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Foveal and parafoveal contrast suppression are different: Mechanisms revealed by the study of healthy aging

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Visual contextual effects enable inference regarding neural mechanisms of cortical function, principally because of similarities between the stimulus properties influencing human perception and those modifying primate visual cortical neural responses. Most neurophysiology assesses nonfoveal cellular function and circuitry, while most human studies are foveal. Here we use parafoveal stimuli to measure center-surround perception of contrast in older and younger adults. We measure the influence of both near and far surround because neurophysiology demonstrates different circuitry for these areas. Contrast suppression from the near surround was reduced in older observers, while that from the far surround was intact. Our results are consistent with reduced intracortical inhibition with age and normal extrastriate feedback. Interestingly, in the same older observers, foveal surround suppression of contrast was strengthened relative to younger adults, demonstrating a clear distinction between foveal and parafoveal center-surround behavior. We assume that underlying alterations in cortical neurotransmitter levels with age should not differ substantially between the areas of visual cortex representing foveal and near foveal regions. Consequently, our results suggest regional differences in center-surround circuitry. That older adults have varied contextual effects of visual contrast as a function of retinal eccentricity suggests complex effects of aging on scene and object perception.

Introduction

Visual perceptual measures are widely used to study human cortical function. In the past decade, visual contextual effects in humans have been extensively studied for this purpose, primarily because there are clear similarities between stimulus properties that influence normal human performance and those that influence primate cortical visual neural responses (Cannon & Fullenkamp, 1991; Cavanaugh, Bair, & Movshon, 2002; Levitt & Lund, 1997; Petrov, Carandini, & McKee, 2005). Examples include the study of center-surround contrast perception and surround suppression of motion discrimination in schizophrenia (Dakin, Carlin, & Hemsley, 2005; Serrano-Pedraza et al., 2014; Tibber et al., 2013; Yang et al., 2013; Yoon et al., 2010; Yoon et al., 2009), migraine (Battista, Badcock, & McKendrick, 2010, 2011), and in older adults to assay the effects of aging on cortical processing (Betts, Taylor, Sekuler, & Bennett, 2005; Karas & McKendrick, 2009, 2011, 2012, 2015). In addition to allowing specific hypotheses to be tested regarding the human conditions of interest, such experiments importantly allow exploration and testing of assumptions regarding the intersection between normal visual processing and underlying neural mechanisms. To clarify, some rethinking of the purported mechanisms is required if a series of tasks that are assumed to invoke the same neural processes are substantially differentially affected by a single disease entity. It is within this context that we have been studying the effects of healthy normal aging on perceptual surround suppression of contrast.

