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Is There a Negative Interpretation Bias in Depressed Patients? An Affective Startle Modulation Study

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Key Words

Depression · Affective startle modulation · Ambiguity · Interpretation bias · Cognitive theory

Abstract

Background/Aims: Scientists proposed that patients with depression favour negative interpretations when appraising ambiguity. As self-report measures seem prone to response bias, implicit measures of emotional valence should be additionally used. ***Methods:*** A total of 16 patients with depression and 19 controls underwent an acoustic imagery task comprising neutral and negative words, as well as ambiguous words that could be understood either way. Affective startle modulation and direct interrogation were used to assess implicit and explicit emotional valence, respectively. We expected a negative bias for ambiguous words in the patient group, resulting in augmented startle magnitudes and preference for negative interpretations of the ambiguous words in the interrogation. ***Results:*** Surprisingly, both groups preferred neutral interpretations and showed augmented startle magnitudes to ambiguous words. Furthermore, both groups displayed an emotional startle potentiation for negative words. ***Conclusion:*** In summary, our results do not confirm a negative interpretation bias or a blunted emotional response in patients with major depression. The mismatch between self-report and affective startle reaction to ambiguous targets might reflect defensive mobilization or attention effects.

Introduction

In the 1960s, cognitive scientists proposed that information processing in patients with depression is characterized by a negative interpretation bias, i.e. patients tend to interpret ambiguous information negatively [1–5]. Based on this assumption, therapists have tried to modify this bias during treatment [6, 7]. However, the general

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existence of such a bias is not unequivocally supported. Some authors doubt its existence in depression [8]. Whereas a number of studies on information processing have provided evidence for a negative interpretation bias, negative attentional bias, and negative memory bias, respectively, in depression [5, 9–11], other studies have revealed that patients with depression tend to interpret information in a more negative but concurrently more realistic manner compared to controls [12, 13]. These studies have suggested that interpreting ambiguous information in healthy people is influenced by a protective positivity bias, which leads to a more positive but sometimes unrealistic interpretation [14].

Thus, it is still a matter of debate whether a negative interpretation bias in depression actually exists [11, 15]. So far, most studies implementing ambiguous situations used text comprehension tasks, homophone tasks or self-evaluation tasks. Such measurements of negative bias have been criticized as they rely on self-reports, which may be prone to response bias or demand effects [5, 8, 16]. That is, patients only tend to *report* negative meanings, although the actual *interpretation* may not differ from healthy controls [5]. To avoid such problems, Lawson et al. [17] added the affective startle modulation as an objective, implicit measure of affective interpretation. The affective startle modulation is a well-established paradigm applied in animal and translational human research on emotion [18]. The magnitude of the human blink reflex is augmented when elicited while being confronted with negative rather than neutral stimuli [19] and reduced by positive stimuli [20], which has been replicated using different stimulus materials [19, 21–24]. For unambiguous stimuli, studies in patients with depression are not as consistent as for healthy subjects. Some found the expected modulation in moderate depression, whereas it may be absent in more severe depression or even increased for positive pictures. Also, augmented startle responses for neutral versus positive pictures have been reported [25–27].

The startle reflex might aid in investigating negative bias in depression: if ambiguous information is processed negatively, leading to a negative emotional state, the startle reflex should be augmented. Lawson et al. [17] argued that the blink magnitude provides information about whether the interpretation of ambiguous information was negative or neutral. To examine this, sound files were constructed of words that could be interpreted differently – a common method for creating ambiguity [5, 10, 17, 28]. These sounds consisted of neutral and negative target stimulus pairs that differed in valence but were acoustically identical except for one phoneme (e.g. dress and stress). After merging pairs, the acoustically presented word (e.g. *ress) could be understood in either its negative or neutral meaning with equal probability. Additionally, unambiguous negative and neutral target stimuli were used. Students were divided into a depressive and a non-depressive subgroup (lowest vs. highest tertile) according to their scores on the Beck Depression Inventory II (BDI-II) [29]. They were instructed to imagine situations evoked by the presented words. Results showed that the blink magnitude elicited during the imagery of unambiguous negative words was greater than after unambiguous neutral words. Furthermore, the high BDI group showed a significant augmentation of the startle reflex after listening to ambiguous words, indicating a negative interpretation. In contrast to studies using self-reports, these results provide a more objective evidence for a negative interpretation bias in participants with high BDI scores.

