Affective Modulation of the Startle reflex in Schizophrenic patients

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Preface

This research project was performed as a part of the study Psychology at the Erasmus University Rotterdam, the Netherlands. It was performed at the department of Psychiatry at the Erasmus Medical Centre in Rotterdam.

First of all, I would like to thank Roelie Hempel and Joke Tulen for their daily support, comments and advice. Thank you both for your patience, swift feedback and for making my stay a pleasant time and a valuable learning experience. Second, thanks to Ingmar Franken for his supervision and comments on my thesis.

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Abstract

Startle eyeblink reflex can be influenced by valence of emotion. This is known as affective modulation of the startle reflex. This effect can provide an objective measure of emotional processes. Schizophrenic patients are known to have emotional disturbances. The aim of this study was to investigate whether patients with schizophrenia differ from healthy controls in their involuntary eyeblink response on an affective startle modulation task. Affective modulation of the startle reflex was studied in 17 schizophrenic patients and 33 healthy controls to investigate possible emotional deficits in schizophrenic patients. Moreover, subjective evaluations of the pictures were investigated to examine potential differences in subjective emotional experience.

Results indicated that there were no significant differences in the affective modulation of the startle response to the pictures between patients and controls. Furthermore, there were no significant differences in the subjective valence ratings of the pictures between patients and controls. Schizophrenic patients rated all pictures as more arousing, but the pattern of the arousal ratings of patients did not differ from that of the controls.

These findings suggest that involuntary emotional reactions as well as subjective emotional experience are unimpaired in schizophrenia. However, because patients as well as controls did not exhibit a prototypical startle pattern, it cannot be conclusively argued from this data that schizophrenics have a normal affective startle modulation. Further research is needed to conclude if schizophrenics have deficits in affective startle modulation.

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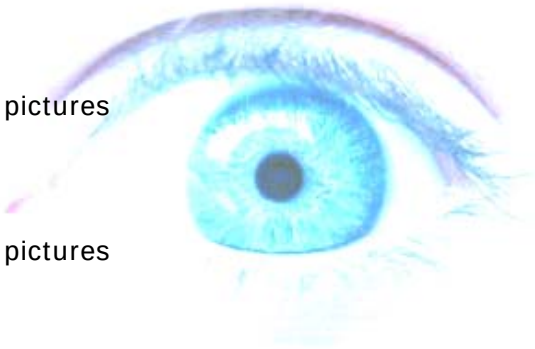

Introduction

Schizophrenia is a serious psychiatric illness. The lifetime prevalence of schizophrenia (1%) is lower than other psychiatric illnesses such as depression or anxiety. However, the illness has a chronic course and often a more poor prognosis compared to these other psychiatric illnesses (Gelder, Mayou & Geddes, 2005). Although the presentation of the symptoms of schizophrenia varies a great deal between patients, the illness can be characterized by three types of symptoms: psychotic symptoms, negative symptoms and cognitive impairment (Mueser & McGurk, 2004).

Psychotic symptoms are most characteristic of schizophrenia. These symptoms entail the loss of contact with reality. Delusions (false beliefs) and hallucinations (bizarre perceptual experiences) are among the most striking features of schizophrenia. Psychotic symptoms in schizophrenia tend to be acute and episodic.

States in which basic emotional or behavioral processes are diminished or absent compile the negative symptoms of schizophrenia. Among these symptoms are anhedonia (inability to experience pleasure), blunted affect, apathy (lack of initiative and drive) and alogia (reduced speech). These negative symptoms have a propensity to be chronic.

Cognitive impairment is also a common feature of schizophrenia. Cognitive impairments include reduced attention and concentration, poor learning and memory and problems with executive functions such as planning and organization.

