ELECTROPHYSIOLOGICAL EVIDENCE FOR AFFECTIVE NORMALITY IN SCHIZOPHRENIA

by

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(Under the Direction of Gregory Strauss)

ABSTRACT

Anhedonia has long been considered a core symptom of schizophrenia. Contrary to conclusions obtained from clinical rating scales indicating that most schizophrenia patients are anhedonic, laboratory-based studies indicate intact self-reported and neurophysiological response to pleasant stimuli in schizophrenia. However, prior studies have not comprehensively evaluated the temporal dynamics of emotion response and it is therefore unclear whether anhedonia may exist when measures with good temporal resolution are considered. The current study used electroencephalography, a method with good temporal resolution, to evaluate the time course of the neural response to emotional stimuli in schizophrenia patients (n = 29) and healthy controls (n = 25) who completed an emotional passive viewing task. Several event related potential (ERP) components and self-report were evaluated as measures of emotional response. Schizophrenia patients displayed comparable self-reported and neurophysiological response to controls for pleasant and unpleasant stimuli. Findings provide further support for intact hedonic capacity in schizophrenia.

INDEX WORDS: Schizophrenia, anhedonia, temporal dynamics, event related potentials, electroencephalography

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CHAPTER 1

INTRODUCTION

Anhedonia, traditionally defined as a diminished capacity to experience positive emotion to pleasurable stimuli, has long been considered a core symptom of schizophrenia (SZ) (Bleuler, 1911; Kraepelin, 1919; Meehl, 1962; Rado, 1956). However, recent empirical evidence suggests that this definition may not accurately characterize the nature of affective abnormalities in SZ. For example, laboratory-based studies indicate that SZ patients have comparable self-reported valence and arousal (Cohen & Minor, 2010; Llerena, Strauss, & Cohen, 2012) to non-psychiatric controls (CN) in response to pleasant stimuli. A recent meta-analysis of functional Magnetic Resonance Imaging (fMRI) blood-oxygen-level dependent (BOLD) responses also indicates that patients have similar neurophysiological response to CN while receiving reward feedback or viewing pleasant stimuli in ventral striatum and OFC (Radua et al., 2015). Thus, laboratory-based research suggests that hedonic response may be intact in SZ at both subjective and neurophysiological levels, leading some to conclude that traditional conceptualizations of anhedonia in SZ may be inaccurate (Strauss & Gold, 2012).

Although prior neuroimaging and self-report studies provide valuable information about hedonic response in schizophrenia, these measures lack the temporal resolution to accurately assess the time-course of affective processing. SZ patients may have abnormalities in affective chronometry (i.e., temporal dynamics of emotion), which are missed with global self-report ratings and BOLD response that lack temporal precision. Electroencephalography (EEG) offers excellent temporal resolution and the means for evaluating the time-course of neural response to

emotional stimuli. Few prior studies have used EEG to examine the temporal dynamics of emotion in SZ. The majority of studies conducted to date have examined the integrity of two event related potential (ERP) components: the Late Positive Potential (LPP) and the Early Posterior Negativity (EPN) (for a review, see Hajcak et al., 2012 and Schupp et al., 2006). The LPP is a centroparietal midline component that becomes evident at approximately 300 ms after image onset and persists as a greater relative positivity for emotional than neutral stimuli throughout stimulus presentation (Cuthbert et al., 2000; Foti & Hajcak, 2008; Hajcak et al., 2007; MacNamara & Hajcak, 2009, 2010; Schupp et al., 2003; Weinberg & Hajcak, 2010). The LPP also persists after stimulus offset, as indicated by greater amplitude for pleasant than neutral stimuli for approximately 800 ms and greater amplitude for unpleasant than neutral for 1000 ms (Hajcak & Olvet, 2008). The EPN is a negativity that peaks between 200-300 ms after stimulus onset at occipital electrodes that appears to be sensitive to visual processing of emotional content (Bradley et al., 2007; Hajcak, Weinberg, MacNamara, & Foti, 2012; Schupp et al., 2006).

Six studies have examined the integrity of the LPP in SZ. Findings suggest that like CN, SZ have greater LPP amplitude for unpleasant than neutral stimuli at both early (e.g., 500-1000 ms) and later (e.g., 1000-3000 ms) time windows (Horan et al., 2010; Horan et al., 2012; Patrick, Kiang, & Christensen, 2015; Strauss et al., 2013; Strauss et al., 2015; Sullivan & Strauss, 2017). Greater LPP amplitude for unpleasant stimuli has been associated with higher self-reported state negative emotion to unpleasant stimuli and higher self-reported trait negative affect (Strauss et al., 2013; Sullivan & Strauss, 2017). Fewer studies have examined the LPP for pleasant stimuli. Horan et al. (2010) found that SZ had similar LPP amplitude for both pleasant and neutral stimuli, whereas CN had greater LPP amplitude for pleasant compared to neutral stimuli. However, a follow-up study by Horan et al. (2012) found that similar to CN, SZ have greater

LPP amplitude for pleasant than neutral stimuli. In a third study, Strauss et al. (in preparation) found results similar to Horan et al. (2012), with greater LPP amplitude for both pleasant and unpleasant than neutral in SZ and CN, as well as no between group differences in pleasant, unpleasant, or neutral LPP amplitude. Thus, the majority of studies to date suggest intact LPP amplitude for both pleasant and unpleasant stimuli in SZ, and individual differences in LPP amplitude may be associated with self-reported emotional experience.

Very few studies have examined early emotional ERP components (e.g., P1, N1, P2, N2, or EPN) or early LPP windows (e.g., < 500 ms) to examine the integrity of bottom-up emotion-attention interactions. Of the studies conducted to date, findings regarding early components are inconsistent. For example, Horan et al. (2010) examined early ERP components (e.g., P1, P2, and P3) in response to emotional stimuli, and these components demonstrated normal emotional modulation in SZ. Another study found that both SZ and CN groups showed significantly greater EPN peak negativity for emotional than neutral stimuli (Horan et al., 2012). In a mood induction study using IAPS images, Pinheiro et al. (2013) examined early electrophysiological response to pleasant and unpleasant stimuli in SZ and found that the P1, N1, and P2 mean amplitudes were reduced in SZ compared to CN. Thus, results of studies examining early ERP components provided mixed results, and it is unclear whether early emotional response is intact.

