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Affect Modulated Startle in Schizophrenia: Subjective Experience Matters

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Abstract

Data suggests that emotion reactivity as measured by the affect-modulated startle paradigm in those with schizophrenia (SZ) may be similar to healthy controls (HC). However, normative classification of the stimuli may not accurately reflect emotional experience, especially for those with SZ. To examine this possibility, the present study measured the affect-modulated startle response with images classified according to both normative and subjective ratings. Seventeen HC and 17 SZ completed an image viewing task during which startle probes were presented, followed by subjective valence and arousal ratings. Both groups exhibited inhibited startle responses to positive images, intermediate startle amplitudes to neutral images, and potentiated startle amplitudes to negative images. SZ rated the positive images as less positive than HC. When images were reclassified based on subjective valence ratings, both groups' startle magnitudes increased in response to subjectively rated positive images and decreased to subjectively rated neutral images. The number of trials classified into each valence condition suggested a tendency for SZ to classify neutral images as negative more often than HC. Overall, these findings suggest that affective stimuli modulate the startle response in HC and SZ in similar ways, but subjective emotional experience may differ in those with schizophrenia.

Keywords

Emotion; Reactivity; Startle Reflex; Psychosis; Self-report; Psychophysiology; Symptoms

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1. Introduction

Within schizophrenia research, there is a movement beyond consideration of broadly-defined emotional processing deficits and towards delineating the specific aspects of emotional processing that may be disrupted (Kring and Moran, 2008). Diverse methodologies have been applied in an attempt to conceptualize putative deficits and their relation to everyday functional impairments experienced by individuals with schizophrenia.

Recent reviews have suggested that present-moment subjective emotional experience is unaffected by schizophrenia across physiological and self-report measures (Kring and Moran, 2008; Kring and Caponigro, 2010). As such, individuals with schizophrenia generally rate their emotional response to emotionally-provocative images in a manner comparable to healthy controls across the spectrum of intensity of valence and arousal (Herbener, et al., 2008). However, there is also some evidence to suggest that individuals with schizophrenia may tend to report greater aversive self-reported emotional experience in response to stimuli that are generally classified as pleasant or neutral in valence by healthy controls (Cohen and Minor, 2010). Strauss and Herbener (2011) found subgroups of individuals with schizophrenia displayed “atypical” patterns of subjective emotional experience, suggesting that discrepancies in self-report amongst studies may, at least in part, reflect differences in the composition of the patient samples. Importantly, in their study the subset of patients with “atypical” image ratings had poorer functional outcomes, higher self-reported anhedonia and greater negative symptom severity, which suggests that differences in subjective experience of emotional stimuli is of relevance to the overall clinical presentation and functional impact of the disorder. Moreover, potential disturbances in present-moment emotional experience may be an important differentiating characteristic amongst individuals with schizophrenia that is typically overlooked when examination of group effects are constrained to analyses based on normative image ratings. Reliance on normative ratings may further limit the ability to accurately assess for any possible discrepancy between psychophysiological response and subjective emotional response.

1.1. Emotion-modulated startle paradigm

Investigation of the potential impact of differences in subjective versus normative classifications of affective images on the pattern of physiological response requires a psychophysiological measure that allows for the distinction between positive and negative valence stimuli, such as the startle blink paradigm (Vrana et al., 1988; Bradley et al., 1990). In this paradigm, a white noise burst (i.e. the startle probe) is administered while the participant views images of differing valence. The startle magnitude evoked by the startle probe is measured by recording activity of the *orbicularis oculi* muscle, which is located below the eye. The startle probe evokes a defensive response (the startle blink), and the magnitude of the reflex startle response is modulated by the emotional context in which it occurs (Lang et al., 1990; Lang, 1995). When an aversive motivational state is active, such as when viewing an image of negative valence, the aversive startle stimulus results in an augmented (i.e. larger) startle response. Correspondingly, when a positive motivational state is active, the aversive startle stimulus yields an inhibited (i.e. smaller) startle response (Lang et al. 1998).

1.2. Emotion-modulated startle in schizophrenia

Several previous studies have utilized the startle paradigm to investigate emotional reactivity in individuals with schizophrenia. In the first study, Schlenker and colleagues (1995) observed a comparable linear modulation of the startle response in individuals with schizophrenia and healthy controls. The schizophrenia group tended to rate the images as more arousing compared to the control group. Similar startle findings were reported by Curtis et al. (1999); however, within their sample, the schizophrenia group tended to give lower self-reported valence ratings to positive images (i.e. they found them less positive) and negative images (i.e. they found them less unpleasant) and no difference in valence ratings of neutral images compared to healthy controls. While Volz et al. (2003) also found comparable emotion-modulated startle in schizophrenia, they reported no differences in valence ratings compared to a control group. Yee et al. (2010) replicated the pattern of comparable startle modulation between schizophrenia patients (first episode and chronic patients) and healthy controls. They also reported a linear relationship between self-reported arousal and startle magnitude such that highly arousing negative images were associated with larger startle magnitudes while highly arousing positive images were associated with lower startle magnitudes for both schizophrenia and healthy controls. While valence and arousal ratings were comparable between the schizophrenia and control groups, self-reported valence was lower to positive and neutral images in the prodromal group. More recently, Kring et al. (2011) reported significant differences in startle magnitude between positive and negative images and between positive and neutral images in a schizophrenia sample. However, the startle magnitudes to neutral and negative images did not significantly differ during picture viewing.

