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Attentional biases in patients suffering from unipolar depression: results of a dot probe task investigation

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ABSTRACT

Cognitive models of depression emphasize the relevance of cognitive biases for development, onset and maintenance of major depressive disorder (MDD). Attentional biases consisting of increased attention to negative, mood congruent stimuli and reduced attention to positive, mood-incongruent stimuli are postulated but have rarely been tested for early attentional processing. Furthermore, the role of concurrent depressive mood as a moderating factor has not been studied to date. Participants comprised 30 patients suffering from MDD and 30 healthy control subjects. All participants performed a dot-probe task with pictorial stimuli displaying affective facial expressions, presented either for 100 ms or for 500 ms. Attentional biases towards faces displaying joy in both MDD patients and control subjects and towards faces displaying pain in MDD subjects were found at presentation times of 100 ms. In the MDD sample, the bias indices at 100 ms were correlated with concurrent depressive mood. In patients with pronounced depressive mood, significant biases towards happy and angry faces were observed that exceed the biases obtained in control subjects and patients with less depressive mood. The results provide first evidence that MDD patients with pronounced depressive mood show an increased early attentional engagement towards emotional salient stimuli, independent from valence.

1. Introduction

Unipolar depression is a disorder that also affects cognition. In current classification systems, cognitive deficits, especially attentional problems, are listed as diagnostic criteria. And indeed, it could be shown that depressed persons suffer from cognitive impairments persisting beyond acute depressive episodes (Bora et al., 2013; Lee et al., 2012). However, the magnitude of these impairments is comparably smaller than in patients suffering from bipolar disorder, schizoaffective disorder or schizophrenia (Harvey, 2011).

Instead of focusing on pure cognitive functioning, cognitive models of depression like Beck's schema theory (Beck et al., 1987; Beck, 2008) or associative network models (Bower, 1981) predict that dysfunctional cognitive structures and cognitive biases affecting perception, attention, memory and reasoning play a major role in development, onset and maintenance of affective disorders.

Thus, deviations in information processing of emotionally relevant stimuli would be expected for depressive patients and indeed, for several cognitive domains, MDD patients performed differently compared to healthy controls in so-called "hot cognition" tasks using emotionally relevant stimuli (Roiser and Sahakian, 2013). For example, stimuli related to depression are better recalled by depressive patients than neutral and happy stimuli (Moritz et al., 2005; Matt et al., 1992), and there is evidence that altered "hot cognition" might not only be a state marker of depression but might also function as a vulnerability factor (Wells and Beevers, 2009; Baert et al., 2010).

Given the crucial role of attention for other cognitive domains as well as for emotion processing and regulation, the investigation of attentional engagement to and disengagement from emotionally relevant stimuli during early stages of information processing in depressive patients is an interesting topic (see de Raedt et al., 2010). One widely used paradigm to investigate such attentional biases is the dot probe task, which was first introduced by MacLeod et al. (1986). Based on the assumption that subjects respond faster to probes presented at the spatial location that was previously attended, pairs of stimuli (usually one neutral and one emotional) are presented, while the primary task is to detect a probe (usually a dot) as fast as possible. The probe appears at the position of either the emotional or the neutral stimulus immediately after both stimuli have disappeared. If the emotional stimulus was attended, then reaction time should be shorter when the dot appears at the position of the emotional stimulus. Recently, emotional faces have been preferred as stimuli over emotional words, as faces represent

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social situations better than words (Mogg and Bradley, 2002), are more salient (Segrin, 2000) and seem to have privileged access to brain structures responsible for rapid and automatic processing of emotional contents (Le Doux, 1995).

For depressive patients, past research has found contradicting results using the DPT, yielding attentional biases in some studies but not in others. However, most reviewers (e.g. De Raedt and Koster, 2010) agree that if emotional stimuli are presented for one second or longer, there is stronger evidence of mood congruent biases (faster reaction to dots at the spatial position where sad faces were presented immediately before) and weaker evidence of an absence of attentional biases towards positive stimuli, which usually can be found in non-depressed persons (Fritzsche et al., 2010; Hankin et al., 2010; Joormann and Gotlib, 2007; Gotlib et al., 2004a, 2004b). These results are commonly interpreted by the authors as a difficulty to disengage from affective salient information (see also Bradley et al., 1997a, 1997b). For shorter presentation times, especially relevant for early engagement processes, there is no clear evidence of any biases in depressive patients (see for example Donaldson et al., 2007; Neshat-Doost et al., 2000). These results could be interpreted as in line with the emotion context insensitivity theory (see for example Rottenberg and Cowden Hindash, 2015), which suggests a generalized loss of emotional reactivity and would predict no favour towards any emotion.

