

Impaired emotion regulation in schizophrenia: evidence from event-related potentials

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Background. Although several aspects of emotion seem to be intact in schizophrenia, there is emerging evidence that patients show an impaired ability to adaptively regulate their emotions. This event-related potential (ERP) study examined whether schizophrenia is associated with impaired neural responses to appraisal frames, that is when negative stimuli are presented in a less negative context.

Method. Thirty-one schizophrenia out-patients and 27 healthy controls completed a validated picture-viewing task with three conditions: (1) neutral pictures preceded by neutral descriptions ('Neutral'), (2) unpleasant pictures preceded by negative descriptions ('Preappraised negative'), and (3) unpleasant pictures preceded by more neutral descriptions ('Preappraised neutral'). Analyses focused on the late positive potential (LPP), an index of facilitated attention to emotional stimuli that is reduced following cognitive emotion regulation strategies, during four time windows from 300 to 2000 ms post-picture onset.

Results. Replicating prior studies, controls showed smaller LPP in Preappraised neutral and Neutral *versus* Preappraised negative conditions throughout the 300–2000-ms time period. By contrast, patients showed (a) larger LPP in Preappraised neutral and Preappraised negative *versus* Neutral conditions in the initial period (300–600 ms) and (b) an atypical pattern of larger LPP to Preappraised neutral *versus* Preappraised negative and Neutral conditions in the 600–1500-ms epochs.

Conclusions. Modulation of neural responses by a cognitive emotion regulation strategy seems to be impaired in schizophrenia during the first 2 s after exposure to unpleasant stimuli.

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Introduction

People with schizophrenia often demonstrate diminished emotional expression and engagement in pleasurable activities on clinical assessments of negative symptoms (Blanchard *et al.* 2011). However, laboratory studies using affective science methods have revealed that several components of emotion seem remarkably intact in schizophrenia. On tasks involving exposure to emotionally evocative stimuli (e.g. pictures, films, foods), people with schizophrenia report feeling pleasant emotions as strongly as unaffected people (Cohen & Minor, 2008). Similarly, they report feeling unpleasant emotions as strongly as, or sometimes more strongly than, people without schizophrenia. These intact responses extend beyond

self-reported emotions as patients show normal emotion-modulated cardiovascular, electrodermal and startle eyeblink responses to evocative stimuli (Kring & Moran, 2008).

People with schizophrenia also show largely normal event-related potentials (ERPs) during even the initial stages of processing emotional stimuli. A series of studies has focused on emotional modulation of the late positive potential (LPP), an index of motivated attention that is thought to reflect increased allocation of attentional resources to, and sustained attentional processing of, motivationally relevant stimuli (Hajcak *et al.* 2010). In healthy adults, emotional modulation of the LPP begins about 300 ms following stimulus onset at midline central–parietal sites. The LPP can persist for several seconds during picture presentation and demonstrates somewhat different characteristics during early and later time windows. For example, the P300 and the early portion of the LPP seem fairly similar in terms their temporal and spatial characteristics, and also their sensitivity to emotional stimuli.

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In contrast to the transient P300, the LPP is sustained at central sites and is thought to reflect more elaborated processing related to the significance and meaning of stimuli (Hajcak *et al.* 2012). People with schizophrenia have generally shown normal patterns of LPP enhancement to emotional *versus* neutral pictures; this was true under experimental conditions in which subjects were explicitly instructed to attend to the pictures in a passive viewing paradigm and when the emotional pictures were incidental to task demands (Horan *et al.* 2010, 2012).

Although emotional responses to evocative stimuli seem to be largely intact in schizophrenia, adaptive functioning in daily life also requires the capacity to regulate one's emotions to meet goals and manage arousal. Emotion regulation is the process by which people influence which emotion will be experienced, when it will be experienced and how it will be experienced and expressed (Gross & Thompson, 2007).

Gross and colleagues distinguish between regulation strategies that are antecedent focused, that is before emotion response tendencies have become fully activated to change behavioral and physiological responding, and response focused, that is after the response tendencies have been generated (Gross, 1998; Gross & John, 2003). Cognitive reappraisal, an extensively studied antecedent-focused strategy, is a form of cognitive change that involves construing a potentially emotion-eliciting situation in a way that changes its emotional impact (Lazarus, 1991; Gross, 2002; Ochsner & Gross, 2005; Hajcak & Nieuwenhuis, 2006). For example, during a stressful job interview, an individual might down-regulate negative emotions by viewing the experience as an opportunity to find out how much they are suited to a particular work environment rather than as a test of their worth. Reappraisal may be a particularly effective emotion regulation strategy because it serves to change the fundamental meaning and personal significance of an emotional stimulus prior to an unpleasant emotional response being elicited. Contrasted with less optimal response-focused strategies, such as suppression of emotional expression (e.g. maintaining a poker face), changing the personal significance of an unpleasant stimulus is efficient and effective, with few physiological or cognitive costs (Gross, 2002).

Several studies have investigated the neural correlates of cognitive reappraisal in healthy adults. For example, functional magnetic resonance imaging (fMRI) studies examining the impact of reappraisal instructions (e.g. 'Reappraise' *versus* 'Attend') on emotional responses after unpleasant stimuli are presented have identified a key neural circuit that shows increased activity in prefrontal brain areas involved in cognitive control coupled with decreased activity in

the amygdala and other brain areas involved in emotional responses (Ochsner & Gross, 2005). In addition, ERP paradigms have begun to shed light on the time course of appraisal manipulations.

