Reduced Contextual Effects on Visual Contrast Perception in Schizophrenia and Bipolar Affective Disorder

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Abstract

Background—The salience of a visual stimulus is often reduced by nearby stimuli, an effect known as surround suppression of perceived contrast, which may help in locating the borders of an object. Weaker surround suppression has been observed in schizophrenia but it is unclear whether this abnormality is present in other mental disorders with similar symptomatology, or is evident in people with genetic liability for schizophrenia.

Methods—By examining surround suppression among subjects with schizophrenia or bipolar affective disorder, their unaffected biological relatives, and healthy controls we sought to determine whether diminished surround suppression was specific to schizophrenia, and if subjects with a genetic risk for either disorder would show similar deficits. Measuring perceived contrast in different surround conditions also allowed us to investigate how this suppression depends on the similarity of target and surrounding stimuli.

Results—Surround suppression was weaker among schizophrenia patients regardless of surround configuration. Subjects with bipolar affective disorder showed an intermediate deficit, with stronger suppression than in schizophrenia but weaker than control subjects. Surround suppression was normal in relatives of both patient groups. Findings support a deficit in broadly-tuned (rather than sharply orientation- or direction-selective) suppression mechanisms.

Conclusions—Weak broadly tuned suppression during visual perception is evident in schizophrenia and bipolar affective disorder, consistent with impaired gain control related to the clinical expression of these conditions.

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Conflict of interest

None

Keywords

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Introduction

Visual processing is context-specific, such that the neural response to a visual stimulus depends on nearby stimuli or backgrounds. One well-studied example is known as surround suppression, wherein the response to a visual stimulus is reduced by similar nearby stimuli (Angelucci and Bressloff, 2006, Cavanaugh *et al.*, 2002, Nurminen and Angelucci, 2014, Webb *et al.*, 2005). The perceived luminance contrast of a stimulus is also reduced by surrounding stimuli with similar features (e.g., orientation, direction of motion; Yu *et al.*, 2001). This surround suppression effect is believed to be important for visually detecting edges and determining the salience of image features during camouflage.

Patients with schizophrenia (SZ) show a number of visual processing abnormalities including a reduced influence of surrounding context. It has been suggested that studying these impairments may provide insight into the neural underpinnings of this disorder; by precisely characterizing visual deficits in SZ, one may be able to attribute them to specific neural mechanisms (Butler *et al.*, 2008, Notredame *et al.*, 2014, Phillips and Silverstein, 2013, Yoon *et al.*, 2013). A number of recent studies have shown weaker surround suppression among SZ patients compared with healthy controls (HC; Dakin *et al.*, 2005, Robol *et al.*, 2013, Schallmo *et al.*, 2013, Seymour *et al.*, 2013, Tadin *et al.*, 2006, Tibber *et al.*, 2013, Yang *et al.*, 2013a, b, Yoon *et al.*, 2009), but see (Barch *et al.*, 2012, Chen *et al.*, 2008). However, it is not clear whether this deficit is specific to SZ, or if it is also observed in other psychiatric conditions such as bipolar affective disorder (BP; Dakin *et al.*, 2005, Yang *et al.*, 2013a). Further, it is not known to what extent persons with genetic liability for such disorders, such as first-degree biological relatives of schizophrenia patients (SZrel; Schallmo *et al.*, 2013) or of patients with bipolar affective disorder (BPrel), show similar deficits. Finally, the extent to which diminished surround suppression in SZ depends on the similarity between targets and surrounding stimuli is not well established (Seymour *et al.*, 2013, Yoon *et al.*, 2009).

The current study examines suppression of visual contrast perception by surrounding stimuli among SZ and BP patients, SZrel, BPrel, and HC subjects, to determine whether deficits in surround suppression are present in each group. We varied the configuration of surrounding stimuli to examine how such deficits depend on the similarity between target and surround. Understanding whether diminished surround suppression is diagnostically specific to SZ or reflects mechanisms underlying genetic liability will help clarify the role of basic visual functions in severe psychopathology.

Methods

Participants

The following subjects were recruited: 32 outpatients with SZ, 1 outpatient with schizoaffective disorder – depressed type (grouped with SZ for analysis), 23 BP outpatients, 7 outpatients with schizoaffective disorder – bipolar type (grouped with BP), 28 unaffected first-degree biological relatives of SZ patients (SZrel), 11 relatives of BP patients (BPrel), 10 relatives of patients with schizoaffective disorder – bipolar type (grouped with BPrel), and 45 healthy controls (HC). Diagnoses were made from structured interview (DSM-IV-TR, SCID, and Psychosis Module from DIGS; APA, 2000, First, 1997, Nurnberger *et al.*, 1994) and clinical data reviewed in a consensus process by a doctorate-level clinical psychologist or advanced doctoral students. During consensus diagnosis, 1 SZrel and 1 BPrel were found to have diagnoses of SZ and BP, respectively. These were retained as relatives; repeating our analyses without them yielded an equivalent pattern of results. Additionally, we repeated our analyses excluding schizoaffective disorder – bipolar type patients, to explore the effect of grouping them with BP patients. Results were equivalent; analysis and results for the larger group are reported.