Given these findings, several further questions could be raised. First, in concordance with Beck' s cognitive model, if presentation times of 1000 ms or longer are used, several series of top-down driven engagement and disengagement processes could have taken place and finally resulted in enduring engagement. Thus, it is unclear whether initial attentional biases bound to bottom-up mechanisms responsible for the instantiation of negative perceptions are being captured at all. Second, to complicate this situation even further, attentional biases seem to be influenced by current depressive mood. For example, the depletion of tryptophan (a precursor to serotonine) seems to reduce biases towards happy faces in healthy subjects, while administration of SSRIs or a single nasal dose of oxytocin (Zhou et al., 2015; Domes et al., 2016) reduces biases toward sad faces in depressive patients (see for example the review of Merens et al., 2007). Similar results can be found when current mood is considered in healthy and depressed subjects (Bradley et al., 1997a, 1997b; Shane and Peterson, 2007). Third, there is substantial evidence of elevated autonomic arousal following stimuli of any emotional valence (Guinjoan et al., 1995; Falkenberg et al., 2012; Schneider et al., 2012), which makes it even thinkable that immediate attentional responses are independent from emotional content.

In the present study we therefore administered a dot-probe task that uses stimulus presentation times of 100 ms and 500 ms in a sample of patients suffering from major depressive disorder (MDD) with no comorbidity of anxiety as well as in a control sample without history of psychiatric illness. Furthermore, we used faces expressing joy, anger and pain as pictorial stimuli in our DPT study, because all of these pictures have been used by our workgroup in previous studies investigating pain-related processing (see for example Scheel et al., 2017; Dimova et al., 2013; Baum et al., 2013a, 2013b) and represent distinct positive and negative states that are at the same time distant to sadness, which is the mood congruent emotion for depression. By that procedure, we tried to avoid unfavourable top down effects created by primes for depressive mood which cannot be offset by later presentations of other emotions. These primes might confound perception of later stimuli, as repeated sad mood inductions may – especially in individuals with a vulnerability for depression – result in emotional sensitization, which is difficult to counterbalance (Mata et al., 2013).

We hypothesized that during initial engagement (at a presentation time of 100 ms) the fact that stimuli contain emotional content of any kind might be more important than the specific emotional content during early bottom-up instantiation of negative perceptions for the depressive group. Thus, we expected enhanced early attentional engagement for all emotional stimuli, independent from their emotional content. As depressive mood might influence attentional biases, we supposed that attentional engagement even in depressed subjects might be stronger for participants suffering from more severely depressed mood. In contrast, presentation times of 500 ms might reveal later engagement or early disengagement, which could already be under the control of top-down processes after the emotional stimulus content has been recognized. Thus, for the control group, joy faces should lead to more engagement whereas pain and anger faces should lead to more disengagement. On the other hand, patients with depression may be more likely to display attention biases toward pain and anger faces and away from joy faces.

2. Methods

2.1. Participants

Thirty inpatients of a psychiatric hospital in Bamberg, Germany were included. All of them fulfilled the International Classification of Diseases-10 (ICD-10) as well as the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for a current major depressive disorder and were diagnosed based on the Structured Clinical Interview for the DSM-IV (SCID, First et al., 1997). Exclusion criteria were other medical diagnoses associated with neurocognitive impairment, prior or concurrent diagnosis of anxiety disorders and uncorrectable deficits in vision or hearing that would prevent performing the tests. Furthermore, 30 control subjects matched by age, educational level and gender from a larger sample that had been recruited for a former study of our research group (Baum et al., 2013) via announcement in local newspapers and amongst university students in Bamberg took part. Participants of the control group were without any history of psychiatric or neurological disorders. None of the participants (of either group) took analgesics or reported any acute or chronic pain conditions or previous major surgical intervention.

After a complete description of the study, written informed consent was obtained from all subjects. The study adhered to the principles of Good Clinical Practice of the International Conference on Harmonization and the Declaration of Helsinki and was approved by the local ethics board (University of Bamberg).