It has been argued that severity of depression is an important factor for the degree of bias [11, 12]. One might ask whether the results referring to students [17] also hold true for depressed inpatients. Therefore, we investigated a clinical sample of patients. As self-focusing and self-relevance of information provoke distortion tendencies in patients with depression [7, 30, 31], we instructed the patients to imagine autobiographic, personally relevant situations evoked by the presented words to foster a negative interpretation bias. First, we hypothesized that all participants would show an augmented startle reaction evoked by unambiguous negative versus neutral words [17, 25–27]. Second, we hypothesized that depressive patients tend to interpret ambiguous words negatively, i.e. reporting more negative words and showing an augmented startle reflex for ambiguous words compared to healthy controls [17].

Methods

Participants

Patients were recruited at the Department of Psychiatry, Psychosomatics and Psychotherapy at the University Hospital Wuerzburg. They were diagnosed by two psychiatrists according to ICD-10 criteria using a semi-structured interview analogous to the AMDP interview [32]. Patients with past or present bipolar affective disorder were excluded. None of the patients had neurological comorbidities, mental retardation or severe somatic disorders in order to exclude organic affective disorders. Hospitalization time at measurement ranged between 1 day and 6 months, and the number of inpatient stays was between 1 and 10. Controls were recruited from lists of volunteers and the university community and participated without payment. From the original

Table 1. Sample characteristics

Variable	Patients (n = 16)	Controls (n = 19)	Statistics
Age, years	36.44±11.71	31.95±10.06	t_{33} = 1.221, p = 0.231
Gender (female/male)	10/6	10/9	χ_1^2 = 0.345, p = 0.557
Handedness (right/left/ambidextrous)	16/0/0	14/4/1	p = 0.071[a]
Education level			p < 0.001[a]
General school	8	0	
Intermediate school	4	2	
A levels	4	17	
BDI (min, max)	29.25±12.82 (11, 47)	2.68±3.32 (0, 10)	t_{16} = 8.06, p < 0.001
STAI state	46.63±10.07	29.74±6.61	t_{25} = 5.75, p < 0.001
DAS	158.75±31.85	98.68±20.61	t_{24} = 6.49, p < 0.001
MWT-B	104.81±11.87	128.32±10.54	t_{33} = 6.21, p < 0.001
Days since admission[b]	39.50±42.73		
Number of stays[c]	2.63±2.36		
Duration of illness[d]	13.33±10.26		

Values are expressed as mean ± SD or as numbers. d.f. adjusted in cases of unequal variances.

BDI = Beck Depression Inventory; STAI = State-Trait Anxiety Inventory; DAS = Dysfunctional Attitude Scale; MWT-B = Multiple Choice Word test version B.

[a] Fisher's Exact Test (Freeman-Halton extension). [b] range: 1–180. [c] range: 1–10. [d] range: 0.5–35 years.

sample (22 patients, 21 controls), 1 patient was excluded for discontinuing the experiment, 1 for technical problems and 4 for being startle non-responders, as were 2 controls.

The final sample included 16 patients with a depressive episode [ICD-10: F32.2 (n = 6), F32.3 (n = 1)] or recurrent depressive disorder [ICD-10: F33.1 (n = 1), F33.2 (n = 7), F33.3 (n = 1)]. Mean BDI-II [33] score in the patients was 29.25 (range: 11–47). All controls had BDI-II scores below 10. All participants were native speakers, had normal or corrected-to-normal vision and were free of any kind of amblyacousia. Sample characteristics are displayed in table 1.

Patients displayed the following comorbid mental disorders: dysthymia [F34.1 (n = 1)], narcissistic personality disorder [F60.8 (n = 1)], and harmful use of alcohol [F10.1 (n = 1)]. All patients were on antidepressant medication as follows: selective serotonin reuptake inhibitors (n = 2), serotonin noradrenalin reuptake inhibitors (n = 5), noradrenergic and specific serotonergic antidepressants (n = 5), tricyclic antidepressants (n = 9), second generation tricyclic antidepressants (n = 3), antipsychotics (n = 9), antiepileptics (n = 1), benzodiazepines (n = 8) and lithium (n = 1).