In a series of studies, Hajcak and colleagues demonstrated that the magnitude of the LPP to unpleasant picture stimuli is sensitive to manipulations that impact how the stimuli are interpreted (Foti & Hajcak, 2008; MacNamara *et al.* 2009, 2011). These studies involved reappraisal in which auditory descriptions were presented before unpleasant and neutral pictures that framed the images in either a more negative or a more neutral manner (Hajcak *et al.*, in press). For example, a picture of a fierce-looking snake might be preceded by either 'This is a poisonous snake that is very dangerous' or 'This is a snake that is completely harmless – it doesn't even have teeth'; the latter description is designed to down-regulate the emotional response elicited by the unpleasant image. Reappraisal with verbal descriptions removes the potential confound of task difficulty (i.e. greater effort involved in 'Reappraise' *versus* 'Attend' conditions in many fMRI studies), such that each condition simply involves listening to descriptions and viewing pictures. Unpleasant images preceded by descriptions that framed them in a more neutral light elicited reliably smaller LPPs than unpleasant images preceded by more negative descriptions; LPPs to unpleasant images in both conditions were larger than those found for neutral pictures preceded by neutral descriptions. Modulation of the LPP began within 300 ms after stimulus onset and was sustained for at least several hundred milliseconds during picture presentation, indicating that shifts in the meaning due to reappraisal exert an early, sustained influence on emotion processing in the healthy adult brain. These findings have been extended to young children and applied to understanding emotion regulation processes associated with vulnerability to depression and anxiety disorders (Dennis & Hajcak, 2009; Mocaiber *et al.* 2009; DeCicco *et al.* 2012). Thus, it is possible to modulate early electrocortical responses to unpleasant pictures by reappraisal and this paradigm is well suited for use in clinical populations.

The primary aim of the current study was to examine whether people with schizophrenia can modulate their electrophysiological responses (i.e. LPP) to unpleasant stimuli through reappraisal-based manipulations of stimulus meaning. We are unaware of prior studies that have used ERP paradigms to study emotion regulation in schizophrenia, although the few relevant studies using alternative methods suggest impaired emotion regulation in this population. In the most directly relevant work,

a recent fMRI study found that people with schizophrenia ($n=12$) showed ventrolateral prefrontal cortex (VLPFC) hypoactivation, along with decreased PFC–amygdala coupling, during down-regulation of unpleasant emotion through cognitive reappraisal (Morris *et al.* 2012). At a broader level, several studies indicate that people with schizophrenia demonstrate lower scores on the ‘Managing Emotions’ branch of the Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT; Mayer *et al.* 2003), which assesses, in part, the ability to adaptively regulate one’s own emotions (e.g. Eack *et al.* 2008; Kee *et al.* 2009). There have also been a few studies using self-report emotion regulation questionnaires in schizophrenia, although the findings are mixed. Some studies found that patients reported lower habitual use of cognitive reappraisal (Livingstone *et al.* 2009; van der Meer *et al.* 2009) or greater use of suppression (van der Meer *et al.* 2009) than healthy controls but others found no group differences on these measures (Henry *et al.* 2008; Badcock *et al.* 2011; Perry *et al.* 2011). The available evidence led us to predict that schizophrenia patients would show diminished modulation of the LPP to unpleasant pictures preceded by more neutral than more negative descriptions as compared to matched healthy controls.

A secondary aim was to explore relationships among ERP indices from the emotion regulation task, scores on a self-report emotion regulation questionnaire assessing habitual use of cognitive reappraisal and suppression, and clinical symptoms within the patient group. The few prior studies that have examined relationships between indices of emotion regulation and symptoms are inconsistent, reporting relationships to negative symptoms (Henry *et al.* 2007; Kee *et al.* 2009; Perry *et al.* 2011), positive symptoms (Badcock *et al.* 2011) or no relationship to symptoms (Henry *et al.* 2008). We therefore did not have specific directional hypotheses for these analyses.

Method

Participants

Thirty-one out-patients with schizophrenia and 27 healthy control subjects participated in this study. The schizophrenia patients were recruited from out-patient treatment clinics at the Veterans Affairs Greater Los Angeles Healthcare System (VAGLAHS) and through presentations in the community. Patients met criteria for schizophrenia based on the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First *et al.* 1996). None of the patients were in a depressed or manic episode at the time of testing. Additional exclusion criteria for patients included:

substance abuse or dependence in the past 6 months; IQ <70 based on chart reviews; a history of loss of consciousness for more than 1 h; an identifiable neurological disorder; or insufficient fluency in English. All patients were clinically stable as defined by: no hospitalizations in the past 3 months, no changes in living situation in the past 2 months, and no medication changes in the past 6 weeks. Patients were medicated at clinically determined dosages, with 26 receiving atypical antipsychotics, four receiving typical antipsychotics and one receiving both types of antipsychotic medication. The average antipsychotic medication dosage in chlorpromazine (CPZ) equivalent units (Andreasen *et al.* 2010) was 269.59 (S.D. = 160.07).

Healthy controls were recruited through flyers posted in local newspapers, websites and posted advertisements. An initial screening interview excluded potential control participants with identifiable neurological disorder or head injury, those whose first-degree relatives had schizophrenia or other psychotic disorder, or participants not sufficiently fluent in English. Potential controls were screened with the SCID-I and excluded for history of schizophrenia or other psychotic disorder, bipolar disorder, recurrent depression, lifetime history of substance dependence or any substance abuse in the past 6 months. Potential controls were also administered portions of the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II; First *et al.* 1994) and excluded if they had avoidant, paranoid, schizoid or schizotypal personality disorder.

All SCID interviewers were trained through the Treatment Unit of the Department of Veterans Affairs VISN 22 Mental Illness Research, Education, and Clinical Center (MIRECC) to a minimum κ of 0.75 for key psychotic and mood items (Ventura *et al.* 1998). All participants had the capacity to give informed consent and provided written informed consent after all procedures were fully explained in accordance with procedures approved by the Institutional Review Boards at the University of California, Los Angeles (UCLA) and the VAGLAHS.

Demographic information for both groups and clinical data for the schizophrenia group are presented in Table 1. The groups did not significantly differ in sex, age or ethnicity. The patients had lower personal education levels than controls but the groups did not differ in parental education. We intended to match the groups for parental education as a control for family socio-economic status because personal education can be influenced by the illness itself. Patients in the schizophrenia group had a typical age of onset, were chronically ill, and showed mild to moderate levels of clinical symptoms at the time of testing.