2.2. Measures

2.2.1. Dot-probe task

The dot-probe paradigm used in this study is described in further detail in Baum et al. (2013a). Monochrome photographs of affective facial expressions (pain, anger, joy, neutral faces; displayed by three male and three female actors) extracted from the Montreal Pain and Affective Face Clips (Simon et al., 2008) served as stimulus material. There were 24 pictures for each category. Affective pictures were always paired with pictures displaying neutral faces. Additionally, neutral-neutral picture pairs served as control items. Only pictorial emotions where joy, pain and anger were expressed very distinctly by the actors were included in the dot-probe task. Additionally, the displays were FACS coded to guarantee that they indeed matched typical basic emotions and that the intensities of displays were similar. Furthermore, we tested whether the most similar facial expressions, namely those of anger and pain, were still clearly distinguishable in our set of pictures and obtained a positive result (Baum et al., 2013b).

In each trial, first a fixation cross was presented for 500 ms in the centre of a computer screen. Next, two pictures (either a neutral picture paired with an affective picture, or two neutral pictures) were presented concurrently, left and right of the central fixation point. Each pair of pictures was presented twice, at 100 ms and 500 ms. Immediately after the concurrent presentation of the two pictures, a dot appeared in the same position as one of the two pictures. The participants were instructed to indicate as quickly as possible the side the dot had appeared, using a response box with a three button response panel.

The central button (holding button) had to be released only to respond to the appearance of the dot. The dot-probe task reaction time was taken from the time interval between appearance of the dot and the release of the holding button for correct responses. By measuring pure reaction time (time until release of hold button for correct responses), we tried to circumvent distorting effects of a possible motor slowing in our subsample of depressive patients (see for example the results of van Hoof et al., 1998). To indicate both attentional engagement and disengagement, two different bias indices, namely the congruency and the incongruency index, were calculated. The indices were calculated based on the reaction times following the formula suggested by Asmundson and collegues (Asmundson et al., 2005; Asmundson et al., 2007): The congruency index (CI) was computed using the formula: CI = (reaction time for neutral trials) – (reaction time for congruent trials), where neutral trials are trials in which neutral faces were displayed on both sides and congruent trials are trials in which the dot appears at the side of the affective face. The incongruency index (ICI) was computed by: ICI = (reaction time for incongruent trials) – (reaction time for neutral trials), where incongruent trials are trials in which the dot appears at the opposite side of the affective face. The CI, reflecting attentional engagement, was computed for presentation times 100 ms and 500 ms (CI_{100}, CI_{500}) whereas the ICI, reflecting problems in disengagement, could only be calculated for 500 ms (ICI_{500}) presentation because disengagement cannot occur as early as at 100 ms. Thus, a positive score on the CI (CI_{100}, CI_{500}) reflects attentional engagement with the affective stimuli. Difficulty in disengaging from the affective stimuli is indicated by a positive score in the ICI_{500}, whereas a negative score in this bias parameter represents attentional disengagement from affective pictures.

2.2.2. Assessment of sad and anxious mood: BDI and State Trait Anxiety Depression Inventory

All participants completed the 2nd edition of the Beck Depression inventory (BDI, Hautzinger et al., 2009).

Additionally, the State Trait Anxiety Depression Inventory (STADI, Laux et al., 2013) was administered in the patients with MDD. This self-rating questionnaire consists of a state and a trait part, each comprising 20 items. Total scores for trait as well as state anxiety and depression were computed and used for further analyses. The development of the STADI was based on the experience with the State-Trait Anxiety Inventory (Spielberger et al., 1983) and allows differentiating between anxiety and depression both as a state as well as a trait feature. Reliability (Cronbach's alpha) scores for the scales used in this study lie between .88 and .90. The STADI was chosen to assess depressive and anxious mood in our depressive patients because of time economical and content reasons: As the STADI covers state and trait anxiety as well as acute and enduring depressive mood, only one questionnaire was needed to examine these variables' potential effects on attentional engagement and disengagement. In contrast to the BDI, which contains many questions unrelated to depressive mood, like those targeting fatigue, changes in appetite, loss of interests or changes in sleep patterns, the items of the STADI mainly cover depressive and anxious mood. As we suspected that attentional biases towards emotional stimuli are moderated by depressive mood, the STADI was preferred for that purpose while the BDI was mainly used to compare MDD patients with healthy control subjects.

2.3. Statistics

Kolmogorov Smirnov tests were performed to verify deviation from normal distribution for all bias indices.

T-Tests for independent samples were computed to compare control subjects and MDD patients with respect to depressive symptoms, age and years of education.

