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Attentional bias scores in patients with depression and effects of age: a controlled, eye-tracking study

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Abstract

Objective: To compare the attentional bias of depressed patients and non-depressed control subjects and examine the effects of age using eye-tracking technology in a free-viewing set of tasks.

Methods: Patients with major depressive disorder (MDD) and non-depressed control subjects completed an eye-tracking task to assess attention of processing negative, positive and neutral facial expressions. In this cross-sectional study, the tasks were separated in two types (neutral versus happy faces and neutral versus sad faces) and assessed in two age groups ('young' [18–30 years] and 'middle-aged' [31–55 years]).

Results: Compared with non-depressed control subjects ($n = 75$), patients with MDD ($n = 90$) had a significant reduced positive attentional bias and enhanced negative attentional bias irrespective of age. The positive attentional bias in 'middle-aged' patients with MDD was significantly lower than in 'young' patients, although there was no difference between the two age groups in negative attentional bias.

Conclusions: These results confirm that there are emotional attentional biases in patients with MDD and that positive attentional biases are influenced by age.

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Introduction

Attentional bias for emotional stimuli has become recognised as a key mechanism of affective disorders and is an important factor in the persistence of depressive symptoms.[1] Although the aetiology and phenomenology of depression has been the focus of research into attentional bias,[2] experimental evidence of attentional bias in depressive patients is inconsistent.[3–13]

Some studies support a negative attentional bias in depressive patients. For example, using free-viewing tasks, one study found that compared with control subjects, depressed patients had a longer gaze on negative pictures and had difficulty relieving attention from negative stimuli.[3] Another study using visual search tasks also reported that patients with depression were more likely to pay attention to negative stimuli compared with control subjects.[4] A meta-analysis of 33 studies using eye-tracking research concluded that the attentional bias for negative stimuli in patients with depression was significantly higher than in non-depressed subjects.[5]

Using happy and sad faces as stimuli to investigate depressive disorders in hospitalized patients, researchers found that compared with never-depressed controls, patients with depression failed to inhibit negative information but positive material was not affected.[6] In one study where subjects were free to browse neutral and emotional images of the same face (i.e. happy, sad or angry), investigators showed that compared with never-depressed controls, patients with depression showed attentional bias to sad faces but not to angry faces.[7] These results indicated that patients with depression tended to look at the stimuli that were consistent with their mood and confirmed that they had significant negative attentional bias.

However, other studies using emotional faces have shown that compared with controls, depressed patients have a lack of attentional bias for positive stimuli.[8,9] A study of event-related evoked potentials found that patients with depression had less attention to positive information.[10] Another study using a free-viewing paradigm, reported that while currently depressed and remitted depressed participants paid attention to sad faces significantly more than never-depressed participants, only the depressed participants showed a significant lack of attentional bias to happy faces.[11] Nevertheless, although one study using a browsing paradigm to study the attentional bias of patients with depression showed that compared with controls patients with depression had an inadequate positive attentional bias,[5] another study using eye-tracking research did not find any significant attentional bias toward positive stimuli in patients with depression.[7] Moreover, some studies have failed to find any attentional biases in patients with depression.[12,13]

People of different ages will undoubtedly have differences in their psychological and physiological makeup that will lead to differences in emotional perception. For example, one study showed that with increasing age, the impact of negative emotions gradually decreased and that of positive emotions remained constant.[14] Another study found that older people were more likely to look at happy faces and avoid angry faces whereas younger people only showed a tendency towards afraid faces.[15] Studies have also found that with increasing age,

attention to negative expressions gradually decreases.[16,17] To date, research on the effect of age on emotional attention has tended to focus on healthy individuals and not on depressed individuals. Interestingly, one study compared the clinical treatment of depressed adults from different age groups and found that the dose of medication for middle-aged patients with depression is often larger than that for the young and the elderly.[18] This may indicate that depression in middle-aged depressed patients is more severe than in other age groups. Furthermore, antidepressant medications may increase positive emotional conditioning and reduce the negative emotional conditioning that may affect attention to different emotional images.[19,20]

The current study was designed to assess attentional bias in depressed patients and non-depressed subjects when presented with negative, positive, and neutral facial expressions in a free-viewing paradigm. Importantly, stimulation time is a crucial factor in any study of attentional bias. Studies have shown that in depressed patients, negative attentional biases are related to the time of stimulus and are not found with short presentation times (i.e. 500 ms) but are present with longer presentation times.[21–24] The presentation time chosen for this present study was 3000 ms.

