2=0.08, p=0.93$
Age (years) (mean±SD)	38.9±10.6	37.1±10.2	$t=0.67, p=0.50$
Education (years) (mean±SD)	13.8±1.9	14.8±1.3	$t=-1.92, p=0.06$
Work status (employed/unemployed)	22/9	22/5	$\chi^2=0.87, p=0.35$
WAIS-Overall IQ score (mean±SD)	92.9±9.2	97.08±10.0	$t=-1.58, p=0.12$
ACT total score [median (min-max)]	58.5±1.8	59±1.8	$t=-1.0, p=0.32$
YMRS score (mean±SD)	0.9±2.1	-	-
HAM-D score (mean±SD)	1.16±1.69	-	-

F: female, M: male, HAM-D: Hamilton depression scale, YMRS: Young mania rating scale, ACT: auditory consonant trigrams test.

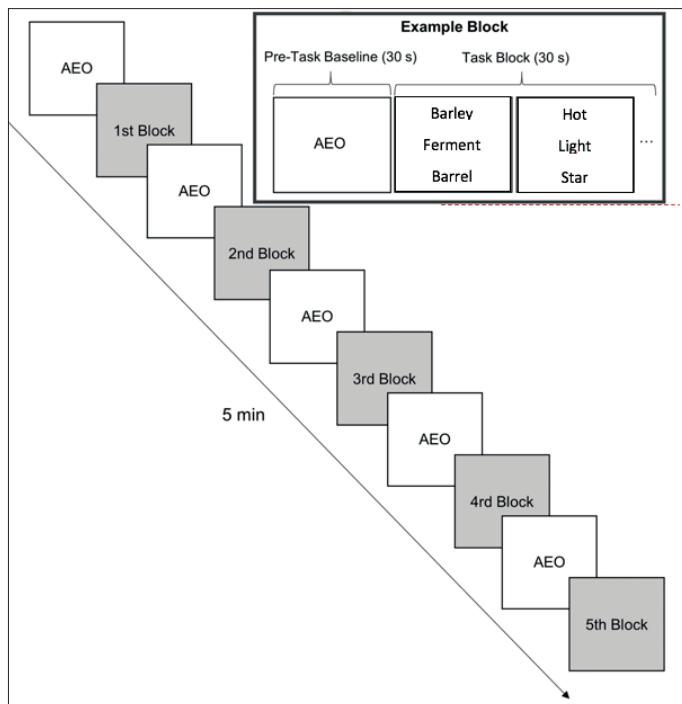


Figure 3. The RAT activation task

total RAT scores and Δ oxy-Hb values during the correspondent activation paradigm.

Δ Oxy-Hb measurements from 16 channels during the AuT and RAT were analyzed with 2 (Groups: BPD vs. Control) \times 2 (Condition: AuT vs. RAT) \times 2 (ROIs: pPFC vs. aPFC) mixed ANOVA design. Group was the between-subject independent variable; Condition and ROI were within-subject independent variables. To prevent Type-1 errors resulting from sphericity violations, Greenhouse-Geisser corrections (F-test); and to prevent Type-1 errors resulting from multiple comparisons in the post-hoc tests, Bonferroni corrections (t-test) were applied.

RESULTS

Control subjects displayed higher performance than the index subjects in the tests of divergence and remoteness. This was true not only for the AuT

Table 2. Comparison of the study groups for tests of thought divergence and remoteness

Creativity Test Scores	IG (N=31)	CG (N=27)	Statistics
RAT-NCR score (mean \pm SD)	5.32 \pm 3.16	7.84 \pm 3.65	t=-2.77, p=0.008
RAT-total score	13.29 \pm 8.86	19.96 \pm 9.54	t=-2.71, p=0.009
AuT-If _{coal} [median (min-max)]	3 (0-8)	4 (1-10)	Z=-2.95, p=0.003
AuT-If _{water} [median (min-max)]	4 (1-11)	5 (2-12)	Z=-1.67, p=0.09
AuT-If _{paperbox} [median (min-max)]	4 (1-8)	6 (3-8)	Z=-2.65, p=0.008
AuT-If _{total} [median (min-max)]	11 (5-27)	14 (8-27)	Z=-3.08, p=0.002
AuT-Dv _{coal} [median (min-max)]	25 (0-70)	40 (3-118)	Z=-3.22, p=0.001
AuT-Dv _{water} [median (min-max)]	26 (6-83)	44 (13-90)	Z=-1.85, p=0.065
AuT-Dv _{paperbox} (mean \pm SD)	39.9 \pm 22.06	61.07 \pm 21.34	t=-3.70, p<0.0001
AuT-Dv _{total} (mean \pm SD)	101.39 \pm 49.36	147.29 \pm 44.75	t=-3.69, p=0.001

RAT: Remote Associations Test, AuT: Alternate uses Test

and RAT total scores, but for the item scores in the AuT and the NCR score in the RAT as well (Table 2). Behavioral results are presented in Table 2.