Several behavioral and eye tracking findings suggest that early emotion response may be abnormal in SZ. For example, in an emotional Stroop task, SZ patients failed to show greater interference for pleasant than neutral words (Strauss et al., 2008), a deficit that was associated with greater severity of anhedonia. Stroop interference for unpleasant words was intact or elevated depending on the discrete stimulus category. Patients also failed to show normal modulation of T1 and T2 emotional attentional blink effects for both pleasant and unpleasant

stimuli (Strauss et al., 2013). Lack of bottom-up competitive advantage for emotional stimuli on the emotional attentional blink task was associated with greater severity of negative symptoms. In an eye tracking task that placed emotional and neutral stimuli in competition for selective attention while eye movements were recorded, CN and low negative symptom SZ patients were both more likely to have their first fixation allocated toward pleasant or unpleasant than neutral stimuli (Strauss, Llerena, & Gold, in preparation); however, high negative symptom patients only showed this selective orienting effect for unpleasant stimuli. The bottom-up competitive advantage for pleasant stimuli was absent, as indicated by no differences in probability of first fixating on pleasant versus neutral stimuli. However, CN, low negative symptom patients, and high negative symptom patients all demonstrated greater probability of fixating on pleasant and unpleasant over neutral stimuli across the entire 3-second stimulus duration (minus the first fixation). Collectively, these behavioral and eye-tracking findings suggest that SZ patients may have intact top-down attention to pleasant and unpleasant stimuli, but that they may lack the bottom-up competitive advantage for pleasant stimuli. Additionally, this bottom-up deficit may be specific to high negative symptom patients. Additional studies are needed to explore bottom-up attention to emotional stimuli using ERPs given that so few studies have examined whether emotional stimuli modulates early ERP components.

The current study examined early ERP components (P1, N1, P2, N2, EPN, and LPP) in relation to emotional and neutral stimuli from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999) in SZ and CN participants using a Rapid Serial Visual Presentation (RSVP) task that applied a brief stimulus-presentation duration (500 ms) designed to evaluate bottom-up attention to affective stimuli. The following hypotheses were made. First, it was hypothesized that SZ and CN participants would display significantly greater P1, P2, and

LPP mean amplitude and greater N1, N2, and EPN negativity for unpleasant than neutral stimuli, suggesting intact emotional reactivity to unpleasant stimuli. Second, SZ participants would display reduced P1, P2, and LPP mean amplitude and reduced N1, N2, and EPN negativity for pleasant compared to neutral stimuli, whereas CN will show greater LPP mean amplitude and EPN peak negativity for pleasant compared to neutral stimuli. Third, in SZ participants, reduced modulation of ERP components to pleasant stimuli (pleasant – neutral difference score) was expected to be associated with reduced self-reported state positive emotion and arousal to pleasant stimuli on the IAPS rating task, lower trait positive emotion on the positive and negative affect scale (PANAS), and greater severity of clinically rated negative symptoms—particularly anhedonia, avolition, and asociality. In contrast, modulation of ERP components in relation to unpleasant stimuli was expected to significantly correlate with higher state negative emotion to unpleasant stimuli, higher trait negative emotion on PANAS, and greater severity of negative symptoms in SZ participants.

CHAPTER 2

METHODS

Participants

Data were collected from 32 participants with a DSM-IV-TR (American Psychiatric Association, 2000) diagnosis of schizophrenia or schizoaffective disorder (SZ) and 29 non-psychiatric controls (CN). Three SZ and four CN participants with excessively noisy EEG data (50% or more noisy epochs) following artifact correction were excluded, yielding a final sample of 29 SZ and 25 CN. The final sample included a mean of 85% of potential trials in the CN group and 84% of potential trials in the SZ group.

Participants in the SZ group were initially referred by their treating psychiatrist from local community outpatient mental health centers. Patients were evaluated only if they were clinically stable, as defined by no changes in antipsychotic medication type or dose in the past four weeks. Psychiatric diagnosis was established via a best-estimate approach based on consultations with treating clinicians and/or medical record review, and confirmed via the Structured Clinical Interview for DSM-IV-TR (SCID: First et al., 2002). Participants were either stably unmedicated, prescribed first-generation, second-generation, or a combination of first and second-generation antipsychotics.

CN participants were recruited from the community using posted flyers, electronic advertisements, and word of mouth among enrolled participants. SCID I and SCID II (First et al., 2002; Pfol et al., 1997) interviews were conducted to ensure that CN participants did not meet

criteria for any Axis I disorder or Axis II schizophrenia-spectrum diagnoses. Also, controls did not have family history of psychosis and were not taking psychotropic medications.

Both groups were free from lifetime neurological disease and substance use disorders within the last six months. All participants provided written informed consent for a protocol approved by the University Institutional Review Board prior to any study related tasks and received monetary compensation for their participation.

General Procedures

Participants first completed a structured clinical interview, which was performed by a PhD clinical psychologist or graduate student trained to reliability standards (ICC > 0.80 for all symptom rating measures) using gold standard rating and training videos. Following the interview, the following measures were rated: Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962), Brief Negative Symptom Scale (BNSS; Kirkpatrick et al., 2011; Strauss et al., 2012), Level of Functioning Scale (LOF; Hawk et al., 1975). Participants also completed a self-report measure of trait positive and negative emotional experience, the Positive and Negative Affect Scale (PANAS; Watson & Clark, 1992). Chlorpromazine equivalent dosage was calculated using the method published by Leucht et al. (2014).

Rapid Serial Visual Presentation (RSVP) Task

All participants completed a Rapid Serial Visual Presentation (RSVP) paradigm while the electroencephalogram (EEG) was recorded (see trial diagram in Figure 1). The RSVP paradigm included pictures from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1999). Participants were instructed to minimize body and head movements while

passively viewing a series of photographs. Trials began with a white fixation cross presented against a black background for 1200 ms. Each IAPS image was then presented for 500 ms across the entirety of the screen on a 19" monitor (1280 x 1024 resolution) and a viewing distance of approximately 70 cm to the center of the screen and a visual angle of 32.6° x 21.0°).

The RSVP task included a familiarization phase and an experimental phase. Participants were first familiarized with the task by viewing one pleasant, one neutral, and one unpleasant stimulus. The experimental phase consisted of 90 IAPS stimuli (30 pleasant, 30 neutral, and 30 unpleasant stimuli) presented in random order. Content in the pleasant condition included human interactions, erotica, babies, cute pets, delicious food, sports scenes, and adventure. Unpleasant scenes consisted of natural disasters, car accidents, ill people, mutilation, human and animal threat, and dirty toilets. Neutral stimuli consisted of humans and animals in everyday situations, landscapes, and common objects. Task duration consisted of approximately 5 minutes and the task was presented via E-Prime v2.0 software (PST Technologies, Pittsburgh, PA).

Among the experimental stimuli, the three stimulus conditions differed in normative stimulus valence and arousal. However, pleasant and unpleasant conditions did not differ in arousal. The three conditions did not significantly differ in lower-level visual features, including complexity, luminance, or red/green/blue saturation (Nummenmaa et al., 2006) (See Table 1).