The symptoms described above illustrate that schizophrenia involves serious cognitive disturbances. Besides these cognitive disturbances, schizophrenic patients also experience various emotional disturbances. Emotional disturbances in schizophrenia consist of a wide range of deficits, in addition to the aforementioned symptoms such as anhedonia and blunted affect. Reviewing the research on emotion processing in schizophrenia, Shayegan and Stahl (2005) found schizophrenics to have difficulties identifying and processing emotional information. More specifically, emotion expression and recognition are impaired in schizophrenic patients. For example, schizophrenics show fewer outward signs of emotion (Aghevli, Blanchard & Horan, 2003) and have difficulties recognizing emotions from facial expressions in others (Mueser et al., 1996). These impairments can lead to difficulties in social interactions. One of the methods to study emotional processes and emotional deficits in schizophrenia is the method of cue-modulated startle reflex.

Startle reflex

The startle reflex can be used as an effective objective measure of attentional and emotional processes (Vrana, Spence & Lang, 1988). The startle response is usually measured by recording of the eyeblink reflex in response to an unexpected sensory event: the startle stimulus or probe. Although the startle response is not a modality

specific response, the startle probe is usually presented in the form of a loud noise burst (Bradley & Lang, 2000). The eyeblink reflex can be characterized as an involuntary reaction to a startle probe and is the first, fastest and most stable autonomic response to startle stimuli (Lang, Bradley & Cuthbert, 1990). Furthermore, the eyeblink reflex is resistant to demand aspects and response bias. In startle research, the amplitude of the eyeblink reflex is commonly measured by use of EMG (electromyography). This method is widely used because it is straightforward and relatively inexpensive (Grillon & Baas, 2003).

Startle modulation

The amplitude of the startle reflex can be influenced by a stimulus preceding the startle probe. This process is known as startle modulation. There are two ways in which a preceding stimulus can influence the response to a startle probe, namely attentional and affective modulation.

Attentional modulation occurs when a nonstartle-eliciting stimulus precedes the startle probe by a short duration (Bradley, Cuthbert & Lang, 1993). The startle response is then attenuated compared to the response without a preceding stimulus or prepulse. This effect is also known as prepulse inhibition (PPI). It is hypothesized that the attentional resources allocated to the prepulse will draw attention away from the startle probe, thereby attenuating the startle response (Lang et al., 1990). The underlying construct of PPI is believed to be the process of sensorimotor gating. In this process, excess stimuli are ‘gated out’ of awareness so that attention can be focused on the most important aspects of the environment (Braff, Geyer & Swerdlow, 2001). Sensorimotor gating thereby serves the function of avoiding behavioral interference that might arise from the simultaneous processing of different stimuli (Kumari & Sharma, 2002).

Affective modulation is an emotional process rather than an attentional process. When a startle probe occurs in the context of an emotional state of the subject, the startle response is influenced by this emotional state. Lang et al. (1990) suggested that this effect is caused by an affective match or mismatch. The startle probe elicits negative affect. When this matches the emotional foreground (i.e. when a person is in a negative emotional state), the startle response is enhanced. If there is a mismatch, with a negative startle probe and a positive emotional state, the startle response is inhibited (Bradley, Cuthbert & Lang, 1990).

In a typical paradigm to record affective modulation of the startle reflex, subjects are viewing pictures of varying emotional valence. A startle probe is then presented, usually in the form of a loud noise burst. The startle reflex is found to be enhanced when viewing aversive pictures compared to neutral ones. Also, the startle reflex is reduced when viewing pleasant pictures, compared to neutral pictures. However, this latter finding is

controversial and not as widely replicated as the startle potentation in response to aversive pictures (Grillon & Baas, 2003).

Bradley et al. (1993) studied the temporal relationship between affective modulation effects and PPI. Subjects in this study viewed pleasant, neutral or unpleasant slides for 6 seconds. An acoustic startle probe was presented at either 300, 800, 1300 or 3800 ms after slide onset. They found that probe times (i.e. time between stimulus/picture onset and startle probe) of 800, 1300 and 3800 ms are sensitive to affective modulation effects. At 300 ms effects of prepulse inhibition were observed. However, the finding of affective modulation effects is contradictory for probe times under 1000 ms. Volz et al. (2003) also investigated the temporal course of startle modulation using the same probe times as Bradley et al. (1993). They found that for the earlier probe times (300 and 800 ms) attention-related processes are dominant. Affective modulation of the startle occurred for the later probe times (1300 and 3800 ms).

