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The Impact of Depression and Antidepressant Pharmacotherapy on Early-stage Visual Functioning in the Magno-, Parvo-, and Koniocellular Pathways

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Abstract

Vision research has contributed to an increased understanding of the neurophysiological substrates and disease processes of a number of neurological conditions, recently including the investigation of psychiatric disorders. Initial studies among individuals with depressive disorders have documented subtle vision abnormalities. However, this research has not yet assessed the impact of antidepressant pharmacology. In addition to contributing to knowledge regarding depression, investigation of the visual consequences of antidepressant treatment is important given the increased prevalence of prescription medication for both depressive and nondepressive disorders. Thus, the present study examined fundamental processes of photopic visual functioning associated with the use of selective-serotonin reuptake inhibitors (SSRIs), the most commonly prescribed type of antidepressant medication. The impact of depression was also assessed, both in terms of mood symptoms and clinical criteria, and measures of anxiety were included due to high comorbidity with depression and the use of antidepressant medications to treat anxiety disorders. Expanding on recent psychophysical studies that have measured only luminance-based spatiotemporal contrast sensitivity associated with depression (Szabo et al., 2004; Wesner & Tan, 2006), the present study additionally measured isoluminant "red-green" and "blue-yellow" chromatic contrast sensitivity, as well as S-cone sensitivity assessed by short-wavelength perimetry. Participants included 44 adult volunteers from the university student population and larger community. Results indicated that SSRI medications were associated with reductions in "red-green" chromatic contrast sensitivity and a trend of

decreased luminance contrast sensitivity limited to high spatial frequencies. Depression was associated with overall reductions in luminance contrast sensitivity, most apparent in the low-to-mid range of spatial frequency, as well as overall reductions in "blue-yellow" chromatic contrast sensitivity and selective decreases in "red-green" chromatic contrast sensitivity. By contrast, S-cone sensitivity enhancements were observed among depressed participants in their peripheral (30-50°) temporal hemiretinas. Anxiety appeared to have the opposite effects of depression, showing a trend of enhanced luminance contrast sensitivity for low-to-mid spatial frequencies, significant overall enhancement of "red-green" contrast sensitivity, and a trend of increased "blue-yellow" contrast sensitivity at certain spatiotemporal frequencies, as well as significant reductions of S-cone sensitivity in the peripheral (30-50°) temporal and paracentral (10-22°) superior nasal sections of their retina. Results are discussed with reference to involvement of the magno-, parvo-, and koniocellular streams of visual perception.

Introduction

Anomalies of vision have been documented in both seasonal and non-seasonal depression. These abnormalities are subtle and generally not detected by standard clinical tests of vision, but instead require noninvasive psychophysical assessment for the identification of dysregulated pathway operations. Although usually unnoticed by affected individuals, these types of vision abnormalities have nevertheless been important for investigation of pathophysiology, as well as diagnostic and treatment considerations, in a number of neurological diseases. In the area of psychiatric disorders, psychophysical measures of vision have been used extensively in schizophrenia research and are beginning to be applied to the study of mood disorders. The present study seeks to add to the psychophysical research that has been initiated with respect to visual functioning in depressive disorders. Specifically, this study will attempt to clarify the nature of the luminance contrast anomalies that have been observed in depressive disorders and will additionally introduce an exploration of chromatic visual functioning and an examination of the effects of antidepressant pharmacology on early-stage visual processes.

Psychophysical Assessment and Neurological Disorders

Psychophysical assessment of visual functioning is increasingly being used as a tool to investigate neurological disorders not typically characterized by visual impairment. For example, abnormal visual functioning has been identified in several neurodegenerative disorders, including Parkinson's disease, multiple sclerosis, Huntington's chorea, Alzheimer's disease and other dementias (e.g., Bassi, Solomon, &

Young, 1993; Bodis-Wollner et al., 1987; Caruana et al., 2000; Cronin-Golomb et al., 1991; Gilmore & Levy, 1991; Hutton, Morris, Elias, & Poston, 1993; Lakshiminarayanan, Lagrave, Keane, Dick, & Shankle, 1996; Logi et al., 2001; O'Donnell et al., 2003; Silva et al., 2005; Skrandies & Gottlieb, 1986) as well as neurodevelopmental disorders, such as autism and fragile X syndrome (e.g., Bertone, Mottron, Jelenic, & Fauber, 2005; Davis, Bockbrader, Murphy, Hetrick, & O'Donnell, 2006; Kogan et al., 2004). In some cases, vision deficits are manifest as overt ophthalmologic impairment, adding significantly to the disability associated with the disease. In other cases, anomalies of vision are subtle, highly specific, and not detected by standard clinical vision tests. These may be reported as vague visual complaints of blurring or dullness, but are more often not noticed by affected individuals. However, even when asymptomatic, visual abnormalities can serve as important markers of neurological disease processes.

The utility of psychophysical assessment of visual functioning in neurological disorders is manifold. First, psychophysical tests provide a sensitive and noninvasive method of identifying discrete visual anomalies overlooked by standard clinical procedures. Second, the information provided by psychophysical assessment contributes to an increased understanding of the potential substrates of the disorder. Psychophysical paradigms can be designed to isolate distinct and localized functions of the visual system, shedding light on physiological and anatomical components of neurological pathology (Caruana et al., 2000; Silva et al., 2005). Additionally, investigators have explored visual dysfunction as contributing to an explanation of core symptoms of certain neurological

diseases. For example, deficits in visual processing have been suggested as contributing to the observed motoric and cognitive impairments associated with Parkinson's and Alzheimer's, respectively (Bodis-Wollner, 2002; Cormack, Tovee, & Ballard, 2000; Cronin-Golomb, Corkin, & Growdon, 1995; Pieri, Diederich, Raman, & Goetz, 2000). Third, psychophysical findings provide valuable information for diagnostic considerations. Research has demonstrated that closely related disorders, such as Parkinson's disease and multiple system atrophy (Delalande et al., 1996; Tebartz van Elst, Greenlee, Foley, & Lucking, 1997) or Alzheimer's disease and other dementias (Bassi et al., 1993), can be distinguished on the basis of sub-clinical differences in visual functioning. Psychophysical assessment has also identified vision deficits in the earliest stages of some illnesses, such as multiple sclerosis, before many of the core symptoms have emerged, thus highlighting possible prodromal indicators (Blumhardt, 1984; Bodis-Wollner & Camisa, 1980; Halliday, McDonald, & Mushin, 1973). Fourth, psychophysical testing has the potential to inform treatment considerations. For some neurological diseases, such as Parkinson's disease, visual dysfunction has been linked to the severity of illness, and can thus provide an indication of disease progression (Bodis-Wollner, 2002; Bodis-Wollner, Yahr, & Thornton, 1981; Diedrich, Raman, Leurgens, & Goetz, 2002). Knowledge of sub-clinical visual dysfunction is also being used in treatment strategies aimed at reducing functional disability and enhancing activities of daily living among individuals with Alzheimer's disease (Cormack et al., 2000; Cronin-Golomb, 1995). Thus, psychophysical procedures have contributed to a better understanding of the sites and mechanisms associated with a given neuropathology, have

provided information useful for early and differential diagnosis, and have assisted with symptom management.

Phototherapy and Vision Research in Mood Disorders

The visual system became a point of interest in mood disorder research with the demonstrated efficacy of light therapy for seasonal affective disorder (SAD; Eastman, Young, Fogg, Liu, & Meaden, 1998; T.M. Lee & Chan, 1999; Rosenthal, 1995; Rosenthal et al., 1985; Terman et al., 1989) and the observation that its antidepressant effect is mediated through the eyes (Wehr, Skwerer, Jacobsen, Sack, & Rosenthal, 1987). Two opposing theories of pathophysiology have been proposed. The hyposensitivity hypothesis suggests that individuals with SAD do not absorb enough light in the winter months to maintain a euthymic state (Reme, Terman, & Wirz-Justice, 1990). Specifically, based on animal studies (Parker & Williams, 1995; Penn & Williams, 1986), it is proposed that most individuals are able to accommodate for decreased light levels in the winter months with an ocular compensatory mechanism that increases their sensitivity to ambient light. Individuals with SAD are thought to have deficient compensatory mechanisms and thus require the additional light exposure of phototherapy. By contrast, the hypersensitivity hypothesis suggests that the visual systems of SAD individuals have a heightened sensitivity to ambient light which causes them to process and respond to artificial indoor illumination as if it were natural environmental light (Beersma, 1990). In the winter months, because indoor illumination generally extends much later than the natural outdoor light, individuals with SAD experience a lengthening of their natural photoperiod, instigating a depressogenic phase

delay of their natural circadian rhythms. Early morning phototherapy is thought to anchor their rhythms. While these two theories propose opposite dysfunction, both emphasize light-gathering processes of the visual system and have guided investigation of retinal mechanisms in individuals with SAD.

Support for either the hyposensitivity or hypersensitivity hypotheses appears to depend upon the method by which retinal sensitivity is studied. Dark adaptation studies use psychophysical procedures to determine thresholds of light sensitivity and have generally found increased sensitivity among SAD individuals in the winter months compared to healthy control participants (Oren, Joseph-Vanderpool, & Rosenthal, 1991; Terman & Terman, 1999), although no differences in dark adaptation thresholds were noted in one study (Oren et al., 1993). Studies of electrooculogram (EOG) ratios instead support the theory of hyposensitivity during the winter (Lam, Beattie, Buchanan, Remick, & Zis, 1991; Ozaki, Rosenthal, Moul, Schwartz, & Oren, 1993; Ozaki, Rosenthal, Myers, Schwartz, & Oren, 1995) and have also demonstrated a significant increase in EOG ratios among healthy control participants from the summer to the winter months, but no seasonal change among individuals with SAD (Ozaki et al., 1995). Similarly, electroretinography (ERG) research tends to support the hyposensitivity hypothesis, although results are mixed. Most ERG studies have found retinal sensitivity to be reduced among individuals with SAD or subsyndromal SAD compared to healthy control participants in the winter (Hebert, Beattie, Tam, Yatham, & Lam, 2004; Hebert, Dumont, & Lachapelle, 2002), although this was only evident among women in one study (Lam, Beattie, Buchanan, & Mador, 1992), while another study found no

differences (Oren et al., 1993). With respect to phototherapy, some research has found that anomalies in retinal sensitivity among individuals with SAD were normalized with clinically effective light therapy (Tam, Lam, Yatham, & Zis, 1998; Terman & Terman, 1999), while another study found that differences in retinal sensitivity persisted despite effective phototherapy (Oren et al., 1993).

Since its success with SAD, phototherapy has been explored as a treatment option for a number of other mood disorders. Recent meta-analyses provide support for the use of phototherapy with non-seasonal major depression (Golden et al., 2005; Tuunainen, Kripke, & Endo, 2004) and treatment trials for premenstrual depression (Lam et al., 1999), postpartum depression (Epperson et al., 2004), and bipolar disorder (Benedetti et al., 2004) have also found phototherapy to be effective. Investigations of visual mechanisms in non-seasonal mood disorders have found increased light sensitivity among depressed individuals when using dark adaptation thresholds and ERG procedures (Seggie, Canny, Mai, McCrank, & Waring, 1989; Seggie & Steiner, 1990). An early study of EOG ratios suggested that depressed individuals with psychomotor retardation had low sensitivity to light, while manic individuals had heightened sensitivity to light (Economou & Stefanis, 1979), although subsequent EOG research has found little difference between depressed individuals and healthy control participants (Seggie et al., 1991). Thus, results vary according to the procedure used, with the most consistent findings suggesting that non-seasonal depression may be associated with a heightened retinal sensitivity to light.

Retinal light sensitivity in depression may be instigated by an inability of the retina to process appropriate amounts of ambient light. The effect of ambient light exposure on mood has been explored in naturalistic studies with non-clinical populations, which have demonstrated a correlation between reduced daily illumination and depressed mood (Espiritu et al., 1994; Kripke et al., 1994, 2004; Youngstedt, Kripke, Elliot, Baehr, & Sepulveda, 1998). One such study of older adults included an investigation of various ophthalmic factors and determined that the relationship between daily light exposure and depressed mood was mediated by visual impairment (Jean-Louis, Kripke, Cohen, Zizi, & Wolintz, 2005). Both visual deficits and reduced daily illumination were associated with depressed mood, but the relationship between illumination levels and mood was minimized when specific vision factors were accounted for. More specifically, although several ophthalmic features were measured, including intraocular pressure, nerve fiber layer thickness, vertical and horizontal cup-to-disk ratios, and visual field defects, only visual acuity was significantly correlated with measures of mood.

Other studies among geriatric populations have found a similar correlation between depressive symptoms and various visual deficits, such as low visual acuity and macular degeneration (Rovner, Casten, & Tasman, 2002; Rovner & Ganglui, 1998; Shmuely-Dulitzki & Rovner, 1997; Tsai et al., 2003). Interpretations of these findings have generally attributed decreased mood to the functional disability, and consequent reduction in quality of life, associated with having a vision impairment. However, in the study by Jean-Louis et al. (2005), depressed mood was only linked to visual acuity deficits and not to the other ophthalmic factors investigated. This suggests that it is not

visual impairment in general, or the resulting disability, that contributes to depressed mood, but rather a process specific to visual acuity. The researchers also determined that there was no direct relationship between vision deficits and daily illumination, meaning that illumination levels were similar among those with and without visual impairment. Thus, ophthalmic factors had a direct impact upon mood, whereas reduced daily illumination was only associated with substantial reductions in mood among individuals with vision impairments, and specifically among those with visual acuity deficits. Relatedly, bright light treatment has been found effective in improving circadian rhythm functions in Alzheimer's patients, but does not work among those who have visual impairment resulting from cataracts (Van Someren, Kessler, Mirmiran, & Swaab, 1997).

Despite a focus on retinal mechanisms in phototherapy research, visual perception has not yet been extensively explored in clinical populations with mood disorders. Instead, the vast majority of research on the visual system in phototherapy has examined the eye as a gateway to circadian rhythm mechanisms. Studies of sensitivity and adaptation to environmental light have been interpreted in terms of circadian phototransduction, which involves the retinohypothalamic pathway connecting the eye to the suprachiasmatic nucleus of the hypothalamus, considered the major circadian pacemaker. However, this pathway does not involve perceptual components of the visual system, which are instead processed along the retinogeniculostriate pathway connecting the eye to the cortex through the lateral geniculate nucleus. Perceptual processes comprise the largest portion of the visual system and may provide a non-invasive avenue for studying neurophysiological correlates of depression. Additionally, the circadian

effects of light on mood disorders may be mediated by processes associated with visual perception.

Early Stages of the Visual System

Of the various perceptual systems, vision has been the most extensively studied, due in part to the accessibility of the eye as the first stage of a highly sophisticated network of neural communication. Light information from the environment is collected through photoreceptors in the retina and transmitted from the eye through the optic nerve to multiple levels of pre-cortical regions, including the lateral geniculate nucleus, and on to the primary visual cortex and subsequent cortical areas. Early stages of this system process basic components of the visual environment, including chromatic and luminance differences, edge orientations, and temporal or dynamic pattern contrasts. This information is combined in later stages to create richly detailed and complex representations of the visual scene.

Throughout these hierarchical levels, the existence of at least two anatomically and functionally distinct parallel visual processing streams have been established: the magnocellular stream with its predominately dorsal occipito-parietal poststriatal projections, and the parvocellular stream with its predominately ventral occipito-temporal poststriatal projections (Bassi & Lehmkulle, 1990; Kessels, Postma, & Haan, 1999; Livingstone & Hubel, 1988; Merrigan & Maunsell, 1993; Shapley, 1992; Ungerleider & Mishkin, 1982). The magnocellular stream carries information involving rapid temporal changes and low spatial frequencies in the visual environment from the retina to layers IV-B and IV-C_{α} of the primary visual cortex (V1). This information is

projected dorsally to areas in the parietal lobe, where it is synthesized into perception of motion and spatial location. The parvocellular stream is sensitive to lower temporal frequencies and medium to high spatial frequencies, and transmits information concerning fine detail of static or slow-moving stimuli. Additionally, the parvocellular stream is responsible for colour information. From the retina, the parvocellular stream carries information to layers IV-A and IV-C_β of the primary visual cortex, and projects ventrally to the inferior temporal lobe, where information is synthesized into recognition of colour and object properties. There is some cross-communication in higher cortical areas, but the magnocellular and parvocellular streams remain fairly distinct in earlier stages of visual processing (Merrigan & Maunsell, 1993; Sawatari & Callaway, 1996; Vidyasagar, Kulikowski, Lipnicki, & Dreher, 2002).

A third parallel stream has more recently been confirmed as being part of perceptual processing. Originally believed to be more involved with the vegetative visual functions associated with the superior colliculus (i.e., analogous to the W-cell pathway in cats), the koniocellular stream now appears to also relay information from the retina to both the colour processing blobs and layer I of the primary visual cortex (see Hendry & Reid, 2000, for review). Evidence has accumulated that closely links the koniocellular stream with S-cone information and "blue-yellow" colour opponent channels (Calkins, Tsukamoto, & Sterling, 1998; Dacey, 1999; Dacey & Lee, 1994; Martin, White, Goodchild, Wilder, & Sefton, 1997; Mullen & Kingdom, 2002). Although the parvocellular stream was previously considered to be responsible for all chromatic processing, it now appears to be primarily limited to M- and L-cone information and

"red-green" colour opponency (Sun, Smithson, Zaidi, & Lee, 2006a; Martin et al., 1997; Mullen & Kingdom, 2002). The koniocellular stream has additionally been associated with low acuity visual information and responds maximally to spatial frequencies intermediate to those of the magnocellular and parvocellular streams (Forte, Hashemi-Nezhad, Dobbie, Dreher, & Martin, 2005; Hendry & Reid, 2000; Roy et al., 2009; White, Solomon, & Martin, 2001).

Due to the highly structured organization of the human visual system, knowledge of anomalies in visual perception can point to particular mechanisms or sites of disruption. Psychophysical tests can be constructed to isolate specific visual processes and pathways. One of the simplest and most thorough psychophysical techniques for analyzing basic visual functioning involves the use of sinusoidal gratings, perceived as alternating bands of dark and light, in order to measure thresholds of sensitivity to luminance contrast (Campbell, 1983; Campbell & Robson, 1968; Kelly, 1977; Robson, 1966).

Contrast is the primary feature by which the visual system distinguishes an object from its background. Luminance contrast denotes intensity edges, which contribute to perception of form and texture, and it is therefore integral in object identification. The perception of luminance contrast, without nuances of colour, motion, or directionality, is a response which begins in the retina and underlies the functioning of much subsequent central visual processing (DeValois & DeValois, 1990). Higher-level visual abilities are contingent upon the performance of these basic functions in early stages of the visual system.

Sensitivity to luminance contrast varies with spatial and temporal frequency. Thus, contrast sensitivity is different when viewing coarse patterns (i.e., low spatial frequency) than patterns with fine detail (i.e., high spatial frequency). Similarly, contrast sensitivity is different for static visual scenes than when the visual stimuli involve motion. Thresholds of the minimum amount of contrast needed to detect a stimulus can be determined for gratings representing the full spectrum of observable spatial and temporal frequencies. Contrast sensitivity values, which are the inverse of contrast thresholds, can be plotted across these ranges to create a contrast sensitivity function. Under average luminance conditions, the contrast sensitivity function of normal adult observers resembles an inverted U-shape (Kelly, 1977, 1979; B.B. Lee et al., 1990; Legge, 1978; Tolhurst, D.J., Sharpe, C.R., & Hart, C., 1973; Wandell, 1995; Woodhouse & Barlow, 1982). When temporal modulation is low (i.e., 0-1 cycles per second or Hz), the contrast sensitivity function has a bandpass characteristic across a full range of spatial frequencies, with peak sensitivity to spatial frequencies between 2-4 cycles per degree (cpd) of visual angle. When temporal modulation is increased, the contrast sensitivity function becomes low-pass, with better sensitivity to lower spatial frequencies. At these low spatial frequencies, contrast sensitivity is maximized for temporal frequencies of approximately 10 Hz.

The observation of shifts in the contrast sensitivity function due to varying spatial and temporal parameters led to the theory of at least two separate perceptual channels in visual processing, referred to as the transient and the sustained channels (Legge, 1978). Although a complete contrast sensitivity function represents an envelope of the

sensitivities from the different visual streams, the use of minimum thresholds helps to isolate only the most sensitive channel when there is functional overlap at given spatial and temporal frequencies (Smith, 1991). The transient channel has been shown to have higher sensitivity for stimuli with low spatial frequencies (i.e., less than 3 cpd) and high temporal frequencies (i.e., 4-15 Hz), whereas the sustained channel is better stimulated by higher spatial and lower temporal frequencies (Bassi & Lehmkuhle, 1990; Breitmeyer, 1992; Green, 1981; Legge, 1978; Livingstone & Hubel, 1978; Wilson, 1980). These characteristics resemble the distinct neuronal responses of the different anatomical visual streams, with the magnocellular stream responsive to motion, but only coarse patterns, and the parvocellular stream responsive to fine detail, but not motion. Although there is a notable association between the perceptual channels and the anatomical pathways, it should be noted that the mapping is not exact (Merrigan & Maunsell, 1993). Further, the koniocellular stream has not yet been considered in reference to transient and sustained channels. Nevertheless, by assessing contrast sensitivity across a range of spatial and temporal frequencies, the functioning of parallel visual streams can be compared.

Schizophrenia, Luminance Contrast Sensitivity, and Medication

Within the area of psychiatric disorders, contrast sensitivity tests have been used extensively in research on schizophrenia. The first series of studies were conducted by Schwartz and colleagues (Schwartz, McGuinn, & Winstead, 1987; Schwartz, Nelson, Wall, & Winstead, 1985; Schwartz & Winstead, 1985). Deficits were most reliably observed for temporally modulated gratings, indicating transient channel dysfunction.

The sustained channel appeared to be largely intact, although some anomalies were observed. Keri, Antal, Szekeres, Benedek, and Janka (2002) similarly found reduced contrast sensitivity among individuals with schizophrenia compared to healthy control participants when viewing drifting gratings, but additionally noted lower contrast sensitivity to static gratings of medium to high spatial frequencies, suggesting both a transient and sustained channel dysfunction. Broad-band spatial and temporal deficits were also noted in Slaghuis (1998, 2004), but only among individuals with mainly negative symptomology (i.e., anhedonia, affective flattening, paucity of speech content, reduced motivation, deficits in social functioning). Individuals with predominantly positive symptomology (i.e., hallucinations, delusions, thought disorder, odd behaviours) either had moderate difficulty with medium to high spatial frequencies or no impairment at any spatial frequency. Cimmer et al. (2006) more recently found no contrast sensitivity differences between different symptom groups; all schizophrenic individuals performed worse than control participants in response to a low spatial and high temporal frequency grating, indicative of a transient channel deficit. By contrast, Chen, Palafox, et al. (1999) found that a nonsignificant trend of reduced contrast sensitivity for static low spatial frequencies was eliminated with the addition of temporal modulation, indicating a greater motion gain among individuals with schizophrenia compared to healthy controls. This was interpreted as a hyperactive or compensatory mechanism within the transient channel of individuals with schizophrenia. Additionally, two other studies of contrast sensitivity demonstrated no differences between individuals with schizophrenia and healthy control participants (Antal, Keri, Szekeres, Benedek, & Janka, 1999; Chen,

Nakayami, Levy, Matthysse, & Holzman, 1999). Overall, while there is some variability, results of contrast sensitivity tests in schizophrenia most often implicate the transient channel or magnocellular stream, which is consistent with other psychophysical studies of vision for this disorder.

Some variation in results may be due to differences in the medication regimes of individuals with schizophrenia. A study by Chen et al. (2003) found that individuals with schizophrenia who were taking typical antipsychotic medications demonstrated reduced contrast sensitivity to transient channel stimuli, while those receiving atypical antipsychotic medications performed similar to healthy control participants. A review of the medication status of participants in previous studies indicates that this finding may account for many of the discrepant results of earlier research. Further, the Chen et al. (2003) study found that individuals not taking any antipsychotic medications demonstrated elevated contrast sensitivity. This was also observed in a preliminary report by Keri, Antal, Szekeres, Benedek, and Janka (1998) which showed the contrast sensitivity of never-medicated, first-episode schizophrenic patients to be enhanced compared to healthy matched control participants for static and drifting gratings at low spatial frequencies. No differences were noted for medium to high spatial frequencies. These findings suggest that contrast sensitivity deficiencies of individuals with schizophrenia may only be evident among those receiving typical antipsychotic medications, whereas unmedicated schizophrenic individuals may actually possess enhanced contrast sensitivity when mediated by the transient channel or magnocellular stream of the visual system. This has been interpreted as a reflection of enhanced retinal

sensitivity to luminance contrast caused by the elevated levels of endogenous dopamine among individuals with schizophrenia (Chen et al., 2003). The dopamine-antagonist effects of antipsychotic medications are hypothesized to correct, and may even over-compensate for, the contrast sensitivity enhancements associated with schizophrenia.

