



Orientation-dependent contextual modulation of contrast in schizophrenia



Victor J. Pokorny ^{a,*}, Scott R. Sponheim ^{a,b,c}, Cheryl A. Olman ^a

^a University of Minnesota, Department of Psychology, United States of America

^b Minneapolis Veterans Affairs Health Care System, United States of America

^c University of Minnesota, Department of Psychiatry and Behavioral Science, United States of America

ARTICLE INFO

Keywords:

Schizophrenia

Context

Vision

Contrast

Orientation

V1

ABSTRACT

Introduction: Schizophrenia is associated with weakened contextual modulation of visual contrast perception, which is generally predicted by population average neural firing rates in primary visual cortex (V1). We use high field fMRI and a novel task to assess V1-intrinsic and V1-extrinsic mechanisms of atypical contextual modulation in schizophrenia.

Methods: We examined the BOLD responses of individuals with schizophrenia (SCZ = 34), bipolar disorder (BP = 25), unaffected first-degree relatives of SCZ (SREL = 20), unaffected first-degree relatives of BP (BPREL = 13) and healthy controls (CON = 23). Participants were presented with near- and far-surrounds oriented at 20° and 70° relative to center gratings.

Results: We observed orientation-dependent modulation of V1 BOLD activation to near-surrounds across groups. In particular, the SCZ and CON groups showed significant orientation-dependent contextual modulation (Cohen's d_z SCZ = 0.56; CON = 0.63). Surprisingly, the direction of the modulation was opposite of predicted: greater BOLD activation for the condition that was expected to produce suppression.

Conclusions: Our results differ from previous reports: we observed successful orientation-dependent modulation of V1 activation in SCZ. Furthermore, our results suggest that spatial attention and figure-ground modulation may play an important role in determining the direction and magnitude of orientation-dependent modulation.

1. Introduction

Suppression of perceived contrast by surrounding context (i.e., surround suppression) is altered in people with schizophrenia (Dakin et al., 2005; Pokorny et al., 2023; Schallmo et al., 2015; Serrano-Pedraza et al., 2014; Seymour et al., 2013; Yoon et al., 2009) and, to a lesser extent, bipolar disorder (Pokorny et al., 2023; Salmela et al., 2021; Schallmo et al., 2015). However, the neural mechanisms of such altered contextual modulation are unknown. In the present manuscript, we examine primary visual cortex (V1) activity as a possible neural mechanism.

Neurons in the primary visual cortex (V1) encode contrast information. The firing rate of a given V1 neuron will generally increase as the contrast within its classical receptive field increases. However, V1 firing rates cannot be explained purely by their classical receptive fields; firing rates are suppressed by features presented in the extra-classical receptive field (Cavanaugh et al., 2002). Such surround suppression at the neural level is thought to explain behavior-level suppression of perceived contrast (Zenger-Landolt and Heeger, 2003).

Within V1, surround suppression is thought to occur via horizontal

inhibitory connections between neurons that have similar orientation preferences, but sample different parts of the visual field (Stettler et al., 2002). Such orientation-dependent suppression at the neural-level can explain the modulation of perceived contrast by surrounds of differing orientations (Self et al., 2014). Previous studies of schizophrenia have provided evidence for weakened orientation-dependent surround suppression (Seymour et al., 2013; Yoon et al., 2009) suggesting alterations in V1-intrinsic horizontal inhibitory connections.

A variety of mechanisms outside of V1 also influence surround suppression. Bair et al. (2003) showed that the propagation rate of suppression throughout V1 is too fast to be mediated purely by V1-intrinsic unmyelinated horizontal connections. Instead, myelinated feedback connections from higher level visual regions (with larger receptive fields) can explain the speed of propagation. Furthermore, global stimulus features encoded by higher level visual regions can dramatically alter suppression effects (Schwartz and Coen-Cagli, 2013). In particular, figure-ground modulation, an effect in which neural firing is stronger for perceived figures relative to perceived backgrounds, likely contributes to many classical surround suppression effects (Self

* Corresponding author at: University of Minnesota, Minneapolis, MN, United States of America.

E-mail address: pokor076@umn.edu (V.J. Pokorny).

et al., 2016).

Visual attention is also known to play an important role in surround suppression: Flevares and Murray (2015) showed that V1 BOLD activation shifted from suppression to enhancement depending on attentional allocation. Characterizing the effects of visual attention on surround suppression is especially important in the context of schizophrenia because the disorder is associated with alterations in visual attention. Indeed, it is possible that previously observed atypical surround suppression in SCZ is driven by altered spatial attention rather than V1-intrinsic mechanisms.

Given the roles of both V1-intrinsic and extrinsic mechanisms of contextual modulation, there is a need to disentangle which mechanisms are altered in schizophrenia. One way to parse these mechanisms is to manipulate the distance between center and surround. Suppression from far-surrounds is mediated by feedback connections from higher visual areas while suppression from near-surrounds is mediated primarily by V1-intrinsic horizontal inhibition (Bair et al., 2003; Shushruth et al., 2013). We used high field fMRI and a novel surround suppression paradigm to isolate V1-intrinsic and extrinsic mechanisms in orientation-dependent contextual modulation. Importantly, our paradigm incorporated an incidental fixation task in which participants attended to a fixation stimulus rather than the peripherally presented center-surround stimuli. This is important because group differences in task engagement and attentional allocation may spuriously suggest group differences in contextual modulation.

We are aware of one other published fMRI study of orientation-dependent contextual modulation in schizophrenia (Seymour et al., 2013). However, this study used orthogonal and parallel surrounds that abutted the target grating which led to strong figure ground cues. We avoided this confound by using non-abutting center-surround configurations with less obvious orientation grouping cues (20° and 70° orientation offsets). Furthermore, the V1-intrinsic suppression observed in the Seymour et al. (2013) task might have been confounded with feature-based attention because the attended fixation was superimposed on a central surround grating. Our task avoids this confound by spatially separating fixation and grating stimuli. Also, the Seymour et al. (2013) study did not include a bipolar group or an unaffected first-degree relative group. Thus, it is unclear whether atypical contextual modulation is specific to schizophrenia or whether it extends to other disorders and first-degree relatives of people with schizophrenia (SREL) or bipolar disorder (BREL). Clarifying specificity will inform whether altered contextual modulation is a clinically useful biomarker of schizophrenia. Furthermore, if first degree relatives also exhibit altered contextual modulation, then the alteration is likely a marker of genetic predisposition rather than a consequence of having the disorder.