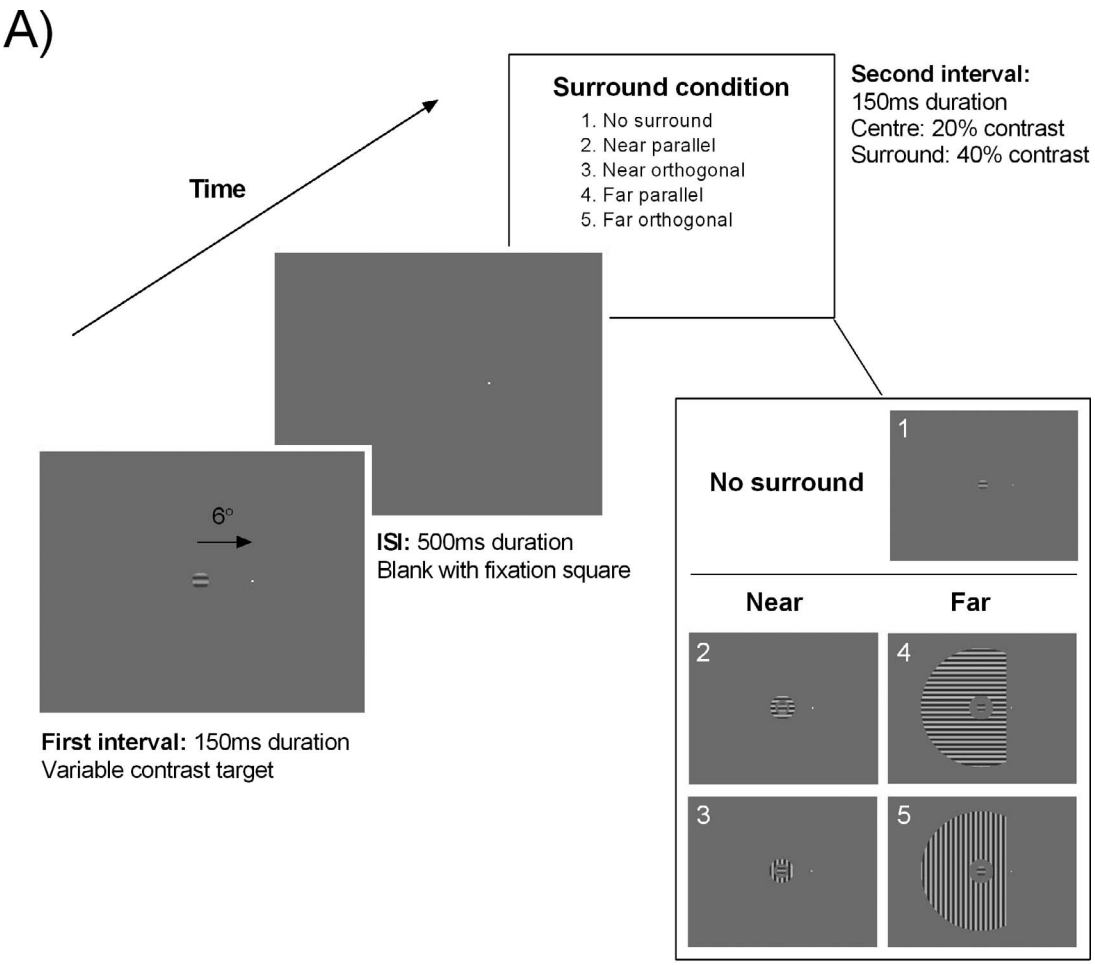
The systems neuroscience of surround suppression of contrast within the visual cortex is incompletely understood; however, it is being pieced together by numerous single-unit recording studies in primate (reviewed by Angelucci & Bressloff, 2006; Nurminen & Angelucci, 2014). Neural data are typically collected parafoveally. The aging process reduces orientation selectivity and decreases the surround suppression of many V1 cells in macaque monkeys (Fu et al., 2010), consistent with a model of an overall reduction in GABA-mediated inhibition in the aging visual cortex (Leventhal, Wang, Pu, Zhou, & Ma, 2003; Schmolesky, Wang, Pu, & Leventhal, 2000). The simple analogous

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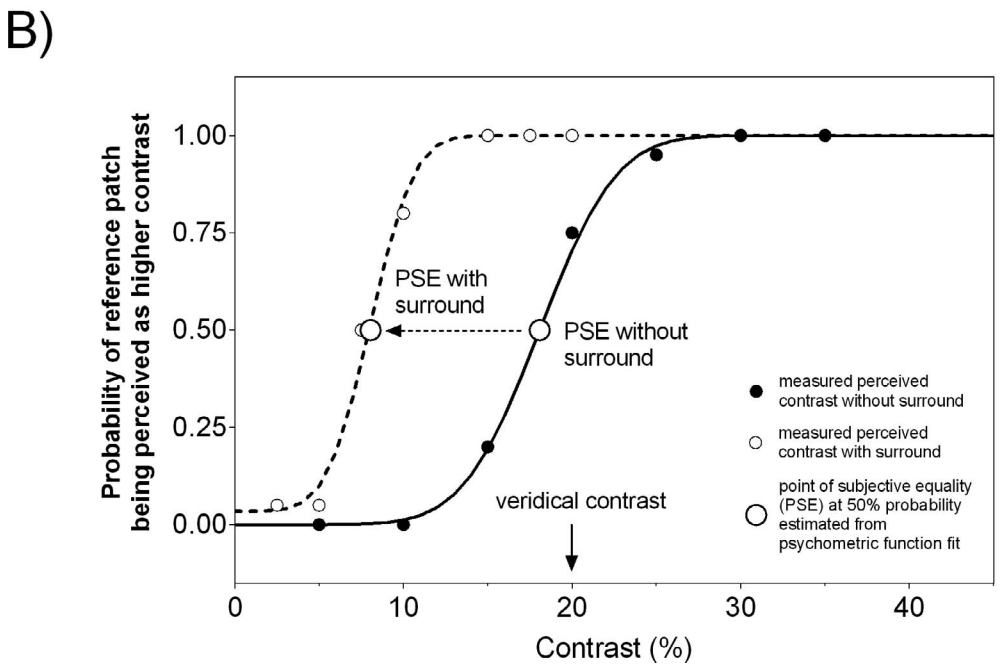