Not all studies with luminance contrast gratings reveal the same patterns, however. Harris, Calvert, Leendertz and Phillipson (1990) showed that the depot injection of a typical antipsychotic medication resulted in an increase in contrast sensitivity to low spatial frequency gratings and a decrease with medium to high spatial frequency gratings. Because there were no control participants included in this study, it is unclear whether the contrast sensitivity values were above or below normal levels, but the pre- to post- injection changes do not easily fit the hypothesis by Chen et al. (2003) regarding typical antipsychotics. Recent studies with atypical antipsychotics also present some contradiction. O'Donnell et al. (2006) found that individuals with schizophrenia who were taking atypical antipsychotic medications and those who had recently withdrawn from medication performed similarly on tests of contrast sensitivity for transient and sustained channel stimuli, and both groups performed worse than healthy control participants. Similarly, most of the schizophrenic participants in a study by Butler et al. (2005) were taking atypical antipsychotic medications, but nevertheless demonstrated reduced contrast sensitivity with low and medium spatial frequency grating presentations. These researchers noted possible methodological differences that may account for the discrepancy with previous investigations, and called for further research to clarify the effects of medication on contrast sensitivity in schizophrenia.

Anomalies in early-stage visual processing among individuals with schizophrenia are often interpreted as a reflection of the underlying neurotransmitter dysfunction of this disorder. Specifically, schizophrenia is characterized by abnormal transmission of dopamine, which is also a primary neuromodulator of the retina. Disturbance of basic visual functions in schizophrenia may thus be related to the same dopaminergic dysregulation that causes schizophrenic symptomology. In fact, it has been suggested that some of the core symptoms of schizophrenia, such as cognitive fragmentation, thought disorder, and visual hallucinations, may be the result of disturbed visual input causing dysregulation of higher cortical functions (Braff, 1989; Braff & Sacuzzo, 1981; Butler et al., 2006). Variation in early-stage visual processes among individuals with schizophrenia appears to be partly related to the distinct pharmacodynamic actions of different medications. Although all antipsychotic drugs act on dopamine receptors, atypical antipsychotics are characterized by shorter occupancy periods than typical antipsychotics (Seeman & Tallarico, 1999) and also demonstrate more involvement with additional neurotransmitter systems, including serotonergic, histaminergic, and adrenergic processes (Chen et al., 2003). Understanding the effects of medication on visual functioning is important to clarify results of vision studies in schizophrenia. Additionally, neurotransmitter pathology can be explored through the visual corollaries of both medication and the disorder itself.

Depressive Disorders and Luminance Contrast Sensitivity

A handful of studies have begun to explore visual contrast sensitivity within the area of depressive disorders. Early investigations focused exclusively on SAD and relied

on contrast cards and charts to measure contrast sensitivity. Murphy et al. (1993) found no differences in contrast sensitivity between control participants and individuals with SAD measured in the winter season. Gallin et al. (1995) also found no pathological deficits in contrast sensitivity among SAD patients while depressed. However, for 20 of the 40 tested eyes (in 12 of the 20 SAD patients), contrast sensitivity values were borderline low according to normative performance values. Two weeks of phototherapy corrected the baseline abnormality in 9 cases, while contrast sensitivity remained borderline low in the other 11 cases.

Since these earlier studies, computerized measures have been developed to allow for more sensitive assessments of contrast sensitivity which use stimuli that have specific spatial frequency and temporal modulation parameters. Employing these technologies, Szabo et al. (2004) found a nonsignificant trend of lower contrast sensitivity for static gratings among individuals with SAD during a depressive phase, compared to healthy control participants. Four weeks of phototherapy led to increases in contrast sensitivity for both SAD and healthy individuals, although the change was only significant among SAD patients and only for static gratings at low and medium spatial frequencies. Following phototherapy, static contrast sensitivities of SAD individuals and control participants were comparable. Szabo et al. also investigated moving gratings but found no trends or significant results, either in terms of differences between SAD and controls or between pre- and post-treatment performances.

Contrary to the findings of Szabo et al. (2004), which suggested marginal deficits in baseline contrast sensitivity, Wesner and Tan's (2006) investigation of SAD

participants demonstrated enhanced contrast sensitivity to high spatial frequencies in the winter months compared to healthy control participants. These enhancements were noted for static gratings and for gratings modulated at low temporal frequencies, but were not observed for gratings with high temporal modulation. Phototherapy was conducted with a subset of participants and indicated a return-to-normal decrease in contrast sensitivity for high spatial frequency gratings among individuals with SAD (Ly, Wesner, & Tan, 2001).

Although the direction of abnormality is different, the findings of both Szabo et al. (2004) and Wesner and Tan (2006) indicate anomalies in the contrast sensitivity of SAD patients which may be normalized following phototherapy. Also apparent in both studies is the observation that temporal modulation was generally not associated with abnormal contrast sensitivity, pointing away from the transient channel and magnocellular stream of visual processing. This interpretation is consistent with the spatial frequency results of Wesner and Tan, in which affected contrast sensitivities were limited to high spatial frequencies, processed by the parvocellular stream or sustained channel. In Szabo et al. contrast sensitivity enhancements in response to phototherapy were evident for low and medium, but not high, spatial frequencies, suggesting a possible magnocellular involvement that is less coherent with the lack of temporal modulation effects they observed.

Several methodological differences can be noted for these investigations. For example, Wesner and Tan's (2006) study included 46 SAD individuals, while only 10 SAD participants were involved in the study by Szabo et al. (2004). Also, while both studies relied on a forced choice detection paradigm, Wesner and Tan presented

alternatives simultaneously, while Szabo et al. displayed alternatives consecutively, which may affect adaptational processes related to retinal gain mechanisms. Additionally, none of the participants in the Szabo et al. study were taking medication at the time of testing, while a minority of the SAD patients in Wesner and Tan's study were receiving antidepressant medication.

Non-seasonal depression was also explored in Wesner and Tan's (2006) study, with results paralleling those found with SAD. Although less pronounced than among the SAD participants, individuals with non-seasonal depression similarly exhibited elevated contrast sensitivities for high spatial frequencies compared to control participants in the winter months. These enhancements were noted in response to static and low temporal frequency gratings, but not high temporal frequency gratings, comparable to SAD results. Phototherapy also resulted in return-to-normal decreases in the high spatial frequency enhancements of individuals with non-seasonal depression (Ly et al., 2001). Thus, evidence for elevated performance in the sustained channel or parvocellular stream of the visual system was common to both SAD and non-seasonal depression.

Wesner and colleagues (Gallant & Wesner, 2004; Pavlou & Wesner, 2006) conducted preliminary investigations of the effect of season and antidepressant medication on contrast sensitivity in depressive disorders. When measured in the summer months, elevations in contrast sensitivity for high spatial and low temporal frequencies persisted among individuals with SAD compared to control participants, with neither group demonstrating notable seasonal variation in contrast sensitivity functions. Surprisingly, non-seasonally depressed individuals displayed the most seasonal

variability in contrast sensitivity, with their wintertime enhancements diminishing in the summer months to levels comparable to control participants. Standard SSRI treatments did not appear to impact the contrast sensitivity functions of SAD individuals in either the winter or summer testing sessions, with consistent high spatial frequency enhancements displayed regardless of medication status (Gallant & Wesner, 2004). Antidepressant medication similarly did not affect the wintertime contrast sensitivity enhancements of participants with non-seasonal depression, but did exacerbate their summertime reductions. Consequently, among individuals with non-seasonal depression, contrast sensitivity values for high spatial frequency gratings decreased to control participants' levels among those not taking medication, while those receiving standard SSRI treatment demonstrated high spatial frequency contrast sensitivity that was lower than that of control participants in the summer months. Thus, although characterized by seasonal fluctuation in mood symptoms, SAD does not seem to exhibit variability in visual functioning. Instead, non-seasonal depression may be more affected by season and pharmacology with respect to early-stage visual processes.

Both SAD and non-seasonal depression have demonstrated subtle anomalies in basic visual functioning, as indicated by recent psychophysical assessments of luminance contrast sensitivity. However, the nature of abnormality remains to be clarified. Both marginal deficits and significant enhancements in luminance contrast sensitivity have been observed. Further, indications of transient or magnocellular stream involvement are inconsistent, and the degree to which the sustained or parvocellular stream is affected is not clear. Thus, more research is required to verify recent findings and extricate the

contributions of parallel visual streams. The present study will examine luminance contrast sensitivity associated with the magnocellular and parvocellular streams to help clarify these initial findings with respect to depression.

Chromatic Visual Functioning

In addition to spatial and temporal distinctions, magnocellular and parvocellular streams are also distinguished by responsiveness to colour, with chromatic signaling only occurring in the latter. The possible involvement of the parvocellular stream in depressive disorders suggests that an exploration of chromatic visual functioning may be useful. Additionally, the chromatic visual system is itself comprised of distinct channels, which may facilitate further localization of visual anomaly.

The human retina contains three types of cone photoreceptors, which are selectively responsive to different wavelengths of light. Short-wavelength (S-) cones are most sensitive to wavelengths of light around 440 nm; middle-wavelength (M-) cones have peak sensitivity around 530 nm; and long-wavelength (L-) cones are maximally responsive around 560 nm. Signals from the three cone classes are recoded into post-receptoral channels of opponency. One chromatic channel contrasts the signals from L-cones and M-cones, giving rise to a perceptual opponency of "red" and "green". The second chromatic channel contrasts the signals from S-cones with some combination of L- and M-cone signals, resulting in a perceptual opponency of "blue" and "yellow". A third channel focuses on luminance comparisons and corresponds to a perceptual dimension of black and white, with no chromatic distinctions. This luminance channel combines L- and M-cone signals additively, and avoids S-cone input.

Colour and luminance contrast vision in neurodegenerative disorders. Both luminance and chromatic contrast sensitivity have been investigated in neurodegenerative disorders. Studies of multiple sclerosis have found vision deficits in both areas, with chromatic contrast sensitivity more notably affected than luminance contrast sensitivity (e.g., Caruana et al., 2000; Fallowfield & Krauskopf, 1984; Flanagan & Markuleve, 2005; Flanagan & Zele, 2004; Travis & Thompson, 1989). Impairment for "red-green" contrasts has been found to be more severe than impairment for "blue-yellow" contrasts, although both are associated with worse performance in multiple sclerosis patients than among healthy control participants (Flanagan & Markuleve, 2005; Flanagan & Zele, 2004; Travis & Thompson, 1989). Alzheimer's disease has similarly demonstrated both broad-band luminance and selective chromatic contrast deficits, in the latter case related to short-wavelength or "blue" light (e.g., Cronin-Golomb et al., 1995; Gilmore, Koss, Wenk & Whitehouse, 1993; Kurylo et al., 1994). Studies of Parkinson's disease have documented pronounced losses of luminance contrast sensitivity, most commonly associated with the middle range of spatial frequencies, to which normal observers are most sensitive (e.g., Bodis-Wollner, 1990, 2002; Bodis-Wollner et al., 1987; Diederich et al., 2002; Marx et al., 1986), as well as some impairment in colour vision which also appears to be selective for short-wavelength or "blue" light (e.g., Buttner et al. 1995; Haug, Kolle, Trenkwalder, Oertel, & Paulus, 1995; Pieri, Diederich, Raman, & Goetz, 2000; Price, Feldman, Adelberg, & Kaynes, 1992).

Colour vision and depressive disorders. Colour vision has received little attention in the area of psychiatric disorders. Isolated studies of vision in schizophrenia

have tested chromatic functioning, relying on a battery of standard clinical tests (Shuwairi, Cronin-Golomb, McCarley, & O'Donnell, 2002) or psychophysical tests using patterns of squares or vernier stimuli (Butler et al., 2001; Keri, Kelemen, Benedek, & Janka, 2004; Keri, Kelemen, Janka, & Benedek, 2005), but not contrast gratings. These have not evidenced any colour vision impairments, which fits with the most consistent finding of magnocellular deficits in schizophrenia.

In mood disorder research, psychophysical measurements of chromatic visual functioning have not been reported. Instead, clinical tests of colour vision have been described in two ophthalmic investigations of SAD. Specifically, Oren et al. (1993) found no colour vision deficiencies in his study of SAD patients in the winter months and Gallin et al. (1995) similarly found that two weeks of phototherapy was not associated with changes in colour perception. Interestingly, three patients had a previous diagnosis of "red-green" colour deficiency, but nevertheless demonstrated an antidepressant response to bright light therapy.

Some wavelength specificity has been found in research exploring parameters of effective phototherapy in SAD. A meta-analysis conducted by T.M. Lee, Chan, Paterson, Janzen and Blashko (1997) concluded that long-wavelength light was neither necessary nor sufficient to produce antidepressant effects in SAD patients. By comparison, short- and medium-wavelengths of light were related to symptom improvement. The studies used for analysis by Lee and colleagues were limited, however, in their ability to isolate specific wavelengths. Light sources used at the time were associated with relatively large bandwidths, even when designed to focus on specific wavelengths. A recent study,

relying on an LED light source to produce more narrow-bandwidth light, exposed SAD patients to three weeks of either bright light limited to short-wavelengths (468 nm) or dim long-wavelength light (654 nm) included as a placebo control (Glickman, Byrne, Pineda, Hauck, & Brainard, 2005). Symptom improvement was evident in both groups of SAD patients, but the change was significantly higher among those treated with bright short-wavelength light. Because a condition of broad-band "white" light was not used, it is unclear how the narrow-band short-wavelength light compares to the current standard protocol for phototherapy treatment. Nevertheless, this study does indicate that short-wavelength or "blue" light is sufficient to induce an antidepressant effect significantly better than placebo. Short-wavelength light has also been found to be more potent than longer wavelengths at shifting circadian rhythms of melatonin (Lockley, Brainard, & Czeisler, 2003), which has been discussed as a possible mechanism for phototherapeutic efficacy.

Ly et al. (2001) investigated the effects of bright light treatment on luminance contrast sensitivity among individuals with SAD and non-seasonal depression, as well as healthy control individuals. Participants underwent seven days of one-hour light sessions involving either broad-band "white" light, narrow-band short-wavelength or "blue" light (440 nm), or narrow-band "yellow" light (580 nm). Prior to treatment, individuals with SAD and non-seasonal depression demonstrated higher contrast sensitivity at medium and high spatial frequencies than control participants. These enhancements were reduced to normal levels following treatment with broad-band "white" light and narrow-band "blue" light. No changes in contrast sensitivity resulted from the narrow-band "yellow"

light. Thus, it was concluded that the contrast sensitivity enhancements among individuals with SAD and non-seasonal depression were corrected by bright light treatment, but only if it included short-wavelength light. Of note, the narrow-band "blue" light condition was also associated with some reduction of CS in healthy control participants.

Seggie et al. (1989) has similarly demonstrated enhanced dark adapted sensitivity to "blue" light points that was normalized following treatment with antidepressant medication. His study was not designed to test chromaticity, however, so no other wavelengths of light were used for comparison. A report by Lagerloff (1982) assessed colour vision directly among a group of individuals being treated with tricyclic psychotropics. Fourteen participants were taking tricyclic antidepressants, ten were taking neuroleptics with a tricyclic molecular structure, and twelve were taking benzodiazepines with a tricyclic molecular structure. Of the 72 eyes tested, 60 demonstrated "blue-yellow" colour deficiency as measured by clinical tests, while none showed evidence of "red-green" impairment. Among participants taking standard tricyclic antidepressants, 24 of the 28 eyes tested displayed "blue-yellow" deficits. These rates are substantially higher than those in the general population and Lagerloff accordingly concluded that acquired Type III colour deficiency is common with tricyclic pharmacology. However, it is not clear whether Lagerloff controlled for the age of his participants, most of whom were over 50 years old. Since increasing age is associated with reduced sensitivity to short-wavelength light (Gaillard, Zheng, Merriam, & Dillon,

2000; Packer & Williams, 2003; Werner, Peterzell, & Scheetz, 1990), this could offer an alternative explanation to his findings other than the effects of tricyclic medication.

In sum, psychophysical assessment of chromatic visual functioning has not yet been conducted within the area of depressive disorders. Although studies of SAD have reported no impairment on standard clinical tests of colour vision, these measurements often lack the sensitivity to detect anything less than clinical dysfunction (see Silva et al., 2005) and are also not capable of identifying possible enhancements in performance. Treatment studies have provided some suggestion that chromatic processes are involved in depressive disorders. For instance, effective phototherapy has been associated with wavelength selectivity; visual mechanisms which process short-wavelength light, and possibly medium-wavelength light, are important for an antidepressant response in SAD patients, whereas the processing of long-wavelength light appears ineffective. One interpretation is that short-wavelength or "blue" light corrects circadian mechanisms related to mood impairment. At the same time, repeated exposure to short-wavelength light has been shown to normalize contrast sensitivity elevations in SAD and non-seasonal depressed individuals, which may mean that the adaptation or desensitization of short-wavelength light mechanisms also corrects vision abnormalities. Additionally, tricyclic antidepressant medication may diminish "blue-yellow" colour vision, although this needs to be confirmed. Overall, information on chromatic visual functioning in depressive disorders is sparse, but does indicate that further research, particularly in relation to short-wavelength visual processing, is warranted. The present study will examine chromatic contrast sensitivity and S-cone sensitivity in order to gain a better

understanding of the involvement of distinct channels of colour vision in depression and its treatment.

Summary of Vision Research in Depressive Disorders

The investigation of early visual processing in mood disorders is still in its infancy and more research is needed to extend knowledge regarding the full range of mood disorders, clarify the involvement of parallel visual streams, elucidate seasonal patterns, and confirm the effects of treatment, including phototherapy and antidepressant medications. Nevertheless, initial research does suggest that depressive disorders are associated with abnormal functioning in early stages of the visual system. Both SAD and non-seasonal depression have been associated with abnormal luminance contrast sensitivity, as well as chromatically selective effects involving the processing of short-wavelength light. Chromatic mechanisms related to S-cones comprise a distinct channel of colour vision, with demarcation beginning in the first layer of the retina. Fundamental aspects of luminance and chromatic contrast detection, such as those measured by sinusoidal gratings, are processed in early stages of the visual system (DeValois & DeValois, 1990; Sclar, Maunsell, & Lennie, 1990; Shapley & Enroth-Cugell, 1984). Although contrast sensitivity degradation may, in fact, arise anywhere along the visual hierarchy, the finding of possible enhancement argues strongly for mechanisms involved in the initiation of the signal. In particular, with the lowest signal to noise ratios of the visual system, the retina acts as the limiting neural agent, setting ceiling levels for higher order visual performance (Attwell, 1986; Atwell & Wilson, 1983). In concert with observations of abnormal retinal light sensitivity in dark adaptation, ERG, and EOG

studies of SAD and non-seasonal depression, the observed irregularities in chromatic processing and luminance contrast sensitivity suggest that visual anomalies in depressive disorders are at least partly associated with early stages of the visual system, are retinally based, and involve not only vegetative functioning, but visual perception pathways as well.

The retina is a particularly accessible part of the brain for investigation, both in terms of structure and function. Consequently, understanding of the retina has proceeded faster than that of other areas of the nervous system, and retinal research has greatly contributed to knowledge regarding phenomena of general importance to the field of neuroscience (Ames & Nesbett, 1981; Dowling, 1987; Kolb, Nelson, Ahnelt, & Curcia, 2001). Representing approximately 0.5% of the human brain, the retina involves the same mechanisms of communication found throughout the nervous system, including the same neurotransmitter and neuromodulator systems (Sterling & Demb, 2004). Dysfunction in retinal communication processes may reflect dysfunction in similar processes elsewhere in the brain. Thus, in both schizophrenia and Parkinson's disease, early-stage vision dysfunctions are considered to be a consequence of the neurotransmitter dysregulation inherent to the illness.

Neurotransmitters in Depressive Disorders

Neurotransmitters have played a central role in biological theories of mood disorders, beginning with the original monoamine theories of the 1960s which first implicated norepinephrine (Schildkraut, 1965), then serotonin (Coppen, 1967), in the pathogenesis of depression. The following decade saw an additional interest in dopamine

as a forerunner in monoaminergic models of mood disorders (Randrup et al., 1975). These early theories proposed that symptoms of depression were the result of reduced levels of the specified monoamine and were based upon the observed therapeutic effectiveness of pharmaceutical compounds acting on respective monoaminergic transmitter systems (Slattery, Hudson, & Nutt, 2004). Subsequent research, however, suggests that a simple deficiency model is insufficient to explain the involvement of monoamines in mood disorders.

While some research has found support for reduced levels of monoamine transmitters in depression, results are inconsistent overall (e.g., Cheetham, Katona, & Horton, 1991; Duman, Heninger, & Nestler, 1997; Kalia, 2005; Manji, Drevets, & Charney, 2001; Nestler et al., 2002). Moreover, antidepressant medications cause an immediate increase in synaptic levels of monoamines, but the associated mood improvements are generally not evident until after at least ten to fourteen days of continued administration. Thus, contemporary biological theories of depression do not address monoamines as direct etiological agents, but rather emphasize their extensive modulatory actions on a range of other neural processes, including mechanisms of neurogenesis and interactions with stress hormones (e.g., Arborelius, Owens, Plotsky, & Nemeroff, 1999; Duman, 2002, 2004; Malberg & Schecter, 2005; McEwen, 2005; Nestler et al., 2002; Norman, 2006; Pariante & Miller, 2001; Slattery et al., 2004; Young, Bakish, & Beaulieu, 2002) . Indeed, the number of monoaminergic neurons in the brain is relatively small compared to other transmitter systems, but their axonal projections are

distributed widely throughout the central nervous system and interact with a diversity of other neurochemicals and receptors (Kalia, 2005).

Recent investigations have begun to explore the relationship between mood disorders and the more prevalent amino acid transmitters. A growing body of evidence implicates both GABA, which is the primary inhibitory neurotransmitter in the brain, and glutamate, the main excitatory neurotransmitter. Abnormal levels of these transmitters have been associated with mood disorders (Brambilla, Perez, Barale, Schettini, & Soares, 2003; Choudry et al., 2005; Kelmendi, Saricicek, & Sanacora, 2006; Paul & Skolnick, 2003; Sanacora et al., 2004). Pharmacological compounds which affect the GABAergic and glutamateric systems have shown antidepressant efficacy (Brambilla et al., 2003; Kendell, Krystal, & Sanacora, 2005; Sanacora, Rothman, Mason, & Krystal, 2003; Slattery & Cryan, 2006; Zarate et al., 2004, 2006). Current medication treatments for mood disorders exert modulatory effects on both of these systems (Kelmendi et al., 2006; Sanacora, Mason, Rothman, & Krystal, 2002; Slattery & Cryan, 2006), which is likely related to the known interactions of both GABA and glutatmate with serotonin and dopamine in the CNS (Gong, Neil, & Justice, 1998; Kelmendi et al., 2006; Kendell et al., 2005; Varga, Sik, Freund, & Kocisis, 2002).

Antidepressant medications. Although recent inquiries are exploring neural processes beyond a simple monoamine deficiency model, it should be noted that the currently approved antidepressant medications in clinical use exert their primary effects through increases in synaptic levels of serotonin, norepinephrine, and dopamine, alone or in combination, and this increase does lead to therapeutic improvements in mood

(Slattery et al., 2004). There are several classes of antidepressants that vary in terms of their method of increasing monoamine functioning as well as their degree of involvement with the different monoamines (Marangell & Martinez, 2006; Schatzberg, Cole, & DeBattista, 2005). First generation antidepressant medications, including monoamine oxidase inhibitors (MAO-Is) and tricyclic antidepressants (TCAs), increase the availability of monoamines in a non-selective manner, leading to notable side-effects along with symptom improvement. Second generation antidepressants have been designed to limit their actions to specific monoamines. Serotonin has been a primary focus of the majority of these newer drugs, which include several selective serotonin reuptake inhibitors (SSRIs), as well as 5-HT receptor antagonists. The norepinephrine system is targeted by selective norepinephrine reuptake inhibitors and mirtazapine, a norepinephrine modulator. Dual-action antidepressants include those which affect both serotonin and norepinephrine levels, as well as bupropion, which increases norepinephrine and dopamine. It is worth noting that the various pharmacological profiles of antidepressant medications may also have differential effects on retinal neurotransmission.

