EMOTIONAL SCENE PROCESSING ACROSS THE SCHIZOBIPOLAR SPECTRUM: A MULTIVARIATE APPROACH

by

REBEKAH TROTTI

(Under the Direction of Brett Clementz)

ABSTRACT

Reward and motivation deficits may underlie symptoms of psychosis syndromes. Research suggests impaired emotional abilities in psychosis, including reduced cognitive control over emotions and deficient facial emotion processing and identification. Emotional scenes elicit a robust neural response and are a well-researched aspect of emotion. Previous studies investigating the emotional scene response in psychosis using electroencephalography (EEG) have focused on non-affective psychosis and yielded mixed findings. The current study employs EEG and self-report in a large, transdiagnostic sample to investigate emotional scene processing. Two temporal components of the neural response (early and late processing) were extracted using principal component analysis. The early component suggested impaired visual processing in groups with high psychosis and affective disturbance, while the late component and self-reported arousal indicated emotional impairments following a severity continuum with increasingly less-affective psychosis. Emotional measures correlated with cognition and social functioning, supporting a relationship between emotional scene processing and social cognition.

INDEX WORDS: Psychosis, mood, emotion, electroencephalography

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CHAPTER 1

INTRODUCTION

Psychosis syndromes are often characterized by negative symptoms, including flattened affect and avolition. Evidence suggests that deficits in reward processing and motivation present in schizophrenia and other psychosis syndromes may underlie these symptoms (Strauss, Waltz, & Gold, 2014). Given that reward and motivation drive emotional processes (Löw, Lang, Smith, & Bradley, 2008), emotional stimulus processing is of particular interest in psychotic disorders. Prior event-related potential (ERP) studies of the emotional scene response have used images from the International Affective Picture System (IAPS) to examine emotion processing in schizophrenia and found mixed results. However, few studies have used a large, transdiagnostic sample to examine diagnostic specificity or phenomenological overlap with affective psychosis syndromes.

Emotional abnormalities are present across a wide range of functions in psychosis syndromes. Individuals with schizophrenia have deficits in emotion regulation, indicating an inability to exert cognitive control over the automatic emotional response (Strauss et al., 2013; Sullivan & Strauss, 2017). Facial affect recognition and processing is also impaired in schizophrenia (Earls, Curran, & Mittal, 2016; Lynn & Salisbury, 2008; Turetsky et al., 2007) and across the psychosis spectrum (Culbreth, Foti, Barch, Hajcak, & Kotov, 2018; Ruocco et al., 2014). Emotion deficits affect social cognition, which involves recognizing and responding to emotions expressed by others. Social cognitive difficulties impact functional disability and

outcomes in psychosis syndromes (Fett et al., 2011; Green, Horan, & Lee, 2015), highlighting the importance of understanding and targeting neural abnormalities in emotional processing.

Early and late ERP components index different aspects of the affective scene response. Early components ranging from 100 to 250 ms reflect the initial encoding of visual stimuli. An early emotion-sensitive component is the early posterior negativity (EPN), which is apparent from approximately 150-300 ms after cue onset at occipito-temporal sensor locations (Junghöfer, Bradley, Elbert, & Lang, 2001; Schupp, Junghöfer, Weike, & Hamm, 2004). The EPN likely originates in occipital and parietal cortices (Codispoti, Ferrari, Junghöfer, & Schupp, 2006; Junghöfer et al., 2001), but could be modulated by other stimulus features along with emotion content (Farkas, Oliver, & Sabatinelli, 2019; Sabatinelli, Keil, Frank, & Lang, 2013).

Elaborative processing of emotional content is commonly measured by the late positive potential (LPP), a slow-wave ERP modulated by emotional intensity of affective stimuli (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000; Schupp, Flaisch, Stockburger, & Junghofer, 2006) and the P300, which indexes stimulus salience and is increased by emotional content (Hajcak, Macnamara, & Olvet, 2010). Emotional modulation of these components is associated with the motivational significance of the stimulus, with pleasant stimuli prompting appetitive motivation and unpleasant stimuli prompting defensive motivation (Löw et al., 2008). These components are topographically localized along the midline at central and parietal recording sites beginning roughly 300 ms after stimulus onset (Hajcak et al., 2010; Schupp et al., 2000). As indicated by correlations with the BOLD response, late components likely originate from widespread activity across lateral occipital, inferotemporal, and parietal cortex, as well as the amygdala, ventral striatum, nucleus accumbens, anterior cingulate, and anterior insula (Liu,

Huang, McGinnis-Deweese, Keil, & Ding, 2012; Mini, Palomba, Angrilli, & Bravi, 1996; Sabatinelli, Keil, Frank, & Lang, 2013).

Early components have occasionally been reported as abnormal in schizophrenia-spectrum disorders (Rockstroh, Junghöfer, Elbert, Buodo, & Miller, 2006), but most evidence supports intact early responses (Horan et al., 2012, 2010; Weber et al., 2009). There is also some evidence for abnormal late ERP responses in schizophrenia and youth at risk for psychosis, specifically with reduced discrimination between neutral and emotional scenes (Horan, Wynn, Kring, Simons, & Green, 2010; Strauss, Ruiz, Visser, Crespo, & Dickinson, 2018), but this finding is not always significant (Horan, Foti, Hajcak, Wynn, & Green, 2012). These previous studies could be limited by samples dominated by non-affective psychosis, and a categorical representation of psychosis syndromes.

Despite growing evidence from genetic and phenomenological studies showing a great deal of overlap between affective and non-affective psychosis syndromes (Cardno & Owen, 2014; Tamminga et al., 2013), most electrophysiological studies of emotion focus on schizophrenia. Additionally, schizoaffective disorder is seldom studied on its own, but rather grouped with schizophrenia or excluded, and studies on bipolar disorder rarely employ emotional scenes. In behavioral measures of emotion, most trans-diagnostic work suggests deviations follow a severity continuum progressing from affective to non-affective psychosis (Aminoff, Jensen, Lagerberg, Andreassen, & Melle, 2011; Ruocco et al., 2014; Thaler, Allen, Sutton, Vertinski, & Ringdahl, 2013), so examinations of the emotional response in psychosis may benefit from using a dimensional approach. The Schizo-Bipolar Scale provides such an approach, with a continuum ranging from primarily affective to non-affective psychosis (Keshavan et al., 2011). This scale will be used in the current study.

