Stronger tilt aftereffects in persons with schizophrenia

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Abstract

Symptoms of schizophrenia have been explained as a failure to appropriately apply past environmental regularities to the interpretation of incoming sensory information, thus leading to abnormal perceptions and beliefs. Here we use the visual system as a test bed for investigating how prior experience shapes perception in individuals with schizophrenia. Specifically, we use visual aftereffects, illusory percepts resulting from prior exposure to visual input, to measure the influence of prior events on current processing. At a neural level, visual aftereffects arise due to attenuation in the responses of neurons that code the features of the prior stimulus (neuronal adaptation) and subsequent disinhibition of neurons signaling activity at the opposite end of the feature dimension. In the current study, we measured tilt aftereffects and negative afterimages, two types of aftereffects that reflect, respectively, adaptation of cortical orientation-coding neurons and adaptation of subcortical and retinal luminance-coding cells in persons with schizophrenia (PSZ; $n=36$) and demographically-matched healthy controls (HC; $n=22$). We observed stronger tilt aftereffects in PSZ compared to HC, but no difference in negative afterimages. Stronger tilt aftereffects were related to more severe negative symptoms. These data suggest over-sensitivity to recent regularities at cortical, but not subcortical, levels in schizophrenia, which is in line with a growing literature that predictive processes in schizophrenia are altered at multiple cortical levels. More broadly, the results underscore the value of aftereffect paradigms as a tool for the quantitative examination of canonical computations whose dysfunction may underpin symptom genesis in schizophrenia.

Keywords: schizophrenia, visual perception, aftereffects, predictive coding, adaptation

Introduction

Schizophrenia—characterized by vivid hallucinations and rigid delusions, disorganized thinking, and profound social, cognitive, and motivational deficits—is often considered among the most debilitating of mental health conditions. Even with currently-available pharmacological and behavioral interventions, individuals are often left with residual symptoms, functional impairments, and decreased quality of life. Comprehensive, explanatory mechanistic frameworks for schizophrenia symptoms hold tremendous promise for guiding treatment development. One such framework posits that symptoms of schizophrenia arise due to an abnormality in forming or using stored regularities to make predictions in order to infer the causes of sensory input. This abnormality is argued to lead to the misinterpretation of sensory information and over-interpretation of meaningless associations that characterize the positive syndrome of schizophrenia (Fletcher & Frith, 2009; Gray, Feldon, Rawlings, Hemsley, & Smith, 1991; Hemsley, 2005; Sterzer et al., 2018). In addition, although speculative, noisy and unreliable sensory data may also lead to the amotivation characteristic of the negative syndrome (Demmin, Davis, Roche, & Silverstein, 2018; Fletcher & Frith, 2009; Keri, Kiss, Kelemen, Benedek, & Janka, 2005). The so-called predictive processing framework that centers on the abnormal use of regularities unites several levels of explanation—linking diverse clinical phenomenology with cognitive and computational processes and the neurobiological mechanisms that underlie them. More specifically, prediction abnormalities are formalized within a Bayesian inference model (Friston, 2005) and can be implemented at the level of hierarchical brain systems and local neural circuits (Bastos et al., 2012; Kanai, Komura, Shipp, & Friston, 2015), as well as neuromodulatory systems (Moran et al., 2013). Although this framework provides a compelling canonical and biologically plausible perspective from which to understand schizophrenia, empirical data remains scant.

The visual system can serve as a unique model system within which to understand the role of experience in how individuals perceive and interpret the world as our constructed internal model of the world, formed by acquired knowledge, informs our current visual perception (Barlow, 1990; Clifford, Wenderoth, & Spehar, 2000; Knill & Richards, 1996). More specifically, visual aftereffects reflect and provide a quantitative measure of the role of prior experience in ongoing visual processing. Visual aftereffects occur after prolonged viewing of a visual stimulus and are the illusory perception of ‘the opposite’ of the initial stimulus (e.g., opposite direction of motion, complementary color, etc.; see **Figure 1** for a demonstration). Aftereffects range from the basic—for example, color and orientation—to the more complex, for example, involving facial identity. They are caused by adaptation of neurons in the visual brain that are tuned to particular features. For example, the tilt aftereffect that appears after prolonged viewing of a grating of a particular orientation arises due to adaptation (i.e., attenuation of the firing rate) of neurons responsive to the orientation of that adapter stimulus, and subsequent disinhibition of neurons that signal components of the feature dimension (e.g., orientation) away from those of the current stimulus (**Figure 2**). Aftereffects and the neuronal adaptation that underpins them reflect a fundamental assumption about temporal regularities in the environment—that one’s current experience is a reliable predictor of future experience (Kohn, 2007). In this way, altered visual aftereffects in schizophrenia can be considered within a predictive processing framework.

Visual aftereffects can provide a computationally and biologically-informed behavioral assay of predictive processing abnormalities in schizophrenia for several reasons. First, aftereffects have been explained using formal mathematical models and thus behavioral findings can be interpreted within the context of these models’ parameters. Second, different aftereffects reflect neuronal adaptation at different levels of the visual processing hierarchy, from the retina up to higher order integration areas, and thus can reveal at what level of a sensory hierarchy altered

predictive processing in psychosis is emerging. Third, visual aftereffects likely arise due to transient changes in the strength of lateral inhibitory interactions between local processing units (Bednar & Miikkulainen, 2000; Tolhurst & Thompson, 1975) and, in this way, visual aftereffects are sensitive to an imbalance between neuronal excitation and inhibition in local circuits. Finally, there are known neuromodulatory influences on visual aftereffect strength: dopamine antagonists reduce aftereffect strength in healthy observers (Harris, Gelbtuch, & Phillipson, 1986; Harris, Phillipson, Watkins, & Whelpton, 1983).

An older body of work—conducted largely before 1970—is suggestive of altered visual aftereffects in schizophrenia. As we recently reviewed (Thakkar, Silverstein, & Brascamp, 2019), however, there are significant sources of variability across studies and methodological issues related to experimental design and clinical characterization that preclude conclusive interpretation of these aftereffect findings in schizophrenia. Our goal in the current study was to use rigorous psychophysical paradigms and comprehensive and current clinical characterization to investigate putative differences in aftereffect strength in individuals in schizophrenia and to explore correlations with clinical symptom severity.