The use of antidepressant medications has increased steadily since their introduction, with a particularly dramatic rise in prevalence in recent years. Analysis of a province-wide person-specific pharmacy database found that 7.2% of British Columbia residents had filled an antidepressant prescription in 2004, compared to only 3.4% in 1996 (Raymond, Morgan, & Caetano, 2007). These prevalence rates were consistent with other Canadian reports (Beck et al., 2005; Fransoo et al., 2005) and reflect a trend of

increasing antidepressant use that has been observed in several North American and European studies (Mant et al., 2004; Olfson et al., 2002; Poluzzi et al., 2004; Rosholm, Andersen, & Gram, 2001; Stagnitti, 2005, as cited in Patten, Esposito, & Carter, 2007). One explanation for this trend is the notable expansion of therapeutic indications for antidepressant medications. Various SSRIs and serotonin norepinephrine reuptake inhibitors (SNRIs) have been approved for the treatment of anxiety disorders, including obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), generalized anxiety disorder (GAD), and social phobia (Marangell & Martinez, 2006; Physicians' Desk Reference, 2007; Schatzberg et al., 2005). Additionally, antidepressant medications are prescribed for the treatment of bulimia, borderline personality disorder, attention-deficit disorder, autism, neuropathic pain conditions, sexual dysfunction, migraine headaches, and smoking cessation (Larson, Miller, & Fleming, 2007; Marangell & Martinez, 2006; Patten et al., 2007; Schatzberg et al., 2005; Stone, Viera, & Parman, 2003). In 2005, just under two-thirds of the antidepressant medication treatments recommended by a representative sample of Canadian physicians were for reasons related to depression (Patten et al., 2007). Thus, there is widespread applicability for antidepressant pharmacology, especially the second generation drugs which are generally better tolerated than original antidepressant medications, although nevertheless associated with their own sets of side-effects (Marangell & Martinez, 2006; Schatzberg et al. 2005). Diverse uses of antidepressant medication make it possible to examine their effects outside of depression, which may help disentangle the influence of drug versus disorder in studies of visual functioning.

Visual consequences of antidepressant medication. Ophthalmic side-effects are common with the use of antidepressant medications. Tricyclic antidepressants, in particular, are frequently accompanied by visual disturbances due to their high affinity for muscarinic acetylcholine receptors leading to notable anticholinergic side-effects (Schatzberg et al., 2005). Blurred vision occurs in 30% of patients beginning TCA treatment (Oshika, 1995) and is usually caused by interference with accommodation due to cycloplegia, a paresis of the ciliary muscles of the lens (Pollack & Rosenbaum, 1987; Pollack & Smoller, 1996; Riedel & van Praag, 1995). Disturbances of near vision or presbyopia are also common with TCAs as a result of mydriasis, which involves pupillary dilation and sluggish pupillary reaction to light (Pollack & Rosenbaum, 1987; Pollack & Smoller, 1996; Riedel & van Praag, 1995). These conditions tend to remit after a few weeks of treatment and are generally reported as mild to moderate disturbance. However, more serious ophthalmic conditions are also possible with TCA use, such as increased intraocular pressure and increased risk of acute glaucoma (Oshika, 1995; Pollack & Rosenbaum, 1987; Pollack & Smoller, 1996; Riedel & van Praag, 1995). Other types of antidepressant drugs, including newer medications, are similarly associated with visual disturbances, despite minimal anticholinergic effects. Duloxetine is linked to an increased risk of glaucoma due to mydriasis (Marangell & Martinez, 2006). Imipramine and nefazodone are commonly discontinued by patients due to complaints of amblyopia (Preskorn, 1995). Nefazodone and trazodone are both associated with blurred and abnormal vision, including scotoma, palinopsia, and visual trails (Marangell & Martinez, 2006; Mosberian, Leung, Hollander, & Remick, 1999;

Schatzberg et al., 2005; Schwartz, 1997). MAO-Is have mild effects on accommodation, leading to blurred vision (Oshika, 1995). In fact, blurred or abnormal vision is listed as a side-effect for nearly all antidepressant medications (P hysician's Desk Reference, 2009). Side-effects studies generally do not investigate causal mechanisms or report on the severity or duration of these side-effects, so the nature of these visual disturbances is often unclear. Nevertheless, taken as a whole, the literature indicates that antidepressant pharmacologies are commonly associated with ophthalmic dysfunction.

Only one study has directly examined the effect of antidepressant medication on early-stage visual processing. Seggie et al. (1989) found that two to six weeks of treatment with doxepin, a TCA, decreased the light sensitivity of depressed participants in a dark adaptation study. Specifically, cone-mediated sensitivity, which had been elevated prior to treatment, was normalized to levels similar to those of healthy control participants. Rod-mediated sensitivity, which had previously been comparable to control levels, was significantly lower in depressed individuals following treatment. This finding of reduced retinal light sensitivity is similar to results regarding the visual effects of lithium (Wirz-Justice et al., 1997), a mood stabilizer used to treat bipolar depressive disorder.

Contrast sensitivity has been explored in a study using nomifensine, a dopamine reuptake inhibitor which was originally used as an antidepressant in the 1970s, but is now restricted to research purposes due to concerns about its long-term use. An investigation of healthy volunteers found that a single dose of nomifensine increased contrast sensitivity for medium and high spatial frequencies and lowered contrast

sensitivity to spatial frequencies below 2 cpd (Domenici, Trimarchi, Piccolino, Fiorentini, & Maffei, 1985). The same study also examined the effects of levodopa, a precursor to dopamine commonly used to treat Parkinson's disease. Results were similar among healthy volunteers, with a single dose of levodopa increasing contrast sensitivity for medium spatial frequencies most notably, as well as high spatial frequencies. This is consistent with other studies of levodopa that found contrast sensitivity improvements for patients with Parkinson's disease (e.g., Hutton, Morris, & Elias, 1993; Mestre, Blin, van den Brand, Azulay, & Serratrice, 1996; Pierelli et al., 1988). Other medications used in the treatment of Parkinson's disease have also been associated with contrast sensitivity effects. For example, healthy volunteers were tested with apomorphine, a dopamine agonist, and demonstrated reduced contrast sensitivity for low spatial and high temporal frequencies, as well as elevated contrast sensitivity for high spatial frequencies (Blin, Mestre, Masson, & Serratrice, 1991). Piribedil, another dopamine agonist used for Parkinson's disease, improved age-related contrast sensitivity deficits for low spatial frequencies among healthy elderly individuals (Corbe, Arnaud, Brault, & Janiak-Bolzinger, 1992). Finally, contrast sensitivity has also been explored in relation to lorazepam, which acts on GABA receptors, and is most commonly used as an anxiolytic. A single dose of lorazepam in healthy volunteers resulted in reduced contrast sensitivity to moving gratings which was most pronounced at lower spatial frequencies and not apparent above 8 cpd (Harris & Phillipson, 1995). Among long-term lorazepam users, impaired contrast sensitivity was observed in the low to middle range of spatial

frequencies, particularly between 1 and 4 cpd (Giersch, Speeg-Schatz, Tondre, & Gottenkiene, 2006).

The use of antidepressant medication has commonly been linked with certain visual side-effects, but these are generally related to disturbances in the optics of the eye, including the lens and pupil. Investigation of visual functions related to the retina and other early neural processes has been minimal, but does indicate that antidepressant medication can impact early-stage neural functions of the visual system. As evident in schizophrenia research, an understanding of pharmacological effects is important at the outset of vision research in depressive disorders. Thus, one of the primary purposes of the present study is to examine the consequences of antidepressant medication on basic visual functions, including luminance and chromatic contrast sensitivity.

Retinal Connections and Communication

A number of disorders that involve substantial dysregulation of brain neurotransmitters have demonstrated abnormal visual functioning. Similarly, the neurotransmitter actions of neuropharmacological medications are also known to induce visual disturbances related to both the optics and neural processes of the early visual system. In the area of mood disorders, vision research is relatively new but does indicate anomalies of light sensitivity, luminance contrast sensitivity, and chromatic functioning, all of which are dependent upon the connections and neurotransmission of information in the retina before being processed by central visual systems.

Several layers of neurons compose the retina (see Sterling & Demb, 2004, for review). Photoreceptors are the first of these, collecting light which has traveled through

the pupil and lens and arrived at the back of the eye. Their primary job is to transduce light energy into neural energy. Photoreceptors connect to bipolar cells in the outer plexiform layer, which connect to ganglion cells in the inner plexiform layer, whose axons gather to form the optic nerve. These connections represent the forward transmission of neural information through the eye to visual areas in the rest of the brain. There are also neurons for lateral communication at each of these layers; horizontal cells extend across the outer plexiform layer and amacrine cells run laterally throughout the inner plexiform layer. Lateral processes coordinate information across the expanse of the eye and are integral in shaping the receptive fields of bipolar and ganglion cells involved in forward transmission.

There is substantial diversity in the methods of neural communication observed in the retina, including conventional chemical synapses, chemical synapses that involve synaptic ribbons, and electrical synapses, such as gap junctions between neighbouring neurons. Most retinal neurons use graded potentials, signaling an increase or decrease of activity through an incremental disruption of sustained transmitter release. Action potentials are only observed in ganglion cells, whose axons extend a notable distance through the optic nerve, as well as certain amacrine cells. Chemical communication occurs both traditionally, with neurotransmitters released into synaptic clefts, as well as in a paracrine or hormone-like manner, where certain transmitters diffuse throughout retinal space to affect neurons distant from the site of release (Witovsky, Nicholson, Rice, Bowmaker, & Meller, 1993; Yazulla & Studholme, 1995).

Neurotransmitters in the retina. Essentially all of the neurotransmitters found throughout the CNS are evident in the retina (Sterling & Demb, 2004). Glutamate and GABA are the most prominent retinal transmitters, involved in excitatory and inhibitory responses, respectively. Glutamate is the primary transmitter of forward transmission, released by photoreceptors onto bipolar and horizontal cells and by bipolar cells onto ganglion and amacrine cells. GABA is the primary transmitter of lateral transmission, released by horizontal cells onto cone terminals and bipolar cells and by amacrine cells onto bipolar and ganglion cells. Many retinal neurons contain more than one transmitter. For example, certain bipolar cells release both glutamate and GABA (Kao et al., 2003). Half of amacrine cells contain glycine, while the other half contain GABA. The latter also often contain a second transmitter, such as acetylcholine, various neuropeptides, or monoamines, including dopamine and serotonin (Casini & Brecha, 1992; Sagar, 1987; Vaney, 1990, 2003).

Dopamine has been established as a major retinal neurotransmitter and neuromodulator, involved in multiple processes throughout the retina, including mechanisms of contrast detection and light adaptation. It is present in certain amacrine and interplexiform cells of mammalian retina (Djamgoz, Hankins, & Archer, 1997; Frederick, Rayborn, Laties, Lam, & Hollyfield, 1982; Massey & Redburn, 1987), synthesized in conditions of light and released in a graded light-dependent manner (Djamgoz & Wagner, 1992; Haggendal & Malmfors, 1965; Iuvone, Galli, Garrison-Gund, & Neff, 1978). Several classes of dopamine receptors have been identified in the retina, associated with different processes or in some cases, associated with the same

process, but with antagonistic regulatory effects (Djamgoz et al., 1997). As well as working at conventional synapses, dopamine also acts in a paracrine fashion. For example, dopamine released by amacrine cells in the inner plexiform layer diffuses through the retina to inhibit the gap junction connections of horizontal cells and photoreceptors in the outer plexiform layer (DeVries & Schwartz, 1989; Dowling, 1991; Piccolino, Neyton, Gerschenfeld, 1984; Lasater & Dowling, 1985; Sterling & Demb, 2004; Teranishi, Negishi, & Kato, 1983, 1984).

Contrast sensitivity is affected by dopamine modulation of receptive field organization (Djamgoz et al., 1997). This is largely achieved through inhibition of gap junction coupling in horizontal cells, which feed the surround portion of receptive fields in forward transmission (Kaneko, 1973). By regulating the spatial summation of lateral neurons, dopamine modulates the center-surround signal of forward neural pathways, which is critical for contrast detection. Dopamine deficiency, induced experimentally in animal studies and in pathological hypodopaminergic conditions, such as Parkinson's disease, results in decreased contrast sensitivity, with some studies finding reductions limited to low spatial frequencies and other studies reporting decreases most apparent for medium and high spatial frequencies (e.g., Bodis-Wollner, 1988, 1990; Ghilardi, Bodis-Wollner, Onofrj, Marx, & Glover, 1988; Masson, Mestre, & Blin, 1993; Tagliati, Bodis-Wollner, & Yahr, 1996). Conversely, an excess of dopamine may lead to increased contrast sensitivity. In pharmacological studies with healthy volunteers, the administration of a dopamine agonist results in enhanced contrast sensitivity for medium to high spatial frequencies and a tendency toward reduced sensitivity to low spatial

frequencies (Domenici et al., 1985; Masson et al., 1993). Investigation of drug treatments for Parkinson's disease and animal studies have similarly observed that the effects of dopamine on contrast sensitivity vary according to spatial frequency, causing low frequency attenuation and medium to high frequency amplification (Bodis-Wollner, 1987, 1990; Hutton, Morris, Elias, 1993). This may be due to different dopamine receptors; some evidence suggests that D1 receptors are associated with low spatial frequencies, attributed to their presumed involvement with large-centre ganglion cells, while D2 receptors are associated with medium and high spatial frequencies, related to possible center-response amplification of ganglion cells with smaller centres (Bodis-Wollner & Tzelepi, 1998; Stormann, Gdula, Weiner & Brown, 1990). Dopamine has also been implicated in the contrast gain associated with temporal modulation and illumination levels (Jensen & Daw, 1986; Masson et al., 1993).

The bipolar and ganglion cells of forward retinal pathways are thought to be affected by dopamine directly, as well as the indirect effects caused by dopaminergic modulation of the lateral neurons they connect with. Specifically, both the spontaneous and light-evoked responses of bipolar and ganglion cells have been shown to be influenced by dopamine (Djamgoz et al., 1997; Djamgoz & Wagner, 1992; Holopigan, Clewner, Seiple, & Kupersmith, 1994; Jensen & Daw, 1988; Maguire & Hamasaki, 1994; Maguire & Werblin, 1994; Shiells & Falk, 1985; Wellis & Werblin, 1995). Additionally, some ganglion cells use dopamine as a neurotransmitter in their communication with central areas of the visual system (Simon & Nguyen-Legros, 1995).

Dopamine is also known to regulate the efficiency of other retinal transmitter systems, including GABA and glutamate (Yazulla & Kleinshmidt, 1982).

Dopamine is mainly active in light or day phases, and is thus linked primarily to cone-mediated vision and the transition to photopic vision (Djamgoz et al., 1997; Djamgoz & Wagner, 1992; Dong & McReynolds, 1991; Godley & Wurtman, 1988). Photoreceptor disc shedding is inhibited by dopamine (Besharse, Iuvone, & Pierce, 1988). Additionally, dopamine potentiates the glutamatergic input of photoreceptors to horizontal cells (Hankins & Ikeda, 1991; Hedden & Dowling, 1978; Knapp & Dowling, 1987). Because there is cone selectivity in connections between photoreceptors and horizontal cells (Ahnelt & Kolb, 1994), dopamine regulation at this level may be associated with chromatic signal specificity (Djamgoz et al., 1997).

There is a mutually antagonistic relationship between dopamine and melatonin in the retina which optimizes the visual system's adaptation to natural cycles of dark and light (Morgan & Boelen, 1996). Specifically, dopamine production is stimulated by light and inhibited by melatonin, while melatonin synthesis occurs in dark conditions (Dubocovich, 1983; Dubocovich, Lucas, & Takahashi, 1985) and is inhibited by dopamine (Cohen, Todd, Harmon, & O'Malley, 1992; Tosini & Dirden, 2000). Importantly, serotonin is a precursor to retinal melatonin. Processes which affect the conversion of serotonin to melatonin thus alter the availability of retinal serotonin.

Serotonin has been implicated in retinal functioning for several decades (Ames & Pollen, 1969). Indoleamine accumulating cells (IACs) are specific amacrine cells in the retina that actively take up serotonin through both high and low affinity transporter

mechanisms (Brunken, Jin, & Pis-Lopez, 1993; Ehinger & Holmgren, 1979; Holmgren-Taylor, 1982; Matsumoto, Ueda, & Kawata, 1992; Osborne & Barnett, 1990; Osborne, Nesselhut, Nicholas, Patel, & Cuello, 1982; Sandell & Masland, 1986; Sandell, Masland, Raviola, & Dacheux, 1989; Wassle, Voigt, & Patel, 1987). IACs do not appear to synthesize notable amounts of endogenous serotonin, however. In fact, only low levels of endogenous serotonin have been found in mammalian retina, most of which appears to be synthesized by photoreceptors as a precursor for melatonin (Chanut, Nguyen-Legros, Labarthe, Trouvin, & Versaux-Botteri, 2002; Ehinger & Floren, 1978; Gastinger, Tian, Horvath, & Marshak, 2006; Osborne, 1980, 1984; Osborne & Barnett, 1990; Redburn & Churchill, 1987). However, all major serotonin receptors have been identified in the retina (Mitchell & Redburn, 1985; Osborne et al., 1993; Perez-Leon, Sarabia, Miledi, & Garcia-Alcocer, 2004; Pootanakit & Brunken, 2000, 2001; Pootanakits, Prior, Hunter, & Brunken, 1999), indicating that, in addition to serving as a melatonin precursor, serotonin also plays a role in retinal neuromodulation and/or neurotransmission.

Serotonin is the primary transmitter for one of two sets of retinopetal axons that extend into the retina from other parts of the brain (Chanut et al., 2002; Gastinger et al., 2006; Gastinger & Marshak, 2005; Lima & Urban, 1998). These are not specialized to supply the retina, but rather are a subset of ascending arousal systems that project throughout the CNS. The centrifugal fibers of the serotonergic retinopetal system originate in the dorsal raphe and branch mainly in the layer of retinal ganglion cells (Gastinger et al., 2006). Serotonin released by these fibers is used as a transmitter by retinal neurons and collected by IACs (Gastinger et al., 2006). The majority of IACs

arborize extensively in the inner plexiform layer, forming a dense network that spans the retina, while a smaller number of IACs distribute sparsely through both the inner and outer plexiform layers (Sandell & Masland, 1986).

Indoleamine accumulating cells form reciprocal synaptic connections specifically with rod bipolar cells, suggesting a role for serotonin in scotopic or mesopic conditions of illumination (Daw, Brunken, & Parkinson, 1989; Daw, Jensen, & Brunken, 1990; Fletcher & Wassle, 1999; Sandell et al., 1989). Serotonin is also important in scotopic or mesopic vision as a precursor for melatonin, which is synthesized in dark conditions. Alternatively, investigators have observed a light-evoked release of retinal serotonin (Ames & Pollen, 1969; Brunken & Daw, 1988a; Mangel & Brunken, 1992; Valenciano, Alonso-Gomez, & Iuvone, 1999). This may be related to the serotonergic retinopetal axons, which fire most rapidly during waking hours, thus releasing more serotonin during the day among diurnal animals (Gastinger et al., 2006). Consequently, serotonin is also involved in photopic vision.

All classes of ganglion cells receive input from IACs and appear to be the primary target of most serotonin activity in the retina (Brunken & Daw, 1987, 1988a; Brunken et al., 1993). Serotonergic agents impact the principal functions of ganglion cells, which are responsible for retinal output to higher areas of the visual system. Specifically, serotonin affects the spontaneous activity, light-evoked response, and receptive field surrounds of ganglion cells (Brunken & Daw, 1986, 1987, 1988a, 1988b; Brunken et al., 1993; Brunken & Jin, 1993; Sandell et al., 1989). The direction of effect is dependent on which serotonin receptors are activated. Pharmacological studies indicate

that 5-HT_2 receptors are linked to enhanced ganglion cell activity, whereas 5-HT_{1A} receptors are associated with reduced ganglion cell activity (Brunken et al., 1993; Mangell & Brunken, 1992; Osborne & Barnett, 1990). Although the application of serotonergic agents does not appear to have direct impact on photoreceptors, horizontal cells, or bipolar cells, part of their influence on ganglion cell activity is mediated through these preliminary processes. For instance, while serotonin does not alter the responding of horizontal cells, it does modulate their ability to affect ganglion cells' surround fields (Mangel & Brunken, 1992). Also, the application of serotonin does not lead to any immediate effects on bipolar cells, but is associated with a slower, long-lasting potentiation of their response to photoreceptor input, suggesting that serotonin may be involved in the adaptational processes of bipolar cells (Skrandies & Wassle, 1988). Additionally, serotonin affects the release of other retinal neurotransmitters, including modulation of GABA and inhibition of dopamine (Neal, Cunningham, & Matthews, 2001; Perez-Leon et al., 2004; Gastinger et al., 2006).

Both serotonin and dopamine have been the focus of monoamine theories of depression and pharmacological intervention. Although a simple deficiency hypothesis has been excluded, alterations in brain levels of serotonin and dopamine exert significant modulatory effects on other processes and downstream systems, and they remain the initial locus of currently available antidepressant medications. Their important role in basic visual functions provides a link between depressive disorders and possible vision disturbance. That is, dysregulation of serotonergic and dopaminergic systems in central brain regions may also manifest in disruption of these systems in the retina and other

early stages of visual processing. Similarly, GABA and glutamate, the primary retinal neurotransmitters, have recently been implicated in the pathophysiology of depressive disorders.

Chromatic visual channels. The possible involvement of chromatic processes in visual anomalies of depressive disorders also draws attention to distinct pathways of colour vision communication in the early stages of the visual system. Wavelength specific signals from the S-, M-, and L-cone photoreceptors are recoded into "red-green" and "blue-yellow" colour opponent channels in subsequent retinal neurons; the "red-green" channel contrasts signals from L- and M-cones and the "blue-yellow" channel contrasts S-cone signals with L- and M-cone signals combined. The two chromatic channels are thought to have evolved at different times and for different purposes and their substrates remain anatomically distinct. The majority of cone photoreceptors in the human retina are of the L- and M-cone types, which are densely packed in the fovea and decline in number with increasing eccentricity. S-cones comprise fewer than 10% of all cones (Dartnall, Bowmaker, & Moller, 1983). They are sparsely distributed across the retina, being most prevalent just outside the fovea, then declining gradually with increasing eccentricity. Inside the fovea, S-cones are scarce and appear to be entirely absent at the fovea centralis. It was initially believed that both colour-opponent channels were mediated by the parvocellular stream. However, it is now understood that not only are the "red-green" and "blue-yellow" channels associated with distinct cell morphologies and physiologies, but they also occupy separate retino-cortical projecting

streams (Dacey, 1999; Goodchild & Martin, 1998; Hendry & Reid, 2000; Martin, White, Goodchild, Wilder, & Septon, 1997).

The retinal connections related to S-cones are discrete and largely independent from L- and M-cone connections. Among L- and M-cones, small gap junctions couple immediate neighbours, but S-cones are excluded from this interreceptor pathway (Ahnelt & Kolb, 1994; Hornstein, Verweij, & Schnapf, 2004; Li & DeVries, 2004). Of the two types of lateral processes in the outer plexiform layer, the wide-field horizontal cell, which has thick dendrites and couples strongly to its neighbours, avoids S-cone contact, while the narrow-field horizontal cell, with thin dendrites and weak gap junctions, connects especially strongly to S-cones (Dacey, Lee, Stafford, Pokorny, & Smith, 1996; Mills & Massey, 1994; Piechl & Gonzalez-Soriano, 1994; Sandmann, Boycott, & Peichl, 1996; Vaney, 1990). There is also a distinct population of bipolar cells which connect exclusively to S-cones (Herr, Klug, Sterling, & Schein, 2003; Kolb, Goede, Roberts, McDermott, & Gouras, 1997; Kouyama & Mashak, 1992, 1997; Mariani, 1984). These supply a family of ganglion cell types that carry "blue-yellow" opponent signals to higher areas of the visual system. The most prominent is the small-field bistratified ganglion cell type, which signals blue-ON, yellow-OFF colour opponency with one set of dendritic connections contacting S-cone bipolar cells and another set contacting bipolar cells conveying L- and M-cone information (Calkins, et al., 1998; Dacey, 1993; Dacey & Lee, 1994; Dacey et al., 1996; Ghosh, Martin, & Grunert, 1997). S-cone bipolar cells also connect to a large-field bistratified ganglion cell, which signals a blue-ON type of response (Dacey, Peterson, Robinson, & Gamlin, 2003), as well as to a sparse

monostratified ganglion cell type that is thought to carry an S-OFF signal by sign inverting the bipolar cell signal (Dacey & Packer, 2003; Klug, Herr, Ngo, Sterling, & Schein, 2003). These S-cone related ganglion cells project in parallel to the LGN. Both the midget ganglion cells of the parvocellular system and the parasol ganglion cells of the magnocellular system collect information derived from L- and M-cones, but avoid input from S-cone related processes (Sun, Smithson, Zaidi, & Lee, 2006a, 2006b).