The current study uses the Schizo-Bipolar Scale to compare healthy individuals and groups with affective and non-affective psychosis on electrophysiological and self-report measures of the affective scene response. Two primary hypotheses are investigated: 1) groups with psychosis will have differing patterns of neural and self-reported emotional responding and 2) these abnormalities will follow a severity continuum progressing from affective to non-affective psychosis. Exploratory analyses assess multivariate relationships between emotional measures and symptom scales, including measures of social functioning and cognition. We expect individuals with increasingly non-affective psychosis to exhibit reduced early and late emotional ERP amplitudes and abnormal ratings of image pleasantness and arousal, particularly for emotional scenes.

CHAPTER 2

MATERIALS AND METHODS

Participants

We recruited 410 healthy participants and 613 participants with a DSM-IV-TR psychotic disorder across five sites of the Bipolar-Schizophrenia Network for Intermediate Phenotypes (B-SNIP2) and Psychosis and Affective Research Domains and Intermediate Phenotypes consortia (PARDIP). Individuals with psychotic disorders were divided into groups based on their total score on the Schizo-Bipolar Scale (SBS), a dimensional measure of an individual's symptom profile based on the proportion of psychotic and affective symptoms. Low scores on the scale, which ranges from zero to nine, indicate a larger proportion of mood symptoms (with a score of 0 indicative of prototypical affective psychosis) while high scores on the scale indicate a low proportion of mood symptoms (with a score of 9 indicative of prototypical non-affective psychosis; Keshavan et al., 2011). The SBS ranges of each group were chosen to best equate group sizes. 186 participants fell into SBS 0-3, 125 to SBS 4-5, 129 to SBS 6-7, and 173 to SBS 8-9. Detailed group demographics are reported in Table 1.

Trained masters- or doctoral-level clinicians diagnosed participants with psychotic disorders according the Structured Clinical Interview for DSM-IV-TR disorders (SCID; First, Spitzer, Gibbon, & Williams, 2002). Clinical features were assessed using a wide range of clinical scales described in Tamminga et al., 2013. Group scores on these scales are reported in Table A1. Medications varied between groups, as expected with differing symptomology, and

are reported in Tables A2-A4. Associations between medications and neural measures were minimal and are reported in Table A5.

Healthy subjects were free of any lifetime psychotic or mood disorders and had no first-degree relatives with a history of psychotic or bipolar disorders according to the Family History Research Diagnostic Criteria (Endicott, 1978). Exclusion criteria for all subjects included current illegal drug use (established by a urine toxicology screening), substance abuse within one month of testing, substance dependence within three months, extensive past substance use, presence of a major neurological disorder (including loss of consciousness for greater than 30 minutes), and a major medical disorder affecting the central nervous system. For more detailed information about recruitment and procedures, see Tamminga et al., 2013.

All subjects provided informed consent prior to inclusion after receiving a full description of the study. The institutional review board approved this project at all participating sites, and procedures were in accordance with the Declaration of Helsinki 2013.

Procedures

Across all sites, stimulus presentation and recording equipment were identical, and testing conditions were similar. Researchers were trained and monitored to guarantee uniform data collection procedures.

Emotional stimuli. Stimuli consisted of 60 pseudorandomly ordered scenes from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1997) including 20 unpleasant (UP: human threat, animal threat, mutilations), 20 pleasant (P: erotica, romantic couples, families), and 20 neutral (N: people, landscapes, cityscapes) stimuli. Participants viewed each scene three times during the experimental session. Scenes were presented in grayscale and

balanced to be statistically equivalent ($p > .20$) in luminance and 90% quality JPEG file size, as a rough index of complexity.

Data collection. Participants wore a 64 EEG sensor net plus mastoid and CP 1/2 sensors, with nose reference and forehead ground (QuikCap, Compumedrics Neuroscan, El Paso, Texas). Individual sensor impedances were kept below 10 kΩ, and data were sampled at 1000 Hz with a bandpass filter of direct current (DC) to 100 Hz. During data recording, participants viewed a fixation cross, then an IAPS image for 1000 ms, followed by 3.5 seconds of a black screen. After the EEG recording, participants rated each scene according to experienced arousal and valence using the Self-Assessment Manikin (Bradley & Lang, 1994). Arousal indicates how alarming or exciting a stimulus is and valence indicates its degree of pleasantness or unpleasantness.

EEG data processing. Raw data were inspected for bad sensor recordings (no more than 5% for any subject) were interpolated using a spherical spline method in BESA® (MEGIS Software, Gräfelfing, Germany). Data were transformed to an average reference and digitally filtered from 0.1 (12 dB/oct, zero phase) to 50 (48 dB/oct, zero phase) Hz. Eye blink, cardiac, and muscle artifacts were minimized using the Independent Component Analysis (ICA) toolbox in EEGLAB (Delorme & Makeig, 2004) under Matlab (MathWorks, Natick, Mass). Data were downsampled to 500 Hz. Epochs containing activity greater than 120 μV at any sensor were not included, and no less than 25 trials were included in each subject's ERP waveform average, per scene content. A 250 ms pre-stimulus period was used to baseline-adjust post-stimulus data.

Data reduction

To provide an comprehensive quantification of neural responses to scenes and use information from all rather than a few selected timepoints, a temporal principal component analysis (PCA) was carried out on grand average data using the ERP PCA Toolkit (Dien, 2010)

in Matlab. The PCA used all sensors, task types, and subjects as observations, a promax vector rotation, and Kaiser normalization (per the suggestions in Foti, Hajcak, & Dien, 2009), and was calculated on the 876 x 876 timepoint covariance matrix (100 ms before stimulus onset to 1500 ms after stimulus onset). Based on the resulting Scree plot, two components were identified, each accounting for 47% of the variance. Component 1 weighted primarily on early activity (peaking around 200 ms, later referred to as the Early Component), and component 2 weighted primarily on late activity (peaking around 1000 ms, later referred to as the Late Component). The early component captures the EPN and other early visual components. The late component encompasses the emotionally-dominated P300 and late positive potential. Component weights were multiplied by each subject's grand average data, summed across time points, and divided by the plus sum of component weights, reducing each subject's data to one spatial topography per component (Figure 1).

To reduce spatial information, sensor clusters were chosen where voltage was maximal based on the resulting average topographies (Figure 1), yielding one value per subject per task type. A posterior cluster was chosen for the early component (PO7, PO5, PO3, PO4, PO6, PO8, O1, O2) and a centro-parietal cluster was chosen for the late component (CP1, CPz, CP2, P1, Pz, P2). These values were then adjusted for linear and quadratic effects of age by calculating age regression coefficients in the healthy group, and removing these age-related effects from all groups' data, as documented in Dukart, Schroeter, Mueller, & The Alzheimer's Disease Neuroimaging Initiative, 2011.

Data analysis

All statistics were performed in SPSS (IBM, Version 26). For tests that violated Mauchley's Test of Sphericity, Greenhouse-Geisser corrections were used. Original degrees of freedom are reported in the text.