Figure 1. Measurement and analysis of parafoveal contrast suppression. (A) Schematic of the 2IFC contrast matching task. The order of the trials was fixed. The first interval (150 ms) contained the target grating (2° diameter) of variable contrast, followed by an ISI of 500 ms. The second interval (150 ms) contained the reference grating of fixed center contrast (20%). Five surround conditions were →

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tested: no surround, near surround (3°–5° diameter) parallel and orthogonal, far surround (5°–24° diameter) parallel and orthogonal. The surround contrast was fixed at 40%. The observer indicated with a button press which of the two intervals contained the central target of higher contrast. (B) Example psychometric functions when tested with (unfilled circles) and without a surround (filled circles). A leftward shift (dashed arrow) of the PSE (mean of best-fitting cumulative Gaussian) indicates suppression.

human prediction is that a decrease in GABA-mediated inhibition should reduce visual surround suppression in older adults. There is some support for this prediction with Betts et al. (2005) demonstrating that older adults have improved motion discrimination thresholds for large, high-contrast gratings consistent with a reduced high-contrast suppressive effect. However, older adults consistently demonstrate increased surround suppression of perceived contrast relative to younger adults (Karas & McKendrick, 2009, 2011, 2012, 2015; McKendrick, Weymouth, & Battista, 2013). In contrast to the neurophysiological research, the behavioral research has used foveal viewing.

Recently, Shushruth and colleagues (2013) demonstrated that human suppression of perceived contrast mirrored macaque V1 single-cell responses when both perceptual and neurophysiological measures were made at approximately 6° eccentricity. Orientation tuning profiles were qualitatively similar in human observers and primate V1 neurons for two spatially distinct surround regions: the "near" surround between 3° and 5° in diameter and the "far" surround, extending up to 24° in diameter. Convergent evidence suggests that the near and far surrounds are likely generated by different anatomical circuits (Angelucci & Bressloff, 2006) with properties of the near surround originating from multiple sources—feed-forward connections from lateral geniculate nucleus (LGN), feedback connections from extrastriate cortex, and intra-V1 horizontal connections (Angelucci & Bressloff, 2006; Sceniak, Chatterjee, & Callaway, 2006)—whereas far surround suppression is attributed exclusively to feedback from extrastriate cortex (Angelucci & Bressloff, 2006).

Here we study parafoveal near and far surround suppression of perceived contrast in older and younger observers in order to (a) understand the consequences of human aging on center-surround visual processing and (b) determine whether age-related differences in performance support or question current models of center-surround neural circuitry. Far surround suppression was not altered in older adults, implying no age-related change to the extrastriate feedback that generates the far surround. Intriguingly, we found that healthy aging results in less near suppression of contrast parafoveally (consistent with models of reduced GABA-ergic inhibition) but increased suppression foveally, pointing to a distinct difference in the mechanisms of surround suppression of contrast across the visual field.

Methods

Participants

The study was approved by the Human Research Ethics Committee of the University of Melbourne. Participants provided written informed consent prior to testing, and the study protocol was compliant with the tenets of the Declaration of Helsinki. Nineteen younger (11 females, ages 24–35, $M = 28$ years) and 19 older adults (14 females, ages 62–78, $M = 69$ years) participated in the study. Participants were screened to ensure the following inclusion criteria were met: visual acuity at least 6/7.5, refractive error within ±5.00 D sphere and −2.00 D cylinder, normal ocular health findings on ophthalmoscopic and slit-lamp examination, no significant lens opacities (grade 1.5 or better on the Lens Opacities Classification System III scale; Chylack et al., 1993), and no systemic conditions (e.g., diabetes, epilepsy) or medications known to affect visual or cognitive function (e.g., antidepressants).

Stimuli

Stimuli were written in Matlab V7.6 (Mathworks, Natick, MA) and displayed on a gamma-corrected Sony G500 21-in. CRT monitor (frame rate: 100 Hz, resolution: 1024 × 768 pixels) using a ViSaGe graphics system (Cambridge Research Systems, Kent, UK). The screen was viewed binocularly in a darkened room with the appropriate refractive correction for 57 cm, maintained by a chin rest. Each test session lasted approximately 2 hr with regular breaks between each trial.