An analysis of variance for repeated measurements was performed using the CI_{100} bias as dependent variables in order to look for differences in biases between the three affective picture categories (joy, anger, pain) as within-factor and between the diagnostic groups (control subjects vs. MDD patients) as between-factor.

One-sample *T*-tests were run to determine whether bias-indices deviated significantly from zero, which is the score that suggests unbiased processing (only deviations from zero indicate different processing of affective and neutral facial stimuli). Since for a presentation duration of 500 ms no biasing effects of the affective pictures could be detected, the CI_{500} and ICI_{500} indices were excluded from further analyses.

To investigate whether state and trait anxiety and depression levels measured by the STADI were associated with the bias indices of our patient group, the bias scores were correlated with the STADI scores using Pearson correlation coefficients.

As state anxiety and depression scores were correlated with the CI_{100} bias indices, an analysis of covariance using the STADI state anxiety and state depression scores as covariates was performed for the CI_{100} scores as dependent variables and the three affective picture categories (joy, anger, pain) as within-subject factor.

Because the analysis of covariance showed main and interaction effects only for the depression but not for the anxiety scores, a new group variable denoting high vs. low state depression was created by median splits for the STADI state scores. Thereafter, an analysis of variance using the new dichotomous variable (high vs. low depressive mood) as between-subject group factor and the affective category (joy, anger and pain) as within-subject factor was carried out for the CI_{100} index as dependent variable. One-way analyses of variance with Scheffé a posteriori comparisons were performed to compare the subsamples (controls, MDD patients with high levels and MDD patients with low levels of depressed mood) with respect to age and reaction times. Chi-square tests were used to test for differences in antidepressant or antipsychotic medication between the two depressive groups.

Finally, the CI_{100} index differences between the subgroups were examined by *t*-tests for independent samples, and the deviations from zero, indicating biased attention, were again tested for significance by one-sample *t*-test.

For all analyses, results with a minimum alpha-levels of 0.05 are reported as significant.

3. Results

3.1. Demographic and clinical characteristics

The group of 30 MDD patients (16 females; mean age = 38.7 years (*SD* = 12.3 years); mean years of education = 13.2 (*SD* = 2.5 years)) did not differ from the 30 control subjects (16 females; mean age = 38.7 years (*SD* = 12.2 years); mean years of education = 13.2 (*SD* = 3.9 years)) with respect to age and years of education ($t < 0.001$, $p = 1.0$, each). However, as to be expected, the MDD group had higher BDI depression scores (mean = 26.03, *SD* = 12.27) than the control group (mean = 5.77, *SD* = 4.57; $t = 8.460$, $p < 0.0005$). The MDD patients reached average STADI scores of 25.57 for state depression (*SD* = 7.47, *T* = 65), 26.93 for trait depression (*SD* = 7.39, *T* = 65), 24.60 for state anxiety (*SD* = 6.88, *T* = 65) and 27.10 for trait anxiety (*SD* = 5.62, *T* = 65). According to the t-score distribution, the STADI scores indicate moderately enhanced depressive and anxious mood in the patients. All but 2 depressive patients (93.3%) received antidepressant medication, some of them additionally received mood stabilizers (2 patients, 6.7%), benzodiazepines (1 patient, 3.3%) or antipsychotics (10 patients, 33.3%).

3.2. Attention biases for depressive patients and controls

Tables 1, 2 show the reaction times and the bias indices of all participants obtained for all affective categories. Kolmogorov-Smirnov tests do not point to any deviations from normal distribution for any of

Table 1
Bias indices for depressive patients and control subjects.

		Control subjects		Depressive patients					
				Total		Less severe depressive mood		More severe depressive mood	
Bias indices		Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*
Joy	CI_{100}	7.68	20.52	13.55	32.66	1.87	13.00	26.88	42.72
	CI_{500}	−4.65	24.75	−.76	32.00	−4.11	18.58	3.06	43.08
	ICI_{500}	3.38	31.28	−6.87	22.13	−2.34	14.75	−12.05	28.06
Anger	CI_{100}	6.89	24.41	7.81	33.64	−8.17	20.11	26.07	37.21
	CI_{500}	−4.25	23.43	−11.65	27.77	−3.76	16.29	−20.76	35.31
	ICI_{500}	−0.72	23.90	−9.93	31.52	−14.56	23.27	−4.64	39.18
Pain	CI_{100}	5.83	25.22	10.70	21.60	7.28	16.72	14.60	26.22
	CI_{500}	5.27	30.79	2.83	29.79	3.83	16.70	1.70	39.86
	ICI_{500}	−6.38	25.66	−10.11	31.71	−8.92	26.19	−11.47	38.05

the bias indices (Z between 0.372 and 1.214, $p > 0.10$).