Self-report analyses. Ratings were examined for group and stimulus differences in self-reported pleasantness and arousal. 982 (HC: N=399, SBS 0-3: N=179, SBS 4-5: N=121, SBS 6-7: N=124, SBS 8-9: N=159) of the total 1023 subjects completed at least 75% of the items on each scale, so this subset was used for statistical analysis of emotional ratings. Mixed-design ANOVAs were conducted with a 3 (scene valence: N / P / UP) X 5 (group: HC / SBS 0-3 / 4-5 / 6-7 / 8-9) design. ANOVAs were corrected using the Holm-Bonferroni procedure. Follow-up Tukey HSD tests and within-subject t-tests were conducted as appropriate.

EEG analyses. Mixed design ANOVAs with a 3 (scene valence: N / P / UP) X 5 (group: HC / SBS 0-3 / 4-5 / 6-7 / 8-9) design were carried out on EEG amplitude values and corrected using the Holm-Bonferroni procedure. Follow-up Tukey HSD tests and within-subject t-tests were conducted as appropriate.

Discriminant analysis. To summarize variables that maximally differentiated groups based on emotional response, a canonical discriminant analysis was conducted using all self-reported and neural measures that exhibited significant group effects. For each significant canonical variate, means and standard error were calculated, and a Tukey's test was performed to identify homogenous sub-groupings.

Canonical correlation for relationship with clinical measures. Canonical correlations were conducted to assess relationships between emotional processing and clinical features. Emotion measures included self-reported and neural measures exhibiting significant group

effects and clinical measures included measures of functioning, psychosis symptoms, mood symptoms, and cognition (details on clinical scales in Appendix).

Table 1

Demographics by group

	HC	SBS 0-3	SBS 4-5	SBS 6-7	SBS 8-9	Statistic	*p*
N	410	186	125	129	173		
Mean age	34	38	39	42	40	F(4,1018)= 13.99***	<.001
Age SD	12	12	11	11	12		
Sex (% F)	58	55	58	43	39	$x^2(4)$= 24.40***	<.001
N from each site						$x^2(16)$= 58.50***	<.001
Boston	85	25	16	8	31		
Chicago	51	56	31	31	33		
Dallas	76	42	13	30	38		
Georgia	89	20	26	26	31		
Hartford	109	43	39	34	40		
N with each diagnosis							
SZ	N/A	4	3	61	159		
SZA	N/A	17	116	67	13		
BDP	N/A	165	6	1	1		

Note. SZ = schizophrenia, SZA = schizoaffective disorder, BDP = bipolar I disorder with psychotic features. ***$p < .001$

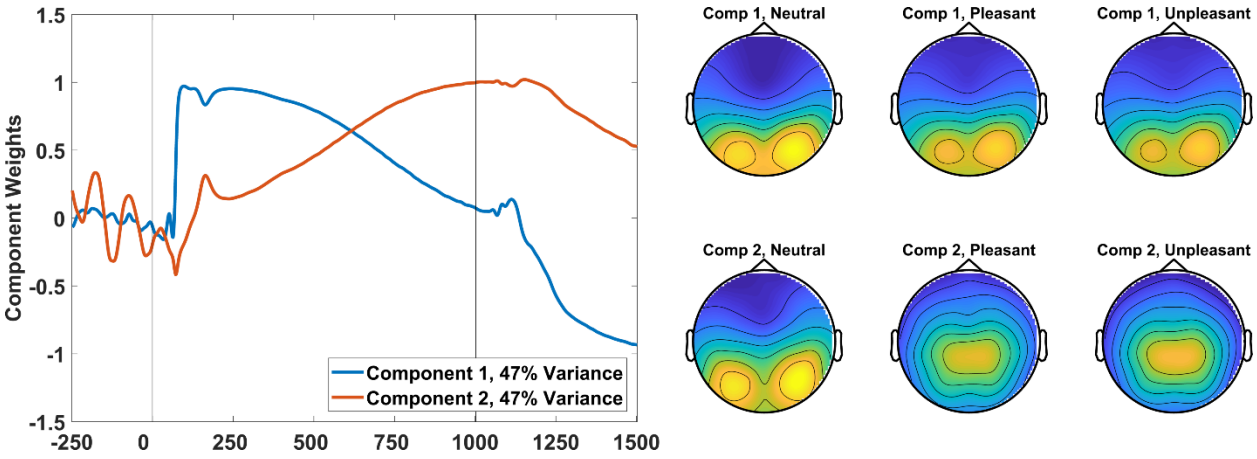

Figure 1. Component weights and resulting healthy topographies by scene type. Weights are shown across time with vertical lines indicating stimulus onset and offset. In topographies, yellow indicates positive voltage and blue indicates negative voltage. Component 1 (early component) and component 2 (late component) each account for 47% of the variance.

CHAPTER 3

RESULTS

Self-report measures

Analysis of self-reported scene ratings yielded a significant main effect of scene content for pleasantness [$F(2,1954) = 2573.96$, $p < .001$; $\alpha = .025$] and arousal [$F(2,1954) = 213.172$, $p < .001$; $\alpha = .05$]. Pleasantness ratings followed the expected pattern of pleasant (P) < neutral (N) < unpleasant (UP; all $p < .001$), with lower ratings indicating more perceived pleasantness. Arousal ratings followed the expected pattern of UP & P < N (both $p < .001$), with lower ratings indicating more perceived arousal.

A primary aim of the current study was if scene ratings differ across psychosis groups (Figure 2). Main effects of group were not significant [pleasantness: $F(4,977) = 1.24$, $p = .29$; $\alpha = .025$, arousal: $F(4,977) = 1.04$, $p = .39$; $\alpha = .05$]. There was not a group by valence interaction for pleasantness ratings [$F(8,1954) = .74$, $p = .66$; $\alpha = .05$], but there was a group by valence interaction for arousal [$F(8,1954) = 13.90$, $p < .001$; $\alpha = .025$]. For arousal ratings of neutral images, group ratings showed larger deviations from HC along the SBS. With increased SBS scores (or increasingly non-affective psychosis), neutral images were rated as higher in arousal (Table 2). Pleasant image ratings did not differ between groups. For unpleasant images, deviations again increased along the SBS, but with increased SBS scores reporting lower arousal to unpleasant images (Table 2). This indicates a reduced range of arousal with increasingly non-affective psychosis.