Once the RSVP paradigm concluded, participants completed the stimulus rating task. Participants were presented with 10 pleasant, 10 neutral, and 10 unpleasant IAPS images that have been included within the RSVP task and were presented in random order. Participants were given unlimited time to make three self-report ratings for each image; how positive, how negative, and level of arousal. All ratings were on a 1-5 scale (1 = not at all; 5 = extremely)(see trial diagram in Figure 2).

EEG Recording and Data Reduction

EEG Recording: EEG signal was recorded using a 64 Ag/AgCl electrode elastic cap manufactured by BrainVision (actiCap model). Online signals were recorded using a right mastoid reference and re-referenced offline using the average of left and right mastoid electrodes (Hajcak, Weinberg, MacNamara, & Foti, 2012). Horizontal electro-oculogram (EOG) was used to measure horizontal eye movement and was recorded as the voltage between electrodes placed lateral to the external canthi. The vertical EOG was used to detect eye blinks and was recorded from electrodes above and beneath the left eye. Impedance levels from all electrodes were maintained below 15KΩ. EEG and EOG signals were amplified by a BrainVision actiCHamp amplifier with a gain of 5,000, a band-pass filter of 0.05 to 100 Hz, and a 60 Hz notch filter. The amplified signals were digitized at 500 Hz and averaged offline.

EEG Data Reduction: Signal processing was done in Matlab using EEGLAB and ERPLAB toolboxes (Lopez-Calderon & Luck, 2014). A high-pass filter of 0.01 was applied offline to the continuous EEG signal to prevent LPP attenuation (Hajcak, Weinberg, MacNamara, & Foti, 2012). EEG signal containing excessive muscle activity (i.e., EMG) identified via visual inspection was manually removed, and an Independent Component Analysis (ICA) was conducted to identify and correct eye blink activity.

ERP Measurement Procedures

The ICA-corrected signal was used to construct all ERP variables. EEG signal was divided into epochs that began 200 ms before stimulus onset and continued for 500 ms after stimulus onset. Epochs were baseline corrected using a 200 ms pre-stimulus period. Six ERP

components were evaluated as follows: 1) P1 computed as the mean amplitude of lateral occipital electrodes O1 and O2 in the range of 60-120 ms; 2) N1 computed as the peak negativity of centroparietal electrodes Cz, Pz, CP1, and CP2 in the range of 120-190 ms; 3) P2 computed as the mean amplitude of central electrode Cz in the range of 150-250 ms; 4) N2 computed as the mean amplitude of central electrode Cz in the range of 230-260 ms; 5) EPN computed as the peak negativity of occipital electrodes Oz, O1, and O2 between 200-300 ms; and 6) LPP computed as the mean amplitude of centroparietal electrodes Cz, Pz, CP1, and CP2 from 300-500 ms. These measurement procedures are consistent with prior studies (Foti, Hajcak, & Dien, 2009; Hajcak, Weinberg, MacNamara, & Foti, 2012; Horan et al., 2010; Horan et al., 2012; Schupp et al., 2006; Sabatinelli et al., 2013; Strauss et al., 2013).

Data Analysis

Analyses: To examine hypotheses related to these ERP components, separate 2 (Group: SZ, CN) X 3 (Stimulus Valence: pleasant, neutral, unpleasant) repeated measures ANOVAs were conducted. Significant interactions were followed-up by post hoc one-way ANOVAs and within-group paired-sample t-tests. To examine the effect of Group on stimulus ratings, three separate 2 (Group: SZ, CN) X 3 Stimulus Valence (pleasant, neutral, unpleasant) repeated measures ANOVAs were conducted using self-reported positive emotion, negative emotion, and arousal as dependent variables. Bivariate correlations were conducted to determine whether ERP variables are associated with subjective ratings and symptom severity.

CHAPTER 3

RESULTS

Demographic information is presented in Table 2. Groups did not differ on age, ethnicity, sex, or parental education. As expected, SZ had significantly lower personal education than CN. Results from separate 2 (Group: SZ, CN) X 3 (Valence: pleasant, unpleasant, neutral) repeated measures ANOVAs examining each ERP component are summarized in Table 3. Figures 3-6 include overall waveforms for the ERP components for each group.

Late Positive Potential

Repeated measures ANOVA indicated that the Group X Valence interaction and the main effect of Group were nonsignificant. However, the main effect of Valence was significant.

To evaluate the valence effect and verify that both groups displayed normal affective modulation of the LPP, within-group paired-sample t-tests were conducted. Results indicated that CN had more positive LPP amplitude for pleasant and unpleasant compared to neutral stimuli. However, SZ had more positive LPP amplitude for unpleasant compared to neutral and a trend toward higher LPP amplitude for pleasant than neutral. Findings are generally consistent with intact emotional reactivity in both groups.

Other ERP Components (EPN, P1, N1, P2, & N2)

For the EPN, the Group X Valence interaction was nonsignificant. However, the main effects of Group and Valence were significant. Within-group paired-sample t-tests indicated that

CN had more negative amplitude for pleasant and neutral compared to unpleasant stimuli, but there was no difference between pleasant and neutral. EPN peak negativity did not differ among pleasant, unpleasant, and neutral stimuli in SZ.

All interactions and main effects were nonsignificant for P1, N1, and N2 components. Significant main effects for Group were found for P2 indicating that SZ had more positive P2 amplitude relative to CN.

Self-Report Ratings

Table 4 summarizes results for self-reports of valence and arousal. For self-reports of positive emotion, negative emotion, and arousal to the stimuli, there were no significant Group x Valence interactions (see Figure 7). The main effect of Group was also nonsignificant for each dependent variable. However, the main effect of valence was significant for each effect. These findings indicate that both groups displayed comparable modulation of levels of positive emotion, negative emotion, and arousal across the stimulus categories.

To further examine the valence effects and verify that both groups did show the expected modulation across stimulus conditions, within-group paired samples t-tests were conducted. SZ and CN reported the expected pattern of modulation for reports of positive emotion (pleasant>neutral>unpleasant), negative emotion (unpleasant>neutral>pleasant) and arousal (pleasant, unpleasant > neutral).

Correlations

LPP difference scores (emotional – neutral) were computed as a marker of emotional reactivity to pleasant and unpleasant stimuli. Higher LPP difference score for pleasant stimuli

positively correlated with positive symptoms ($r = 0.47$, $p < 0.05$), indicating that greater reactivity was associated with higher severity of psychosis. In both groups, pleasant and unpleasant stimulus difference scores were not significantly correlated with self-reported emotional experience to the stimuli or trait emotional experience on the PANAS. In SZ, correlations between LPP difference scores and clinical ratings of negative symptoms and chlorpromazine equivalent dosage were nonsignificant.