No main ($F_{(2,57)/(1/58)} = 0.490$ and 0.543, p 0.487 and 0.584) or interaction effect ($F_{(2,57)} = 0.245$, $p = 0.783$) could be found in the repeated measures analyses of variance using the CI_{100} indices as dependent variables, diagnostic group (control subjects vs. MDD patients) as between-subject factor and the affective picture categories (joy, anger and pain) as within-subject factor. This indicates that the dot-probe performance regarding CI_{100} - whether biased or unbiased – appeared similar in both groups.

No main ($F_{(2,57)/(1/58)} = 1.920$, 0.378 and for emotional category, type of index (ICI vs. CI) and diagnostic group) 0.490 and 0.543, p 0.487 and 0.584)) or interaction effect ($F_{(2,57)} = .245$, $p = 0.783$) could be found in the repeated measures analyses of variance using the CI_{500} and ICI_{500} indices as dependent variables, diagnostic group (control subjects vs. MDD patients) as between-subject factor and the affective picture categories (joy, anger and pain) as within-subject factor. This indicates that the dot-probe performance regarding CI_{100} - whether biased or unbiased - appeared similar in both groups.

One sample t-tests indicated significant deviations from zero for the CI_{100} indices regarding the facial display of pain and joy ($t = 2.712$, $p = 0.011$; $t = 2.272$, $p = 0.031$, respectively) in MDD patients and regarding the facial display of joy in control subjects ($t = 2.051$, $p = 0.049$), indicating attentional biases (towards increased engagement) to pain-related stimuli for the depressive group and to joyful stimuli for both groups. All ICI_{500} and CI_{500} indices failed to reach statistical significance, discarding any biases in the form of attentional engagement or disengagement at 500 ms.

3.3. Mood – bias correlations and mood effects on attention biases in the patient sample

CI_{100} indices were correlated with STADI values for state and trait depressive and anxious mood within the group of MDD patients: Significant correlations of state depression with the CI_{100} indices for joy ($r = 0.403$, $p < 0.05$) as well as anger ($r = 0.547$, $p < 0.01$) and of state anxiety with the CI_{100} index for anger ($r = 0.463$, $p < 0.01$) were found, indicating stronger attentional engagement at 100 ms in patients with more enhanced depressive and anxious mood.

Consistently, a repeated measures analysis of covariance using the CI_{100} indices as dependent variables and the STADI state depression and anxiety scores as covariates yielded no significant main effect for the repeated measures factor (emotional category, $F_{(2/26)} = 0.556$, $p = 0.580$), the STADI state anxiety as covariate ($F_{(1/27)} = 0.348$, $p = 0.560$) and the interaction effect for STADI state anxiety and emotional category ($F_{(2/26)} = 1.003$, $p = 0.380$). However a significant main effect for STADI state depression as covariate ($F_{(1/27)} = 7.294$, $p = 0.012$) as well as a significant interaction effect for STADI state depression and emotional category ($F_{(2/26)} = 5.349$, $p = 0.011$) was found. These results point to an effect of state depression on attentional biases acting differently regarding the facial expression of joy, anger and pain.

To analyze this in further detail, a new group variable denoting high (scores higher than 26) vs. low state depression (scores less or equal to 26) was created by median splits for the STADI state depression scores.

The subsamples of high (mean/std = 35.56/11.96 yrs.) and low depressive mood (mean/std = 42.29/11.99 yrs.) did not differ from each other with respect to age ($t = 1.54$, $p = 0.136$), antidepressant (Chi2(1) = 0.010, $p = 0.922$) or antipsychotic medication (Chi2(1) =

Table 2
Reaction times and error rates for depressive patients and control subjects.