Stimuli were matched to the perceptual contrast matching experiment of Shushruth et al. (2013) (Figure 1A). The target stimulus was a circular, horizontal sinusoidal grating (1 c/°) subtending 2° diameter and centered in the middle of the display. Participants were instructed to fixate on a small white square (0.2° diameter) at 6° eccentricity that remained on screen at all times. Continuous monitoring by direct visual inspection confirmed steady fixation throughout testing. The target either appeared on its own or surrounded by a 40% contrast annular grating of the same phase and spatial frequency. The near surround annulus subtended 3°–5°, and the far surround annulus subtended 5°–24° in diameter. To avoid overlapping

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with the fixation square, the far surround was truncated at 1.5° from the fovea.

Contrast detection task

Contrast sensitivity declines with age (reviewed by Owsley, 2011); hence we measured contrast detection thresholds to ensure that the target stimulus (20% contrast grating) was suprathreshold for all observers. Each trial consisted of two 150-ms stimulus intervals indicated by auditory cues and separated by a 500-ms interstimulus interval (ISI) at mean luminance. The target was presented in one of the intervals chosen at random, and observers nominated by button press which interval contained the target (two-interval forced choice, 2IFC). The contrast of the target was varied using a three-down, one-up staircase with a step size of 20% and converging on the 79% level (Wetherill & Levitt, 1965). The staircase terminated after six reversals and was performed twice. The last four reversals of each staircase were averaged, and the average of the two staircases was the final threshold estimate.

Parafoveal contrast matching task

The perceived contrast of the target grating was measured using a 2IFC contrast matching task (Figure 1A). In the first interval (150 ms), the target stimulus of variable contrast was displayed on its own. In the second interval (150 ms), a center-surround target of fixed contrast (20% center, 40% surround) appeared (the reference). Several surround conditions were used in different experimental runs as described below. The two intervals were indicated by audio cues and separated by 500 ms. Participants pressed one of two buttons to indicate the interval that contained the central target stimulus of higher contrast. No feedback was provided. Participants first completed a "no-surround" condition, then four "surround" conditions to test the effect of surround (near vs. far) and surround orientation (parallel vs. orthogonal). The surround conditions were performed in separate runs with the order randomized between observers to balance effects of learning/fatigue.

To train participants on the task and to choose which contrast levels to test in the main experiment, an initial abbreviated method of constant stimuli (MOCS, 10 levels, four trials each) was performed. Psychometric functions were then measured using a MOCS consisting of seven contrast levels (Figure 1B, 20 trials each). The data were fitted with a modified cumulative Gaussian (Wichmann & Hill, 2001) using a maximum-likelihood fitting procedure in Microsoft Excel (Microsoft, Redmond, WA):

$$\psi(t) = FP + (1 - FP - FN) \times G(t, \mu, \sigma) \quad (1)$$

where $G(t,\mu,\sigma)$ is the cumulative Gaussian with mean μ and standard deviation σ for value t. FP and FN represent the false positive and false negative error rates, respectively, that are made independently of the Gaussian response distribution. The perceived contrast was defined as the mean of the fitted psychometric function (μ), i.e., the point of subjective equality (PSE) when both the reference and target stimulus appeared subjectively the same. To compare suppressive effects between groups, a suppression index was calculated (Equation 2). A positive index indicates suppression, a negative index indicates facilitation, and an index of 0 indicates no effect of the surround.

$$\text{Suppression index} = 1 - \frac{\text{PSE with surround}}{\text{PSE no surround}}. \quad (2)$$

Foveal contrast matching task

A subgroup of observers comprising 10 younger (mean age: 27 years) and 10 older (mean age: 68 years) participants completed a second experiment to compare foveal and parafoveal suppression of perceived contrast. The subgroup of people was chosen at random based on their availability to return at short notice, i.e., recruitment was not influenced by performance in the first experiment. The contrast matching procedures were identical to the parafoveal measures except that the stimuli were scaled by a cortical magnification factor (Rovamo & Virsu, 1979). The central target subtended 0.6° diameter, and the near surround annulus subtended 1°–1.6°. The spatial frequency was adjusted (3.2 c/°) to ensure the same number of cycles were visible for both foveal and parafoveal conditions. Four nonius lines in the cardinal directions were displayed at the center of the screen at all times to reduce the observer's uncertainty about the target location, particularly for the no-surround condition. Only the near parallel surround condition was tested in this experiment because parallel surrounds produce the greatest perceptual contrast suppression (Cannon & Fullenkamp, 1991; Xing & Heeger, 2000; C. Yu, Klein, & Levi, 2001).