CHAPTER 4

DISCUSSION

The current study examined emotional reactivity in individuals with SZ using electrophysiology. Multiple ERP components were evaluated in a rapid serial visual presentation task to examine the impact of emotional stimuli on early emotion processing, and their relation to symptoms. Several key findings emerged.

The first major finding was that both groups generally displayed greater amplitude for emotional than neutral stimuli on the LPP. Specifically, both CN and SZ groups showed greater LPP amplitude for unpleasant than neutral stimuli. For pleasant stimuli, the CN group displayed significantly greater LPP amplitude for pleasant than neutral stimuli, and the patients displayed a trend toward greater amplitude for pleasant than neutral stimuli ($p = .08$). These findings are inconsistent with the hypothesis that the LPP amplitude for pleasant stimuli would be reduced for SZ compared to CN and that SZ would fail to show within-group differences for pleasant compared to neutral stimuli. These findings are consistent with prior studies indicating higher LPP amplitude for pleasant (Horan et al., 2012; Pinheiro et al., 2013) and unpleasant (Horan et al., 2010, 2012; Pinheiro et al., 2013; Patrick et al., 2015; Strauss et al., 2013, 2015; Sullivan & Strauss, 2015) than neutral stimuli in SZ. Thus, findings generally provide evidence for intact neurophysiological reactivity in SZ for both pleasant and unpleasant stimuli.

Contrary to hypotheses, there were no significant correlations between LPP amplitude for pleasant stimuli and state positive emotion, trait positive emotion, or negative symptoms. There were also no significant correlations between LPP amplitude for unpleasant stimuli and state

negative emotion, trait negative emotion, or negative symptoms. These findings are consistent with some prior studies (Horan et al., 2012; Pinheiro et al., 2013; Strauss et al., 2015) indicating that LPP reactivity to affective stimuli is not predictive of state emotional experience, trait emotional experience, or negative symptom severity. However, results are inconsistent with other studies indicating that the LPP amplitude for unpleasant stimuli is significantly associated with state and trait negative emotional experience (Strauss et al., 2013; Sullivan & Strauss, 2017). There was a significant correlation between LPP amplitude for pleasant stimuli and positive symptoms, which did not survive Bonferroni correction. This correlation has not been significant in prior studies and may reflect a spurious association.

Findings did not support hypotheses related to the EPN, as valence effects were not in the expected directions on the early EPN components for either group (i.e., EPN means were expected to be pleasant, unpleasant < neutral; however, we observed that pleasant<neutral<negative). One prior study found higher EPN peak negativity for affective versus neutral stimuli in both SZ and CN despite omitting extreme affective images (e.g., nudity and violence). Although the EPN is not always observed in RSVP studies, this discrepancy could be explained by differences in study design including differences in the stimuli used, stimulus presentation time, or ITI duration. Moreover, research is mixed on the effects of lower level visual of stimulus characteristics on early emotional ERP components. For example, Junghöfer et al. (2001) found that lower level properties (color, brightness, complexity, and spatial frequency) did not modulate the EPN response, whereas Löw et al. (2005) proposed that picture type (single object vs. complex scene, object vs. people) modulated the EPN response. Future studies should directly manipulate lower level visual properties to evaluate their effect on early emotional ERPs in schizophrenia given that these patients display impairments in lower-level visual perception

that may impact emotional reactivity with brief stimulus durations (Sergi & Green, 2003; Green et al., 2011).

Valence effects in other early ERP components were nonsignificant in both groups for P1, N1, P2, and N2 components. Importantly, both groups showed similar patterns of early neurophysiological response. These findings are consistent with two prior studies showing that early neural processing of affective stimuli is similar between SZ and CN (Horan et al., 2010; Horan et al., 2012). On the other hand, Pinheiro et al. (2013) found evidence for abnormal N1 and P2 responses to affective stimuli in SZ and suggested a generalized visual processing deficit in SZ. This inconsistency could be explained by methodological and stimulus characteristic differences. In the Pinheiro et al. (2013) study, the authors compared absolute ERP amplitudes between groups but did not compare ERP responses to affective stimuli by examining difference scores (affective – neutral), which prevents the examination of within-group affective response. However, our findings did not change when this approach was taken and raw amplitudes, rather than difference scores, were analyzed. Variations between low-level stimulus characteristics may also explain this inconsistency. Rigoulot et al. (2008), for example, found a P1 reduction for affective stimuli. These early ERP components have not always been found on emotional ERP tasks (Hajcak et al., 2012) and may therefore not be reliable.

There were several limitations of the current study. First, it is possible that the sample size could not have been adequate to examine small to medium effects on ERP and behavioral variables. In this study, patients showed larger LPP amplitude for pleasant compared to neutral stimuli, but this difference did not reach statistical significance potentially due to reduced power. Second, since most patients were on second-generation antipsychotic medications, it is possible that medication could have had effects on affective processing. The effects of antipsychotic

medications can only been examined in a broad sense using chlorpromazine equivalent dosage estimates (Leucht et al., 2014; Woods 2003). Consistent with prior studies (Berenbaum & Oltmanns, 1992; Kring & Earnst, 1999; Kring & Neale, 1996; Pinheiro et a., 2013), there was no association between ERP variables and chlorpromazine equivalent dosage, suggesting that medication effects cause minimal to no effects on ERP variables. Future studies examining neurophysiological reactivity to affective stimuli in unmedicated first-episode patients could directly evaluate the effects of antipsychotics. Third, we implemented a fixed ITI of 1200 ms, which may have systematically impacted ERP amplitudes. Inspection of individual channels provided no evidence for a contingent negative variation effect as participants anticipated the effect of predictably timed stimuli (i.e., there was no evidence of a negative slow wave in the central electrodes during the baseline period) in either group, suggesting that this was unlikely to influence results. Fourth, since the LPP was measured as the mean amplitude between 300 and 500 ms, it is possible that this component instead reflects the P3 component, which is sensitive to attention allocation to motivational salient stimuli. Prior studies have found emotional modulation of the P3 in healthy individuals when presented with affective pictures (Johnston et al., 1986; Palomba et al., 1997). However, others have proposed that the P3 is actually an early component of the LPP (Hajcak et al., 2012). Findings from this study are consistent with prior studies indicating that the LPP becomes evident around 300 ms post stimulus, consistent with the notion that this component is better termed LPP than P3. Lastly, it is possible that the stimulus content may not have been high enough in arousal to produce the component effect. Future studies should examine the LPP at longer stimulus durations to examine if the higher LPP amplitude for emotional than neutral stimuli continues past 500 ms (i.e., past stimulus offset).

