

Attentional Bias in Remitted Depressed Patients: Evidence from an Eye-Tracking Study

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Abstract

Objectives: To investigate the attentional bias characteristics of remitted depressed (RD) patients toward both happy and sad facial expressions.

Methods: Eye-movement data for the free-viewing facial expressions information of two groups (RD patients and healthy control (HC)) were acquired using the eye-tracking technique. The RD patients' initial attentional orientation toward different pieces of emotional information and their attentional bias related to the attention-maintenance components were analyzed.

Results: (1) On the initial orienting indicators (direction of initial gaze and initial fixation latency) and the initial attention maintenance indicators (first fixation duration), the RD patients showed no attentional bias toward the emotional faces; (2) For the late-stage attention maintenance indicators (total fixation time), both the RD group and the HC group exhibited attentional bias toward happy faces; the bias was smaller in the RD group than in the HC group; (3) For the RD group, there was a positive correlation between the direction of the initial gaze toward happy faces and total fixation time and a negative correlation between the initial fixation latency toward happy faces and total fixation time, whereas there were no such correlations in the HC group.

Conclusions: The RD group displayed an attentional bias trend for happy faces, and this increase in the positive bias reflected the RD patients' subjective, active efforts to establish a "protective bias" that would both alleviate and improve depressive symptoms.

Keywords: Remitted depression; Emotional faces; Attentional bias; Eye tracking

Introduction

Attention is the basis of all cognitive activities. Accordingly, the attentional function of depression patients has been extensively studied. Numerous studies have indicated that depression patients exhibit attentional bias toward negative information when processing emotional information [1], which plays an important role in the occurrence and maintenance of depression. Many studies have primarily focused on depression patients' negative attentional bias, whereas studies on the absence of positive information bias are lacking. Some investigations have found that in addition to their excessive attentional processing toward negative emotions, depression patients also exhibit the loss of positive information bias [2], leading to insufficient experience with positive emotions and the absence of the "protective bias." The "protective bias" is the typical attentional bias characteristics that are present in healthy individuals and that enable those individuals both to avoid paying attention to negative information and to be more inclined to pay attention to happy or neutral information [3,4]. The loss of the "protective bias" resulted in reduced sensitivity to reward and rendered the reward stimuli unable to capture attention successfully [5]. Therefore, the lack of positive emotions in depression patients in turn promoted declined attention to positive stimulations [6], further aggravating the loss of happy feelings.

These studies have shown that depression patients' attentional bias toward negative stimuli leads to over-processing of negative

information, whereas their attentional avoidance toward positive information leads to under-processing of positive information. Under these circumstances, the protective bias (biased toward positive information and avoiding negative information) that is present in mentally healthy individuals is absent in patients with depression, leading to deficient positive emotional experiences and excessive negative emotional experiences, the combination of which sustains and develops depression. This phenomenon also suggests that depressed mood in depression patients is caused not only by the biased attention toward negative information but also by the loss of happiness induced by the absence of attentional bias toward positive information.

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Numerous studies have shown that individuals with dysphoria had attentional bias toward threatening stimuli in both early and late attentional stages [5], whereas depressed patients' attentional bias toward negative information only appeared in either the late attentional stage or the attention-maintenance stage. For example, in the emotional Stroop color-naming task, depression patients were found to have a significantly elongated reaction time to the intervention of negative words only when the stimulus rendering time was over 1000 ms [7,8]. In the dot-probes detecting tasks, when the stimulus rendering time was 500 ms, the negative attentional bias was not observed in the depression patients, and when the stimulus rendering time was 1000 ms, the patients showed attentional bias toward the negative stimuli of sad faces [9,10], indicating both that the depressed individuals spent more time viewing negative images than the healthy people and that the negative attentional bias occurred in the late attentional stage [11]. Studies based on eye tracking [1,12] showed that when the fixation on negative information was significantly elongated, it was difficult to remove the attention, indicating that attention to negative information had a maintenance tendency.

For initial gaze direction and initial orienting speed, most of the existing investigations have shown that the initial gaze of patients with depression did not have a biased direction toward negative information. For example, it was found that depression patients' orienting speed toward negative information was not significantly different from that of the control group [13]. Other studies based on eye tracking also found that depression patients' initial gaze direction toward negative information showed no bias [12,14].

Studies of depression patients' attentional bias toward positive information demonstrated that they either showed deficiency or lacked an attentional bias toward positive information. Relative to the healthy control group, the depressed group showed a shorter fixation toward positive stimuli and insufficient maintenance of positive attentional bias, leading to the patients' loss of positive emotions [2,6,15]. With respect to initial attention orientation, the low level of positive emotions caused reduced sensitivity toward reward stimuli in the exogenous system and thus led to the defect in orientated positive stimulation [15], resulting in the reduced speed of the patients' orientation toward positive stimuli [5].