The study was approved by the Ethics Committee of the University of Wuerzburg, and all procedures involved were in accordance with the latest version of the Declaration of Helsinki.

Materials

Target Stimuli. Stimuli were created at the Department of Psychology at the University of Wuerzburg [34]. Ambiguous target stimuli were generated using a neutral and a negative noun differing only in one phoneme (e.g. Falle [trap]/Halle [hall], Raub [robbery]/Laub [leaves]). These words were read out by a female volunteer, recorded, digitized and processed with sound-editing software (Adobe Audition 2.0; Adobe Systems, San Jose, Calif., USA). The waveforms representing the unambiguous negative and neutral target stimuli were split into one identical and one different part and overlaid to construct the ambiguous target stimulus (i.e. *alle, *aub), which could be understood either in its negative or neutral meaning. In a pilot study, 187 words (60 unambiguous negative, 60 unambiguous neutral and 67 ambiguous) were evaluated by 10 healthy volunteers. Stimuli were presented binaurally at 70 dB through headphones. Following Lawson et al. [17], a background white noise at 60 dB was applied. The participants listened to the 187 words in a randomized order and were required to repeat the words aloud. All unambiguous target stimuli were named correctly; 20 ambiguous target stimuli that were judged negative and neutral in comparable frequency were selected for the main experiment; 20 stimuli were selected each from the unambiguous negative and neutral words. According to the CELEX database [35] the neutral and negative stimuli selected for the final experiment did not differ with respect to word frequency (in the ambiguous and unambiguous condition).

Experimental Apparatus. We used Presentation (version 9.90; Neurobehavioral Systems, Albany, Calif., USA) for programming the experiment. Target stimuli were presented binaurally at 70 dB via headphones (K 516 TV; AKG, Vienna, Austria) with a background white noise at 60 dB. Startle reflexes were elicited by a 92-dB sound burst. Electromyographic activity from the right and left eye were measured with Ag/AgCl electrodes placed over the musculus orbicularis oculi and at the lateral canthus, respectively. The ground electrode was placed on the participant's forehead close to the hair line. Before attaching the electrodes, the skin on these sites was cleaned with an abrasive gel and a conducting paste (Electrode cream for EKG, EEG and cardioversion; GE Medical Systems Information Technologies, Freiburg, Germany). Electromyographic signals were amplified using an electrode input box EIB64 and a 64-channel BrainAmp MR amplifier and recorded using the BrainVision Recorder software (Brain Products, Munich, Germany). The sampling rate was 5 kHz, and the time constant was 0.01 s, according to a high cut-off of 15.915 Hz.

Demographic Questionnaire and Psychometric Scales. Participants provided information about age, gender, residence, native language, handedness, amblyacousia, amblyopia, medication, education, graduation and profession in a demographic questionnaire. Severity of depressive symptoms was measured with the BDI-II, cognitive distortion with the Dysfunctional Attitude Scale (DAS) [36], and state anxiety in the experimental situation with the State-Trait Anxiety Inventory (STAI) [37]. Verbal intelligence was assessed with the Multiple Choice Word test (MWT-B) [38]. Present or past mental disorders in the controls were assessed using the SKID screening interview of the DSM-IV [39].

Assessment of Ambiguous Stimuli Interpretation. After the experiment, a questionnaire regarding the experiment's ambiguous target stimuli was administered. Participants had to write down the words as they understood them in the experimental session. Items were coded as missing if the answer fit neither the neutral nor the negative source of the ambiguous target stimulus.

Valence and Arousal Ratings. The evoked personal situation was rated for arousal and valence with the Self-Assessment Manikin (SAM) scale [40], a non-verbal 5-point Likert scale pictorial assessment technique measuring affective reactions towards a variety of stimuli. Scales were assigned to numerical values from –2 (very negative) to +2 (very positive) for valence and from 0 (no arousal) to 4 (high arousal) for arousal.