Exclusion criteria used during recruitment were identical to those previously reported (Schallmo *et al.*, 2013). All subjects had normal or corrected-to-normal visual acuity. HC subjects had no history of SZ, BP, or other psychotic diagnoses for themselves and their first-degree biological relatives. Subjects provided written informed consent and were compensated $15/hr. This protocol was approved by the Institutional Review Boards of the University of Minnesota and the Minneapolis VA Medical Center.

Subjects reported their parents' level of education using a 7-point scale. IQ was estimated using the Wechsler Adult Intelligence Scale (WAIS-III; Jeyakumar *et al.*, 2004). The following behavioral measures were used to assess symptom levels: Brief Psychiatric Rating Scale (BPRS; Overall and Donald, 1962), Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1982), Scale of the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), Schizotypal Personality Questionnaire (SPQ; Raine, 1991), and Sensory Gating Inventory (SGI; Hetrick *et al.*, 2012). Medication levels were converted to chlorpromazine (CPZ), Lithium (Li), and Imipramine (Imip.) equivalent doses (Andreasen *et al.*, 2010).

Stimuli

Stimuli were generated using MATLAB and Psychtoolbox (Brainard, 1997, Pelli, 1997) on a MacMini running OSX, and displayed on a 19 inch LCD monitor that subtended 35.1×26.7 degrees of visual angle at a viewing distance of 61cm. Display luminance was linearized using custom software. Mean luminance was 84 cd/m^2. The stimuli comprised two circular patches of sinusoidal luminance modulation (gratings hereafter) 1° in diameter, with a spatial frequency of 2 cycles/°, presented at 2° eccentricity to the left and right of a central fixation mark (blue square 8 pixels across) along the horizontal meridian. In most conditions, an annular stimulus surrounding one circle was also presented, with an outer diameter of 3°. Gratings drifted at 3.75 cycles/sec. The orientation of the circular gratings

and direction of stimulus motion was randomly assigned on each trial from 4 orientations (0–135°), each with 2 relative directions of motion.

Different stimulus conditions were defined by the presence and configuration of an annular sine wave grating stimulus surrounding one of the circular gratings (Figure 1). We refer to the circular stimulus presented with the surround as the target, and the stimulus presented alone as the reference. Note that target and reference were always presented peripherally. We included different surround conditions to examine whether greater similarity between target and surround would evoke stronger perceived contrast suppression, as predicted (Cavanaugh *et al.*, 2002, Yu *et al.*, 2001). These surround conditions were designed to probe whether low-level differences in visual stimulus features (e.g., orientation, motion direction) may differentially affect surround suppression in certain subject groups. A suppression deficit specific to conditions with more similar targets and surrounds may suggest impairment in feature-selective suppression in early visual cortex, while an impairment across conditions might reflect deficiencies in more broadly tuned mechanisms (Angelucci and Bressloff, 2006, Nurminen and Angelucci, 2014).

In the Parallel condition, target and surround had the same orientation and spatial phase. The inner diameter of the surround was 1°, so target and surround were abutting. The Gap condition was identical to Parallel, except that a 0.1° mean luminance gap separated target and surround (edges not blurred), to mitigate brightness induction (Yu *et al.*, 2001). The Opposite condition was identical to Parallel, except target and surround drifted in opposite directions. In Figure 1, target and surround are illustrated with opposite spatial phase to convey that the opposite drift direction disrupts their relative phase relationship. In the Orthogonal condition, target and surround stimuli were oriented orthogonally (90°). Finally, there was a None condition in which no surround was presented. Surrounds were displayed at 70% Michelson contrast, and target contrast was 50%. The position of the target and surround versus reference stimuli (left or right of fixation) was random in each trial.

Paradigm

Subjects fixed their eyes on the central square and used their peripheral vision to compare target and reference contrast. In each trial, stimuli were presented for 300 msec; afterward subjects indicated which circular stimulus (left or right; i.e., target or reference) was higher contrast by pressing the corresponding arrow key. Response time was unlimited. The fixation mark was displayed for 400 msec between trials. Twenty-five trials were presented for each condition in a random intermixed order, which composed one run. Each subject completed at least 4 runs. Prior to the experiment, subjects completed several practice trials during which they viewed static and drifting stimuli. They were instructed to attend to the peripheral stimuli while maintaining fixation, and to compare the perceived contrast of the target and reference, but not the surround. Total experiment duration including practice was approximately 10 minutes.