Summarizing, attentional modulation or PPI and affective modulation of the startle reflex are two related processes of startle modulation that occur within different time windows.

Startle modulation as a measure of emotional dysregulation in psychopathology

The affective startle paradigm has been used as a measure for emotional dysregulation in different psychiatric groups, for example depressed patients and psychopaths. A few of these studies will be described hereafter.

Allen, Trinder & Brennan (1999) studied affective modulation of the startle reflex in depressed participants. They found that while the moderately depressed group showed a normal response pattern, the severely depressed patients showed a disturbed startle pattern. Specifically, they showed that the startle response was potentiated while viewing pleasant pictures, suggesting that depression might be associated with aversive responses to pleasant stimuli. Kaviani et al. (2004) also investigated startle modulation in depressed patients. They found a lack of startle modulation, but only for the highly depressed patients or patients with high levels of anhedonia. These results show that reactivity to pleasant and even unpleasant stimuli is diminished in severely depressed and anhedonic patients.

Miranda et al. (2003) studied affective modulation of the startle reflex in alcoholics with antisocial personality disorder. Results indicated a lack of startle potentation for negative pictures and a lack of startle inhibition for positive pictures in this group, compared to healthy controls and an alcohol-dependent group who showed a normal pattern of affective startle modulation. Psychopaths have been found to show a lack of normal startle modulation. Specifically, they show startle inhibition for both the pleasant and unpleasant pictures (Patrick, Bradley & Lang, 1993; Levenston et al., 2000). These

results can indicate a stronger threshold for unpleasant information or negative emotion in the psychopaths.

Although this is not a complete overview of the numerous studies using the affective startle paradigm, the aforementioned studies illustrate the use of this paradigm to investigate emotional processes in psychiatric groups.

Startle modulation in schizophrenic patients

There is ample evidence that PPI is disturbed in schizophrenic patients (Cadenhead et al., 2000; Dawson et al., 1993; Dawson et al., 2000; Ludewig et al. 2002; Ludewig et al., 2003; Meincke et al., 2003). In a review on human studies of prepulse inhibition of startle, Braff et al. (2001) found PPI to be reduced in the schizophrenic population. Specifically, the normal reduction of the startle response in the presence of a prepulse is absent. It is believed that the underlying mechanism of sensorimotor gating is disturbed. Schizophrenics may have problems filtering excess stimuli out of awareness. This is consistent with the observation that schizophrenics have problems filtering unwanted thoughts (Grillion & Baas, 2003). Although attentional modulation of the startle response has been investigated extensively in schizophrenics, there have been few studies on affective modulation in schizophrenic patients (Gooding et al., 2002).

Schlenker, Cohen & Hopmann (1995) studied affective modulation in schizophrenics and healthy controls. They presented their subjects with pleasant, unpleasant and neutral slides. An acoustic startle probe was delivered at 3.7 or 5.1 seconds after slide onset. They found that schizophrenics differed significantly in their response to the startle probes compared to healthy subjects. There was no difference between the groups in their response to neutral or positive pictures. However, the schizophrenic group showed no difference in their blink amplitudes to unpleasant and neutral pictures. This indicates an absence of normal startle potentation while viewing unpleasant pictures.

Curtis et al. (1999) conducted a similar study with schizophrenic patients, their first degree relatives and healthy controls to investigate if abnormal affective startle modulation could be indicative of a genetic risk for schizophrenia. This study revealed that schizophrenics and their relatives did not differ in their affective modulation compared with normal controls. They concluded that, although there are many emotional disturbances in schizophrenia, the involuntary response to affective stimuli is intact.