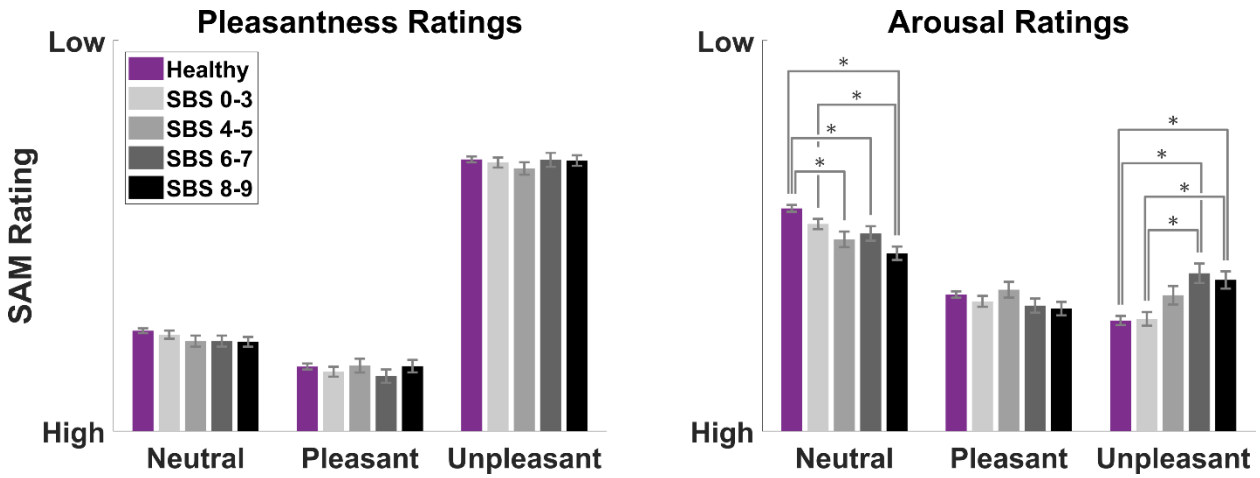

Figure 2. Pleasantness and arousal self-report ratings by group and scene type. Stimulus type is shown along the x-axis and rating (high to low) is shown along the y-axis. The healthy group is shown in purple and the psychosis groups are shown in shades of gray. Lines and stars indicate significant differences between groups. Pleasantness ratings did not vary by group, but neutral and unpleasant arousal ratings exhibited differences from healthy with increasing SBS scores.

Table 2

Tukey HSD tests for arousal ratings

	SBS 0-3		SBS 4-5		SBS 6-7		SBS 8-9	
	MD	*p*	MD	*p*	MD	*p*	MD	*p*
Neutral								
HC	.28	.14	**.56*** **	**.001**	**.45** **	**.01**	**.80*** **	**<.001**
SBS 0-3			.27	.41	.17	.82	**.52** **	**.003**
SBS 4-5					-.11	.97	.25	.54
SBS 6-7							.36	.18
Pleasant								
HC	.12	.86	-.09	.97	.20	.61	.25	.27
SBS 0-3			-.21	.68	.08	.99	.13	.90
SBS 4-5					.28	.46	.34	.24
SBS 6-7							.05	1.0
Unpleasant								
HC	-.03	1.0	-.45	.10	**-.85*** **	**<.001**	**-.73*** **	**<.001**
SBS 0-3			-.43	.24	**-.82** **	**.001**	**-.70** **	**.003**
SBS 4-5					-.40	.41	-.27	.70
SBS 6-7							.12	.98

Note. MD = mean difference (group from row minus column). ** $p < .01$, *** $p < .001$

For within-subjects tests (Table A6), all groups reported significantly higher arousal to emotional scenes (P & UP) than N (all $p < .001$). However, for the difference between P and UP, HC and SBS 0-3 reported significantly *higher* arousal to UP than P ($p < .001$, $p = .02$), ratings did not differ for SBS 4-5 ($p = .63$), and SBS 6-7 and 8-9 reported significantly *lower* arousal to UP than P ($p = .003$, $p = .004$). This indicates that groups with less-affective psychosis show a differing pattern of arousal to P and UP scenes.

Early EEG component

The early component showed the expected main effect of valence [$F(2,2036) = 346.12$, $p < .001$; $\alpha = .05$], with lower voltage to emotional scenes than to N (both $p < .001$), and a lower voltage response to UP than P ($p < .001$). In early processing, this relative negativity indicates enhanced processing of emotional content.

There was a significant main effect of group [$F(4,1018) = 2.84$, $p = .023$; $\alpha = .025$], with lower overall amplitude for SBS 4-5 than HC ($p = .03$). There was also a significant group by valence interaction [$F(8,2036) = 7.63$, $p < .001$; $\alpha = .025$]. Only N scene response significantly separated groups, with higher amplitude for HC than SBS 4-5 and 8-9 (both $p < .01$), though all scene types followed a similar trend, reflected in the overall group effect (Figure 3; Table 3). Groups did not differ in within-subject effects (all comparisons $p < .005$; Table A7).

Late EEG component

The late component also displayed the expected main effect of valence [$F(2,2036) = 437.58$, $p < .001$; $\alpha = .025$], with significantly enhanced voltage positivity to emotional images relative to N (both $p < .001$). Additionally, response amplitudes for UP scenes were higher than those for P ($p < .001$). In late processing, this relative positivity indicates enhanced processing of emotional content.

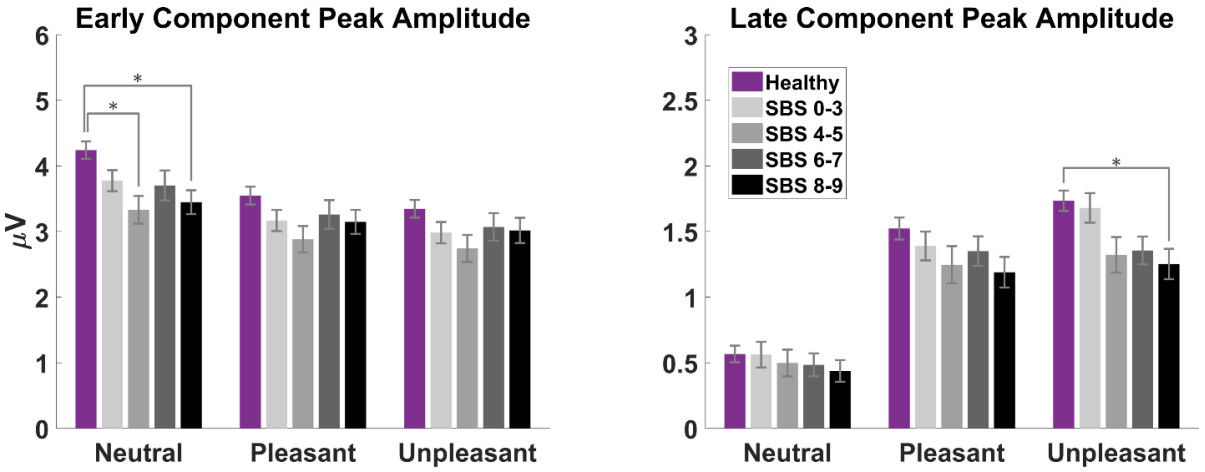

Figure 3. Early and late component amplitudes at peak sensors. Stimulus type is shown along the x-axis and amplitude is shown along the y-axis. The healthy group is in purple and psychosis groups are in gray shades. Lines and stars indicate significant differences between groups. The early component shows overall reduced amplitude in SBS 4-5, while the late component shows a trend of reduced amplitudes to emotional scenes in the less-affective psychosis groups.