Table 1. Demographic and clinical data

	Schizophrenia (<i>n</i> = 31)	Controls (<i>n</i> = 27)	Statistics
Sex (% male)	75.0	77.4	$\chi^2_{(1,58)} = 0.09$
Age (years), mean (s.d.)	47.8 (9.8)	45.5 (6.7)	$t_{56} = 1.01$
Ethnicity (%)			
White	54.8	74	$\chi^2_{(4,58)} = 3.88$
African American	35.5	26	
Asian	3.2	0	
Hispanic	3.2	0	
Other	3.2		
Education (years), mean (s.d.)	12.5 (1.9)	14.93 (1.3)	$t_{56} = 5.52^*$
Parental education (years), mean (s.d.)	13.0 (3.8)	14.5 (3.1)	$t_{56} = 1.72$
Age of onset (years), mean (s.d.)	20.6 (5.7)		
Duration of illness (years), mean (s.d.)	26.9 (11.8)		
BPRS score, mean (s.d.)			
Positive symptoms	1.7 (0.7)		
Negative symptoms	2.0 (0.9)		
Total	36.7 (9.4)		

BPRS, Brief Psychiatric Rating Scale; s.d., standard deviation.

* $p < 0.005$.

Symptom ratings

For all patients, psychiatric symptoms during the previous 2 weeks were rated using the expanded 24-item UCLA version of the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962; Lukoff *et al.* 1986) by a trained rater (Ventura *et al.* 1993). Ratings from the positive and negative symptom subscales, along with total scores, were examined (Kopelowicz *et al.* 2008).

ERP paradigm

Stimulus materials

The paradigm was modeled on prior ERP studies of preappraisal (Foti & Hajcak, 2008; Dennis & Hajcak, 2009; MacNamara *et al.* 2009). A total of 84 pictures were selected from the International Affective Picture System (IAPS; Lang *et al.* 1999); of these, 28 depicted neutral scenes and 56 depicted unpleasant scenes. The two categories differed on normative [1 (unpleasant) to 9 (pleasant)] ratings of valence (mean = 5.05, s.d. = 1.21, for neutral pictures; mean = 2.82, s.d. = 1.64, for unpleasant pictures); in addition, the emotional pictures were reliably higher on normative [1 (low) to 9 (high)] arousal ratings (mean = 5.71, s.d. = 2.16, for unpleasant pictures; and mean = 2.91, s.d. = 1.93, for neutral pictures). People with schizophrenia have consistently been found to report emotional responses to IAPS stimuli that are comparable to healthy control subjects (see Cohen & Minor, 2008 for a meta-analysis).

For the preappraisal manipulation, a brief auditory description (using the established descriptions of Foti & Hajcak, 2008; Dennis & Hajcak, 2009; MacNamara *et al.* 2009) of the upcoming picture was played through speakers, prior to the presentation of the picture. Every participant heard the same neutral description for the 28 neutral images ('Neutral' condition). For each of the 56 unpleasant images, participants heard one of two descriptions: for 28 of the unpleasant pictures, a neutral description preceded the image ('Preappraised neutral' condition) whereas a negative description preceded the other 28 ('Preappraised negative' condition). A complete list of the IAPS image numbers and associated descriptions is presented in the Appendix.

Procedure

After a brief description of the experiment, electroencephalography (EEG) electrodes were attached. Participants were told that they would be viewing pictures and that they would hear a brief description played over the speakers prior to each picture that would describe the upcoming picture. Prior to each picture, a white fixation cross was presented on a black screen for 6 s. During this period, a brief (3–5 s) description of the upcoming picture was presented. Subjects then viewed the pictures passively; the pictures were in color, displayed for 6 s, and occupied the entire monitor (48.26 cm). The viewing distance was approximately 1 m. After each picture, there was a variable 5- to 7-s delay until the next trial. To ensure

that subjects understood the task, six practice trials were administered to all subjects and were repeated with additional instruction if necessary. As in previous studies using a similar paradigm in children (Dennis & Hajcak, 2009; DeCicco *et al.* 2012), self-reported emotional responses were not collected in this initial ERP study of emotion regulation in schizophrenia. After the practice trials, all participants performed the 84-task trials with breaks after every 14 trials. The order of trials and the descriptions were determined randomly for each subject. The task was administered using Eprime software (PST Technologies, USA) to control the presentation and timing of all stimuli.

EEG recording and processing

Participants had their EEG activity recorded continuously from 64 electrodes based on the 10/20 system placed in an electrode cap (Cortech Solutions, USA) and the ActiveTwo BioSemi system (BioSemi, The Netherlands). The signal was preamplified at the electrode with a gain of one; the EEG was digitized at 24-bit resolution with a sampling rate of 512 Hz with a bandpass of 0–100 Hz using a low-pass fifth-order sinc filter with a half-power cut-off of 102.4 Hz. Recordings were taken from the 64 electrodes, and also from two electrodes placed on the left and right mastoids. The electro-oculogram was recorded from four facial electrodes: two 1 cm above and below the left eye, one 1 cm to the left of the left eye, and one 1 cm to the right of the right eye. Each electrode was measured online with respect to a common mode sense electrode that formed a monopolar channel.

Off-line analysis was performed using Brain Vision Analyzer software (Brain Products, Germany). All EEG data were re-referenced to the average of all electrodes and band-pass filtered with cut-offs of 0.1 and 30 Hz. The EEG was segmented for each image beginning 200 ms before each stimulus and continuing for 2000 ms post-stimulus onset (total of 2200 ms). Each EEG segment was corrected for blinks and eye movements using the method developed by Gratton *et al.* (1983). Specific channels were rejected in each trial using a semi-automated procedure, with physiological artifacts identified by the following criteria: a step of more than $50 \mu\text{V}$ between sample points, a maximum difference of less than $0.5 \mu\text{V}$ within 100-ms intervals, and an amplitude that exceeded $\pm 75 \mu\text{V}$. Two patients and two controls were excluded because the quality of the ERP data was poor (less than 50% artifact free trials) and one patient was excluded because of ERP values that differed by more than 3 s.d. from the patient group means. The final sample in this report consisted of 58 individuals (31 patients, 27 controls).

