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Regine Schlenker · Rudolf Cohen · Gereon Hopmann

Affective modulation of the startle reflex in schizophrenic patients

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Abstract Startle-elicited blinks were measured during the presentation of affective slides in order to investigate emotional responsiveness in 24 male healthy subjects and 34 male schizophrenic patients. Although the two groups did not differ with regard to their subjective and autonomic responses to the slide stimuli, there was a significant difference between the groups in their responses to the startle probes. Patients rated low in affective expression showed a linear response pattern comparable to that of normal controls with largest amplitudes during unpleasant slides and smallest during pleasant slides. Patients without apparent deficit in affective expression showed a quadratic relationship with smaller blink amplitudes during both pleasant and unpleasant slides. Diminished affective expression rated on the basis of a clinical interview is not associated with a general attenuation of the blink reflex or of its modulation by exposure to emotional slides. Thus, we found no indication of an impairment in the perception of affective stimuli nor of reduced appreciation of pleasant stimuli (anhedonia) in these patients.

Key words Schizophrenia · Startle response · Reflex modulation · Affective stimuli · Affective expression

Introduction

Affective impairment has long been considered an important feature of schizophrenia. According to Bleuler (1911) "core" symptoms of the disease are abnormalities in association, autism, ambivalence, and affect. Bleuler described blunting or flattening of affect as well as parathymia in patients with schizophrenic disorders. The transition from acute psychosis to chronic stages of the disorder was considered to be accompanied regularly by a loss of affective responsivity (Bleuler 1920). The importance of disordered affect for prognosis has been emphasized by several authors (e.g., Carpenter et al. 1978; Knight et al. 1979). Knight and Roff (1985) conclude from their comprehensive review of the literature that "More recent studies...have consistently found that thought-disorder symptoms lack prognostic utility. ...In contrast, affective deficits have consistently been found to predict poorer outcome among schizophrenic patients." (pp 280–281)

Within the framework of the concept of negative symptoms in schizophrenia, disordered affect has recently attracted new interest (Crow 1980; Andreasen 1982). In studies on negative symptoms patients are usually observed during clinical interviews, and global ratings of their emotional expressiveness and/or responsiveness are performed. In another approach, measurements of nonverbal affective modulation (e.g., by acoustic speech analysis or the Facial Action Coding System) during experimentally manipulated affect-provoking situations have been carried out in order to provide more objective measures of affective flattening or diminished affective expression (Andreasen et al. 1981; Alpert et al. 1989; Steimer et al. 1988; Schneider et al. 1990). Both global rating studies and experimental measurements confirm that schizophrenic patients differ from healthy controls in vocal as well as mimetic aspects of affective responses.

Several attempts have been made to define more closely the areas in which characteristic forms of disturbed affect may occur in schizophrenia; they range from hypersensitivity to emotional stimuli, particularly aversive stimuli (cf. Buss and Lang 1965), to hyposensitivity to emotional stimuli, particularly to a specific genetically determined indifference to positive stimuli, i.e., anhedonia (Meehl 1962, 1990). The sparsity of studies trying to validate such conjectures is most likely due to the difficulty to find experimental stimuli or situations that are both standardized and capable of provoking comparable affect in all subjects.

The present study uses an approach that has recently been shown to invoke a reliable measure of affective valence in healthy subjects. According to Lang (1985) an emotional response is determined by two orthogonal di-

Regine Schlenker (✉) · Rudolf Cohen · Gereon Hopmann
Department of Psychology, University of Konstanz,
Postfach 5560, D-78434 Konstanz, Germany

mensions: affective valence and arousal. Valence refers to the direction of the elicited action disposition, i.e., avoidance vs approach; arousal refers to the degree of activation of the response. Whereas electrodermal activity has been shown to vary primarily with the degree of arousal, it is indifferent to whether the eliciting stimulus is pleasant or aversive: Highly attractive stimuli increase electrodermal activity just as much as frightening stimuli. Valence, on the other hand, has been shown to affect primarily facial expression and the startle probe response. The latter measure has two important advantages over the assessment of facial expressivity: The startle probe response is not subject to voluntary distortion, and it can easily be quantified objectively. Studies with normal subjects have shown that the amplitude of the startle response to sudden and intense acoustic stimuli while the subject is asked to focus his or her attention on slides of pleasant, neutral, or unpleasant contents is a function of the valence of the emotional stimuli. The reflex amplitude is largest while the subject is viewing unpleasant slides, smaller in the context of neutral slides and smallest during the presentation of pleasant slides (Vrana et al. 1988; Bradley et al. 1988; 1990, 1991; Cuthbert et al. 1990).

According to Lang's theory of emotion (Lang et al. 1990) affective behavior is organized in terms of appetitive and defensive action dispositions across all levels of response complexity ranging from reflexes to highly organized behavior. As an inherently aversive stimulus the startle eliciting stimulus evokes defensive behavior such as eye closure (blink). While viewing an aversive slide the subject is in a state of aversive readiness, which matches and therefore increases the response to the startle stimulus presented in this context. Positive slides, on the other hand, prompt a state of appetitiveness, which counters the startle response and therefore attenuates its amplitude. Thus, the startle probe response may provide a direct measure of a subject's valence disposition in relation to emotional stimuli.