In light of the startle modulation studies reviewed above, the majority of studies have found that emotional reactivity as indexed by startle magnitude appears to be similar between individuals with schizophrenia and healthy controls (Curtis et al. 1999; Schlenker et al. 1995; Volz et al. 2003; Yee et al., 2011; although see Kring et al. 2011). In contrast, there is evidence of variability in self-reported valence and arousal amongst individuals with schizophrenia compared to healthy controls within the context of the startle paradigm. Since the emotional content of the stimuli modulate the startle response, differences in how the emotional content are experienced highlight a discrepancy between self-report and psychophysiological response between groups. Therefore, a vital next step is to incorporate subjective ratings of image valence into the startle modulation analysis. Yee and colleagues made an important first step in this direction by examining the relationship between individual subjective arousal ratings and startle magnitude. An alternative approach that may reveal important psychophysiological differences in emotional reactivity between individuals with schizophrenia and healthy controls is to examine the pattern of startle modulation within groups when startle responses are classified into valence categories based on self-reported valence. Such an approach would allow for potential differences in valence ratings at the individual subject level to be accounted for in the classification of psychophysiological responses. Because previous studies have suggested differences in subjective valence ratings between schizophrenia and control groups, classifying images in this way may alter the pattern of psychophysiological response observed for the newly defined valence categories.

1.3. The current study

The present study aimed to investigate patterns of emotion-modulated startle amongst individuals with schizophrenia (SZ) in comparison to healthy controls (HC). A further aim was to explore potential differences in the pattern of startle modulation when individual subject ratings are used to classify the emotion-provoking images into valence categories compared to when they are sorted based on normative classification. Towards this aim, startle responses were first sorted based on normative classification then re-classified into positive, neutral and negative valence categories for each individual based on their valence rating for each image. The startle magnitudes for each method of valence classification were then compared between SZ and HC. In line with most other studies investigating affect modulated startle, we predicted that SZ would show similar patterns of emotion-modulated startle as HC based on normative ratings. Given the findings that patients with schizophrenia subjectively rate positive and neutral emotional stimuli as more negative compared to healthy controls, our second hypothesis was that SZ would have a larger number of startle trials in the 'negative' valence condition compared to HC when the trials are categorized according to subjective valence ratings. Finally, we anticipated that re-analysis of startle amplitudes based on subjective ratings would alleviate the confound of more negatively experienced images being included in the positive and neutral conditions. If patients with schizophrenia truly experience dampened physiological responses to positive and neutral emotional stimuli that they have rated as positive and neutral, then one would expect significantly greater startle magnitudes in response to positive and neutral stimuli in the subjectively classified re-analysis.

2. Methods

2.1. Participants

Seventy participants completed the emotion-modulated startle task; 41 participants were healthy controls and 29 participants met DSM-IV diagnostic criteria for either Schizophrenia ($n = 25$) or Schizoaffective Disorder ($n = 4$). All participants were assessed via structured interview (SCID-I or SCID-NP) by doctoral level psychologists (C.A.B. and A.R.B.) and patients included a mix of hospitalized and those receiving outpatient care. Exclusion criteria included a history of head injury with loss of consciousness of 5 minutes or more, alcohol or illicit drug use at the time of testing as determined by urine screen, current alcohol or drug abuse, history of neurological disorders, diagnosis of a learning disorder, or self-reported hearing loss, and for the healthy control group, the presence of any current Axis-I disorders. Three male SZ participants and one female HC participant was excluded due to the presence of neurological problems. One male SZ participant was excluded due to a history of ECT for psychotic depression. Two HC male participants were excluded due to lack of response to the startle probe (i.e. less than four detectable startles per valence condition) and one female HC was excluded due to less than four useable negative valence startle trials. One SZ subject was excluded as a raw data outlier (more than 3 times the inter-quartile range). Four subjects (two from each diagnostic group) were excluded due to zero trials rated as neutral. Due to time constraints, five SZ and seven HC did not complete image ratings. An additional 11 female HC subjects were randomly chosen to be excluded from the study in order to match the gender distribution of the groups. The final sample of 34

participants with both startle and image rating data were included in the analyses (HC $n = 17$ and SZ $n = 15$, Schizoaffective $n = 2$) (see Table 1). Most ($n=15$) patients were medicated (mean CPZ equivalent= 586.67) while 1 was unmedicated and 1 was unknown due to participation in a double-blind clinical trial. SZ participants completed the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987) within one month of the startle task. Self-reported ethnicities were as follows: African American $n=14$ SZ and $n=10$ HC, Caucasian $n=3$ SZ and $n=6$ HC, and Hispanic/Latino $n=1$ HC.

