Dysfunctional reward learning in bipolar disorder: an event-related potential study

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<ABSTRACT>

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Bipolar disorder is characterized by behavioral changes such as risk taking and increased goal directed activity. These kinds of behaviors may account for the abnormal reward processing in bipolar patients which result from impaired reward learning. Bipolar patients have been reported to show impaired reward learning in situations that require integration of feedbacks over time. In this study, I examine the reward learning in manic and euthymic patients with bipolar disorder behaviorally and electrophysiologically using a probabilistic reward task.

I recruited 24 manic, 20 euthymic patients with bipolar disorder, and 24 healthy controls. They were required to perform the probabilistic reward task. This task is a reward-based paradigm to produce a response bias, in which correct identification of two ambiguous stimuli is rewarded differently.

As a result, both manic and euthymic patients with bipolar disorder showed a reduced acquisition of the response bias toward rich rewarded stimuli ($F = 6.21$, $p = 0.005$) and showed attenuated feedback-related negativity in the early phase of the task ($F = 6.53$, $p = 0.003$) compared to controls. With the Young's Mania Rating Scale, positive correlation was shown with the changes of the response

bias ($p = 0.05$) and negative correlation was seen with the changes of feedback-related negativity ($p = 0.001$).

Conclusively, these findings suggest that manic and euthymic patients with bipolar disorder may have deficits in reward learning. Risk taking behavior and reward processing in bipolar patients may be linked to this deficit.

Key words : probabilistic reward task; response bias; reward learning; bipolar disorder; feedback-related negativity (FRN)

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I. INTRODUCTION

Bipolar disorder is characterized by recurrent mood episodes including manic and depressive mood during the patients' lifetime. Manic patients pursue extremely high goals and ideals, which result in excessive spending, sprees, and excessive involvement of risk taking behaviors.[1] Behavioral alterations can be explained by two motivational systems, the Behavioral Activation System (BAS) and the Behavioral Inhibition System (BIS).[2, 3] BAS is assumed to be linked to elation or increased goal directed behavior in response to positive reward, whereas BIS is proposed to be linked to depression in response to negative reinforcement or punishment.[2, 3] Deactivation of the BAS is related to

depression or anhedonia.[4, 5] In contrast, positive affect associated with BAS which can be activated by positive reward in manic patients.[2, 6] The characteristic behavior of bipolar patients may be associated with the outcome of dysfunctional reward processing.

Manic patients have the tendency to lose money in the gambling task and to choose the high gain option with high risk of losing money rather than the low gain option with low risk of losing money.[7] They scored lower in the gambling task because of their frequent strategy changes.[7] In the task of intermittent or changing reinforcement schedule, manic patient showed the tendency to make more errors. They lack the ability for comprehensive understanding of the reinforcement pattern through reinforcement learning. A PET study reported relatively greater task-related activity in the dorsal anterior cingulate cortex combined with reduced orbitofrontal activation despite matched behavioral performance using the Cambridge Gamble Task.[8]

The study of depressive patients on reinforcement learning showed apathy which is demonstrated by blunted responses to reinforcement and diminished attention, memory and psychomotor speed during task performance.[9] Depressive patients showed dysfunctional response to negative feedback which induced catastrophic reaction when they recognized the error.[10] Therefore, mood states are known to have an influence on the feedback related task performances.

Rewards may act as a reinforcer of behavior to positive events after making correct responses and increase the possibility of similar responses to similar situation, which is termed as reward learning.[11, 12] Response bias is the preferential response to more frequently rewarded stimuli in differently rewarded conditions after reward learning.[13] Probabilistic reward task is an instrument for evaluating reward learning by observing the response bias to differently rewarded stimuli of two ambiguous stimuli.[14]

Bipolar patients are reported to show abnormal shape, size and function of the basal ganglia and increased activity of the amygdala during the manic phase.[15] They are also known to show decreased activity of the mesolimbic dopaminergic area including the nucleus accumbens, ventral tegmental area and anterior cingulate cortex which has a role in reward processing.[16] As a result, manic patients tend to choose the risky options, which is consisted of higher loss for failure and higher gain for success rather than to choose the safe options and they also showed increased behavioral switching, which result in lower scores than healthy controls.[7] Therefore manic patients might have a diminished ability to adapt their behavior in response to altered reward patterns, and they might show deficits in comprehensive understanding of reward patterns through repeated reward learning.[17] Euthymic bipolar patients demonstrated decreased response bias compared to healthy controls, which also correlated with anhedonic levels, suggesting that impairments in reward learning of bipolar patients may be related to anhedonia.[18]