Procedure

After the consent forms and questionnaires had been filled out, the electrodes were attached. The participants were seated in front of the computer screen, received instructions and put on the headphones.

The task consisted of 60 trials (20 unambiguous neutral, 20 unambiguous negative, 20 ambiguous). Presentation order was pseudorandomized, with no more than three successive stimuli of one category. At the beginning of each trial, a green circle for 2,000 ms signalled the participant to listen to the following target stimulus, which was presented 100 ms before green circle offset (i.e. green circle offset and target stimulus offset coincided). Then a yellow circle signalled to imagine a personal situation evoked by the recognized word and lasted on the screen for 8,000 ms. After a constant period of 5,400 ms, the blink reflex was elicited by a sudden burst of 92 dB in 14/20 trials of each category; 2,600 ms later the yellow circle turned off and a red circle was presented for 13 s (intertrial interval), which signalled the end of the trial. During the intertrial interval, a startle burst was elicited after 5,000 ms in 10/60 trials (see fig. 1). This part of the experiment lasted 20 min.

The second part of the experiment was a paper and pencil interrogation. The 20 ambiguous target stimuli were presented in a fixed order. Participants had to write down the word they had understood during the experimental session and to rate arousal and valence of the evoked imagined personal situation using the SAM scales. The interrogation was not integrated into the main experiment to avoid interruption of the provoked emotional imaginations with the cognitively demanding evaluation task. Only interpretations of the 14 words that had been associated with a startle were considered in the analysis.

Startle Response Preprocessing

Offline analysis of the electromyographic activity of both eyes was accomplished with BrainVision Analyzer (version 1.05, Brain Products). Data were filtered with a band-pass from 28 to 500 Hz.

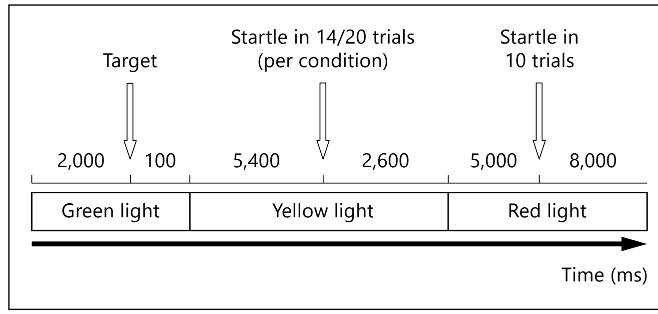

Fig. 1. Schematic illustration of a trial. The green circle indicated the beginning of a trial, at the end of which the word was played. During the yellow circle phase the patient had to imagine a personal scenario; a startle sound was presented in 60% of trials (14/20 per condition). In the intertrial interval (red circle), a startle sound was presented in 17% (10 times).

Segments ranging from 50 ms before until 1,000 ms after the blink reflex-eliciting burst were selected. Trials containing fluctuations over 2 μV in the baseline period (50 ms before startle probe onset) were rejected [41]. The minimum number of valid startles was set to five per category. The software automatically detected the highest amplitude peak in a time frame of 20–120 ms after the onset of the blink reflex-eliciting burst [42]. Magnitudes were calculated for the three categories. Participants with mean magnitudes below 5 μV across all trials were coded as non-responders and excluded from further analyses; therefore, 4 depressive patients and 2 healthy controls from the original sample were eliminated [43].

Raw data of the amplitudes (μV) were standardized for statistical analysis using a z-score transformation within subjects and were subsequently transformed to t scores[1] [17]. This transformation allows for comparing the data and evaluating the relative magnitudes of blink reflexes elicited under the experimental conditions although there are interindividual differences in the strength of the physiological blink response.

Statistical Analysis

Data analysis was performed using SPSS 16 (IBM, New York, USA). For interrogation and rating data, 2 × 2 repeated-measures analyses of variance (ANOVAs) with the within-factor *interpreted target valence* (neutral vs. negative interpretation) and the between-factor *group* (patients, controls) were calculated. Dependent variables were the number of interpreted words and mean valence and arousal rating. For startle data analysis the data from both eyes were averaged. The within-factor *presented target valence* had three levels (negative, neutral, ambiguous) resulting in a 3 × 2 ANOVA. As data within each cell were normally distributed, post hoc tests were performed by means of two-tailed t tests.