Table 3

Tukey HSD tests for early component

	SBS 0-3		SBS 4-5		SBS 6-7		SBS 8-9	
	MD	*p*	MD	*p*	MD	*p*	MD	*p*
Neutral								
HC	.47	.22	**.91****	**.004**	.54	.21	**.79****	**.005**
SBS 0-3			.44	.54	.07	1.0	.33	.73
SBS 4-5					-.37	.76	-.12	1.0
SBS 6-7							.25	.91
Pleasant								
HC	.38	.43	.66	.07	.29	.79	.40	.40
SBS 0-3			.29	.86	-.09	1.0	.02	1.0
SBS 4-5					-.38	.76	-.26	.90
SBS 6-7							.11	1.0
Unpleasant								
HC	.36	.47	.60	.13	.28	.81	.33	.60
SBS 0-3			.24	.92	-.09	1.0	-.03	1.0
SBS 4-5					-.33	.84	-.27	.89
SBS 6-7							.05	1.0

Note. MD = mean difference (group from row minus column). *$p < .05$, **$p < .01$, ***$p < .001$

The main effect of group did not reach the significance threshold [$F(4,1018) = 2.38$, $p = .0503$; $\alpha = .05$], but this sub-threshold effect was reflected in a trend of reduced amplitudes along the SBS (Figure 3). There was a significant group by valence interaction [$F(8,2036) = 3.40$, $p = .001$; $\alpha = .05$]. N and P scenes did not significantly differentiate groups, but UP scene response was significantly higher for HC than SBS 8-9 ($p = .004$) and P scene response followed a similar trend (Figure 3; Table 4). For within subject effects, all groups showed a difference in response amplitude between N and emotional scenes (all $p < .001$), but only HC and SBS 0-3 showed a significant difference between P and UP (both $p < .001$; Table A7).

Canonical discriminant and canonical correlation analyses

Emotional processing measures in the multivariate analyses included arousal ratings of neutral and unpleasant scenes, early EEG component measures for all scene types, and the late EEG component measure for unpleasant scenes.

For the canonical discriminant analysis, one variate was significant ($\Lambda = .33$, Wilks' Lambda = .87, Chi-square = 129.02, df = 24, $p < .001$). The canonical variate driven by arousal ratings and separated groups with less-affective psychosis from HC and highly affective psychosis (HC/SBS 0-3 > SBS 4-9, all $p < .002$; Figure 4; Table 5).

For the canonical correlation analysis, the first pair was significant [$r = .43$, $F(60,2389) = 2.32$, $p < .001$]. The canonical loadings indicated that lower arousal ratings of neutral scenes, rating UP as less arousing than P, higher arousal ratings of unpleasant scenes, and lower amplitude ERPs were associated with lower premorbid IQ, lower cognition, and lower social functioning (Table 6). This finding suggests that the emotional response, primarily characterized by self-report, is highly associated with cognition and social function in psychosis.

Table 4

Tukey HSD tests for late component

	SBS 0-3		SBS 4-5		SBS 6-7		SBS 8-9	
	MD	*p*	MD	*p*	MD	*p*	MD	*p*
Neutral								
HC	.01	1.0	.07	.98	.08	.96	.13	.76
SBS 0-3			.06	.99	.08	.98	.12	.87
SBS 4-5					.01	1.0	.06	.99
SBS 6-7							.05	1.0
Pleasant								
HC	.13	.88	.28	.42	.17	.81	.33	.13
SBS 0-3			.14	.93	.04	1.0	.20	.75
SBS 4-5					-.10	.99	.06	1.0
SBS 6-7							.16	.90
Unpleasant								
HC	.05	.99	.41	.06	.38	.09	**.48****	**.004**
SBS 0-3			.36	.24	.32	.33	.43	.06
SBS 4-5					-.03	1.0	.07	1.0
SBS 6-7							.10	.98

Note. MD = mean difference (group from row minus column). **p<.01

Table 5

Canonical discriminant analysis

Correlation between variable and canonical function								
Neutral Arousal	Unpleasant Arousal		Early Neutral		Early Pleasant		Early Unpleasant	Late Unpleasant
.62	**-.51**		**.37**		.20		.17	**.37**
Centroids	HC		SBS 0-3		SBS 4-5		SBS 6-7	SBS 8-9
N	399		179		121		124	159
M	.35		.12		-.29		-.27	-.57
SD	.99		.92		1.02		1.06	1.06
Tukey tests	SBS 0-3		SBS 4-5		SBS 6-7		SBS 8-9	
	MD	*p*	MD	*p*	MD	*p*	MD	*p*
HC	.22	.10	**.64*****	**<.001**	**.62*****	**<.001**	**.92*****	**<.001**
SBS 0-3			**.42****	**.004**	**.40****	**.006**	**.69*****	**<.001**
SBS 4-5					-.02	1.0	.28	.15
SBS 6-7							.29	.10

Note. **p < .01, ***p < .001, MD = mean difference (group in row minus group in column).