Volz et al. (2003) investigated affective startle modulation in schizophrenia patients using different probe times. They found no difference in affective startle modulation between schizophrenics and controls for the later probe times (1300 and 3800 ms). However, the startle potentation for unpleasant pictures was absent for the earlier probe times (300 and 800 ms) in schizophrenic patients. This suggests that patients with schizophrenia need more time to process the aversive pictures.

Present study

There is still controversy in the field of affective modulation in schizophrenic subjects. There are many reports of disturbed emotion in schizophrenia, and it is possible that the modulation of the startle reflex is also disturbed. From the studies mentioned above, there is no consensus on whether affective startle modulation is disturbed in schizophrenics. The aim of the present study is to examine the influence of emotion on the startle reflex, and investigate whether patients with schizophrenia differ from healthy controls in their involuntary eyeblink response on an affective startle modulation task. Patients and controls will be compared using the affective startle paradigm, where the eyeblink response to a startle probe is measured while subjects are viewing emotional pictures. This study may contribute to increase our insight in the field of disturbances of emotional processing in schizophrenia.

It is hypothesized, based on previous research on affective modulation (Schlenker et al., 1995), that schizophrenics will show an abnormal response pattern of the startle reflex compared to healthy control subjects. Specifically, the startle potentation while viewing aversive pictures will be reduced, compared to control subjects.

Furthermore, the subjective evaluation of the pictures will be investigated to examine whether patients and controls differ in their subjective emotional experience of the pictures.

Methods

Participants

Participants consisted of 17 patients with schizophrenia (age range 16 to 33 years, mean=23.65 years, S.D.=5.33; 3 women*)* and 33 healthy controls (age range 18 to 32 years, mean=22.52 years, S.D.=3.48; 4 women*)*. Patients were rated on the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein & Opler, 1987) by a psychiatrist. Mean total PANNS-score for the patient group was 67.60 (S.D.=19.15).

The patients with schizophrenia were inpatients recruited from the psychiatry ward at the Erasmus Medical Centre, Rotterdam, the Netherlands. Patients were diagnosed according to DSM-IV criteria (American Psychiatric Association, 1994) by a senior psychiatrist. Patients were included if they met the criteria for schizophrenia, schizo-affective disorder, or if they were experiencing a first psychotic episode suggestive for the schizophrenia or schizo-affective syndrome. Patients were informed of the study by the same psychiatrist. If they were interested to participate, patients were informed extensively of the study, both orally and in writing.

Eleven patients used antipsychotic medication. Two patients used typical antipsychotics (haloperidol) and nine atypical antipsychotic medication (5 olanzapine, 4

risperdal). Four of them also used benzodiazepines (lorazepam). Six patients were unmedicated at the time of testing.

Control subjects were recruited by means of advertisement and were primarily medical or psychology students. Control subjects were included if they were physically healthy and drug-free at the time of the experiment (with the exception of the birth control pill for women). Furthermore, controls were excluded from participation in the study if they or their first-degree relatives had any history of psychiatric illness. They were informed of the study by means of an information form. Control subjects received either a monetary reward or course credits for their participation in the study.

The study was approved by the Ethical Committee of the Erasmus Medical Centre, Rotterdam, the Netherlands. All subjects provided written informed consent.

Stimulus material

Forty-eight coloured pictures (sixteen neutral, sixteen positive and sixteen negative) were selected from the International Affective Picture System[1] (IAPS; Centre for the Study of Emotion and Attention, 1999). Neutral pictures included pictures of household objects and nature scenes. Positive pictures included pictures of money, thrilling sports and erotic nudes. Negative pictures included threatening scenes (e.g. aimed guns, knives) and pictures of mutilations. Threat and erotica scenes are believed to induce the greatest modulation of the startle reflex (Bradley et al., 2001). Each picture was presented on a computer screen for 6 seconds. The intertrial interval differed from 10-25 seconds. Pictures were presented in a random order for each participant.

The startle probe consisted of a 50 ms burst of 100-dB noise with instantaneous rise and fall times. The probe was presented binaurally through headphones. The startle probes were presented either 300, 800, 1300 or 3800 ms after stimulus onset. Pictures of each valence category occurred equally in each of the different time conditions. Startles were presented in 75% of all trials. Moreover, 12 startles were delivered during the intertrial interval for purposes of unpredictability.