2.2. Procedure

Study procedures were approved by the Indiana University Ethics Board. Participants viewed thirty-six affective images selected from the International Affective Picture System (IAPS; Center for the Study of Emotion and Attention, 1999). In order to replicate and extend the findings from the schizophrenia group reported by Curtis et al. (1999) we presented the same images¹. Images from each valence condition were randomly distributed throughout the task, and those from the positive and negative conditions contained some highly evocative material (e.g. erotica in the positive condition and bodily injury in the negative condition). The normative valence ratings (using a 1-9 scale) were as follows: Positive $M = 7.38$, $SD = 0.48$; Neutral $M = 4.94$, $SD = 0.35$; Negative $M = 2.54$, $SD = 0.64$. Three startle probes preceded the onset of the task to allow for habituation of the startle response. Startle probes were also delivered during eight positive, seven neutral and eight negative valence images. The startle probe was a 50 ms, 110 dB acoustic white noise burst delivered via ear inserts at three, four or five seconds post-picture onset. Each image was displayed for six seconds. The inter-trial interval (ITI) ranged from 10-18 seconds. Eight startle probes were interspersed with the image trials to assess un-modulated startle reactivity and increase the unpredictability of the startle probe. Raw startle magnitudes of these probe trials are presented in Table 2 to demonstrate the general comparability between groups and maintenance of startle amplitudes over the course of the study. Participants were instructed to look at the image throughout the six second display and were told that on some trials they would hear a loud burst of noise. No behavioral response or subjective ratings of the images were recorded during the startle task; however, after the startle task was completed, participants viewed the images a second time and provided valence and arousal ratings for each image using the 5-point Self Assessment Manikin (SAM; Lang, 1980). Participants were asked to rate how pleasant or unpleasant the images made them feel, therefore, the slide ratings likely reflect subjective emotion experience.

2.3. EMG data processing

Two bipolar 0.5 cm Ag-AgCl electrodes covered the *Obicularis oculi*, with one placed directly below the pupil and the other to the lateral side. Impedance was kept below 10 k Ω and data was collected using Neuroscan SYNAMPS recording system (Neuroscan, Inc., El Paso, TX, USA). Data processing occurred offline using Brain Vision Analyzer 2 (Brain Products, GmbH, Munich, Germany). The EMG data was baseline corrected using a 50 ms

¹IAPS identification numbers for the slides used, in order of presentation (+: positive; =: neutral; -: negative; *: probed) are 550 (=), 803 (+), 139 (=), 626 (-), 818 (+), 925 (-), 808 (+), 709 (=), 960 (-), 171(+), 706 (=), 241 (=), 623 (-), 705 (=), 165 (+), 905 (-), 991 (-), 849 (+), 104 (-), 615 (=), 851 (+), 837 (+), 750 (=), 303 (-), 981 (-), 830 (+), 713 (=), 637 (-), 466 (+), 701 (=), 468 (+), 130 (-), 700 (=), 635 (-), 715 (=), 469 (+).

baseline, filtered with a 28 Hz high pass, rectified, and filtered again with a 40 Hz low pass filter. Startle magnitudes were manually scored as the peak activity between 30 ms and 150 ms after the startle probe. Trials were excluded if excessive noise was present during the baseline period or during the trial either obscuring accurate detection of the startle peak or resulting in failure of baseline correction. Trials with no observable startle response were also excluded. There was no significant difference in the number of trials excluded from each valence condition ($p=0.694$), between diagnostic groups ($p=0.759$) or between males and females ($p=0.331$). Raw startle blink magnitudes were converted to within subject z-scores prior to statistical analysis; raw scores were utilized for the computation of correlations.

2.4. Statistical analysis

To examine the effect of valence on startle modulation both within and across diagnostic groups, the primary analysis consisted of a mixed design Analysis of Variance (ANOVA) with z-score startle as the dependent variable, valence (positive, neutral, negative) as the within subject factor and diagnostic group (SZ, HC) and gender as between subject factors². Multivariate Wilk's Lambda values were reported. Similar ANOVAs were conducted with self-reported valence and arousal ratings as the dependent variables. The startle data was then re-examined after the startle magnitude data was resorted into valence categories based on individual participant valence ratings, which will be referred to as the subjective analysis. Images rated as '1' or '2' were classified as 'negative', '3' as 'neutral' and '4' or '5' as 'positive'. A mixed design ANOVA was also conducted to examine the number of startle trials assigned to each valence condition in the subjectively sorted startle data. The relationship between image valence ratings and startle magnitude was calculated with Pearson correlation coefficients, and group differences in the magnitude of these correlations were examined using the Fisher's r-to-z transform. Finally, the relationship between startle modulation and schizophrenia symptoms was examined by calculating the correlation between PANSS subscale scores and startle magnitudes across genders for both the normative and subjectively classified images.