The long-term goal of the present work is to identify altered neural circuits in people with schizophrenia (SCZ). Identifying such altered circuits has the potential to inform etiology, diagnosis and treatment of psychotic psychopathology. Surround suppression is particularly promising for this aim because it is well studied in both human and animal models. Furthermore, the primary visual cortex is one of the best understood regions of the human brain, making it a useful model for testing hypotheses about altered cortical circuits. In particular, excitation and inhibition imbalance in the primary visual cortex (which is thought to give rise to altered surround suppression) may generalize to other cortical regions that are more difficult to study. For example, excitation/inhibition imbalance in the prefrontal cortex is hypothesized to mediate higher level cognitive deficits such as working memory impairments in SCZ (Murray et al., 2014). In this way, the visual cortex may provide a window into broader brain dysfunction associated with schizophrenia.

The present study sought to characterize the neural mechanisms of atypical orientation-dependent surround suppression in a trans-diagnostic sample of psychotic psychopathology. We predicted that, across groups, we would observe greater suppression of BOLD responses for surrounds with a 20° relative offset and a release from suppression

for 70° offset surrounds. We also predicted reduced orientation-dependent suppression in SCZ, and intermediate suppression in bipolar disorder (BP), and first-degree relatives, consistent with previously published behavioral results. Finally, we predicted that altered surround suppression would be more evident for near-surrounds than far-surrounds, suggesting altered V1-intrinsic mechanisms.

2. Methods

2.1. Participant Information

Study recruitment practices are detailed in previous work (Longenecker et al., 2021; Pokorny et al., 2020, 2023; Pokorny and Sponheim, 2021; Stevens et al., 2023). Exclusion criteria for SCZ, BP, and healthy controls (CON) included age <18 or >60 , drug/alcohol dependence in the past 6 months, intellectual disability (IQ <70), or any central nervous system condition. Subjects were also excluded for history of electroconvulsive therapy, epilepsy, or severe head injury (e.g. skull fracture, loss of consciousness for >30 min). CON were additionally excluded if they endorsed history of a psychotic disorder, depressive episode, attention-deficit disorder, learning disability, or family history of depression, schizophrenia, or bipolar disorder. First-degree relatives were only excluded for medical conditions that would make study completion difficult. All procedures complied with the ethical standards of the University of Minnesota/Minneapolis VA institutional review boards and the Declaration of Helsinki.

2.2. Near/far orientation-dependent surround suppression task

Task stimuli were projected onto a screen placed inside the scanner bore using an NEC NP4100 projector (1024×768 px) with a 60 Hz refresh rate. Subjects were able to view projected images via a mirror mounted on the head coil. The viewing distance was 112 cm and the display was calibrated such that pixel intensity values (0–255) linearly scaled with luminance (mean luminance 100 cd/m²). The task was run in PsychoPy using an iMac with the MacOS 10.9 operating system.

Participants were instructed to fixate on a white square in the center of the screen and to press a button with their dominant hand when the square became larger (small square subtended 0.2° and large square subtended 0.4°). The size of fixation was randomly selected for each trial with small fixations assigned to 95 % of trials and large fixations assigned to 5 % of trials. Each trial lasted 500 ms and participants had 900 ms to respond following stimulus onset.

Two thin black circles (0.8° diameter) were always present (see Fig. 1). The center of these circles were 3° from the fixation point to the left and right of the vertical meridian (-1° and 1°) and slightly below the horizontal meridian ($-\sqrt{8}^\circ$). For the near condition, the inner and outer radii of the surrounds were 0.4° and 1.4° . For the far condition, the inner and outer radii of the surrounds were 2.5° and 5° . Far-surrounds were cropped at the horizontal meridian to prevent overlap (see Fig. 1). Both centers and surrounds were composed of sinusoidally luminance-modulated gratings with a spatial frequency of 2 cycles per degree and luminance contrast of 80 %.

There were four center-surround conditions (Near 20° , Near 70° , Far 20° and Far 70°) and a rest condition. For the Near 20° and Near 70° conditions, the orientation of the near-surround and center were offset 20° and 70° , respectively. The Far 20° and Far 70° conditions were identical to the near-surround conditions except the surround was larger, further away from the center and cropped along the vertical meridian to avoid overlapping of left and right surrounds (see Fig. 1). Conditions were presented in 12 s blocks. Within a given block the relative orientation offset between center and surround was consistent, but the absolute orientation of the center was drawn randomly for each trial. Trial duration was 1.5 s (i.e. 8 trials per block). For the rest condition, only the fixation square and black circles were present. The order of the blocks was determined by an m-sequence (Buracas and Boynton,