Feedback-related negativity (FRN) have been used to monitor the reward-related activity in the anterior cingulate cortex (ACC).[19, 20] The FRN usually peaks 200 ~ 400 ms after receiving feedback. The FRN is also known as a different form of the medial frontal negativity (MFN).[21] MFN is elicited in different situations and is named accordingly. MFN has two different forms which are consisted with the FRN and error-related negativity (ERN). FRN is elicited in response to the negative feedback while ERN is evoked by error performances.[20, 22] They have similar time-frequency characteristics although they have different scalp topography.[23] The FRN is thought to reflect the transmission of dopamine signal from the basal ganglia.[24] It is implicated in motivational processing, appearing larger (more negative) for negative feedback or punishment (worse-than expected outcomes), and attenuated (more positive) for positive reinforcement or positive reward (better-than expected outcomes).[25] The FRN can also be used to assess the brain response to positive feedbacks, but is usually used to assess that of negative feedbacks.[26-29] Therefore, positive feedbacks may elicit more positive event-related potential (ERP) deflection.

In this study, I aimed to evaluate the reward learning and related electrophysiological changes in bipolar patients in manic and euthymic phases using the probabilistic reward task. I expect that bipolar patients would show decreased acquisition of the response bias due to difficulties in identification of reward patterns in the probabilistic reward learning. I expected bipolar patients

to show decreased response bias compared to controls, irrespective of the mood status, as well as to show the related electrophysiological changes.

II. MATERIALS AND METHODS

1. Participants

Twenty-four manic patients and 20 euthymic bipolar patients were recruited among inpatients and outpatients of the Severance Mental Health Hospital of Yonsei University Health System. Diagnostic work-ups for bipolar disorder were done according to the criteria of the Diagnostic and Statistical Manual of Mental Disorder, 4th edition. Diagnoses of bipolar disorder were briefly assessed by the Mini-international Neuropsychiatric Interview (MINI).[30] Diagnostic work-ups were performed by two psychiatrists (R.Y.H. and H.S.C). Patients with other psychiatric illnesses such as schizoaffective disorder, severe personality disorder, recent substance abuse or dependence, rapid cycling bipolar disorder, history of closed head injury, mental retardation, neurological disorders or any other current axis I disorders were excluded. For control subjects, I posted a recruitment notice on a website and selected 24 healthy subjects, sex- and age-matched with the patient groups. I also performed the diagnostic work-ups for healthy controls using the MINI. These healthy volunteers had no history of bipolar disorder, schizophrenia or other psychiatric illnesses and did not show any mood or thought problems or symptoms during

the interviews. All subjects were right handed as indicated by the Annett's handedness questionnaire. The intelligence quotients were evaluated using the full version of the Korean Wechsler Adult Intelligence Scale (K-WAIS). The mood status were objectively assessed by Young's Mania Rating Scale (YMRS)[31], and Montgomery-Åsberg Depression Rating Scale (MADRS).[32] This study was approved by the Institutional Review Board of Severance Mental Health Hospital and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants with adequate understanding.

Demographic characteristics of the two patient groups and the control group are presented in Table 1. There were no significant differences between groups with regard to age, sex, IQ, or education level. YMRS score was 12.96 ± 10.07 in manic patients and 2.00 ± 1.62 in euthymic patients. MADRS score was 4.83 ± 2.96 in manic patients and 2.40 ± 3.30 in euthymic patients. Pleasure scale score was 32.79 ± 4.49 in manic patients, 30.45 ± 5.11 in euthymic patients, and 28.58 ± 8.31 in healthy controls ($F(2,65) = 4.03$, $p = 0.02$ (manic > controls)).

Table 1. Demographic characteristics of manic, euthymic patients and healthy controls

	Healthy Controls (n=24)	Manic patients (n=24)	Euthymic patients (n=20)	F, t or X^2	p
Age (years)	31.88±6.96	34.46±9.11	34.75±4.41	1.11	0.34
Sex (M, %)	11 (45.8)	11 (45.8)	8 (40)	0.20	0.91
IQ	106.09±10.76	114.33±12.91	110.00±11.62	2.45	0.10
SHAPS	28.58±8.31	32.79±4.49	30.45±5.11	4.03	0.02 (M>H)
YMRS		12.96±10.07	2.00±1.62	-5.25	<0.001
MADRS		4.83±2.96	2.40±3.30	-2.55	0.01
Mood stabilizers (Lithium / Valproate)		10/14	7/13	0.21	0.76
Chlorpromazine equivalent dose (mg)		829.96±226.00	663.35±225.27	2.44	0.02