As an important stage of depression recovery, remission has recently attracted increasing attention. That notwithstanding, the conclusions drawn from various studies of RD patients' attentional bias have been inconsistent. Hedlund has found that in the emotional Stroop tasks, patients experiencing depressive episodes took a longer time naming negative words and demonstrated a negative attentional bias; however, when the patients fully recovered, the negative attentional bias disappeared [16]. Wenzlaff et al. have reported that relative to negative words, both RD and non-depressed individuals both identified more positive words [17]. Linda Isaac et al. have performed an eye-tracking experiment, finding that RD patients' positive attentional bias had been successfully alleviated, thus attaining the same level as that of healthy individuals [18].

However, some studies have shown that the damage in depression patients' attention function lingered for a long time even after depressive symptoms were alleviated or recovered [19,20]. For example, a dot-probes-detecting task study has shown that RD patients and depression patients both displayed attentional bias toward sad faces and did not exhibit positive attentional bias when the stimulus rendering time was 1000 ms [21]. Behavioral and neuroimaging studies have also revealed that even after depression patients' clinical symptoms alleviated, their

negative attentional bias persisted [22], a result that is supported by other studies that have employed event-related potentials and functional magnetic resonance imaging technology [23-25]. Moreover, Sears has demonstrated that RD individuals exhibited initial directional bias in their attention toward negative information [26].

From the perspective of attentional bias for emotions, there are two indicators of whether depression patients' symptoms are eased: one is negative attentional bias and the other is positive attentional bias. From the studies on attentional bias of healthy individuals and patients in depressive episodes, it was generally believed that healthy individuals had positive attentional bias and attentional avoidance to negative information; conversely, depression patients had negative attentional bias and attentional deficiency with respect to positive information. Thus, if depression patients' symptoms are effectively alleviated, their attentional bias should be similar to that of healthy individuals, i.e., negative attention bias is weakened or disappears and positive attention bias is enhanced. Although the alleviation of negative attentional bias in RD patients has been extensively investigated, the issue of positive attentional bias has rarely been addressed; therefore, it is necessary to investigate RD patients' attentional dysfunction, particularly with respect to their attentional bias.

In this study, which is based on previous studies, pictures of emotional facial expressions and free-viewing tasks were used to investigate RD patients' attentional bias, including the attentional components of both initial gaze orienting and attentional maintenance. The reason for the use of facial expressions as stimuli was as follows: facial expressions contained more interpersonal communication information, were more inductive to individuals' participation, and were more revealing of attentional bias than were emotional words and scene images [27]. However, it is notable that negative facial expressions include sadness, surprise, anger, etc.; it was found that depression-related sad faces could well induce negative attentional bias in depression patients [1,28], whereas the threat stimuli associated with dysphoria could not induce the attentional bias in depression patients [5,29]. Therefore, depression-related sad faces were chosen in this study as the stimuli to detect the negative attentional bias of RD patients, and happy faces were chosen to detect those patients' positive attentional bias.

Early cognitive behavioral studies of attentional bias primarily used the reaction-time technique. As indicated in a review [5], this technique could only assess attentional bias indirectly and implicitly; it could neither adequately describe the time course in real time nor distinguish the components of the attentional bias (orienting attention and attention maintenance). Considering the limitations of the reaction-time technique, an increasing number of investigators have chosen to use the eye-tracking technique, which provides a relatively continuous method of directly measuring attentional bias.

Current studies of attentional bias that are based on the eye-tracking technique primarily use the free-viewing tasks, in which the task matrix contains 2-4 stimuli with the task rendering time varying in the range of 10-30s [5]. The free-viewing tasks can not only monitor the subjects' attentional process more naturally but also more accurately observe and analyze the bias characteristics of each of the attentional components. To simultaneously determine the two components of RD patients' attentional bias, this study adopted the measurements of initial gaze orienting and attention maintenance used in previous studies. Briefly, a 2×2 facial expression matrix was designed, and each matrix included one emotional face and three neutral faces. The attentional bias generated by the 2×2 facial expression matrix is likely more

reliable than that generated by the 1 × 1 paired task (one emotional face and one neutral face). First-fixation location and first-fixation latency duration were used to determine the element of the initial orientation of attention, whereas first-fixation duration and total fixation time were used to determine the elements of attention maintenance [1,12].