We measured two types of visual aftereffects: negative afterimages and tilt aftereffects. Negative afterimages occur after prolonged viewing of a stationary pattern (adapter stimulus). Subsequent presentation of a blank field (test stimulus) can result in the illusion of the ‘photo negative’ of the adapter stimulus in the retinal location that was exposed to that adapter pattern (**Figure 1**). These negative afterimages result from adaptation of luminance-coding neurons in the retina and subcortical visual areas during exposure to the initial pattern (H. Li et al., 2017; Zaidi, 2012). Tilt aftereffects occur after prolonged viewing of, for instance, a slightly tilted grating pattern (adapter stimulus). A subsequently presented vertically-oriented grating pattern

(test stimulus) will appear to be tilted in the opposite direction from the first pattern. This so-called tilt aftereffect (Gibson & Radner, 1937; Wenderoth & Johnstone, 1987) is thought to arise from adaptation of orientation-selective spatial filters in early visual cortex (Clifford, 2002).

Aside from forming a measure of predictive processing, tilt aftereffects can also provide an index of so-called orientation tuning width (defined below). Put another way, in interpreting tilt aftereffect strength in terms of predictive processing, one has to rule out explanations in terms of orientation tuning width. This is relevant because previous studies suggest broader orientation tuning in schizophrenia (Robol et al., 2013; Rokem et al., 2011; Silverstein, Demmin, & Bednar, 2017). The reasoning that ties tuning curve widths to tilt aftereffects is as follows. The measured strength of tilt aftereffects is dependent on the difference in tilt between the adapter stimulus and test stimulus. The more similar the test stimulus is to the adapter stimulus, the greater influence the adapter will have on the perception of the test stimulus (i.e. the stronger the measured tilt aftereffect). This is because of orientation tuning properties of visually-responsive neurons: those neurons respond most vigorously to a particular orientation and decrease in their firing rate to presentation of stimulus orientations that are further from that preferred orientation. More neuronal adaptation accumulates for neurons that are sensitive to orientations nearer to that of the adapter, whereas neurons that are tuned to an orientation that is far removed from the adapter orientation will adapt weakly if at all (Schwartz, Hsu, & Dayan, 2007). The implication here is that broader orientation tuning in schizophrenia could conceivably lead to a different aftereffect strength, depending on the measurement parameters (i.e. the orientation difference between adapter and test). We thus manipulated these parameters in our paradigm in order to distinguish whether putatively altered tilt aftereffects would be best explained by broader orientation tuning curves or by altered neuronal adaptation based on

previous regularities. Specific hypothesized outcomes under these two potential scenarios are detailed in **Figure 3**.

Our primary question in the current study was whether there are alterations in aftereffect strength in individuals with schizophrenia, and, if so, whether the alterations in neural adaptation that putatively underlie visual aftereffect differences is primarily cortical or subcortical in nature, or both. Given prior work (reviewed in Thakkar, Silverstein, et al., 2019), we hypothesized that aftereffects of cortical origin (i.e. tilt aftereffects) would be stronger in persons with schizophrenia; investigation of negative afterimages was exploratory. We additionally hypothesized that putative alterations in visual aftereffect strength would be related to severity of clinical symptoms, given altered predictive processing as a purported mechanism of positive symptom, and possibly negative symptom, genesis. Our secondary exploratory question was whether putative alterations in tilt aftereffect strength could be explained by differences in tuning curve widths in schizophrenia. As visual aftereffects are a manifestation of the visual system incorporating information about past events and past states of the visual system into its current processing, findings from the current study have the potential to shed further light on the nature of predictive processing abnormalities in schizophrenia.

Methods and Materials

Participants

36 persons with schizophrenia or schizoaffective disorder (PSZ) and 22 healthy controls (HC) were recruited from outpatient mental health facilities and via community advertisements.

Demographic characteristics are presented in **Table 1**. Diagnoses were based on results of the NetSCID (Brodey et al., 2016), an electronic version of the Structured Clinical Interview

for *DSM-5* Axis I disorders, and material from medical records and collateral informants, when available. Final diagnosis was reached at a consensus conference with study staff. 31 PSZ were taking antipsychotic medication, and many PSZ were also medicated with antidepressants, anxiolytics, mood stabilizers, or a combination thereof (*Supplemental Table 1*). Chlorpromazine (CPZ) equivalent dosages of antipsychotic medication were calculated for each patient (Andreasen, Pressler, Nopoulos, Miller, & Ho, 2010).

Clinical symptoms were assessed with the Brief Psychiatric Rating Scale (BPRS; Overall & Gorham, 1962), Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), and Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1983). IQ was measured with the Wechsler Test for Adult Reading (WTAR; Wechsler, 2001). Handedness was assessed using the Modified Edinburgh Handedness Inventory (Oldfield, 1971).

Exclusion criteria included meeting *DSM-5* criteria for moderate or severe substance use disorder within the previous six months, history of neurological disorders, history of head injury with loss of consciousness >10 minutes, and vision that was not normal or corrected-to-normal. HC were excluded if they had a personal history of *DSM-5* Axis-I disorders or family history of schizophrenia spectrum disorders or bipolar disorder. A handful of participants were excluded from analyses based on task performance (see *Supplemental Methods* for performance exclusion criteria). Groups were matched for age, gender, and handedness. All subjects gave written informed consent approved by the Michigan State University Institutional Review Board and were paid.

Apparatus and stimulus presentation

Participants were seated in a dimly lit room, their head stabilized 59 cm away from a computer screen. Stimuli were presented on a 20" CRT monitor (spatial resolution: 1280x1024

pixels, vertical refresh rate: 85 Hz). Eye position was recorded to ensure fixation using an Eyelink 1000 (SR Research, Canada). Manual responses were recorded with a keyboard. Stimulus presentation and response collection were controlled with Python using PsychoPy (Peirce et al., 2019).

Experimental paradigms and procedure

Participants completed a negative afterimage and tilt aftereffect paradigm, the order of which was counterbalanced across participants. Participants were instructed to keep their gaze fixated at the center of the display throughout each trial. Both experiments were preceded by a practice session, which was repeated until it was clear that the participant understood the task.