Based on the topographical maps from this sample, we selected a set of six electrodes (C1, C2, Cz, CPz, CP1, CP2) where the LPP was maximal for analyses. Based on prior studies (Foti & Hajcak, 2008; Dennis & Hajcak, 2009) and the morphology of the waveforms from the current study, we evaluated the LPP across four time epochs: (1) 300–600 ms, (2) 600–1000 ms, (3) 1000–1500 ms and (4) 1500–2000 ms. ERPs were constructed by separately averaging segments of the three experimental conditions (Neutral, Preappraised neutral, Preappraised negative). In each case, the average activity in the 200-ms window prior to picture onset served as the baseline. The LPP was quantified as the mean activity during each epoch across the six electrode sites for each participant.

Emotion Regulation Questionnaire (ERQ)

All participants completed the ERQ (Gross & John, 2003). On this 10-item questionnaire, six items focus on cognitive reappraisal (e.g. 'When I want to feel more positive emotion, I change the way I'm thinking about the situation') and four focus on suppression (e.g. 'I keep my emotions to myself'). Subjects were asked to indicate to what extent the statements apply to them, scoring from 1 (strongly disagree) to 7 (strongly agree). Higher scores reflect the more frequent use of a particular strategy. The ERQ has been shown to be a reliable and valid measure of emotion regulation strategies in healthy subjects (Gross & John, 2003) and in people with schizophrenia (e.g. Henry *et al.* 2008; van der Meer *et al.* 2009; Perry *et al.* 2011).

Data analyses

For demographic data, group differences for continuous variables were evaluated with *t* tests and for categorical variables with χ^2 tests. Preliminary analyses of the distributional properties of the demographic, clinical, ERP and self-report measures indicated that parametric statistical tests were appropriate. Primary analyses were conducted in three stages. First, for the ERP data, separate 3 (condition: Neutral, Preappraised neutral, Preappraised negative) \times 2 (group: patient, control) repeated-measures analyses of variance (ANOVAs) were conducted for each of the four time epochs. Greenhouse–Geisser ϵ corrections were used for repeated-measures analyses with more than one degree of freedom. In these cases, we report the uncorrected degrees of freedom and the corrected *p* values. Second, group differences on the self-report emotion regulation scales were evaluated with *t* tests. Third, within the schizophrenia group, Pearson correlation coefficients examined associations among ERP, symptom and self-report emotion regulation

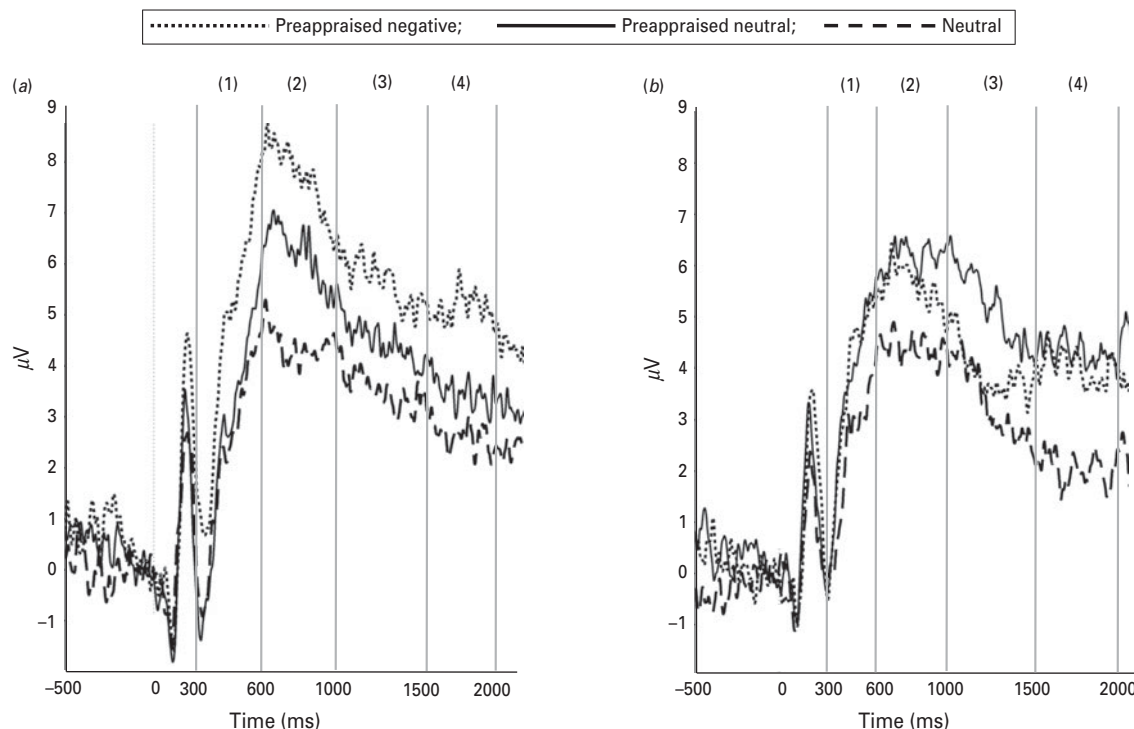


Fig. 1. Late positive potential (LPP) grand averages at pooled electrodes C1, Cz, C2, CP1, CPz and CP2 in Preappraised negative, Preappraised neutral, and Neutral conditions for (a) control and (b) schizophrenia groups. Stimulus onset occurred at 0 ms. Positive is plotted upward. The four epoch numbers are given in parentheses.

variables. For the ERPs in these correlational analyses, LPP difference wave scores during each epoch for the Preappraised negative minus Preappraised neutral conditions were used as the electrophysiological index of emotion regulation.