Methods

Subjects

Twenty-seven unipolar depression patients (8 males and 19 females) with successfully remitted depressive symptoms in the RD group were recommended by doctors at Beijing Anding Hospital, Capital Medical University. They were 22-65 years of age, right-handed, had normal verbal communication and normal vision (or corrected-to-normal vision), and were able to perform the eye-tracking experiment. The patients were assessed by Hamilton Depression Rating Scale (HAMD-17) ≤ 7 and Beck Depression Inventory (BDI) ≤ 10.

Twenty-seven subjects (eight males and 19 females) in the HC group were recruited through advertisement. They were 18-65 years of age with education levels matching those in the RD group and with BDI ≤ 4. These control subjects did not have a past or present history of depression or other mental illness at present; they had no first-degree relatives with a history of severe mental disease or nerve system illness; and they were right-handed, had normal or corrected-to-normal vision, lacked color blindness or other eye diseases, and were capable of completing the eye-tracking test.

All of the subjects signed written informed consent and were remunerated after the test was completed.

Materials and experimental procedure

Both of the groups were subjected to identical experimental stimuli, including 20 images representing happy, neutral and sad facial expressions from the NimStim set of facial expressions [30]. To enable consistency in all of the facial expression images, Picture Manager

software was used both to formalize the images and to render uniform their size, grayscale, and resolution.

The free-viewing tasks method was used; the tasks included viewing tasks on two types of facial expressions: happy and sad faces. Each type of task consisted of four images of facial expressions and in each task, four images were rendered at four different quadrant positions (upper left, upper right, lower left and lower right), as shown in the example in Figure 1.

To minimize the impact of non-facial expression factors, each stimulus task used images of different facial expressions (three neutral and one happy, or three neutral and one sad) made by the same person. The reason for not using paired images (one neutral face and one emotional face) was that the pair-images method tends to be more appropriate for investigating initial attentional orienting. To reduce the position effect, the number of happy or sad faces appearing at various positions was balanced.

The fixation point on the screen could directly affect initial attentional orienting prior to the free-viewing tasks. Accordingly, before the task, a white "+" sign appeared first in the center of the black screen for 1000 ms, and the subject was asked to indicate when the color of the "+" sign changed (to ensure that his or her fixation point was at the center of the screen) [1,31]. Next, four images were simultaneously rendered in the four quadrants for a duration of 10000 ms [18] and followed by the "*" sign to indicate a rest period of 2000 ms, after which the next trial proceeded. The stimulus tasks were rendered pseudo-randomly. During the test, the Tobii T120 eye tracker was used to simultaneously acquire and record eye-movement data for the subject viewing the stimulus tasks.

Statistical analysis

Eye-movement indicators: Four indicators were extracted from the eye-movement data acquired with the eye-tracking device

1. Direction of initial gaze (i.e., location of the first fixation): the location of the first fixation on each stimulus task.
2. First-fixation latency: the time used by the subject from the



start of the stimulus task rendering to the first fixation at the interest area in each stimulus task.

3. First-fixation duration: the maintenance period of the subject's initial fixation in each stimulus task.
4. Total fixation time: the total time the subject gazed at a certain interest area in each stimulus task.

Calculation method of bias score: In relation to the absolute indicators, the relative bias score is likely more reflective of depression-associated emotional bias [4]. In terms of initial gaze direction, the subject's first fixation on happy and sad face stimuli compared to neutral face stimuli was calculated; higher than 25% indicated the existence of attentional bias toward emotional faces, whereas lower than 25% indicated the existence of attentional bias toward neutral faces [1]. In calculating the first-fixation latency, first-fixation duration and total fixation time, each stimulus's bias score was the value obtained from the emotional faces, which were determined using the average of the values obtained from the three neutral faces. The scoring indicators were based on the differences that had been used in the previous studies [1,32]. For first-fixation latency, a bias score of greater than 0 indicated the absence of attentional bias toward emotional faces and a score of less than 0 indicated the presence of attentional bias for emotional faces. For first-fixation duration and total fixation time, a bias score of greater than 0 indicated the presence of attentional bias for emotional faces and a score of less than 0 indicated the absence of attentional bias toward emotional faces.

Results

Demographics and clinical data

As shown in Table 1, compared with the control group, the RD patients group showed no significant differences in age ($t(52)=0.033$, $p=0.974$), sex ratio ($\chi^2(1, 54)=0.000$, $p=1.000$) and education level ($t(52)=0.118$, $p=0.906$).

Attentional bias analysis of emotional information

Initial gaze direction:

Analysis of attentional bias: The indicator for the initial gaze direction was the first fixation location. The scores of the two groups' initial gaze direction are shown in Figure 2. The comparison results with the no-bias score value of 25% are shown in Table 2. The RD group's bias scores for the happy and sad faces were not significantly different from the no-bias value of 25%; this result was the same for the HC group's bias scores for the happy faces, but that group's bias scores for the sad faces was significantly lower than the no-bias value of 25%. These results indicate that the RD group had no bias in their initial gaze direction for emotional faces, and the HC group showed an avoidance bias toward sad faces.