We hypothesized that compared with non-depressed, control subjects, depressed patients would have an inadequate positive attentional bias and an enhanced negative attentional bias.[2] Our second hypothesis was that compared with controls, both 'young' and 'middle-aged' depressed patients would show inadequate positive attentional bias and enhanced negative attentional bias.[3] The third hypothesis was that compared with 'young' patients with depression, 'middle-aged' patients would have significant inadequate positive attentional bias and enhanced negative attentional bias.

Patients and methods

Study participants

For this cross-sectional study, all study participants were recruited from the Department of Automation, Faculty of Information Technology, Beijing University of Technology, and the Mood Disorders Centre & China Clinical Research Centre for Mental Disorders, Beijing Anding Hospital, Capital Medical University, Beijing, China. The control subjects (non-depressed) were recruited following advertisement. All prospective participants were screened by one of two psychiatrists (L.F & B.B.F) using the Mini-international neuropsychiatric interview based on Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) to identify cases of major depressive disorder (MDD).[25] The control subjects had never suffered with depression.

Inclusion criteria were as follows: (i) $\geq$18 years of age; (ii) right-handed; (iii) Patient Health Questionnaire (PHQ-9) score $>$5;[26] (iv) no drugs or alcohol in the previous 2 weeks; (v) normal or corrected to normal vision. Exclusion criteria included: (i) colour blindness; (ii) presence of concurrent eye disease; (iii) inability to complete the eye-tracking experiment; (iv) presence of an obstacle to facial expression recognition such as inability to have normal language exchange. All study participants provided signed informed consent and this study was approved by the Ethics Committee at Beijing Anding Hospital, Capital Medical University, Beijing, China (no. 2014065).

Experimental procedures

A set of images that included 12 happy faces (six males, six females), 12 sad faces (five males, seven females) and 24 neutral faces (11 males, 13 females) were selected from the NimStim Set of Facial Expressions image library.[27] All images were processed by

Photoshop software and the size, gradation and resolution were all consistent (i.e. image size 354 × 472 pixels; 8 × 6 cm). Stimuli consisted of pairs of images that included an emotional and a neutral facial expression made by the same person (Figure 1). There were two types of tasks separated into 12 neutral versus happy faces and 12 neutral versus sad faces and they appeared in random order. The positions of the two images in each task type were counterbalanced. The total task took 144 s to complete.

Eye-tracking information was collected using a Tobii T120 Eye Tracker (Tobii Pro, Stockholm, Sweden) with a sampling frequency of 120 Hz. The experimental stimuli were shown on a 17 in liquid crystal display monitor. Participants' eyes were kept at a distance of approximately 60 cm from the monitor and 60 cm from the eye tracker.

Practice trials preceded the main study to ensure the participants were familiar with the experimental procedures and the data were collected correctly. Each trial began with a white cross on a grey background presented as the prompt for 1 s in the centre of the screen and the participant was required to pay attention to the symbol and fixate on the cross. Afterwards, a pair of faces was displayed for 3 s and the participants were instructed to view them freely. A rest time of 2 s preceded the next trial.

Initially, an area in each image was selected as an area of interest and the fixation time on that area was designated the total fixation time. All measurements were made in milliseconds (ms) and collected by two researchers (J. Xu & J. Xue). The data were analysed by one researcher (J. Xu) The total fixation time on happy faces was denoted t_h, on sad faces t_s, and on neutral faces t_n. Therefore, happiness bias score was $t_h - t_n$, and sadness bias score was $t_s - t_n$ Scores greater than zero indicated an attentional bias for emotional faces while scores less than zero indicated a preference toward neutral faces. Score indices based on differences such as these have been used in previous research.[7]

Statistical analyses

All statistical analyses were performed using IBM SPSS® software, version 20.0 for Windows® (IBM Corp, Armonk, NY, USA). Data were expressed as mean ± SE. A 2 group (i.e. depressed, non-depressed) × 2 group (i.e. emotional category: happy, sad) × 2 group (i.e. age:

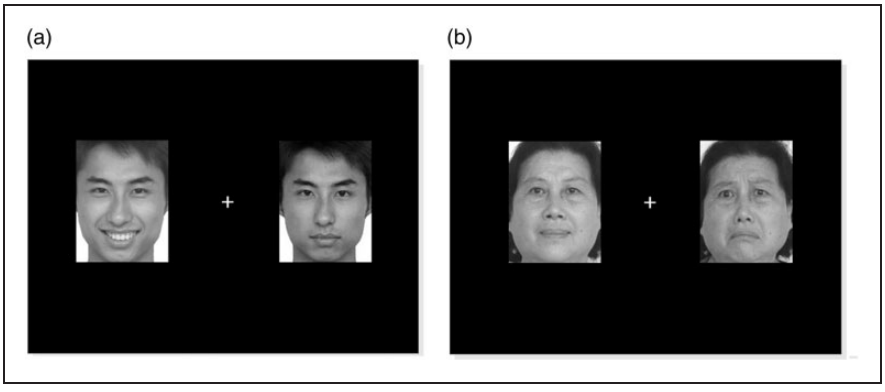

Figure 1. Examples of the facial expression stimulus tasks used in the eye-tracking trials: the two types of tasks were separated into happy versus neutral faces (a) and neutral versus sad faces (b).

young, middle-aged) mixed-model analysis of variance (ANOVA) was used to analyse the data. Differences between groups in attentional bias scores of total fixation time were analysed using a two sample *t*-test. A P-value < 0.05 (2-sided) was considered statistically significant.

Results

In total, 75 (27 men, 48 women) patients with depression were enrolled into the study; their ages ranged from 18–55 years (mean ± SE age, 42.5 ± 12.0 years) and they had attended school for a mean ± SE of 12.9 ± 3.4 years. In addition, 90 (40 men, 50 women) non-depressed control subjects were recruited whose ages ranged from 18–55 years (mean ± SE age, 31.2 ± 9.9 years) and they had attended school for a mean ± SE of 14.6 ± 3.2 years.

Study participants were subdivided into 'young' and 'middle-aged'. In the depressed group, there were 17 (7 men, 10 women) 'young' patients whose ages ranged from 18–30 years (mean ± SE age, 24.9 ± 3.1 years) and they had been in education for a mean ± SE of 14.7 ± 2.4 years. There were 58 (20 men, 38 women) 'middle-aged' patients with depression whose ages ranged from 31–55 years (mean ± SE age, 44.2 ± 7.7 years) and they had been in education for a mean ± SE of 12.5 ± 3.6 years. In the non-depressed control group, there were 56 (26 men, 30 women) 'young' subjects whose ages ranged 18–30 years (mean ± SE age, 24.6 ± 3.0 years) and they had been in education for a mean ± SE of 15.8 ± 2.1 years. There were 34 (14 men, 20 women) 'middle-aged' control subjects whose ages ranged from 31–55 years (mean ± SE age, 42.2 ± 7.1 years) and they had been in education for a mean ± SE of 12.7 ± 3.8 years.

In the three factor (i.e. $2 \times 2 \times 2$) ANOVA, group factor was not significant (F [1, 161] = 0.18, $P \geq 0.05$, $\eta^2 = 0.001$). However, expression factor was significant (F [1, 161] = 111.14, $P < 0.05$, $\eta^2 = 0.26$), but age factor was not significant (F [1, 161] = 0.17, $P \geq 0.05$, $\eta^2 = 0.001$). Group × expression interaction was significant (F [1, 161] = 12.00, $P < 0.05$, $\eta^2 = 0.04$), group × age interaction was not significant (F [1, 161] = 0 .40, $P \geq 0.05$, $\eta^2 = 0.003$), but expression × age interaction was significant (F [1, 161] = 5.74, $P < 0.05$, $\eta^2 = 0.02$). Finally, group × expression × age interaction was significant (F [1, 161] = 4.15, $P < 0.05$, $\eta^2 = 0.03$).

Results from the 2 (group: depressed, non-depressed) × 2 (emotional category: happy, sad) ANOVA showed a nonsignificant main effect for the group (F [1, 163] = 0.41, $P \geq 0.05$, $\eta^2 = 0$ .003) and a significant interaction between emotion and group (F [1, 163] = 54.80, $P < 0.05$, $\eta^2 = 0$ .25). Analysis of attentional bias scores showed that by comparison with control subjects, depressed patients had a reduced attentional bias for happy faces and an enhanced attentional bias for sad faces (Table 1).