Results

LPP results

Grand average ERPs for the control and schizophrenia groups are presented in Fig. 1†. Table 2 displays

† We also evaluated whether the positive deflection seen before 300 ms in Fig. 1 revealed any effects involving group. Mean amplitude was evaluated in the time window from 165 to 215 ms (centered around a peak at 190 ms) and this positive deflection was maximal in the same six central/parietal electrodes used in the primary analyses; we therefore based the mean on a pooling of these six electrodes. Notably, this deflection seems to reflect the beginning of the LPP rather than an independent, earlier ERP component such as P1 or P2, an interpretation that is consistent with prior research (Foti et al. 2009; Hajcak et al. 2009). A significant main effect of condition ($F_{2,56} = 6.44$, $p < 0.02$), indicated a significant difference between the Preappraised negative versus Neutral conditions ($t_{57} = -4.00$, $p < 0.001$) but not between the other conditions: Preappraised neutral versus Neutral ($t_{57} = -1.72$, $p = 0.09$) and Preappraised negative versus Preappraised neutral ($t_{57} = -1.68$, $p = 0.10$). However, the group ($F_{1,56} = 0.37$, $p > 0.05$) and group \times condition interactions ($F_{2,56} = 1.02$, $p > 0.05$) were not significant. There were no significant correlations between the Preappraised negative minus Preappraised neutral difference scores and self-reported regulation strategies or symptoms in either group.

results of the repeated-measures ANOVAs along with corresponding follow-up within-group comparisons during each LPP epoch.

LPP during epoch 1 (300–600 ms)

There were significant condition and interaction effects during the earliest LPP epoch. For controls, preappraisal effects were evident: the LPP was significantly larger during the Preappraised negative condition compared to both the Preappraised neutral and Neutral conditions, which did not differ significantly from each other. By contrast, for patients the LPP was significantly larger during both the Preappraised negative and Preappraised neutral conditions compared to the Neutral condition, and the two Preappraise conditions did not differ from each other. Thus, the patients showed larger LPPs to unpleasant pictures than neutral pictures but no dampening of the LPP for the Preappraised neutral condition during this initial epoch.

LPP during epoch 2 (600–1000 ms)

There were again significant condition and interaction effects in this epoch. Controls continued to show a significant preappraisal effect evidenced by significant differences among the three conditions. The LPP amplitude showed a linear decrease across conditions,

Table 2. Group comparisons on the late positive potential (LPP)

	ANOVA results			Group means (s.d.)			Within-group <i>t</i> tests		
	Group	Condition	Group × condition	Neutral	Preappraised neutral	Preappraised negative	Neutral versus		Preappraised neutral versus preappraised negative
							<i>F</i> _{1,56}	<i>F</i> _{2,56}	
Epoch 1 : 300–600 ms	0.06	8.51***	4.29*	Control 2.67 (3.68)	3.07 (4.87)	5.02 (4.11)	–0.59	–4.00***	2.52*
				Scz 2.38 (4.47)	4.11 (3.67)	3.55 (3.88)	–2.90*	–2.30*	–1.14
Epoch 2 : 601–1000 ms	1.26	13.32***	5.82**	Control 4.42 (3.50)	6.23 (4.56)	7.80 (3.74)	–2.81**	–5.43***	2.83**
				Scz 4.21 (4.22)	6.23 (3.89)	5.03 (3.54)	–2.64*	–1.33	–2.12*
Epoch 3 : 1001–1500 ms	0.86	2.73†	3.58*	Control 3.62 (3.88)	4.60 (3.75)	5.74 (3.33)	–1.19	–2.82***	1.97†
				Scz 3.42 (4.39)	5.12 (3.35)	3.25 (4.50)	–1.7†	0.18	–2.64*
Epoch 4 : 1501–2000 ms	0.21	3.40*	1.51	Control 2.65 (3.77)	3.52 (3.80)	5.06 (3.19)	–1.03	–2.79**	1.94†
				Scz 2.45 (5.06)	4.35 (3.11)	3.48 (4.81)	–1.66	–0.83	–1.06

Scz, Schizophrenia; s.d., standard deviation.
 † $p < 0.10$, * $p < 0.05$, ** $p < 0.01$, *** $p < 0.005$.

with the LPP largest during the Preappraised negative, intermediate during the Preappraised neutral, and smallest during the Neutral condition. Patients showed a strikingly different pattern. Their LPP was significantly larger during the Preappraised neutral condition than during both the Preappraised negative and Neutral conditions, which did not differ from each other. The patients therefore demonstrated an atypical pattern of relatively enhanced LPP for the Preappraised neutral condition.

LPP during epoch 3 (1000–1500 ms)

During the third epoch, a trend-level condition effect was accompanied by a significant interaction. The controls continued to show separation among the conditions in line with the expected preappraisal influence. The LPP was larger in the Preappraised negative versus Neutral condition whereas there was no difference between the Preappraised neutral and Neutral conditions; there was also a trend for larger LPP during the Preappraised negative versus Preappraised neutral conditions. For patients, the pattern was again different. Their LPP during the Preappraised neutral condition was significantly larger during than the Preappraised negative condition and different from the Neutral condition at a trend level. There was no difference between the Preappraised negative and Neutral conditions, again indicating an enhanced LPP during the Preappraised neutral condition.

LPP during epoch 4 (1500–2000 ms)

During the final epoch there was a significant condition effect but the interaction effect was not significant. Across the two groups, the LPP was larger for the Preappraised negative versus Neutral conditions ($t_{56} = -2.17, p < 0.05$) and there was a trend for larger LPP in the Preappraised negative versus Preappraised neutral conditions ($t_{56} = -1.96, p = 0.09$). For consistency, within-group *t* tests are also presented in Table 2. The control group continued to show a pattern similar to the previous epoch (the LPP was larger in the Preappraised negative versus Neutral condition and no difference between the Preappraised neutral and Neutral conditions; there was also a trend for larger LPP during the Preappraised negative versus Preappraised neutral conditions). There were no significant differences across condition within the patient group.