Procedure

The experimental session always took place in the morning. Participants were asked to refrain from having any coffee or cigarettes before and during the laboratory session. The data were collected during a single session (duration 45 minutes). In the laboratory session, physiological sensors were attached and headphones were placed. Subjects sat

[1] IAPS: negative: 3000, 3010, 3065, 3069, 3080, 3102, 3120, 3170; 6200, 6212, 6230, 6260, 6300, 6313, 6350, 6550; neutral: 5120, 5510, 5530, 5535, 5711, 5731, 5740, 5900, 7000, 7002, 7004, 7006, 7009, 7010, 7020, 7025; positive: 4220, 4290, 4490, 4520, 4608, 4660, 4670, 4680; 5260, 5470, 5621, 5910, 8030, 8170, 8490, 8501.

in a chair approximately 70 centimeters from the 19 inch computer screen. The experiment started with a five minute resting period. After five preliminary startle probes were delivered, participants were instructed that a series of pictures would be presented. They were informed to sit relaxed, watch the fixation point and look at the pictures the entire time they were on screen. Participants were told that they would occasionally hear loud noises through the headphones like they heard before, and that they could ignore these noises. Then, the pictures were presented on the screen and the probe stimuli were presented. The experimenter was seated behind the subject. The headphones were removed directly after the experiment. After another five minute resting period, all physiological sensors were removed. Then the same pictures were presented again on the screen. In this second task the participant was asked to subjectively rate the pictures on two dimensions, valence and arousal, using a computerized version of the Self-Assessment Manikin (SAM; Bradley & Lang, 1994).

Physiological measures

According to the guidelines described by Blumenthal et al. (2005) startle reflex was measured using Ag/AgCl-electrodes filled with electrode paste. The skin below the eye was cleaned with alcohol to reduce skin impedance. Two cup electrodes were then placed below the left eye, on the orbicularis oculi muscle, approximately 10 mm apart. The medial electrode was placed in line with the pupil. The EMG signal was recorded with a portable digital recorder (VITAPORT^{TM} System; TEMEC Instruments BV, Kerkrade, The Netherlands) and digitized using Columbus software, with a sampling rate of 1024 Hz. Online filters were used with a lowpass of 500 Hz and a time constant of 0.015 seconds.

Self-report measures

Demographic data on the subjects were collected using a self-report form. Subjective evaluation of the IAPS-pictures was measured using a computerized version of the Self-assessment manikin (SAM). Subjects were asked to rate all pictures on a scale from 1 to 9 regarding valence (1=very unpleasant and 9=very pleasant) and arousal (1=very calm and 9=very aroused).

Data reduction and analysis

All physiological signals were analyzed using specialized software. The eyeblink EMG responses were digitally rectified and then smoothed. Eyeblink responses were also visually inspected to reduce baseline contamination due to noise or movement artefacts (Blumenthal et al., 2005).

The eyeblink response was defined as the relative amplitude of the peak response. The relative peak amplitude was calculated as the amplitude of the peak response minus

the amplitude at the time the response exceeded the mean baseline by two standard deviations. Baseline activity was determined over a 50 ms interval preceding the startle stimulus. Startle responses were not scored if the peak response did not exceed the prestimulus baseline level plus 2 standard deviations. Furthermore, if the eyeblink response occurred outside the 20-100 ms time window, the trial was rejected and excluded from further analysis. Following the criteria defined by Graham and Murray (1977), participants with more than 33% missing trials were excluded from further analysis. Two participants were excluded from analysis (one control subject and one patient) because they exhibited little or no startle reflex.

For purposes of the present paper, only the startle responses at the later probe times (1300 and 3800 ms) were used for analysis. These probe times were averaged to enhance power. The startle response magnitudes for the later probe times were subsequently analyzed using a repeated measures analysis of variance (ANOVA). A 2 x 3 design with group (patients vs. controls) as between subjects variable and picture category (negative vs. neutral vs. positive) as a within subjects variable was used.