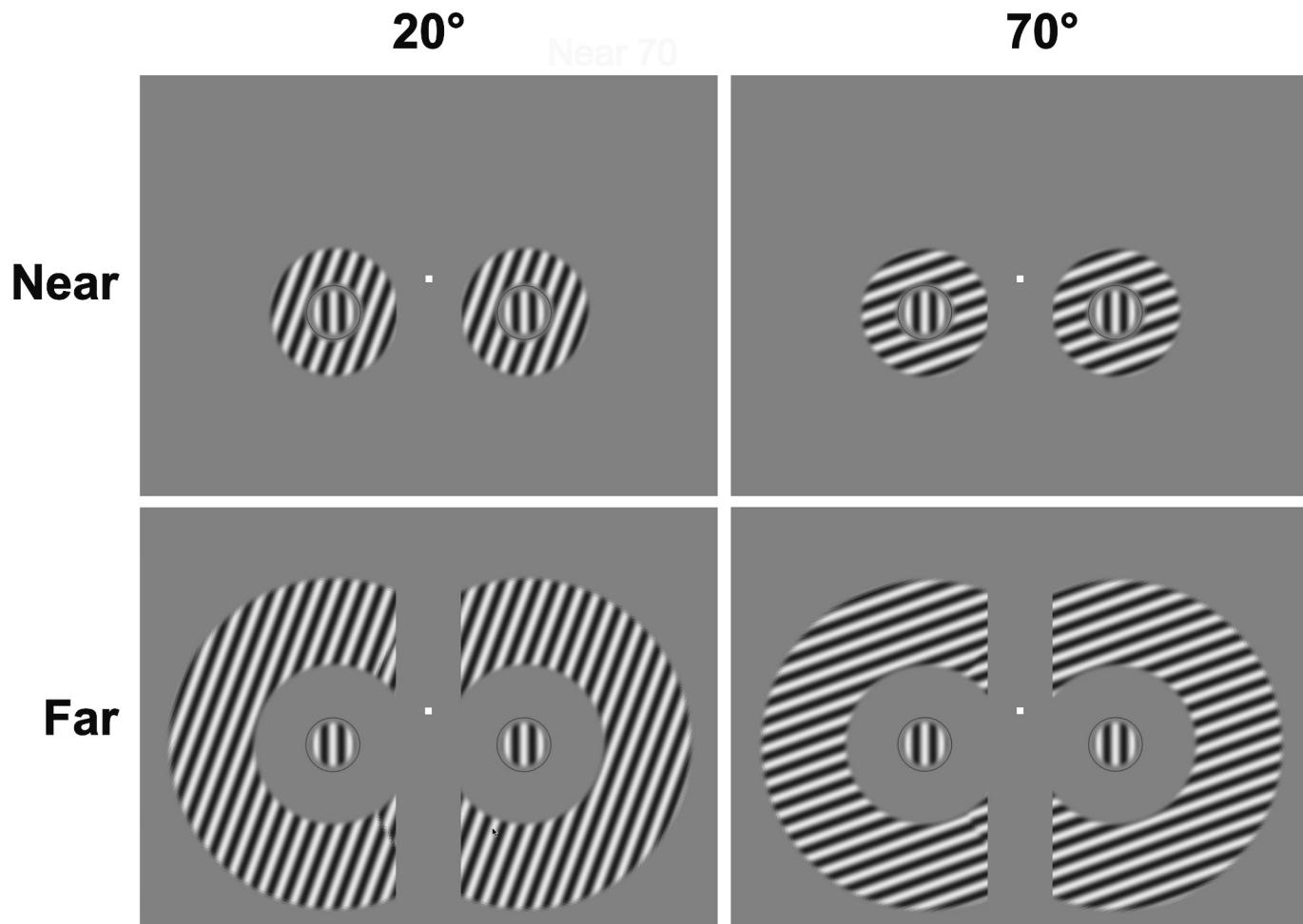


Fig. 1. Task stimulus examples. The task consisted of four center-surround conditions. Top left: Near 20°. Top Right: Near 70°. Bottom Left: Far 20°. Bottom Right: Far 70°. Not shown: rest condition in which only the fixation and thin black rings were present. Participants attended to the central fixation square and pressed a button when the fixation doubled in size.

2002). A single task run consisted of 24 condition blocks. The majority of participants ($n = 107$) completed two runs of the task; 8 did not complete the second run due to scanning time constraints. We included these 8 subjects in subsequent analyses; however whether they were included or not did not substantially change the results (see supplemental materials).

Prior to the task scan, participants completed a localizer scan to identify individualized V1 center regions of interest (ROIs). The localizer consisted of two alternating conditions: center only, and near-surround only. One localizer run consisted of 17 blocks (12 s block duration) and all participants completed a single run. All other aspects of the localizer were identical to the task.

2.3. MRI collection and processing

Images were collected on a 3 T Siemens Prisma system using a 32-channel head coil. We acquired T1-weighted anatomical volumes using magnetization-prepared rapid acquisition gradient echo (MPRAGE) with 1-mm isotropic resolution, collected sagittally. We then collected whole-brain EPI (echo-planar imaging) data with a 208 mm field-of-view and an 88 by 88 matrix size. Thus, the in-plane resolution was 2.36 mm isotropic. We collected 60 pseudo-axial (rotated toward coronal 20°) slices with an anterior-posterior phase encode direction, ensuring whole brain coverage. Slices were acquired using a multiband factor of 3 and the slice thickness was 2.4 mm. The repetition time (TR) was 1.5 s and the flip angle was 75°. Echo time (TE) was 30 ms, echo

spacing was 0.54 ms, and the total slice read-out time was 47 ms. Eye position was not monitored during the scanning session; however, the fixation task encouraged participants to keep their eyes on the center of the screen.

We removed thermal noise from all scans using the noise reduction with distribution corrected (NORDIC) PCA approach (Vizioli et al., 2021). All other preprocessing was performed using the Analysis of Functional NeuroImages (AFNI) software (21). We performed motion correction using AFNI's 3dvolreg with each scan's initial EPI as reference. Data were unwarped (3dQwarp) using a reverse phase-encoded EPI. For subject-level general linear models (GLMs), TRs for which motion was >0.3 mm were removed. All subjects retained >60 % of their total TRs.

2.4. Analysis

V1 ROIs were identified by visually inspecting localizer scans and identifying a central vertex in the patch of voxels that responded more strongly to the central disk (see Fig. 2). Voxels contained within a 5 mm spherical radius of this central vertex were defined as V1 ROI voxels. The majority of individuals ($n = 90$) had identifiable V1 ROIs in both hemispheres. There were 10 individuals with identifiable ROIs in only one hemisphere and 16 individuals with no identifiable ROIs. We also conducted whole brain group-level GLMs to identify ROIs outside of V1 that significantly modulated as a function of task manipulations (see supplemental materials for more information).