Beyond the retina, the "blue-yellow" channel appears to remain distinct. While projections from some types of the S-cone family of ganglion cells are not yet clear, the small bistratified ganglion cells are known to project to koniocellular zones of the lateral geniculate nucleus (Hendry & Reid, 2000; Martin et al., 1997), and not to the main parvocellular layers, as was orginally presumed. Information from the koniocellular areas of the LGN projects directly to the colour-processing blobs of layers II and III of the primary visual cortex (Hendry & Yoshioka, 1994), whereas information from LGN parvocellular layers first projects to layer IV-C_β of the primary visual cortex, before connecting to the blobs in layers II and III. Thus, the koniocellular stream is now considered to represent a distinct stream for "blue-yellow" chromatic processes driven by S-cone mediated mechanisms of the retina (Hendry & Reid, 2000). Psychophysical tests can be used to separately assess the performance of "red-green" and "blue-yellow" opponency channels, thus distinguishing possible involvement of the parvocellular and koniocellular visual streams.

Proposed Model of Retinal Mechanisms and Visual Anomalies in Depression

Communication in the retina, as in the rest of the brain, involves an intricate network of diverse and specialized interconnections. Despite our enormously improved understanding of retinal physiology within the last 50 years, a complete and detailed understanding of the full complexity of retinal communications has yet to be achieved. Consequently, while pathway localization is possible, it is difficult to state with certainty which specific mechanisms or substrates are responsible for given vision abnormalities. This is particularly challenging in the area of depressive disorders, where vision research has only recently been initiated and early findings require much clarification. Further, the elusiveness of the biological underpinnings of mood disorders also makes interpretation difficult. Nevertheless, it is possible to construct a working hypothesis about specific retinal mechanisms that can account for many of the visual anomalies that have so far been observed in depressive disorders: abnormal retinal light sensitivity; potential enhancement of contrast sensitivity at high spatial frequencies, with low spatial and high temporal frequencies relatively unaffected; and S-cone selectivity in phototherapeutic and, possibly, pharmacological treatments.

The serotonergic system has received the most attention in biological theories of depression and is the target of the most commonly prescribed antidepressants. Dysfunction in the serotonin system could affect the early stages of visual processing. Serotonin is integral to the production of melatonin, which is a major inhibitor of dopamine synthesis in the retina (Brunken et al., 1993; Dubocovich et al., 1985; Tosini & Dirden, 2000). Low levels of serotonin impede melatonin production, contributing to an

excess of retinal dopamine. Because dopamine is a primary neurotransmitter and neuromodulator in the retina involved in basic visual functions of light adaptation and contrast sensitivity, its dysregulation would have an extensive impact on early-stage visual processes.

Retinal dopamine is stimulated by light. Thus, an increase of dopamine levels in the retina normally signals an increase in light levels, and initiates relevant mechanisms of adaptation, including adjustments of retinal light sensitivity (Iuvone, 1978; Godley, Flaherty, & Wurtman, 1985). Abnormally elevated dopamine would instigate retinal adaptation processes not concordant with actual light conditions. This may account for the findings of atypical retinal sensitivity to ambient light among individuals with SAD and non-seasonal depression (e.g. Oren et al., 1991; Seggie et al., 1989; Terman & Terman, 1999). Light levels are also associated with contrast sensitivity, fundamental to higher-end pattern or form perception. Under normal conditions, increases of surrounding light trigger a shift in the peak of contrast sensitivity functions toward higher spatial frequencies (Ehinger, 1983; Shapley & Enroth-Cugell, 1984). This resembles the high spatial frequency enhancement in luminance contrast sensitivity that was observed in Wesner and Tan (2006). Essentially, the contrast sensitivity functions of depressed individuals may be similar to what is observed in healthy individuals under increased light conditions. However, in the case of depression, it may be deficits of serotonin, rather than light changes, that cause the elevated dopamine levels associated with contrast sensitivity shifts (Wesner & Tan, 2006).

By uncoupling the gap junction connections of horizontal cells, dopamine modulates the size of the surround portions of receptive fields (Djamgoz et al., 1997). An excess of retinal dopamine would intensify this uncoupling, effectively reducing receptive field size. Smaller receptive fields are better suited to the processing of finer details or higher spatial frequencies of the visual image. Thus, elevated levels of dopamine would enhance retinal sensitivity to higher spatial frequencies. This effect would be particularly pronounced among narrow-field horizontal cells, which have relatively weaker connections to their neighbours than wide-field horizontal cells (Mills & Massey, 1994; Peichl & Gonzalez-Soriano, 1994; Peichl, Sandmann, & Boycott, 1998; Sandmann, et al., 1996). Since narrow-field cells are involved in the processing of higher spatial frequencies, dopamine dysregulation can be expected to disrupt the parvocellular and koniocellular streams more than the magnocellular stream, which is primarily associated with wide-field cells. Additionally, narrow-field horizontal cells make strong connections to S-cones, while these are explicitly avoided by wide-field horizontal cells (Dacey et al., 1996; Sandmann et al., 1996; Sterling & Demb, 2004). Effects specific to narrow-field horizontal cells may therefore selectively impact S-cone mediated processes, while L- and M-cone processes may remain intact through their interconnections with wide-field horizontal cells.

In sum, this hypothesis suggests that a reduced availability of serotonin among individuals with depression results in an excess of dopamine in the retina, leading to enhanced luminance contrast sensitivity for higher spatial frequencies. The increased vulnerability to dopaminergic de-coupling between narrow-field horizontal cells would

also selectively impact S-cone connections. Thus, the koniocellular stream is expected to be most susceptible to the neurotransmitter dysregulation associated with depression. The parvocellular stream is also expected to be impacted, but to a lesser degree, due to more redundancy and interconnections, while the magnocellular stream is expected to remain unaffected. Antidepressant medications are anticipated to reverse these visual abnormalities.

This working hypothesis does not refer to a number of other important links between the biology of depression and basic visual functions. For example, serotonergic dysregulation in depression may also have a direct impact upon retinal processes, outside of any interaction with dopamine. Conversely, disturbances in retinal dopamine may not be mediated by serotonin, but may instead be related to the proposed dopaminergic dysfunction in depression. Other neurotransmitters which play an important role in visual processes, such as GABA and glutamate, have also been implicated in depressive disorders and may contribute to visual disturbances.

The Present Study

The proposed model is based upon observations of visual anomalies which need to be confirmed and clarified. Since psychophysical investigation of visual processes has only recently begun to be applied in the area of depressive disorders, further research is required to establish the nature and pathway involvement of potential vision abnormalities. Awareness of the effects of antidepressant medication on vision is crucial to avoid confounds and misinterpretation of causality. Investigation of antidepressant treatment additionally contributes to an increased understanding of the relationship

between visual perception and neurobiological substrates of depression. Further, given the rising prevalence and increased range of uses for antidepressant pharmacology, knowledge of the visual effects of antidepressant medications is important in its own right, regardless of diagnosis. Current information concerning antidepressant treatment and vision is largely limited to self-reported side-effects studies assessing non-specific visual complaints, such as blurring or dullness.

The present study was intended to collect detailed and objective information about the impact of depression and antidepressant medication on fundamental processes of visual perception. Specifically, spatiotemporal luminance contrast sensitivity and chromatic processes were explored with a set of non-invasive psychophysical tests designed to assess the involvement of the magno-, parvo-, and koniocellular streams. Analyses included a comparison of medicated and unmedicated individuals, with and without symptoms of depression. Measures of anxiety were also included due to high comorbidity with depression and the use of antidepressant medication in the treatment of anxiety disorders.

Method

Participants

Participants were recruited from among the university population and the larger community. At the university, announcements were made in psychology classes and advertisements were posted on bulletin boards across campus, at the library, and at the student health centre. In the community, radio and newspaper advertisements were used, as well as postings at clinics and other health care facilities. Advertisements indicated

that the study was about the effects of antidepressant medication on visual functioning. It was noted that participants would have the opportunity to enter their name in a draw for $100. Additionally, students enrolled in certain psychology classes were eligible for three bonus points toward their course mark. There were no other direct incentives for participation.

Fifty-one individuals completed the study. However, five were removed from analysis due to various exclusion criteria, including confounding medical conditions and pharmacological prescriptions, eye disease (i.e., macular degeneration), concurrent light therapy, and age. Additionally, since only two participants were prescribed bupropion, which involves a dopaminergic effect, their data was excluded and the study focused on antidepressant medications involving a primary effect on the serotonergic system. A final total of 44 participants were included in analyses. Of these, 29 were university students and 15 were recruited from the larger community. Participants ranged from 18 to 41 years of age, with a mean of 23.86 (SD = 6.88). Seventy-five percent were women. All had normal or corrected-to-normal visual acuity and no evidence of colour vision deficits.

The SSRI group included a total of 13 participants (Table 1), who were taking either citalopram (n = 3), fluoxetine (n = 2), paroxetine (n = 3), or sertraline (n = 5). These had been taken for between 1 and 120 months, with a median duration of 42 months (M = 45.46, SD = 36.23). Dose regiments were within standard recommended protocols (Physicians' Desk Reference, 2007). All participants indicated either depression or anxiety as the reason for their SSRI prescription. In some cases, symptoms

of both depression and anxiety were endorsed and participants were required to choose one as the primary reason, which was found to be consistent with responses to mood and symptom questionnaires.

Measures

Screening measures. The Freiburg Visual Acuity Test (Bach, 1996) was used to screen for possible visual acuity problems. All participants included in analysis demonstrated normal or corrected-to-normal visual acuity. Colour vision deficits were assessed using Ishihara pseudoisochromatic plates (1993; 24-plate edition), and no problems with colour vision were found among participants.

The Digit Symbol subtest of the the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III; Wechsler, 1997) was included as a measure of general attention capability, since the psychophysical vision tests are sometimes described as repetitive and monotonous, and may present a problem for individuals with limited attention abilities. Raw scores on the Digit Symbol subtest were not significantly correlated with the dependent variables in any experimental condition ($p > .05$), nor did they alter the pattern of ANCOVA results when entered as a covariate. Thus, Digit Symbol scores were not included in primary analyses.

Current mood symptoms. Participants were asked to complete a set of standardized self-report questionnaires pertaining to current symptoms of depression and anxiety. These included the Depression Anxiety Stress Scales (S.H. Lovibond & P.F. Lovibond, 1995), the Diagnostic Inventory for Depression (Zimmerman, Sheeran, &

Young, 2004), and the State-Trait Anxiety Inventory (Spielberger, Gorsuch, & Lushene, 1983).

The Depression Anxiety Stress Scales (DASS) were designed to distinguish between respondents' experiences of depression, anxiety, and stress over the previous week. These three dimensions have been confirmed by exploratory and confirmatory factor analysis of the DASS (Brown, Chorpita, Korotitsch, & Barlow, 1997). Within the three scales, test-retest reliability and internal consistency indices are high, with the latter demonstrating alpha coefficients of 0.91 for Depression, 0.84 for Anxiety, and 0.90 for Stress (P.F. Lovibond & S.H. Lovibond, 1995). The standard DASS form includes 42 items, with content from the different scales interspersed throughout the questionnaire. Response options are presented in a 4-point Likert scale format. Scores are totaled to provide a dimensional score for each scale. Additionally, the authors provide category cut-off scores for classifications of normal, mild, moderate, severe, and extremely severe. The DASS Depression and Anxiety scales were used to create dichotomous variables of depressed and anxious mood for data analysis, with participants reporting at least mild symptoms being categorized as having depressed or anxious mood.

The Diagnostic Inventory for Depression (DID) evaluates the presence of an episode of depression according to criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev.; DSM-IV-TR; American Psychiatric Association, 2000). It includes 38 items that are rated with reference to the preceding week. For each item, four response options are provided representing a range of severity for the particular symptom being assessed. A scoring guide is provided to evaluate the items

related to each DSM-IV symptom and to determine if DSM-IV diagnostic criteria are met for an episode of depression. Internal consistency of the DID is high (alpha = .91), as is test-retest reliability (Zimmerman et al., 2004). It has also demonstrated good convergent and discriminant validity when compared to other related measures (Zimmerman, Chelminski, McGlinchey, & Young, 2006; Zimmerman, McGlinchey, Young, & Chelminski, 2007; Zimmerman et al., 2004). The DID was used to create a dichotomous variable of clinical depression for data analysis.

The State-Trait Anxiety Inventory (STAI) differentiates between the temporary experience of 'state' anxiety and a more general and long-standing quality of 'trait' anxiety. It includes 20 items for each scale, which are presented separately. State anxiety items refer respondents to how they feel at that moment, while trait anxiety items refer to how they generally feel. Response options are presented in a 4-point Likert scale format, resulting in total scores for state and trait anxiety. Scores on the STAI-Trait scale were used as a covariate in primary data analysis. In some cases, it was necessary to instead include trait anxiety as a between-subjects variable. This was accomplished by dividing the sample in half according to STAI-Trait scores, creating a low trait anxiety group and a high trait anxiety group.

Antidepressant medication questionnaires. In order to determine the reason for antidepressant medications, participants were asked to complete the following questionnaires with reference to the 6-month time period prior to beginning treatment: symptom questionnaires based on DSM-IV-TR criteria for Mood Disorders, Anxiety Disorders, and Eating Disorders; DASS and STAI-Trait with instructions adapted to the

relevant time period; and a checklist of possible reasons for taking antidepressant medications.

Psychophysical Stimuli and Apparatus

S-cone sensitivity. Short-wavelength automated perimetry (SWAP) was conducted to assess retinal sensitivity to short-wavelength light across the visual field. This procedure isolates short-wavelength sensitive mechanisms by using a high luminance "yellow" background to saturate M- and L-cones and suppress rod activity, while leaving S-cones relatively unaffected. The SWAP program used for this study was run on an OPTO AP200 Automated Perimeter (Opto-Global; Adelaide, South Australia). The background was set to a luminance of 100 cd/m^2 and included dominant wavelengths higher than 530 nm. Against this background, "blue" target stimuli were presented to preferentially stimulate S-cones. The target stimuli consisted of Goldmann size V points of narrow-band light with a peak transmission of 440 nm. Each target was presented for 200 ms to maximize the temporal summation of S-cone channels (Wild, 2001).

Participants were seated in front of the bowl background, with their heads situated on a chin rest to facilitate constant fixation. SWAP testing was conducted monocularly, so an eye patch was used to cover the untested eye. Following 7 minutes of dark adaptation, participants were adapted to the bright "yellow" light of the bowl background for 3 minutes prior to presentation of target stimuli. For testing, participants were instructed to press a joystick button whenever they saw a blue circle flash on the background. It was emphasized that a constant focus on the central fixation dot be

maintained, as loss of fixation would lengthen test duration. This instruction was especially important, since the digital infrared eye-tracking option proved inconsistent and overly sensitive to slight deviations in pupil image. Thus, loss of fixation was sometimes recorded when participants were, in fact, focusing on the central dot, as observed in their pupil image on the experimenter monitor. To examine the possible impact of lost fixation on SWAP results, Pearson correlations were computed between SWAP measurements and the percentage of stimulus presentations associated with a reported loss of fixation. No significant correlations were found for any visual field locations, with correlations ranging from $r = .04$ to .20 and significance ranging from $p = .206$ to .776. Thus, although the fixation losses recorded by the SWAP program were inflated to some degree, they did not appear to influence the results of SWAP measurement.

Standard perimetry methods are designed to assess for retinal anomalies at multiple locations across the full visual field. In the current study, 162 target locations were tested, with the "blue" stimulus circle presented in each of these locations 3-5 times, depending on participant response. Stimulus presentations began in central areas of the visual field, then moved peripherally. Within these general areas, each presentation of target stimuli was in a random location. S-cone sensitivity at each target location was expressed in decibels (dB).

The level of detail provided by the 162 target locations was not considered necessary for the purposes of the current study. Instead, mean S-cone sensitivity values were computed by averaging the decibel values for target locations across various sub-

divisions of the visual field, based upon the known spatial heterogeneity of S-cone distributions and functional symmetries across the retina (e.g., Ahnelt, Schubert, Kubber-Heiss, Schiviz, & Anger, 2006; Bierne, Zlatkova, & Anderson, 2005; Curcio & Allen, 1990; Sample, Martinez, & Yamagishi, 1997). The first set of analyses divided the retina into three zones according to eccentricity, with the central zone referring to 1-6° of visual angle, the paracentral zone referring to 10-22°, and the peripheral zone referring to 30-50°. The second set of analyses divided retinal area into five hemiretinal locations involving a central section (1-6°) and four outer quadrants (10-50°) corresponding to the superior nasal, inferior nasal, inferior temporal, and superior temporal sections of the retina. The final analyses combined sub-divisions from the previous two analyses, resulting in a detailed division of the retinal area into 11 sections, including three concentric rings of the central retina, representing 1°, 3°, and 6° of visual angle, and eight sections in the remainder of the retina, referring to the paracentral (10-22°) and peripheral (30-50°) areas of the superior nasal, inferior nasal, inferior temporal, and superior temporal quadrants.

Luminance contrast sensitivity. Luminance contrast thresholds were measured using achromatic vertically-oriented Gabors, created by convolving sinusoidal gratings with a Gaussian luminance profile (see Figure 1). Specifically, each sinusoidal luminance grating was presented in a circular window overlayed with a two-dimensional Gaussian envelope with space constant values (σ_{xy}) of 1.3, 1.0, or 0.8, according to the peak spatial frequency. These vertical luminance patterns were presented against a space-averaged "gray" background. Contrast was defined according to the Michelson formula [(L_{max}-

$L_{min}) / (L_{max} + L_{min})]$, where L_{max} and L_{min} refer to peak and trough luminances, respectively. At 0% contrast, there was no difference in luminance across the grating, and the stimulus appeared as a uniform field. The minimum amount of contrast needed to detect a grating represented contrast threshold, the inverse of which defined luminance contrast sensitivity.

Luminance gratings were created using a Vision Research Graphics™ program and presented on a high-resolution Nanao 9080i RGB monitor driven by a 32-bit microprocessor (Texas Instruments 34020 GSP) configured for monochromatic presentations. The monitor was positioned 75 cm from the participant's entrance pupil, subtending a height and width of 13° and 16° of visual angle, respectively. The size of the circular stimulus window was 7.5° of visual angle for gratings under 1.0 cpd (cycles per degree), 5.0° for gratings between 1.0 and 2.0 cpd, and 3.0° for gratings of 4.0 cpd and higher spatial frequencies. A centrally positioned cross-hair was used to facilitate center fixation. The homogenous "gray" background of the monitor screen was set at a space-averaged luminance of 13.6 cd/m^2.

Testing was conducted binocularly and in a darkened room. Participants were dark adapted for 7 minutes, followed by 3 minutes of light adapt to the monitor background screen, after which contrast sensitivity trials began. Stimulus trials involved a two-alternative forced choice (2AFC) procedure in which participants were asked to report whether a grating was presented to the left or right of the cross-hair. They used a corresponding two-button keypad to indicate the left or right position. Each trial was signaled by a tone, followed by a 975 ms presentation of the stimulus grating.

Subsequent trials were not presented until a response had been entered; consequently, participants were required to guess when they were unsure or unable to see a grating.

The luminance contrast of the gratings was modulated using two interwoven staircases of relative log contrast proportions, beginning at either 0.75 or 0.01, and adjusted according to participant response. Three successive correct responses resulted in a decrease of contrast by 0.10 log units. A single error response resulted in an increase of contrast by 0.10 log units. Additionally, in order to avoid artificially low contrast thresholds, four successive error responses reset the luminance contrast to initial levels. When the contrast proportions of the two interleaved staircases converged, a reversal was considered to have occurred. Participants practiced through four reversals before completing the six trial reversals needed to compute their contrast threshold. The geometric means of the six trial reversals were used to determine a Michelson contrast threshold at 75% detection. The inverse of this contrast threshold equals the luminance contrast sensitivity for each participant at the presented spatial frequency.

In order to plot a complete contrast sensitivity function, luminance contrast thresholds were determined for ten randomly presented static (i.e., 0 Hz) Gabors with center spatial frequencies of 0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd. Additionally, a subset of Gabors with center spatial frequencies of 0.5, 1.5, and 4.0 cpd were randomly presented with temporal modulation; their peaks and troughs were 180° counterphase flickered at 4 Hz. Altogether, participants viewed 13 luminance gratings, presented as a set in random order.

Chromatic contrast sensitivity. In these trials, a near-isoluminant, heterochromatic sinusoidal pattern was modulated between two pairs of opponent chromaticities processed by either L-M weighted ("red-green") or S-(L+M) weighted ("blue-yellow") opponency streams. In other words, periodic gratings with alternating peak "red" and trough "green" bands were presented to probe parvocellular functioning and periodic gratings of alternating peak "blue" and trough "yellow" bands were used to assess koniocellular functioning (see Figure 1). These Gabors were vertically oriented with a space-averaged constant value (σ_{xy}) of 1.0. Maximum chromatic contrast, defining a relative contrast proportion of 1.0, involved using intial x,y pairs that were near complimentary and equiluminant in CIE (1931) space (Figure 2). Relative chromatic contrast was then reduced by adjusting the chromaticities of each "red-green" or "blue-yellow" peak-to-trough compliment toward the intermediate chromaticity of the background (i.e., a yellowish background for red-to-green modulation and a grayish background for blue-to-yellow modulation). Thus, at 0% contrast, the stimulus appeared as a uniform field indistinguishable from the background. Chromatic contrast sensitivity, as the inverse of threshold (i.e., the minimum level of chromatic contrast needed to detect the stimulus grating), was calculated in the same manner as the achromatic luminance contrast sensitivities described above, using two interleaved staircases in a 2AFC task. Participants were asked to indicate whether a stimulus grating had been presented to the left or right of the centrally positioned "white" cross-hair.

Whereas luminance contrast gratings were achromatic to ensure that chromaticity did not contribute to a participant's response, chromatic contrast gratings were designed

to be near-isoluminant in order to minimize the influence of luminance stream operations in the determination of threshold. An instrument-based approach to isoluminance was used rather than a perceptually-based method involving the determination of unique isoluminance values for each participant (e.g., heterochromatic flicker photometry). Although there is inter-individual variability in the M- and L-cone ratios of the retinal mosaic, the impact of these variations is reduced post-receptorally and does not translate into substantial individual differences in colour perception (e.g., "red-green" or "blue-yellow" hue cancellation; Cicerone, 1990; Cicerone & Nerger, 1989). Due to the logistical challenge of measuring each participant's unique isoluminance points accompanied with chromatic stimulus recalibration prior to experimental presentations, it was decided that an instrument-based approach would sufficiently approximate isoluminance for our purposes. Thus, normative population values of isoluminance were taken from previous literature and adjusted according to spectroradiometric luminance measurement. Specifically, the chromaticities used to create the near-isoluminant peaks and troughs were derived from a hue scaling study by DeValois et al. (1997), which was based upon MacLeod & Boynton's (1979) isoluminant colour space. Plots of contrast sensitivity functions (see Results) for chromatic conditions conformed to the low-pass characteristics expected of chromatic stimuli, rather than the bandpass properties of luminance stimuli, suggesting that the influence of luminance was indeed minimized for measures of chromatic contrast sensitivity.

For the grating assessing parvocellular processing, at relative contrast of 1.0, the initial "red" was set to CIE (1931) coordinates of x = .3828 and y = .2846, and the initial

"green" to x = .2639 and y = .3772. Spectroradiometric measurements also confirmed near-isoluminance of the stimuli, with a luminance of 35.3 cd/m^2 and 35.1 cd/m^2 for "red" and "green", respectively. For the grating probing the koniocellular stream, the initial "blue" was set to x = .2739 and y = .2263, and the initial "yellow" to x = .4280 and y = .4976. Spectroradiometric measurements indicated 35.6 cd/m^2 for the "blue" peak and 35.4 cd/m^2 for the "yellow" trough. Luminance for the background screen was measured at 36.8 cd/m^2 for the "red-green" condition and 33.91 cd/m^2 for the "blue-yellow" condition.

Chromatic Gabors were presented on a gamma corrected Viewsonic G225 21-inch CRT monitor with a resolution of 1024x768 pixels at 150 Hz. The display was driven by a NVIDIA GeForce 6600 LE graphics card on a Dell Dimension DXP051 PC with a 3.2 GHz processor. Participants were situated on a chin rest at a distance of 75 cm from the monitor screen. Testing was conducted binocularly and in a darkened room. Participants were dark adapted for 7 minutes, followed by 3 minutes of light adaptation to the background screen. Gabors were presented at three spatial frequencies (0.5, 1.5, and 4.0 cpd) and two temporal frequencies (0 and 4 Hz). The circular windows of the Gabors subtended 7.5°, 5.0°, and 3.0° of visual angle for the 0.5, 1.5, and 4.0 cpd spatial frequency stimuli, respectively. Each grating was presented for 975 ms.