Negative afterimage

The negative afterimage task is presented in **Figure 4A**, and full paradigm details are presented in the *Supplemental Methods*. On each trial the subject was presented with a blurry disk, with one bright half and one dark half for 1.5 seconds (adapter stimulus). We used a so-called nulling method to measure the strength of the negative afterimage. The *nuller stimulus* was a 'photo negative' of the afterimage (in other words, a low-contrast version of the adapter stimulus) that was presented for 0.5 seconds immediately following the adapter stimulus. Participants were asked to indicate which part of the nuller appeared brightest, with perception of this nuller being formed by the illusory negative afterimage superimposed on the physically present nuller stimulus. If the nuller is strong enough to overpower the afterimage, then the participant typically reports seeing a pattern that is consistent with the nuller stimulus--light where the nuller is light, and dark where it is dark. Alternatively, if the nuller is not strong enough to counteract the afterimage, then the participant will see a pattern that is of opposite contrast polarity to the nuller

stimulus, that is light and dark where the afterimage is light and dark. The strength (luminance contrast) of the nuller is varied across trials, and the goal of the nulling procedure is to find the nuller strength at which the nuller cancels out the afterimage (i.e. at which the participant provides either response equally often). This nuller strength was taken as an index of afterimage strength (Brascamp, van Boxtel, Knapen, & Blake, 2010; Georgeson & Turner, 1985; Leguire & Blake, 1982). Practically, this is quantified as the 50% point on the psychometric curve fitted to responses plotted against the strength of the nuller (see *Quantifying Aftereffects* section below). A third image followed the nuller and masked any lingering afterimage; it remained on screen until the response. Participants were instructed to select the area in which the nuller image appeared brightest using a mouse click. Their response was followed by a 1-second pause, a gaze drift correction procedure, and then another 3-second inter-trial interval. In order to minimize the possibility of participants accidentally reporting their perception of the adapter stimulus rather than the nuller stimulus, we slightly modified the conventional nulling method (described in the *Supplemental Methods*) in which the nuller is simply the photo negative of the afterimage. This modification leaves our experimental method identical in rationale and interpretation.

Tilt aftereffect paradigm

The tilt adaptation task is depicted in **Figure 4B** (see *Supplemental Methods* for full paradigm details). On each trial a flashing grating tilted at 20 degrees from vertical—the adapter stimulus—was presented for 2 s. Analogous to the negative afterimage task, tilt aftereffect strength was quantified using a nulling procedure. In this paradigm, the nuller stimulus was a second grating tilted at various degrees from vertical from trial to trial. Participants indicated whether the nuller appeared to be tilted leftward or rightward from vertical. Tilt aftereffect strength was then quantified as the degree of physical tilt away from vertical, in the direction of

the adapter's tilt, that is required for the participant to perceive it as vertical reach a subjective sense of vertical, again corresponding to the 50% point of the psychometric curve plotting responses against nuller strength (here, tilt); see *Quantifying Aftereffects* section below). The nuller lasted 0.4 s and was separated from the adapter by a 0.3 s blank. Then, a circle with two lines originating from the center, one oriented rightward and the other oriented leftward, was presented, and the participant was instructed to indicate whether the nuller appeared to be oriented leftward or rightward by making a mouse click on the corresponding line. Their response was followed by a 0.5 s pause, a gaze drift correction procedure, and a 4 s inter-trial interval. After this the next adapter stimulus appeared.

To investigate whether putatively altered tilt aftereffects in schizophrenia may be secondary to wider orientation tuning curves (rationale outlined in **Figure 3**), the trials described above—which we refer to as ‘near’ trials—were interleaved with ‘far’ trials. These far trials were the same as in the near condition with one exception: the adapter stimulus was tilted at a much steeper angle (65 degrees from vertical). In healthy individuals, adaptation at this steep of an angle has little influence on the perception of near-vertical orientations (Schwartz et al., 2007). However, with wider orientation tuning curves, adaptation to these steep angles may be expected to exert an effect on the perception of near-vertical orientations. Should PSZ have wider tuning curves, we may expect stronger aftereffects when measured at these far angles.

Data analysis

Quantifying aftereffects

For both negative afterimage and tilt aftereffect paradigms (and for both near and far adapter-nuller separations in the latter case), we calculated the proportion of trials in which the participant's perceptual report was consistent with the nuller (i.e. the proportion of trials where

the nuller “beat” the aftereffect); this was done for each nuller strength. For each participant the relationship between this proportion and the nuller strength was fitted with a cumulative Gaussian function with three free parameters: mean, standard deviation and ‘lapse rate’. Lapse rate indicates the proportion of trials in which the participant makes a response error regardless of the clarity of their perception. A lapse rate of 0 indicates that the functions spans the full range between proportions of 0 and 1; otherwise, its vertical range is scaled down. The fitted mean parameter corresponds to the nuller strength at which both response options are selected equally often, and it served as our estimate of aftereffect strength. For the tilt aftereffect paradigm, we fit the data from the near and far conditions separately.

To ensure data quality, we applied several previously employed data exclusion criteria, (Brascamp, Becker, & Hambrick, 2018; Thakkar, Antinori, Carter, & Brascamp, 2019), which are detailed in the *Supplemental Methods*. 3 PSZ and 1 HC were excluded from the negative afterimage analysis (leaving a total sample of 33 PSZ and 21 HC), and 6 PSZ and 1 HC were excluded from the tilt aftereffect analysis (leaving a total sample of 30 PSZ and 21 HC).

Controlling for the effect of eye movements

As there is some degree of spatial selectivity in aftereffects, breaks in fixation would be expected to yield weaker aftereffects. Thus, for participants for whom we had usable eye data for that particular task, we repeated the quantification of aftereffect strength as described above after removing trials in which the participant’s gaze deviated more than 2.5 degrees of visual angle during the adapter stimulus (Knapen, Rolfs, Wexler, & Cavanagh, 2010) or in which more than 25% of the samples were missing (i.e. due to blinks, head movements, recording errors, etc.). Of those participants with usable behavioral data, eye movement data were either partially

or completely missing from 3 PSZ and 2 HC in the negative afterimage paradigm and from 4 PSZ and 3 HC in the tilt aftereffects paradigm.

Statistical analyses

First, to test for the presence of significant aftereffects, the magnitude of negative afterimages and tilt aftereffects (in both the near and far adapter-nuller deviation conditions) were compared to 0 using a one sample t-test. Negative afterimage strength was compared between PSZ and HC using independent samples t-tests. Mixed model ANOVAs were used to examine tilt aftereffect strength, with group included as a between-subjects factor and condition (near, far) included as a within-subjects factor. The above analyses were repeated after removing trials based on eye gaze data. Spearman's rho (r_s) was computed to evaluate correlations between negative afterimage strength, tilt aftereffect strength in both the near and far conditions and both positive and negative symptoms and CPZ equivalent antipsychotic doses. The alpha level for correlations between aftereffect strength and symptoms was Bonferroni-corrected to $0.05/6=0.008$.