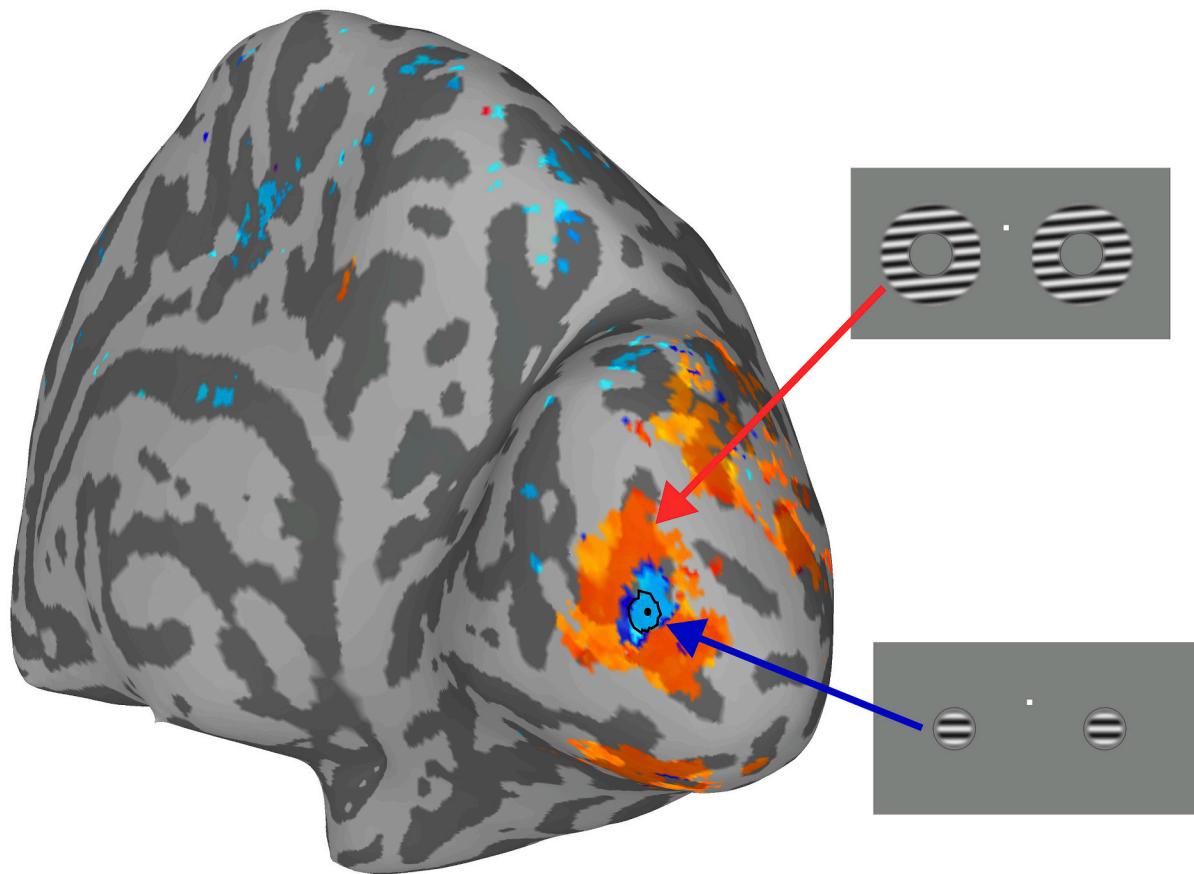
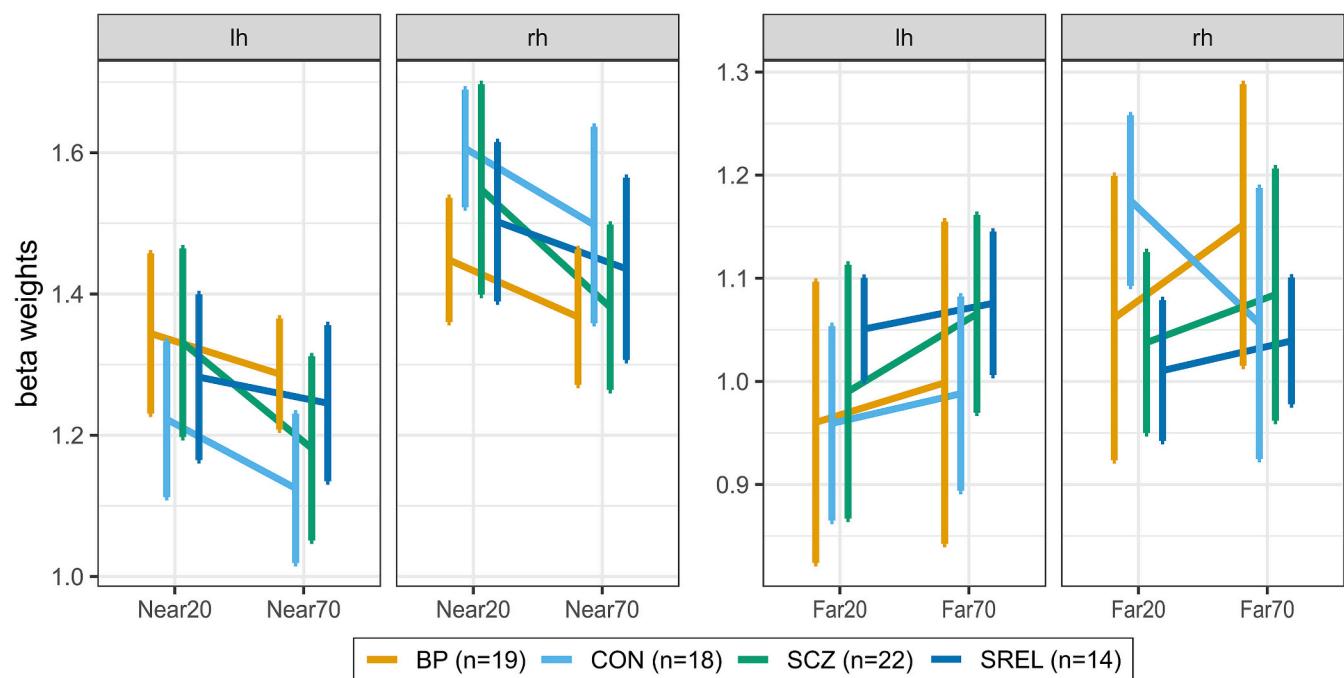
A.**B.**