"Red-green" and "blue-yellow" Gabors were presented in separate trial blocks, with the block order counter-balanced across participants. Within the two blocks, the different spatial and temporal frequency stimuli were presented randomly. Similar to the luminance contrast test design, chromatic contrast was modulated using two interwoven

staircases of relative log contrast proportions, adjusted according to participant response. Three successive correct responses resulted in a decrease of contrast, while a single error response resulted in an increase of contrast. Additionally, four successive error responses reset contrast to initial levels. Participants practiced through four reversals before completing the six trial reversals that were required to compute their contrast threshold. Specifically, the geometric means of the six trial reversals were used to determine chromatic contrast thresholds.

Procedure

Participants were introduced to the nature and procedures of the study and provided written informed consent (Appendix A). Screening measures for visual acuity, colour vision, and attention capability were conducted. Participants were then asked to complete a questionnaire regarding demographic information, eye conditions, medical conditions, mental health, and pharmacology (Appendix B). For participants who were taking antidepressant medications, an additional questionnaire was included referring to prescription details and reasons for antidepressant medication (Appendix C). Current mood measures were completed by all participants, followed by a series of psychophysicial vision tests. These began with the luminance contrast sensitivity test, followed by SWAP, and concluded with the heterochromatic, near-isoluminant "red-green" and "blue-yellow" contrast sensitivity measurements. Participation took approximately 2.5 hours to complete the experiment.

Design

Dependent variables included S-cone sensitivity, luminance contrast sensitivity, chromatic R-G contrast sensitivity, and chromatic B-Y contrast sensitivity. These were examined separately. Independent variables involved between- and within-subjects variables. The original between-subject variables were SSRI medication status (SSRIs, no SSRIs), DASS depressed mood (depressed mood, no depressed mood), and DID clinically-defined depression (clinical depression, no clinical depression).

The DASS Anxiety scale score was intended to be used as a covariate, but demonstrated significant interactions with independent variables in some analyses, violating assumptions of homogeneity of regression for covariates. It was therefore converted to a dichotomous between-subjects variable, referred to as DASS anxious mood (anxious mood, no anxious mood), and included as an independent variable in all analyses, for the sake of consistency. Similarly, the STAI-Trait Anxiety scale score was included as a covariate, but demonstrated significant interactions with independent variables in analysis of S-cone sensitivity. Thus, it was converted into a dichotomous variable of trait anxiety (high trait anxiety, low trait anxiety) and entered as a between-subjects variable in S-cone sensitivity analysis. This was only done for S-cone sensitivity analysis, since violations of homogeneity of regression assumption were limited to this dependent variable. Trait anxiety remained a covariate in analysis of luminance and chromatic contrast sensitivity. Age was used as a covariate in all analyses because of progressive age-related declines in visual functioning (e.g., Fiorentini, Porciatti,

Morrone, & Burr, 1996; Haegerstrom-Portnoy, Hewlett, & Barr, 1989; Hardy, Delahunt, Okajima, & Werner, 2005).

Within-subjects independent variables for contrast sensitivity measures included spatial frequency, with ten levels for analyses restricted to static luminance conditions (0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd) and with three levels for the remaining contrast sensitivity analyses (0.5, 1.5, and 4.0 cpd), as well as temporal frequency (0 and 4 Hz). Within-subject variables for S-cone sensitivity (SWAP) measurement included three sets of retinal location divisions: retinal eccentricity (3 levels), hemiretina sections (5 levels), and specific retinal locations (11 levels).

Data Analysis

Between-subjects variables. Two primary sets of between-subjects variables were used to examine different aspects and interactions of medication and symptomology on visual functioning. Specifically, they were constructed to disentangle the effects of potentially transient and less severe mood states compared to clinically relevant and chronic conditions. The first set included SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood), and DASS anxious mood (anxious mood, no anxious mood) as three dichotomous between-subjects variables, with age entered as a covariate. The second set included SSRI medication status (SSRI, no SSRI) and DID clinically-defined depression (clinical depression, no clinical depression) as two dichotomous between-subjects variables, with age and trait anxiety scores (STAI-Trait scale) used as covariates. However, it was sometimes necessary to instead include trait anxiety scores as a between-subjects variable rather than a covariate. Thus, a

dichotomous trait anxiety (high trait anxiety, low trait anxiety) variable was created by dividing the sample in half according to STAI-Trait scores. Cell sizes for these primary sets of between-subjects variables are presented in Tables 2, 3, and 4. Demographic and clinical characteristics associated with the between-subjects variables are presented in Table 5 and average values on the DASS, STAI, and DID are presented in Table 6.

For plotting and further analysis with contrast sensitivity measures, the second set of between-subjects variables were combined into a single four-level medication/depression variable consisting of participants who were not taking SSRI medication and did not meet DID clinical criteria for depression (HEALTHY), participants who were taking SSRI medication but did not demonstrate current clinical depression (MEDONLY), participants who met clinical criteria for depression and were not taking SSRI medication (DEPONLY), and participants who were both clinically depressed and taking SSRI medication (DEPMED). This medication/depression variable was entered into analyses of contrast sensitivity as a single between-subjects variable, along with age and trait anxiety scores as covariates.

S-cone sensitivity. Mixed-model ANCOVAs were conducted on S-cone sensitivity, with the three retinal eccentricity zones (central, paracentral, peripheral) entered as a single within-subjects variable in one analysis, the five hemiretinal sections (central, superior nasal, inferior nasal, inferior temporal, superior temporal) entered as a single within-subjects variable in another analysis, and the eleven specific retinal locations (central 1°, central 3°, central 6°, paracentral superior nasal, peripheral superior nasal, paracentral inferior nasal, peripheral inferior nasal, paracentral inferior temporal,

peripheral inferior temporal, paracentral superior temporal, peripheral superior temporal) entered as a single within-subjects variable in a final analysis. The two primary sets of between-subjects variables, described above, were included in separate ANCOVAs for each of the three retinal divisions. Age was entered as a covariate in all ANCOVAs. Trait anxiety scores from the STAI-Trait scale were initially entered as a covariate, along with age, for ANCOVAs that included SSRI medication status and DID clinically-defined depression as between-subjects variables. However, due to significant interactions between trait anxiety scores and retinal area locations violating the ANCOVA assumption of homogeneity of regression for covariates, ANCOVAs were re-run with trait anxiety (low trait anxiety, high trait anxiety) instead entered as a dichotomous between-subjects variable, alongside SSRI medication status and DID clinically-defined depression.

A summary of the ANCOVAs conducted on average S-cone sensitivity is presented in Table 7. This includes two mixed-model ANCOVAs for the three retinal eccentricities: (a) SSRI Medication Status (SSRI, no SSRI) x DASS Depressed Mood (depressed mood, no depressed mood) x DASS Anxious Mood (anxious mood, no anxious mood) x Eccentricity (central, paracentral, peripheral), with age as a covariate; and (b) SSRI Medication Status (SSRI, no SSRI) x DID Clinically-Defined Depression (clinical depression, no clinical depression) x Trait Anxiety (high trait anxiety, low trait anxiety) x Eccentricity (central, paracentral, peripheral), with age as a covariate. Two mixed-model ANCOVAs were also used to examine average S-cone sensitivity for the five hemiretinal locations: a) SSRI Medication Status (SSRI, no SSRI) x DASS

Depressed Mood (depressed mood, no depressed mood) x DASS Anxious Mood (anxious mood, no anxious mood) x Hemiretinal Location (central, superior nasal, inferior nasal, inferior temporal, superior temporal), with age as a covariate; and (b) SSRI Medication Status (SSRI, no SSRI) x DID Clinically-Defined Depression (clinical depression, no clinical depression) x Trait Anxiety (high trait anxiety, low trait anxiety) x Hemiretinal Location (central, superior nasal, inferior nasal, inferior temporal, superior temporal), with age as a covariate. Finally, two mixed-model ANCOVAs were conducted on S-cone sensitivity for the eleven specific retinal locations: (a) SSRI Medication Status (SSRI, no SSRI) x DASS Depressed Mood (depressed mood, no depressed mood) x DASS Anxious Mood (anxious mood, no anxious mood) x Retinal Location (11 levels, described above), with age as a covariate; and (b) SSRI Medication Status (SSRI, no SSRI) x DID Clinically-Defined Depression (clinical depression, no clinical depression) x Trait Anxiety (high trait anxiety, low trait anxiety) x Retinal Location (11 levels, described above), with age as a covariate. Bar graphs representing age-adjusted S-cone sensitivity means were created for variables demonstrating significant effects.

Homogeneity of variance was assessed with the F(max) test, which demonstrated no violations. Although Mauchly's W indicated sufficient sphericity for several of the analyses, Huynh-Feldt corrections were used throughout, due to sample size. Type-III sum of squares was applied to balance unequal cell sizes for most ANCOVAs. However, Type-IV sum of squares was used for the mixed-model ANCOVAs involving SSRI medication status, DID clinically-defined depression, and trait anxiety as between-subjects variables, due to an empty cell. Specifically, no participants who were taking

SSRI medications and experiencing clinical depression were classified as having low trait anxiety. Post-hoc simple effects analysis was used to examine significant interactions. Significance levels were set to $p < .05$.

Contrast sensitivity (CS). Luminance CS functions were examined across the ten spatial frequencies (0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd) presented in the static condition (0 Hz). Luminance CS was also assessed at the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (no temporal modulation - 0 Hz) and dynamic (counterphase flickered at 4 Hz) conditions. Similarly, "red-green" (R-G) chromatic CS and "blue-yellow" (B-Y) chromatic CS were examined at three spatial frequencies (0.5, 1.5, and 4.0 cpd) for both the static (0 Hz) and dynamic conditions (4 Hz).

The first method of analysis involved the use of traditional CS plots, whereby unadjusted mean sensitivity values were plotted as a function of spatial frequency on logarithm-scaled axes. Curves were fit according to a double exponential template (Movshon & Kiorpes, 1988), with error bars expressing the standard error of the means (SEM). In order to highlight patterns, group differences of 0.10 log units or more were noted and are reported in the Results section. Although a cut-off of 0.10 log units is somewhat arbitrary, it nevertheless reflects a difference that is well beyond suprathreshold levels of discrimination, as traditionally defined by a relative contrast difference larger than 2% (i.e., Weber fraction at 0.02).

The second method of analysis used mixed-model ANCOVAs to assess CS differences, with spatial and temporal frequency entered as within-subjects variables.

Age was included as a covariate in all ANCOVA analyses. For those ANCOVAs that included SSRI medication status and DID clinically-defined depression as between-subjects variables, trait anxiety scores from the STAI-Trait scale were also entered as a covariate, along with age.

A summary of the ANCOVAs conducted on CS is presented in Table 7. Specifically, analyses for the ten static luminance Gabors involved three mixed-model ANCOVAs: (a) SSRI Medication Status (SSRI, no SSRI) x DASS Depressed Mood (depressed mood, no depressed mood) x DASS Anxious Mood (anxious mood, no anxious mood) x Spatial Frequency (0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd), with age as a covariate; (b) SSRI Medication Status (SSRI, no SSRI) x DID Clinically-Defined Depression (clinical depression, no clinical depression) x Spatial Frequency (0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd), with age and trait anxiety scores as covariates; and (c) Medication/Depression (HEALTHY, MEDONLY, DEPONLY, and DEPMED) x Spatial Frequency (0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd), with age and trait anxiety scores as covariates. Analyses for the luminance Gabors that were presented in both static and dynamic conditions also involved three mixed-model ANCOVAs: (a) SSRI Medication Status (SSRI, no SSRI) x DASS Depressed Mood (depressed mood, no depressed mood) x DASS Anxious Mood (anxious mood, no anxious mood) x Spatial Frequency (0.5, 1.5, and 4.0 cpd) x Temporal Frequency (0 and 4 Hz), with age as a covariate; (b) SSRI Medication Status (SSRI, no SSRI) x DID Clinically-Defined Depression (clinical depression, no clinical depression) x Spatial Frequency (0.5, 1.5, and 4.0 cpd) x Temporal Frequency (0 and 4 Hz), with age

and trait anxiety scores as covariates; and (c) Medication/Depression (HEALTHY, MEDONLY, DEPONLY, and DEPMED) x Spatial Frequency (0.5, 1.5, and 4.0 cpd) x Temporal Frequency (0 and 4 Hz), with age and trait anxiety scores as covariates. A similar set of three mixed-model ANCOVAs was conducted for R-G chromatic CS and B-Y chromatic CS separately.

Homogeneity of variance for the ANCOVAs was assessed with the F(max) test, which demonstrated no violations. Although Mauchly's W indicated sphericity for several of the analyses, Huynh-Feldt corrections were nevertheless used throughout, due to sample size. Type-III sum of squares was applied to balance unequal cell sizes. Post-hoc simple effects analysis examined significant interactions and significant main effects for non-dichotomous variables. Significance levels were set to $p < .05$.

Of note, significant effects involving only spatial and/or temporal frequency variables are omitted from the Results section for brevity and because the effects conformed to expected patterns of spatiotemporal contrast sensitivity which are unrelated to the questions posed in the current study. For example, significant main effects of spatial frequency on luminance contrast sensitivity across the range of 0.5 to 12.0 cpd were expected, and found, for all groups of participants, due to the bandpass properties of typical luminance contrast sensitivity functions. Of course, significant interactions of spatial and/or temporal frequency with any of the between-subjects variables are reported in the Results section, as are significant main effects for the between-subjects variables.

SSRI dosage. Effective doses vary notably across SSRI medications and there is no common equivalency scale with which to compare the dosing potency of different

medications. In order to explore the effects of dosage on visual functioning, a relative dosage scale was created for the current study based upon standard dose protocols indicated for depression (Physicians' Desk Reference, 2007). Specifically, the standard range of dosage is between 20 mg and 60 mg for citalopram, between 20 mg and 80 mg for fluoxetine, between 20 mg and 60 mg for paroxetine, and between 50 mg and 200 mg for sertraline. The prescription of doses outside of these ranges is not uncommon in clinical practice. Nevertheless, these ranges were used to construct a relative scale to compare SSRI doses in the current study. This scale ranged from 1 to 10, with the lowest standard dose for each medication equaling 1 and the highest standard dose for each medication equaling 10. Intermediate doses were divided with equal spacing according to each medication's standard dose range. This resulted in six scale scores being used to represent the different dose prescriptions evident in the current study (Table 8). It should be noted that this is only a rough approximation with which to compare relative doses across medications, and does not reflect actual psychopharmacological equivalency. Further, the number of participants taking SSRIs in the current study involved a relatively small sample size to be examined on its own ($n = 13$). Thus, analyses related to SSRI dosage were considered exploratory and results tentative.

The relationship between relative SSRI dose and contrast sensitivity for the luminance, R-G, and B-Y conditions was examined with Spearman rank correlations. Similarly, Spearman rank correlations were used to assess the relationship between relative SSRI dose and average S-cone sensitivity for each of the retinal location divisions. Significance was set at $p < .05$.

Month of testing. Although the present study was not designed to examine seasonal effects, correlations between month of testing and visual functioning were conducted to assess whether test month may have contributed to primary findings. Specifically, Spearman rank correlations were computed between month of testing and each aspect of visual functioning examined in primary analysis, including average S-cone sensitivity at the various retinal area divisions, luminance CS, R-G chromatic CS, and B-Y chromatic CS. Chi-square tests were used to assess whether there were differences in month of testing between the groups of each between-subjects variable, including SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood), DASS anxious mood (anxious mood, no anxious mood), and DID clinical depression episode (clinical depression, no clinical depression). Significant differences in month of testing were observed for DASS depressed mood and DID clinically-defined depression (see Results). Thus, Spearman rank correlations between test month and visual functioning were also conducted within groups of depressed and non-depressed participants, with the sample split by DASS depressed mood (depressed mood, no depressed mood) in one analysis and by DID clinically-defined depression (clinical depression, no clinical depression) in another analysis.

Results

Data Screening

Prior to analysis, data were screened for normality and outliers within groups. Examination of Mahalonobis distances revealed no multivariate outliers; however, a number of univariate outliers were noted. Of the 1100 contrast sensitivity values

recorded across the 25 spatial, temporal, and chromatic conditions, 20 (1.8%) cases were identified as extreme values based upon interquartile range distances, z-scores, and detrended normal probability plots. Dummy coding analysis confirmed that these outliers were not associated with medication status, mood variables, specific individuals, or experimental conditions of spatial and temporal frequency. The extreme values contributed to significant non-normality within their respective group by experimental condition. Logarithmic and inverse transformations were attempted but discarded, since they did not produce notable improvement in distributions. In order to lessen the influence of these extreme scores, their original values were winsored at 0.5 of an interquartile range beyond the next highest or lowest value within their group and experimental condition. Thus, they retained their rank order and some distance from the remainder of values, but the severity of their separation was reduced. The same screening and adjustment procedure was undertaken with S-cone sensitivity, resulting in modification for 15 (3.1%) extreme cases from among the total 484 observations. Following these adjustments, the distributions of contrast sensitivity and S-cone sensitivity values within groups and conditions were within acceptable limits of normality.

S-cone Sensitivity

Retinal location: Eccentricity. Mixed model ANCOVAs were conducted on S-cone sensitivity with retinal eccentricity (central, paracentral, peripheral) as the within-subjects variable and age as a covariate. The first ANCOVA entered SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood),

and DASS anxious mood (anxious mood, no anxious mood) as between-subjects variables. No significant main effects or interactions involving the between-subjects variables were observed. The second ANCOVA entered SSRI medication status (SSRI, no SSRI) and DID clinically-defined depression (clinical depression, no clinical depression) as between-subjects variables, and included trait anxiety scores as a covariate, along with age. However, trait anxiety scores demonstrated a significant interaction with retinal eccentricity, $F(2,152) = 5.56$, $p = .010$, partial $\eta^2 = .13$, violating the assumption of homogeneity of regression for covariates. Thus, the ANCOVA was re-run with trait anxiety (high trait anxiety, low trait anxiety) instead entered as a dichotomous between-subjects variable. No significant main effects were observed for SSRI medication status, DID clinically-defined depression, or trait anxiety. However, significant two-way interactions were apparent for DID Clinically-Defined Depression x Eccentricity, $F(2,152) = 7.74$, $p = .001$, partial $\eta^2 = .18$, and for Trait Anxiety x Eccentricity, $F(2,152) = 10.06$, $p < .001$, partial $\eta^2 = .22$.

For the two-way interaction involving DID clinically-defined depression, simple effects analysis found significant differences in the peripheral portion of the retina (Figure 3, top panel), $F(1,36) = 4.34$, $p = .044$, partial $\eta^2 = .11$, with participants who reported clinical depression ($M_{adj} = 21.42$, $SE = 1.58$) demonstrating higher S-cone sensitivity than those who did not describe clinical depression ($M_{adj} = 17.82$, $SE = 0.84$), but no significant differences in either the central or paracentral portions of the retina. For the two-way interaction involving trait anxiety, significant differences were also limited to the peripheral portion of the retina (Figure 3, bottom panel), $F(1,36) = 6.01$, p

= .019, partial η^2 = .14, with lower S-cone sensitivity observed among people reporting high trait anxiety (M_{adj} = 17.58, SE = 0.80) compared to low trait anxiety (M_{adj} = 21.73, SE = 1.59). The three-way interaction between DID Clinically-Defined Depression x Trait Anxiety x Eccentricity was also significant, F(2,125) = 11.22, p < .001, partial η^2 = .24, with post-hoc analysis revealing results consistent with the two-way interactions. That is, differences in S-cone sensitivity were limited to peripheral portions of the retina, with higher sensitivity associated with low trait anxiety and the presence of clinical depression. SSRI medication status was not involved in significant interaction effects.

Retinal location: Hemiretina sections. Mixed model ANCOVAs were conducted on S-cone sensitivity, with hemiretinal location (central, superior nasal, inferior nasal, superior temporal, and inferior temporal) entered as the within-subjects variable and age as a covariate. The first ANCOVA entered SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood) and DASS anxious mood (anxious mood, no anxious mood) as between-subjects variables. These were not associated with significant main effects or interactions. The second ANCOVA entered SSRI medication status (SSRI, no SSRI) and DID clinically-defined depression (clinical depression, no clinical depression) as between-subjects variables and included trait anxiety score as a covariate, along with age. However, a significant interaction between trait anxiety score and hemiretinal location was observed, $F(4,152)$ = 3.18, p = .015, partial η^2 = .08, which violated the assumption of homogeneity of regression for covariates. Thus, the ANCOVA was re-run with trait anxiety (high trait anxiety, low trait anxiety) as a dichotomous between-subjects variable instead of a

covariate. No significant main effects were observed for SSRI medication status, DID clinically-defined depression, or trait anxiety. Significant two-way interactions were demonstrated for DID Clinically-Defined Depression x Trait Anxiety, $F(1,36) = 4.28$, $p = .046$, partial $\eta^2 = .11$; for DID Clinically-Defined Depression x Hemiretinal Location, $F(4,144) = 2.80$, $p = .028$, partial $\eta^2 = .07$; and for Trait Anxiety x Hemiretinal Location, $F(4,144) = 2.47$, $p = .047$, partial $\eta^2 = .06$.

Post-hoc simple effects analysis of the DID Clinically-Defined Depression x Hemiretinal Location interaction demonstrated higher S-cone sensitivity among people experiencing clinical depression compared to those who were not (Figure 4, top panel) in the superior temporal quadrant, $F(1,36) = 5.11$, $p = .030$, partial $\eta^2 = .12$ (Clinical depression: $M_{adj} = 25.09$, $SE = 1.18$; No clinical depression: $M_{adj} = 22.17$, $SE = 0.63$), and in the inferior temporal quadrant, $F(1,26) = 6.05$, $p = .019$, partial $\eta^2 = .14$ (Clinical depression: $M_{adj} = 24.33$, $SE = 1.60$; No clinical depression: $M_{adj} = 20.01$, $SE = 0.86$). For the Trait Anxiety x Hemiretinal Location interaction, simple effects analysis showed lower S-cone sensitivity among people with high anxiety compared to those with low anxiety (Figure 4, bottom panel) for the superior temporal quadrant, $F(1,36) = 5.38$, $p = .026$, partial $\eta^2 = .13$ (High trait anxiety: $M_{adj} = 22.16$, $SE = 0.60$; Low trait anxiety: $M_{adj} = 25.10$, $SE = 1.19$) and for the inferior temporal quadrant, $F(1,36) = 5.23$, $p = .028$, partial $\eta^2 = .13$ (High trait anxiety: $M_{adj} = 20.17$, $SE = 0.81$; Low trait anxiety: $M_{adj} = 24.11$, $SE = 1.62$). The three-way interaction between DID Clinically-Defined Depression x Trait Anxiety x Hemiretinal Location was also significant, $F(4,144) = 2.86$, $p = .026$, partial $\eta^2 = .07$, and consistent with the patterns observed in the two-way

interactions. Specifically, differences in S-cone sensitivity were observed in the inferior and superior temporal quadrants, with higher S-cone sensitivity associated with low anxiety and the presence of an episode of clinical depression. SSRI medication status was not involved in any significant interactions.

Retinal location: Eleven levels. In order to explore the effects of retinal location in further detail, the retinal area was sub-divided into 11 sectors: the central 1°, 3°, and 6°, and the paracentral and peripheral sections of the superior nasal, inferior nasal, inferior temporal, and superior temporal quadrants. Mixed-model ANCOVAs were conducted on S-cone sensitivity with retinal location (11 levels) as the within-subjects variable and age included as a covariate. The first ANCOVA included SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood), and DASS anxious mood (anxious mood, no anxious mood) as the between-subjects variables. These variables demonstrated no significant main effects and were not involved in significant interactions. The second mixed-model ANCOVA included SSRI medication status (SSRI, no SSRI) and DID clinically-defined depression (clinical depression, no clinical depression) as the between-subjects variables. Trait anxiety scores were initially entered as a covariate, along with age. However, a significant interaction was observed between trait anxiety and retinal location, $F(7, 276) = 4.183$, $p < .001$, partial $\eta^2 = .10$, violating the ANCOVA assumption of homogeneity of regression for covariates. Thus, the ANCOVA was re-run with trait anxiety (high trait anxiety, low trait anxiety) entered as a dichotomous between-subjects variable. Main effects were not significant for SSRI medication status, DID clinically-defined depression, or trait

anxiety. Significant interactions were observed for DID Clinically-Defined Depression x Retinal Location, $F(8, 286)= 3.69, p <. 001$, partial $\eta^2 = .09$, for Trait Anxiety x Retinal Location, $F(8,286) = 4.237, p < .001$, partial $\eta^2 = .11$, and for DID Clinically-Defined Depression x Trait Anxiety, $F(8, 286) = 5.19, p < .001$, partial $\eta^2 = .13$. SSRI medication status was not involved in any significant interactions.