Statistical analysis

Groups were compared using a repeated-measures analysis of variance (RM-ANOVA) in SPSS Statistics V22.0 (SPSS, Chicago, IL). Data were tested to confirm statistical normality (Kolmogorov-Smirnov normality test) and homogeneity of variances (Mauchly's test of sphericity).

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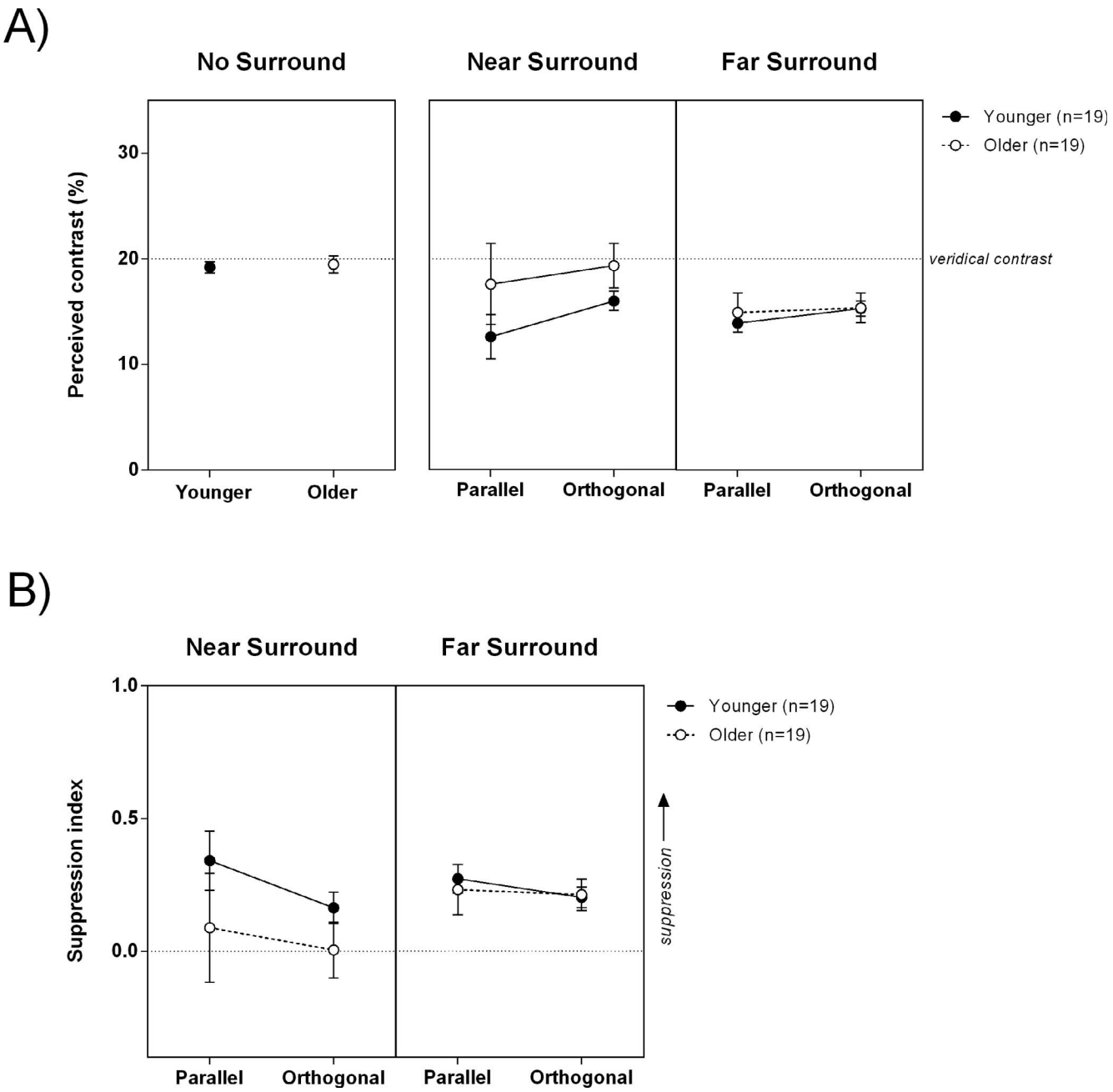


Figure 2. Group results of the parafoveal contrast matching task. (A) Mean perceived contrast. Surround suppression is indicated by a reduction in perceived contrast relative to the no-surround condition. (B) Mean suppression index. Positive indices indicate suppression. Error bars = 95% confidence intervals of the mean.