The purpose of the present study was to examine emotional responses of schizophrenic patients to a series of affect-laden slides. Patients were rated on their degree of affective flattening, which was mostly, but not exclusively, based on a global assessment of diminished facial and vocal expressiveness during a clinical interview. We hypothesized that patients with diminished affective expression do not show the startle modulation induced by the valence of emotional stimuli typically seen in normals. In addition, we wanted to investigate for Meehl's concept of anhedonia by testing whether patients who describe themselves as highly anhedonic in a questionnaire show diminished reflex inhibition relative to patients with low anhedonia scores.

Subjects and methods

A heterogeneous group of 34 male schizophrenic inpatients of the Psychiatric State Hospital Reichenau, as well as a group of 24 healthy men, participated in the study. Patients were included in the study when they fulfilled DSM-III-R criteria for schizophrenia. Patients were diagnosed on the basis of the Present State Examination (Wing et al. 1973) and clinical files. At the time of testing patients were largely free of psychotic symptoms, and many were considered close to discharge. The patients' ages ranged from 21 to 47 years (mean age 31.2 years), and number of years of education ranged from 8 to 13 years (mean 10.3 years). None of the patients were married; three were divorced. Age of disease onset was on average 24 years (range 18–35 years). Patients had been hospitalized for an average of 18 months (range 0–99 months). All except 3 patients were receiving neuroleptic treatment (mean 329 mg CPE; range: 0–733 mg CPE). Patients with any obvious extrapyramidal side effects according to clinical judgment were excluded. In a subsample of 22 schizophrenic patients extrapyramidal side effects were assessed with the Simpson/Angus Scale. Of these patients, 87% had total scores ≤ 3, and the others ≤ 9. Twelve patients received neuroleptic drugs with strong anticholinergic effects, mostly clozapine (11 patients), and 1 patient received antiparkinson medication. Patients with clozapine did not differ from patients with standard neuroleptics with regard to extrapyramidal side effects ($t = 0.70$; $df = 20$).

The control group was recruited from hospital staff or subjects who responded to a local newspaper advertisement. Subjects were asked about intake of psychopharmacological medication and their history of psychiatric problems, and were excluded from the study if there was a positive response. The mean age of normals was 32.2 years (range 23–50 years), and mean years of education was 11.1 years (range 9–13 years). Of the subjects, 92% were employed or were in school at the time of testing, and 30% were married.

Whereas age and years of education were comparable in the two groups, patients and controls clearly differed with regard to occupational and marital status.

Stimulus materials and presentation

Subjects were presented with a series of 27 stimuli selected to elicit emotional responses. The stimuli consisted of colored slides and varied along two dimensions: (a) valence (positive vs negative), and (b) level of arousal (high vs low). The stimuli were taken from a series that was provided by Lang et al. (1988). Nine of these slides were rated as extremely pleasant and exciting, nine slides were considered extremely unpleasant and exciting, and nine slides were of neutral valence and not exciting. Pleasant and unpleasant slides were considered comparably interesting. Pleasant slides depicted female nudes, appetizing food, a smiling child, and a pair of lovers; neutral slides showed household objects such as a basket, a fork, and a book; negative slides showed mutilated bodies, an aimed gun, a spider, and a starving child. Subjects sat in a reclining chair situated approximately 2 m from the screen. Slides were projected through a window from an adjoining room using a Kodak Carousel slide projector (Kodak, Stuttgart). Presentation and timing was controlled by a Hewlett Packard (HP 1000, Cupertino, California) minicomputer. Slides were presented randomly in blocks of nine with an equal number of positive, neutral, and negative slides within each block. There were three orders of presentation with each slide occurring equally often in the first, second, and third block.

On two-thirds of the slides (balanced over the three subsets of slides) an acoustic startle stimulus (50 ms white noise; 103 dB(A) with instantaneous rise time) was presented binaurally over Sony Dynamic Stereo headphones (Sony, Tokyo). The probe occurred 3.7 or 5.1 s after slide onset during the 6-s slide-viewing period. Additional startle probes were presented eight times during the interslide interval to minimize the predictability of the startle stimulus. The interslide interval varied randomly between 15 and 25 s.

Physiological measures

Skin conductance change, heart rate, and finger pulse volume (FPV) to emotional stimuli (slides) was measured, as well as the startle-probe response via the electromyogram of M. Orbicularis.

Slide presentation was triggered by a respiratory maximum during the predetermined interslide interval.

Blink responses to the startle probes were measured with Beckman miniature (Ag/ACl) electrodes positioned over the orbicularis muscle beneath the left eye. The signal was low-pass filtered at 1000 Hz and digitized at a sampling rate of 500 Hz. In addition, the raw electromyographic (EMG) signal was digitally filtered offline at 70 Hz (high-pass), rectified, and integrated at a time constant of 200 ms. Amplitudes (in arbitrary AD units) and latency (in ms) of the startle response were determined according to the algorithms of a program by Balaban et al. (1986).

Electrodermal activity was recorded from the medial phalanges of the third and fourth fingers of the left hand using 1-cm Beckmann Ag/AgCl electrodes filled with Unibase (0.05 *M*/l NaCl) electrode cream. Changes in skin conductance of more than 0.025 microSiemens (μS) beginning in the interval of 1–3.5 s after slide onset were counted as skin conductance responses to the slide stimuli.

The FPV was recorded using a Zack transilluminated photoplethysmographic transducer placed on the second finger of the left hand. The amplitudes of the finger pulses were determined by a computer program running on an IBM AT from the first to the seventh second after the beginning of the trial and related to the amplitudes measured during a baseline 7-1 s before slide onset. An FPV response was scored when a constriction of at least two standard deviations below the level predicted from the respective baselines appeared 1–7 s after slide onset.