[1] z-scores were calculated by using this formula: $z = (x - \mu)/\sigma$ where x is the raw score, μ is the individual mean and σ is the individual standard deviation. The z-scores were then transformed to t scores with the formula: $50 + 10z$.

Results

Interpretation of the Ambiguous Target Stimuli

Figure 2 depicts the mean number of negative and neutral interpretations of ambiguous stimuli for patients and controls. In both groups less than one answer was coded as missing on average (i.e. neither the unambiguous neutral or negative word was named). A 2 × 2 ANOVA revealed a significant effect of *condition*, F(1, 33) = 12.78, partial $\eta^2 = 0.279$, $p < 0.001$, and a trend effect of *group*, F(1, 33) = 3.51, partial $\eta^2 = 0.096$, $p = 0.07$. The interaction was not significant, F(1, 33) = 2.47, partial $\eta^2 = 0.070$, $p = 0.13$. Both groups more often reported the neutral (7.89 ± 1.89) than the negative word (5.69 ± 1.76). Although the interaction effect was not significant, it might be useful to look at specific post hoc contrasts [for rationale, see 44]. Patients tended to interpret fewer ambiguous stimuli in a neutral meaning than controls, t(33) = 1.89, d = 0.66, $p = 0.07$, while there was no difference in the number of negatively interpreted words, t(33) = 1.17, d = 0.41, $p = 0.25$. Whereas controls significantly interpreted more words in a neutral than negative meaning, t(18) = 4.13, d = 0.95, $p = 0.001$, this was not the case for the patients, t(15) = 1.25, d = 0.31, $p = 0.23$.

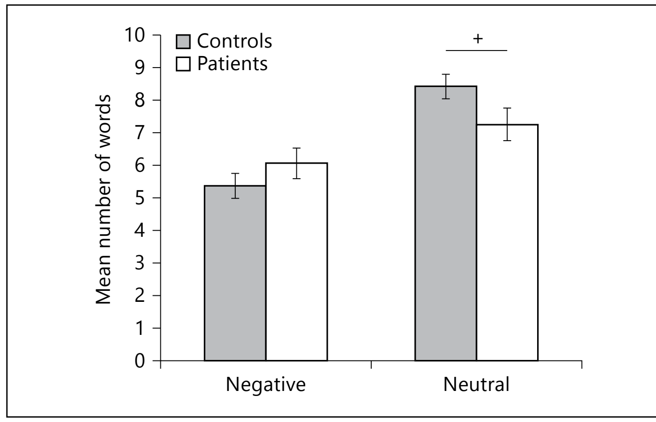

Fig. 2. Mean number of negative and neutral interpretations of ambiguous stimuli (and standard error of the mean, SEM) for patients and controls ($^+$ $p < 0.10$).

Valence and Arousal Ratings

Mean valence and arousal ratings are depicted in figure 3. For valence, a 2 × 2 ANOVA revealed a significant main effect for *condition*, F(1, 33) = 190.09, partial $\eta^2 = 0.853$, $p < 0.001$, indicating, as expected, more negative ratings for negatively versus neutrally interpreted ambiguous words. A significant main effect of *group*, F(1, 33) = 5.57, partial $\eta^2 = 0.144$, $p = 0.02$, indicated generally lower ratings in the patient group. Although the interaction effect did not reach significance, F(1, 33) = 1.65, partial $\eta^2 = 0.048$, $p = 0.21$, exploratory analyses within the words with a negative meaning hint at a more negative rating in the patients, t(33) = 2.57, d = 0.90, $p = 0.02$, which is in line with the expectation. This effect was not found for words interpreted neutrally, t(33) = 1.40, d = 0.49, $p = 0.17$.