Results

Negative afterimages

Results are depicted in **Figure 5**. Robust negative afterimages were observed in both HC ($t(20)=20.6$, $p<0.0001$, $d= 4.5$ (95% CI [3.0 5.9])) and PSZ ($t(32)=14.8$, $p<0.0001$, $d= 2.6$ (95% CI [1.9 3.3])). However, there was no difference in negative afterimage strength between groups ($t(52)=1.0$, $p=0.32$, $d=0.3$ (95% CI [-0.3 0.8])).

Tilt aftereffects

Results are depicted in **Figure 6**. Robust tilt aftereffects were observed in both HC ($t(20)=6.6$, $p<0.0001$, $d=1.4$ (95% CI [0.8 2.1])) and PSZ ($t(29)=12.1$, $p<0.0001$, $d=2.2$ (95% CI [1.5 2.9])) in the near condition. Neither group showed a significant tilt aftereffect in the far condition (HC: ($t(20)=1.3$, $p=0.22$, $d=-0.3$ (95% CI [-0.7 0.2])); PSZ: $t(29)=1.3$, $p=0.20$, $d=0.2$ (95% CI [-0.1 0.6])), consistent with findings from non-clinical samples that adaptation to particular tilted grating has little influence on the perception of a stimulus that is tilted at a much different angle than the adapter (Schwartz et al., 2007). A mixed model ANOVA on tilt aftereffect strength revealed significant main effects of both condition ($F(1,49)=102.7$, $p<0.0001$, $\eta^2=0.7$ (95% C.I. [0.5 0.8])) and group ($F(1,49)=10.5$, $p=0.002$, $\eta^2=0.2$ (95% CI [0.0 0.4])). Tilt aftereffects were larger in the near condition, and PSZ had significantly stronger tilt aftereffects than HC. There was no significant group-by-condition interaction ($F(1,49)=1.0$, $p=0.32$, $\eta^2=0.02$ (95% C.I. [0.0 0.1])). We take this lack of a significant interaction as evidence that differences in tilt aftereffect strength cannot be explained by broader tuning curves; otherwise, we would have specifically expected larger aftereffects in PSZ compared to HC in the far condition and perhaps even the opposite difference in the near condition (see **Figure 3B**), resulting in a significant group-by-condition interaction. On the other hand, a lack of group-by-condition interaction indicates that differences in tilt aftereffect strength between PSZ and HC are not significantly larger in the near compared with the far condition, thus suggesting that stronger tilt aftereffects occur alongside marginally broader orientation tuning curves.

Correlations with clinical symptoms and medication

Correlations are presented in **Figure 6**. Stronger tilt aftereffects in the near condition only (where significant tilt aftereffects were observed in both groups) were related to more severe

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negative symptoms ($p=0.50$, uncorrected- $p=0.005$), even after stringent Bonferroni-correction for the number of correlation analyses. There were no other relationships between clinical symptoms and aftereffect strength, nor any relationships with normalized medication dose (all r_s 's < 0.34 , all uncorrected- p 's > 0.13).

Controlling for eye movements

Analyses controlling for gaze deviations during the presentation of the adapter stimulus are presented in the *Supplemental Results*. The above-reported group differences in aftereffect strength were replicated even when using stringent gaze deviation criteria to exclude individual trials.

Discussion

In the current study, we observed stronger tilt aftereffects, but no difference in negative afterimages, in individuals with schizophrenia. Although data were suggestive of broader orientation tuning curves in individuals with schizophrenia, consistent with previous studies (Rokem et al., 2011), differences in tuning curve width did not explain group differences in tilt aftereffect strength. Attesting to their clinical relevance, stronger tilt aftereffects were related to more severe negative symptoms, but only in the experimental condition in which significant aftereffects were observed to begin with. These data corroborate findings that hinted at stronger aftereffects for orientation and motion in schizophrenia (reviewed in Thakkar, Silverstein, et al., 2019), and circumvent methodological confounds present in those early studies. In the following sections, we consider mechanistic interpretations of these findings and relate these data to comprehensive computational and pathophysiological accounts of the illness. Furthermore, we consider these findings in relation to other visual abnormalities in

schizophrenia, highlight their limitations, and conclude by speculating upon their clinical relevance.

These findings may suggest a difference in neuronal adaptability of specific populations in individuals with schizophrenia. Different types of visual aftereffects arise from adaptation in neuronal populations that differ in their selectivity to visual input. Tilt aftereffects emerge primarily from dynamic interactions between orientation-tuned neurons in visual cortex (Clifford, 2002), while negative afterimages are based largely in adaptation of retinal and subcortical neurons (Craik, 1940; H. Li et al., 2017; Zaidi, 2012). At the level of local microcircuits, single neurons that are tuned to particular dimensions of visual input interact through both excitatory and inhibitory connections (Z. Li, 1998), and aftereffects have been theorized to arise due to short-term changes in the strength of lateral inhibitory interactions between these neurons (Bednar & Miikkulainen, 2000). Thus, one mechanistic interpretation of our findings of stronger tilt aftereffects and equivalent negative afterimages is that individuals with schizophrenia have altered cortical, but not retinal or subcortical, neuronal adaptation, potentially driven by more dynamic updating of lateral interaction strength. Such altered interactions between local processing units in visual cortex is consistent with a prominent pathophysiological account of schizophrenia, which proposes a central imbalance in cortical excitation and inhibition (E/I imbalance) as a result of NMDA receptor hypofunction (Anticevic & Lisman, 2017). Altered excitatory and inhibitory dynamics in visual cortex of PSZ is supported by behavioral work (Barch et al., 2012; Dakin, Carlin, & Hemsley, 2005; Schallmo, Sponheim, & Olman, 2015; Serrano-Pedraza et al., 2014; Tadin et al., 2006a; Tibber et al., 2013; Yang et al., 2013; Yoon et al., 2009) and magnetic resonance spectroscopy (Thakkar et al., 2017; Yoon et al., 2010). Findings from the current study are furthermore consistent with data suggesting a predominantly

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cortical origin of predictive coding impairments in schizophrenia and visual dysfunction more generally (reviewed in Silverstein, 2016).