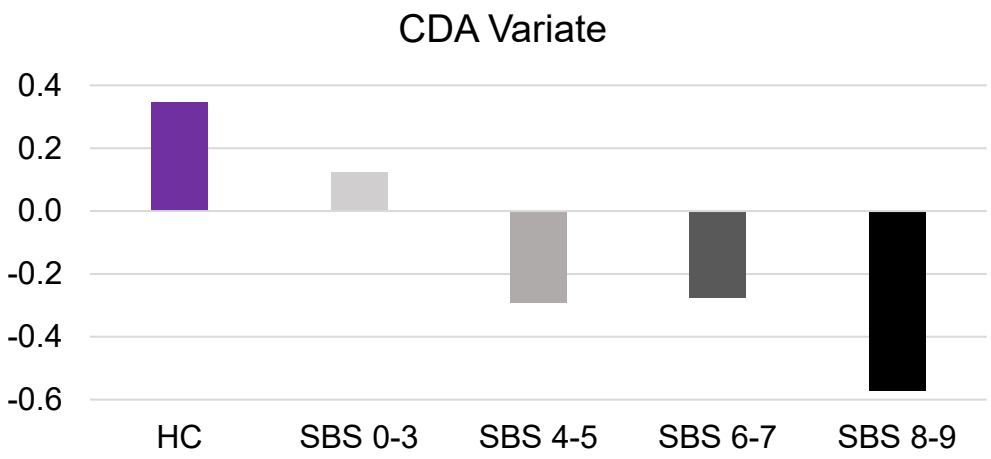

Figure 4. Centroids of each group from the canonical discriminant analysis. Groups are labeled along the x-axis and variate scores are shown on the y-axis. Tukey tests indicated that HC and the most affective group significantly differed from all the less-affective psychosis groups.

Table 6

Canonical correlation variate pair loadings

Set 1	Loading
Arousal rating, unpleasant	**0.685**
Arousal rating, neutral	**-0.661**
EEG early, neutral	**-0.419**
EEG late, unpleasant	**-0.340**
EEG early, pleasant	**-0.312**
EEG early, unpleasant	**-0.303**
Set 2	**Loading**
Premorbid IQ (WRAT)	**-0.861**
Cognition (BACS)	**-0.747**
Social Function (SFS)	**-0.363**
Global Function (GAF)	-0.293
PANSS Negative Symptoms	0.204
PANSS Positive Symptoms	0.196
PANSS General Symptoms	0.071
Mania (YMRS)	0.066
Depression (MADRS)	-0.028
Anxiety (CAS)	-0.022

Note. Cells are color coded according to loading strength and direction (positive = red, negative = blue). Loadings in bold (absolute value ≥ .3) contribute meaningfully to the relationship between variable sets.

CHAPTER 4

DISCUSSION

This study examined the emotional scene response across psychosis syndromes. Psychosis syndromes were classified using the Schizo-Bipolar Scale, a measure of affective (0 end of scale) to non-affective (9 end of scale) psychosis. The emotional scene response was quantified by self-reported pleasantness and arousal, as well as early- and late-occurring EEG components in response to neutral, pleasant, and unpleasant scenes. Findings supported abnormal neural and behavioral emotional responses with increasingly non-affective psychosis. Self-reported arousal, early ERP amplitudes, and late emotional amplitudes showed patterns of increasingly abnormal responses along the Schizo-Bipolar Scale from most to least affective. Differences between groups were best characterized by self-reported arousal, and emotional measures tracked with clinical measures of cognition and functioning. Overall, findings support abnormal emotional processing in psychosis, related to socio-cognitive deficits.

Self-report

Subjects with psychosis reported higher arousal to neutral images and lower arousal to unpleasant images, but there were no group differences in experiences of pleasantness. Furthermore, the least-affective SBS groups reported lower arousal to unpleasant images than pleasant, while HC and the most-affective SBS group reported the opposite pattern. Findings support an abnormal subjective experience of emotion with increasingly "schizophrenia-like" psychosis. Previous research supports these findings, with a meta-analysis reporting similarly abnormal arousal to neutral and unpleasant stimuli in schizophrenia (Llerena, Strauss, & Cohen,

2012) and another large trans-diagnostic study reporting lower arousal to unpleasant images in non-affective psychosis but not affective illness, and no differences in valence ratings (Aminoff et al., 2011). The theory of intact hedonic responses in psychosis perhaps explains the lack of significant differences in pleasantness ratings (Strauss & Cohen, 2018). However, recent work suggests that pleasantness responses in non-affective psychosis may actually be characterized by higher emotional coactivation, or simultaneous experience of positivity and negativity (Strauss, Visser, Lee, & Gold, 2017). Future work should consider using a bivariate model of pleasantness to investigate this possibility transdiagnostically.

ERP responses

Early ERP responses were characterized by overall lower amplitudes in SBS 4-5, with a trend of lower amplitudes in all less-affective psychosis groups, and the most prominent difference for neutral images. This suggests that early visual responding is deficient in groups with both prominent mood and psychosis symptoms, regardless of emotional content. Late ERP responses showed lower unpleasant response amplitudes in SBS 8-9 and a trend of lower amplitudes along the SBS for both pleasant and unpleasant scene responses. Additionally, only HC and SBS 0-3 displayed differing responses between pleasant and unpleasant scenes, likely reflective of their arousal ratings, since they were they only groups to score unpleasant scenes as more arousing than pleasant. These findings in the late component indicate that elaborative emotional processing is slightly blunted in less-affective psychosis.

Given the rather small effect sizes of these differences (Table A8), it is not surprising that similar studies with smaller samples have found inconsistent ERP results. Additionally, patterns of significance at the early component and effect sizes in the SBS 4-5 group indicate that inclusion of this group in schizophrenia samples (though individuals in SBS 4-5 are typically

diagnosed with schizoaffective disorder; Table 1) could boost the likelihood of significant findings in emotional processing studies. This possibility emphasizes the need for studying members of this group specifically, rather than lumping them into schizophrenia samples.

Multivariate analyses

The discriminant analysis suggested that self-reports of arousal separate groups better than electrophysiological responses. This interpretation is supported by the moderate to large effect sizes for neutral and unpleasant arousal ratings in psychosis groups (Table A8). Differences on discriminant scores reflected the pattern of results seen throughout most examined measures, with differences from healthy seen in less-affective psychosis and increasing differences along the SBS. These findings indicate that overall, emotional scene processing is intact in affective psychosis, but shows increasing impairments with less-affective psychotic illness.

The multivariate correlation indicated that arousal scores and cognition best characterize the relationship between emotional scene processing and clinical features, further highlighting the importance of self-reported arousal to clinical differences. Three clinical measures stood out in this correlation: The Wide Range Achievement Test (WRAT), which is often used as a proxy for premorbid IQ or cognitive reserve (Barnett, Salmond, Jones, & Sahakian, 2006; Olsen, Fellows, Rivera-Mindt, Morgello, & Byrd, 2015), the Brief Assessment of Cognition in Schizophrenia (BACS), and the Social Functioning Scale (SFS). The high loadings on these measures indicates that, as expected, emotional scene processing is linked to socio-cognitive functioning. This finding raises the potential for emotional scene processing as a neurobehavioral marker of response to cognitive and social therapies.

Limitations

Participants in the current study were taking a wide range of psychoactive medications. Lithium, second-generation antipsychotics, and anticonvulsants had associations with neural measures (Table A5), but additional effects of interacting medications cannot be ruled out. Future visual and emotional studies of mood and psychotic disorders should consider potential effects of these medications. Additionally, placebo-controlled studies should examine how specific drugs in these classes affect similar neural measures.