Fig. 2. V1 BOLD responses. Panel A: Right hemisphere localizer activations for an example subject. Blue corresponds to increased activation for center gratings, while red corresponds to increased activation for surround gratings. Black dot denotes the central vertex of the center ROI and the black line around it is the 5 mm spherical ROI projected onto surface space. Panel B: Task activations to retinotopically localized V1 regions for center gratings by condition, group and hemisphere. Right and left hemispheres are denoted as rh and lh, respectively. Error bars represent within-subject standard errors of the mean. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Statistical analyses were conducted in R (R Core Team, 2023). Using the afex package (Singmann et al., 2023), we conducted separate repeated measures ANOVAs (rmANOVAs) for near-surround conditions and far-surround conditions with orientation and hemisphere as within-subject factors, group as a between subjects factor and gender as a covariate. Note: we conducted two separate rmANOVAs rather than a single rmANOVA with an additional within-subject factor of “surround distance” because we were not confident in the validity of directly comparing BOLD activations for near and far conditions. In particular, non-specific blood flow effects are likely to differently impact BOLD responses for near relative to far surrounds. Thus, any differences in BOLD activation between near and far surround conditions reflects a mixture of genuine surround suppression and non-specific blood flow. This is also why we did not include a center-only condition in the task: non-specific blood flow effects are confounded with genuine suppressive effects when comparing center-surround responses to center-only responses (see supplemental materials for more information). To measure the degree of orientation modulation, we computed Cohen's d_z effect sizes as the mean difference score divided by the standard deviation of the difference scores. Finally, we used the Rmisc package to compute within-subject error bars for plotting purposes (Hope, 2022).

2.5. Data quality exclusions

A total of 115 individuals completed the NF-ODSS fMRI task (SCZ = 34, BP = 25, CON = 23, SREL = 20, BPREL = 13). Of these 115, we excluded one BP who had zero recorded button presses. We also excluded individuals without identifiable V1 localizer activations in either hemisphere (SCZ = 8, BP = 2, CON = 2, SREL = 2, BPREL = 2). Finally, we excluded individuals with negative V1 BOLD activations for more than four conditions (SCZ = 6, BP = 5, CON = 5, SREL = 2, BPREL = 2). Given the small number of BPREL after exclusions, we did not include their data in categorical analyses, but we did include their data in correlational analyses.

3. Results

3.1. Demographic, clinical & behavioral measures

Participant demographic, clinical and behavioral information are presented in Table 1. SCZ had a larger proportion of men than the other groups. Age and visual acuity (LogMAR) did not significantly differ between groups. Years of education and IQ significantly differed between groups with CON having the highest values and SCZ having the lowest values. SCZ had higher CPZ equivalent dosages than BP. BPRS and SPQ scores were indicative of a spectrum of psychopathology with SCZ having the highest scores, BP the next highest, and relative groups scoring lower than patient groups, but higher than CON.

3.2. V1 results

We observed a strong effect of near-surround orientation on V1 activity ($F(1,64) = 13.91, p < 0.001, \eta^2 = 0.179$). Surprisingly, V1 activation was larger for the condition that we expected to produce more suppression (see Fig. 2). We did not observe a significant main effect of group ($F(3,64) = 0.34, p = 0.8, \eta^2 = 0.016$) nor group by orientation interaction ($F(3,64) = 0.78, p = 0.51, \eta^2 = 0.035$). Cohen's d_z effect sizes (Near 20°-Near 70°) were as follows: SCZ = 0.56, BP = 0.38, CON = 0.63, and SREL = 0.44. Additionally, we observed a significant effect of laterality in which right hemisphere activations tended to be larger than left hemisphere activations ($F(1,64) = 5.05, p = 0.03, \eta^2 = 0.073$).

We did not observe a significant effect of far-surround orientation on V1 activity ($F(1,64) = 0.86, p = 0.36, \eta^2 = 0.013$). We did not observe a main effect of group ($F(3,64) = 0.97, p = 0.41, \eta^2 = 0.043$) or group by condition interaction ($F(3,64) = 0.69, p = 0.56, \eta^2 = 0.031$). Cohen's d_z effect sizes for Far 20° vs. Far 70° within each group were as follows:

Table 1
Demographic and symptom severity.

	SCZ (n = 22)	BP (n = 19)	SREL (n = 17)	BPREL (n = 10)	CON (n = 18)	Statistic
% Women	23 %	53 %	71 %	50 %	56 %	X ² (4) = 9.66, p = 0.05
Age	43.86 (11.05)	46.16 (9.84)	46.65 (9.64)	44.6 (9.73)	46.61 (10.27)	F(4,81) = 0.29, p = 0.89
LogMAR	0.11 (0.12)	0.12 (0.1)	0.12 (0.12)	0.07 (0.09)	0.09 (0.14)	F(4,81) = 0.48, p = 0.75
Years	13.73 (1.7)	15.11 (2.64)	15 (1.97)	15.6 (1.65)	16 (1.24)	F(4,81) = 3.89, p = 0.01
Education						
IQ	100.36 (13.91)	102.47 (13.5)	111.35 (17.65)	105.9 (20.25)	112.83 (12.01)	F(4,81) = 2.47, p = 0.05
CPZ Equivalent	9.72 (17.79)	1.1 (1.28)				F(1,39) = 4.43, p = 0.04
BPRS Total	42.23 (10.49)	36.53 (8.13)	29.71 (5.61)	30.4 (4.67)	25.28 (1.6)	F(4,81) = 16.26, p < 0.001
SPQ Total	39.79 (20.02)	23.63 (15)	15.71 (10.14)	15.5 (11.21)	6.75 (5.86)	F(4,76) = 14.17, p < 0.001

LogMAR: normal is 0.0, better than normal is <0. IQ was estimated using the Block Design and Vocabulary subtests of the Wechsler Adult Intelligence Scale, Third Edition.