Within a predictive processing framework, stronger tilt aftereffects may be interpreted as an abnormality in the way individuals with schizophrenia are making or utilizing predictions about the future based on past input. Bayesian observer accounts of tilt aftereffects may provide a nuanced computational perspective here (Chopin & Mamassian, 2012; Stocker & Simoncelli, 2005). According to one such account (Stocker & Simoncelli, 2005) exposure to a tilted grating may have two simultaneous and, in a sense, opposite effects. On the one hand, prolonged exposure to that stimulus causes the system to direct more processing resources toward features (i.e. orientation) that are present in that adapting stimulus. This tendency would relate to the posited functional role of neuronal adaptation, which is to adjust sensory systems' limited resources to optimally process prevalent inputs—in the case of the visual system, to see best what it sees most. In the context of the Bayesian observer account, it is this reallocation of processing resources that leads to the system interpreting new stimuli that do not match the adapting stimulus as being more different from it than they actually are: the repulsive effect observed in tilt aftereffect experiments. The basic idea is this: the increased allocation of processing resources to the features of the adapting stimulus (e.g. to left-tilted orientations) leads to a particularly reliable signal in response to such features. As a consequence, a neural signal that indicates *different* features (e.g. one that indicates a vertical orientation) is particularly unlikely to have originated from a stimulus with the features of the adapting stimulus (e.g. one with a left-tilted orientation), and this leads to an interpretation of the sensory data (in Bayesian terms, a likelihood function) that is biased away from those adapting features. In this context, the increased tilt aftereffect strength we observe in schizophrenia patients could correspond to an increased readiness to reallocate processing resources to those inputs that

were encountered in the recent past. The same Bayesian account, however, also stipulates a second effect of the adapting stimulus, namely a shift in the system's prior expectations toward the adapting features: a growing expectation that newly encountered stimuli will have those features, too. This shift in expectation (in Bayesian terms, the system's prior) would, to some extent, counteract the repulsive effect that is observed in the tilt aftereffect, and diminish its strength. Under this view, then, a second interpretation of increased tilt aftereffect strength in schizophrenia could be a reduction in this shift in prior expectation. One interesting observation is that both simultaneous effects—the reallocation of processing resources on the one hand and the shift in, or updating of prior expectation on the other—can be considered adjustments of neural processing in response to prior input, but that an interpretation of our data in terms of these two effects would lead to an opposite conclusion in each case. Specifically, increased tilt aftereffect strength is consistent with an increase in the readiness to reallocate processing resources, but also with a reduction in the readiness to adjust expectations.

This idea of two oppositely-acting components to history-dependent updating may also be helpful in framing the wider literature investigating the influence of history and knowledge on visual processing in schizophrenia, which is rife with mixed findings. On the one hand there are findings suggesting of a weaker top-down influence on perception. Studies using the hollow mask illusion provide a notable example. Here, a concave face is perceived to be convex due to the powerful influence of prior knowledge that faces are convex (Gregory, 1997). Individuals with schizophrenia, particularly those in more acute illness phases, are more immune to this illusion (Keane, Silverstein, Wang, & Papathomas, 2013; Schneider et al., 2002). In addition, individuals with schizophrenia show diminished modulation of brain responses in a way that suggests they are less sensitive to repetition and the temporal regularities of events—findings which include reduced sensory gating (Judd, McAdams, Budnick, & Braff, 1992; McGhie &

Chapman, 1961), reduced mismatch negativity (Naatanen & Kahkonen, 2009), and reduced suppression of the fMRI BOLD response with repeated exposure to an object (Lee et al., 2019). Other data, however, point to a *larger* top-down influence on perception. For example, previous exposure to an image confers better discrimination of a degraded version of that same image presented later, and individuals prone to psychosis show an even greater reliance on that prior information (Davies, Teufel, & Fletcher, 2018; Teufel et al., 2015). Furthermore, the degree to which experimentally induced beliefs affect the perception of an ambiguous stimulus was found to relate to positive symptoms in schizophrenia (Schmack, Rothkirch, Priller, & Sterzer, 2017). Corlett and colleagues (2019) attempted to reconcile such apparently contradictory results by considering *when and where* predictions are formed along a sensory hierarchy, positing that weaker priors at earlier stages of a hierarchy might lead to greater reliance on more complex priors from later stages in the hierarchy to help structure the input. The Bayesian account discussed above (Stocker & Simoncelli, 2005) also hints at potential reconciliations that center on a distinction between changes in resource allocation (related to the likelihood function in a Bayesian context) and changes in expectation (related to the prior).

In interpreting these findings, we must consider potential confounds—the most obvious being medication. However, antipsychotic medication likely does not explain our findings. In healthy observers, antipsychotics *reduce* the strength of tilt aftereffects (Harris et al., 1986; Harris et al., 1983)—we observed the opposite. Furthermore, antipsychotic dose did not correlate with aftereffect strength in our sample. Findings in non-clinical samples may provide further insights into a potential role of medication. In an undergraduate sample, we found that the strength of tilt aftereffects, but not negative afterimages, was related to schizotypal traits (Thakkar, Antinori, et al., 2019). However, the direction of that relationship was opposite to what the current findings would predict; increased schizophrenia-like traits were associated with weaker tilt aftereffects.

Although these findings in healthy individuals may seem at odds with the current findings, we must consider the restricted range and minimal levels of schizotypal traits in that sample as well as the compensatory and homeostatic neural processes that likely occur in response to core disturbances associated with schizophrenia—all of which muddy a direct comparison. A further potential confound is perceived stimulus contrast. Individuals in the chronic stage of schizophrenia, which would characterize the majority of our sample, have reduced contrast sensitivity (e.g. Butler et al., 2005; e.g. Slaghuis, 1998). In healthy individuals, both negative afterimages and tilt aftereffects become weaker as the physical contrast of the adapter stimulus decreases (Georgeson & Turner, 1985; Parker, 1972) raising the question of whether group differences in contrast sensitivity might be related to the current findings. Our pattern of results and previous findings in the literature would suggest that stronger tilt aftereffects are not secondary to altered contrast sensitivity (see *Supplemental Discussion*). It may well be, however, that common properties of early visual processing in schizophrenia produce both altered contrast sensitivity and altered tilt aftereffect strength, but more work is needed to understand the nature of these properties.

The observed correlation between tilt aftereffect strength (in the near condition in which significant tilt aftereffects were observed) and negative symptoms attests to the clinical relevance of these findings. Predictive processing accounts of schizophrenia have typically focused on the positive symptoms of the illness; however, the observed correlation with negative symptoms is not without precedent. The strength of context in the spatial domain (i.e. surround suppression) has been associated with negative symptoms (Robol et al., 2013; Tadin et al., 2006b; Yang et al., 2013). More generally, these findings are consistent with a set of findings that may be broadly construed as increased attentional perseveration in the chronic stage of schizophrenia when negative symptoms would be expected to be more prominent. For

example, individuals with severe negative symptoms are more resistant to conditioning to a stimulus that was previously uninformative (Cohen et al., 2004), suggesting an undue influence of history on learning. These data can also be viewed as in line with a recent proposal of attentional hyper-focusing in individuals with chronic schizophrenia, whereby they have an abnormally narrow and intense focusing of attentional resources—which may then drive stronger aftereffects (Luck, Hahn, Leonard, & Gold, 2019).