In conclusion, the current study found evidence for normal emotional reactivity in SZ at neurophysiological and subjective levels. These findings are consistent with prior self-report studies, indicating that individuals with SZ do not differ from controls in how they experience pleasant and unpleasant stimuli (Cohen & Minor, 2011; Llerena et al., 2012). Although SZ is a heterogeneous disorder, individual differences in symptoms, antipsychotic medication regimen, and self-reported emotional experience did not predict reductions in neurophysiological emotional reactivity. These findings support recent theories that anhedonia should be reconceptualized in SZ and no longer be consider diminished hedonic capacity (Strauss & Gold, 2012). Hedonic capacity appears intact at the subjective and neurophysiological level, suggesting that some other aspect of emotionality may be impaired and contributing to low self-reports of pleasure obtained during clinical ratings of anhedonia. One possibility is that anhedonia reflects a behavioral abnormality characterized by a reduction in pleasure seeking behavior. This behavioral abnormality has been associated with other aspects of reward processing, but not hedonic response (Strauss, Waltz, Gold, 2014; Kring & Barch, 2014). It may therefore be the case that aspects of reward processing other than hedonic response are critical elements of the pathophysiology of anhedonia in SZ and whether patients engage in behaviors aimed at obtaining rewards (e.g., value representation, effort-cost computation, reinforcement learning).

Table 1. Stimulus Characteristics

	Unpleasant	Pleasant	Neutral	F, P-Value
Valence	2.51 (0.64)	7.09 (0.61)	5.10 (0.52)	$F(2,87) = 552.1$, $p<0.001$
Arousal	5.64 (0.84)	5.61 (1.13)	2.80 (0.50)	$F(2,87) = 127.9$, $p<0.001$*
Complexity	229 (188)	191 (108)	191 (113)	$F(2,87) = 1.3$, $p = 0.37$
Luminosity	104 (39)	101 (31)	93 (46)	$F(2,87) = 0.57$, $p = 0.63$
Red Saturation	109 (43)	124 (40)	119 (38)	$F(2,87) = 0.21$, $p = 0.81$
Green Saturation	107 (41)	100 (49)	96 (43)	$F(2,87) = 1.2$, $p = 0.33$
Blue Saturation	89 (39)	94 (49)	86 (41)	$F(2,87) = 0.22$, $p = 0.79$

Note. * The arousal comparison for pleasant versus unpleasant did not significantly differ: $F(1,58) = 0.03$, $p = 0.92$.

Table 2. Demographics

	SZ = 29 Mean (SD)	CN = 25 Mean (SD)	Test-Statistic	P-value
Age	35.8 (11.8)	39.4 (12.7)	F = 1.12	0.29
Parental Education	13.3 (2.2)	13.3 (3.1)	F = 0.01	0.96
Sex (female)	37.9%	40.0%	X^2 (1) = 0.02	0.88
Race			X^2 (4) = 2.48	0.65
Caucasian	79.3%	84.0%	--	--
African-American	6.9%	4.0%	--	--
Asian	3.4%	4.0%	--	--
Hispanic	3.4%	8.0%	--	--
Biracial	6.9%	0.0%	--	--

Note. SZ = schizophrenia; CN = control; CPZ = Chlorpromazine

Table 3. Repeated Measures ANOVA for ERP Measures

	Test Statistic	p-value	η_p^2
LPP			
Group	F(1,52) = 0.67	0.42	0.01
Valence	F(2,104) = 8.88	**< 0.001**	0.15
Group X Valence	F(2,104) = 0.18	0.84	<0.01
EPN			
Group	F(1,51) = 8.00	**< 0.01**	0.14
Valence	F(2,102) = 4.96	**< 0.01**	0.09
Group X Valence	F(2,102) = 2.08	0.14	0.04
N1			
Group	F(1,52) = 2.46	0.12	0.05
Valence	F(2,104) = 0.29	0.75	0.01
Group X Valence	F(2,104) = 0.01	0.99	<0.01
P1			
Group	F(1,52) = 0.22	0.65	<0.01
Valence	F(2,104) = 2.58	0.08	0.05
Group X Valence	F(2,104) = 0.31	0.74	0.01
N2			
Group	F(1,52) = 2.32	0.13	0.04
Valence	F(2,104) = 0.96	0.39	0.02
Group X Valence	F(2,104) = 0.01	0.98	<0.01
P2			
Group	F(1,52) = 5.39	**< 0.05**	0.09
Valence	F(2,104) = 0.12	0.89	<0.01
Group X Valence	F(2,104) = 0.02	0.98	<0.01

Note. LPP = Late Positive Potential; EPN = Early Posterior Negativity; η_p^2 = Partial Eta Squared

Table 4. ANOVA for Self-Reported Emotional Experience to Stimuli

	Test Statistic	p-value	η_p^2
How Positive?			
Group	F(1,51) = 0.03	0.87	<0.01
Valence	F(2,102) = 119.56	**< 0.001**	0.70
Group X Valence	F(2,102) = 1.51	0.23	0.03
How Negative?			
Group	F(1,51) = 2.83	0.10	0.05
Valence	F(2,102) = 224.45	**< 0.001**	0.82
Group X Valence	F(2,102) = 0.29	0.75	0.01
Arousal			
Group	F(1,51) = 0.15	0.70	<0.01
Valence	F(2,102) = 56.37	**< 0.001**	0.53
Group X Valence	F(2,102) = 0.64	0.53	0.01

Note. η_p^2 = Partial Eta Squared

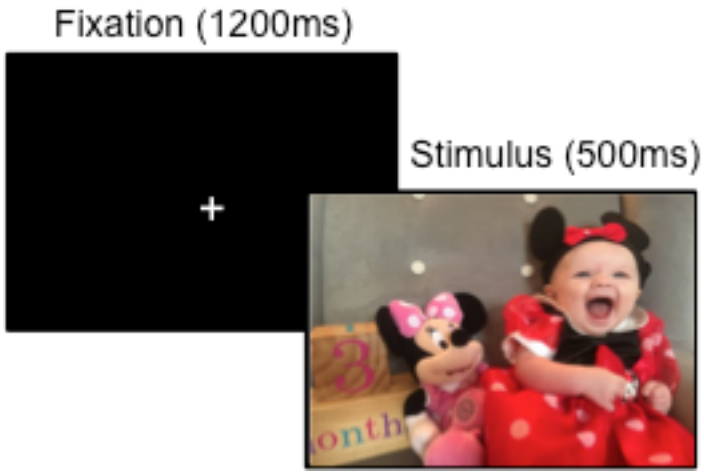

Figure 1. RSVP Trial Diagram. Participants passively viewed a total of 90 IAPS images (30 pleasant, 30 unpleasant, and 30 neutral) randomly presented while EGG was recorded. The inter-trial interval consisted of 1200 ms.