Post-hoc simple effects analysis of the DID Clinical Depression x Retinal Location interaction revealed higher S-cone sensitivity among people meeting clinical criteria for depression compared to those who did not (Figure 5), in the peripheral section of the inferior temporal quadrant, $F(1,36) = 9.23, p = .004$, partial $\eta^2 = .20$ (Clinical depression: $M_{adj} = 21.85$, $SE = 2.22$; No clinical depression: $M_{adj} = 14.50$, $SE = 1.18$) and in the peripheral section of the superior temporal quadrant, $F(1,36) = 6.66, p = .014$, partial $\eta^2 = .16$ (Clinical depression: $M_{adj} = 21.54$, $SE = 1.61$; No clinical depression: $M_{adj} = 17.02$, $SE = 0.86$). This pattern approached significance in the paracentral section of the superior nasal quadrant, $F(1,36) = 3.98, p = .054$, partial $\eta^2 = .10$ (Clinical depression: $M_{adj} = 30.83$, $SE = 1.06$; No clinical depression: $M_{adj} = 28.53$, $SE = 0.56$).

Post-hoc simple effects analysis of the Trait Anxiety x Retinal Location interaction demonstrated lower S-cone sensitivity among people in the high trait anxiety group compared to the low trait anxiety group (Figure 6) for the peripheral section of the inferior temporal quadrant, $F(1,36) = 7.90, p = .008$, partial $\eta^2 = .18$ (High trait anxiety: $M_{adj} = 14.78$, $SE = 1.12$; Low trait anxiety: $M_{adj} = 21.46$, $SE = 2.23$), the peripheral section of the superior temporal quadrant, $F(1,36) = 6.54, p = .015$, partial $\eta^2 = .15$ (High trait anxiety: $M_{adj} = 17.07$, $SE = 0.81$; Low trait anxiety: $M_{adj} = 21.47$, $SE = 1.62$), as well

as the paracentral section of the superior nasal quadrant, $F(1,36) = 9.20$, $p = .004$, partial $\eta^2 = .20$ (High trait anxiety: $M_{adj} = 28.04$, $SE = 0.53$; Low trait anxiety: $M_{adj} = 31.48$, $SE = 1.06$). The pattern of results for the interaction between DID Clinically-Defined Depression x Trait Anxiety x Retinal Location was consistent with the two-way interactions, showing that significant simple effects were limited to the peripheral sections of the superior and inferior temporal quadrants, as well as the paracentral superior nasal quadrant, and that higher S-cone sensitivity was associated with low trait anxiety and the presence of an episode of clinical depression.

Luminance Contrast Sensitivity Functions

SSRI medication, DID depressed mood, and DID anxious mood. Mean log luminance CS was plotted as a function of the ten spatial frequencies used for static Gabor presentations. The resulting luminance CS functions revealed typical bandpass properties, which were plotted separately for SSRI medication status (Figure 7), DASS depressed mood (Figure 8), and DASS anxious mood (Figure 9). Differences in mean luminance CS for each group and each spatial frequency are summarized in Table 9. Contrast sensitivity functions for participants taking SSRIs were generally similar to those not taking SSRIs, with exceptions apparent for high spatial frequencies. Specifically, lower average luminance CS was observed among participants taking SSRIs at 10.0 cpd (0.12 log units) and 12.0 cpd (0.19 log units). Mean luminance CS tended to be lower among participants reporting depressed mood compared to those who did not, especially in the low-to-mid range of spatial frequency, with differences most notable at 2.0 cpd (0.11 log units) and 2.5 cpd (0.12 log units), as well as 10.0 cpd (0.10 log units).

The low-to-mid range of spatial frequency also demonstrated differences in luminance CS among participants reporting anxious mood, who yielded higher mean CS values than those without anxious mood at 2.0 cpd (0.12 log units) and 2.5 cpd (0.12 log units). No other differences exceeded 0.10 log units.

A mixed-model ANCOVA was conducted on luminance CS, with spatial frequency (0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd) entered as the within-subjects variable and age as the covariate. SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood), and DASS anxious mood (anxious mood, no anxious mood) were included as between-subjects variables. Of these, only DASS depressed mood was associated with a significant main effect, $F(1,35) = 5.15$, $p = .029$, partial $\eta^2 = .13$, with lower overall luminance CS evident among participants who reported depressed mood ($M_{adj} = 353.11$, $SE = 19.84$) than among those who did not ($M_{adj} = 437.67$, $SE = 19.84$). Interaction effects involving the between-subjects variables were not found to be significant.

SSRI medication status and DID clinically-defined depression. Mean log luminance CS was plotted as a function of the ten spatial frequencies used for static Gabor presentations. Luminance CS functions demonstrated typical bandpass properties. Separate plots were created for SSRI medication status (Figure 7, discussed above) and DID clinically-defined depression (Figure 10). As previously described, luminance CS functions differed only at the highest spatial frequencies for the SSRI medication status variable, with lower luminance CS at 10.0 cpd (0.12 log units) and, especially, 12.0 cpd (0.19 log units) among participants taking SSRI medications compared to those who

were not (see Table 9). For DID clinically-defined depression, lower luminance CS was most notable at 1.0 cpd (0.10 log units) and 2.5 cpd (0.13 log units) among participants describing clinical depression compared to those who did not. No other differences exceeded 0.10 log units.

A mixed-model ANCOVA was conducted on static luminance CS with spatial frequency (0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd) entered as the within-subjects variable. SSRI medication status (SSRI, no SSRI) and DID clinically-defined depression (clinical depression, no clinical depression) were entered as between-subjects variables, controlling for trait anxiety score and age as covariates. DID clinically-defined depression demonstrated a significant main effect, $F(1,38) = 5.08$, $p = .030$, partial $\eta^2 = .12$, with lower luminance CS among participants who met clinical criteria for a depressive episode ($M_{adj} = 326.15$, $SE = 44.02$) compared to those who did not ($M_{adj} = 437.39$, $SE = 17.78$). No other significant main effects or interactions were found for the between-subject variables.

Combined medication/depression variable. To examine the effects of SSRI medication and clinical depression in relation to one another, they were combined to create a medication/depression between-subjects variable, consisting of four mutually exclusive groups (HEALTHY, MEDONLY, DEPONLY, and DEPMED). Mean static luminance CS values were plotted as a function of spatial frequency for each of the medication/depression groups (Figure 11). The luminance CS function of the MEDONLY group was highly similar to that of the HEALTHY group, with the exception of a 0.20 log unit difference at 12.0 cpd in favour of healthy control

participants (see Table 9). The CS function for the DEPONLY group showed somewhat lower sensitivity than the HEALTHY group for the low-to-mid range of spatial frequency, with the largest difference observed at 1.0 cpd (0.11 log units). At higher spatial frequencies, the luminance CS values of the DEPONLY group were somewhat elevated compared to the HEALTHY group, with the largest difference observed at 6.0 cpd (0.11 log units). Comparison of these two clinical groups showed that the MEDONLY group was higher than the DEPONLY group at 1.0 cpd (0.19 log units), whereas the DEPONLY group was higher than the MEDONLY group at 12.0 cpd (0.25 log units). The CS function for individuals who were both depressed and taking SSRIs (DEPMED) was consistently lower than that of the HEALTHY group. Differences exceeded 0.10 log units for eight of the ten spatial frequencies, with the largest differences observed at 2.5 cpd (0.27 log units) and 10.0 cpd (0.21 log units). The CS function of the DEPMED group was also lower than those of the other clinical groups, with differences higher than 0.10 log units for seven of the ten spatial frequencies in each case. The largest luminance CS differences between the DEPMED and DEPONLY groups were evident at 2.5 cpd (0.21 log units), 6.0 cpd (0.28 log units), and 10.0 cpd (0.24 log units). The largest CS differences between the DEPMED and the MEDONLY groups were also observed at 2.5 cpd (0.30 log units) and 6.0 cpd (0.23 log units).

The medication/depression variable was also entered as a between-subjects variable in a mixed-model ANCOVA of luminance CS, with spatial frequency (0.5, 1.0, 1.5, 2.0, 2.5, 4.0, 6.0, 8.0, 10.0, and 12.0 cpd) as the within-subjects variable, and age and trait anxiety scores included as covariates. The main effect of the medication/depression

variable was not significant, $F(3,38) = 2.18$, $p = .106$, partial $\eta^2 = .15$. It was also not involved in significant interaction effects.

Static and Dynamic Luminance Contrast Sensitivity

SSRI medication status, DASS depressed mood, and DASS anxious mood. Mean log luminance CS values were plotted for the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (0 Hz) and dynamic (4 Hz) conditions. Separate plots were created for SSRI medication status (Figure 12), DASS depressed mood (Figure 13), and DASS anxious mood (Figure 14) variables. There was little difference in plot values between participants who were taking SSRIs and those who were not. Luminance CS differences were also minimal between participants reporting anxious mood and those who did not. Some separation was noted for DASS depressed mood at 1.5 cpd in the dynamic condition (see Table 10), with lower mean luminance CS among participants describing depressed mood compared to those who did not (0.10 log units). There were no other instances where groups differed by 0.10 log units or greater.

A mixed-model ANCOVA was conducted on luminance CS with spatial frequency (0.5, 1.5, and 4.0 cpd) and temporal frequency (0 and 4 Hz) included as within-subjects variables, and age entered as a covariate. SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood), and DASS anxious mood (anxious mood, no anxious mood) were entered as the between-subjects variables. Of these, DASS depressed mood was the only variable to demonstrate a significant main effect, $F(1,35) = 5.01$, $p = .032$, partial $\eta^2 = .13$. Comparison of adjusted marginal means indicated that luminance CS was lower for participants who reported

depressed mood (M_{adj} = 481.81, SE = 40.21) than for those who did not (M_{adj} = 587.32, SE = 25.10). Interaction effects involving any of the between-subjects variables were not significant.

SSRI medication status and DID clinically-defined depression. Mean log luminance CS values were plotted for each of the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (0 Hz) and dynamic (4 Hz) conditions. Separate plots were created for the SSRI medication status variable (Figure 12, discussed above) and the DID clinically-defined depression variable (Figure 15). As previously described, the plots for participants taking SSRIs were highly similar to those for participants not taking SSRIs in both the static and dynamic conditions. For DID clinically-defined depression, lower luminance CS values were most notable in the dynamic condition at 0.5 cpd (0.11 log units) and 1.5 cpd (0.13 log units) for participants describing clinical depression compared to those who did not (see Table 10). Otherwise, no differences equal to or greater than 0.10 log units were observed.

A mixed-model ANCOVA was conducted on luminance CS with spatial (0.5, 1.5, and 4.0 cpd) and temporal (0 and 4 Hz) frequency entered as within-subjects variables. SSRI medication status (SSRI, no SSRI) and DID clinically-defined depression (clinical depression, no clinical depression) were entered as the between-subjects variables, controlling for trait anxiety score as a covariate, along with age. The main effect of SSRI medication status approached significance, $F(1,38) = 3.82$, $p = .058$, partial $\eta^2 = .09$, suggesting a trend toward lower luminance CS among people taking antidepressant medications (M_{adj} = 453.43, SE = 45. 40) compared to those who were not (M_{adj} =

548.76, SE = 22.58). DID clinically-defined depression demonstrated a significant main effect, $F(1,38) = 9.81$, $p = .003$, partial $\eta^2 = .21$), with lower luminance CS found among people reporting clinical criteria for a depressive episode ($M_{adj} = 411.85$, $SE = 50.85$) compared to those who did not ($M_{adj} = 590.34$, $SE = 20.54$). Further, there was a three-way interaction between DID Clinically-Defined Depression x Spatial Frequency x Temporal Frequency, $F(2,76) = 5.27$, $p = .007$, partial $\eta^2 = .12$. Post-hoc analysis of simple effects found lower luminance CS among people reporting clinical depression than among those who did not at 1.5 cpd in the static condition, $F(1,38) = 4.23$, $p = .047$, partial $\eta^2 = .10$ (Clinical depression: $M_{adj} = 455.93$, $SE = 116.68$; No clinical depression: $M_{adj} = 724.96$, $SE = 47.13$), and at 0.5 cpd in the dynamic condition, $F(1,38) = 11.37$, $p = .002$, partial $\eta^2 = .23$ (Clinical depression: $M_{adj} = 430.80$, $SE = 110.90$; No clinical depression: $M_{adj} = 849.90$, $SE = 44.80$). SSRI medication status was not involved in any significant interaction effects.

Combined medication/depression variable. The SSRI medication status and DID clinically-defined depression variables were combined to create a four level medication/depression variable (HEALTHY, MEDONLY, DEPONLY, DEPMED). Mean log luminance CS values were plotted for this variable at each of the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (0 Hz; Figure 16, top panel) and dynamic (4 Hz; Figure 16, bottom panel) conditions. In the static condition, mean luminance CS values were similar between the HEALTHY, MEDONLY, and DEPONLY groups, with no differences of 0.10 log units or greater (see Table 10). By contrast, the CS plot for the DEPMED group was notably lower than the other three

groups at all three spatial frequencies, with differences of 0.13 to 0.16 log units compared to the HEALTHY group, 0.14 to 0.16 log units compared to the MEDONLY group, and 0.11 to 0.18 log units compared to the DEPONLY group. In the dynamic condition, there was similarly little difference in the plots for the HEALTHY and MEDONLY groups. The DEPONLY group exhibited lower luminance CS than the HEALTHY group at 1.5 cpd (0.14 log units). The DEPONLY group was also somewhat lower than the MEDONLY group at 0.5 cpd (0.12 log units) and 4.0 cpd (0.10 log units). Participants who were both depressed and taking SSRIs (DEPMED) had lower mean luminance CS than participants in the HEALTHY group at 0.5 cpd (0.15 log units) and 1.5 cpd (0.18 log units). They were also lower than the MEDONLY group at 0.5 cpd (0.20 log units). No other group differences greater than 0.10 log units were apparent in the dynamic condition.

The medication/depression variable (HEALTHY, MEDONLY, DEPONLY, DEPMED) was entered as the between-subjects variable in a mixed-model ANCOVA of luminance CS, with spatial (0.5, 1.5, and 4.0 cpd) and temporal (0 Hz and 4 Hz) frequency entered as within-subjects variables, and age and trait anxiety scores included as covariates. A significant main effect was observed for the medication/depression variable, $F(3,38) = 3.55$, $p = .023$, partial $\eta^2 = .22$. Simple effects analysis found overall luminance CS to be significantly higher for the HEALTHY group ($M_{adj} = 246.85$, $SE = 14.75$) than both the DEPMED ($p = .005$; $M_{adj} = 345.76$, $SE = 71.47$) and DEPONLY ($p = .046$; $M_{adj} = 477.95$, $SE = 48.98$) groups. The MEDONLY group ($p = .004$; $M_{adj} = 561.11$, $SE = 38.50$) also showed significantly higher luminance CS than the DEPMED

group. No interaction effects involving the medication/depression variable were found to be significant.

"Red-Green" Chromatic Contrast Sensitivity

SSRI medication status, DASS depressed mood, and DASS anxious mood. Mean chromatic CS values for the "red-green" (R-G) Gabors were plotted as a function of the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (0 Hz) and dynamic (4 Hz) conditions. Plots depicted low-pass properties, which are commonly found with isoluminant heterochromatic stimuli. Separate plots were created for SSRI medication status (Figure 17), DASS depressed mood (Figure 18), and DASS anxious mood (Figure 19) variables. Measurements of R-G chromatic CS were lower among participants taking SSRI medications compared to those who were not at 4.0 cpd in the static (0.11 log units) and dynamic (0.15 log units) conditions (see Table 11), whereas differences were minimal at other spatial frequencies. Mean R-G chromatic CS was similar between participants reporting depressed mood and those who did not, and also between participants describing anxious mood compared to those who did not, with no differences of 0.10 log units or more.

A mixed-model ANCOVA was conducted on R-G chromatic CS values, with spatial frequency (0.5, 1.5, and 4.0 cpd) and temporal frequency (0 and 4 Hz) as the within-subjects variables and age as a covariate. SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood), and DASS anxious mood (anxious mood, no anxious mood) were entered as between-subjects variables. Although significance was not observed for the main effects of between-

subjects variables, the main effect of medication approached significance, $F(1,35) = 4.03$, $p = .052$, partial $\eta^2 = .10$, with a trend toward lower R-G CS among participants taking SSRI medication ($M_{adj} = 161.77$, $SE = 18.65$) compared to those who were not ($M_{adj} = 215.33$, $SE = 16.44$). Interactions involving the between-subjects variables were not significant.

SSRI medication status and DID clinically-defined depression. Mean R-G chromatic CS values were plotted for the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (0 Hz) and dynamic (4 Hz) conditions. Again, plots revealed a low-pass property typical of isoluminant heterochromatic stimuli. Separate plots were created for the SSRI medication status variable (Figure 17, described above) and the DID clinically-defined depression variable (Figure 20). As discussed previously, mean R-G chromatic CS was lower among participants taking SSRI medications compared to those who were not at 4.0 cpd in the static (0.11 log units) and dynamic (0.15 log units) conditions. Lower R-G chromatic CS was also observed among participants meeting clinical criteria for depression compared to those who did not at 1.5 cpd in the static condition (0.10 log units; see Table 11). Differences of 0.10 log units or greater were not observed at any other spatial or temporal frequency for these between-subjects variables.

A mixed-model ANCOVA was conducted on R-G chromatic CS, with spatial (0.5, 1.5, and 4.0 cpd) and temporal (0 and 4 Hz) frequency as the within-subjects variables. SSRI medication status (SSRI, no SSRI) and DID clinically-defined depression (clinical depression, no clinical depression) were entered as between-subjects variables, and trait anxiety scores were included as a covariate, along with age. A

significant effect was observed for trait anxiety scores, $F(1,38) = 5.40$, $p = .026$, partial $\eta^2 = .12$; beta-coefficients indicated a positive relationship between trait anxiety and R-G CS, indicating that higher trait anxiety was associated with higher R-G chromatic CS values. SSRI medication status exhibited a significant main effect, $F(1,38) = 12.64$, $p = .001$, partial $\eta^2 = .25$, involving lower R-G chromatic CS values among participants taking SSRI medication ($M_{adj} = 122.49$, $SE = 21.43$) than among those who were not ($M_{adj} = 204.27$, $SE = 10.66$). Interactions involving SSRI medication status were not significant.

DID clinically-defined depression also demonstrated a significant main effect, $F(1,38) = 12.33$, $p = .001$, partial $\eta^2 = .25$), as well as a significant DID Clinically-Defined Depression x Spatial Frequency interaction, $F(2,76) = 3.84$, $p = .026$, partial $\eta^2 = .09$, and a significant DID Clinically-Defined Depression x Spatial Frequency x Temporal Frequency interaction, $F(2,76) = 3.26$, $p = .044$, partial $\eta^2 = .08$. Post-hoc analysis of simple effects for the three-way interaction showed that R-G chromatic CS was significantly lower among people reporting clinical criteria for a depressive episode compared to those who did not at: 0.5 cpd – 0 Hz, $F(1,38) = 7.14$, $p = .011$, partial $\eta^2 = .16$ (Clinical depression: $M_{adj} = 122.38$, SE = 54.11; No clinical depression: $M_{adj} = 284.51$, SE = 21.86); at 1.5 cpd – 0 Hz, $F(1,38) = 8.61$, $p = .006$, partial $\eta^2 = .19$ (Clinical depression: $M_{adj} = 102.27$, SE = 57.33; No clinical depression: $M_{adj} = 290.86$, SE = 23.16); and at 0.5 cpd – 4 Hz, $F(1,38) = 10.82$, $p = .002$, partial $\eta^2 = .22$ (Clinical depression: $M_{adj} = 124.49$, SE = 32.11; No clinical depression: $M_{adj} = 242.89$, SE = 12.97).

Combined medication/depression variable. The SSRI medication status and DID clinical depression variables were combined into a four-level medication/depression variable (HEALTHY, MEDONLY, DEPONLY, DEPMED). Mean R-G chromatic CS values were plotted for this variable at each of the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (0 Hz; Figure 21, top panel) and dynamic (4 Hz; Figure 21, bottom panel) conditions. In the static condition, the mean R-G chromatic CS values of the HEALTHY group were similar to those of the DEPONLY group at all spatial frequencies (see Table 11) and were somewhat lower than those of the MEDONLY group at 1.5 cpd (0.12 log units). Between these latter two groups, MEDONLY had higher mean R-G chromatic CS values at 1.5 cpd (0.11 log units), whereas DEPONLY had higher mean CS values at 4.0 cpd (0.17 log units). Individuals who were both depressed and taking SSRI medications (DEPMED) showed notable reductions in mean R-G CS values compared to participants in the HEALTHY group at all spatial frequencies, with differences ranging from 0.10 to 0.22 log units. The R-G chromatic CS values were also lower for the DEPMED group than the DEPONLY group at all spatial frequencies in the static condition, with differences between 0.18 and 0.24 log units. Similarly, R-G CS values were lower for the DEPMED group than the MEDONLY group at 0.5 cpd (0.23 log units) and 1.5 cpd (0.35 log units). No other group differences exceeded 0.10 log units in the static condition. For plots of the dynamic condition, group differences were only apparent at 4.0 cpd. Specifically, individuals in the HEALTHY group had higher mean R-G chromatic CS values than those in the MEDONLY group (0.19 log units) and DEPMED group (0.13 log units).

The DEPMED group also showed lower R-G CS means than the DEPONLY group (0.11 log units). Group differences in R-G CS did not exceed 0.10 log units in the dynamic condition at either 0.5 cpd or 1.5 cpd.

The combined medication/depression variable (HEALTHY, MEDONLY, DEPONLY, DEPMED) was entered as the between-subjects variable in a mixed-model ANCOVA of R-G chromatic CS, with spatial (0.5, 1.5, and 4.0 cpd) and temporal (0 and 4 Hz) frequency entered as the within-subjects variables, and age and trait anxiety scores included as covariates. Trait anxiety scores exhibited a significant effect, $F(1,38) = 5.40$, $p = .026$, partial $\eta^2 = .12$, with beta-coefficients indicating a positive relationship between trait anxiety and R-G chromatic CS. The medication/depression variable demonstrated a significant main effect, $F(1,38) = 5.60$, $p = .003$, partial $\eta^2 = .31$, but no significant interactions. Post-hoc simple effects analysis found R-G chromatic CS to be significantly higher for the HEALTHY group ($M_{adj} = 246.85$, $SE = 14.75$) than all other groups and significantly lower for the DEPMED group ($M_{adj} = 70.60$, $SE = 33.73$) than all other groups (MEDONLY: $M_{adj} = 174.38$, $SE = 18.17$; DEPONLY: $M_{adj} = 161.69$, $SE = 23.12$).

"Blue-Yellow" Chromatic Contrast Sensitivity

SSRI medication status, DASS depressed mood, and DASS anxious mood. Mean chromatic CS values for the "blue-yellow" (B-Y) Gabors were plotted as a function of the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (0 Hz) and dynamic (4 Hz) conditions. Plots demonstrated low-pass properties which are commonly found with isoluminant heterochromatic stimuli. Separate plots were created

for SSRI medication status (Figure 22), DASS depressed mood (Figure 23), and DASS anxious mood (Figure 24). Plots related to SSRI medication status revealed differences at 4.0 cpd in the static condition, with lower mean B-Y chromatic CS observed among participants taking SSRIs compared to those who were not (0.13 log units; see Table 12). For the DASS depressed mood variable, B-Y chromatic CS was lower among participants describing depressed mood compared to those who did not at 0.5 cpd (0.15 log units) and 1.5 cpd (0.14 log units) in the static condition . For the DASS anxious mood variable, differences were also apparent at 4.0 cpd in the static condition, but with higher mean B-Y chromatic CS among individuals reporting anxious mood compared to those who did not (0.10 log units). No other differences of 0.10 log units or more were observed at any of the spatial or temporal frequencies.

A mixed-model ANCOVA was conducted on B-Y chromatic CS, with spatial frequency (0.5, 1.5, and 4.0 cpd) and temporal frequency (0 and 4 Hz) as within-subjects variables and age as a covariate. SSRI medication status (SSRI, no SSRI), DASS depressed mood (depressed mood, no depressed mood), and DASS anxious mood (anxious mood, no anxious mood) were entered as the between-subjects variables. Results indicated significant two-way interactions for DASS Depressed Mood x Temporal Frequency, $F(1,35) = 4.92$, $p = .033$, partial $\eta^2 = .12$, and for DASS Depressed Mood x Spatial Frequency, $F(2,70) = 3.47$, $p = .037$, partial $\eta^2 = .09$. For the interaction involving temporal frequency, post-hoc analysis of simple effects found lower B-Y chromatic CS at 0 Hz, $F(1,35) = 4.92$, $p = .034$, partial $\eta^2 = .12$, among people reporting depressed mood ($M_{adj} = 92.85$, $SE = 15.48$) compared to those who did not ($M_{adj} =$

133.09, SE = 9.66), but no significant differences at 4 Hz, $F(1,35) = 0.51$, $p = .478$, partial $\eta^2 = 0.14$. For the interaction involving spatial frequency, significantly lower B-Y chromatic CS was found at 1.5 cpd, $F(1,35) = 4.16$, $p = .049$, partial $\eta^2 = .11$ among people who reported depressed mood ($M_{adj} = 117.98$, $SE = 18.61$) compared to those who did not ($M_{adj} = 162.49$, $SE = 11.62$), with no significant differences found at 0.5 or 4.0 cpd. SSRI medication status and DASS anxious mood were not involved in any significant effects.