Abbreviations: IQ: Intelligent Quotient, SHAPS: Snaith-Hamilton Pleasure Scale, YMRS: Young's Mania Rating Scale, MADRS: Montgomery-Åsberg Depression Rating Scale ion Rating Scale

2. Tasks

Participants performed the probabilistic reward task, in which they made

decisions about whether the length of the ambiguous - mouth stimulus is short or long. Participants were instructed to focus on the cross sign in the center of the screen. After 500ms, participants viewed the schematic face stimuli without the mouth for 500ms. The ambiguous mouth stimulus was shown for a short duration after which the participants were required whether the length of the mouth was short or long. The length of long stimuli was 13 mm, - and that of short stimuli was 11.5 mm. During the task, participants were not rewarded to all correct responses. They were rewarded for some of their correct responses with a message "Correct!! You won ₩100". The probability of the reward for the correct response was 3 out of 5 for the rich stimulus and 1 out of 5 for the lean stimulus. Participants were explicitly informed that they will not receive the reward feedback to all correct responses. They are not informed that one of the stimuli types would be rewarded more. This difference in reward probability made the response bias.[33] This task consisted of 3 blocks with 100 trials for each block. (Figure 1)

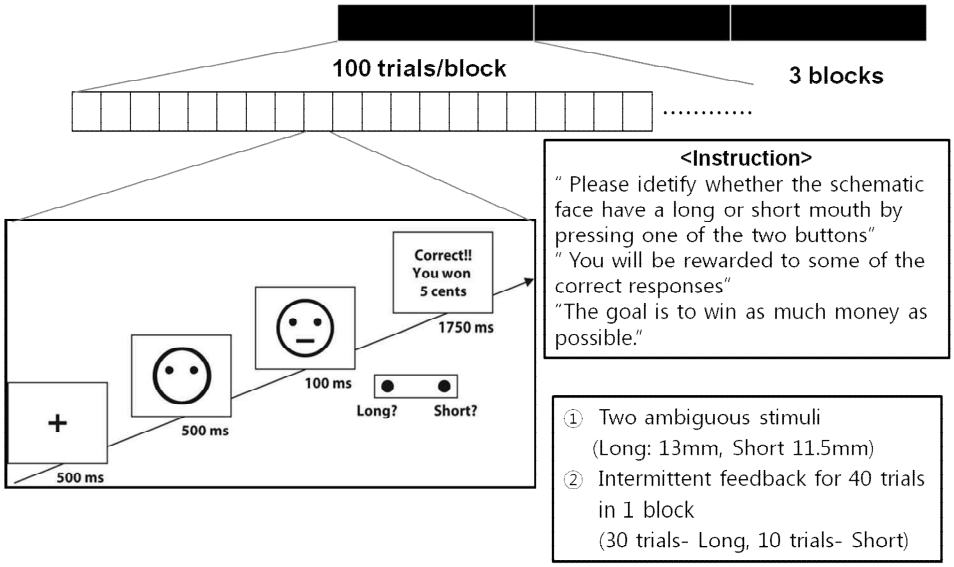

Figure 1. Schematic diagram of probabilistic reward task[33]

3. Data

I calculated response bias, discriminability, and response time to assess the task performances.[34, 35] Response bias and discriminability were calculated by the following formulae.[18, 34, 35]

A. Response bias (RB):

$$\log b = \frac{1}{2}\log\frac{Rich_{correct} \times Lean_{incorrect}}{Rich_{incorrect} \times Lean_{correct}}$$

B. Discriminability:

$$\log d = \frac{1}{2}\log\frac{Rich_{correct} \times Lean_{correct}}{Rich_{incorrect} \times Lean_{incorrect}}$$

Response bias increases if participants make more choices of rich rewarded

stimuli in cases of correct rich stimuli and incorrect lean stimuli. This means that RB may increase when participants prefer the more frequently rewarded stimuli. Positive reinforcements produce preferences to the more frequently rewarded stimuli as the task is executed. Therefore, RB may be an index of reward learning modulated by positive reinforcement. Discriminability represents the ability to distinguish between the two ambiguous stimuli, which may be used to assess the task difficulty.

4. Clinical assessment

I interviewed participants for assessment of demographics including age, sex and education level. Full version of the Korean Wechsler Adult Intelligence Scale (K-WAIS)[36] was performed for all participants. Young's Mania Rating Scale (YMRS)[31] , Montgomery-Åsberg Depression Rating Scale (MADRS)[32], and State-Trait Anxiety Inventory (STAI)[37] were done to assess mood status. Korean version of the Snaith-Hamilton Pleasure Scale (SHAPS)[38] was used to evaluated the subjective hedonic or anhedonic levels.