This study included people with a range of illness lengths and varying histories of medication use. While these factors could affect behavioral and neural measures, this diverse sample is highly representative of community populations with psychosis. Furthermore, most participants were clinically stable and not experiencing severe mood and psychosis symptoms. Perhaps the low loadings on positive, negative, and mood symptoms are affected by this limited range of symptomology. Studies of inpatients and first-episode psychosis should examine this possibility.

Future directions

The BSNIP consortium previously identified three biological subtypes, "Biotypes," of psychosis during the first iteration of the BSNIP project (Clementz et al., 2016). These Biotypes repeatedly display larger between-group differences on biological measures than DSM diagnoses (Hudgens-Haney et al., 2017; Ivleva et al., 2017; Meda et al., 2016). The current project was part of the second iteration of the BSNIP project, in which we have replicated the Biotypes, so we will soon examine how emotional scene processing differs across these subtypes of psychosis. Evidence suggests there may be subtypes of psychosis with intact and impaired emotional experience (Strauss & Herbener, 2011). These subtypes could potentially line up with Biotypes or reflect an additional level of behavioral differences. Moreover, a critical factor that

distinguished the Biotypes was cognition, which we have demonstrated is closely related to the emotional scene response. Future studies will examine emotional scene processing and other emotional measures (specifically emotion recognition; see Ruocco et al., 2014) in the Biotypes and experimentally tax cognition to further examine its relationship with emotional measures.

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APPENDIX

Clinical scales

Clinical measures included the Global Assessment of Functioning (GAF; Axis V of the DSM-IV-TR), the Birchwood Social Functioning Scale (SFS; Birchwood et al., 1990), the Positive and Negative Syndrome Scale for Schizophrenia (PANSS; Opler et al., 1999), the Young Mania Rating Scale (YMRS; Young et al., 1978), the Montgomery-Åsberg Depression Rating Scale (MADRS; Montgomery and Asberg, 1979), the Clinical Anxiety Scale (CAS; Snaith et al., 1982), the Wide Range Achievement Test (WRAT; Wilkinson & Robertson, 2006), and the Brief Assessment of Cognition in Schizophrenia (BACS; Keefe et al., 2004). Group scores on these scales are reported in Table A1.

Table A1

Clinical scales by group

	HC	SBS 0-3	SBS 4-5	SBS 6-7	SBS 8-9	Statistic	*p*
Global Assessment of Function (GAF)						F(4,907)= 479.32***	<.001
						F(3,570)= 9.62***	<.001
N	338	173	114	124	163	HC > SBS 0-9***	
M	83.69	56.18	54.28	53.09	49.36	SBS 0-3***, SBS 4-5**,	
SD	6.63	12.99	10.81	11.99	11.32	SBS 6-7* > SBS 8-9	
Birchwood Social Functioning Scale (SFS)						F(4,955)= 152.17***	<.001
						F(3,570)= 14.15***	<.001
N	386	176	118	122	158	HC > SBS 0-9***	
M	153.85	129.99	121.08	114.95	116.18	SBS 0-3 > SBS 4-5**,	
SD	17.81	23.71	24.52	21.66	21.76	SBS 6-9***	
Wide Range Achievement Test (WRAT)						F(4,960)= 25.33***	<.001

						F(3,583)= 13.99***	<.001
N	378	179	118	123	167	HC, SBS 0-3 > SBS 4-9***	
M	100.03	98.85	92.58	91.72	89.38		
SD	12.47	13.44	14.57	15.07	13.97		
Brief Assessment of Cognition in Schizophrenia (BACS)						F(4,977)= 77.84***	<.001
						F(3,584) = 17.61***	<.001
N	394	181	119	125	163	HC > SBS 0-7*** > SBS 8-9***	
M	-.21	-.76	-.95	-1	-1.39		
SD	.74	.78	.80	.83	.82		
Positive and Negative Syndrome Scale (PANSS) Positive						F(3,553)= 14.85***	<.001
N	N/A	170	111	120	156	SBS 0-3 < SBS 4-9***	
M	N/A	14.04	17.39	17.94	18.21		
SD	N/A	6.16	6.30	6.27	6.64		
PANSS Negative						F(3,552)= 10.78***	<.001
N	N/A	170	111	120	155	SBS 0-3 < SBS 6-7**, SBS 8-9*** SBS 4-5 < SBS 8-9**	
M	N/A	13.93	14.91	16.65	17.86		
SD	N/A	6.49	6.37	6.89	6.80		
PANSS General						F(3,553)=1.54	.20
N	N/A	170	111	120	156		
M	N/A	30.82	32.50	32.66	33.03		
SD	N/A	10.47	9.16	9.52	10.53		
PANSS Total						F(3,552)= 7.79***	<.001
N	N/A	170	111	120	155	SBS 0-3 < SBS 6-7**, SBS 8-9***	
M	N/A	58.79	64.80	67.25	69.20		
SD	N/A	21.12	19.27	19.93	21.23		
Montgomery-Åsberg Depression Rating Scale (MADRS)						F(3,562)= 5.74**	.001
N	N/A	172	115	119	160	SBS 0-3**, SBS 4-7* > SBS 8-9	
M	N/A	14.26	13.13	13.66	9.80		
SD	N/A	11.60	10.58	10.62	8.96		
Young Mania Rating Scale (YMRS)						F(3,558)=2.01	.11
N	N/A	172	113	118	159		
M	N/A	8.89	11.22	9.72	10.17		
SD	N/A	8.72	7.98	7.48	7.66		
Clinical Anxiety Scale (CAS)						F(3,564)= 4.35**	.005

N	N/A	172	115	120	161	SBS 0-3 > SBS 8-9** SBS 6-7 > SBS 8-9*
M	N/A	5.89	5.62	5.85	4.17	
SD	N/A	5.53	4.84	4.74	4.23	

Note. For scales with two sets of ANOVA statistics, the first was done including HC, and the second included only those with psychosis. *$p < .05$, **$p < .01$, ***$p < .001$. Group comparisons performed with Tukey tests.