SSRI medication status and DID clinically-defined depression. Mean B-Y chromatic CS values were plotted for the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in the static (0 Hz) and dynamic (4 Hz) conditions. A low-pass property typical of isoluminant heterochromatic stimuli was observed. Separate plots were created for the SSRI medication status variable (Figure 22, described above) and the DID clinically-defined depression variable (Figure 25). As previously discussed, mean B-Y chromatic CS values were lower among participants taking SSRIs than those not taking SSRIs at 4.0 cpd in the static condition (0.13 log units), but were comparable at other spatial and temporal frequencies. For the DID clinically-defined depression variable, lower B-Y chromatic CS was observed among participants reporting clinical depression compared to those who did not, with the most substantial reductions noted at 0.5 cpd (0.20 log units) and 1.5 cpd (0.13 log units) in the static condition (see Table 12). No other group differences equal to or greater than 0.10 log units were observed.

A mixed-model ANCOVA was conducted on B-Y chromatic CS with spatial frequency (0.5, 1.5, and 4.0 cpd) and temporal frequency (0 and 4 Hz) as within-subjects

variables. SSRI medication status (SSRI, no SSRI) and DID clinically-defined depressin (clinical depression, no clinical depression) were entered as the between-subjects variables, with trait anxiety scores included as a covariate along with age. A significant main effect was observed for DID clinically-defined depression, $F(1,38) = 4.15$, $p = .049$, partial $\eta^2 = .10$. Specifically, lower B-Y chromatic CS was observed among participants reporting clinical criteria for a depressive episode ($M_{adj} = 87.37$, $SE = 15.15$) compared to those who did not ($M_{adj} = 121.97$, $SE = 6.12$). No other significant effects were demonstrated for the between-subject variables.

Combined medication/depression variable. The SSRI medication status and DID clinically-defined depression variables were combined into a four-level medication/depression variable (HEALTHY, MEDONLY, DEPONLY, DEPMED). Mean B-Y chromatic CS values were plotted for this variable at each of the three spatial frequencies (0.5, 1.5, and 4.0 cpd) presented in both the static (0 Hz; Figure 26, top panel) and dynamic (4 Hz; Figure 26, bottom panel) conditions. Several group differences were apparent in the static condition (see Table 12). Mean B-Y chromatic CS values were higher for the HEALTHY group than the DEPONLY group at 0.5 cpd (0.14 log units), and were also higher for the HEALTHY group than the MEDONLY group at 4.0 cpd (0.15 log units). When these two clinical groups were compared, the MEDONLY group had a higher mean B-Y CS value than the DEPONLY group at 0.5 cpd (0.20 log units) and 1.5 cpd (0.14 log units), whereas the reverse was true at 4.0 cpd (0.17 log units). The lowest mean B-Y chromatic CS values were consistently observed for individuals who were both medicated and clinically depressed (DEPMED). Specifically,

lower B-Y CS was observed among the DEPMED group than the HEALTHY group at 0.5 cpd (0.28 log units) and 1.5 cpd (0.21 log units). Mean B-Y chromatic CS was lower for the DEPMED group than the DEPONLY group at all three spatial frequencies, with differences between 0.10 and 0.17 log units. Lower B-Y CS was also found for the DEPMED group compared to the MEDONLY group at 0.5 cpd (0.35 log units) and 1.5 cpd (0.31 log units).

In the dynamic condition, the mean B-Y chromatic CS values for DEPONLY and MEDONLY were not substantially different than those for the HEALTHY group. Similarly, differences between the DEPONLY and MEDONLY groups were minimal. However, at all spatial frequencies in the dynamic condition, B-Y chromatic CS was lower among individuals who were both medicated and depressed (DEPMED) than all other groups (see Table 12). Differences ranged from 0.16 to 0.17 log units when compared to participants in the HEALTHY group; 0.17 to 0.22 log units compared to the MEDONLY group; and 0.12 to 0.19 log units compared to individuals in the DEPONLY group.

The combined medication/depression variable was entered as the between-subjects variable in a mixed-model ANCOVA of B-Y chromatic CS, with spatial (0.5, 1.5, and 4.0 cpd) and temporal (0 and 4 Hz) frequency entered as within-subjects variables, and age and trait anxiety scores included as covariates. Significance was not observed for the main effect of medication/depression, $F(1,38) = 2.21$, $p = .103$, partial $\eta^2 = .15$, nor its interactions.

SSRI Dosage

Spearman's rank correlations were computed between relative SSRI dose (see Table 8) and luminance CS for each of the spatial frequencies of the ten static luminance Gabors. A significant correlation was observed at 12.0 cpd (r_s = -.68, p = .010), indicating that higher relative doses of SSRI medication were associated with lower luminance CS at this spatial frequency. The next highest correlation was apparent at 1.0 cpd (r_s = -.51, p = .073), but was not significant. Correlations for the remaining spatial frequencies were not significant and ranged from r_s = -.27 to .12, with significance ranging from p = .373 to .890. The relationship between relative SSRI dose and luminance CS was also explored in the subset of spatial frequencies presented in both the static and dynamic conditions. Correlations were not significant, ranging from r_s = -.28 to .40, and from p = .182 to .712.

Correlations were computed between relative SSRI dose and R-G chromatic CS for the three spatial frequencies in both the static and dynamic conditions. A significant correlation was observed in the static condition at 4.0 cpd (r_s = -.58, p = .037). Remaining correlations ranged from r_s = -.41 to .06, with significance ranging from p = .159 to .934. Correlations between relative SSRI dose and B-Y chromatic CS were not significant at any of the three spatial frequencies in either the static or dynamic conditions, ranging from r_s = -.30 to .38, p = .207 to .890.

The effect of SSRI dose was also explored in relation to S-cone sensitivity. Spearman's rank correlations were not significant for any of the retinal locations, ranging from r_s = -.46 to .30, with significance ranging from p = .115 to .861.

Month of Testing

Participants were tested between February and June. There no significant differences in month of testing between participants taking SSRI medications and those who were not, $\chi^2(4, N = 44) = 6.08, p = .193$, nor between participants describing anxious mood on the DASS compared to those who did not, $\chi^2(4, N = 44) = 3.33, p = .505$. Significant differences in month of testing were observed between participants reporting DASS depressed mood compared to those who did not, $\chi^2(4, N = 44) = 10.78, p = .029$. Specifically, participants describing depressed mood tended to be tested later in the year than those who did not (Table 13). Similarly, significant differences in month of testing were evident between participants describing an episode of clinical depression on the DID compared to those who did not, $\chi^2(4, N = 44) = 17.91, p = .001$. Again, participants reporting clinical depression tended to be tested later in the year than those who did not (Table 13).

The relationship between month of testing and visual functioning was examined with Spearman's rank correlations. No significant correlations were observed for any of the spatial or temporal frequencies used to assess luminance CS. Specifically, correlations ranged from $r_s = -.20$ to .19 and significance ranged from $p = .202$ to .944. Similarly, no significant correlations were observed at any of the spatial or temporal frequencies used to assess B-Y chromatic CS, with correlations ranging from $r_s = -.25$ to .04 and significance ranging from $p = .097$ to .881. Significant correlations were also not observed for dynamic R-G Gabors; however, for static R-G Gabors, a significant correlation between month of testing and R-G chromatic CS was observed at 4.0 cpd (r_s

= .30, p = .048) and correlations approached significance at 0.5 cpd (r_s = .29, p = .057) and 1.5 cpd (r_s = .29, p = .055). These were in the positive direction, indicating that later months were associated with higher R-G chromatic CS. Correlations between month of testing and S-cone sensitivity were also computed. None were significant at any of the retinal location divisions, with correlations ranging from r_s = -.27 to .25 and significance ranging from p = .070 to .963.

Because depression was associated with significant differences in month of testing, the relationship between test month and CS was assessed within groups of depressed and non-depressed participants. Correlations were higher and more often significant when the DID clinically-defined depression variable was used to split the sample, rather than the DASS depressed mood variable. Thus, detailed results are presented for the sample divided according to DID clinical depression status. For luminance CS, significant correlations were observed among people describing clinical depression at 2.5 cpd – 0 Hz (r_s = .84, p = .001), 10.0 cpd – 0 Hz (r_s = .75, p = .007), 0.5 cpd – 4 Hz (r_s = .68, p = .022), and 1.5 cpd – 4 Hz (r_s = .70, p = .016). These correlations were positive, indicating that later months of testing were associated with higher luminance CS. Remaining correlations for the clinically depressed group ranged from r_s = -.21 to .58 and significance ranged from p = .060 to .676. Among participants who did not report clinical depression, correlations between test month and luminance CS were not significant, ranging from r_s = -.28 to .32 and p = .073 to .930.

For R-G chromatic CS, significant correlations were observed among participants reporting clinical depression at 0.5 cpd (r_s = .80, p = .003), 1.5 cpd (r_s = .72, p = .013),

and 4.0 cpd ($r_s = .91, p < .001$) in the static condition. Again, these correlations were positive, indicating that later test months were associated with higher R-G CS in the static conditions. For the dynamic R-G conditions, correlations were not significant among clinically depressed individuals, ranging from $r_s = -.10$ to .21 and from $p = .529$ to .781. Among people not reporting clinical depression, correlations between month of testing and R-G chromatic CS were not significant at any temporal or spatial frequency, with correlations ranging from $r_s = -.29$ to .06 and significance ranging from $p = .102$ to .763.

For B-Y chromatic CS, a significant positive correlation was observed among individuals reporting clinical depression at 1.5 cpd – 4 Hz ($r_s = .69, p = .019$), indicating that later test months were associated with higher B-Y chromatic CS. Remaining correlations among clinically depressed individuals ranged from $r_s = -.05$ to .45 and $p =$ .169 to .890. A significant negative correlation was observed at 1.5 cpd – 4 Hz among people not describing clinical depression ($r_s = -.36, p = .042$), indicating that later test months were associated with lower B-Y chromatic CS. The remaining correlations among individuals without clinical depression ranged from $r_s = -.25$ to .09 and $p = .153$ to .694.

For S-cone sensitivity in different retinal locations, the clinically depressed group demonstrated significant correlations in the peripheral sections of the superior nasal quadrant ($r_s = .61, p = .048$) and inferior temporal quadrant ($r_s = .82, p = .002$), again indicating that later test months were associated with higher S-cone sensitivity. The remaining correlations among the clinically depressed group ranged from $r_s = -.23$ to .54,

with significance ranging from $p = .089$ to .989. Among participants who did not report clinical depression, correlations were not significant at any of the retinal locations, ranging from $r_s = -.27$ to .13 and from $p = .148$ to .902.

Discussion

Psychophysical techniques have proved to be an informative and noninvasive method of exploring visual functioning in neurodegenerative diseases (e.g., Alzheimer's disease, multiple sclerosis, Parkinson's disease) and psychiatric disorders (e.g., schizophrenia). Initial psychophysical investigation with depressive disorders has documented anomalies in vision that are limited to specific visual streams, rather than global dysfunction, indicating the utility of more detailed investigations of the visual system in depression. Additionally, the appearance of at least mild visual disturbances on the side-effects profiles of most antidepressant medications also indicates the need for research into the specific effects of these medications on visual functioning.

The present study was designed to examine and disentangle the impact of depression and antidepressant pharmacotherapy on visual functioning. In order to isolate the functions of the magno-, parvo-, and koniocellular streams of the visual system, minimum thresholds of luminance, "red-green", and "blue-yellow" contrast sensitivity were determined across a range of spatial frequencies in both static and dynamic conditions. An additional focus on S-cone sensitivity was incorporated through short-wavelength automated perimetry (SWAP) in order to further explore the hypothesis of koniocellular stream vulnerability. The available sample compared individuals who were taking SSRI antidepressant medications with those who were not. Participants were

assessed with respect to the presence of depressed mood, as well as whether they met clinical criteria for a depressive episode. In addition, due to the high comorbidity of depression and anxiety, and the prescription of antidepressant medications to treat anxiety disorders, measures of anxious mood and trait anxiety were also employed.

Summary of Results

SSRI medications. Measures of S-cone sensitivity did not demonstrate significant results associated with SSRI medications, when potential effects of depression and anxiety were accounted for. The luminance CS function for individuals taking SSRI medications was similar to control participants at all but the highest spatial frequencies. That is, at 10.0 cpd and especially 12.0 cpd, SSRI medications tended toward lower achromatic luminance CS. For chromatic CS, significant sensitivity shifts were observed for R-G but not B-Y Gabors. Specifically, SSRI medications were associated with lower R-G chromatic CS when compared to participants not taking SSRI medications, regardless of mood status.

Higher relative SSRI dosages were associated with lower luminance CS at 12.0 cpd – 0 Hz and with lower R-G CS at 4.0 cpd – 0 Hz. This suggests a possible dose-response relationship between SSRI medications and parvocellular functioning. However, due to the lack of a standardized dose equivalency for SSRI medications, this finding is tentative and remains to be confirmed, either with larger numbers of participants taking the same medication to allow for within-group dose comparisons or with a direct biological measure of serotonin concentrations.

Depression. Significant elevations in S-cone sensitivity were observed in the SWAP measurements of participants reporting clinical depression on the DID, when accounting for potential effects of SSRI medications and trait anxiety. These elevations were demonstrated in peripheral portions of the temporal hemiretina, with a non-significant trend found in the paracentral section of the superior nasal quadrant. No significant results related to S-cone sensitivity were observed with the DASS depressed mood variable.

Both DASS depressed mood and DID clinically-defined depression were associated with a significant overall reduction in luminance CS, when accounting for potential effects of SSRI medications and anxiety. Sensitivity losses were most apparent at low-to-mid spatial frequencies, especially 2.0 and 2.5 cpd. For higher spatial frequencies, beginning with 6.0 cpd, luminance CS functions were similar among participants describing symptoms of depression and those who did not. The dynamic 4.0 Hz counterphase flicker conditions assessing luminance CS also revealed lower luminance CS among depressed participants at certain spatial frequencies.

Depression was found to contribute to significantly reduced sensitivity in R-G chromatic CS, but only when the DID clinically-defined depression variable was used and only at specific spatial and temporal frequency combinations (i.e., 0.5 and 1.5 cpd in the static condition and 0.5 cpd in the dynamic condition). For B-Y Gabors, a global decrease in B-Y chromatic CS was demonstrated for DID clinical depression, and DASS depressed mood also led to reductions which were most pronounced at certain spatial (1.5 cpd) and temporal (0 Hz) frequencies. Thus, the unique contribution of depression

was more consistent across a broader range of spatiotemporal frequencies for the B-Y Gabors than the R-G Gabors, although in both cases the effect was significantly lower chromatic contrast sensitivities.

Anxiety. S-cone sensitivity was significantly reduced among individuals with high trait anxiety, when accounting for effects of SSRI medications and DID clinically-defined depression. This effect was observed in peripheral portions of the temporal hemiretina and the paracentral section of the superior nasal quadrant. Of note, these retinal locations were the same as those affected by clinical depression, albeit with an opposite direction of effect.

Luminance CS was not associated with significant findings related to anxiety. However, plots demonstrated notable elevations in static luminance CS limited to specific low-to-mid spatial frequencies (i.e., 2.0 and 2.5 cpd) among individuals reporting anxious mood on the DASS. No trends were apparent for dynamic luminance gratings.

Trait anxiety demonstrated a significant effect on R-G chromatic CS when included as a covariate in analysis with SSRI and clinical depression variables. The direction of effect was positive, indicating that increased trait anxiety was associated with increased R-G CS. Significant effects of anxiety were not observed for B-Y CS. However, plot values showed a tendency toward increased B-Y CS at 4.0 – 0 Hz among participants describing anxious mood on the DASS.

Retinal Enhancements and Contrast Sensitivity Deficits for Depression

The current study hypothesized that depression would be associated with enhancements in visual functioning related to neurotransmitter changes in the retina, and that the koniocellular stream would be most impacted by these enhancements, as suggested by previous findings that short-wavelength light is most effective in influencing neurometric and psychometric dysphoric symptoms (Glickman et al., 2005; Ly et al., 2001). The finding of higher S-cone sensitivity in depression for certain retinal locations supports the hypothesis of enhancements at the retinal level. That is, in peripheral temporal portions of the retina, S-cones were more sensitive among people reporting clinical depression than among those who did not.

The increase in S-cone sensitivity among participants with clinical depression did not translate into enhanced B-Y chromatic CS. Rather, depression was associated with reduced B-Y CS, which suggests the possibility of over-compensatory activity in post-receptoral or post-retinal mechanisms. Alternatively, depression may differentially impact the distinct S-on and S-off cell pathways of the koniocellular stream, both of which are involved in the processing of B-Y CS, whereas SWAP assessment relies more prominently on the S-on pathways. At the same time, increased S-cone sensitivity in the current study was restricted to peripheral (30-50°) portions of the retina, whereas CS stimuli were presented just off center, at 2.5° eccentricity, and SWAP assessment was conducted monocularly, whereas CS measurement was conducted binocularly. Thus, the observed enhancements in S-cone sensitivity for depression may be independent of the reductions that were noted for B-Y CS.

Contrast sensitivity deficits for depression in the current study were not limited to B-Y CS, but also appeared for R-G CS and luminance CS. Although the effects were widespread across the various conditions, the potential of a global reduction is countered by some spatial frequency specificity in static luminance CS, as well as more spatiotemporally extensive reductions in B-Y than R-G CS. Thus, selectivity of deficit was apparent. Early stages of visual functioning were implicated in prior research documenting enhanced luminance CS among individuals with depression (Wesner & Tan, 2006). With the lowest signal to noise ratios of the visual system, the retina sets ceiling levels for higher-order visual performance, and enhancements suggest mechanisms involved in the initiation of the signal. However, CS reductions can occur at any stage of the visual system. Thus, the source of CS deficits among depressed individuals in the current study cannot be isolated to a particular hierarchical stage. Functional anomaly, including possible over-compensation, may occur at the retinal level, where chromatic opponency and luminance contrast arise, or at later stages which integrate these fundamental components of visual information.

Mood versus Disorder Symptoms

Effects on visual functioning were more consistent and significant for the clinical depression variable than the depressed mood variable. Indeed, for S-cone sensitivity and R-G CS, contributions of depressed mood were unremarkable, whereas significant differences were demonstrated for clinical depression. More pronounced results tended to also be observed for trait anxiety compared to anxious mood. This pattern suggests that,

although alterations of mood did have some impact in certain test conditions, visual functioning is most affected by more severe or chronic affective disturbances.

Combination of SSRI Medications and Depression

A common finding throughout analyses was that the combined effect of SSRI medication and clinical depression resulted in larger CS reductions than either on its own. For instance, although SSRI medication did not exert a notable unique influence on luminance CS throughout most of the CS function, it did appear to exacerbate the reductions associated with clinical depression in the low-to-mid range and counteract potential elevation or normalization at the highest spatial frequencies. Similarly, the unique contribution of clinical depression led to significant reductions in B-Y CS, whereas no significant effects were found for SSRI medication; yet, plots demonstrated that the combination of SSRI medication and clinical depression resulted in the lowest levels of B-Y CS. For R-G CS, reductions associated with SSRI medication were more consistent and pronounced than those of depression, but again, the lowest R-G CS was observed among participants who were both clinically depressed and taking SSRI medications.

These findings challenge the hypothesis that anomalies in visual functioning associated with depression would be corrected for by pharmacotherapy. Specifically, if disruption of visual functioning in depression were related to monoamine deficits in the retina, then antidepressant medications, which exert their primary influence on monoamines, were expected to rectify the visual disturbance. However, an opposite pattern was observed in the current study. When significant unique effects were observed

for both SSRI medication and depression, as was the case with R-G CS, they demonstrated the same direction of effect, acting to reduce CS. Further, when significant findings were not observed for SSRI medication, as was the case for most conditions in the assessment of luminance and B-Y CS, it nevertheless exacerbated the deficits demonstrated for depression. Thus, although participants who reported depression demonstrated reduced CS, those who were also taking SSRI medications showed the most extreme reductions, while participants who were taking SSRI medications but were no longer depressed often demonstrated CS levels that were comparable to those of healthy control participants. This pattern points away from a simple imbalance in retinal monoamines as causing visual disturbances in depression, and instead suggests a more complex interplay between the downstream neurotransmitter or neuromodulatory actions of SSRI medication, other neurochemical correlates of depression, and anomalies of visual functioning. GABA and glutamate, which are primary neurotransmitters in the retina and throughout later stages of the visual system, may be involved in the visual effects noted in the current study, since they have been implicated in both anxiety and depressive disorders (Brambilla et al., 2003; Choudry et al., 2005; Kelmendi et al., 2006; Paul & Skolnick, 2003; Young et al., 2002), and are known to be affected by SSRI medications (Kelmendi et al., 2006; Sanacora et al., 2002; Slattery & Cryan, 2006).

When SSRI medications did demonstrate unique contributions to CS, the effects of depression were not as consistent. Specifically, at the highest spatial frequencies of the static luminance condition, SSRI medications were associated with reduced luminance CS, whereas luminance CS for depression was comparable to normal levels. Also, SSRI

medications showed significant main effects for R-G CS, whereas depression was only linked to lower CS at certain spatial and temporal frequencies, and even then, only if it was the variable of clinical depression and not depressed mood. By contrast, SSRI medications failed to demonstrate unique effects in conditions where the most consistent and prominent results were apparent for depression, in the low-to-mid range of luminance CS and for B-Y CS. This suggests that although an interaction between SSRI medication and depression is indicated by the observation of their combined effects leading to more extreme results than either alone, their strongest unique contributions to visual functioning appear to be produced in separate visual streams or perceptual channels.

Opposite Effects of Depression and Anxiety

The effects of anxiety and depression were in opposite directions for both CS and S-cone sensitivity. Anxiety was associated with CS enhancements, which were apparent at the low-to-mid spatial frequencies of static luminance CS conditions and for R-G CS, as well as a tendency toward some elevation at certain spatiotemporal frequencies for B-Y CS. By comparison, the results of depression indicated reduced CS in these conditions. The reverse pattern was evident for S-cone sensitivity, for which depression was associated with significant elevations in S-cone sensitivity in the peripheral sections of the temporal hemiretina, while anxiety was associated with significant reductions in these areas, as well as the paracentral portion of the superior nasal quadrant.

These results suggest that anxiety and depression are largely impacting the same mechanisms of visual functioning, but with opposite effects. This is consistent with the

diverging symptom dimensions of anxiety and depressive disorders, despite frequent co-occurrence and similar treatments. Specifically, symptoms of anxiety relate to physiological and cognitive over-activity, including arousal and hypervigilance, whereas symptoms of depression more often reflect diminished energy and concentration, and dulled responsivity in terms of motivation, pleasure, and interest (American Psychiatric Association, 2000). Yet, there is high co-morbidity between anxiety and depressive disorders, and many of the same pharmacotherapies are used for their treatment.

For both depression and anxiety, the shifts in S-cone sensitivity observed in the current study were largely limited to peripheral portions of the temporal hemiretina. The retinal location specificity of these results parallels the various asymmetries of retinal function and physiology which have been documented. For instance, visual acuity for achromatic and short-wavelength-isolating stimuli has been found to be significantly higher in the nasal than the temporal retina beginning around 25° eccentricity (S.J. Anderson, Mullen, & Hess, 1991; R.S. Anderson, Wilkinson, & Thibos, 1992; Bierne et al., 2005; Rovamo, Virsu, Laurinen, & Hyvarinen, 1982). This has been linked with an increase in corresponding retinal ganglion cell densities along the nasal horizontal meridian compared to the temporal horizontal meridian (Curcio & Allen, 1990). At 25° eccentricity, a similar increase in ganglion cell densities has been observed in superior portions of the retina compared to inferior portions (Curcio & Allen, 1990). Differential acuity and contrast thresholds for S-on pathways compared to S-off pathways has also been observed in peripheral locations, but not more central locations (Zlatkova, Vassilev, & Anderson, 2008). A previous SWAP study found enhanced peripheral sensitivity in the

temporal quadrant compared to the nasal quadrant in healthy participants (Sample et al., 1997). Examination of S-cone distributions has indicated a slight increase in S-cone density in superior portions of human retina (Ahnelt et al., 2006). A nasal-temporal asymmetry has not been reported for humans (Curcio et al., 1991), although studies with other primates have noted such asymmetry (DeMonasterio, McCrane, Newlander, & Schein, 1985; Martin & Grunet, 1999). Asymmetries in retinal physiology and function could make certain retinal locations more susceptible to the effects of depression and anxiety.