A. Young's Mania Rating Scale (YMRS) [31]

YMRS is commonly used for measuring the severity of manic symptoms based on the interviewer. Assessment includes items of elevated mood, increased motor activity (energy), sexual interest, sleep changes, irritability, speech (rate and amount), language-thought disorder, language content,

disruptive-aggressive behavior, appearance, and insight. Seven items are rated on an explicitly defined severity scale of 0 to 4. Four items (irritability, speech rate and amount, language content, and disruptive-aggressive behavior) are rated on a scale of 0 to 8.

B. Montgomery-Åsberg Depression Rating Scale (MADRS) [32]

MADRS is used for measuring changes in depression severity. Scales include ten items that measure the major components of clinical depression. The items are apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, pessimistic thoughts, and suicidal thoughts. Each item is rated on a seven-point scale (0 to 6).

C. State-Trait Anxiety Inventory (STAI) [37]

This inventory is used for measuring the anxiety level, based on a 4-point likert scale. Higher score positively correlates with higher level of anxiety positively. This inventory measures two types of anxiety – state and trait anxiety.

D. Snaith-Hamilton Pleasure Scale (SHAPS) [38]

SHAPS is developed for the self-administered assessment of hedonic capacity. A higher total score of SHAPS means higher level of present anhedonia. This instrument consists of 14 self-reported items.

5. Electrophysiological recordings and analyses

Electroenecephalogram was recorded from 64-channel AgCl lead cap according to the international 10/10 system with a 0.05 and 100 Hz band-pass filter and a sampling rate of 1000 Hz/Channel (SynAmpsII). The recordings were referenced to linked electrodes placed on the left and right mastoid processes. Eye blinks and movements were monitored by electrodes placed near the outer canthus and beneath the left eye.

Recording procedures were performed in a dimly lit, quiet, and electrically shielded electroencephalography room. Subjects were seated in a comfortable reclining chair at an eye distance of 50 cm from the computer monitor (visual angle of 9° x 12°). Subjects were instructed to concentrate on the center of the monitor and to avoid eye-blinking as much as possible. The subjects' performances were monitored by the closed-circuit camera, and subjects were not sleepy during the experiments.

Analysis of electroencephalography was carried out on an off-line basis. Salient noises of the electroencephalography were removed by inspection. The electroencephalography was amplified by a 0.1 - 30 Hz band-pass filter. To control for eye movement artifacts, trials were adjusted by regression from electro-oculograms.[39] Artifacts were rejected if their amplitude exceeded ±50 uV. A low-pass filter at 8.5 Hz was used to remove muscular movement, noise,

and alpha-wave activity. Epochs were included in the analysis of cases of correct responses to rich rewarded stimuli.

Distribution map was calculated by means of Low Resolution Electromagnetic Tomography (LORETA) which is used to estimate intracerebral current density underlying the scalps effects.[40] The LORETA algorithm is a form of Laplacian-weighted minimal norm solution for the inverse problem.[41] On the basis of activation time of FRN peak, analyses focused the Global Field Power (GFP) in the anterior cinglulate area (Talairach coordinates (X, Y, Z) = (1, 28, 9)).[42]

6. Statistical analyses

Behavioral data was analyzed by mixed analyses of variances (ANOVA) to assess effects of blocks (response bias of three blocks) and group (manic, euthymic patients and healthy controls). FRN amplitudes at F_z electrodes were analyzed by mixed ANOVA to assess the effects of group, blocks. Greenhouse-Geisser corrections for non-sphericity were applied. Pairwise comparisons for the response bias in each block were performed with the one-way ANOVA with post-hoc analysis of Bonferroni corrections. FRN amplitudes were analyzed in Fz electrodes. I performed multiple regression analysis to simultaneously evaluate contribution to change of response bias and FRN amplitude according to block progression in the manic patient group. Results were considered significant when the two-sided probability was less

than 0.05 in the multiple regression analysis. SPSS version 17.0 was used for statistical analyses. I calculated Pearson's correlational coefficient between the FRN amplitude at F_z electrodes and symptom severity.

III. RESULTS

1. Response bias

A 2-way group x block analysis of variance (ANOVA) revealed a main effect for block, in which the response bias of block 1 was lower than that of block 3 ($F(2,130) = 6.21$, $p = 0.005$). There were interaction of group x block ($F(4,130) = 2.47$, $p = 0.05$). RB of each block and group were shown in Figure 1. In block 1, ANOVA revealed that RB of controls were higher than those of the two patient groups ($F(2,67) = 4.11$, $p = 0.02$). However, there were no differences among the groups in block 2 ($F(2,67) = 0.22$, $p = 0.80$) and block 3 ($F(2,67) = 0.14$, $p = 0.87$) (Figure 2).