Results

For the 1 c/° target, parafoveal contrast detection thresholds (mean ± standard deviation) for older participants (1.79% ± 0.37%) were significantly higher than for younger observers (1.15% ± 0.18%), $t_{36} = 6.70$, $p < 0.0001$. Thresholds did not exceed 2.5% in either group, indicating that all stimuli presented were indeed suprathreshold. In the subgroup of observers who additionally completed the foveal task, the older group similarly showed a trend for higher parafoveal contrast detection thresholds (2.65% ± 1.26%) than did the younger group (1.74% ± 0.54%), $t_{18} = 2.09$, $p = 0.05$, for 3.2 c/° targets. In this case, the highest detection threshold was 5.81% in the older group and well below the target contrast (20%).

Figure 2A shows the perceived contrast matches made by the older and younger observers with and

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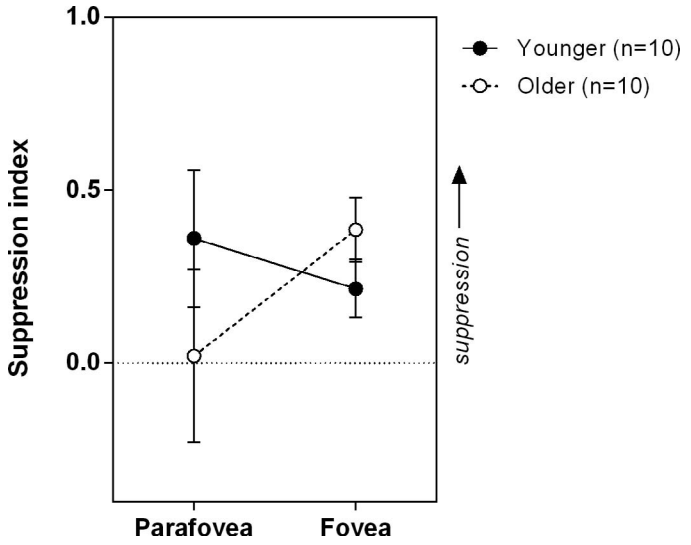


Figure 3. Group results of the foveal versus parafoveal contrast matching tasks. Mean suppression index for the near parallel surround under foveal and parafoveal (6° eccentricity) viewing in a subset of participants. Surround suppression is indicated by a positive suppression index. Error bars = 95% confidence intervals of the mean.

without a surround parafoveally. For the target grating alone, both groups matched to approximately 20%, the veridical contrast, demonstrating a similar capacity to perform the task. In the presence of a surround, perceived contrast was reduced (below the horizontal dotted lines in Figure 2A). For the near surround, older observers perceived the contrast as higher than did younger observers. This translates to a significant reduction in the near surround suppression index in the older group, regardless of orientation (Figure 2B; RM-ANOVA main effect of group: $F(1, 36) = 7.96$, $p = 0.008$; group × orientation interaction: $F(1, 36) = 0.89$, $p = 0.35$). On the other hand, far surround suppression (Figure 2A, B, right panels) was similar in both groups for parallel and orthogonal conditions (RM-ANOVA main effect of group: $F(1, 36) = 0.17$, $p = 0.69$; group × orientation interaction: $F(1, 36) = 1.22$, $p = 0.28$).

Figure 3 shows the suppression indices for the participants that performed both the foveal and parafoveal tasks for the near surround only, using the same contrast matching method. The difference in suppression index between groups was dependent on eccentricity (RM-ANOVA group × eccentricity interaction: $F(1, 18) = 12.15$, $p = 0.003$). The older group showed increased suppression relative to the younger group foveally but reduced suppression parafoveally. Foveal near surround suppression did not predict parafoveal near surround suppression; there was no statistically significant relationship between foveal and parafoveal measures for the younger group ($r = -0.19$, $p = 0.61$), older adults ($r = 0.59$, $p = 0.08$), and both groups combined ($r = -0.14$, $p = 0.55$).