3. Results

The potential influence of demographic variables was examined prior to the statistical analyses (Table 1). The groups did not significantly differ in age, gender or ethnicity distribution.

3.1. Normative classification of startle modulation

There was a significant main effect of Valence, Wilks' lambda = 0.645, $F(2,29) = 7.97$, $p=0.002$, $\eta_p^2=0.355$ ³ (Figure 1). There was a trend toward a Valence x Gender x Diagnosis interaction, Wilks' lambda= 0.832, $F(2,29) = 2.93$, $p=0.069$, $\eta_p^2=0.168$. Separate mixed

²Reported results are based on z-score startle magnitudes. The pattern of raw startle data was the same except in instances where differences are noted.

³Using raw startle magnitude, there was a significant main effect of Valence, Wilks' lambda = 0.563, $F(2,29) = 11.27$, $p<.001$, $\eta_p^2=0.437$. There was also a significant Valence x Gender interaction, Wilks' lambda= 0.770, $F(2,29)=4.34$, $p=0.023$, $\eta_p^2=0.230$ and a significant Valence x Diagnosis x Gender interaction, Wilks' lambda= 0.785, $F(2,29)=0.030$, $\eta_p^2=0.215$.

design ANOVAs were conducted for each gender separately. For males, there was no longer a main effect of Valence, Wilks' lambda= 0.907, $F(2,20) = 1.03$, $p=0.375$, $\eta_p^2=0.093$. For females, there was a main effect of Valence, Wilks' lambda= 0.291, $F(2,8) = 9.75$, $p=.007$, $\eta_p^2=0.709$. Paired samples t-tests within females revealed that negative image startle magnitude was significantly greater than positive, $t(10) = 4.02$, $p=0.002$, and neutral was significantly larger than positive, $t(10) = 3.22$, $p=0.009$. Negative startle magnitude did not significantly differ from neutral within females, $p=0.096$.

3.2. Normative classification of image ratings

There was a significant main effect of Valence, Wilks' lambda= 0.126, $F(2,29) = 100.25$, $p<0.001$, $\eta_p^2=0.874$. There was also a significant Valence x Diagnosis interaction, Wilks' lambda= 0.756, $F(2,29) = 4.68$, $p=0.017$, $\eta_p^2=0.244$. Independent sample t-tests comparing the valence ratings between diagnostic groups revealed that SZ rated the positive images as less positive compared to HC, $t(32)=2.91$, $p=0.007$ (Table 3).

There was a significant main effect of Image Valence on Arousal Rating, Wilks' lambda = 0.304, $F(2,29) = 33.19$, $p<0.001$, $\eta_p^2=0.696$ (Table 3), and a significant Valence x Gender interaction, Wilks' lambda= 0.802, $F(2,29) = 3.57$, $p=0.041$, $\eta_p^2=0.198$. Males rated the positive valence images as more arousing than negative, $t(22)=4.15$, $p<0.001$ and neutral images, $t(22)=9.25$, $p<0.001$ with negative images also rated as more arousing compared to neutral images, $t(22)=3.21$, $p=0.004$. In females, positive and negative valence images did not significantly differ in arousal rating, but only the positive image valence condition was rated as significantly more arousing than the neutral valence images, $t(10)=4.16$, $p=0.002$.

Across diagnostic groups there were no significant correlations between image valence rating and startle magnitude. Correlation coefficients within diagnostic groups separately revealed significant negative correlations between neutral image valence ratings and raw startle magnitude across valence conditions for the HC group (Table 4). There were no significant correlations between valence ratings and raw startle magnitudes within the SZ group. The magnitude of the relationship between neutral image valence ratings and raw startle magnitude in response to negative images was significantly larger in the HC group than it was in the SZ group. No other group differences in correlation magnitude were found between groups.

3.3. Subjective classification of startle modulation

There was a significant main effect of Valence, Wilks' lambda = 0.693, $F(2,29) = 6.41$, $p=0.005$, $\eta_p^2=0.307^4$ (Figure 2). Paired samples t-tests indicated that subjectively negative startle magnitudes were significantly larger than positive image startle magnitudes, $t(33)=2.71$, $p=0.011$. There was also a trend for a significant Valence x Gender interaction, Wilks' lambda=0.815, $F(2,29)=3.30$, $p=0.051$, $\eta_p^2=0.185$. There were no other significant main effects or interactions.