This task was designed to measure the perceived contrast of the target stimulus. For the first 85 subjects, the contrast of the reference was adjusted across trials using a 1-up, 1-down staircase method to determine the point of subjective equality between perception of target and reference contrast. This method converges on the reference contrast reported as higher

50% of the time (Garcia-Perez, 1998), which we refer to as the perceived contrast. For the remaining 72 subjects, reference contrast was adjusted across trials using the Psi adaptive staircase procedure (Prins and Kingdom, 2009) to determine the point of subjective equality. This method (not readily available when the task was designed) provides a more efficient estimate of psychometric function slope, which quantifies the noise associated with estimates of perceived contrast (Kingdom and Prins, 2010). The proportion of subjects that completed each version of the task did not differ between groups ($X^2_{(4)} = 4.60$, $p = 0.3$). Perceived contrast was measured separately in each run for each surround condition. Reference contrast varied between 14 and 74%, starting at 40 or 60% (on alternating runs).

Data Analysis

For the 1-up, 1-down staircase, perceived contrast was defined as the average contrast from the last 6 trials in each condition. For the Psi staircase, perceived contrast and corresponding psychometric function slopes were calculated by fitting a Logistic function to the staircase responses using a Maximum Likelihood criterion (Prins and Kingdom, 2009). Guess rate and lapse rate were both set to 4%. Psi staircases with perceived contrast values < 0% or > 100% were excluded (196 out of 1140). We saw no significant difference in perceived contrast values between the two staircase methods (1-way ANOVA, $F_{(1,145)} = 0.13$, $p = 0.7$); data from both were subsequently combined.

Change in perceived contrast was quantified for each condition, run, and subject as the difference between perceived and veridical target contrast (50%), with negative values indicating suppression. To quantify the relative effect of different surround configurations, Contextual Modulation Indices were calculated by subtracting the change in perceived contrast from the Parallel condition from values in the Gap, Orthogonal, and Opposite conditions for each run in every subject.

A number of datasets showed around +20% perceived contrast (i.e., enhancement) for all or most surround conditions. This contradicts the well-established pattern of surround suppression (Yu *et al.*, 2001). We believe that these subjects failed to follow task instructions and erroneously compared the reference contrast to the surround contrast (70% in all conditions). As the actual target contrast was 50%, such a pattern of responses would resemble 20% enhancement of perceived target contrast. Data sets that met the following criteria were analyzed as a separate Enhancement group: change in perceived contrast in 3 or more surround-present conditions was +10% (averaged across runs), and change in perceived contrast was not −10% in any condition. 10 SZ, 11 BP, 3 SZrel, 4 BPrel, and 7 HC subjects showed such enhancement.

The proportion of subjects exhibiting enhancement did not significantly differ across diagnosis groups ($X^2_{(4)} = 8.27$, $p = 0.082$). For Enhancement subjects, perceived contrast did not vary across surround conditions (excluding None; 2-way ANOVA, 5 groups x 4 conditions; $F_{(3,30)} = 0.93$, $p = 0.4$) or groups ($F_{(4,30)} = 1.78$, $p = 0.16$), and there was no significant group by condition interaction ($F_{(16,120)} = 1.49$, $p = 0.11$). Overall, Enhancement group data are inconsistent with feature-selective surround modulation (Cavanaugh *et al.*, 2002, Yu *et al.*, 2001), but instead suggest that subjects were responding to surrounding

stimulus contrast (70%), rather than perceived target contrast (~50%). Therefore, Enhancement group data were excluded from further analyses.

Results

We sought to determine how surrounding stimulus configuration affected perception of target contrast among SZ and BP patients, their unaffected first-degree biological relatives, and healthy controls (demographics reported in Table 1). Figure 2 shows the change in perceived contrast for each condition in each group, following exclusion of subjects who did not comply with task instructions (see Methods). Stimulus conditions are arranged in Figure 2 with greatest target-surround feature similarity (Parallel) on the left, to least (Orthogonal) on the right, followed by the None condition in which no surround was present. Weaker surround suppression was expected for less-similar surrounding stimuli (Cavanaugh *et al.*, 2002, Yu *et al.*, 2001).