Group comparisons on self-reported emotion regulation strategies

The groups differed on both types of self-reported habitual emotion regulation strategies. Cognitive

reappraisal scores were significantly higher in controls (mean = 5.3, S.D. = 1.0) than patients (mean = 4.5, S.D. = 1.3, $t_{56} = -2.45$, $p < 0.05$). By contrast, suppression scores were significantly lower in controls (mean = 3.2, S.D. = 0.9) than patients (mean = 3.9, S.D. = 1.6, $t_{56} = 2.27$, $p < 0.05$).

Exploratory correlations within the schizophrenia group

First, we examined whether the four LPP difference wave scores (Preappraised negative minus Preappraised neutral) correlated significantly with self-reported habitual emotion regulation strategies (reappraisal, suppression) and clinical symptoms (positive, negative, total). Of the 40 correlations, only one was significant and the direction of the correlation was counterintuitive. Higher difference scores (i.e. greater reappraisal effect) during the 300–600-ms epoch correlated with higher positive symptoms ($r_{31} = 0.37$, $p < 0.05$). There were also no significant correlations with CPZ equivalent units. (There were no significant correlations between ERPs and self-reported emotion regulation strategies in the control group.) Second, we examined correlations between the self-reported emotion regulation and clinical symptom variables. Higher levels of suppression correlated significantly with higher positive ($r_{31} = 0.36$, $p < 0.05$), negative ($r_{31} = 0.45$, $p < 0.05$) and total ($r_{31} = 0.41$, $p < 0.05$) symptom levels. Reappraisal levels did not correlate significantly with symptoms.

Discussion

This ERP study evaluated whether people with schizophrenia alter their neurophysiological responses to unpleasant stimuli following appraisal-based manipulations of stimulus meaning. Consistent with prior studies (Foti & Hajcak, 2008; Dennis & Hajcak, 2009; MacNamara et al. 2009; DeCicco et al. 2012), healthy controls showed a pattern in which the LPP was significantly reduced when unpleasant pictures were reappraised in less negative terms. Specifically, the LPP in the Preappraised neutral condition did not differ from the Neutral condition during the earliest epoch (300–600 ms) and fell between the Neutral and the Preappraised negative conditions during the middle two epochs (600–1500 ms). By contrast, patients failed to down-regulate their LPP responses, instead showing (a) larger LPP in response to both reappraise conditions versus Neutral conditions in the initial epoch and (b) the opposite pattern from controls in the middle periods with larger LPP to Preappraised neutral versus Preappraised negative and Neutral conditions. The patients also reported

lower habitual use of cognitive reappraisal and higher expressive suppression than controls, although there were no significant correlations between these self-reports and LPP variables. This study provides the first electrophysiological evidence of impaired sensitivity to reappraisal manipulations of emotional stimulus meaning in schizophrenia.

The patients' absence of LPP reappraisal effects converges with the results of a few prior studies of cognitive reappraisal in schizophrenia using self-report, behavioral and fMRI paradigms (e.g. Eack et al. 2008; Kee et al. 2009; Livingstone et al. 2009; van der Meer et al. 2009). A likely explanation for this impairment is a disturbance in top-down cognitive control of emotional responses. Disturbances in cognitive control and associated prefrontal cortical circuitry are well documented in schizophrenia (Barch & Braver, 2005; Lesh et al. 2011) and cognitive control plays a central role in cognitive reappraisal (Ochsner & Gross, 2005). This explanation converges with a recent fMRI study in schizophrenia in which subjects were instructed to voluntarily decrease, maintain or increase their emotional responses to unpleasant pictures (Morris et al. 2012). When attempting to decrease their responses, patients displayed hypoactivation of prefrontal regions and significantly less corticolimbic coupling than healthy controls, consistent with impaired cognitive control. A key aspect of the fMRI study that affects interpretation was that subjects had to generate their own reinterpretations in the decrease condition. This leaves open the possibility that the patients' impairment merely reflected increased cognitive demands associated with generating alternative interpretations after unpleasant stimuli are presented, rather than an inability to benefit from a shift in meaning of the stimuli. The current ERP paradigm eliminated these differences in cognitive demands across conditions by presenting subjects with descriptions before each type of trial. In this way, the shifts in meaning occurred in a more implicit manner (for further discussion, see Foti & Hajcak, 2008; MacNamara et al. 2009). Even under these task conditions, schizophrenia patients showed impaired modulation of the neurophysiological responses.

We previously found that patients and controls showed comparable increases in LPP amplitudes for unpleasant versus neutral pictures across tasks in a passive viewing paradigm (Horan et al. 2010) and when emotional pictures were incidental to task demands (Horan et al. 2012). By contrast, patients in the current study showed a smaller LPP difference between the Preappraised negative and Neutral conditions than controls; this dampening was true even during the first epoch ($t_{56} = 2.80$, $p < 0.005$). Because the recruitment process and sample characteristics were

similar across studies, the most likely explanation for this discrepancy is differences in the experimental tasks. An important difference is that the current study provided descriptive sentences before each trial whereas the previous studies did not provide any such information. The sentence frames essentially provide a context in which the images can be perceived. Thus, the patients' atypical LPP pattern in the current preappraisal manipulation may be associated with impaired context processing, an aspect of cognitive control that has also received considerable investigation in schizophrenia (Park *et al.* 2003; Hemsley, 2005; MacDonald *et al.* 2005).