For arousal, a 2 × 2 ANOVA revealed a significant main effect for *condition*, F(1, 33) = 14.53, partial $\eta^2 = 0.306$, $p = 0.001$, indicating, as expected, higher arousal ratings for negatively versus neutrally interpreted ambiguous words. However, this was only valid for the controls as indicated by a significant interaction effect, F(1, 33) = 4.88, partial $\eta^2 = 0.129$, $p = 0.03$. Patients did not rate negatively versus neutrally interpreted words differently, t(15) = 0.95, d = 0.24, $p = 0.36$, and thus rated neutrally interpreted words more arousing than controls, t(33) = 3.03, d = 1.06, $p < 0.01$. There was no significant *group* effect, F(1, 33) = 0.91, partial $\eta^2 = 0.027$, $p = 0.35$.

Startle Magnitude Analysis

The mean startle magnitudes are listed in table 2 and depicted in figure 4. The main effect of *condition*, F(2, 66) = 11.60, partial $\eta^2 = 0.260$, $p < 0.001$, was significant. There was no main effect of *group*, F(1, 33) = 0.73, partial $\eta^2 = 0.022$, $p = 0.40$, and no interaction *group* × *condition*, F(2, 66) = 0.25, partial $\eta^2 = 0.007$, $p = 0.78$.

Post hoc t tests revealed that blink magnitudes were larger when elicited during imagery evoked by a negative compared to a neutral target stimulus, t(34) = 3.98, d = 0.67, $p < 0.001$. Furthermore, the startle magnitude was larger during imagery evoked by ambiguous compared to neutral target stimuli, t(34) = 4.13, d = 0.70, $p < 0.001$.

Discussion

This study applied the affective startle modulation paradigm to investigate whether patients with depression interpret ambiguous stimuli negatively. The main result is that no negative interpretation bias in patients could be discerned, conforming with some previous findings [5, 14, 45]. Self-report data showed that although patients tended to interpret fewer ambiguous words neutrally than controls, there was no difference in the number of negatively interpreted words. However, we found a slight hint for a negative bias in patients concerning the valence ratings. Thus, ambiguous words that had been interpret-

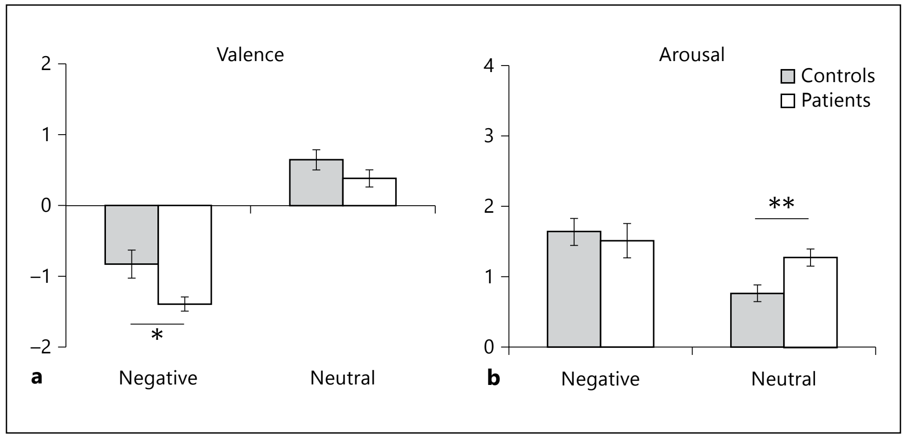

Fig. 3. Mean valence (**a**) and arousal (**b**) ratings (and SEM) for ambiguous words written down in their negative vs. neutral meaning (* $p < 0.05$, ** $p < 0.01$).

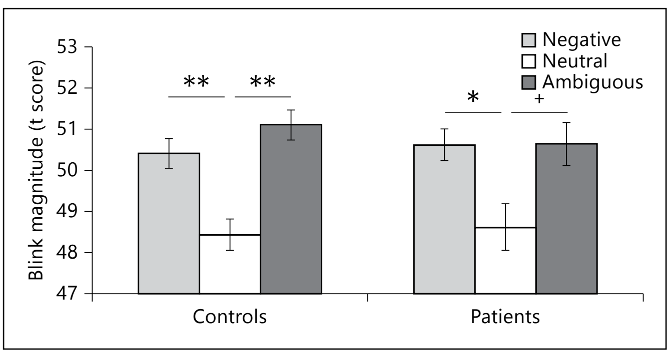

Fig. 4. Mean blink reflex magnitudes (and SEM) for all participants in each target valence condition separated for the right and left eye ($^{+}$ $p < 0.10$, * $p < 0.05$, ** $p <0 .01$).