Heart-rate activity was recorded from Beckman Ag/AgCl electrodes positioned on the right and left inner forearms (EKG Lead I). Amplifier and filter (30 Hz low-pass, time constant 0.03 s) were chosen in order to achieve a clear R-wave that exceedes a fixed threshold that functions as a trigger. Interbeat intervals were measured in milliseconds and transformed to heart rate (beats per minute) for each second of the slide interval and the preslide baseline. Heart-rate responses were defined as mean changes during the 6-s slide-viewing period from the 1-s baseline immediately preceding slide onset.

Procedure and additional assessments

Anhedonia

Subjects completed an inventory for the assessment of anhedonia. The inventory, considered to be equally applicable for normals and psychiatric patients, has been developed according to Chapman et al. (1976), and consists of 50 items on physical and social anhedonia. An item analysis based on the responses of 170 psychiatric patients indicated that all items could be combined in a total score (Cronbach's $\alpha = 0.87$).

Affective expression

Affective expression was rated on the basis of the video recording of a clinical interview conducted within 1 week before the experimental investigation. The interviews were evaluated by two trained psychologists on three different rating scales: the SANS (Scale for the Assessment of Negative Symptoms; Andreasen and Olsen 1982), the PANSS (Positive and Negative Symptom Scale; Kay et al. 1987), and the BPRS (Brief Psychiatric Rating Scale; Lukoff et al. 1986). The ratings on the individual items of these scales of 100 schizophrenics patients from a long-term study on Negative Symptoms were entered into a Principal Component Analysis. Three components were extracted and rotated according to Varimax criteria, representing different aspects of negative symptoms: (1) Diminished Affective Expression (33%), (2) Social Dysfunction (17%), and (3) Cognitive Disorganization (10%). Diminished Affective Expression has its highest loadings on "Paucity of Expressive Gestures" (SANS), "Unchanging Facial Expression" (SANS), "Decreased Spontaneous Movements" (SANS), and "Lack of Vocal Inflections" (SANS, $a \geq 0.73$); Social Dysfunction has its highest loadings on "Grooming and Hygiene" (SANS) and "Physical Anergia" (SANS; ≥ 0.68); Cognitive Disorganization has its highest loadings on "Impaired Abstract Thinking" (PANSS) and "Inattention During Testing" (SANS; $a \geq 0.72$). In the following analyses we focus on Diminished Affective Expression. The two other factors were not considered relevant for the present research questions. Furthermore, the factor scores on these components did not correlate significantly with affective startle modulation.

Startle experiment

Subjects were instructed to attend to a series of slides presented on the screen. They were also told that they would occasionally hear a brief noise over the headphones, which they were asked to ignore as much as possible. Two startle stimuli were presented as examples. Each of the 27 slides was shown on the screen for 6 s. In a second run the same slides were presented again, and subjects were instructed to view the slides as long as they wanted (up to 15 s). By pressing a button subjects terminated a slide and were shown the next slide. Slide-viewing time was recorded (in milliseconds) as a behavioral measure of interest in the slides. In a third run subjects rated their subjective experience of valence (pleasure) and arousal using a paper-and-pencil version of Lang's (1980) Self-Assessment Manikin (SAM).

Data analysis

Hypotheses involving subjects' responses to affective stimuli (slides) were tested using multivariate analysis of variance (Wilk's Lambda; SAS) with slide-valence category (pleasant, neutral, unpleasant) as a repeated measurement factor. Following Bradley et al. (1990, 1991) the predicted linear or quadratic relationship between slide valence and the subjective and autonomic responses to slides and the startle responses was tested using a univariate analysis of trend separately for each group. From the results with normals a linear trend was expected for the valence dimension, and a quadratic trend for the arousal dimension. Because the blink-amplitude data were highly skewed, raw data were subjected to a log transformation (i.e., log(ampl+1)).

Results

In a first step schizophrenic patients were compared with the control group with regard to their autonomic, motoric, and subjective responses to the slide stimuli. Two-way multivariate analyses of variance were carried out with Groups (schizophrenic patients vs healthy controls) as an independent factor and slide valence (pleasant vs neutral vs unpleasant) as a repeated measurement factor. An overview on the results of the MANOVAs is presented in Table 1.

In order to examine the relationships between startle and affective flattening, and between startle and anhedonia, the schizophrenic patients were categorized into two groups according to the median values of the factor Diminished Affective Expression and the global score of the anhedonia questionnaire. The resulting patient groups were then compared in two separate analyses.

Startle response amplitude

In 4 patients the amplitudes of the blink reflex (startle response) could not be evaluated due to failures of the apparatus or unstable baselines (see Balaban et al. 1986).