Although preappraisal modulated the LPP in the control group, it did not affect the patients in a similar way. In the initial epoch, patients showed a larger LPP to unpleasant pictures in both the Preappraised negative and Preappraised neutral conditions compared to the Neutral condition. Although this indicates some early sensitivity to the emotional significance of unpleasant pictures, no preappraisal modulation was evident. During the two middle epochs, the sentence frames seemed to have a paradoxical effect in the patients: they showed larger LPP amplitude in the Preappraised neutral condition *versus* Preappraised negative and Neutral conditions, suggesting that the Preappraised neutral condition in fact resulted in enhanced, sustained neural processing. Perhaps the relative incongruity between the context provided by the more neutral frames and the evocative unpleasant pictures was more difficult or effortful for patients to process than the other conditions in which the sentence and picture pairings were congruous. One might consider whether this effect is impacted by N400, a centro-posteriorly distributed negative-going waveform found to be larger (more negative) to words that are semantically incongruous (*versus* congruous) with preceding words or sentences (van Petten & Luka, 2006). If N400 accounted for the patients' unusual pattern, we would expect a more negative LPP in the Preappraised neutral condition than in the Preappraised negative condition in this group. However, the patients showed the opposite pattern. Furthermore, prior research in healthy subjects suggests that LPP preappraisal modulation in this paradigm is not driven by N400 (MacNamara *et al.* 2009). Thus, patients failed to show an adaptive benefit from the meaning shift typically associated with the contextual frames. Context is a complex, multi-faceted construct (Park *et al.* 2003; Hemsley, 2005; MacDonald *et al.* 2005) and behavioral studies that examined socio-emotional context processing in schizophrenia have found both impaired (Green *et al.* 2007; Huang *et al.* 2009) and intact (Chung & Barch, 2011; Lee *et al.* 2012) context effects. Further investigations will help to

clarify the factors that influence how contextual information impacts emotional responses in schizophrenia.

This study also examined self-reported habitual use of emotion regulation strategies. In addition to an atypical LPP pattern, the schizophrenia group reported less frequent use of cognitive reappraisal and more frequent expressive suppression than healthy controls. This pattern is consistent with some (Livingstone *et al.* 2009; van der Meer *et al.* 2009) but not all (Henry *et al.* 2008; Badcock *et al.* 2011; Perry *et al.* 2011) prior studies. Although there were no significant correlations between self-reported emotion regulation strategies and LPPs, higher levels of suppression were associated with higher levels of positive, negative, and overall symptoms. Again, some prior studies have found suppression to be related to higher negative or positive symptoms (Henry *et al.* 2007; Kee *et al.* 2009; Badcock *et al.* 2011), and to worse social functioning (Perry *et al.* 2011), but others did not (Henry *et al.* 2008). It is unclear why the results have been inconsistent across studies, although differences in sample characteristics (e.g. some included mixed samples of out-patients and in-patients, and in one study patients were selected for high levels of hallucinations) and symptom assessment measures may be relevant. The current findings are consistent with the notion that expressive suppression is associated with greater levels of psychopathology (Werner & Gross, 2010), even among people with schizophrenia.

Some limitations of this study should be considered. First, this study focused on an ERP index of emotional regulation and did not include self-reported levels of valence or arousal after each trial. Future studies could examine the coherence between ERP's and self-reported emotions, along with other aspects of emotional responding such as facial electromyography (Wu *et al.* 2012). Second, this study only examined the preappraisal of unpleasant images. We focused on this emotion regulation process to eliminate differences in difficulty across task conditions and focus on contextual modulation of the LPP. It remains an open question whether similar LPP results would be seen for other types of regulation strategies (e.g. cognitive reappraisal, expressive suppression) or for pleasant stimuli. Third, patients were taking various antipsychotic medications at clinically determined dosages and the impact of these medications on the LPP are unknown. Although there were no significant correlations with CPZ equivalents and atypical antipsychotics have in fact been reported to improve some aspects of emotional processing (Juckel *et al.* 2006; Schlagenhauf *et al.* 2008), further research on antipsychotic medication effects and in unmedicated samples is needed. Fourth, the patients were clinically

stable, predominantly male and chronically ill, which may limit the generalizability of these findings. Research in other types of samples, such as patients in the early phases of schizophrenia, can help to address these limitations.

Although recent research has highlighted several areas of intact emotional responding in schizophrenia, the current findings contribute to emerging evidence of disturbances in the regulation of emotion in this disorder. Impairments in emotion regulation may show linkages to clinical symptoms and could also contribute to social cognitive impairments associated with poor functional outcome (Green & Horan, 2010). For example, emotion regulation has been described as a key component of empathy (Decety & Lamm, 2006), a core social cognitive processes that seems to be disturbed in schizophrenia (e.g. Smith et al. 2012). Difficulties in emotion regulation have been associated with various forms of psychopathology and empirically supported interventions have been developed to treat them (Aldao et al. 2010). The current results support recent suggestions that emotion regulation interventions may also be useful in treating people with schizophrenia (Bassam & LeCompte, 2012).

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Declaration of Interest

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Appendix 1. Descriptions for International Affective Picture System (IAPS) pictures

IAPS picture no.	Picture valence	Negative interpretations	Neutralizing interpretations
2716	Negative	This man is addicted to crack cocaine	This man is an actor in a movie about addiction
9800	Negative	This is a photo of a German Nazi	This is an actor in a movie about neo-Nazis
6312	Negative	This woman is being abducted by a rapist	This is an actress in a self-defense training video
6831	Negative	This is a police officer investigating the scene of a murder	This is the set of a 1960s crime show
2691	Negative	This is a protester during a riot where 50 people were killed	This is a scene from a movie about a riot in the Middle East
9480	Negative	People have come to see their families' bones; they make them very sad	These are bones of ancient people; scientists are studying them to learn about the past
1120	Negative	This is a snake that is about to attack and bite another animal	This snake has a very large mouth; he is begging for a snack
9425	Negative	This man has just been taken hostage by terrorists	This is a scene from a movie called 'The Terrorists'
9921	Negative	The firefighters do not save this woman in time	The firefighters get this woman to safety just in time
9600	Negative	This ship sinks and no one survives	This is a scene from a movie much like 'Titanic'
2683	Negative	This is a bloody clash between police and protestors	These are actors in a movie about tension in the Middle East
9470	Negative	This building collapsed on the people who were sleeping in it; they were badly hurt	This old building was knocked down; everyone was happy to see it go
1201	Negative	A poisonous tarantula is about to bite this man	This is a harmless pet tarantula sitting on his owner's shoulder
1930	Negative	This is a shark that attacked and killed a diver	This is a mechanical shark from the movie 'Jaws'
9901	Negative	The victims in this accident could not be saved in time	No one was in this car when it was totaled at a construction site
9911	Negative	The driver in this accident was killed before help could arrive	This is contrived scene from an educational film about drunk driving
3220	Negative	This man is dying in a hospital	This man is recovering from illness in a hospital
6370	Negative	This person is dangerous and is hiding his face because he is a criminal	This person is visiting his friend; he is wearing a mask because it is cold
9042	Negative	This man has been punished by his tribe	This tradition is a rite of passage and is actually not painful
1300	Negative	This is a wild dangerous dog that will attack anyone	This dog just went to the dentist – look how clean her teeth are
2661	Negative	This premature baby may not live more than a couple of days	Thanks to early care this baby develops into a healthy toddler
3168	Negative	This man suffers from a number of deformities since birth	The costume worn in this horror film won an Academy award in 1982
9050	Negative	This is a terrible plane crash in which many people were killed	This plane veered off the runway but no one was seriously hurt
9920	Negative	Two people died in this horrendous car crash	No one was seriously injured in this car accident
9611	Negative	All passengers were killed in this plane crash	This fake plane crash was put together for a movie
2700	Negative	These women are mourning the loss of their close friend	These women are overwhelmed with joy at a friend's wedding
6190	Negative	This woman is about to pull the trigger on her husband	This is a picture from a training video on gun safety