The subjective experience of the IAPS pictures was also analyzed for arousal ratings and valence ratings, using separate repeated measures ANOVA's, with a 2 (group) x 3 (picture category) design.

For all ANOVA's a Greenhouse-Geisser correction on the degrees of freedom was used when appropriate. An alpha-level of 0.05 was used for all statistical analysis.

Results

Startle response

The relative response amplitudes of the startle reflex elicited during negative, neutral and positive pictures for the control and patient group are reported in figure 1 and table 1. The results of the repeated measures ANOVA with the relative amplitude of the startle response as a dependent variable did not reveal a main group effect [$F(1,46)=1.82$, n.s.].

Startle responses were modulated by picture category, the main effect for picture category was significant [$F(2,92)=4.84$, $p<.05$]. Post hoc contrasts revealed that relative response amplitude was significantly higher for the negative than for the positive pictures [$F(1,46)=10.90$, $p<.01$]. The responses to the positive pictures were significantly lower than for neutral pictures [$F(1,46)=4.26$, $p<.05$]. However, the responses to the negative pictures did not significantly differ from the neutral picture category [$F(1,46)=.78$, n.s.].

The group by category interaction effect was not significant [$F(2,92)=1.59$, n.s.]. This indicates that there was no difference for the two groups in their response to the different picture categories.

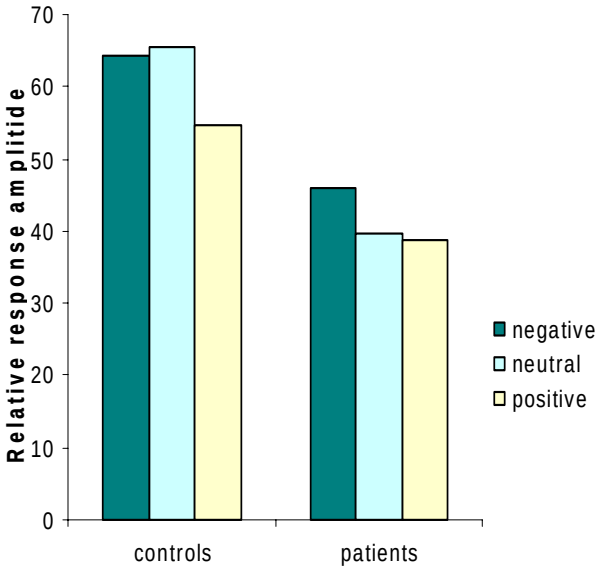

Figure 1: Relative amplitude of the startle response (in microvolts)

	Control subjects (N=32)	Schizophrenia patients (N=16)
Negative pictures	64.25 (58.97)	46.06 (32.09)
Neutral pictures	65.60 (60.64)	39.55 (27.59)
Positive pictures	54.66 (49.69)	38.84 (30.52)

Table 1: Mean (S.D.) relative response amplitude (in microvolts)

Subjective ratings of the pictures

Means and standard deviations of the SAM ratings of the pictures on valence and arousal are presented in table 2.

	Control subjects (N=32)			Schizophrenia patients (N=16)		
	Affective categories			Affective categories		
	Negative	Neutral	Positive	Negative	Neutral	Positive
SAM valence rating	3.06 (0.97)	5.30 (0.65)	6.32 (0.76)	2.43 (1.69)	5.34 (0.62)	6.38 (0.83)
SAM arousal rating	4.48 (1.55)	2.22 (1.31)	3.81 (1.36)	5.36 (2.43)	3.38 (1.70)	4.68 (1.74)

Table 2: Mean (S.D.) subjective ratings of the IAPS pictures on valence (1=very unpleasant to 9=very pleasant) and arousal (1=calm to 9=very aroused)

Analysis on the valence ratings revealed that there was no difference between patients and controls in their subjective evaluation of the pictures: the category by group interaction effect was not significant [$F(1.46,67.04)=2.30$, n.s.]. There was no main group effect [$F(1,46)=0.83$, n.s.]. The picture categories were rated significantly different on valence [$F(1.46,67.04)=202.25$, $p<.001$]. Picture ratings on valence were

consistent with the a priori designation of the pictures into categories. Ratings on valence increased from negative to neutral to positive pictures, linear trend analysis [$F(1,46)=250.37$, $p<.001$].