Table 2. Startle magnitudes (t values) for controls and patients in the different target conditions

Target word	Controls (n = 19)	Patients (n = 16)
Unambiguously negative	50.42±1.57	50.61±1.54
Unambiguously neutral	48.43±1.66	48.61±2.27
Ambiguous	51.10±1.59	50.64±2.09

Values are expressed as mean ± SD.

ed negatively were rated more negative by depressive patients than by healthy controls – as seen in the exploratory analysis. Valence of the evoked personal situations was rated more negatively by patients than healthy controls. However, this finding might actually be based on a negative response bias, but not a negative interpretation bias as confirmed by previous studies [16]. These results have to be considered preliminary, as they only emerged in exploratory post hoc analyses.

Besides self-report data, the startle reflex is less likely to be prone to response bias. Regarding the affective startle modulation, we did not find any difference between patients and controls. Consistent with Lawson et al. [17], unambiguous negative target stimuli evoked higher blink magnitudes than unambiguous neutral target stimuli. This effect was shown for healthy samples in numerous studies with different stimulus material [19, 21–24, 46]. By contrast, studies trying to replicate this phenomenon in depressive patients or subjects with nonclinical depression have produced inconsistent results [25–27]. Some researchers — consistent with the present study — have succeeded in showing the characteristic affective startle modulation with augmented startle amplitudes after negatively valenced stimuli [27, 47], whereas others did not [26, 48, 49]. The present study provides evidence that the affective startle modulation found in healthy samples can also be found in patients with depression. Summarizing, neither self-report nor startle data indicate profound differences between patients and controls when interpreting ambiguous information.

Regarding modulation of startle responses, we found comparable amplitudes for ambiguous and unambiguous negative information in both groups, contrary to the hypothesis derived from the work of Lawson et al. [17]. According to their results, startle responses for ambiguous information should have been comparable to unambiguous neutral information in controls but comparable to unambiguous negative information in patients. Consequently, the question arises why our results deviate from those of Lawson et al. [17]. Interestingly, it is the controls