The 'Area' main effect revealed by ANOVA was significant [F(1.56)=9.44, p=0.003, η^2 =0.144]. Post-hoc analyses showed that aPFC was more active than pPFC (MD=0.014, SE=0.004, p=0.003). 'Group' \times 'Condition' \times 'Area' interaction was also significant [F(1.56)=5.33, p=0.025, η^2 =0.09]. When we approach this interaction from the 'area' perspective, post-hoc analyses showed that this interaction stems from (i) higher activity among the control group during the AuT in the anterior compared to the posterior PFC (MD=0.23, 0.008, p=0.04), (ii) higher activity among the index group during the RAT in the posterior PFC (MD=0.016, SE=0.007, p=0.022) (Table 3). When we approach this interaction from the condition perspective, post-hoc analyses showed that the triple interaction only stems from higher activity in the aPFC during the AuT than the RAT (MD=0.21, SE=0.009, p=0.03) (Table 4).

Table 3. Triple interaction from the area perspective

Study Group	Condition	Area	MD	SE	p	95% CI
Bipolar Group	AuT	pPFC-aPFC	-0.13	0.007	0.087	-0.27, 0.02
	RAT	pPFC-aPFC	-0.16*	0.007	0.022	-0.029, -0.002
Control Group	AuT	pPFC-aPFC	-0.23*	0.008	0.04	-0.038, 0.008
	RAT	pPFC-aPFC	-0.003	0.007	0.69	-0.017, 0.012

aPFC: anterior prefrontal area, pPFC: posterior prefrontal area, AuT: Alternate uses Test, RAT: Remote Associations Test, MD: mean difference, SE: standard error.
*statistically significant. The oxy-Hb gradients are presented as mMmm.

Table 4. The triple interaction from the condition perspective

Study Group	Area	Condition	MD	SE	p	95% CI
Bipolar Group	pPFC	AuT-RA	0.002	0.008	0.99	-0.15, 0.16
	aPFC	AuT-RA	-0.003	0.009	0.71	-0.21, 0.14
Control Group	pPFC	AuT-RA	0.001	0.008	0.93	-0.16, 0.17
	aPFC	AuT-RA	0.021*	0.009	0.03*	0.002-0.04

aPFC: anterior prefrontal area, pPFC: posterior prefrontal area, AuT: Alternate uses Test, RAT: Remote Associations Test, MD: mean difference, SE: standard error.
*statistically significant. The oxy-Hb gradients are presented as mMmm.

RAT score was negatively correlated with the activity of the aPFC ($r=-0.37$, $p=0.041$) only in the index group.

DISCUSSION

We found that the index subjects displayed lower performance than healthy controls during the AuT and the RAT. This is rather an unexpected finding since previous research suggested that bipolar subjects perform better than healthy controls during creativity tasks (6, 25). In a meta-analysis, Taylor suggested that the relationship between creativity and mood disorders may be mediated by methodological issues (26). That is, most research reporting bipolar subjects as more creative than healthy controls rely on biographical studies or self-reported artistic creativity (3, 27, 28). Strong et al. (2007) compared bipolar subjects with healthy controls with the Barren Welsh Art Scale (BWAS) that assesses artistic creativity and the Torrence test that assesses creative thinking (originality, fluency and abstraction), and found that bipolar subjects performed better in the BWAS but not in the Torrence test (7). Johnson et al. (2015) compared bipolar-1 subjects to healthy controls with the Unusual Uses Test, and reported no difference between the two groups (8). Medication status may also affect creativity. For example, use of lithium carbonate has been associated with decreased creativity performance (29), and 21 among 31 participants in this study were under lithium treatment which may indeed interfere with creative performance. Sample characteristics may also be important. Some studies with positive results enrolled both Type-1 and Type-2 bipolar patients (6, 16, 25) while our sample consists of only Type-1 bipolar subjects which may reduce performance in AuT and RAT.

The difference between the two study groups in terms of education levels was on the verge of significance in favor of the control group. However, we found that level of education was not correlated with AuT and RAT performance, and therefore education levels are unlikely to have confounded our findings. At least one study found relationship between general cognitive performance and creativity (2, 25). However, we found that ACT performance was comparable among the study groups, and therefore did not interfere with the results.