The association between tilt aftereffect strength and negative symptoms also highlights the inherent heterogeneity of schizophrenia. It is possible that stronger tilt aftereffects are only present in chronically-ill individuals with predominant negative symptom presentation. Indeed, the observed over-reliance on past history in shaping current perception in schizophrenia may develop over time and in response to disruptions present earlier in the illness or during acute psychosis. Future studies in individuals across illness stages and with more diverse symptom severities will be an important area of future study.

To conclude, a wealth of findings suggest that the reading of information is tuned differently to prior experience in schizophrenia, which may provide a compelling cognitive and mechanistic explanation for clinical phenomenology. Clearly, however, the story is not as simple as more or less history dependence. There are likely a multitude of task and illness-related factors that bear on experimental findings. Visual aftereffect paradigms may provide a tool with which to systematically address these considerations. As an example, the degree to which perception is shaped by past experience may depend on the duration of that past experience. The effect of very recent history may be amplified in schizophrenia, relative to controls (Salzinger, 1984), whereas the effect of more remote history may be attenuated. This can be tested in the context of aftereffect paradigms by varying the adapter duration, as aftereffects become stronger with

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longer adapter durations in healthy observers (Harris & Calvert, 1989) . If indeed the influence of recent experience is amplified at the expense of remote experience in schizophrenia, one testable prediction is that individuals with schizophrenia would have stronger tilt aftereffects at short adapter durations relative to controls, but weaker tilt aftereffects at longer adapter durations. Furthermore, as different aftereffects reflect neuronal adaptation at different levels of the visual processing hierarchy, using a battery of different aftereffect paradigms across illness stages may reveal at what level of a sensory hierarchy altered predictive processing in psychosis is emerging across development of the illness. In short, visual aftereffect paradigms provide behavioral assays that may prove useful in illness detection and monitoring, as well as refine predictive processing accounts of schizophrenia.

Table 1. Demographic characteristics of the patient and control groups.

	HC (n=22) Mean (s.d.)	PSZ (n=36) Mean (s.d.)	Statistic	p
Age	36.4 (10.3)	37.8 (10.2)	t = 0.51	0.61
Gender	11 F / 11 M	16 F / 20 M	ϕ = 0.17	0.79
IQ	109.2 (7.8)	99.6 (11.9)	t = 3.21	0.002
Education (yrs)	17.1 (2.4)	13.6 (2.2)	t = 5.69	<0.0001
Handedness	69.5 (37.3)	49.3 (53.9)	t = 1.54	0.14
Years of Illness		12.7 (9.4)		
CPZ Equivalent		349.9 (360.9)		
BPRS		46.3 (12.0)		
SAPS		22.1 (16.3)		
SANS		34.4 (21.0)		

Figure Legends

Figure 1. Negative afterimage. Stare at the crosshair for 20 seconds, then look at a blank wall. You should perceive the inverse of this image, which is an example of a visual aftereffect. This figure is reproduced from Thakkar, Silverstein, et al. (2019).

Figure 2. Schematic of single neuron implementing visual aftereffects (tilt, in this case). The response of a neuron that responds to the adapter stimulus (leftward grating) is depicted as a function of stimulus presentation. Upon presentation of a left oriented grating, the neuron responds vigorously, but soon begins to attenuate its firing rate (i.e. adapt) with repeated presentation. Upon the onset of a blank screen, the neuron returns to a below-baseline level of firing. Because orientation perception depends on the aggregation of responses across neurons with many orientation preferences, this reduced firing for the adapted neurons results in the perceptual phenomenon of a rightward bias in the perception of stimulus orientation (i.e. aftereffect). This figure is adapted from Thakkar, Silverstein, et al. (2019).

Figure 3. Hypothesized tilt aftereffect findings in PSZ (orange lines) compared to HC (grey lines). Neuronal adaptation is stronger in neurons that are sensitive to orientations nearer to that of the adapter (labeled near on the x-axis), and neurons that are tuned to an orientation that is far removed from the adapter orientation will adapt weakly if at all (labeled far on the x-axis). That means that when the adapter orientation and the nuller orientation are similar, aftereffects will be strong, in contrast to when they are far apart. Thus, we expect that in both groups, tilt aftereffects in the near condition will be stronger than in the far condition. Aftereffect strength

will also depend on the width of tuning curves (i.e. how selective orientation-tuned neurons are to a particular orientation). If putative group differences in aftereffects are due to true amplitude differences, then we would expect that individuals with schizophrenia would show weaker or stronger tilt aftereffect strength in the near condition, but make no prediction about the far condition (A). However, if putative differences in tilt aftereffect strength in schizophrenia was due to wider tuning curves, we would expect that tilt aftereffects would be stronger in PSZ than HC in the far condition, but expect weaker or equal aftereffect strength in PSZ in the near condition (B).

Figure 4. Task figures of the negative afterimage (A) and tilt aftereffect (B) paradigms. See main text and *Supplemental Methods* for details.

Figure 5. Negative afterimage results. The main panel depicts the proportion of trials on which the observer reported perception that was consistent with the nuller (i.e. the proportion of trials where the nuller outweighed the aftereffect) plotted against the strength of the nuller stimulus. Curves for individual participants are depicted in thin lines and curves fit to the average data for each group separately are depicted in thick lines. The inset depicts the average 50% point for each group, which represents aftereffect strength. Error bars represent 95% confidence intervals.

Figure 6. Tilt aftereffect findings for PSZ and HC in the near (A) and far (B) conditions. The main panel depicts the proportion of trials on which the observer reported perception that was consistent with the nuller (i.e. the proportion of trials where the nuller outweighed the aftereffect) plotted against the strength of the nuller stimulus. Curves for individual lines are depicted in thin lines and curves fit to the average data for each group separately are depicted in thick lines.

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The inset depicts the average 50% point for each group, which represents aftereffect strength.

Error bars represent 95% confidence intervals.

Figure 7. Relationships between clinical symptoms and the strength of negative afterimages (A) and tilt aftereffects in the near (B) and far (C) conditions.