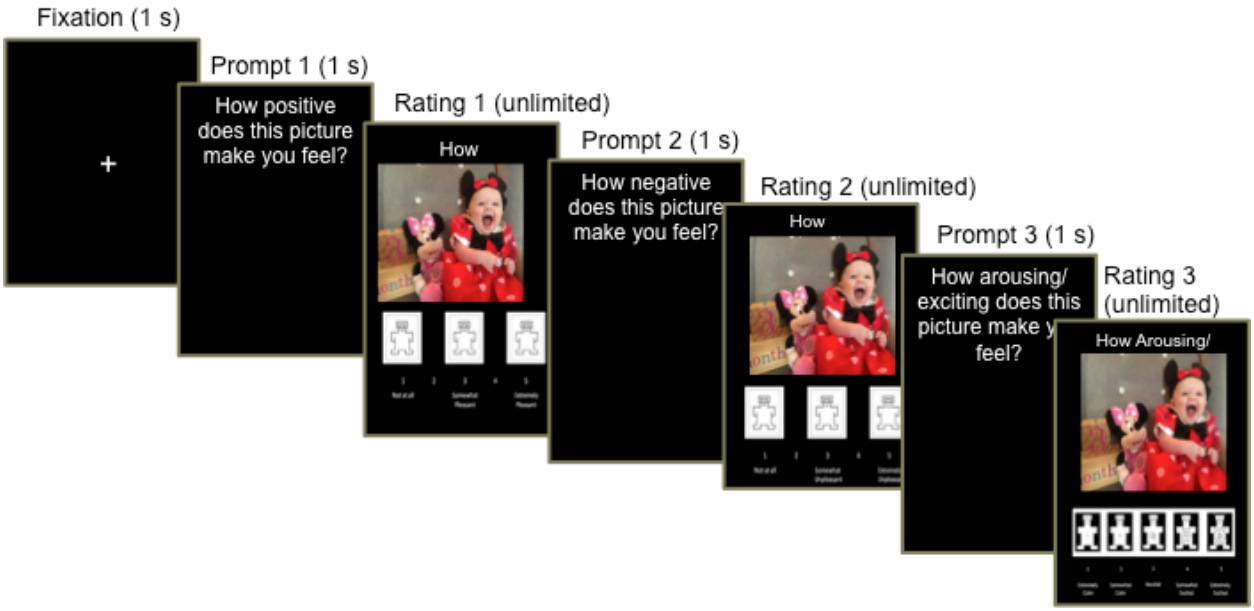

Figure 2. Self-Report Task. Participants were presented 30 IAPS images (10 pleasant, 10 neutral, and 10 unpleasant) previously presented within the RSVP task in a random order and were given unlimited time to indicate how positive, how negative, and level of arousal for each image on a 1-5 scale (1 = not at all; 5 = extremely).

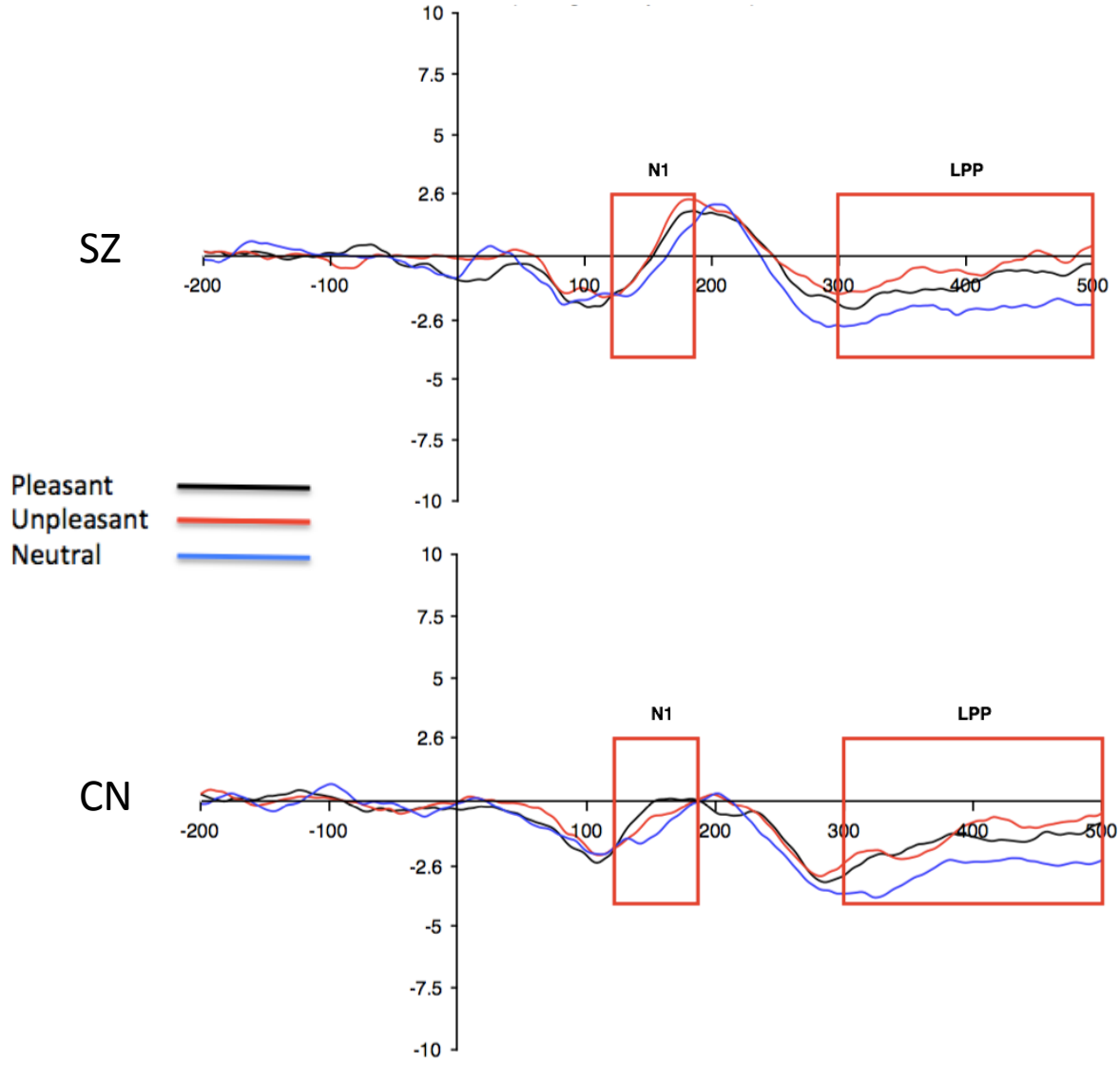

Figure 3. LPP & N1 (Cz, Cp1, Cp2, Pz)