We first compared changes in perceived contrast across all surround conditions and subject groups (2-way ANOVA, 5 conditions × 5 groups); a significant main effect of condition ($F_{(4,117)} = 97.0$, $p < 0.001$) indicated that surround configuration significantly affected target contrast perception, as expected. Collapsing across groups, changes in perceived contrast differed significantly in post-hoc tests between each surround condition, with more negative values when target and surround were more similar (Parallel < Gap < Opposite < Orthogonal < None; Tukey's HSD, $q_{(236-239)} > 3.89$, $p < 0.05$). This matches the expected form of configuration-dependent surround suppression (Cavanaugh *et al.*, 2002, Yu *et al.*, 2001): greater feature similarity (e.g., orientation and direction of motion) evoked greater suppression of perceived target contrast. We also observed a main effect of subject group ($F_{(4,117)} = 2.70$, $p = 0.034$); post-hoc tests showed significantly weaker suppression of perceived contrast in SZ subjects than in all other groups (across all conditions), while BP subjects showed weaker suppression than HC, BPrel and SZrel groups, but stronger than SZ subjects (Tukey's HSD, $q_{(31-56)} > 4.35$, $p < 0.05$; Figure 2A). Effect sizes were fairly small (HC vs. SZ, $q_{(56)} = 11.6$, Cohen's $d = 0.42$; HC vs. BP, $q_{(52)} = 6.08$, $d = 0.26$; BP vs. SZ, $q_{(37)} = 4.35$, $d = 0.20$). No difference in contrast perception was observed between HC, SZrel and BPrel groups (Figure 2B). This indicates that surround suppression is greatly diminished during contrast perception among SZ subjects (Dakin *et al.*, 2005, Tibber *et al.*, 2013, Yang *et al.*, 2013b, Yoon *et al.*, 2009), reduced among BP subjects (but less so than in SZ), and equally strong among relatives with a genetic risk for SZ or BP as in HC subjects.

We next sought to determine whether suppression deficits among patients were more evident in certain conditions. Although the group by condition interaction for perceived contrast was not significant ($F_{(16,465)} = 1.35$, $p = 0.16$), we computed Contextual Modulation Indices as the difference in perceived contrast between the Parallel and Gap, Orthogonal, or Opposite conditions (Figure 3), to further examine how surround similarity affected the strength of suppression. Indices differed across conditions as expected (2-way ANOVA, 3 conditions x 5 groups; $F_{(2,115)} = 76.6$, $p < 0.001$). However, we saw no significant effect of group ($F_{(4,\ 115)} = 0.25$, $p = 0.9$), and no interaction between group and condition ($F_{(8,\ 221)} = 1.25$, $p = 0.2$). These results indicate that different surround configurations evoked similar changes in contrast perception across all subject groups.

We examined relationships between task performance and demographic data to determine whether such factors might influence the magnitude of surround suppression. Although gender composition and IQ scores differed significantly across groups (Table 1), we still observed a significant difference in suppression of perceived contrast across groups with gender and IQ included as covariates ($F_{(4, 82)} = 3.67$, $p = 0.009$). No significant correlations were observed between changes in perceived contrast and age, education, parents' education, symptomatology scores (BPRS, SANS, SAPS, SPQ, and SGI), or medication levels (CPZ, Li, or Imip. equivalents). Only 2 subjects reported daily use of benzodiazepines (1 BP, 1 SZrel), and excluding these subjects yielded equivalent results. For both SZ and BP subjects, symptom dimension scores from the BPRS, SANS and SAPS (Wilson and Sponheim, 2014) and factor scores for Sensory Gating Inventory (SGI; Hetrick *et al.*, 2012) were un-correlated with surround suppression levels. There was no difference in suppression between HC, SZrel, and BPrel subjects with low SPQ scores (≤ 1, n = 23) and those with high scores (≥ 12, n = 22; $t_{(37)} = 0.48$, $p = 0.6$). In contrast, weaker surround modulation has been reported among non-clinical schizotypal subjects (Uhlhaas *et al.*, 2004), which may reflect differences in study sample composition. We did observe significant negative correlations between estimated IQ and perceived contrast changes for all subjects in the Parallel, Gap, and Opposite conditions (Pearson's $r_{(105-107)} < -0.34$, $p < 0.016$, Bonferroni corrected). Subjects with higher IQ showed stronger surround suppression, consistent with a recent study in healthy subjects (Melnick *et al.*, 2013). However, as there was a significant difference in suppression between groups with IQ as a covariate, IQ scores alone cannot account for our observation of diminished surround suppression among SZ and BP subjects.

Finally, we examined whether surround suppression deficits might be attributed to non-visual factors such as off-task performance (e.g., lapses of attention, lack of effort; see Barch *et al.*, 2012, Tibber *et al.*, 2013). We conducted two additional analyses, the first of which compared the standard deviations of perceived contrast measurements for each subject acquired in 4 separate runs. If a particular group had a higher level of off-task performance, then this would lead to less stable estimates of perceived contrast and greater variability across runs. However, variability in perceived contrast measurements did not differ significantly between groups (2-way ANOVA, 5 conditions × 5 groups; $F_{(4,117)} = 0.39$, $p = 0.8$). We also examined psychometric function slopes from the Psi staircase version of our task (see Methods). Greater slope values indicate a more reliable perceptual transition at the point of subjective equality. We expected that greater off-task performance would be associated with smaller (less reliable) slopes. We found no evidence for any difference in slopes across groups (2-way ANOVA, 5 conditions x 5 groups; $F_{(4,52)} = 0.66$, $p = 0.6$). These results are not consistent with group differences in perceived contrast being attributable to off-task performance.