		Control subjects		Depressive patients					
				Total		Less severe depressive mood		More severe depressive mood	
Reaction times		Mean	*SD*	Mean	*SD*	Mean	*SD*	Mean	*SD*
Joy	*Congruent 100 ms*	392.11	58.96	445.52	94.83	397.35	48.97	515.91	107.70
	Congruent 500 ms	383.42	62.96	444.28	104.79	395.84	49.10	499.64	124.61
	incongruent 500 ms	383.39	62.73	437.57	95.25	387.24	43.93	495.10	106.45
Anger	*Congruent 100 ms*	387.78	59.96	451.26	92.81	407.40	48.43	501.39	106.93
	Congruent 500 ms	382.53	62.76	454.01	112.47	393.25	40.34	523.46	128.85
	incongruent 500 ms	377.04	61.77	435.25	98.63	379.32	46.20	499.16	104.84
Pain	*Congruent 100 ms*	386.80	57.25	448.37	109.70	391.94	43.24	512.85	127.63
	Congruent 500 ms	377.59	59.74	441.22	96.91	387.75	46.22	502.32	104.62
	incongruent 500 ms	373.78	57.86	436.83	103.46	385.02	45.51	496.05	120.03
Neutral	*100 ms*	390.01	56.36	459.06	109.71	399.22	43.78	527.45	123.26
	500 ms	381.41	61.99	444.12	99.57	391.70	40.09	504.03	114.08
% errors		.87	1.01	1.53	2.99	.91	1.03	2.23	4.21

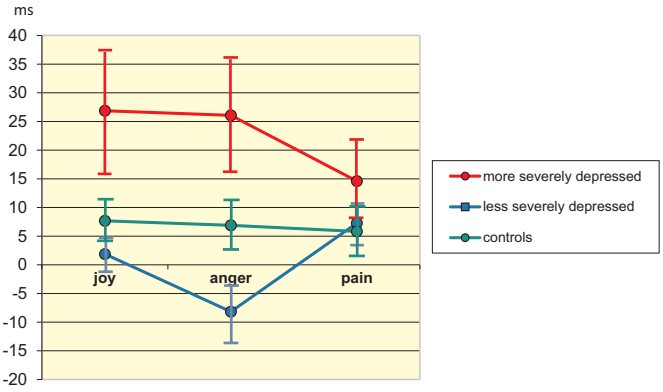

Fig. 1. Mean values and standard errors for CI_{100} bias indices for depressive patients suffering from more or less severely depressed mood and control subjects.

1.071, $p = 0.301$). However reaction times in general were slower for patients suffering from high depressive mood ($F_{(2/57)}$ between 12.738 and 17.528) compared to both patients suffering from less severe depressed mood and control subjects (Scheffé a posteriori comparisons, p between < 0.0005 and 0.008) who do not differ from each other (Scheffé a posteriori comparisons, p between 0.260 and 0.833).

Significant deviations from zero as evidence for biased attention were found only for patients with enhanced depressive mood with regard to the facial display of joy and anger ($t = 2.355$ and 2.621, $p = .035$ and .021, respectively; near-to-significant deviation for pain: $t = 2.083$, $p = 0.058$) and not for those showing less depressive mood (t-values = 0.577, −1.626 and 1.742 for joy, anger and pain, p-values = 0.573, 0.125 and 0.102).

Fig. 1 displays the CI_{100} scores for the two subgroups of patients with low and high current depressive mood and the healthy participants. Post-hoc testing revealed that CI_{100} indices for anger and joy of the patients with enhanced depressive mood were significantly higher compared to the corresponding index scores for control subjects and patients with less depressive mood (t-values between 3.197 and 2.028, p between 0.003 and 0.049). These findings made it obvious that enhanced early attentional engagement with emotional stimuli (facial expression of joy or anger) occurred only in MDD patients with a high level of current depressive mood.

4. Discussion

Our main aims were to study attentional engagement towards emotional stimuli (emotional faces) in depressive patients by using a dot-probe task and to identify biased attention. We hypothesized that during initial engagement emotional stimuli of any kind are preferred over neutral stimuli and that attentional biases are influenced by current depressive mood even in patients suffering from MDD.

We observed biased attention only for very early attentional engagement in all participants. Specifically, we found attentional biases towards faces displaying negative and positive emotions as well as pain only after a picture presentation time of 100 ms but not after 500 ms.

Moreover, in the MDD sample, the extent of these biases was shown to be dependent on the level of current depressed mood in the patients. The CI_{100} indices were significantly correlated with depressive mood. This mood effect on attentional bias was pronounced to such an extent that significant attentional biases towards happy and angry stimuli as well as almost significant biases toward sad stimuli were only found for patients with high levels of current depressive mood, but not for patients with low levels.