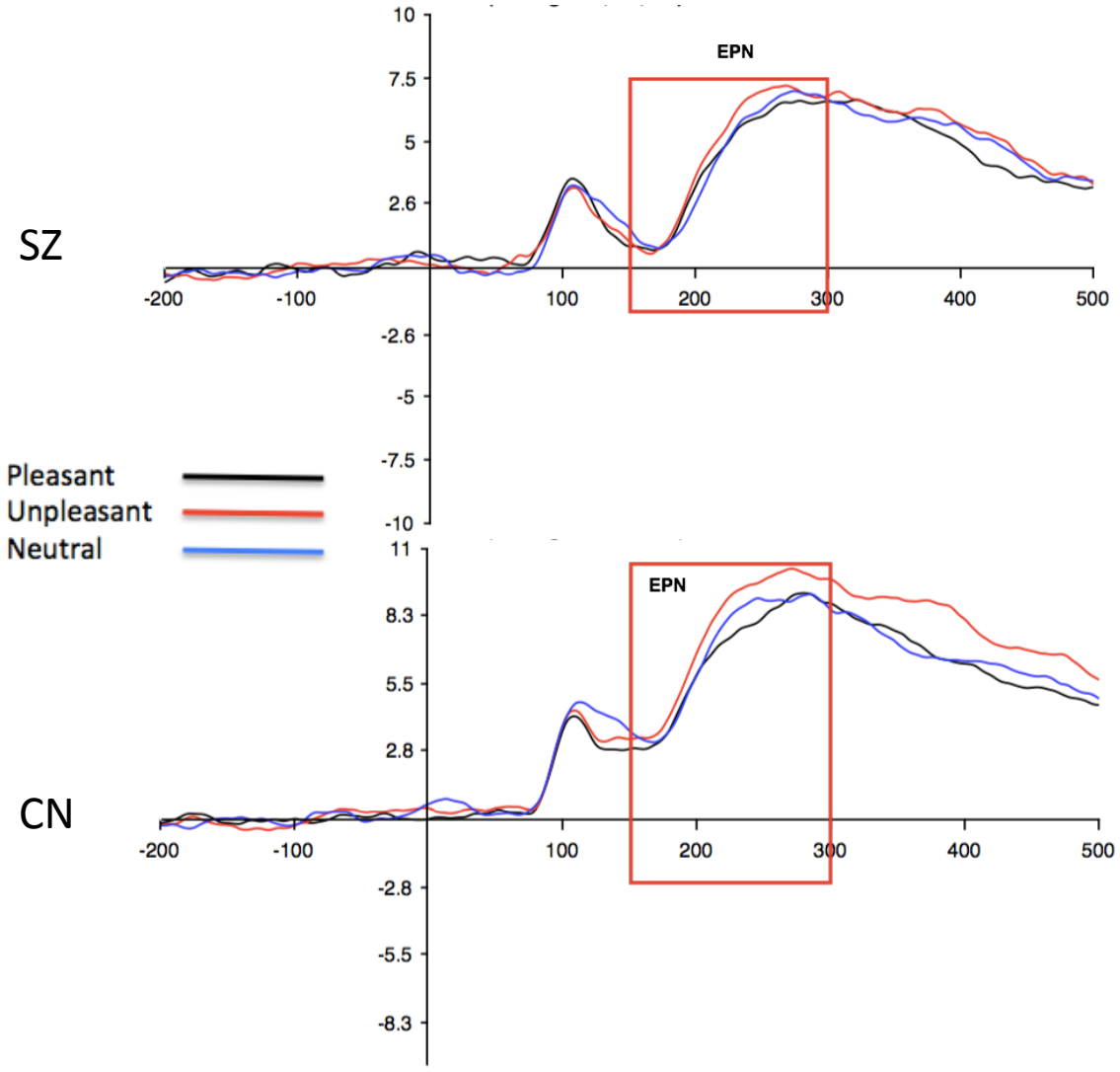

Figure 4. EPN (Oz, O1, O2)

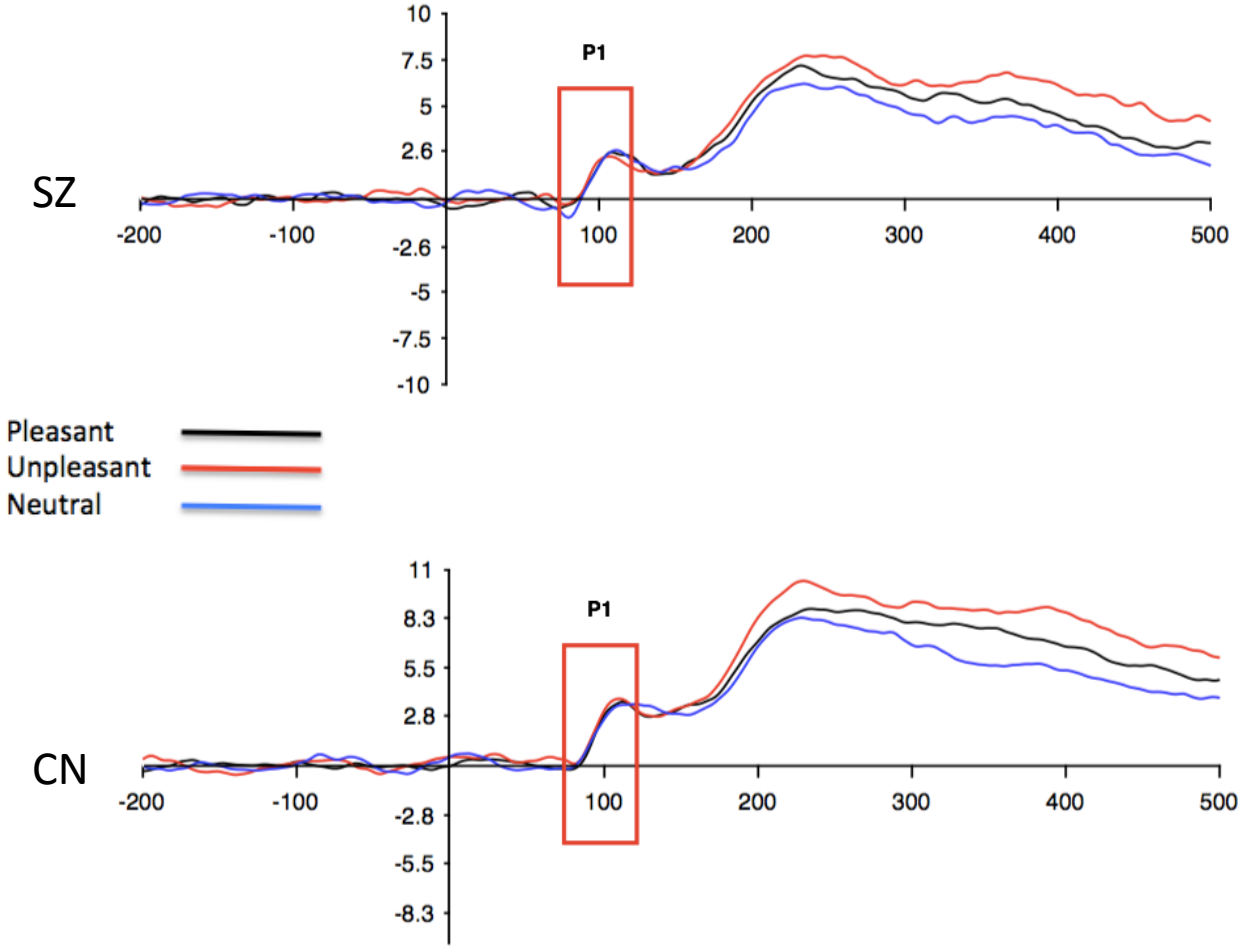

Figure 5. P1 (O1, O2)