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Figure 1.

Visual aftereffects in schizophrenia

Figure 2.

Visual aftereffects in schizophrenia

Figure 3.

Visual aftereffects in schizophrenia

Figure 4.

Figure 5.

Figure 6.

Figure 7.

Supplemental Methods

Negative afterimage paradigm

On each trial our participants viewed an adapting pattern that essentially consisted of a blurry disk divided down the middle into a dark half and a bright half, shown upon a gray background (35 cd/m^2). Specifically, they viewed a Gabor patch created by presenting a sine wave grating (Michelson contrast 1; mean luminance same as background luminance) within a Gaussian envelope. The relation between the grating's spatial frequency ($0.15 \text{ cycles/degrees of visual angle; dva}$) and the Gaussian's standard deviation (1.7 dva) was such that less than 1 grating cycle was visible, resulting in the half dark, half light appearance. The afterimage of such an adapter is a similarly blurry patch that appears bright where the adapter was dark and vice versa (Supplemental Figure 1A; 'b' represents a subsequent blank screen, and 'ai' stands for afterimage; the reason for separating 'ai' from the participant's actual percept in this figure will become clear momentarily). The strength of such an afterimage can be assessed using a so-called nulling method, in which the display after adaptation does not revert to a blank field, but to a pattern that is a 'photo negative' of the afterimage or, in other words, a low-contrast version of the original adapting pattern itself (Supplemental Figure 1B; here 'n' represents the nuller). The goal of such a nulling procedure would be to find the nuller strength at which the percept during the nulling period indicates a balance between the nuller and the afterimage, and this strength would then be taken as an index of the strength of the afterimage (Brascamp, van Boxtel, Knapen, & Blake, 2010; Georgeson & Turner, 1985; Kelly & Martinezuriegas, 1993; Leguire & Blake, 1982). In the specific case of our Gabor adapter, a conventional approach would be to use a Gabor patch as the nuller stimulus as well, and vary its contrast from trial to trial, asking each time which half of the stimulus area appears brighter during the nulling period

(Supplemental Figure 1B). To avoid potential confusion about whether to respond to the luminance of the adapter stimulus or the nuller, we modified the stimulus used during the nulling period, to achieve a percept that could not be confused with the adapting Gabor patch. As illustrated in Supplemental Figure 1C, our stimulus during the nulling period consisted of a superimposed combination of a Gabor patch that would conventionally be used to null our participants' afterimages, and that we refer to as the nuller, and a second Gabor patch that was similar but orthogonal to the nuller. This second Gabor patch, which we refer to as the carrier ('c' in Supplemental Figure 1C), had a strength that was fixed across trials and it played no role in canceling the afterimage. Instead, as illustrated in Supplemental Figure 1C, the inclusion of the carrier resulted in a percept, during nulling, of a type of dipole that could not be confused for the adapting Gabor patch. This dipole was characterized by a dark corner and a bright corner, and the perceived location of the bright corner (or, equivalently, of the dark corner) on a given trial was now diagnostic of whether the nuller overpowered the afterimage or not. Accordingly, the strength of the nuller was varied across trials and observers were asked to report on each trial which of four corners (top left, top right, bottom left or bottom right) appeared brightest during the nulling period. The dissimilarity in perceptual appearance between adaptation and nulling also reduced the possibility of other types of cognitive response biases associated with having seen the adapter. Across consecutive trials, the adapting stimulus was alternately oriented vertically or horizontally (i.e. the transition that separated the bright and dark half ran either vertically or horizontally), while the nuller contrast was chosen quasi-randomly out of 6 different values (Michelson contrasts of 0, 0.12, 0.24, 0.36, 0.48, 0.60, counterbalanced), and the carrier contrast was always fixed (0.3 Michelson). In addition, the contrast polarity (i.e. which half was bright and which half was dark) of both adapter and carrier were independently randomized across trials (the polarity of the nuller was yoked to that of the adapter). We note that this design, although potentially complicated from the perspective of experimenters and

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readers, was extremely straightforward from the participants' perspectives, because neither adapter orientation nor adapter or carrier polarity had any bearing on the nature of their task, i.e. to report the bright corner of the dipole seen during the nulling period. Central fixation of gaze was facilitated by a circle (radius 2.7 dva) that framed the stimulus area and a circular fixation mark at its center (radius 0.15 dva). The circle was white during presentation of the adapter stimulus, and then turned green during presentation of the nuller so as to distinguish it from the adapter stimulus.

There were 6 possible nuller strengths, each of which was presented 12 times, resulting in 72 total trials that were equally distributed across 3 runs. After each sequence of 6 such trials observers were informed what percentage of trials had been completed, and were allowed a self-timed break.

Tilt aftereffect paradigm

Our adapting stimulus was a sine wave grating (1.6 cycles/dva, radius 4.4 dva, Michelson contrast of 1, mean luminance same as background luminance), oriented at 20 degrees (in either direction away from vertical, randomly selected each trial) and presented on a gray background (35 cd/m²) for 2 s at a time. The adapter grating's phase jumped randomly between 8 evenly spaced values every 0.024 s in an effort to provide as strong an adapting stimulus as possible and thereby maximize adaptation. The orientation of our nulling stimulus varied randomly from trial to trial (between -1, 0, 1, 2, 3 and 4 degrees relative to vertical, counterbalanced between trials. Here 0 degrees means physically vertical and positive numbers indicate tilts in the direction of the adapting grating). Participants were asked to report the tilt (clockwise or counterclockwise from vertical) during each nulling period. Central gaze fixation

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was again facilitated by presenting stimuli within a circle (radius 5.1 dva) and with a circular fixation mark shown at the center of the display (radius 0.15 dva). In order to discourage participants from reporting the appearance of the adapting stimulus itself, we again took measures aimed at clearly distinguishing the adapting pattern and the nulling pattern. For this reason, the nulling pattern was a type of annulus (Figure 4B), formed by presenting a grating pattern (of the same spatial frequency as the adapter; 0.2 Michelson contrast; mean luminance same as background luminance) within a radial Gaussian envelope (envelope centered on ring with radius 3.1 dva, with a standard deviation of 0.73 in the radial direction). In addition, the ring surrounding the stimulus area turned from white to green at the moment the nuller stimulus appeared so as to distinguish the nuller from the adapter stimulus. Because the anticipated absence of a tilt aftereffect during far condition trials, nuller tilts during these far condition trials were drawn from a different range, centered on vertical (-2.5, -1.5, -0.5, 0.5, 1.5, and 2.5 degrees).