SCZ = -0.29, BP = -0.34, CON = 0.15, SREL = -0.1. We also did not observe a difference between the left and right hemispheres ($F(1,64) = 0.41, p = 0.53, \eta^2 = 0.006$).

3.3. Group GLM results

We conducted group-level mass univariate *t*-tests for three contrasts: “Near 20°-Near 70°”, “Far 20°-Far 70°” and “All Conditions-Rest”. We did not observe any significant clusters of activation for the “Near 20°-Near 70°” or “Far 20°-Far 70°” contrasts. This suggests these task conditions were well-matched for higher level cognitive processes. For the “All Conditions-Rest” contrast, we observed four significant clusters of activation (see Fig. 3). The first was a large bilateral positive cluster over the occipital cortex representing general visual responses. The remaining three clusters appeared to represent different nodes of the default mode network: bilateral precuneus, right middle frontal cortex and right temporoparietal cortex. We did not observe any group differences in the deactivation of these clusters.

3.4. Correlational results

We ran mass bivariate correlations between brain variables, symptom ratings, visual acuity, and estimated IQ (see Fig. 4). Across all groups, we observed two interesting associations between neural and symptom variables: greater contextual modulation for near surrounds was associated with greater BPRS total scores and BPRS positive scores. However, these associations did not remain significant after correction for multiple comparisons (see Supplemental Table 1) and should be regarded as exploratory.

We also examined correlations within the psychotic psychopathology groups only (i.e., SCZ and BP). We observed significant correlations between occipital activation and clinical variables: weaker occipital activations were associated with greater BPRS total, BPRS disorganized, SPQ Total, SPQ Cognitive Perceptual, SPQ Interpersonal and SPQ Disorganized scores. This suggests that individuals with greater

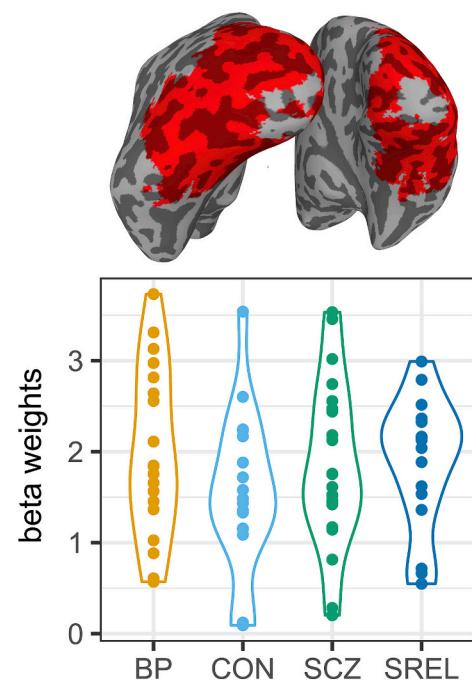
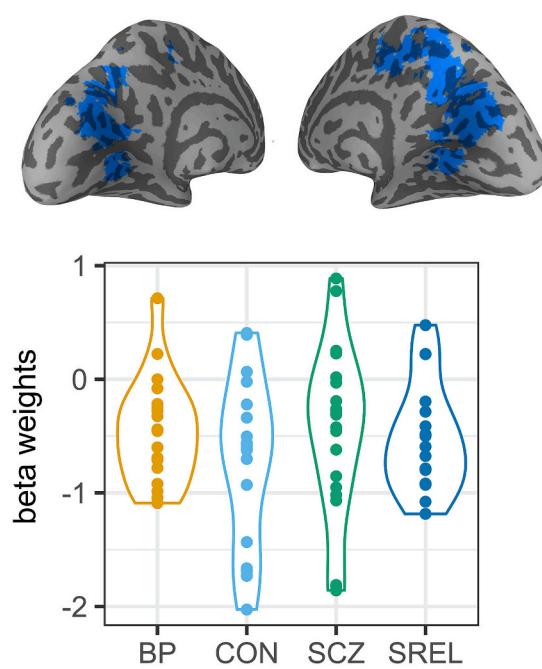
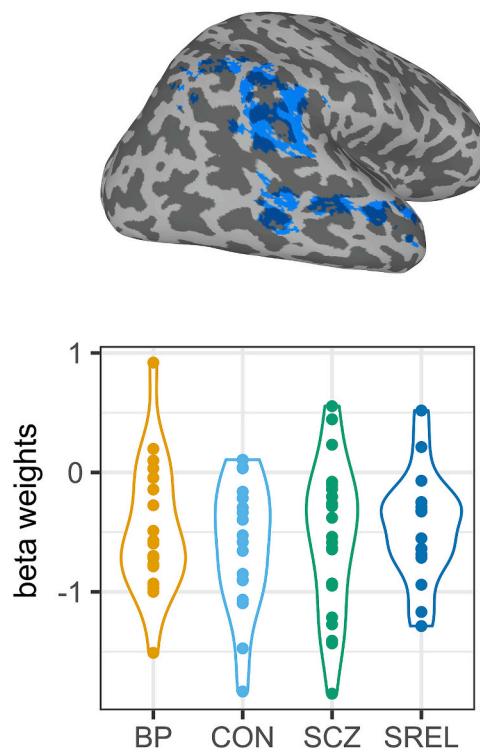
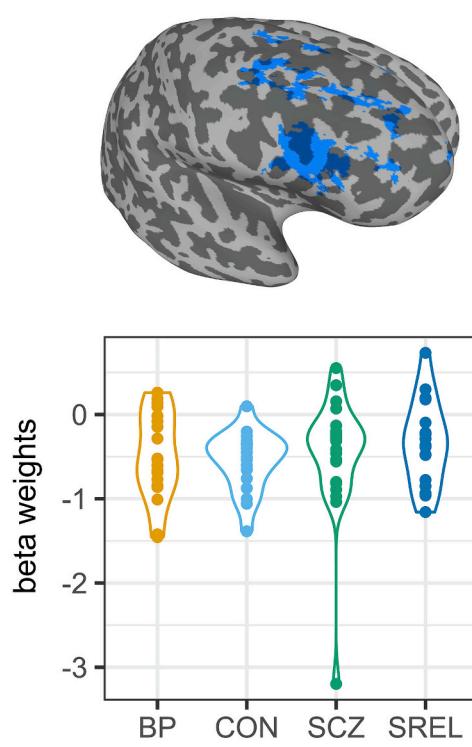
Bilateral Occipital**Bilateral Precuneus****Right Parietotemporal****Right Frontal**

Fig. 3. Group GLM all stimuli clusters. Top left: Occipital cluster of voxels that generally increased when center-surround stimuli were presented. Top right, bottom left and bottom right: clusters of voxels that decreased activation when center-surround stimuli were presented. The three negative clusters likely reflect deactivation of the default mode network. No significant differences between groups were observed for any of these clusters.