A comparative analysis of the two groups: A 2 (group: RD, HC) \times 2 (emotional types: Happy, Sad) two-factor, mixed-model analysis of variance (ANOVA) was performed to investigate the difference in the initial fixation location when the subjects gazed upon faces that showed different emotions. It was found that no significant interaction of group \times type of emotion was observed ($F(1, 52)=0.640$, $p=0.427$, $\eta^2=0.012$). The main effect between the groups was not significant ($F(1, 52)=0.132$, $p=0.718$, $\eta^2=0.003$), indicating no significant difference between the two groups with respect to the initial gaze direction toward the facial expressions. The main effect between the types of emotion was significant ($F(1, 52)=7.840$, $p=0.007$, $\eta^2=0.131$); the subjects' initial gaze direction toward happy faces was significantly greater than that toward sad faces.

To understand which group caused the differences in gaze direction for each type of emotion displayed, an intra-group paired t test was performed; the result is shown in Figure 2. With respect to the difference between the happy and sad faces, subjects in the HC group showed a significant difference ($t(26)=3.122$, $p=0.004$, $d=0.716$), whereas those in the RD group showed no significant difference ($t(26)=1.224$, $p=0.232$, $d=0.352$), indicating that the RD group exhibited no bias in the initial gaze direction toward emotional faces.

First-fixation latency:

Analysis of attentional bias: First-fixation latency reflects the orienting speed of the first fixation. The bias scores for the two groups' first-fixation latency toward two facial expressions are shown in Figure 3. The comparison results with the no-bias value of 0 are shown in Table 3. The bias scores of the RD group related to happy and sad faces had no significant difference from the no-bias value of 0. The bias score of the HC group related to happy faces was significantly lower than the no-bias value of 0, whereas the score related to sad faces was significantly higher than the no-bias value of 0.

Analysis shows that in terms of initial orienting speed, the RD group showed no bias toward the emotional faces, whereas the HC

	RD (n = 27)	HC (n = 27)	p-value
Gender (M:F)	08:19	08:19	1
Age(years)	49.37 \pm 12.39	49.26 \pm 12.49	0.974
Educational level (years)	12.04 \pm 3.50	11.93 \pm 3.40	0.906

RD: Remitted Depressed; HC: Healthy Control; M: mean; SD: standard deviation.

Table 1: Comparison of the demographic differences between the two groups (M \pm SD).

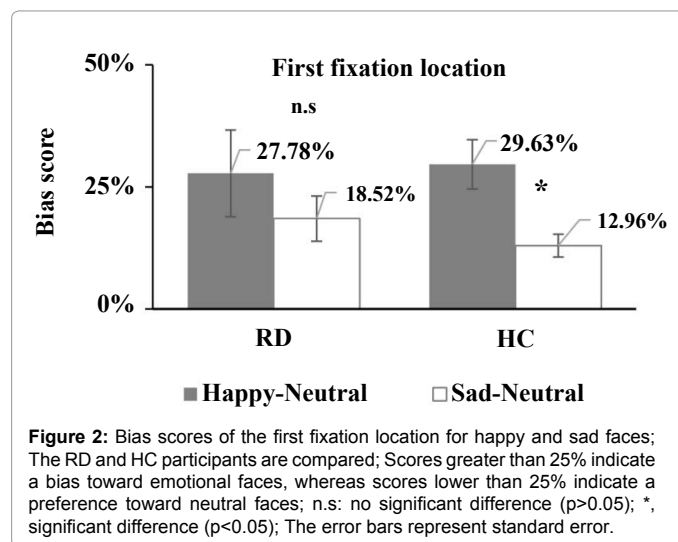


Figure 2: Bias scores of the first fixation location for happy and sad faces; The RD and HC participants are compared; Scores greater than 25% indicate a bias toward emotional faces, whereas scores lower than 25% indicate a preference toward neutral faces; n.s: no significant difference ($p>0.05$); *, significant difference ($p<0.05$); The error bars represent standard error.

Groups	Bias	t (26)	p-value	Effect Size (d)	
RD	Happy	0.5	0.621	0.962	N
	Sad	-1.369	0.183	0.008	N
HC	Happy	0.961	0.345	1.183	N
	Sad	-2.801	0.009	0.58	N*

N denotes no bias for emotional faces, and * denotes the bias for neutral faces.

Table 2: Bias scores for initial gaze direction and their comparison with the no-bias value of 25%.