Table 1 MANOVA results and results of trend analyses for all dependent variables

	MANOVA results			Schizophrenic patients		Normal controls	
	Valence	Groups	Valence × groups	Linear	Quadratic	Linear	Quadratic
Startle amplitude	F(2/51) = 26.8***	F(1/52) = 0.4	F(2/51) = 5.8 **	F(1/29) = 18.9***	F(1/29) = 9.9**	F(1/23) = 33.1***	F(1/23) = 2.8
Startle-onset latency	F(2/51) = 3.2	F(1/52) = 0.1	F(2/51) = 2.6	F(1/29) = 2.5	F(1/29) = 4.0	F(1/23) = 4.2	F(1/23) = 1.6
Skin-conductance response	F(2/54) = 6.71**	F(1/55) = 3.7	F(2/54) = 1.5	F(1/33) = 0.5	F(1/33) = 6.5*	F(1/22) = 2.3	F(1/22) = 7.0*
Finger-pulse volume response	F(2/53) = 7.4**	F(1/54) = 7.8**	F(2/53) = 2.5	F(1/32) = 1.0	F(1/32) = 1.1	F(1/22) = 2.3	F(1/22) = 12.4**
Heart-rate deceleration	F(2/54) = 3.1	F(1/54) = 0.0	F(2/54) = 1.7	F(1/33) = 6.5*	F(1/33) = 3.6	F(1/22) = 0.0	F(1/22) = 0.5
Valence ratings	F(2/55) = 311.4***	F(1/56) = 0.30	F(2/55) = 0.6	F(1/33) = 310.2***	F(1/33) = 1.74	F(1/23) = 344.9***	F(1/23) = 0.05
Arousal ratings	F(2/55) = 144.6***	F(1/56) = 3.96	F(2/55) = 0.96	F(1/33) = 29.4***	F(1/33) = 119.70***	F(1/23) = 16.21***	F(1/23) =124.4***
Viewing time	F(2/55) = 15.4***	F(1/56) = 2.38	F(2/55) = 1.27	F(1/33) = 9.56**	F(1/33) = 17.1***	F(1/23) = 2.1	F(1/23) = 27.5***

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$

Therefore, the size of the patient group was reduced to 30 subjects for this analysis. Means and standard deviations for the two groups are presented in Table 2. The main effect of Valence was highly significant (F(2,51) = 26.8; $P <$ 0.001), as was the Valence × Groups interaction (F(2/51) = 5.8; $P < 0.01$). There were no significant overall group effects with regard to the startle-response amplitude (F(1/52) = 0.4). Trend analyses across the factor Valence were performed separately for the two groups. As illustrated in Fig. 1, normal subjects show a significant linear increase of the blink amplitudes across the valence dimension (F(1/23) = 33.06; $P < 0.001$) with smallest amplitudes for the pleasant and largest amplitudes for the unpleasant valence condition. In schizophrenic patients blink amplitudes are smallest for pleasant as well, but in addition to a significant linear trend (F(1/29) = 18.92; $P < 0.001$) a quadratic trend (F(1/29) = 9.86; $P < 0.005$) was found to be significant. Blink amplitudes of the patients during negative slides do not increase over the level during neutral slides. Parallel analyses were performed with the other dependent variables.

Startle onset latency

In normal subjects there was a tendency for blink latencies to be shortest for aversive slides and longest for neutral slides. In patients, the shortest latencies were observed in the neutral context, and the longest latencies in the positive context. This different pattern was reflected in a Valence × Groups interaction, which was, however, *not significant* (F(2/51) = 2.6; $P < 0.10$). The same was true for the main-effect Valence (F(2/52) = 3.2; $P < 0.10$). A main effect of Groups was not obtained (F(1/52) = 0.11) (Means and standard deviations are presented in Table 2).

Visceral responses

For the number of skin conductance responses (SCR) a significant main effect of Valence was obtained (F(2/55) = 6.70) with less responsivity in the neutral valence condition than in both affectively significant conditions. This response pattern was reflected in a quadratic trend that was comparable for both groups (schizophrenic patients: F(1/33) = 6.47; $P < 0.05$; normal subjects: F(1/22) = 6.98; $P < 0.05$). A marginally significant main effect of Groups shows normal subjects to be more responsive autonomically than schizophrenic patients (F(1/56) = 3.70; P = 0.06). For FPV we obtained a significant main effects of Valence as well (F(2/55) = 7.40; $P < 0.005$), but the quadratic trend was significant only in normal subjects (F(1/22) = 12.35; $P < 0.01$). The significant main effect of Groups again reflects the reduced autonomic responsivity of schizophrenic patients (F(1/56) = 7.8; $P < 0.01$): This attenuation of visceral responsivity in schizophrenic patients may account for the decreased response modulation by simulus contents. Heart-rate change scores (HR deceleration during slide viewing) did not differ between groups

Table 2 Means and standard deviation for physiological and self-report measures

	Schizophrenic patients			Normal controls		
	Slide category			Slide category		
	Pleasant	Neutral	Unpleasant	Pleasant	Neutral	Unpleasant
Startle amplitude (A/D units)	3.41 0.35	3.51 0.34	3.50 0.34	3.35 0.34	3.39 0.33	3.50 0.30
Startle-onset latency (ms)	39.4 7.9	37.4 8.4	38.2 7.5	37.9 8.2	38.4 8.5	36.6 9.0
Skin-conductance response (n)	0.05 0.10	0.03 0.07	0.05 0.07	0.14 0.23	0.06 0.12	0.12 0.22
Finger-pulse volume response (%)	11.7 7.5	9.5 8.2	10.1 9.0	19.5 12.0	11.1 6.1	16.2 10.7
Heart-rate deceleration (bpm)	−1.5 1.5	−1.5 1.5*	−2.2 1.5	−1.8 2.0	−1.6 1.7	−1.8 1.3
Valence ratings (0–29)	8.5 2.8	14.6 3.6	22.2 2.7	8.2 2.3	15.4 2.4	22.2 2.5
Arousal ratings (0–29)	15.0 5.0	9.7 5.0	19.6 4.5	13.9 4.8	6.7 3.6	17.5 5.0
Viewing time (ms)	6083 3907	3779 2390	4398 2800	4429 2340	3076 1570	3896 1864

NOTE: For each column of numbers, the first number is the mean and the second number is the SD