Discussion

The aim of this study was twofold: First, we investigated whether a putative deficit in surround suppression is only evident in SZ or is also observed in BP and unaffected first-degree biological relatives of SZ and BP patients. Second, we examined how such deficits might depend on similarity between target and surrounding stimuli. We observed overall weaker surround suppression among SZ patients, and to a lesser extent those with BP,

compared with their unaffected relatives who showed no difference from HC subjects. The magnitude of deficits among patients did not depend strongly on the configuration of surrounding stimuli. Diminished surround suppression is fairly well documented in SZ, having been observed by a number of groups using different paradigms and stimuli (Dakin *et al.*, 2005, Robol *et al.*, 2013, Schallmo *et al.*, 2013, Seymour *et al.*, 2013, Tadin *et al.*, 2006, Tibber *et al.*, 2013, Yang *et al.*, 2013b, Yoon *et al.*, 2009). Here we have clearly demonstrated that BP patients also show weaker surround suppression (Dakin *et al.*, 2005, Yang *et al.*, 2013a), albeit to a lesser degree than those with SZ. Our results are also the first observation that the magnitude of surround suppression during contrast perception is not tightly linked to genetic liability for SZ or BP, as SZrel and BPrel showed equivalent suppression to HC subjects.

Our results align with a growing literature showing impaired visual context processing in SZ (Butler *et al.*, 2008, Notredame *et al.*, 2014, Phillips and Silverstein, 2013, Yoon *et al.*, 2013). Some of these deficits may be specific to peripheral vision, such as abnormal temporal processing (Chen *et al.*, 2014) and spatial crowding (Kraehenmann *et al.*, 2012, but see Robol *et al.*, 2013). Conversely, weaker surround suppression has been observed in SZ using both foveal (Barch *et al.*, 2012, Dakin *et al.*, 2005, Tadin *et al.*, 2006) and peripheral stimuli (Tibber *et al.*, 2013, Yang *et al.*, 2013b), suggesting a deficit that extends across the visual field. However, a more precise understanding of the neural mechanism(s) underlying weaker suppression in SZ has remained elusive. For example, it is not yet clear to what extent this deficit is selective for similarity (e.g., parallel orientation) between target and surrounding stimuli, as few studies have examined multiple stimulus configurations (Seymour *et al.*, 2013, Yoon *et al.*, 2009).

Overall, we found little evidence to support a specific deficit in suppression for particular surround configurations; no group by condition interaction was observed for changes in perceived contrast, and Contextual Modulation Indices did not vary significantly across groups. The most parsimonious explanation for these results is that SZ patients show a broad deficit in the strength of surround suppression that is not selective for surrounding stimulus features. This proposal contrasts with previous findings showing weaker surround suppression in SZ for parallel but not orthogonal stimuli (Seymour *et al.*, 2013, Yoon *et al.*, 2009). However, those two studies employed larger (2.2 or 3.3° wide) lower spatial frequency (both 1.1 cycles/°) annular gratings that were presented more peripherally (3.3 or 6.2° eccentricity) than our stimuli (1° diameter circular gratings, 2 cycles/°, 2° eccentricity). One might therefore attribute this discrepancy to differences in surround suppression across the visual field. Suppression may be stronger and less selective at greater eccentricities (Xing and Heeger, 2000; but see Williams *et al.*, 2003), which could reflect differences in the relative contribution of selective and non-selective suppression mechanisms (Angelucci and Bressloff, 2006; see below). Variability in the balance between these mechanisms, which could be differentially affected by SZ, may explain why others using more peripheral stimuli have found orientation-specific impairments in SZ (Seymour *et al.*, 2013, Yoon *et al.*, 2009), while the deficit we observed in this study was clearly non-selective.

Beyond reducing surround suppression, SZ may impair overall perception of contrast and/or motion. Specifically, a deficit in magnocellular contrast sensitivity has been proposed

(Butler *et al.*, 2005, Martinez *et al.*, 2012, Martinez *et al.*, 2008), though this has been disputed (Skottun and Skoyles, 2007). Deficits in motion perception observed in SZ (Chen *et al.*, 2005, Chen *et al.*, 2008, Tadin *et al.*, 2006) but not in BP or SZrel (Chen *et al.*, 2005) may also depend on impaired functioning in the magnocellular pathway and/or motion-selective cortical areas such as MT. Reports conflict regarding the effect of surrounding context during motion perception in SZ and BP (Chen *et al.*, 2008, Tadin *et al.*, 2006, Yang *et al.*, 2013a, b). In contrast perception, previous studies examining surround suppression in SZ used static (Dakin *et al.*, 2005, Tibber *et al.*, 2013, Yang *et al.*, 2013b) or contrast-reversing stimuli (Seymour *et al.*, 2013, Yoon *et al.*, 2009), while the current study used drifting target and surround gratings. Thus, motion perception deficits (Tadin *et al.*, 2006) might have enhanced the group differences we observed. Further study is warranted to clarify how specific neural pathways (e.g., magnocellular versus parvocellular) contribute to perceptual surround suppression in both HC and SZ subjects.