⁴Using raw startle magnitude, there was a significant main effect of Valence, Wilks' lambda = 0.602, $F(2,29) = 9.58$, $p=0.001$, $\eta_p^2=0.398$. There was also a significant Valence x Gender interaction, Wilks' lambda = 0.758, $F(2,29) = 4.63$, $p=0.018$, $\eta_p^2=0.242$. Independent samples t-tests indicated that males exhibited significantly lower startle amplitudes to subjectively negative images compared to females, $t(32) = -2.41$, $p=0.022$.

The mean number of trials contributing to the average startle magnitude for each valence condition based on the participants' self-reported valence rating was compared between valence conditions (Table 5). There was a significant main effect of Valence, Wilks' lambda = 0.693, $F(2,29) = 6.41$, $p=0.005$, $\eta_p^2=0.307$, and a significant Valence x Diagnosis interaction, Wilks' lambda = 0.767, $F(2,29) = 4.40$, $p=0.021$, $\eta_p^2=0.233$. Separate ANOVAs for each diagnostic group were calculated. In the HC group, there were no significant main or interaction effects. For the SZ group, there was significant a main effect of Valence, Wilks' lambda=0.532, $F(2,14) = 6.15$, $p=0.012$, $\eta_p^2=0.468$. Paired samples t-tests show significantly fewer trials in the neutral condition compared to positive $t(16) = 2.67$, $p=0.017$ and negative $t(16) = 2.97$, $p=0.009$ which did not significantly differ from each other, $p=0.382$.

3.4. Subjective classification of image ratings

There was a significant main effect of Valence on subjective arousal ratings, Wilks' lambda = 0.499, $F(2,29) = 14.57$, $p<.001$, $\eta_p^2=0.501$ with all valence conditions significantly different from each other (Table 3). There were no other significant main effects or interactions. Within the HC group positive, $t(16)=5.95$, $p<0.001$ and negative, $t(16)=4.53$, $p<0.001$ images were rated as significantly more arousing than neutral and did not differ from each other, $p=0.418$. In SZ, arousal was rated as higher in response to positive images compared to neutral, $t(16)=3.41$, $p=0.004$. The difference between positive and negative approached significance, $t(16)= 1.96$, $p=0.068$, with no significant difference between arousal in response to neutral and negative images, $p=0.285$.

We could not calculate correlation coefficients between subjective image ratings and raw startle magnitude as there was no variability in ratings for the neutral condition (only values of '3' were assigned to the neutral condition).

3.5. Psychopathology and startle reactivity

There were no significant correlations between PANSS symptom ratings and raw startle magnitudes for either the normative or the subjective categorization.

4. Discussion

The present study examined subjective emotional experience in individuals with schizophrenia. The findings replicated and extended the study by Curtis et al. (1999) by examining emotional reactivity in individuals with schizophrenia as indexed by subjective report and a psychophysiological measure of emotional reactivity (i.e. emotion-modulated startle). The psychophysiological data was examined in two ways: (1) according to normative classification and (2) according to subjective valence classification. The rationale for this approach was to identify potential differences in psychophysiological emotional reactivity that may be masked when the interpretation of the psychophysiological data does not take subjective emotional experience into account.

4.1. Startle amplitudes

In line with our prediction and previous research, the pattern of emotion-modulated startle observed for SZ was comparable to that of HC for both the normative and the subjective conditions. However, the pattern of startle amplitudes was atypical in the normative condition and was largely impacted by gender. The valence x gender x diagnosis interaction indicated that the emotional content of the stimuli did not significantly impact startle amplitudes for the male participants. For female participants, startle magnitude in response to negative and neutral stimuli were larger than those in response to positive stimuli, but there was not a significant difference between startle magnitudes in response to negative and neutral slides. Therefore, in this sample, affective stimuli based on normative classification may contribute more to the modulation of the startle response in women compared to men, consistent with previous studies of emotion modulated startle in healthy samples (Bradley et al., 2001). Interestingly, these effects largely disappeared in the subjective condition in which startle magnitudes in response to negative slides remained larger than those observed in response to positive images, while startle magnitudes in response to neutral images no longer differed from either positive or negative images. This was due to decreased startle magnitude to neutral images and increased startle magnitude to positive images for both groups and genders (Figure 2). These findings indicate that when able to more closely match valence condition to emotional experience, the typical pattern of emotion modulated startle was still apparent. These results do not support our hypothesis of greater startle magnitudes during viewing of subjectively positive and neutral images in individuals with schizophrenia, and further highlight the importance of accurately classifying the emotional stimuli to the subjective experience of the participants.