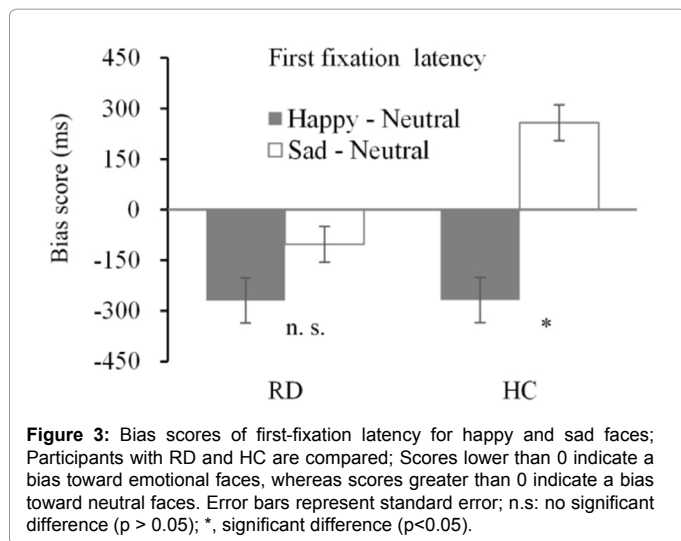


Figure 3: Bias scores of first-fixation latency for happy and sad faces; Participants with RD and HC are compared; Scores lower than 0 indicate a bias toward emotional faces, whereas scores greater than 0 indicate a bias toward neutral faces. Error bars represent standard error; n.s: no significant difference ($p > 0.05$); *, significant difference ($p < 0.05$).

Groups	Bias	t (26)	p-value	Effect Size (d)	
RD	Happy	-1.754	0.091	0.338	N
	Sad	-1.017	0.319	0.196	N
HC	Happy	-3.431	0.002	0.66	Y
	Sad	2.378	0.025	0.458	N*

N/Y denotes no bias/bias toward emotional faces, and * denotes bias toward neutral faces.

Table 3: Bias scores of first-fixation latency and their comparison with the no-bias value of 0.

group displayed expedited bias toward happy faces and slowed bias toward sad faces.

Comparative analysis between the two groups: The 2 (group: RD, HC) \times 2 (emotional types: Happy, Sad) two-factor mixed-model ANOVA showed that no significant interaction group \times type of emotion was observed ($F(1, 52)=2.671, p=0.108, \eta^2=0.049$), and the main effect between the groups was not significant either ($F(1, 52)=2.382, p=0.129, \eta^2=0.044$), indicating that there was no significant inter-group difference in the first-fixation latency for different emotion types. The main effect between the types of emotion was significant ($F(1, 52)=9.950, p=0.003, \eta^2=0.161$), indicating that the orienting speed of the two groups was significantly faster toward happy faces than toward sad faces.

To understand which group caused the difference in the emotion types, further intra-group analysis showed that the orienting speed toward happy faces by the subjects in the HC group was significantly faster than in the RD group ($t(26)=-3.988, p=0.000, d=1.091$), whereas the difference in the orienting speed between the two groups was insignificant ($t(26)=-0.950, p=0.351, d=0.252$).

It can be concluded that the RD group showed no attentional bias in the initial orienting speed toward emotional faces.

First-fixation duration:

Analysis of attentional bias: First-fixation duration reflects the attention maintenance time of the first fixation. The bias scores of

the two groups' first-fixation duration on two facial expressions are shown in Figure 4. The comparison results with the no-bias value of 0 are shown in Table 4. The bias scores of the two groups' first-fixation duration on happy faces and sad faces exhibited no significant difference from the no-bias value of 0.

The analysis shows that with respect to first-fixation duration, both the RD group and the HC group showed no attentional bias toward the emotional faces.

A comparative analysis of the two groups: The 2 (group: RD, HC) \times 2 (emotional types: Happy, Sad) two-factor, mixed-model ANOVA showed that no significant interaction of group \times type of emotion was observed ($F(1, 52)=0.884, p=0.351, \eta^2=0.017$), and the main effect between the groups was not significant ($F(1, 52)=0.342, p=0.561, \eta^2=0.007$), indicating that there was no significant inter-group difference in the first-fixation duration for different types of emotion. The main effect between the types of emotion was not significant ($F(1, 52)=0.914, p=0.334, \eta^2=0.017$), indicating that the effect of different emotional faces on the two groups' first-fixation duration was identical. It can be concluded that there was no bias in either group's initial attention maintenance.