Analysis of the 'young' participants (aged 18–30 years) from the 2 (group: depressed, non-depressed) × 2 (emotional category: happy, sad) ANOVA showed a nonsignificant group effect (F [1, 71] = 0.06, $P \geq 0.05$, $\eta^2 = 0.001$) and a significant interaction between emotion and group (F [1, 71] = 9.33, $P < 0.05$, $\eta^2 = 0.12$). Likewise, analysis of the 'middle-aged' participants (aged 31–55 years) from the 2 (group: depressed, non-depressed) × 2 (emotional category: happy, sad) ANOVA showed a nonsignificant group effect (F [1, 90] = 0.14, $P \geq 0.05$, $\eta^2 = 0.002$) and a significant interaction between emotion and group (F [1, 90] = 35.39, $P < 0.05$, $\eta^2 = 0.28$). Analysis of attentional bias scores showed that both 'young' and 'middle-aged' depressed patients had a reduced attentional bias for happy faces and an increased attention bias for sad faces when compared with non-depressed control subjects (Tables 2 and 3).

Table 1. Attentional bias scores for the depressed patients and non-depressed control subjects who participated in the study.

	Depressed patients $n = 75$	Non-depressed control subjects $n = 90$	t	Statistical significance[a]
Happiness bias score,[b] ms	247 ± 125	1003 ± 166	-6.97	$P < 0.05$
Sadness bias score,[b] ms	-570 ± 184	-1447 ± 189	6.39	$P < 0.05$

Data are presented as mean ± SE.
[a]Two sample *t*-test.
[b]Happiness bias score was t_h–t_n and sadness bias score was t_s–t_n, where total fixation time on happy faces was t_h, on sad faces was t_s and on neutral faces was t_n.

Table 2. Attentional bias scores for 'young' (i.e. 18–30 years) depressed patients and non-depressed control subjects.

	Depressed patients $n = 17$	Non-depressed control subjects $n = 56$	t	Statistical significance[a]
Happiness bias score,[b] ms	305 ± 158	992 ± 167	-3.07	$P < 0.05$
Sadness bias score,[b] ms	-804 ± 206	-1435 ± 187	2.43	$P < 0.05$

Data are presented as mean ± SE.
[a]Two sample *t*-test.
[b]Happiness bias score was t_h–t_n and sadness bias score was $t_s - t_n$, where total fixation time on happy faces was t_h, on sad faces was t_s and on neutral faces was t_n.

Table 3. Attentional bias scores for 'middle-aged' (i.e. 31–55 years) depressed patients and non-depressed control subjects.

	Depressed patients $n = 58$	Non-depressed control subjects $n = 34$	t	Statistical significance[a]
Happiness bias score,[b] ms	162 ± 110	1031 ± 162	-6.26	$P < 0.05$
Sadness bias score,[b] ms	-440 ± 175	-1361 ± 186	4.87	$P < 0.05$

Data are presented as mean ± SE.
[a]Two sample *t*-test.
[b]Happiness bias score was t_h–t_n and sadness bias score was $t_s - t_n$, where total fixation time on happy faces was t_h, on sad faces was t_s and on neutral faces was t_n.

For the depressed patients, results from the 2 (age: young, middle-aged) × 2 (emotional category: happy, sad) ANOVA showed a non-significant effect of group (F [1, 73] = 1.21, $P \geq 0.05$, $\eta^2 = 0.016$) and a significant interaction between emotion and age (F [1, 73] = 4.42, $P < 0.05$, $\eta^2 = 0.057$). For the non-depressed control subjects, results from the 2 (age: 'young', 'middle-aged') × 2 (emotional category: happy, sad) ANOVA showed a significant group factor interaction between emotion and age

Table 4. Attentional bias scores for 'young' and 'middle-aged' depressed patients.

	Young depressed patients[a] $n = 17$	Middle-aged depressed patients[a] $n = 58$	t	Statistical significance[b]
Happiness bias score,[c] ms	305 ± 158	162 ± 110	2.03	$P < 0.05$
Sadness bias score,[c] ms	-804 ± 206	-440 ± 175	–0.83	NS

Data are presented as mean ± SE.
[a]Young = 18–30 years; middle-aged = 31–55 years.
[b]Two sample *t*-test.
[c]Happiness bias score was $t_h - t_n$ and sadness bias score was $t_s - t_n$, where total fixation time on happy faces was t_h, on sad faces was t_s and on neutral faces was t_n.
NS, no significant between-group difference ($P \geq 0.05$).