Surround suppression is believed to be driven by multiple neural mechanisms whose anatomical substrates include feed-forward, recurrent, lateral, and feedback connections within and between early visual cortical areas (e.g., primary visual cortex, V1; Angelucci and Bressloff, 2006, Nurminen and Angelucci, 2014). Previous work suggests that these separate processes include an early stage that is insensitive to the configuration of surrounding stimuli, and a later stage that is more sharply tuned (Webb *et al.*, 2005). This early stage produces a baseline level of surround suppression, and may operate within the lateral geniculate nucleus of the thalamus (LGN), or the input layers of V1 (Webb *et al.*, 2005). Broadly tuned early suppression may serve as a mechanism for visual gain control (Nurminen and Angelucci, 2014); recent work in SZ has suggested impaired gain control in this disorder (Butler *et al.*, 2008, Dakin *et al.*, 2005, Phillips and Silverstein, 2013). On the other hand, the later stage evokes stronger suppression for more-similar surrounds, consistent with cortical mechanisms that are more strongly selective for visual stimulus features such as orientation. Thus, our observation of weaker suppression among SZ and BP patients across surround configurations appears consistent with a deficit in the putative early stage. This agrees with reduced gain control (Butler *et al.*, 2008, Dakin *et al.*, 2005, Phillips and Silverstein, 2013), and may suggest impaired neural suppression within the LGN or V1.

Abnormal inhibition by the neurotransmitter γ-ammino butyric acid (GABA) has been reported in SZ (Hashimoto *et al.*, 2008, Kelemen *et al.*, 2013, Lewis *et al.*, 2005, Rokem *et al.*, 2011, Yoon *et al.*, 2010). One study measured lower GABA concentrations in visual cortex among SZ versus HC subjects using magnetic resonance spectroscopy, and found lower GABA correlated with weaker surround suppression (Yoon *et al.*, 2010). If surround suppression deficits do indeed depend on GABA, then our results may point to the unique impairment of a particular sub-type of GABA neurons among SZ and BP patients. The role of GABAergic inhibition during surround suppression is not yet fully understood (Ozeki *et al.*, 2009). However, recent work indicates that early- and late-stage suppression may involve different sub-types of GABAergic neurons in V1. The activity of Parvalbumin-positive (PV+) neurons appears consistent with early un-tuned suppression, while Somatostatin-positive (SOM+) inhibition more closely matches the later sharply tuned component described above (Adesnik *et al.*, 2012, Ma *et al.*, 2010). Thus, our observation of

weaker surround suppression across conditions in SZ and BP may suggest a deficit in an early un-tuned suppression mechanism, which may be consistent with impaired PV+ GABAergic functioning. Including a variety of stimulus conditions designed to probe the neural mechanisms underlying surround suppression (Nurminen and Angelucci, 2014) may benefit future studies of the role of GABA in visual abnormalities in SZ.

Dakin and colleagues (2005) reported weaker surround suppression in patients with SZ, but normal suppression among a psychiatric control group, compared with HC. Diagnoses varied among the 13 psychiatric controls in their study, including BP as well as personality disorder, post-traumatic stress disorder, and treatment-resistant mood disorders (the number of subjects with each diagnosis was not provided). Yang and colleagues (2013a) also examined surround suppression among a group of 16 BP patients. They observed suppression that was weaker than in HC but stronger than in SZ, however these group differences were not significant. Studying a larger group of subjects (n = 19) in the current study allowed us to observe a significant deficit in surround suppression among BP subjects that was also significantly attenuated compared to SZ. However, we were not able to examine patients with schizoaffective disorder as a separate group, due to a small sample size (n = 5 following exclusion). Future work may consider whether surround suppression among schizoaffective patients falls on a continuum between SZ and BP.

Reports of impaired visual processing in both SZ and BP are not without precedent; one group found equivalent deficits among SZ and BP subjects in a shine-through Vernier masking task (Chkonia *et al.*, 2012). This differs from other studies showing normal masking in BP (Goghari and Sponheim, 2008, Jahshan *et al.*, 2014, Sponheim *et al.*, 2012), which may reflect differences in Vernier vs. object configuration discrimination. Additionally, in a rapid serial visual presentation task (Jahshan *et al.*, 2014), BP subjects showed better performance than SZ but worse than HC during letter identification at intervals expected to evoke an attentional blink effect. Our observation of a moderate deficit in surround suppression in BP might reflect an impairment in visual context processing shared among patients with SZ and BP (but see also Chen *et al.*, 2005, Kéri *et al.*, 2005).