Total fixation time:

Analysis of attentional bias: Total fixation time reflects the total duration of attentional processing. The bias scores of the two groups' total fixation time toward the emotional faces are shown in Figure

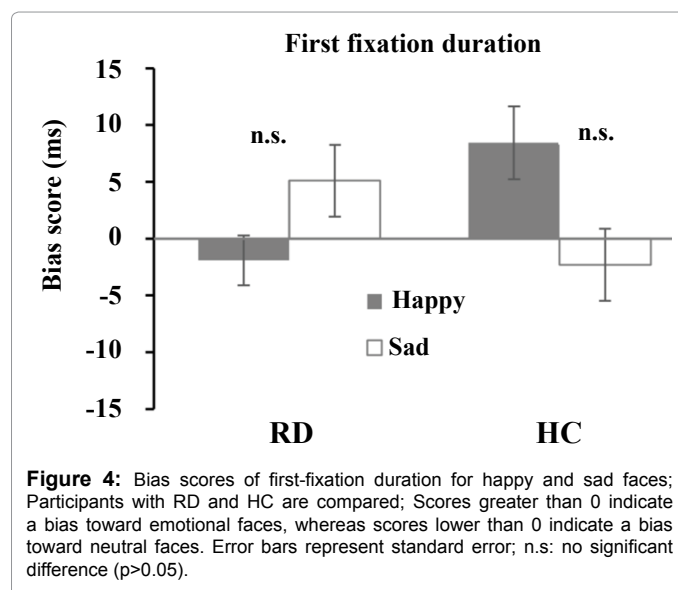


Figure 4: Bias scores of first-fixation duration for happy and sad faces; Participants with RD and HC are compared; Scores greater than 0 indicate a bias toward emotional faces, whereas scores lower than 0 indicate a bias toward neutral faces. Error bars represent standard error; n.s: no significant difference ($p > 0.05$).

Groups	Bias	t (26)	p-value	Effect Size (d)	
RD	Happy	-1.212	0.272	0.216	N
	Sad	-0.624	0.538	0.12	N
HC	Happy	0.967	0.343	0.19	N
	Sad	0.703	0.448	0.14	N

N denotes no bias toward emotional faces.

Table 4: The bias scores of first-fixation duration and their comparison with the no-bias value of 0.

5. The comparison results with the no-bias value of 0 are shown in Table 5. The bias scores of the two groups' total fixation time toward happy faces exhibited significant differences from the no-bias value of 0, whereas the two groups' bias scores for the sad faces showed insignificant differences from the no-bias value of 0.

The analysis result shows that with respect to the total duration of attentional processing, both groups showed attentional bias toward happy faces but no bias toward sad faces.

Comparative analysis between the two groups: The 2 (group: RD, HC) × 2 (emotional types: Happy, Sad) two-factor, mixed-model ANOVA showed that a significant interaction of group × type of emotion was observed ($F(1, 52)=6.005, p=0.018, \eta^2=0.104$), and the main effect between the groups was not significant ($F(1, 52)=1.583, p=0.214, \eta^2=0.030$) and that the difference between the types of emotion was significant ($F(1, 52)=16.248, p=0.000, \eta^2=0.238$), indicating that the subjects showed a bias toward happy faces.

To understand which group caused the bias toward happy faces, further intra-group analysis showed that the bias score of the HC group toward happy faces was significantly higher than the bias score toward sad faces ($t(26)=3.501, p=0.001, d=1.063$) and that the bias score in the RD group toward happy faces was also higher than that toward sad faces, reaching the threshold level ($0.05 < p < 0.10$), $t(26)=1.857, p=0.075, d=0.298$, although the differences were insignificant ($p < 0.05$).

Because of the presence of interaction between the group and the

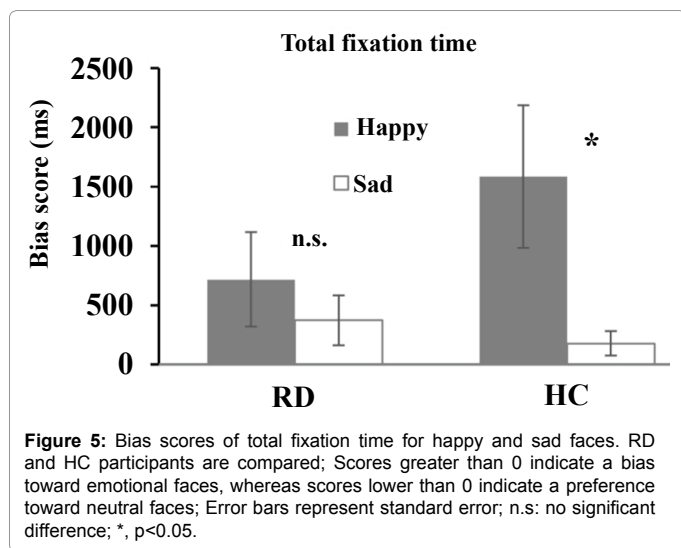


Figure 5: Bias scores of total fixation time for happy and sad faces. RD and HC participants are compared; Scores greater than 0 indicate a bias toward emotional faces, whereas scores lower than 0 indicate a preference toward neutral faces; Error bars represent standard error; n.s.: no significant difference; *, $p < 0.05$.