4.2. Valence ratings

Self-report valence ratings suggest that the images considered to be of positive valence based on normative classification evoked a less positive subjective emotional experience in SZ compared to HC. This finding replicates that of Curtis et al. (1999) who used the same stimuli and Yee et al. (2010) who also found that SZ and prodromal subjects rated the positive slides as less pleasant than controls. These findings are partially in line with the pattern of subjective experience suggested by the Cohen and Minor (2010) meta-analysis. However, the SZ group in the present study appeared to have a specific attenuation of self-reported positive experience rather than a general negative response bias as reported by Cohen and Minor. As Curtis et al. (1999) suggested, dampened positive experience in schizophrenia may be related to symptoms of anhedonia, although several studies have failed to find differences in valence image ratings between patients and healthy controls (Schlenker et al., 1995; Volz et al., 2003; Kring et al. 2011). Therefore, further research is needed to outline the conditions in which patients report dampened positive emotions. Furthermore, the finding of comparable startle modulation along with an attenuated self-reported positive subjective emotional experience suggests a discrepancy between the psychophysiological index and subjective emotional experience in SZ. Such discrepancies between affect modulated startle and self-reported emotional experience are not specific to schizophrenia. Similar discrepancies have been reported in individuals with psychopathy, borderline personality disorder and alexithymia (Patrick et al., 1993; Hazlett et al., 2007;

Vanman et al., 1998) further highlighting the difference between the objective physiological response and the complex processes reflected in self-report.

4.3. Arousal ratings

Arousal ratings for stimuli based on normative classification showed slightly different patterns in healthy controls and schizophrenia patients. The healthy control group exhibited equivalent ratings for positive and negative images that were higher than those for neutral images. These findings mirror those from the normative sample used to develop the stimuli, in which average positive and negative arousal ratings were roughly equivalent (positive mean arousal rating = 6.41, negative mean arousal rating = 6.67) and higher than the arousal ratings for neutral images (neutral mean arousal rating = 3.18) (Lang et al., 1998). In contrast, the schizophrenia patients reported increased arousal in response to positive images compared to both neutral and negative images. These findings indicate that patients with schizophrenia rated positive slides as less pleasant in valence compared to HC and more arousing relative to other image categories. However as with startle magnitudes, these differences in the pattern of arousal ratings in those with SZ tended to normalize in the subjective condition in which arousal ratings did not differ between groups and the pattern of ratings in the schizophrenia group more closely followed the typical pattern found in healthy controls.

4.4. Trial numbers for subjective classification

Analysis of trial numbers included in the subjective condition revealed an even distribution of trials across valence conditions for the HC group. However, the SZ group allocated fewer trials to the neutral condition, and slightly more trials to the negative condition. This suggests that individuals with schizophrenia may have greater difficulty identifying the potentially more ambiguous emotional state that occurs in the absence of strong appetitive or aversive emotional activation (Cohen and Minor 2010). The classification of fewer trials into the neutral condition and a slightly greater number of trials assigned to the negative condition in the subjective analysis is consistent with the equivalent arousal ratings between neutral and negative slides in SZ. In other words, it appears that images which came from the normative neutral category that were given high arousal ratings may have been designated as belonging closer to the negative end of the valence spectrum according to subjective ratings. Such an explanation is in accordance with theories of aberrant attribution of motivational salience to stimuli arising from dysregulation of the dopamine system in psychosis (Kapur, 2003; Kapur et al., 2005), with disruption of emotional experience possibly related to alterations in amygdala activity (Aleman and Kahn, 2005). It is notable that with the inclusion of these normatively 'neutral' images in the subjective negative valence category, the startle magnitudes in this revised negative category remained large and comparable to that observed in HC. This suggests that at a psychophysiological level these images were in fact experienced as negative by the schizophrenia group. Therefore, patients with schizophrenia may tend to label *and* experience emotionally ambiguous stimuli as negative. Therefore, our data suggest that neutral stimuli may have been experienced (and hence re-classified) as negative by those with schizophrenia.

4.5. Startle amplitude correlations

We calculated the correlation coefficients between valence ratings and raw startle magnitudes in HC and SZ separately in order to investigate whether the overall pattern of ratings was consistent with the expected physiological response to the images (e.g. whether those who rated images more negatively responded with higher startle amplitudes, and vice versa for more positive ratings). We found that only in the healthy control group were valence ratings of neutral stimuli negatively correlated with startle magnitudes across all three valence conditions. Our results likely reflect variability in the startle magnitudes toward emotionally ambiguous stimuli in this relatively small sample of healthy controls. These findings further highlight the difference between cognitively complex valence ratings and objective psychophysiological responses to emotionally ambiguous stimuli.

Since the ultimate goal of studying basic emotional processes in the laboratory is to identify their connection to clinical symptomatology, researchers have examined the relationship between startle magnitude and schizophrenia symptoms. Like Curtis et al. (1999), we did not find a relationship between symptoms and startle magnitudes. The current study used the PANSS rating scale while Curtis et al. employed symptom counts derived from Module B of the Structured Clinical Interview for DSM disorders (SCID). Thus, despite methodological differences in the indexing of schizophrenia symptoms, neither study demonstrated reliable relationships between current symptoms and startle magnitudes in patients with schizophrenia.