ANOVA was also done for assessing the discriminability, hit rate, and response time. There were no significant differences in discriminability ($F(2,130) = 2.39$, $p = 0.10$), hit rate ($F(2,130) = 0.87$, $p = 0.41$), and response time ($F(2,130) = 1.89$, $p = 0.16$).

Within-group analysis revealed significantly lower response bias in block 1 compared to block 2 and block 3 in euthymic ($F(2,38) = 7.39$, $p = 0.002$) and manic patients ($F(2,46) = 10.42$, $p = 0.001$), but not in healthy controls ($F(2,46) = 0.22$, $p = 0.75$).

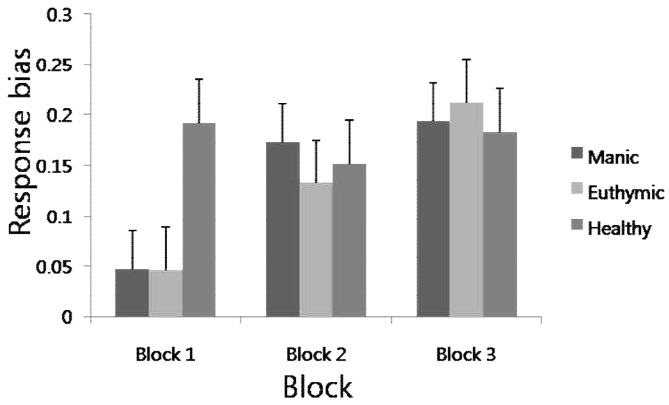

Figure 2. Response bias as a function of blocks

Table 2. The response bias and the amplitude of feedback-related negativity (FRN) among groups

		Manic patients (n=24)	Euthymic patients (n=20)	Healthy controls (n=24)
Block 1	Response bias	0.04 ± 0.13	0.05 ± 0.16	0.19 ± 0.28
	FRN	2.28 ± 3.69	2.04 ± 2.11	0.44 ± 1.67
Block 2	Response bias	0.17 ± 0.20	0.13 ± 0.16	0.15 ± 0.23
	FRN	0.40 ± 3.69	0.61 ± 2.87	0.37 ± 3.08
Block 3	Response bias	0.19 ± 0.11	0.21 ± 0.13	0.18 ± 0.26
	FRN	-0.18 ± 3.96	-0.22 ± 3.12	2.02 ± 4.58

2. FRN components

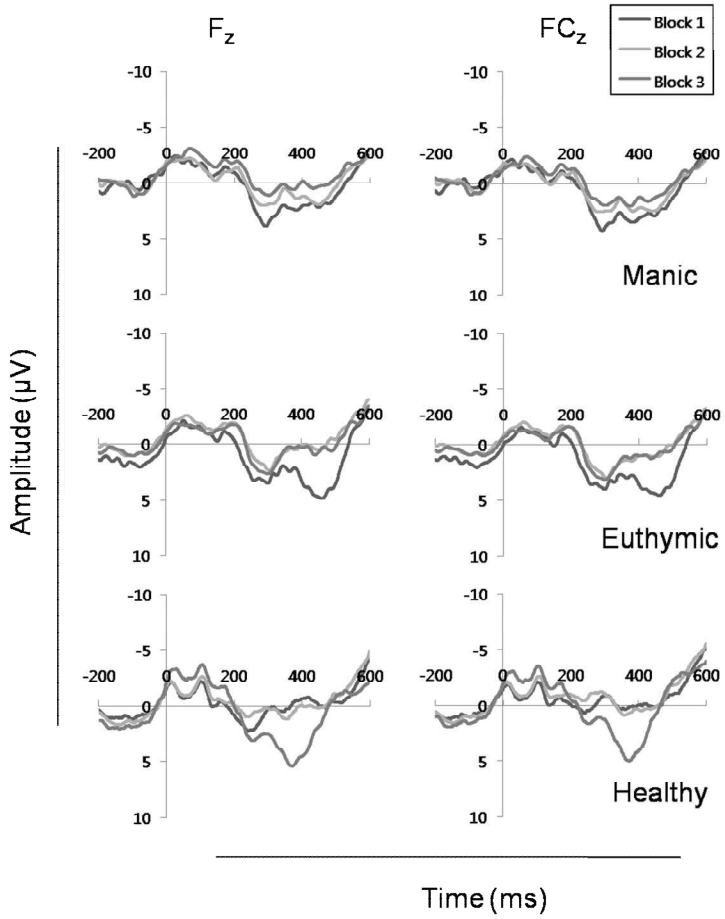

Figure 3. Grand-averages of event-related potential at F_z and FC_z electrodes.