Groups	Bias	t (26)	p-value	Effect Size (d)	
RD	Happy	3.836	0.001	0.738	Y
	Sad	1.499	0.159	0.279	N
HC	Happy	4.797	0	0.923	Y
	Sad	1.108	0.278	0.213	N

N/Y denotes no bias/bias toward emotional faces.

Table 5: The bias scores of total fixation time and their comparison with the no-bias value of 0.

emotional type, the inter-group difference was analyzed. With respect to the bias toward happy faces, the RD group was significantly less than the HC group ($t(52)=-2.286, p=0.026, d=0.634$), indicating that the RD group's attentional bias for happy faces was less than that of the HC group. With respect to the bias toward sad faces, there was no significant difference between the two groups ($t(52)=0.646, p=0.521, d=0.179$), indicating that the negative attentional bias in the RD group was eased, reaching the normal level.

In terms of total fixation time, the RD group showed the attentional bias toward happy faces but still did not reach the level of the HC group.

A correlation analysis of the attention bias of each indicator

To investigate whether there was a relationship between initial attentional orientation and attentional processing time for the emotional faces; a Pearson correlation analysis was conducted to analyze the correlations between the indicators. It was found that in the RD group, initial gaze direction was positively correlated ($r=0.383, p=0.049$) with total fixation time, indicating that the greater the attentional bias for happy faces in the RD group, the more time that group allowed for attentional processing. Furthermore, in the RD group, initial fixation latency showed a significantly negative correlation ($r=-0.387, P=0.046$) with total fixation time, indicating that the more quickly the RD patients gazed at happy faces, the longer they gazed. There were no correlations between the other indicators.

Overall, our analysis showed the following: (1) on the initial gaze direction indicator, regardless of whether that indicator is the initial gaze direction or the initial attentional orientation speed, the RD patients did not show attentional bias, but there was a positive correlation between the initial gaze direction for happy faces and the total fixation time and a negative correlation between the initial fixation latency for happy faces and the total fixation time; (2) for the attentional processing indicators (first-fixation duration and total fixation time), the RD group did not exhibit attentional bias in the initial attentional processing toward the emotional faces; for total fixation time, the RD group behaved the same as the HC group and showed more frequent and longer attentional processing toward happy faces; however, relative to the HC group, the RD group lagged behind and the difference between the biases toward happy faces and sad faces by the RD group itself was insignificant, indicating that the RD group only exhibited a tendency toward positive attentional bias.

Discussion

To investigate the characteristics of attentional bias toward the emotional faces in the RD patients versus the healthy control group, two task types were designed to study the RD patients' attentional processing mode, especially toward positive emotion information. To increase the reliability of the results, two measurements were chosen to examine the attentional orienting indicators and the attentional processing indicators: the bias analyses based on no-bias guideline and the comparison analyses based on the extent of either inter- or intra-group bias.

For the initial orienting indicators, both initial gaze direction (first-fixation position) and initial orienting speed (first-fixation latency) were examined.

For initial gaze direction, the results show that the RD group did not show attentional bias toward happy and sad faces, which is consistent with the results of previous eye-tracking-data studies on patients with depressive episodes. There was no difference in initial

gaze direction among the patients experiencing depressive episodes [5,12,18,33], indicating that neither the RD patients nor the depression patients showed bias in their initial gaze direction, which is likely a common feature of depression patients. However, some studies based on eye-tracking data revealed that the RD patients had bias in their initial gaze direction toward the depression-related image stimuli but no bias toward the positive image stimuli [26], which is inconsistent with this study's results. This inconsistent result is likely caused by the difference in the source and evaluation methods of the RD patients. The RD patients included in this study were found in a professional psychiatric hospital instead of on a campus, as in studies conducted by other investigators. Furthermore, our RD patients were evaluated by two psychiatrists. In addition, the gender difference might be the most direct reason for the discrepancy. Sears et al. have drawn conclusions based solely on female RD patients, whereas both male and female subjects were included in this study. In the future, gender differences in the attentional bias of RD patients should be further investigated.