4.6. Limitations and future directions

The ability to investigate subjective responses in the present study was limited by the restricted range of the five point scale that was used to assess self-reported valence and arousal. While this relatively restricted scale may have particularly affected the number of responses deemed 'neutral', the difference between HC and SZ subjective reports was the main focus of this paper. Nonetheless, future work should continue to examine both normative and subjective classification of emotional stimuli with a more fine-grained assessment tool to measure valence and arousal, as this particularly affected our ability to assess the relationship between subjective valence ratings and startle magnitude (i.e. we could not calculate the correlation coefficient since only items given a rating of '3' were coded as neutral). Such scales might include 9 or 20 point scales as have been used in prior studies (Curtis et al., 1999; Kring et al., 2011). Alternatively, one might examine the continuum of real-time emotional response through the use of a dial, which could be adjusted throughout the entire emotion induction period. Future work with larger sample sizes should pursue the possibility of subgroups and potential links to functional outcomes as suggested by Strauss and Herbener (2011). Another limitation of this study is the medicated status of nearly all the patient sample. While medication, especially atypical antipsychotics, are known to reduce pre-pulse inhibition deficits in patients, (Kumari et al., 2007), Aggernaes et al., (2010) reported that neuroleptic naïve, first-episode patients demonstrate reduced pre-pulse inhibition compared to healthy controls, and Curtis et al., (1999) found no relationship between affect modulated startle and medication status using the same stimuli in a similar paradigm. While the effects of medication on affect modulated startle need further investigation, it is likely that our findings were either unaffected or

attenuated by the use of medication in our sample. Finally, the reanalysis of startle data based on subjective valence ratings resulted in conditions containing different numbers of trials for each individual. While the trial number analyses resulted in an interesting and novel finding, it makes interpretation of the statistical analysis of startle magnitudes difficult (see Supplementary Materials). Therefore, caution is warranted when interpreting these analyses and future studies should include sufficient trials to address this issue.

4.7. Conclusions

This is the first study to evaluate emotion-modulated startle in individuals with schizophrenia via subjective classification of the emotional stimuli. Therefore, the findings of this study are tentative and a similar approach should be employed in future work to further clarify the psychophysiological concomitants of emotional disturbances in schizophrenia. The current study highlights the importance of assessing the subjective experience of both valence and arousal of emotional stimuli and in taking these reports into consideration when interpreting psychophysiological data.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- Measured affect modulated startle in schizophrenia
- Novel analysis sorted startle trials based on subjective valence classification
- There were no startle group differences using normative or subjective classification
- There were group differences on subjective ratings and classification of slides

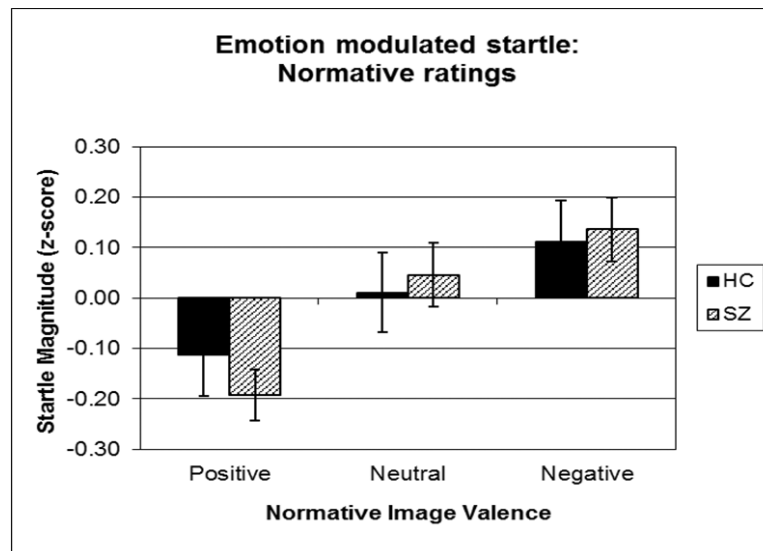


Figure 1.