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that react differently compared to the low BDI group in Lawson et al. [17]. Even if a direct comparison of groups between studies should be taken cautiously, it would be interesting to know if this result is due to differences in the method (e.g. potential differences in instruction or difficulty of the task) or reflects differences in processing of the stimuli between both control groups. As in the aforementioned study [17], no interrogation regarding interpretation of ambiguity was conducted, and it is not known if their subjects differ in this regard. If their low BDI group had interpreted significantly more words neutrally than the high BDI group, it could have substantially influenced startle responses. Another explanation for the discrepancy may be that Lawson et al. [17] examined students divided into two extreme groups according to their BDI scores. The average BDI score in the high BDI group was 15.78 (SD = 7.66), which is possibly not comparable to the extent of depressive symptoms of the inpatients examined in the present study (BDI: mean = 29.25, SD = 12.82). Previous studies have shown qualitative differences between severe and mild depression in the blink reflex, and therefore emotional processing [e.g. 25]. Thus, the relation between blink reflex magnitudes and symptom severity may not be linear. However, this qualitative difference between inpatients and students scoring high on the BDI cannot explain our finding that both patients and controls showed higher startle amplitudes for ambiguous words which were comparable to unambiguous negative words. This result in the affective startle modulation suggests that both patients and healthy controls may have interpreted ambiguous stimuli as aversive or negative. Notably, direct interrogation revealed that participants rather preferred the neutral over the negative interpretation when confronted with ambiguity. Even if dissociations between subjective interrogation (explicit valence) and affective startle modulation (implicit valence) could be confirmed [50, 51], it seems unlikely that the blink magnitudes can be explained by a mere target valence effect. Since the explicit interpretation of the ambiguous stimuli cannot account for the startle findings, it needs to be discussed as to why the ambiguous stimuli elicited startle responses comparable to unambiguous negative stimuli. Two potential explanations may apply: defensive mobilization and/or attention processes. First, an implicit and automatic process to categorize the stimulus, diverging from the explicit process, may exist [52]. Possibly, categorizing ambiguous stimuli implicitly as aversive may result in enhanced arousal and the mobilization of defensive resources, indicating an adaptive and phylogenetic functionality. Due to the automaticity of the defensive reflex, this modulation (i.e. enhanced defensive responses to ambiguous comparable to unambiguous negative stimuli) is not reflected in explicit measures. Second, participants in the experiment might have allocated heightened attention to processing the ambiguous stimuli when deciding which word they had heard. It is known that increased attention to the relevant sensory dimension influences startle magnitudes [53–56], so that greater startle responses found in the ambiguous condition could reflect additional cognitive effort dedicated to the auditory sensory channel. However, it can also be argued that attention might have decreased startle responses, when attention is shifted from the sensory dimension to more internal processes [57] such as imagery of personal situations. Although both explanations might be applicable, it still remains unanswered as to why the low BDI group in Lawson et al. [17] did not display increased startle responses towards ambiguous stimuli. In contrast, participants in the present study had to imagine a personal situation evoked by the presented word. Perhaps in the ambiguous condition participants got irritated because they did not really understand what they heard and therefore experienced negative mood because they could not properly fulfil the task. This negative mood would be totally independent from actual word valence and might have been absent in the low BDI group of Lawson et al. [17]. Furthermore, imagining a personal situation in the present study, thus fostering self-focusing and self-relevance, could also influence the results. One might speculate that in Lawson et al. [17] ambiguous words evoked the image of personal situations in high BDI students but of personally irrelevant situations in low BDI students. Unfortunately, we cannot disentangle these explanations with our study.

Several limitations in the present study need to be considered. First, educational background and verbal intelligence differed between groups, which might have influenced results as language processing and word comprehension also depend on these variables. Second, patients were medicated and received psychotherapy which might have influenced a negative interpretation bias, e.g. by targeting it in psychotherapeutic strategies. Studies found that antidepressants and benzodiazepines can reduce startle responses [17, 58–60]. This, together with heterogeneous treatment regimens and hospitalization durations, constitutes a major caveat. It would be desirable to investigate drug-naïve patients before beginning psychotherapeutic treatment, even though this is not easy to achieve. Third, the investigated groups were rather small, which may have prevented findings of meaningful differences due to statistical power problems. However, effect size calculations and power analyses [61] for the startle data indicated that sample size was sufficient and between-subject differences were in fact not meaningful (estimated sample size would have to be nearly 500). Nonetheless, larger samples should be investigated to further validate the findings.

There are further limitations. The startle sound level was rather low compared to most other studies, which might have concealed effects. Furthermore, the actual instruction to imagine a personal situation according to the understood word differed from the study of Lawson et al. [17] (see above). Thus, plenty of associations could have been evoked by this and sometimes it was not possible to definitely decide whether these imaginations were negative or neutral. Here, we only asked for detailed information about the ambiguous words. Future studies using this paradigm may directly ask for valence and arousal of the personal situations in the ambiguous and unambiguous conditions, preferably on a trial-to-trial basis. The replication of the known affective startle modulation, the comparable pattern for patients and the high BDI group in Lawson et al. [17], and the reasonable effect sizes might at first sight put these limitations into perspective and support the validity of our findings. However, the influence of the above-mentioned limitations cannot be ruled out in our study and need to be cautiously taken into account when drawing conclusions.

In sum, the present study succeeded in showing an affective startle modulation for a sample of depressed patients comparable to healthy controls. Furthermore, we did not find a negative interpretation bias in severely depressed inpatients. That ambiguous stimuli yield comparable results with unambiguous negative stimuli might be explained by additional attentional resources or by an implicit labelling of ambiguous information as negative. Future research is desirable to elucidate the specific impact of attention on ambiguous information processing.

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