Previous work has also examined visual processing in unaffected relatives of patients to assess how a genetic risk for mental illness might contribute to task performance (Chkonia *et al.*, 2010, Kéri *et al.*, 2001, Must *et al.*, 2004, Schallmo *et al.*, 2013, Sponheim *et al.*, 2012). We have recently reported normal performance among SZrels during visual contour detection, as well as normal flanker suppression (Schallmo *et al.*, 2013); the current study builds upon this work by showing that context processing among SZrels (and BPrels) is also not impaired during contrast perception. Conversely, studies of backward masking have reported impairments among SZrels (Chkonia *et al.*, 2010, Kéri *et al.*, 2001, Must *et al.*, 2004, Sponheim *et al.*, 2012). A distinction between temporal and spatial masking may explain the discrepancy between our observation of normal surround suppression among relatives and previously reported impairments in backward masking. Normal performance in SZrels and BPrels suggests that deficient surround suppression reflects the clinical expression of these disorders, rather than marking genetic liability.

Acknowledgments

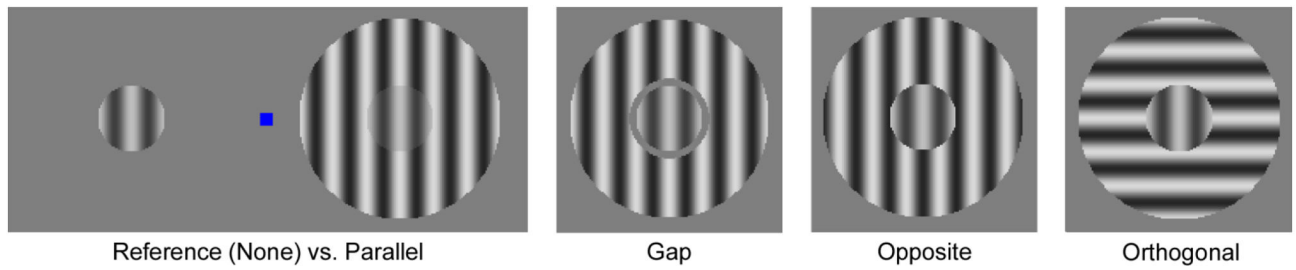## References

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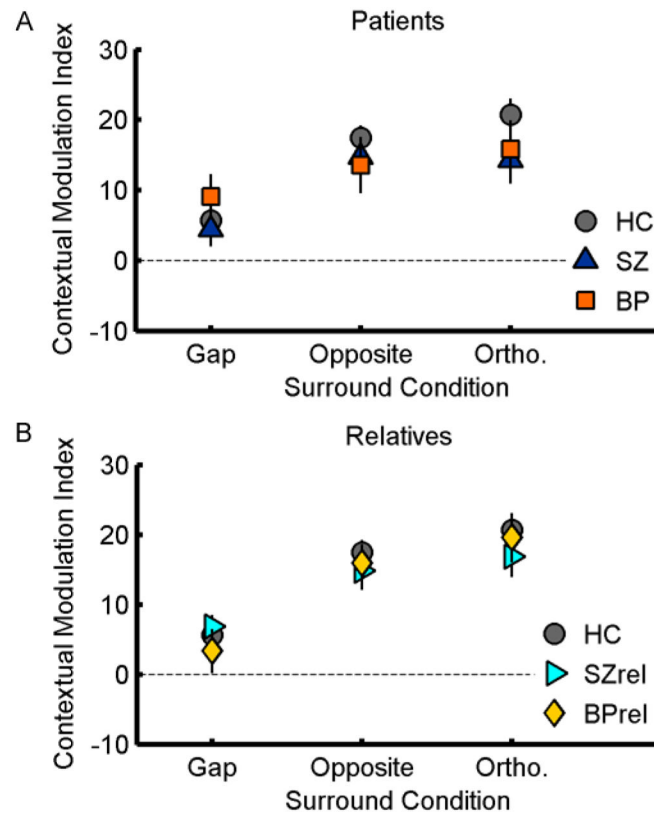
Figure 1.
Surround Suppression Stimuli. Left panel illustrates the stimulus layout, with Reference (left, no surround, identical to the None condition) and Parallel condition stimuli (right) offset horizontally from a blue central fixation square. Target and reference stimuli are shown at 50% contrast, surrounds at 70%.
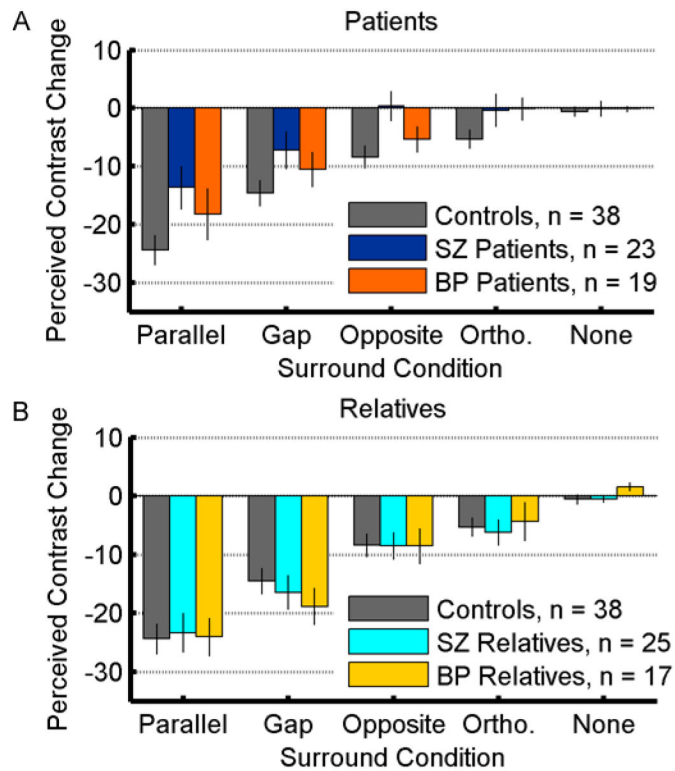
Figure 2.
Surround Suppression Task Results. A) Data from HC, SZ, and BP groups. Surround conditions are shown across the x-axis. Change in perceived contrast relative to the 50% contrast target is plotted on the y-axis; negative values indicate suppression. Error bars show the standard error of the mean (S.E.M.). Across all conditions, suppression is significantly weaker for SZ and BP versus HC, but stronger for BP than SZ. B) Data from HC, SZrel, and BPrel groups.