Grand-averages of FRN and distribution maps are shown in figure 3 and figure 4. A 2-way group by block ANOVA revealed a main effect for block, in which FRN amplitude at F_z electrodes of block 1 was more positive than of

block 3 (F(2,130) = 6.53, p=0.003). There was a significant interaction of group by block (F(4,130) = 7.53, p<0.001) (Figure 5). Between group comparisons in each blocks revealed that FRN amplitude of controls were more negative than those of manic and euthymic patients in block 1 (F(2,67) = 3.32, p = 0.04). There were no differences among groups in block 2 (F(2,67) = 0.03, p = 0.97) and block 3 (F(2,67) = 2.41, p = 0.10) (Figure 5). Within-group analysis revealed more positive amplitude in block 1, compared to block 2 and block 3 in euthymic patients (F(2,38) = 42.82, p<0.001), in manic patients (F(2,46) = 10.98, p<0.001), but not in healthy controls (F2,46) = 2.79, p = 0.08).

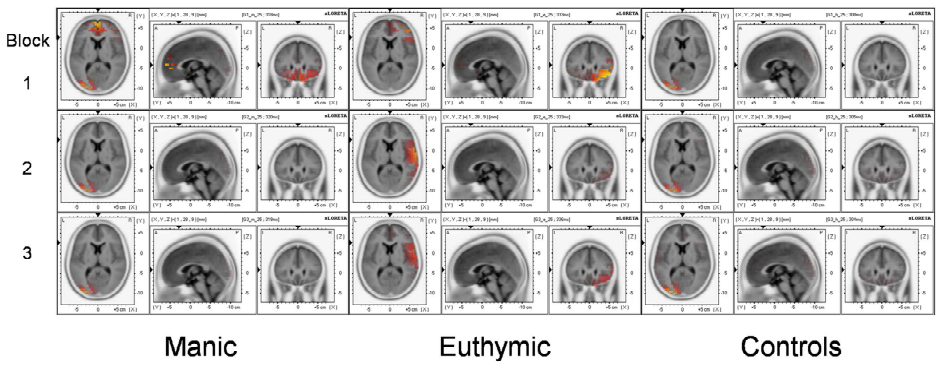

Figure 4. Distribution map of feedback-related negativity among groups

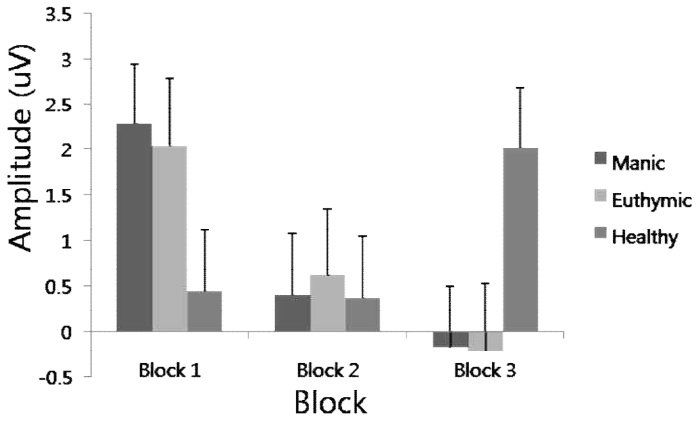

Figure 5. Feedback-related negativity as a function of blocks

3. Multiple regressions

The results of the multiple regression analysis of the association between response bias, feedback-related negativity and clinical variables including YMRS, MADRS, STAI, BDI, and SHAPs in the manic group were shown in Table 3. FRN amplitude was significantly associated with the YMRS score in the manic group, but not with other clinical factors.

Table 3. Multiple regression of clinical variables of response bias and feedback-related negativity

	ΔRB			ΔFRN		
	Coefficient	Std. Error	p	Coefficient	Std. Error	p
YMRS	0.005	0.004	0.153	-0.238	0.081	0.009
MADRS	-0.001	0.011	0.966	0.219	0.244	0.382
BDI	0.026	0.016	0.122	0.151	0.358	0.677
STAI_s	-0.005	0.006	0.496	-0.213	0.146	0.162
STAI_t	0.007	0.008	0.398	-0.101	0.189	0.600
SHAPS	0.009	0.007	0.224	0.045	0.167	0.792

ΔRB = (Response bias of Block 3 – Response bias of Block 1), ΔFRN = (Amplitude of feedback-related negativity of Block 3 – Amplitude of feedback-related negativity of Block 1), $p<0.05$, YMRS: Young's Mania Rating Scale, MADRS: Montgomery-Åsberg Depression Rating Scale, Spielberger's State-Trait Anxiety Inventory, SHAPS: Snaith-Hamilton Pleasure Scale