Table 5. Attentional bias scores for 'young' and 'middle-aged' non-depressed control subjects.

	Young non-depressed subjects[a] $n = 56$	Middle-aged non-depressed subjects[a] $n = 34$	t	Statistical significance[b]
Happiness bias score,[c] ms	992 ± 167	1031 ± 162	0.94	NS
Sadness bias score,[c] ms	-1435 ± 187	-1361 ± 186	–1.18	NS

Data are presented as mean ± SE.
[a]Young = 18–30 years; middle-aged = 31–55 years.
[b]Two sample *t*-test.
[c]Happiness bias score was $t_h - t_n$ and sadness bias score was $t_s - t_n$, where total fixation time on happy faces was t_h, on sad faces was t_s and on neutral faces was t_n.
NS, no significant between-group difference ($P \geq 0.05$).

($F\ [1,\ 88] = 4.04,\ P < 0.05,\ \eta^2 = 0.440$). Analysis of attentional bias scores showed that 'middle-aged' patients with depression had a significantly reduced attentional bias for happy faces when compared with younger patients, but there was no significant difference between the age groups with regard to sadness (Table 4). Finally, there was no significant difference between 'young' and 'middle-aged' non-depressed control subjects in attentional bias for happy or sad faces (Table 5).

Discussion

The results of this study confirmed our first hypothesis that compared with non-depressed control subjects, depressed patients showed inadequate positive attentional bias and enhanced negative attentional bias. These current results were consistent with findings from a previous study that used a visual browsing paradigm.[28] The present results are also partially consistent with another study that also used a visual browsing paradigm and found patients with depression had more negative attentional bias than controls.[7] However, in contrast with the present findings, the previous study did not find inadequate positive attentional bias in depressed patients.[7] A possible explanation for the difference in study outcomes may be the variation in sample size; the previous study only

included 16 depressed patients, which may have been too small to detect a difference.[7] In our opinion, it is reasonable for patients with depression to have inadequate attention to positive stimuli since anhedonia is a typical feature of patients with depression and it can result in patients' decreased sensitivity to reward stimulation,[29,30] which will lead to decreased attention to positive experiences.[31]

Our second hypothesis was also supported by these current results in that irrespective of age, patients with depression showed inadequate positive attentional bias and enhanced negative attentional bias compared with non-depressed control subjects. However, the third hypothesis with regard to differences in attentional biases of 'young' and 'middle-aged' patients with depression was only partially supported. Compared with 'young' depressed patients, 'middle-aged' patients showed a significant deficiency in positive attentional bias but there was no difference between the two age groups in negative attentional bias. Previous studies have reported that in terms of behaviour, the sensitivity of adolescents to positive stimuli was significantly increased while that to negative stimuli was decreased.[32] Changes in the structure and function of the brain with age also follow the trajectory of these behavioural changes.[33,34] Interestingly, a previous study reported that the depressive symptoms in 'middle-aged' patients were more severe than in younger patients.[18] Perhaps the discrepancy in these current results was due to differences in sample size between the 'young' and 'middle-aged' groups, which may have affected statistical power.

Limitations of this study include the small sample size of the group of 'young' patients with depression and the imbalance of the ratio of women to men with depression (i.e. 47 women and 28 men). Studies have shown that there are significant differences between men and women with depression in emotional experience, prevalence and age of onset.[35–37] A further limitation of the study was the imbalance of the number of male and female faces in sad and neutral images, which may have affected the study outcome. Finally, although all drug and alcohol was withdrawn for at least 2 weeks before the study started, some of the patients with depression may have previously taken long-term antidepressants, which may have influenced the results.

In summary, this study showed that patients with depression had inadequate positive attentional bias and enhanced negative attentional bias compared with the non-depressed control subjects. In addition, the positive attentional bias of patients with depression was significantly affected by age: the positive attentional bias in 'middle-aged' patients was significantly lower than in 'young' patients. The results of this study may help us to understand more fully the emotional bias of patients with depression and provide direction for clinical treatment of these patients. For example, it may be possible to adjust the emotional state of depressed patients and reduce their depressive mood by repeated training of paying attention to positive stimuli. Training times would be increased appropriately for older patients.

Declaration of conflicting interests

The authors declare that there are no conflicts of interest.

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