There was no significant interaction effect for category by group, patients and controls did not significantly differ in their subjective arousal ratings of the different picture categories [$F(1.46, 67.25)=0.28$, n.s.]. There was, however, a main group effect [$F(1,46)=5.19$, $p<.05$]. All pictures were rated more arousing by schizophrenic patients. Furthermore, there was a significant main effect for picture category [$F(1.46,67.25)=48.74$, $p<.001$]. Affective pictures were rated more arousing than neutral pictures [negative: $F(1,46)=68.49$, $p<.001$; positive: $F(1,46)=109.79$, $p<.001$]. Negative pictures were rated more arousing than positive pictures [$F(1,46)=7.51$, $p<.01$].

Discussion

In the current study, affective modulation of the startle response was investigated in patients with schizophrenia and healthy control subjects. The affective startle paradigm was used to assess possible differences in emotional processing in schizophrenia compared to control subjects. It was hypothesized that schizophrenic patients and healthy controls would differ in their affective modulation of the startle reflex. Specifically, the startle potentation for the negative pictures would be reduced in schizophrenic patients. Moreover, subjective evaluation of the pictures on valence and arousal were analyzed to investigate possible differences in emotional experience.

Startle modulation

Analysis of the startle data revealed that startle responses were modulated by picture category. Responses to the positive pictures were smaller than to neutral and negative pictures. However, there was a lack of startle potentation for negative pictures compared to the neutral pictures. There were no differences in the responses to the different picture categories between patients and controls. These findings indicate that schizophrenics do not differ in their responses to the startle probes compared to healthy controls. This is consistent with previous findings by Curtis et al. (1999) and Volz et al. (2003). They found no differences in affective modulation between schizophrenic patients and controls. This indicates that involuntary emotional reactions are unimpaired in schizophrenia. The present findings could not support the hypothesis that schizophrenics differ in their affective modulation of the startle compared to controls. Moreover, the data collected in this study seem to suggest that schizophrenic patients do not show a reduced startle potentation in response to negative pictures, but rather an absence of startle inhibition in response to positive pictures. This could indicate that there is a diminished

responsiveness to positive stimuli in schizophrenia. Although abnormal processing of positive stimuli has been primarily linked with depression (Grillon & Baas, 2003), it is possible that specific symptoms of schizophrenia are also related to deviant processing of positive stimuli.

Subjective ratings of the pictures

Analysis of the subjective valence ratings indicated that there were no significant differences between patients and controls in their experience of the different picture categories. The subjective experience of the pictures was consistent with the a priori designation of the pictures into categories. Valence ratings of both groups increased linearly from negative to neutral to positive pictures.

Arousal ratings were found to be consistently higher for schizophrenic patients. They rated all pictures as more arousing. However, subjective arousal ratings did not differ in pattern for the different picture categories for patients and controls. Affective pictures were rated as more arousing than neutral pictures.

These results indicate that there are no differences in subjective emotional experience between patients and controls regarding valence. Although patients rated all pictures as more arousing, overall, patients and controls did not differ in their pattern of subjective ratings for the different picture categories. The fact that there were no differences in subjective emotional experience between patients and controls supports the finding that startle modulation also did not differ for the two groups.

Limitations

There are several limitations that need to be considered when the results of this study are interpreted. Most important, the control subjects in this study did not show a normal affective modulation pattern. The startle potentation while viewing negative pictures was absent. This finding makes it difficult to draw any conclusions from this data, because it is unclear whether the lack of startle modulation in the control sample is due to procedural flaws. The lack of affective startle modulation in the control group could not be explained by deviant subjective experience of the pictures.