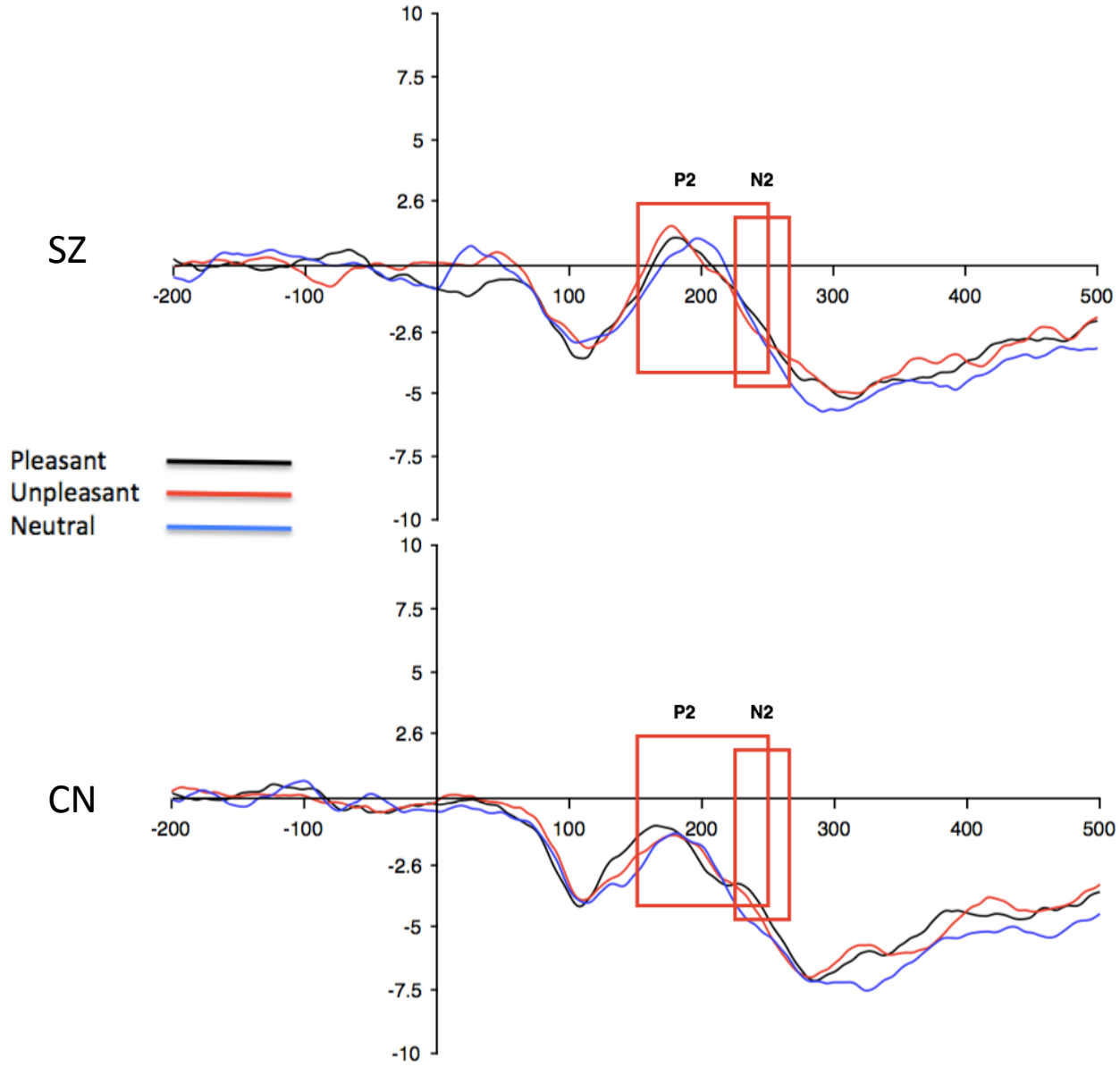

Figure 6. P2 & N2 (Cz)

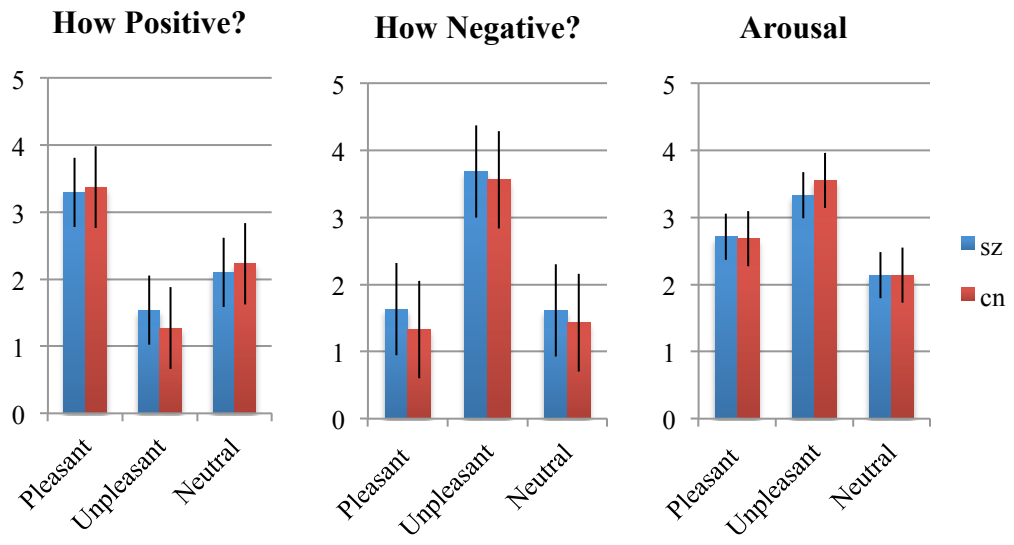

Figure 7. Self-Reported Emotional Experience

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