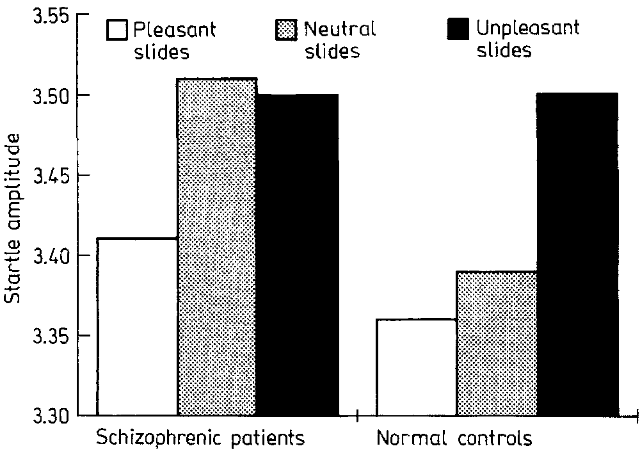

Fig. 1 Mean blink reflex amplitudes to startle stimuli presented during viewing of pleasant, neutral, and unpleasant slides in schizophrenic patients and normal controls

($F(1/55) = 0.01$). The main effect of Valence just failed to reach statistical significance ($F(2/54) = 3.1$; $P = 0.054$). Linear and quadratic trends were not statistically significant in normals, and in patients a significant linear trend ($F(1/33) = 6.53$; $P < 0.05$) was obtained, despite the lack of a significant interaction between Valence and Groups, indicating the largest deceleration in response to slides with aversive valence. (For means and standard deviations see Table 2.)

Affective report and slide-viewing time

The valence ratings of both groups supported the validity of our slide selection: Positive slides were rated as pleasant and negative slides were rated as unpleasant as reflected by a linear trend that was highly significant for both groups ($F(1/23) = 344.9$ controls; $F(1/33) = 310.2$ patients; $P < 0.001$).

Similarly, patients and controls showed comparable response patterns with regard to arousal ratings and slide-viewing time. Neither group differences nor interactions were found to be statistically significant. Pleasant and unpleasant slides were judged to be more arousing than neutral slides by both groups resulting in a highly significant quadratic trend (patients: $F(1/33) = 119.7$; normals: $F(1/23) = 124.4$; $P < 0.001$). In addition, there is a significant linear trend (patients: $F(1/33) = 29.4$; $P < 0.001$; normals: $F(1/23) = 16.2$; $P < 0.001$) indicating that both groups rated aversive slides as more arousing than positive slides. With regard to slide-viewing time, response patterns of both groups also revealed significant quadratic trends (patients: $F(1/33) = 17.1$; normals: $F(1/23) = 27.5$; $P < 0.001$) indicating that positive and negative slides were viewed longer than neutral slides. An additional linear trend that was observed in both groups, but was only significant in the patient group ($F(1/33) = 9.6$; $P < 0.001$), indicates that positive slides were viewed longer than aversive slides. (For means and standard deviations see Table 2.)

Affective expression and the startle-blink response

A total of 17 patients with high factor scores on Diminished Affective Expression (diminished AE) were compared with 17 patients with low scores (normal AE). The two subgroups differed significantly with regard to the Composite Score of the SANS, i.e., the sum of the ratings on all 30 SANS items (mean = 25.8, SD = 10.2, and mean 53.2, SD = 15.1, respectively; $t = 6.2$, $df = 32$, $P < 0.001$).

Regarding the *subscales* of the SANS, the greatest group difference was observed on the Affective Flattening Scale (mean 8.1, SD = 4.8, and mean 22.9, SD = 4.1, respectively; $t = 9.1$; $df = 32$, $P < 0.001$). The two groups did not differ with regard to their scores on the BPRS factors (Guy 1976) "Activation," "Hostility/Suspiciousness," and "Thought Disturbance" ($t(32) \leq 1.16$; $P > 0.25$). In addition, there was no difference between the groups with regard to age, education, age at disease onset, duration of illness, or neuroleptic dosage ($t(32) \leq 0.84$).

Of 17 patients with diminished AE, 9, vs 2 of 17 patients with normal AE, received clozapine ($\chi^2 = 6.56$; $df = 1$; $P < 0.01$). The difference in total duration of hospitalizations approached significance ($t(20.8) = 1.70$; $P = 0.11$), the difference in duration of *present* hospitalization significantly separated the two groups ($t(15.4) = 2.22$; $P = 0.05$), with longer stays in the hospital for patients with diminished AE. Patients receiving clozapine did not differ with regard to duration of present or total hospitalization from the other schizophrenic patients ($t \leq 1.34$; $df = 28$; $P < 0.20$).

In the following analyses these two subgroups of patients with normal and diminished affective expression are compared. Whenever significant group differences or interactions are found each of the subgroups are compared with the group of $n = 24$ healthy controls in a separate analysis.

Blink amplitude

The average amplitudes of the startle responses are presented in Fig. 2. Patients with diminished AE show a *linear* increase of blink amplitudes over the three valence conditions, pleasant, neutral, or unpleasant ($F(1/15) = 23.21$; $P < 0.001$), comparable to that of the normal controls. In patients with normal AE the blink amplitudes did not show a linear trend ($F(1/13) = 2.51$; $P = 0.14$), but a quadratic trend ($F(1/13) = 11.58$; $P < 0.01$) with largest startle responses while viewing the neutral slides. These differential response patterns were supported by a significant Valence × Groups interaction ($F(2/27) = 3.25$; $P < 0.05$). The main effect of Valence was ($F(2/27) = 16.05$; $P < 0.001$). Finally, patients with diminished AE tended to show larger blink amplitudes than patients with normal AE ($F(1/28) = 3.70$; $P = 0.065$).