IV. DISCUSSIONS

This study was aimed to investigate the characteristics of manic and euthymic bipolar patients using the probabilistic reward task. I found that the response bias was reduced and FRN was more increased in both patient groups and FRN compared to healthy controls in the first block of the task, while the discriminability, response time and hit rate were not different among groups, in which the task difficulty were not perceived as different to each groups. This result may suggest that bipolar patients have impairments in reward learning, in

which they have trouble in integrating the repetitive reinforcement pattern of the task, and related reward processing abnormalities even in the euthymic phase. To our knowledge, this is the first study to examine the probabilistic reward learning in manic patients compared with controls and euthymic patients using the probabilistic reward task and to measure the associated event-related potentials.

The main finding of this study was that the RB and FRN were significantly different to controls in block 1. Manic and euthymic patients showed reduced RB in block 1 while RB in block 3 was not different in block 3. Healthy controls tend to achieve similar RB even in block 1. These results were consistent with the previous finding on euthymic patients using the probabilistic reward task, in which the response bias was delayed in the early phase of the task but became similar to healthy controls over time.[18] The main effect of block is observed in RB analysis, but not in the discriminability, hit rate, or reaction time. Depressive patients are reported to show failures in achieving reinforcement learning after completing tasks.[43] However, manic and euthymic patients might achieve reward learning despite the delayed acquisition of reward learning in the early phase of the task. Previous reports using a probabilistic reward task showed larger amplitudes of FRN in non-learners compared to learners during the later phase of task in normal populations.[13] FRN was enhanced while trying to find the proper strategy in non-learners and this neural activity reflects the maintained or enhanced reward sensitivity in the

late phase of the task. [44, 45] Reduced FRN have been reported in some psychiatric diseases characterized by impulsivity or risk-taking such as alcohol dependence, substance abuse, attention-deficit hyperactivity disorder, and pathological gambling.[46-49]

FRN amplitude is known to be positively correlated with anterior cingulate activity and both are correlated with reward learning.[24] Anterior cingulate activity is assumed to reflect dopamine signal conveyed by the basal ganglia in reward related modulation to implement goal-directed behaviors.[24] However, a comparison study between learners and non-learner in normal populations reported that FRN amplitude are positively correlated with anterior cingulate activity in non-learners.[13] The hypothesis suggests that anterior cingulate is inhibited by dopaminergic signal from basal ganglia.[24] When negative feedback is presented, the dopaminergic signal decrease disinhibit the anterior cingulate activity, and larger (more negative) FRN amplitude will be made.[25] Conversely, positive feedback helps to yield smaller (relatively positive or absent) FRN amplitude.[25] In the study mentioned above for learners and non-learners, learners showed greater anterior cingulate activity along with positive FRN amplitude.[13] Posterior cingulate activity was enhanced in non-learners, in which posterior cingulate is connected with the reward-related brain areas including the anterior cingulate, medial prefrontal cortex and caudate nucleus.[13, 50] Relative activation of the posterior cingulate in non-learner may be possibly explained by dysfunctional reward learning. Moreover, posterior cingulate

activity has been noted in response to reward in rodents, monkeys, and humans.[51-54]

Normally, response bias emerges to rich rewarded stimuli when reward frequency to each two correct decision is different.[33] Positive reinforcement may play a role in activating internal system about reward learning to mediate the external stimuli and in reinforcing the reward related behaviors.[55] Several previous studies measuring the response bias reported bipolar patients to show deficient reward learning and processing.[56, 57] That is, risk-taking tendency in bipolar disorder may disturb acquirement of the proper strategy. As a result, patients are dysfunctional in choosing the proper options. However, we should be cautious in interpreting the delayed acquisition of the response bias in the both patient groups due to the different reward frequency. Each patient group may not be identical in reward learning because impulsivity and decision-making of the patients change according to the mood status.[7, 58-60] Studies about more specified reward frequency (2:1 or 4:1) and use of punishment or the negative feedback as well as positive reinforcement will be helpful in understanding the process of reward learning.

Disturbances of anterior cingulate regions have been reported in some imaging studies. This region is activated during task performances requiring attentional controls and selection for action[61] and also contributes to error monitoring.[62] Overactivation of the dorsal anterior cingulate cortex was found to be significant in manic patients in a PET study.[8] Relapsed manic patients

showed a relative increase in perfusion in the superior cingulate cortex compared to stable remitted patients.[63] Positivity of the FRN correlated with the behavioral approach and learning from the positive reinforcement.[18] Our result of increased positivity in each patient groups may reflect delayed reinforcement learning of manic and euthymic patients compared to healthy controls.