Discussion

We measured the perceived contrast of center-surround stimuli in older and younger observers as perceptual analogues of V1 surround suppression. Stimuli were presented parafoveally (6° eccentricity) with a near and far surround to enable comparison to single-cell neurophysiological studies in primate V1 (Shushruth et al., 2013) and infer possible neural underpinnings of age-related changes to surround suppression given that the near and far surround are suggested to arise from different anatomical circuitry (reviewed by Angelucci & Bressloff, 2006; Nurminen & Angelucci, 2014). Far surround suppression at V1 is fast in onset (Bair, Cavanaugh, & Movshon, 2003), has a large spatial extent (Levitt & Lund, 2002; Shushruth, Ichida, Levitt, & Angelucci, 2009), and is thought to arise exclusively from feedback connections from extrastriate cortex (Angelucci & Bressloff, 2006). On the other hand, the near surround has narrower orientation tuning than the far surround (Shushruth et al., 2013) and receives multiple inputs: excitatory feed-forward connections from LGN, intra-V1 inhibitory horizontal connections, and excitatory feedback connections from extrastriate cortex (Angelucci & Bressloff, 2006; Sceniak et al., 2006). Our finding that near but not far surround suppression was altered in the older participants suggests that extrastriate feedback contributions to the far surround are likely unaffected by normal aging. The remaining candidate mechanisms—horizontal intra-V1 connections and feed-forward connections from LGN (Angelucci & Bressloff, 2006)—cannot be disentangled here. Given previous neurophysiological work demonstrating two distinct mechanisms of surround suppression (Webb, Dhruv, Solomon, Tailby, & Lennie, 2005)—one that is transient and monocular and one that is sustained and binocular—further investigations are underway in our laboratory that vary aspects such as timing and eye of presentation to separate the relative effects of aging on these different mechanisms of suppression.

In the parafovea, we found a reduction in near surround suppression of perceived contrast in older adults, which suggests a reduction in inhibition. Previous observations of altered neural activity in primary and extrastriate cortex in aged primate also demonstrate inhibitory dysfunction. Reduced orientation and direction selectivity (Fu et al., 2010; Schmolesky et al., 2000), in conjunction with reduced suppression (Fu et al., 2010), have been reported in V1 cells of aged monkeys along with increased spontaneous neural noise (Schmolesky et al., 2000; Yu, Wang, Li, Zhou, & Leventhal, 2006). The mechanisms underpinning altered functional inhibition in older adults are unclear. Several authors suggest that these age-related differences are due to a reduction in the

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major cortical inhibitory neurotransmitter, GABA (Leventhal et al., 2003; Schmolesky et al., 2000). Key evidence that aging alters GABA-ergic inhibition in the visual cortex is the observation that application of the GABA agonist muscimol restores orientation tuning to cells from older macaque V1 (Leventhal et al., 2003). However, it is important to note that other neurotransmitters modulate cortical excitatory–inhibitory balance and can also modify center-surround antagonistic effects. One example is acetylcholine, whose receptors are ubiquitous throughout mammalian V1 (Avendano, Umbriaco, Dykes, & Descarries, 1996; Lysakowski, Wainer, Bruce, & Hersh, 1989; Mechawar, Cozzari, & Descarries, 2000). Activation of different cholinergic receptors can alter the release of inhibitory and excitatory neurotransmitters, including GABA (Gulledge, Bucci, Zhang, Matsui, & Yeh, 2009; Sugita, Uchimura, Jiang, & North, 1991; Thiele, 2013), and can influence the amplitude of excitatory and inhibitory postsynaptic potentials in the mammalian brain (Kimura & Baughman, 1997). The orientation tuning of many primate V1 neurons is broadened by application of acetylcholine, presumably by reducing cortical inhibitory drive (Zinke et al., 2006). Similarly, perceptual contrast suppression of iso-oriented (parallel) center-surround stimuli is reduced with human ingestion of a cholinesterase inhibitor, donepezil (Kosovicheva, Sheremata, Rokem, Landau, & Silver, 2012). Normal aging is generally associated with a gradual decline in cholinergic function (Schliebs & Arendt, 2011), which predicts that older adults should have a strengthening rather than a weakening of intracortical inhibition. Our foveal results, and those of previous studies, are consistent with this observation; however, the parafoveal results are not. Naturally, the current experiments can only speculate on neurotransmitter involvement but do demonstrate that a simplistic explanation is unlikely to suffice.