Because significantly more patients with diminished AE received clozapine than patients with normal AE, the effect of medication on the startle modulation was tested within the group of patients with diminished AE. Patients on clozapine ($n = 8$) did not differ from those receiving standard neuroleptic medication ($n = 8$) with regard to modulation of the startle amplitude (valence × clozapine: $F(2,13) = 1.22$; $P = 0.33$). A separate comparison of *normal AE* patients with *normals* resulted in a significant Valence × Groups interaction ($F(2/35) = 9.19$; $P < 0.001$), whereas the parallel comparison of *diminished AE* patients and *normals* showed no interaction ($F(2/37) = 2.04$; $P = 0.14$).

To further analyze the relationship between reflex modulation and affective expression in schizophrenic patients, measures for both startle inhibition and startle potentiation were defined and correlated with psychopathology. The differences between blink amplitudes in the pleasant and the neutral conditions were considered as a measure of reflex inhibition while pleasant slides were being viewed, and the differences between blink amplitudes in the unpleasant and neutral conditions were considered as a measure of startle potentiation while unpleasant slides were viewed. The factor scores on Diminished Affective Expression as well as the SANS composite score were positively associated with the degree of reflex potentiation indicating that diminished affective expression and negative symptoms (see Table 3) are accompanied by higher blink amplitudes during unpleasant, rather than neutral, stimulation. When duration of present hospitalization was determined, the relationships remained basically the same.

Blink-onset latency

A 2 × 3 MANOVA revealed significant main effects of Valence ($F(2/27) = 3.78$; $P = 0.035$) with a marginally significant quadratic trend ($F(1/28) = 3.79$; $P = 0.06$) indicating that blink latencies were shortest during the neutral condition in both groups. In addition, the main effect of

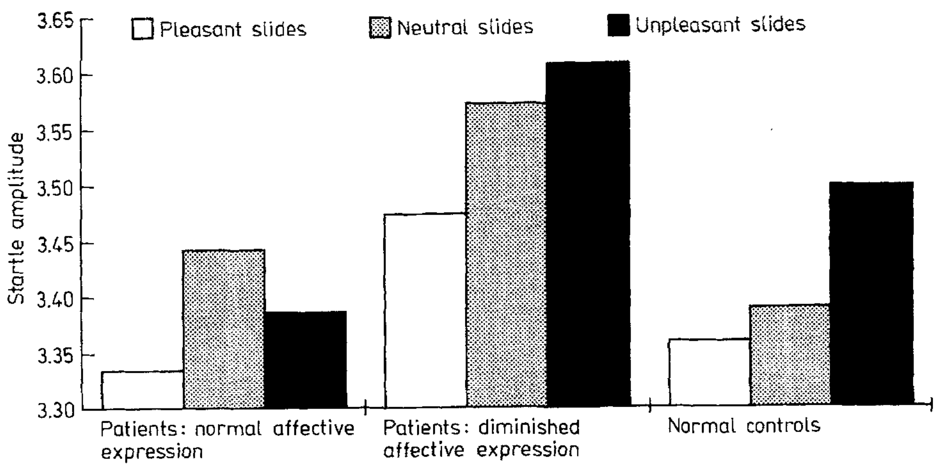

Fig. 2 Mean blink reflex amplitudes of patients with high and with low factor scores on affective flattening, and of normal controls

Table 3 Pearson correlations between reflex modulation and affective flattening (SANS), anhedonia, and duration of hospitalization

	Affective expression (factor scores)	SANS (composite score)	Anhedonia (total score)	Duration of present hospitalization
Reflex inhibition (neutral – pleasant)	– 0.01	– 0.16	– 0.28	– 0.26
Reflex potentiation (unpleasant – neutral)	0.33*	0.34*	0.05	0.18
Duration of present hospitalization partialled out				
Degree of inhibition (neutral – pleasant)	– 0.02	– 0.02	– 0.26	
Degree of potentiation (unpleasant – neutral)	0.31*	0.32*	0.03	

* $P < 0.010$

Groups was significant ($F(1/28) = 4.26$; $P < 0.05$). Diminished AE patients had shorter latencies than normal AE patients. There was no significant interaction ($F(2/27) = 0.86$; $P = 0.43$). When the two groups were compared with normals no significant main effects of Groups or interactions emerged in either of the two analyses ($P \geq 0.11$).

Visceral measures

Both patient groups were comparable with regard to the number skin-conductance responses and heart-rate change ($F(1/32) \leq 1.40$). There were no significant Valence × Groups interactions ($F(2/31) \leq 0.94$). With regard to the amplitudes of FPV responses, there was a significant main effect of Groups ($F(1/31) = 5.18$; $P = 0.03$) indicating diminished AE patients to show less vascular responsivity to slide stimuli than normal AE patients. The same pattern was found in the comparison of diminished AE patients with normals $F(2/36) = 11.29$; $P < 0.001$).

Subjective and behavioral measures

Both patient groups were comparable with regard to valence and arousal ratings, and to slide-viewing time ($F(1/32) \leq 0.32$). There was no significant Valence × Groups interaction ($F(2/31) \leq 1.15$).

Anhedonia and startle

According to expectations schizophrenic patients described themselves as more anhedonic than normals, and the average total score from our anhedonia questionnaire was mean = 18.0 (SD = 7.3) for schizophrenic patients and mean = 7.7 (SD = 4.5) for healthy controls. This difference was highly significant ($t(55.3) = 6.593$; $P < 0.001$).