4.1. Biases in first and later attentional processing

As already covered in the introduction section, there is substantial evidence for mood congruent attentional biases in depressive patients gathered from dot-probe studies when longer presentation times of 1000 ms or more are used. When shorter presentation times were used in order to investigate early attentional engagement, the few studies that have been performed provided no consistent evidence for biases in any form. While studies using presentation times of 100 ms or less are very rare - to the knowledge of the authors, no study using faces as stimuli and shorter presentation times in MDD patients has been performed so far - results regarding presentation times of 500 ms are mainly negative. Only one study (Mathews et al., 1996) found significant attentional biases for socially threatening words, whereas in other studies no biases for emotional stimuli were reported (MacLeod et al., 1986; Bradley et al., 1997a, 1997b; Donaldson et al., 2007) for clinically depressed subjects. The findings regarding presentation times of 500 ms might be due to the fact that regular top-down driven content-specific emotion processing already might have started in this time window and might have outweighed effects of early attentional engagement. The general pattern of results of no biases for shorter presentation times and mood congruent biases for longer presentation times however is consistent with data from studies using eye-movement technology. While no differences from control subjects were shown when only direction and latency of first glance were analyzed, prolonged fixation times on either sad pictures or sad regions of pictures could be found. This can be interpreted as a deficit to disengage from negative mood congruent stimuli (see for example De Raedt et al., 2010), while currently various assumptions about attentional biases concerning early attentional engagement are plausible. Theoretically, similar to the findings for longer presentation times, a negativity bias resulting in preferred engagement with negative and diminished engagement with positive emotional stimuli could be predicted. But also, following emotional context insensitivity theory, which would predict a deficit in depressed persons to recognize emotions of any valence (see for example Rottenberg and Hindash, 2015), an absence of any bias towards positive or negative stimuli would be a reasonable suggestion. Finally, there is also robust data concerning elevated galvanic skin response to emotionally relevant stimuli of any valence (Schneider et al., 2012; Falkenberg et al., 2012; Gross and Levenson, 1997), which may reflect elevated attentional engagement following autonomic arousal. Thus, it is also plausible that all emotional stimuli whatsoever are attended. This hypothesis is consistent with newer neurobiological approaches like Helen Mayberg's model of depression, proposing a cortical limbic dysbalance (Mayberg, 2003). In this model, hypoactivity in neocortical regions like the dorsolateral prefrontal and dorsal cingulate cortex hamper regulation of fast autonomous reactions to negative emotional input caused by hyperactivity in limbic and subcortical areas. Thus biases occurring under longer presentation times of emotional stimuli may be under the control of top-down emotion processing in prefrontal areas involving reappraisal, decision making and self-regulation, whereas early biases during shorter presentation times might reflect "hot" bottom-up processes that are under the control of limbic areas like the amygdala, the hippocampus or the subgenual cingulate (Roiser and Sahakian, 2013).

In this context, it is interesting to note that a recent meta-analysis of fMRI data for depressive patients found hyperactivity in depressive patients' salience networks that include limbic structures (insula, dorsal cingulate cortex and amygdala) during the processing of negative stimuli as well as hyperactivity of the pulvinar nuclei in the thalamus during rest (Hamilton et al., 2012). The authors argue that the increased excitability of the salience network may be mediated by the pulvinar nuclei. When considering this, it should be noted that in neurobiological models covering visuospatial attention the pulvinar is assigned a key role in early engagement of attention onto a new target (Fan et al., 2009).

Hence our findings of elevated early attentional biases towards all kind of emotional material, while contraintuitive, are plausible.

4.2. Mood effects on the attentional bias in MDD patients

Our hypothesis that the extent of depressive symptoms has an impact on attentional biases in depressive patients was clearly confirmed. In our data, the effect of current depressive mood on attentional biases is pronounced to such an extent that attentional biases for stimuli displaying engagement only occur in patients with high levels of depressed mood and no biases for low levels of depressed mood are found.

As already stated in the introduction, there are multiple findings that current depressive mood affects attentional biases.

Moreover, there are a number of hints from other studies that the current level of depressive symptoms in MDD patients is of great importance for cognitive biases regarding the recognition of facial expression of emotions (see also the section below). Likewise, the negative perceptual bias of positive facial expressions (a greater intensity of a happy expression is needed to recognize a face as happy) vanishes along with the reduction of depressive symptoms (Münkler et al., 2015).

In this context, the weaker attentional engagement with pain faces may result from the fact that their recognition is more difficult than the recognition of faces displaying basic emotions (Kappesser and Williams, 2002; Simon et al., 2008). Thus, the recognition of facial expressions of pain might have been too difficult to prompt early attentional orientation.