I also investigated the multiple regression of RB, FRN and clinical variables. A previous study of euthymic patients reported that anhedonic level was negatively correlated with response bias.[18] In this study, I could only find that the symptom severity was dedicated to FRN amplitude negatively in block 1. But I could not observe the regression of RB, FRN and pleasure and anxiety level.

This study has several limitations. First, although our study recruited more participant than previous study using the probabilistic reward task, small sample size may hinder the generalization of this result to most of the bipolar patients. Second, because all patients were medicated, I could not rule out possible medication effects. However, I thought that medication effects could be minimized because discriminability and response time were not different comparing both patients groups and the control group were compared. The chlorpromazine equivalent dose was not correlated with RB (p value: 0.66 ~ 084) and FRN (0.21 ~ 0.87). And Lithium using and divalproex using group were also not different in RB (p value: 0.49 ~ 0.76) and FRN (p value: 0.41 ~ 0.87). Third, I used the probabilistic reward task which is not standardized to

the Korean population. I tried to apply this task to participants with the original diagram, and the translation of the instructions was enough to deliver the exact study objectives.

V. CONCLUSIONS

I investigate the characteristic reward learning of euthymic and manic bipolar patients, and the results indicated reduced reward learning behaviorally and electrophysiologically. This result may suggest abnormal reward learning in manic and euthymic patients with bipolar disorder.

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< ABSTRACT(IN KOREAN)>

양극성장애의 보상학습이상: 사건유발전위 연구

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유 빈

양극성장애 환자는 고위험 행동, 목적 지향적 활동의 증가, 과잉 행동 등의 행동상의 변화를 흔히 보이며, 이는 조증기에 두드러지게 관찰된다. 이러한 양극성장애 환자의 행동 특성에 대한 설명으로 보상 학습의 이상과 관련된 보상 자극의 처리의 이상이 제시되고 있다. 양극성장애 환자의 보상 학습과 관련된 이상은 꾸준히 보고되고 있으며, 이는 안정기에도 관찰되고 있다. 본 연구에서는 안정기와 함께 조증기의 양극성장애 환자들을 대상으로 하여 보상학습과 관련된 확률론적 보상과제를 수행하게 하여 행동상의 변화와 함께 관련된 사건유발전위의 변화도 관찰하고자 하였다.

본 연구에서는 24 명의 조증, 20 명의 안정기 환자들이 실험에 참여하였다. 또한 24 명의 기분장애는 물론, 다른 정신과적 질환의 과거력이나 가족력이 없는 정상인이 참여하였다. 참여자들은 선택에 따른 보상 확률이 다른 과제인 확률론적 보상과제를 수행하였으며, 이와 함께 64 채널의 증폭기를 이용하여 뇌파를 측정하였다. 확률론적 보상과제는 정반응에 대한 보상 확률을 3:1 로 차이를 두어 피험자의 반응이 보상확률이 높은 쪽으로 편향성을 유도하는 과제로 알려져 있다. 이 과제는 한 블록당 100 의 시행으로 구성되어 있으며, 총 세 블록을 시행하여 보상학습을 관찰할 수 있도록 이루어져 있다.

본 연구의 결과, 안정기 양극성장애 환자는 물론 조증기 양극성장애 환자에서도 첫번째 블록에서의 반응 편향이 낮아져 있으며, 이후 블록에서는 대조군과 차이를 보이지 않아 두 환자군의 보상 학습이 지연되어 있는 결과를 관찰할 수 있었다. ($F = 6.21$, $p = 0.005$) 또한, 두 환자군 모두에서 첫번째 블록에서 보상관련음전위의 감소가 관찰되었으며 그 변화는 행동 결과와 같은 변화 양상이었다. 상관 분석의 결과, 영조증척도로 측정한 조증 증상의 심각도와 반응편향은 양적 상관 관계를 ($p = 0.05$), 보상관련음전위의 전압과는 부적 상관 관계를 보였다 ($p = 0.001$).

결론적으로 이러한 결과는 안정기는 물론, 조증기 양극성장애 환자의 보상 학습의 이상과 함께 전기생리학적인 변화를 시사한다. 양극성장애 환자에서의 이러한 변화는 고위험 행동 등의 행동 변화와 관련된 보상 처리 과정의 이상에 대한 전기생리학적 근거로 생각할 수 있다.

핵심되는 말 : 확률론적 보상 과제, 반응 편향, 보상 학습, 양극성장애, 보상관련음전위