There were 6 possible nuller orientations for both near and far conditions, each of which was presented 9 times, resulting in 108 total trials that were distributed across 3 separate runs. After each sequence of 9 trials, observers were informed what percentage of trials had been completed, and were allowed a self-timed break.

Performance exclusion criteria

To ensure data quality, we applied several data exclusion criteria. In particular, data were discarded if: (1) fit quality was poor (a sum of squared errors above 0.25), indicating a large degree of randomness in the data; (2) the fitted 50% point fell far outside of the range of the nuller strengths we applied, precluding an accurate estimate (tilt aftereffects-far condition:

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outside a $[-5\ 5]$ degree range; tilt aftereffects-near condition: outside a $[-3.5\ 6.5]$ degree range; negative afterimage: outside a $[0.25\ 0.85]$ contrast range; (3) the curve was very flat, indicating a weak response to the independent variable, calculated as the difference in y-values from the leftmost and rightmost nuller < 0.4 .

Eye tracking

At the start of every session the experimenter adjusted the angle and focus of the eye tracker camera to get a clear view of both eyes. After that, the participant performed a standard Eyelink calibration during which he/she was instructed to fixate on a disk on the screen, while this disk appeared at various locations. This procedure establishes the relation between the eye tracker camera image and gaze position on the screen. Before every trial throughout all sessions the participant also performed a drift correction procedure, aimed at verifying whether the calibration was still accurate and performing a new calibration if not. During drift correction, the participant was shown a small white circle (radius 0.3 dva) at the center of the screen and instructed to press a key once he/she was fixating on the white circle. The first on-screen gaze position recorded by the eye tracker during the 100 ms time interval following key release was then compared to the actual position of the white circle (i.e. the center of the screen). If the difference between the two exceeded 2 dva, or if no gaze position was recorded at all during the 100 ms interval, this was considered a failed attempt and the procedure was repeated; otherwise drift correction was considered successful and the experiment continued to the next stage. After three failed attempts in a row, the original calibration procedure was repeated, overwriting the previous calibration.

Supplemental Results

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Analyses of aftereffect strength were repeated after removing trials based on gaze deviation or missing gaze samples criteria.

Negative afterimages

There was no significant difference between PSZ and HC in the percentage of trials removed (PSZ: mean=12.2%, std=8.5%; HC: 6.5%, std=5.8%; $t(46)=1.83$, $p=0.07$). Robust negative afterimages were observed in both HC ($t(18)=20.6$, $p<0.0001$) and PSZ ($t(28)=18.6$, $p<0.0001$). However, there was no difference in negative afterimage strength between groups ($t(45)=1.66$, $p=0.10$).

Tilt aftereffects

There was no significant difference between PSZ and HC in the percentage of trials removed in either the near (PSZ: mean=8.1%, std=10.8%; HC: 3.4%, std=3.4%; $t(38)=1.76$, $p=0.09$) or far (PSZ: mean=11.1%, std=12.0%; HC: 5.7%, std=5.1%; $t(38)=1.76$, $p=0.08$) conditions. Robust tilt aftereffects were observed in both HC ($t(17)=6.1$, $p<0.0001$) and PSZ ($t(22)=8.8$, $p<0.0001$) in the near condition. Neither group showed a significant tilt aftereffect in the far condition (HC: $t(17)=-1.5$, $p=0.014$; PSZ: $t(21)=1.9$, $p=0.07$). Mixed model ANOVA on tilt aftereffect strength revealed significant main effects of both condition ($F(1,38)=59.3$, $p<0.0001$) and group ($F(1,38)=9.9$, $p=0.003$). Tilt aftereffects were larger in the near condition, and PSZ had significantly stronger tilt aftereffects than HC. There was no significant group-by-condition interaction ($F(1,38)=0.01$, $p=0.92$).

Supplemental Discussion

Contrast sensitivity

An important consideration for interpreting these results is perceived stimulus contrast. Contrast sensitivity is altered in individuals with schizophrenia: those in the chronic stage of the illness, which would characterize the majority of our sample, show reduced sensitivity (Butler et al., 2005; O'Donnell et al., 2006; Skottun & Skoyles, 2007; Slaghuis, 1998). In healthy individuals, both negative afterimages and tilt aftereffects become weaker as the physical contrast of the adapter stimulus decreases (Georgeson & Turner, 1985; Parker, 1972) raising the question whether differences in contrast sensitivity might be related to the current findings. While it is plausible that reduced contrast sensitivity (Silverstein, Demmin, & Bednar, 2017) and increases in tilt aftereffect strength in schizophrenia are both rooted in altered early visual processing, closer inspection reveals no straightforward connection. Most importantly, while perceived contrast is reduced in schizophrenia, reduced adapter contrast usually produces weaker tilt aftereffects (Parker, 1972): the opposite of what we report for our schizophrenia patients. Moreover, there is evidence that contrast deficits in schizophrenia may be relatively mild for visual patterns that contain high spatial frequencies (i.e. spatially fine patterns; Butler, Silverstein, & Dakin, 2008; Calderone et al., 2013), yet we observe altered aftereffects specifically in the tilt aftereffect paradigm that uses such a pattern, and not in the negative afterimage paradigm that uses a spatially coarse pattern. Attempts to directly link our findings to altered contrast sensitivity are further complicated by the facts that our tilt aftereffect paradigm adapter was dynamic while the negative afterimage paradigm adapter was static (another factor that influences the degree of altered contrast sensitivity in schizophrenia; Butler et al., 2008; Keri, Antal, Szekeres, Benedek, & Janka, 2002), and that tilt aftereffect strength in healthy controls has opposite dependences on the contrast of the adapter stimulus and that of the nuller stimulus (Parker, 1972). In sum, it may well be that common properties of early visual

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processing in schizophrenia produce both altered contrast sensitivity and altered tilt aftereffect strength, but more work is needed to understand the nature of these properties.

Supplemental Table 1. Psychotropic medication information for individuals with schizophrenia.

Medications	n
Antipsychotics only	5
Antidepressants only	1
Antipsychotics+mood stabilizers only	5
Antipsychotics+antidepressants only	8
Mood stabilizers+antidepressants only	1
Antipsychotics+mood stabilizers+antidepressants	4
Antipsychotic+anxiolytic	2
Antipsychotic+anxiolytic+antidepressants	5
Antipsychotic+anxiolytic+mood stabilizers+antidepressants	2

Supplementary Figure 1.

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