4.3. Impairments of MDD patients regarding the recognition of emotion?

Possibly, the attentional bias of MDD patients toward positive and negative emotional stimuli during shorter presentation times of 100 ms was caused by deficits in recognition of emotion.

Indeed there are repeated findings that neutral faces are more likely to be misinterpreted as sad faces by MDD patients, while sad faces are significantly better recognized (Leppänen et al., 2004; Bourke et al., 2010). Although we tried to circumvent such distorting effects by excluding sad facial expressions from our design and using only pictorial stimuli that displayed anger, joy and pain very distinctly, the biases found in our study could have been influenced by misinterpreting neutral faces as sad ones. However, while this could account for the absence of any biases in the MDD group reporting low levels of depressed mood, false recognition of emotions cannot explain the presence of attentional biases toward all emotional stimuli in the MDD group suffering from more severely depressed mood.

Although we used a response box with a holding button to minimize the impact of motor speed deficits on the bias indices, impairments regarding the recognition of emotions might also be caused by decreased processing speed during acute depression (Bora et al., 2013; Lee et al., 2012). This impairment might have hampered the correct recognition of emotions displayed within the short time window of 100 ms. Indeed, reaction times were slowest for the MDD subgroup with elevated depressive mood, while the other depressive subgroup showed reaction times comparable to the control subjects (see also Table 2).

Considering this, it is possible that the biases toward all kind of emotional stimuli obtained for the MDD group with more severely depressed mood might reflect an earlier stage of processing compared to the two other groups. However, it still remains unclear, why attention would then be disengaged from any emotions by the MDD group with less severely depressed mood.

4.4. Limitations

One shortcoming is that the present study might have been underpowered to detect subtle attentional biases, even though our sample size of 60 is in the midst of the range of comparable studies. For example, the ICI_{500} indices for all three emotional picture categories pointed to disengagement processes, but the corresponding bias scores only reached p- values of < 0.10 each, not reaching the alpha-level of 0.05. Maybe a replication using a larger sample of depressive patients would lead to significant results supporting the hypothesis of later disengagement from mood-incongruent emotional material in MDD patients.

Since all of our depressive patients received psychotropic medication, it cannot be ruled out that this might have influenced attentional biases - most likely towards positive stimuli - in this group. As for none of the MDD groups a corresponding bias pattern could be found, and both groups significantly differ in their bias pattern despite similar medication, it seems questionable whether psychotropic medication has substantially influenced our main findings.

As can be seen in Table 1, the variability in the CI_{100} variable was much higher for the depressed participants higher in depressive mood. This suggests that the difference may be driven by single participants with extreme scores. Although no such participants (scores of 2.5 or more standard deviations from mean) were found in our data, the question why there is more variability in this group remains unresolved.

Furthermore, it would have been desirable to add sad faces as mood congruent stimuli to our dot-probe paradigm. However, our main intention was to investigate attentional biases toward stimuli displaying positive and negative emotions different from the predominating emotion in depressive patients, and we intended to rely on an established dot-probe paradigm that had yielded stable and valid results in past investigations by our work group. Moreover, we wanted to present emotions that are expected to be equally familiar to depressive patients and to the control group. As we thought it necessary to use more elaborated bias indices (Asmundson, 2005; Asmundson, 2007), more trials than usual in dot-probe tasks were necessary, and adding stimuli displaying sad emotions could have extended the dot-probe task beyond the patients' limits of working under stress. In the light of the present results however, it would nevertheless be a promising option to replace the 'painful' stimuli by 'sad' stimuli in future studies.

4.5. Summary

In sum, the results of our study provide first evidence by a dot-probe task that depressive patients with pronounced current depressive mood show an early (first 100 ms) attentional bias towards all kinds of emotional stimuli - independent from their emotional content, whereas later (from 100 ms to 500 ms) attentional processing appeared largely unchanged. If these results could be replicated in future studies, they might point to an interesting starting point for therapeutic interventions, namely to make use of the observed early attentional engagement towards positive stimuli. For instance, in feedback versions of the dot-probe paradigm, patients could gradually be trained to extend engagement with positive stimuli for increasing presentation times. In a second step, patients could then even be trained to prevent engagement with negative stimuli by teaching them to keep their attentional focus on concurrently displayed positive stimuli (i.e. pairs of positive and negative emotions instead of neutral/emotional pairs). Induction of optimism prior to such training of early attentional orientation (King, 2001) might aid in achieving these goals (Peters et al., 2015) and could supplement standard drug and non-drug (cognitive) therapy for MDD.

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Conflicts of interest

None.

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