For initial attentional orienting speed, relative to the HC group, the RD group was not found to have an attentional bias toward either happy faces or sad faces. Previous studies have shown that compared to the control group, depression patients exhibited slowed orienting speed toward positive stimuli [5], whereas their orienting speed toward negative stimuli was not necessarily faster [13]. It is notable that although the orienting speed bias toward happy faces was not observed in the RD group, the analysis using the no-bias guideline showed that compared with the no-bias value of 0, the bias score of the orienting speed toward happy faces reached the threshold level ($0.05 < p = 0.91 < 0.10$), indicating that the RD group had a faster orienting speed toward the positive stimuli. This result shows that to some extent, RD patients alleviated their slow orienting speed toward the positive stimuli. Moreover, the orienting speed bias toward negative information was not observed in the RD patients.

For maintenance indicators of attentional processing, first-fixation duration and total fixation time were examined in the RD group. With respect to first-fixation duration, no attentional bias was found toward the emotional faces in either group or toward either face, findings that are consistent with previous studies' conclusions that RD patients' attentional bias toward negative information occurred in the late stage of information processing [1,11].

For total fixation time, this study found that relative to the HC group, the RD group displayed insufficient attentional bias toward positive information. However, it is worth noting that the analysis based on the no-bias guideline showed that like the HC group, the RD group showed significant attentional bias toward happy faces. In conclusion, the RD patients' tendency toward positive attentional bias has been confirmed, which is essentially consistent with a recent study's conclusions that depression patients had attentional bias toward happy faces [18].

We also analyzed the correlations between the attentional indicators in the two groups, which have not been reported previously. Our results show that in the RD group, the initial gaze direction toward happy faces was positively correlated with total fixation time and the initial fixation latency toward happy faces was negatively correlated with total fixation time, which were all absent in the HC group. These results suggest that the RD patients might have more active attentional motivation for positive information. This active attentional motivation for positive information is likely because during the alleviation of depressive mood, RD patients more actively chose attentional processing toward positive information instead of negative information both to establish

a positive psychological cognitive schema and to destroy their negative psychological cognitive structures, proactively seeking to establish a "protective attentional bias".

Previous studies have shown that training related to the attentional bias toward positive stimuli should be conducted. Training and guidance could improve the attentional bias outcome toward positive stimuli [34]; however, the treatment effect was also associated with the severity of depression [35]. Through repeated training on avoiding depression-related stimuli while enhancing the individual's emotional state with positive information training [1], the patients could improve or adjust their mood in a positive manner to maintain the balance of positive emotion, as healthy individuals do [36].

Negative attentional bias and the deficiency in positive attentional bias have been confirmed as basic features in depression patients. However, whether RD patients have the negative attentional bias is still a matter of dispute. Some investigations have shown that negative attentional bias in RD patients lingered after the depression symptoms of the patients were eased [25], whereas other studies have shown that the RD group also generated attentional bias toward happy faces [18]. Still other studies have even revealed that the subjects with a history of depression showed a bias toward sad faces but no bias toward positive information [21].

The results of our study show that for attentional bias toward sad faces, the RD patients were not significantly different from the HC group either in the indicators of initial gaze orienting or in the indicator of total fixation time, indicating that the RD patients' attentional bias toward negative information disappeared with the alleviation of depressive symptoms.

It is likely that the discrepancy shown in the attentional bias studies on RD patients has been caused by the different degrees to which the patients' depression is alleviating. Mentally healthy individuals have a protective attentional bias, represented by strong attentional motivation toward positive information and weak attentional motivation toward negative information. However, depression patients have an attentional bias toward depression-related negative information and a deficiency in attentional bias toward positive information. On the attentional indicators, the alleviation of depressive symptoms is represented by the strengthening of positive attentional bias and the weakening of negative attentional bias. Therefore, during the alleviation of depression, the evaluation of the alleviation of the symptoms is based on the gap in the attentional bias toward positive information between RD patients and the healthy individuals, along with the gap in the negative attentional bias between RD patients and the healthy individuals. Thus, because RD patients are usually in different stages of remission, there are various possibilities, e.g., their positive attentional bias might or might not be significantly different from that of healthy individuals, or their negative attentional bias might or might not be significantly different from that of healthy individuals.

This study had certain limitations. Only a cross-sectional study was performed, which affected the effectiveness of our explanation of the causality of the attentional bias. That said, this type of cross-sectional investigation has been quite common [1,5,18]. In future studies, the vertical and horizontal investigations will be combined to better understand the characteristics of attentional bias in RD patients.

Conclusion

In conclusion, our study shows that although RD patients'

attentional bias continues to lag that of the mentally healthy population, it eased and improved, as shown by the near disappearance of negative attentional bias while displaying a tendency toward positive attentional bias. Our results are significant for improving the procedures and method for treating depression patients' clinical symptoms and for further alleviating RD patients' depressive symptoms.

Competing interests

The authors declare that they have no competing interests.

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