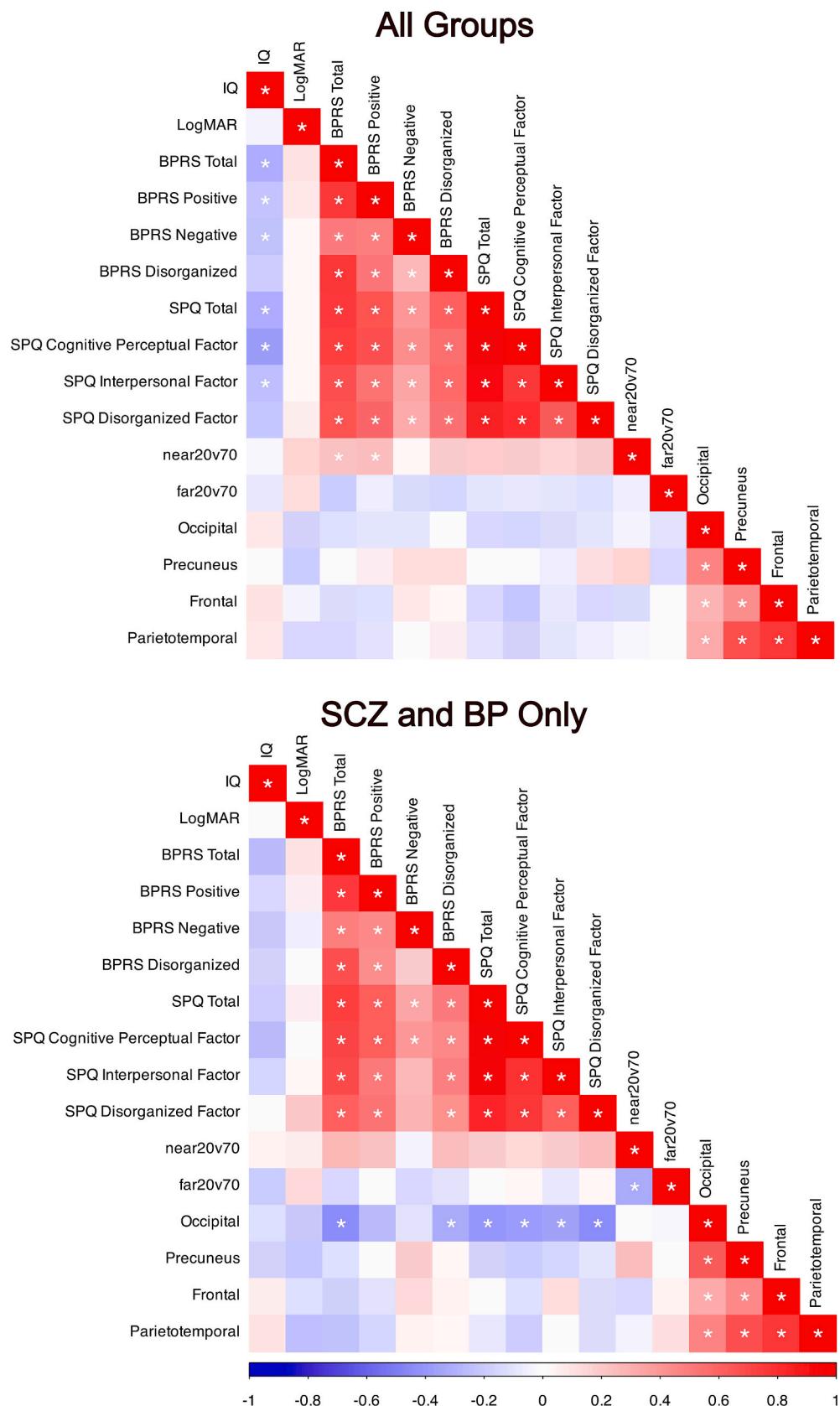


Fig. 4. Correlations between symptoms, brain variables, IQ and visual acuity. White asterisks denote significance at $p < 0.05$ without correction for multiple comparisons. near20v70 and far20vs70 denote subtraction indices for Near 20°-Near70° and Far 20°-Far 70°, respectively. Occipital, precuneus, parietal and frontal refer to the clusters of activations shown in Fig. 3.

psychiatric symptom severity and more prominent schizotypal traits had generally less strong visual responses to center-surround gratings. Again, however, the significance of these associations did not survive correction for multiple comparisons (see Supplemental Table 1).

4. Discussion

The present study sought to clarify the neural mechanisms of altered surround suppression in psychotic psychopathology. With respect to surround suppression of primary visual cortex (V1), we uncovered two surprising findings. First, we observed a significant increase in V1 activation for the condition that we hypothesized would decrease activation (i.e. greater activation for Near 20° relative to Near 70°). Second, we observed intact orientation-dependent modulation for near-surrounds in the schizophrenia group. In what follows, we attempt to reconcile our findings with previous work.¹

4.1. Contextual suppression vs. enhancement

We observed increased V1 activation for near-surrounds with a 20° orientation offset compared to 70° near-surrounds. Schallmo et al. (2016) and Seymour et al. (2013) reported on similar orientation-dependent suppression paradigms and observed decreased V1 activation for parallel surrounds relative to orthogonal surrounds. Our task did not include parallel and orthogonal conditions; however, previous work has demonstrated a monotonic decrease in suppression with increasing relative orientation (DeAngelis et al., 1994; Shushruth et al., 2013; Sil-lito et al., 1995). Thus, we expected the 20° surrounds to produce stronger suppression than the 70° surrounds. The data did not conform to this expectation. This result may be explainable in terms of figure-ground modulation. The present task was designed to reduce the influence of figure-ground modulation via segmentation cues: centers did not abut surrounds, and black circles separated center from surround. Furthermore, 20° and 70° conditions have less clear grouping cues than parallel and orthogonal gratings. Together these features likely reduced the perception of center gratings as figures and surround gratings as background. Therefore, this result suggests that previously measured suppression of V1 BOLD responses by parallel surrounds may be driven by figure-ground modulation rather than surround suppression.