A total of 15 patients with low scores on the anhedonia questionnaire were compared with 15 patients with high scores. The two groups did not differ with regard to age, education, age of onset, duration of illness, duration of hospitalization, or medication dosage (all t-values ≤ 1.05; $df = 32$).

As can be seen in Fig. 3, there was no clear difference in the startle-response pattern between patients scoring

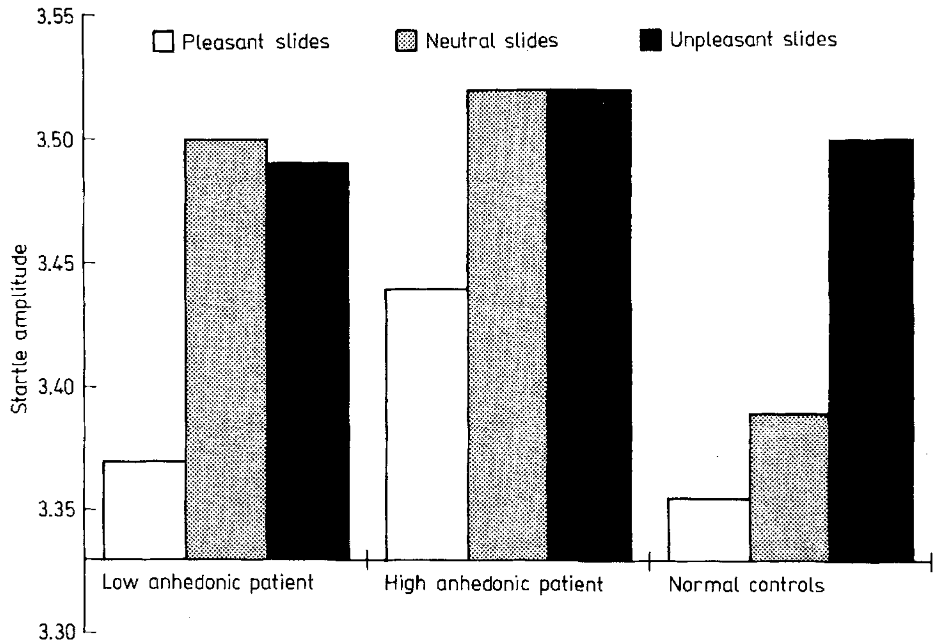

Fig. 3 Mean blink reflex amplitudes of patients with high and with low total scores on the Anhedonia Questionnaire, and of normal controls

high or low on the anhedonia questionnaire. Neither the main effect of Groups ($F(1/28) = 0.12$) nor the Valence × Groups interaction ($F(2/27) = 0.98$) approached significance. Accordingly, the correlation coefficients (Table 3) between the Anhedonia score and the degree of reflex inhibition or potentiation were not statistically significant. The highest correlation of $r = -0.28$ between reflex inhibition in the pleasant condition and anhedonia may nevertheless indicate some validity of the questionnaire, showing that the degree of self-reported anhedonia trends to correspond with a weaker startle-reflex inhibition during exposure to pleasant slides.

Discussion

The present study confirms previous studies showing that the eye-blink component of the startle response can be modulated by confronting subjects with pleasant, neutral, and unpleasant slides, and can, therefore, be considered as a valid measure of emotional response in human subjects. Comparable to previous studies (Vrana et al. 1988; Bradley et al. 1990, 1991) the blink amplitudes of normal subjects were potentiated during exposure to unpleasant slides relative to neutral slides, and attenuated during exposure to pleasant slides. Accordingly, the startle-probe amplitude can be considered as a valid measure of emotional response to the affective valence of a stimulus. Traditional autonomic measures were again found to be useful indices of arousal, but to be largely insensitive to differences in affective valence. Our results with healthy subjects also replicate the results of former studies with regard to subjective and behavioral measures (Vrana et al. 1988; Bradley et al. 1991). This is a prerequisite for the interpretation of our results obtained with schizophrenic patients.

It is also important to note that there were no differences between our group of normals and our group of schizophrenic patients in the viewing times or the pleasantness ratings of the slides. Thus, we can assume that our group of schizophrenic patients is comparable to normals in the evaluation of affective valence of pictorial stimuli presented to modulate psychophysiological responses. The only difference between groups in subjective responses was found for the arousal ratings: Schizophrenic patients rated all slides as more arousing. It is difficult to decide whether this difference reflects a response bias or a different perception of the slides. Apart from this, schizophrenic patients categorize the slides similarly to normals, in terms of what is pleasant or unpleasant as well as arousing or dull, and they look longer at pictures they find more arousing. In line with the literature (cf. Zahn et al. 1991), the visceral responsivity of schizophrenic patients is generally reduced relative to normal controls. Both electrodermal and vascular parameters of sympathetic arousal are attenuated when compared with controls. On the other hand, the number of skin-conductance responses is equally related to the arousal value of the slides in schizophrenic patients and normals: more electrodermal responses to arousing – pleasant or unpleasant – than to neutral slides. The vascular responses of schizophrenic patients, especially of those patients with diminished affective expression, seem to be only weakly related to slide stimuli, a result that may be explained by the small vascular responsivity observed particularly in this group.