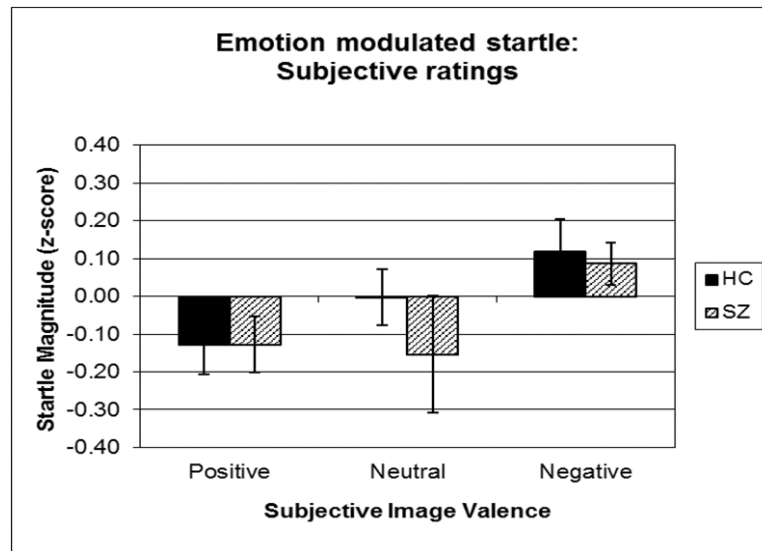


Figure 2.

Table 1

Participant demographics

	Control Group (n=17)	Schizophrenia Group (n=17)
	<i>M (SD)</i>	<i>M (SD)</i>
Age	38.82 (11.57) ^a	36.94 (11.78) ^a
Gender (M/F)	11/6 ^b	12/5 ^b
Ethnicity ^c		
African American	n=10	n=14
Caucasian	n=6	n=3
Latino	n=1	
PANSS Positive Symptoms		15.65 (4.94)
PANSS Negative Symptoms		16.35 (5.23)
PANSS General Psychopathology		27.76 (6.86)

^a $t(32)=0.47, p=0.641$

^b $\chi^2(1, N=34)=0.134, p=0.714$

^c $\chi^2(2, N=34)=2.67, p=0.264$

Table 2

Raw startle magnitudes in response to probe-alone trials

Startle Probe	HC	SZ
	<i>M(SD)</i>	<i>M(SD)</i>
Probe 1	86.61 (69.50)	79.00 (44.49)
Probe 2	79.51 (74.81)	78.63 (84.15)
Probe 3	58.27 (54.51)	82.88 (66.82)
Probe 4	83.72 (74.33)	82.74 (60.63)
Probe 5	85.82 (70.93)	74.00 (52.97)
Probe 6	72.69 (65.68)	61.75 (45.61)
Probe 7	105.48 (125.75)	89.73 (93.26)
Probe 8	69.78 (69.09)	69.64 (83.69)

Table 3

Mean valence and arousal ratings for normative and subjective image valence classification

Valence Ratings				
	Normative Classification		Subjective Classification	
	HC <i>M(SD)</i>	SZ <i>M(SD)</i>	HC <i>M(SD)</i>	SZ <i>M(SD)</i>
Positive	4.27 (0.41)	3.73 (0.64) ^a	4.48 (0.31)	4.70 (0.27)
Neutral	3.10 (0.27)	3.06 (0.66)	3.00 (0.00)	3.00 (0.00)
Negative	1.60 (0.38)	1.83 (0.74)	1.35 (0.28)	1.27 (0.28)
Arousal Ratings				
Positive	3.25 (0.91)	3.52 (0.76)	3.11 (0.89)	3.42 (1.00)
Neutral	1.87 (0.76)	2.26 (0.74)	1.99 (0.80)	2.20 (0.91)
Negative	2.92 (1.05)	2.59 (1.05)	2.89 (1.01)	2.54 (1.04)

^a SZ rated the normatively positive images as significantly less positive than HC

Table 4

Correlations between raw startle magnitudes and normative valence ratings

Valence Ratings	Raw Startle Magnitude (HC)		
	Positive Valence	Neutral Valence	Negative Valence
Positive Image	−0.11	−0.05	−0.19
Neutral Image	−0.57 [*]	−0.52 [*]	−0.61 ^{*†}
Negative Image	−0.03	−0.05	−0.02
	Raw Startle Magnitude (SZ)		
	Positive Valence	Neutral Valence	Negative Valence
Positive Image	0.26	0.34	0.27
Neutral Image	0.03	0.06	0.06 [†]
Negative Image	−0.31	−0.32	−0.33

^{*}
 $p < 0.05$

[†] The relationship between Neutral Image valence ratings and Negative Valence startle magnitude in HC was significantly greater than the corresponding relationship in SZ, $p = .042$.

Table 5

Mean number of startle trials per subjective valence category

Valence Classification	Number of Startle Trials	
	Control Group ^a n=17	Schizophrenia Group n=17
	<i>M(SD)</i>	<i>M(SD)</i>
Positive	7.94 (2.38)	8.29 (2.97)
Neutral	6.41 (2.85)	4.00 (4.25) ^b
Negative	7.35 (1.69)	9.12 (3.22)

^a Main effect of Valence was not significant for HC ($p = 0.480$), indicating that trial numbers were equivalent across valence conditions.

^b Main effect of Valence was significant for SZ ($p < 0.001$), indicating significantly fewer trials were designated neutral.