Appendix 1. (cont.)

IAPS picture no.	Picture valence	Negative interpretations	Neutralizing interpretations
2130	Negative	This woman is very angry and might hit people around her	This woman had her picture taken right when she was about to sneeze
3301	Negative	This child was severely injured in a car accident	This child was injured but makes a full recovery
2141	Negative	This woman just found her mother dead	These are actresses for a movie called 'The Funeral'
2710	Negative	This man was found dead from an overdose in a halfway house	This is an actor from the 1970s film called 'Drug Smuggle'
2688	Negative	The poacher is shooting the bear to sell its fur	A vet is tranquilizing this bear to give him medicine
2120	Negative	This man is very angry and might become violent and dangerous	This man has held his breath to try to make a red face
2399	Negative	This woman suffers from intense migraine headaches	This is an actress posing for an aspirin commercial
5970	Negative	This terrible storm has destroyed many people's homes	This storm is dying away; it is harmless and everyone is safe
9635	Negative	This man was set on fire during a civil war	This daredevil sets himself on fire as a stunt
2900	Negative	This boy is very upset and sad because he found out that his pet ran away	This boy's dad picked him up after he fell; he got scared but is totally okay
2750	Negative	This is a homeless man who lives under a bridge in London	This is an actor who is playing the role of a homeless man
6830	Negative	This man is preparing to rob a bank	This is an actor in a bank robbery film
9584	Negative	This man is undergoing painful dental surgery	The man is having a routine dental checkup
3022	Negative	This person is very scared and is trapped and cannot get out	This person is on a fun ride and he is excited
9582	Negative	This person is having surgery on his teeth and it hurts a lot!	The doctor just finished working on his teeth; he feels all better
2205	Negative	This man has just lost his wife to cancer	This man's wife was ill but is fully recovering
7380	Negative	These disgusting bugs are crawling all over the food and ruining it	These bugs are eating the delicious leftover pizza
9250	Negative	Something terrible has happened to this person; she has been hurt badly	These are the doctors who have saved the woman's life
6571	Negative	This man is having his car stolen by a thief	This is a scene from a movie about an undercover cop
6020	Negative	This is an electric chair used to execute prisoners on death row	This is a prop from a movie about a man who is on death row
3280	Negative	This boy is having a cavity filled; he is in a lot of pain	This boy is having his teeth cleaned; it feels funny but doesn't hurt
2810	Negative	This boy suffers from intense anger problems	This boy is yelling 'Ready or not here I come'
3230	Negative	This man is very sick; he is worried that he might never get better	This man was sick but he is okay now and on his way to getting all better
9520	Negative	These abandoned children are near a nuclear reactor	These children are actors in a movie about poverty
6300	Negative	This person is waiting around the corner and wants to stab someone with the knife	This man is using the tool to fix the wall
8230	Negative	This boxer is being sent into a coma	This is a scene from the movie about boxing

1050	Negative	This is a poisonous snake that is very dangerous	This is a snake that is completely harmless; it doesn't even have teeth
9594	Negative	This person hates to give blood – the needle scares him!	This person gives blood all the time because it helps people who are sick
1321	Negative	This is a mean bear that is angry and could attack people	This is a friendly and harmless bear that is yawning
2102	Neutral	This man reads the stock report every morning	
7595	Neutral	These types of cars were popular in the 1970s	
7130	Neutral	This truck has been used by five different companies	
7217	Neutral	This coat rack is used by three people	
7010	Neutral	This woven basket was made to hold fruit	
7090	Neutral	This book was written in 1950	
5530	Neutral	This is an edible mushroom	
2593	Neutral	This café has outdoor seating	
7030	Neutral	This iron is used to press shirts and dresses	
7037	Neutral	These trains transport commercial goods	
2393	Neutral	This man and woman are working on an assembly line	
7950	Neutral	These tissues sell for 99 cents	
5740	Neutral	This plant is common to the northern United States	
2575	Neutral	This propeller will be used on a small cargo ship	
7056	Neutral	This tool is often used by electricians for wiring	
7150	Neutral	This is a blue umbrella	
7211	Neutral	This clock is in the lobby of an office building	
7175	Neutral	This lamp takes a 60-Watt bulb	
7002	Neutral	This towel was used to clean the floor	
7550	Neutral	This man is working on an old engineering program	
7140	Neutral	This bus travels a route from Boston to Atlanta	
7700	Neutral	This is a poster from a work-training video	
7705	Neutral	This cabinet can hold up to 500 file folders	
7491	Neutral	This building was used in a TV sitcom	
7050	Neutral	This hairdryer is sitting on a laundry basket in a bathroom	
7004	Neutral	This spoon is from a 1970s collection	
7500	Neutral	This is the office of a large law firm	
2580	Neutral	These men play chess three times a week	