Table A2

Medication details by group

	HC	SBS 0-3	SBS 4-5	SBS 6-7	SBS 8-9
N	409	185	123	127	164
% on any medication	48	94	90	89	88
Total medication count- mean	2.3	4.90	4.92	4.88	4.25
Total medication count- SD	1.68	3.56	3.11	2.90	2.70
Psychotropic count- mean	1.21	3.02	2.90	2.83	2.47
Psychotropic count- SD	.54	1.72	1.33	1.31	1.33
N on psychotropic medication	19	166	105	109	148
N on antipsychotic	0	127	91	102	139
N on first generation AP	0	6	14	20	31
N on second generation AP	0	124	85	88	123
N on antidepressant	8	82	60	64	71
N on tricyclic	2	4	1	1	2
N on MAOI	0	0	0	0	0
N on SSRI	5	46	49	55	53
N on other antidepressant	1	52	23	29	27
N on mood stabilizer	3	120	56	38	39
N on lithium	0	45	16	5	13
N on anticonvulsant	3	91	49	34	28
N on anxiolytic/sedative/hypnotic	6	51	24	26	23
N on anticholinergic/antiparkinsonian	0	7	9	27	31
N on stimulant	5	11	5	2	3
N on other psychotropic	0	13	11	5	11

Table A3

Differences in medication status between psychosis groups

	Statistic	*p*
Total medications	F(3,547) = 1.60	.19
Total psychotropic medications	F(3,524) = 4.05**	.01
On antipsychotic	$x^2(3) = 8.55$*	.04
On second generation AP	$x^2(3) = .85$	.84
On antidepressant	$x^2(3) = 2.71$	.44
On SSRI	$x^2(3) = 13.75$**	.003
On mood stabilizer	$x^2(3) = 74.57$***	<.001
On lithium	$x^2(3) = 34.96$***	<.001
On anticonvulsant	$x^2(3) = 48.24$***	<.001
On anxiolytic/sedative/hypnotic	$x^2(3) = 11.20$*	.01

Note. *$p < .05$, **$p < .01$, ***$p < .001$. Statistics only reported for cells with N > 10.

Table A4

Daily dosage information

	SBS 0-3	SBS 4-5	SBS 6-7	SBS 8-9		
Lithium					F(3,60)	*p*
N on lithium	37	12	5	10		
Mean dose	928 mg	913 mg	712 mg	685 mg	1.24	.30
Dose SD	415.63	316.32	494.44	426.91		
CPZ equivalents					F(3,372)	*p*
N	100	79	82	115		
Mean dose	409 mg	620 mg	490 mg	689 mg	1.76	.16
Dose SD	825.44	1189.25	626.61	1088.34		

Note. Only reported for subjects with dose data. CPZ equivalents established with the Andreasen method (Andreasen, Pressler, Nopoulos, Miller, & Ho, 2010).

Table A5

Associations between medication status and EEG measures

	Early Comp, Neutral	Early, Pleasant	Early, Unpleasant	Late, Neutral	Late, Pleasant	Late, Unpleasant
2nd generation APs						
t(611)	-1.68	**-2.20***	**-2.20***	-1.13	-.96	-1.84┼
p	.09	**.03**	**.03**	.26	.34	.07
SSRIs						
t(611)	-.35	-.86	-.64	.94	.15	.78
p	.73	.39	.52	.35	.88	.44
Lithium						
t(611)	**-2.27*** ┼	**-2.33*** ┼	**-2.32*** ┼	-.59┼	-.62	-.86┼
p	**.03**	**.02**	**.02**	.48	.54	.32
Anticonvulsants						
t(611)	.70	1.10	1.08	-1.51	-1.46	**-2.24***
p	.48	.27	.28	.13	.15	**.03**
Lithium dose						
r	-.02	-.03	-.01	.11	.04	-.01
p	.89	.79	.34	.41	.73	.95
CPZ equivalent dose						
r	-.03	-.03	-.05	.05	.04	.00
p	.57	.56	.38	.33	.49	.99

Note. ┼Violated Levene's Test for Equality of Variances, equality of variances not assumed.
*$p < .05$

Table A6

Within-subject t-tests for effects of scene type on arousal

		Neutral / Pleasant		Neutral / Unpleasant		Pleasant / Unpleasant	
	df	*t*	*p*	*t*	*p*	*t*	*p*
HC	398	25.09***	<.001	18.48***	<.001	**4.89*****	**<.001**
SBS 0-3	178	14.95***	<.001	12.03***	<.001	**2.39***	**.02**
SBS 4-5	120	7.10***	<.001	4.50***	<.001	**.49**	**.63**
SBS 6-7	123	9.64***	<.001	3.18**	.002	**-3.08****	**.003**
SBS 8-9	158	7.50***	<.001	2.29*	.02	**-2.96****	**.004**

Note. *$p < .05$, **$p < .01$, ***$p < .001$. The pleasant/unpleasant comparisons show a differing pattern of arousal across groups.

Table A7

Within-subject t-tests for effects of scene type on ERPs

		Neutral / Pleasant		Neutral / Unpleasant		Pleasant / Unpleasant	
	df	*t*	*p*	*t*	*p*	*t*	*p*
Early Component							
HC	409	14.67***	<.001	20.64***	<.001	6.15***	<.001
SBS 0-3	185	10.21***	<.001	12.76***	<.001	4.18***	<.001
SBS 4-5	124	7.54***	<.001	9.58***	<.001	2.93**	.004
SBS 6-7	128	7.10***	<.001	9.87***	<.001	3.67***	<.001
SBS 8-9	172	4.91***	<.001	6.94***	<.001	2.66**	.008
Late Component							
HC	409	-16.0***	<.001	20.52***	<.001	**-4.62*** **	**<.001**
SBS 0-3	185	-10.86***	<.001	-12.74***	<.001	**-4.46*** **	**<.001**
SBS 4-5	124	-8.42***	<.001	-8.47***	<.001	**-1.11**	**.27**
SBS 6-7	128	-10.33***	<.001	-10.34***	<.001	**-.07**	**.94**
SBS 8-9	172	-10.07***	<.001	-10.27***	<.001	**-1.03**	**.30**

Note. All significant except SBS 4-9 P/UP at the late component. $^{**}p < .01$, $^{***}p < .001$

Table A8

Glass' Delta effect sizes in each SBS group

	Neutral	Pleasant	Unpleasant
	Δ	Δ	Δ
Arousal Rating			
SBS 0-3	-.23	-.10	.02
SBS 4-5	-.46	.07	.27
SBS 6-7	-.37	-.17	.51
SBS 8-9	-.66	-.22	.44
Early Component			
SBS 0-3	-.17	-.14	-.13
SBS 4-5	-.34	-.24	-.22
SBS 6-7	-.20	-.10	-.10
SBS 8-9	-.29	-.15	-.12
Late Component			
SBS 0-3	-.00	-.08	-.03
SBS 4-5	-.05	-.16	-.26
SBS 6-7	-.06	-.10	-.24
SBS 8-9	-.10	-.20	-.31

Note. Effects are in comparison to the healthy group.