Despite these similarities of patients and normals, schizophrenic patients show an abnormal pattern of blink-reflex modulation by exposure to pleasant, neutral, and unpleasant slides. Unlike healthy subjects, who show larger startle responses while viewing unpleasant than while viewing neutral slides, schizophrenic patients show no difference in their blink amplitudes to unpleasant and neutral slides, i.e., there was no indication of reflex potentiation in the aversive relative to the neutral context. In contrast, there was no indication of any differential response to pleasant slides: In both groups blink amplitudes while viewing positive slides were smaller than while viewing neutral or aversive slides. The startle-reflex modulation data indicate abnormalities only when blink amplitudes are compared during exposure to neutral and unpleasant slides.

When the group of patients was divided into two subgroups depending on their factor scores on Affective Expression according to clinical ratings, significant differences were found with regard to startle-reflex modulation. Surprisingly, patients with diminished affective expression show a linear increase over the three valence conditions very comparable to that typically found in normals. Patients with normal affective expression, on the other hand, show a deviant pattern of reflex modulation. In these patients response amplitudes are largest in the neutral condition and smaller not only while viewing positive, but also during the presentation of unpleasant slides. Apparently, this subgroup of schizophrenic patients who appear normal with regard to affective flattening seems uninfluenced by the aversive valence of unpleasant slides. Such a response pattern has recently been reported by Patrick et al. (1993) for criminal psychopaths. The authors understand this pattern as indicating a deficit in aversive responding especially in fear. This interpretation is consistent with theories of psychopathy proposed by Lykken (1957) and Gray (1971), who postulate a deficit of psychopaths in avoiding aversive stimuli and punishment, whereas appetitive/approaching behavior as well as acknowledgment of pleasant stimuli or positive reinforcement is intact. It is certainly difficult to assume that some schizophrenic patients are deficient in their capacity to develop anxiety responses as postulated for criminal psychopaths. To our knowledge, it has never been suggested that a substantial subgroup of schizophrenic patients shows a deficit in aversive responding. Early theories of schizophrenia point to *hyper*sensitivity, rather than *hypo*sensitivity, in the context of aversive stimulation, and there are many studies providing evidence for the deteriorating effects of affectively laden stimulus materials (positive and aversive) on the performance of schizophrenic patients (cf. Buss and Lang 1965). In addition, recent research has repeatedly shown that negative attitudes or expressed emotion (EE) in the family predicts symptom relapse in schizophrenic outpatients living with their families, which can hardly be the result of indifference toward aversive stimulation (Vaughn and Leff 1976; Hatfield et al. 1987).

Because our findings with normal subjects successfully replicated the results reported previously by others, it is unlikely that the unexpected results in a subgroup of schizophrenic patients is due to some minor deviation in basic procedure. Although it is speculative at this point, it might be worth considering whether the attenuation of blink amplitudes during unpleasant stimulation and the concomitant dissociation of subjective reports and blink responses might result from different mechanisms in schizophrenic and psychopathic subjects. Postulating two reciprocal motivation systems in the brain for appetitive and aversive effect, Lang et al. (1990) assume that the startle response is larger when the negative valence of the reflex probe matches the valence of the ongoing motivational disposition. Schizophrenic patients with normal affective expression possibly, have a tendency to counteract the classical defense reactions during aversive stimulation as a result of a coping mechanism. In these patients the unpleasant emotional experience elicited by aversive slides may enhance attention and inhibit defensive and withdrawal responses to further aversive stimulation similar to what Byrne (1964) has suggested when differentiating "repressors" and "sensitizers." Obviously, this is a tentative post hoc interpretation that is in need of substantiation in independent studies.

The modulation of blink-response amplitudes observed in patients with diminished affective expression, on the other hand, clearly argues against the notion that these patients with reduced expression are simultaneously impaired in the perception of affective stimuli. Furthermore, our results do not indicate that either schizophrenic patients with diminished expression or patients with high levels of self-reported anhedonia are particularly insensitive to pleasant stimulation as was postulated in Meehl's concept of anhedonia. Our results are more in line with Berenbaum and Oltmanns (1992), who demonstrated that a group of blunted schizophrenics, although showing less facial expression during an affect-eliciting situation, did not differ from nonblunted schizophrenics or normals with regard to their reported emotional experience. Flattening of affect is apparently more a disturbance of expression than an inability to perceive and to experience the action dispositions conceived as emotions. We were not in the position to separate the deficit-syndrome (Carpenter et al. 1988) reliably from what our raters conceived as affective expression. The picture might have been different if only patients with primary negative symptoms had been included in the group. Considering that patients with clinical evidence for extrapyramidal side effects had been excluded from the study, and that significantly more patients with diminished than with normal affective expression received clozapin, it is most unlikely that in our group of patients affective flattening was mimicked by extrapyramidal side effects of neuroleptic medication.

As reported, patients with diminished AE were more likely to be treated with clozapine than patients with normal AE. This confounding of medication and affective expression does not imply that clozapine normalizes startle modulation while standard neuroleptics have a dampening effect. Among patients with diminished AE startle modulation in patients receiving clozapine is similar to that in patients receiving standard neuroleptics.

In conclusion, our results indicate that schizophrenic patients' responses to visual stimuli depicting affectively significant contents are mostly comparable to responses of normal subjects. We observed deviations in startle-response amplitude from the pattern of normals in terms of reduced reflex potentiation while viewing unpleasant slides. On the other hand, reflex inhibition while viewing pleasant slides appeared intact in schizophrenic patients. The differences we obtained between subgroups of schizophrenic patients with diminished vs normal affective expression are not in line with expectations. Consequently, the discussion of these results remains speculative, and for more definite conclusions a replication of the study is warranted.

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