While the subjective ratings of the pictures were consistent with the a priori designation of the pictures into valence categories, it is possible that the stimuli used were insufficiently arousing, especially for the control group. Research has shown that affective modulation effects are highly dependant on arousal level (Bradley & Lang, 2000). Cuthbert, Bradley & Lang (1996) found that affective modulation effects were strongest for both negative and positive pictures if arousal was high. Surprisingly, they found inhibition of the startle response for moderately arousing negative pictures. They consequently concluded that arousal is an important moderating variable in this field of

research. In the current study, the subjective arousal ratings of the pictures were relatively low, especially for the control group. It is possible that the negative pictures were insufficiently arousing for the control subjects. This might provide an explanation for the lack of normal startle modulation for the negative pictures in the control group. However, the negative pictures (mutilations, threat) used in this study are among the pictures usually rated highest in arousal (Bradley et al., 2001). It is therefore more likely that the control subjects had a tendency to moderate their responses on the SAM.

Furthermore, it is possible that some effects have gone undetected due to the low power of the design. The lack of significant findings for the startle response data can possibly be explained by the large standard deviation within these data and the low sample size, especially for the patient group. Also, because only the stimuli presented at the later probe times of 1800 and 3800 ms were used for the present study, only half of the stimuli presented in this study were used for analysis. Besides lowering the power, this has the consequence that not all pictures that the subjects viewed were used for analysis. Perhaps different pictures of similar valence elicited different startle responses. However, because the pictures and probe times were randomized for each participant, it is not likely that this would have influenced the results.

Schizophrenia is a very heterogeneous disorder. The symptoms vary to a great extent between patients. This variation within the patient group may provide an explanation for the lack of consensus from research up to date on whether schizophrenics differ from controls in their affective startle modulation. It is possible that only specific symptoms of schizophrenia are related to deviant affective modulation (Grillon & Baas, 2003). For example, anhedonia or flat affect in schizophrenic patients has been thought to be of influence on emotional processing (Gooding et al., 2002; Suslow, Roestel & Arolt, 2003). Although results up to date have failed to link anhedonia with deviant affective modulation in schizophrenic patients, it is conceivable that specific symptoms are responsible for differences in affective modulation within a schizophrenic patient group. In a heterogeneous patient group, these specific symptoms might not be present, resulting in a lack of significant findings.

Furthermore, the sample included several patients with a first psychotic episode. The diagnosis for these patients as schizophrenic is confirmed after six months. It was not within the time-frame of this study to wait for the confirmation of this diagnosis. Therefore it is possible that non-schizophrenic patients were included in the sample.

Finally, another limitation of this study concerns the fact that most patients (65%) in this sample used medication. Typical and atypical antipsychotic medication have been known to have a normalizing effect on attentional modulation of the startle (Kumari & Sharma, 2002; Weicke, Bauer & Hamm, 1999). Although the effects of medication on affective startle modulation is unknown, it is possible that the medication has a

normalizing effect on both types of startle modulation. Some patients also used benzodiazepines. Although to date, the effects of benzodiazepines seem inconsistent in human studies it is possible that these drugs influenced the results (Grillon, 2002).

Conclusion

In summary, results indicated that patients with schizophrenia did not differ in their affective startle modulation from control subjects. This suggests that involuntary emotional reactions, like the emotion-modulated startle reflex, are unimpaired in schizophrenia. However, since the normal control group did not show the typical affective modulation pattern, concluding that schizophrenics have a normal affective startle modulation would be premature.

Furthermore, although schizophrenic patients rated all pictures as more arousing, there were no differences between patients and controls in their subjective evaluation of the different picture categories. This suggests that schizophrenics and controls do not differ in their subjective emotional experience of emotional pictures.

Further research is needed to confirm definitively if patients with schizophrenia do not differ in their affective startle modulation. Future research should include larger patient samples and preferably include unmedicated patients.

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