The unexpected direction of V1 modulation that we observed can be explained by spatial attention. Flevares and Murray (2015) found that V1 BOLD activation for parallel and orthogonal flankers shifted from suppression to enhancement depending on whether individuals attended to the center or flanker grating. In the paradigm used by Seymour et al. (2013), the fixation was superimposed on a central flanking grating while in our paradigm, participants were neither attending to the center nor the surround. Thus, differences in fixation placement relative to grating stimulus placement could also explain the enhancement we observed.

4.2. Orientation-dependent modulation in schizophrenia

SCZ modulated V1 responses between Near 20° and Near 70° nearly as strongly as healthy controls (SCZ Cohen's $d_z = 0.57$, CON Cohen's $d_z = 0.62$). This pattern is opposite of that reported by Seymour et al., 2013 in which the control group exhibited significantly greater orientation-dependent surround suppression as compared to a schizophrenia group. Again, however, our task differed in important ways from the Seymour task, as detailed in the previous paragraph. Thus, it is possible that the apparent differences in orientation-dependent suppression observed by Seymour et al. were reflective of differences in figure-

ground modulation and/or spatial attention mechanisms.

In addition to the fMRI data reported here, we collected behavioral data from this sample in a separate session (Pokorny et al., 2023). We observed significantly weakened orientation-independent surround suppression in SCZ, but did not observe strong evidence of weakened orientation-dependent suppression. Thus, our finding of orientation-dependent modulation of V1 activation is consistent with these behavioral results. However, the direction of the modulation is not consistent. For example, we observed greater behavioral suppression for the Near 20° condition relative to Near 70°, but less BOLD suppression for the Near 20° condition relative to Near 70°. However, deployment of spatial attention differed between the behavioral and fMRI tasks: the behavioral task required participants to attend to both left and right centers and make judgements about which center had higher contrast. This may explain the opposing directions of the observed contextual modulation.

One limitation of the present work is that we did not track eye movements during the scanning session. However, the presence of identifiable V1 ROIs in the independent localizer scan as well as the lack of group differences in performance on the fixation task provide some evidence that SCZ were able to adequately fixate throughout the task.

4.3. Contextual modulation of near- vs far-surrounds

We observed significant contextual modulation of V1 responses by near-surrounds, but not by far-surrounds. Notably, we observed this same pattern in the psychophysical data collected from this sample (Pokorny et al., 2023). This lack of suppression by far-surrounds may be due to the cropping of the far surrounds along the vertical meridian (see supplemental materials for more information). Previous work has shown robust suppression using cropped far surrounds (Shushruth et al., 2013); however, the extent of the cropping in our stimuli was greater than this previous work. Thus, it is possible that this more severe cropping was responsible for the lack of suppression we observed for far surrounds.

4.4. Higher level brain regions

We attempted to characterize ROIs outside of the primary visual cortex that significantly modulated as a function of task conditions. For “Near 20°-Near 70°” and “Far 20°-Far 70°” contrasts, we did not observe any significant clusters of activation across the brain. This suggests that these conditions were well-matched for features that might activate higher level-brain regions. We also assessed general activation of brain regions to all center-surround conditions (i.e. Near 20°, Near 70°, Far 20°, and Far 70°). We observed three clusters of activation that appeared to reflect different nodes of the default mode network. We did not observe significant differences between groups which suggests that task engagement was relatively uniform across groups. Furthermore, these higher-level clusters of activation overlapped substantially with brain regions associated with visual attention such as the intraparietal sulcus and frontal eye fields (Parks and Madden, 2013). The lack of group differences in the activation of these clusters suggest that allocation of spatial attention did not significantly differ between groups.

4.5. Conclusion

The present study attempted to identify neural mechanisms of altered surround suppression in psychotic psychopathology. Surprisingly, we observed significant contextual modulation of visual cortex responses in SCZ. This suggests that the lateral inhibitory and feedback mechanisms necessary for successful orientation-dependent contextual modulation were not strongly altered in our sample of individuals with schizophrenia. This result is inconsistent with the excitation/inhibition imbalance theory of schizophrenia. Our unexpected results also highlight the profound influences of spatial attention and figure-ground modulation on surround suppression. Further basic visual neuroscience research is needed to disentangle such influences. As a result,

¹ We also observed a surprising hemispheric asymmetry effect, but have relegated discussion of this effect to the supplemental materials due to word count constraints.

clinical studies may become more informative with respect to the pathophysiology of schizophrenia.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.schres.2024.10.021>.

Role of the funding source

Funding sources were not involved in design, analysis or drafting of the present manuscript.

CRediT authorship contribution statement

Victor J. Pokorny: Writing – original draft, Visualization, Formal analysis. **Scott R. Sponheim:** Writing – review & editing, Supervision, Resources, Investigation, Funding acquisition, Data curation. **Cheryl A. Olman:** Writing – review & editing, Visualization, Supervision, Methodology, Formal analysis, Conceptualization.

Declaration of competing interest

None.

Acknowledgments

This work was funded by VA Merit Grant I01CX000227; NIH R01MH112583 and NIH U01MH108150. Andrea N. Grant assisted with developing stimulus presentation code. The following research assistants helped collect data: Joseph Lupo, Haven Hafar, Abraham Van Voorhis, and Collin Teich.

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