Figure 3.
Contextual Modulation Indices. Indices were calculated as the difference in perceived contrast between the Parallel condition and each of the three conditions on the x-axis. Error bars show S.E.M.

Table 1

Subject Demographic Information. All data are presented as mean (standard deviation) unless otherwise noted. Data are presented for subjects retained in the final analyses. Bold index labels indicate significant results at α = 0.05.

Index	SZ (n = 23)	SZrel (n = 25)	BP (n = 19)	BPrel (n = 17)	HC (n = 38)	Statistics
Age (years)	45 (9)	44 (11)	44 (11)	41 (14)	44 (12)	$F_{(4,117)} = 0.37, p = 0.8$
Gender (n)						$X^2_{(4)} = 14.4, p = 0.006$
Male	18	8	15	11	23	
Female	5	17	4	6	15	
Education (years)	13.7 (2.0)	14.6 (2.3)	14.2 (1.6)	14.4 (1.3)	15.2 (1.9)	$F_{(4,103)} = 2.11, p = 0.08$
Parents' Education (7-point scale)	5.1 (1.2)	4.5 (1.1)	4.6 (1.2)	4.8 (0.7)	4.6 (1.3)	$F_{(4,113)} = 0.93, p = 0.4$
Estimated IQ*	93 (20)	104 (14)	105 (14)	113 (19)	106 (16)	$F_{(4,104)} = 3.50, p = 0.01$
Overall Symptomatology† (BPRS Total Score)	47 (12)	31 (7)	39 (10)	34 (9)	28 (4)	$F_{(4,116)} = 22.1, p < 0.001$
Schizotypal Characteristics‡ (SPQ Total Score)	35 (17)	7 (7)	24 (16)	16 (14)	7 (7)	$F_{(4,92)} = 19.7, p < 0.001$
Sensory Gating Phenomena§ **(SGI Total Score)**	70 (32)	47 (32)	66 (26)	60 (35)	31 (19)	$F_{(4,91)} = 7.94, p < 0.001$
Negative Symptoms (SANS Total Score)	36 (18)		19 (15)			$F_{(1,40)} = 11.5, p = 0.002$
Positive Symptoms (SAPS Total Score)	26 (23)		10 (14)			$F_{(1,40)} = 6.68, p = 0.01$
CPZ Equivalents	831 (831)		524 (554)			$F_{(1,23)} = 0.89, p = 0.3$
Li Equivalents	636 (580)		700 (301)			$F_{(1,12)} = 0.07, p = 0.7$
Imip. Equivalents	259 (260)		63 (72)			$F_{(1,18)} = 5.80, p = 0.03$

*
IQ scores in SZ were lower than those of BPrel subjects (Tukey's HSD, $p < 0.05$), but no other differences between groups were significant.

†
BPRS scores were significantly higher in SZ than in all other groups. Scores for BP subjects were higher than in HC, but not significantly higher than BPrel.

‡
SPQ scores were significantly higher in SZ and BP than in HC subjects. SZ scores were higher than SZrel, but scores were not significantly different for BP versus BPrel.

§
SGI scores were significantly higher for SZ, BP, and BPrel groups compared with HC, while other between-group differences were not significant.