The 'area' main effect revealed by ANOVA suggests that, independent from group membership, an antero-posterior gradient was observed on the lateral surface of the frontal region during our experimental paradigm. This result is in line with the general view suggested by several recent models of the brain networks underlying creative thinking that point out to a hierarchical postero-anterior organization within the PFC.

During the alternate uses test, subjects are expected to create original ideas and suppress ideas referring to ordinary uses of that object. It has been suggested that executive control may be involved in this process in order to suppress salient conceptual knowledge and facilitating flexible switching between semantic categories during memory retrieval (30). Similarly, in the model proposed by Beaty et al. (11), divergent thinking process involves an interplay between the default mode network (posterior cingulate cortex and inferior parietal lobe) and executive control (dorsolateral prefrontal cortex). Posterior areas of the PFC are thought to be involved in the systematic control of representations necessary for these higher-level processes (31, 32), and may be required in some creativity tasks such as free generation tasks. Beaty et al. contrasted intrinsic connectivity networks of high- and low-divergent thinking ability groups, and found that high divergent thinking ability was related to greater connectivity between the inferior frontal gyrus and the default network (11). Other models also describe a postero-anterior PFC gradient that serves to create abstract mental representations; more anterior regions of the PFC may support more abstract thinking (2). Gonen-Yaacovi et al. reviewed 34 functional imaging studies that reported activation foci during tasks assumed to engage creative thinking in healthy adults, and showed that

tasks involving the combination of remote information (combination tasks) activated more anterior areas of the lateral PFC than tasks involving the free generation of unusual responses (unusual generation tasks), although both types of tasks shared caudal prefrontal areas (17). We also found a significant 'Area' main effect in favor of the anterior parts in both tasks that suggests that the two measurement areas display different activity during the experimental paradigm. Thus, aPFC may be more sensitive to both divergent and convergent creativity.

The triple interaction revealed by the ANOVA suggests that the activity maps are different for the two study groups during the two creativity tasks. The post-hoc analyses showed that this significance stems from the higher activity in the aPFC compared to the pPFC in the bipolar subjects during the RAT and that among the control subjects during AuT. Prefrontal cortex is among the implicated cortical areas in BD. Bilateral prefrontal cortical thickness is reduced in BD (33). Lee et al. (34) assessed structural alterations in BD with voxel based morphometry analysis, and showed that ventral PFC and dorsal PFC gray matter volumes are lower in bipolar subjects compared to healthy controls. Post mortem studies highlighted reductions in neuronal size and/or changes in neuronal density, reductions in glial cell density, and changes in gene expression particularly in the medial PFC (2). The RAT performance among the index group was also negatively correlated with aPFC activity. We therefore conclude that higher activity in the aPFC may be the functional neuro-anatomical correlate of the low performance displayed by the bipolar subjects during the RAT. In healthy controls both of tests are negatively correlated. We also found that activity in this area is negatively correlated with RAT performance in the index group. These findings highlight the importance of aPFC in creative thinking in BD.

This study has some limitations. First, the sample consists of subjects with remitted BD who are followed at a university hospital, and the results may not be generalized to all subjects with BD. Secondly, creativity is represented by a broader network including some brain regions that were not investigated in this study, such as the temporal lobe, or the cingulate cortex (10), and the difference in the activity of the brain cortex between the study groups may be more significant in these areas. At last, despite not statistically significant, the patient group was older, has lower educational level, and lower IQ and ACT scores compared to the control group which may have an influence on the results. Nevertheless, this study is the first to show that low creative performance in BD may be evident in terms of prefrontal cortical activity.

CONCLUSION

We confirmed previous models that suggested a hierarchical postero-anterior dissociation of cortical activity within the lateral surface of the frontal cortex during two different creativity domains in two groups. However, we did not observe a higher creative performance in subjects with BD: patients displayed lower performance than healthy control subjects in divergence and convergence measures of creativity. Lower behavioral performance in the index group was associated with higher activity in the aPFC, a region that is structurally and functionally disturbed in BD.

Ethics Committee Approval: The study was approved by the Ethics Committee Ankara University.

Informed Consent: Written informed consent was obtained from all participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - YHA, HDÖ, BB; Design - YHA, HDÖ, BB; Supervision - HDÖ, YHA; Resource - HDÖ, BB; Materials - YHA; Data Collection and/ or Processing - YHA, IY; Analysis and/or Interpretation - YHA, HDÖ, BB; Literature Search - YHA; Writing - YHA, HDÖ, BB; Critical Reviews - HDÖ, BB.

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