Previous studies have consistently found increased foveal suppression in older adults using suprathreshold contrast matching methods (Karas & McKendrick, 2009, 2011, 2012, 2015; McKendrick et al., 2013), and this study was no exception. Surround suppression of foveal perceived contrast is also known to gradually increase throughout the adult life span (McKendrick et al., 2013). On the other hand, surround suppression of parafoveal (4°–5° eccentricity) contrast sensitivity is not age-dependent (Serrano-Pedraza et al., 2014; Yazdani, Serrano-Pedraza, Whittaker, Trevalyan, & Read, 2015). This lack of concordance between threshold and suprathreshold measures of surround suppression of contrast is not unexpected, especially as foveal and peripheral measures produce different patterns of results. Snowden and Hammett (1998) measured contrast detection, discrimination, and perceived contrast under comparable conditions in two young observers (ages 28–31 years). A single model that incorporates divisive lateral inhibition did not account for all of the foveal and peripheral effects observed. The effects of aging on suppressive mechanisms at threshold may be further informed by consideration of models proposed by Meese, Challinor, Summers, and Baker (2009) and Petrov et al. (2005).

Primate neurophysiological studies assume an overall decrease in GABA-ergic inhibition within the aged brain (Leventhal et al., 2003; Schmolesky et al., 2000), which is expected to produce an increase in cortical excitation. A plausible explanation for the counterintuitive increase in inhibition found here and in previous human experiments of foveal suppression of perceived contrast with aging (Karas & McKendrick, 2009, 2011, 2012, 2015; McKendrick et al., 2013) is that an overall reduction in GABA-ergic inhibition might increase the excitatory feedback that drives local inhibitory interneurons in V1, hence increasing the perceptual inhibitory response. A novel finding of this study was that the older group showed opposite effects of suprathreshold contextual processing parafoveally (here, decreased suppression of perceived contrast) versus foveally (increased suppression of perceived contrast). Distinct differences in the neural architecture and the practical roles of foveal and peripheral vision are well known. Suppression of perceived contrast occurs both foveally and peripherally with a sharp increase in the strength of suppression with eccentricity until approximately 4°–5° from the fovea and little change thereafter (Xing & Heeger, 2000). Stronger surround suppression in the periphery is thought to mask homogenous or redundant information in visual space. This might assist in identifying salient sites and directing our gaze to objects of interest that are markedly different from their nonuniform backgrounds so that foveal processing of visual information can occur unhindered (Petrov et al., 2005; Xing & Heeger, 2000). Nearby edges are more likely than distant edges to be parallel and belong to the same physical contour (Field, Hayes, & Hess, 1993; Geisler, Perry, Super, & Gallogly, 2001). Orientation-specificity of near surround suppression (Shushruth et al., 2013) is therefore thought to remove homogenous visual information and allow detection of small orientation differences, which is useful for local contour integration in parafoveal vision (Petrov et al., 2005). Consequently, the fact that older adults demonstrate reduced near surround suppression of perceived contrast parafoveally predicts that older adults may have difficulties with tasks requiring contour integration. Indeed, perceptual contour integration is altered in older adults (McKendrick, Weymouth, & Battista, 2010; Roudaia, Bennett, & Sekuler, 2008). Notably, contour integration performance in older adults can be improved by training to levels similar to younger adults pretraining (McKendrick & Battista,

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2013), implying plasticity in the mechanisms underpinning such local spatial interactions.

Conclusions

Our experiments highlight different neural circuitry underpinning perceptual surround suppression of contrast for foveal and parafoveal conditions. The neural circuitry must differ to yield opposing perceptual results because it seems reasonable to assume that any age-related alteration to neurotransmitter level (e.g., GABA) does not selectively affect a small region of visual cortex but is a wider-spread cortical phenomenon. Our findings have implications beyond the study of the aging visual system because similar perceptual tasks have been used to investigate a variety of human disorders where the balance between cortical inhibition and excitation is altered. For example, perceptual contrast suppression has been used as an assay of cortical inhibitory function in conditions such as migraine (Battista et al., 2011) and schizophrenia (Serrano-Pedraza et al., 2014; Tibber et al., 2013; Yang et al., 2013; Yoon et al., 2010; Yoon et al., 2009). Our results suggest distinct mechanistic differences between foveal and parafoveal surround suppression. The study of parafoveal contrast suppressive effects in this wider range of disorders may assist in strengthening the understanding of the underlying circuitry and likely neurotransmitter involvement and hence enhance our knowledge of human visual neurophysiology.

Keywords: contrast, suppression, foveal, parafoveal, aging

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