Peripheral vision narrowing, involving decreased detection of peripheral stimuli, has been reported among athletes in high stress sports situations (e.g., Andersen & Williams, 1999; Rogers & Landers, 2005; Williams & Andersen, 1997; Williams, Tonymon, & Andersen, 1991). This has been attributed to a stress response affecting visual attention. Similarly, human centrifuge studies and examination of aviation pilots in high acceleration have documented a specific pattern of visual effects (Lambert, 1945; Whinnery & Shender, 1993; Wieling et al., 2009; Wood, Lambert, Baldes, & Code, 1946; Yilmaz, Cetinguc, & Akin, 1999), beginning with peripheral "graying" (i.e., loss of colour vision in periphery), followed by complete loss of vision or "blacking out" that begins in the periphery and moves inward, but is not accompanied by a loss of consciousness. This is caused by changes in blood pressure resulting in retinal hypoperfusion but not cerebral hypoperfusion, due to intraocular pressure additionally contributing to the former. Because retinal vasculature becomes less dense as it radiates outward from the optic nerve, initial reductions in blood pressure first impact peripheral

portions of the retina. This suggests the possibility of milder blood pressure changes affecting peripheral vision sensitivity among individuals with anxiety or stress. That is, activation of the sympathetic system due to the physiological arousal associated with anxiety may attenuate retinal perfusion, leading to subtle reductions in peripheral vision sensitivity, as was observed in the current study; however, it is unclear how retinal vasculature may impact peripherally-specific enhancements in S-cone sensitivity among individuals who instead experience depression.

Visual Streams Impacted by SSRI Medications, Depression, and Anxiety

Unique effects of SSRI medications were limited to reduced luminance CS at the highest static spatial frequency and reduced R-G chromatic CS, which corresponds to primary deficits in the parvocellular stream. SSRI medications may also impact other streams indirectly through their exacerbation of the CS reductions associated with depression. Results of chromatic vision tests indicate definite involvement of the koniocellular stream in depression, with respect to significant findings for S-cone sensitivity and B-Y chromatic CS. Anxiety also impacted S-cone sensitivity, implicating the koniocellular stream, although results for B-Y CS were less pronounced. For R-G CS, which reflects parvocellular functioning, a significant overall effect was demonstrated by trait anxiety and clinical depression showed selective spatiotemporal effects.

Interpretation of luminance CS results for depression and anxiety is less straightforward with respect to visual stream localization. The lack of notable group differences at the lowest luminance spatial frequencies for static stimuli points away from the magnocellular stream. However, the finding of significant effects for depression

in certain dynamic luminance CS conditions suggests possible magnocellular involvement, although both the parvocellular and koniocellular streams are known to contribute to motion processing, albeit to a much lesser degree than the magnocellular stream (e.g., Michna, Yoshizawa, & Mullen, 2006; Morand et al., 2000; Nassi & Callaway, 2006; Riecansky, Thiele, Distler, & Hoffman, 2005; Ruppertsberg, Wuerger, & Bertamini, 2003, 2007; Takeuchi, DeValois, & Hardy, 2003). The temporal frequency of 4 Hz was chosen for this study to allow for temporal modulation in chromatic Gabors, which are not perceived well at higher temporal frequencies; however, 4 Hz may not be high enough to exclude possible parvocellular or koniocellular processing of motion for luminance stimuli.

For static luminance CS, the most notable effects of depression and anxiety were observed at spatial frequencies intermediate to exclusive magnocellular and parvocellular functioning. The lowest and highest spatial frequencies of static luminance CS are known to be processed separately by the magnocellular and parvocellular streams, respectively. Intermediate spatial frequencies are thought to be processed by an overlap of channels associated with both magnocellular and parvocellular functions. However, the current study used threshold levels to isolate only the most sensitive channels, and the literature is not clear about whether the magnocellular or parvocellular stream is most sensitive at the affected spatial frequencies. Thus, results could either reflect the low end of parvocellular functioning or the high end of magnocellular functioning. Further, the most sensitive channel at these intermediate spatial frequencies may differ between clinical

and control groups and, consequently, threshold measurements could refer to different channels for different groups of participants.

An alternative explanation has been suggested that intermediate spatial frequencies may be optimally processed by an independent visual stream (e.g., Maddock, Casson, Lott, Carter, & Johnson, 1993), separate from the magnocellular and parvocellular streams. The koniocellular stream may be a candidate. Although the bulk of knowledge that has accumulated over the last decade about the koniocellular stream has focused on its S-cone connections and B-Y chromatic opponency, it has in fact been shown to comprise a diverse collection of cells and LGN layers, many of which have not been studied sufficiently to infer functionality (Casagrande, 1994; Dacey & Packer, 2003; Hashemi-Nezhad, Blessing, Dreher, & Martin, 2008; Hendry & Reid, 2000; Roy et al., 2009; White, Goodchild, Wilder, Sefton, & Martin, 1998; Xu et al., 2001). The assumption that koniocellular functions are limited to processes that involve S-cones is not warranted, given that at least some cells in the koniocellular stream do not appear to process S-cone input (Casagrande & Xu, 2003; Casagrande, Yazar, Jones, & Ding, 2007; Forte, Hashemi-Nezhad, Dobie, Dreher, & Martin, 2005; Szmajda, Grunert, & Martin, 2008). Further, even among koniocellular cells that do process S-cone information, connections with L- and M-cones are required for B-Y opponency, and there is recent evidence to suggest that achromatic luminance signals are also processed by these cells (Forte et al., 2005; Horwitz, Chichilnisky, Albright, 2005; Ripamonti, Woo, Crowther, & Stockman, 2009; Roy, et al., 2009; Tailby, Solomon, & Lennie, 2008; White et al., 2001). The spatial frequency parameters of luminance processing in the koniocellular

system has not yet been clearly specified, but there is suggestion that they may respond to spatial frequencies intermediate to those optimally processed by the magnocellular and parvocellular streams (Forte et al., 2005; Roy et al., 2009; White et al., 2001). If this holds true, then the luminance and chromatic results of the current study would most consistently point to the koniocellular stream as the site of primary effects of depression on visual functioning, with additional involvement of the parvocellular stream and less support for magnocelluar involvement. The effects of anxiety would similarly include both koniocellular and parvocellular streams.

Comparison with Previous Research

The finding that depression was associated with reduced luminance CS in the low-to-mid ranges of spatial frequency corresponds to the luminance CS research conducted by Szabo et al. (2004), which found that marginal CS deficits among individuals experiencing a depressive phase of seasonal depression were corrected to normal levels by light therapy, with the most pronounced increases evident in the low and mid ranges of spatial frequency (i.e., 0.5, 1.2, 3.6, 4.8, and 5.7 cpd). However, results of the current study appear to contradict the only previously published investigation of luminance CS which included a focus on non-seasonal depression. Specifically, Wesner and Tan (2006) found elevated luminance CS at static spatial frequencies above 2.5 cpd among participants with seasonal and non-seasonal depression compared to control participants, with significant increases beginning at 6.0 cpd.

Examination of the luminance CS functions in the current study and the study by Wesner and Tan (2006) indicates a similar broader curve evident among depressed

participants compared to non-depressed individuals, with the two studies differing primarily in terms of baseline levels. In Wesner and Tan, the luminance CS function of depressed individuals begins with sensitivity levels similar to those of control participants at low and mid spatial frequencies, but increases to elevated sensitivities at higher spatial frequencies, whereas in the current study, the luminance CS of depressed individuals is reduced at low-to-mid spatial frequencies, but increases to levels similar to control participants at higher spatial frequencies. Thus, the CS functions of depressed participants in the current study represent a general downward shift in baseline CS when compared to the findings of Wesner and Tan.

One methodological difference between the studies relates to month of testing. A preliminary study by Gallant & Wesner (2004) found a notable reduction in luminance CS in the summer months than the winter months among non-seasonally depressed individuals. This would seem to account for the lower baseline levels of luminance CS in the current study, which had a larger proportion of depressed participants tested in the spring and summer months compared to the study by Wesner and Tan (2006). However, analysis of the correlations between test month and CS in the current study found an opposite trend. Specifically, when significant relationships were present, they indicated higher CS in the summer than in the winter, which does not explain the lower luminance CS levels demonstrated by depressed individuals in the current study and indicates that test month did not impact the pattern of results.

Another methodological difference is the inclusion of anxiety measures in the current study, with plots demonstrating some elevation in luminance CS among

individuals with anxiety. This suggests the possibility that the higher CS among depressed participants in Wesner and Tan (2006) may reflect unmeasured comorbid anxiety. However, in the current investigation, elevations associated with anxiety were most notable at low-to-mid spatial frequencies (i.e., 2.0 and 2.5 cpd), whereas increases among depressed individuals in Wesner and Tan were limited to high spatial frequencies. Antidepressant medications were not controlled for in Wesner and Tan, despite a small proportion taking SSRIs (11.8% of non-seasonally depressed participants and 17.4% of seasonally depressed participants). This is not considered to account for the different results between studies, however, since the current investigation found that SSRIs contributed to reduced luminance CS at the highest spatial frequencies, whereas Wesner and Tan found elevations at these spatial frequencies. The mean age of participants reporting depressed mood ($M = 27.5$, $SD = 7.2$) and clinical depression ($M = 29.3$, $SD = 6.1$) in the current study was somewhat higher than that for non-seasonally depressed participants ($M = 22.41$, $SD = 8.94$) in Wesner and Tan, but comparable to that for SAD participants ($M = 29.33$, $SD = 12.20$). Since contrast sensitivity generally declines with age, it is possible that the higher age in the current study may explain the lower baseline levels for luminance CS functions. However, there were no significant correlations between age and luminance CS in the current study, neither across the total sample nor among participants who reported clinical depression or depressed mood.

Other methodological differences between the current study and Wesner and Tan (2006) were minimal. The procedures and stimuli used for psychophysical measurement of luminance CS were nearly identical. Sample sizes for depressed mood participants (*n*

= 15) and clinical depression participants (n = 11) in the current study were slightly lower, than that of the non-seasonal depression group (n = 17) in Wesner and Tan, but nevertheless demonstrated sufficient power to detect significant results. Thus, the divergent findings for depression of elevated luminance CS at high spatial frequencies in the Wesner and Tan study, compared to reduced luminance CS at low-to-mid spatial frequencies in the current study, are not satisfactorily accounted for by methodological differences. Although an explanation for the different results remains unclear, the similarity of findings is also noteworthy, since the luminance CS function in both studies depicted a similar shaped curve for depressed individuals that was broader than that observed among non-depressed individuals.

Dynamic luminance CS was impacted by depression in the current study, but differences were more apparent for the clinical depression variable than the depressed mood variable, and were also restricted to specific spatial frequencies. These limited findings parallel those found in Wesner and Tan (2006), in which dynamic luminance CS differences were only observed at one spatial frequency in the 2 Hz conditions, but not at higher temporal frequencies, and were only evident for seasonally depressed participants. Again though, differences in the current study indicate dynamic luminance CS reductions, whereas differences in Wesner and Tan were in the direction of elevation. Szabo et al. (2004) did not find any significantly different changes in dynamic luminance CS (8 Hz) between individuals with seasonal depression and healthy control participants.

Comparison with previous research for SSRIs and for anxiety is difficult due to the dearth of psychophysical vision research in these areas. Although general visual side-

effects, such as blurred or "abnormal" vision, are included in the side-effect profiles of most SSRI medications, systematic research into the nature of these visual anomalies has not been reported. Psychophysical research has examined TCAs and dopamine-based antidepressants, with contrast sensitivity research for the latter finding increased luminance CS for medium and high spatial frequencies after a single dose (Domenici et al., 1985). With respect to anxiety, investigations of the effects of lorazepam, a benzodiazepine often prescribed to treat anxiety, have documented losses in CS following acute administration (Harris & Phillipson, 1995). A study of lorazepam among long-term users additionally measured anxiety (Giersch et al., 2006). Lorazepam was associated with reduced luminance CS in median spatial frequencies (1.0 to 4.0 cpd). No correlation was found between luminance CS performance and anxiety; however, the authors noted that indirect correlations suggested a possible partial contribution of anxiety to the effect of lower luminance CS. The current study observed a trend in luminance CS that was similarly limited to intermediate spatial frequencies, although the direction of the trend was toward higher luminance CS among individuals with anxiety.

Chromatic contrast sensitivity has not been investigated in previous research regarding depression, anxiety, or antidepressant medications. Short-wavelength light was found to be sufficient to induce an antidepressant effect among individuals with seasonal affective disorder (T.M. Lee et al., 1997; Glickman et al., 2005). Phototherapy with narrow-band "blue" light (440 nm) was also found to correct for anomalies in luminance CS among individuals with seasonal and non-seasonal depression, whereas phototherapy with narrow-band "yellow" light (580 nm) did not (Ly et al., 2001). This suggests that

depression is associated with chromatically selective effects involving the processing of short-wavelength light. In the current study, both B-Y CS and R-G CS deficits were observed for depression, although effects for B-Y CS were more extensive, lending some support to a possible short-wavelength bias in visual functioning associated with depression. It is not known if the observed shifts in S-cone sensitivity are specific to S-cones, since L- and M-cone sensitivity was not assessed in the current study.

Limitations and Future Directions

The current study would have benefited from increased numbers of participants. This is particularly true since a third between-subjects variable was added to several analyses when anxiety covariates were transformed into independent variables due to violations of homogeneity of regression. Consequently, the number of cells in these analyses was doubled, reducing power and increasing the chance of Type II errors. Thus, there is a greater likelihood that instances of nonsignificance may be due to insufficient power, rather than actual lack of effect. Additionally, multiple analyses were conducted, which could inflate the occurrence of significance to some degree. The current study did not adjust significance values to account for multiple analyses, given the debate about the appropriateness of this practice. However, exact significant levels and effect sizes were reported.

Some indication of a possible dose-response effect of SSRI medication was observed in the current study. However, the composition and sample size of the antidepressant group did not allow for reliable analysis of dose effects. Larger numbers of participants taking the same medication would permit within-group comparisons of

dose effects, as well as interactions with other relevant parameters, such as duration of medication or disorder. Alternatively, biological measurement of neurotransmitter concentrations would enable more precise analysis. In addition, due to participant availability, the present study was limited to investigation of SSRI medications, and it is recommended that antidepressants other than SSRIs be included in future research.

The significant findings related to anxiety, as well as the frequent co-morbidity between anxiety and depression, highlight the importance of continuing to include anxiety as a variable in future vision research with depressive disorders. There was also a tendency for measures of depression and anxiety to be associated with the most consistent results when they referred to more chronic or severe symptom experiences. Thus, future research may be better informed by a focus on diagnosed disorders of depression and anxiety, rather than questionnaire assessments. As well, previous research with seasonal depression suggests that an explicit control for effects of season on mood and visual functioning would help clarify this potential confound.

Results of SWAP measurement in the current study indicate anomalies in S-cone sensitivity associated with depression and anxiety, implicating the earliest levels of retinal processing. Further research examining M- and L-cone sensitivity would be useful for comparison. Additionally, the finding of retinal location specificity with respect to S-cone sensitivity suggests that other psychophysical techniques also sample multiple retinal locations and eccentricities.

Contrast sensitivity measurement, using sine-wave gratings, was chosen for the current study because it represents one of the most thorough methods of assessing and

manipulating a range of fundamental properties of visual perception. Although commonly used in psychophysical investigations, some researchers have suggested that contrast sensitivity gratings may be too complex to reliably isolate visual streams and localize hierarchical stages of the visual system (e.g., Keri et al., 2004, 2005). Indeed, there is some ambiguity with respect to the interpretation of results in the current study related to intermediate spatial frequencies in static luminance CS conditions, although this is more a reflection of the state of recently acquired knowledge regarding visual system complexities, rather than limitations in psychophysical stimuli. Nevertheless, the use of additional psychophysical methods may provide new perspectives to help clarify the nature of visual anomalies associated with depression, anxiety, and antidepressant medication.

Within the more extensively studied areas of visual functioning in neurodegenerative disorders and schizophrenia, some researchers have suggested that Vernier tasks use more basic visual stimuli than contrast sensitivity methods (Keri et al., 2004, 2005). Alternatively, CS gratings have been adapted to include varying pedestal conditions to better isolate visual stream functioning, based upon the work of Pokorny and Smith (1997) and Leonova, Pokorny, and Smith (2003). Various masking and noise procedures have additionally been used to better isolate hierarchical stages of visual processing (e.g., Censor, Bonneh, Arielli, & Sagi, 2009; Georgeson & Meese, 2006; Smith, 2000). Presentation of Gabors at varying orientations would also distinguish hierarchical stages of the visual system, since orientation-specificity is largely a cortical function (Edden, Muthukumaraswamy, Freeman, & Singh, 2009). Additionally,

psychophysical assessements can be supplemented by electrophysiological (e.g., electroretinography, visual evoked potentials) and neuroimaging measures (MRI, fMRI) to help localize visual stream involvement and hierarchical levels of the visual system (e.g., Braus, Weber-Fahr, Tost, Ruf, & Henn, 2002; Butler et al., 2001; Doniger, Foxe, Murray, Higgins, & Javitt, et al., 2002). These types of methods are recommended for future research to more confidently isolate vision abnormalities in depressive disorders, now that such anomalies have been identified.

Conclusions

Psychophysical investigation of visual functioning has only recently been applied in the area of depressive disorders. The current research extends upon a handful of previous studies that have explored luminance contrast sensitivity in depressive disorders. Additionally, the current research is the first known study to systematically examine chromatic visual functioning in depressive disorders, and to investigate the effects of SSRIs in conjunction with depression and anxiety.

Results document various sub-clinical visual anomalies. Depression was associated with reductions in luminance contrast sensitivity that were most apparent at intermediate spatial frequencies; reductions in chromatic contrast sensitivity, especially B-Y conditions; and increased S-cone sensitivity in peripheral temporal portions of the retina. These findings indicate an impact that is most prominent in, but not limited to, the koniocellular stream. The effects of anxiety were opposite to those of depression, with a tendency toward elevated luminance contrast sensitivity at intermediate spatial frequencies, increased chromatic contrast sensitivity, and reduced S-cone sensitivity.

SSRI medications led to deficits that were indicative of primary effects in the parvocellular stream, with decreased luminance CS at the highest spatial frequencies and reduced R-G CS. When unique contributions of SSRI medications were not observed, they nevertheless tended to exacerbate the contrast sensitivity reductions associated with depression.

As a new line of inquiry, results of the current study raise a number of questions for further research. For instance, although the hypothesis of early stage visual anomalies in depression is supported by elevated S-cone sensitivity, the apparently contradictory finding of reduced B-Y chromatic sensitivity negates straightforward interpretation and points to interaction, feedback, or compensatory effects that are at least post-receptoral and may involve higher-order visual system functions as well. Additionally, the hypothesis that antidepressant medications would correct for visual anomalies associated with depression did not hold true for SSRI medications, opposing a simple model of retinal monoamine availability. Thus, more research is required to better localize the effects of depression, anxiety, and antidepressant medications within the visual system and to determine the mechanisms through which these effects are produced. Results of the current study are compelling, however, and confirm the importance of future research in this area.

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Table 1

Participants Taking SSRI Medications: Dose, Duration, and Reason

Age	Gender	SSRI	Daily	Duration (mos.)	Reason for Medication
18	f	citalopram	20 mg	1	depression
31	f	citalopram	40 mg	24	depression
36	m	citalopram	20 mg	62	depression
31	f	fluoxetine	40 mg	30	depression primary, and anxiety
35	f	fluoxetine	20 mg	96	depression
24	f	paroxetine	50 mg	54	depression
36	m	paroxetine	50 mg	58	anxiety primary, and depression
41	f	paroxetine	20 mg	72	anxiety primary, and depression
18	f	sertraline	175 mg	42	depression
19	f	sertraline	150 mg	18	depression primary, and anxiety
20	f	sertraline	150 mg	3	anxiety primary, and depression
24	f	sertraline	50 mg	11	anxiety
40	f	sertraline	100 mg	120	depression

Table 2

Cell sizes for ANCOVAs involving the Between-Subject Variables of SSRI Medication Status, DASS Depressed Mood, and DASS Anxious Mood

DASS Depressed Mood	DASS Anxious Mood	SSRI Medication Status		
		No SSRI	SSRI	
No Depressed Mood	No Anxious Mood	12	3	(15)[a]
	Anxious Mood	10	4	(14)
		(22)	(7)	(29)
Depressed Mood	No Anxious Mood	8	4	(12)
	Anxious Mood	1	2	(3)
		(9)	(6)	(15)

Note. Due to unbalanced cell sizes, ANCOVAs relied on Type III sum of squares.

[a]Numbers in parantheses represent marginal frequency totals.

Table 3

Cell sizes for ANCOVAs involving the Between-Subject Variables of SSRI Medication Status and DID Clinically-Defined Depression

DID Clinically-Defined Depression	SSRI Medication Status		
	No SSRI	SSRI	
No Clinical Depression	24	9	(33)[a]
Clinical Depression	7	4	(11)
	(31)	(13)	(44)

Note. Due to unbalanced cell sizes, ANCOVAs relied on Type III sum of squares.

[a]Numbers in parantheses represent marginal frequency totals.

Table 4

Cell sizes for ANCOVAs involving the Between-Subject Variables of SSRI Medication Status, DID Clinically-Defined Depression, and STAI Trait Anxiety

DID Clinically-Defined Depression	STAI Trait Anxiety	SSRI Medication Status		
		No SSRI	SSRI	
No Clinical Depression	Low Trait Anxiety	19	2	(21)[a]
	High Trait Anxiety	5	7	(12)
		(24)	(9)	(33)
Clinical Depression	Low Trait Anxiety	1	-	(1)
	High Trait Anxiety	6	4	(10)
		(7)	(4)	(11)

Note. Due to an empty cell, ANCOVAs relied on Type IV sum of squares.

[a]Numbers in parantheses represent marginal frequency totals.

Table 5

Demographic and Mental Health Characteristics for Primary Between-Subjects Variables

Between-Subjects Variables	*n*	Age		Gender		SSRI	Prev. Dep. Diagnosis[a]	Prev. Anx. Diagnosis[b]	Prev. Hospital.[c]
		M (SD)	Range	Men	Women	*n* (%)	*n* (%)	*n* (%)	*n* (%)
SSRI Medication Status									
SSRI	13	28.7 (8.6)	18-41	2	11	13 (100.0)	12 (92.3)	7 (53.8)	3 (23.1)
No SSRI	31	21.8 (4.9)	18-33	9	22	0 (0.0)	7 (22.6)	5 (16.1)	2 (6.5)
DASS Depressed Mood									
Depressed Mood	15	27.5 (7.2)	18-40	4	11	6 (40.0)	11 (73.3)	3 (20.0)	2 (13.3)
No Depressed Mood	29	22.0 (7.1)	18-41	7	22	7 (24.1)	8 (27.6)	9 (31.0)	3 (10.3)
DASS Anxious Mood									
Anxious Mood	17	21.0 (5.7)	18-40	4	13	6 (35.3)	7 (41.2)	7 (41.2)	4 (23.5)
No Anxious Mood	27	25.7 (7.1)	18-41	7	20	7 (25.9)	12 (44.4)	5 (18.5)	1 (3.7)
DID Clinically-Defined Dep.									
Clinical Depression	11	29.3 (6.1)	18-40	2	9	4 (36.4)	9 (81.8)	2 (18.2)	2 (18.2)
No Clinical Depression	33	22.1 (6.2)	18-41	9	24	9 (27.3)	10 (30.3)	10 (30.3)	3 (9.1)
Total Sample	44	23.9 (6.9)	18-41	11	33	13 (29.5)	19 (43.2)	12 (27.3)	5 (11.4)

[a]Previous Depression Diagnosis. [b]Previous Anxiety Diagnosis. [c]Previous Hospitalization for Mental Illness.

Table 6

Mood Characteristics for Primary Between-Subjects Variables

Between-Subjects Variables	*n*	DASS Depressed Mood *M*(*SD*)	DASS Depressed Mood Range	DASS Anxious Mood *M*(*SD*)	DASS Anxious Mood Range	STAI – Trait Anxiety *M*(*SD*)	STAI – Trait Anxiety Range	DID Clinical Depression *n* (%)
SSRI Medication Status								
SSRI	13	13.23(10.91)	0-35	7.31(4.63)	0-16	50.15(10.08)	30-67	4 (30.8)
No SSRI	31	6.81(8.34)	0-33	5.23(4.49)	0-18	38.26(12.38)	20-68	7 (22.6)
DASS Depressed Mood								
Depressed Mood	15	19.53(8.43)	10-35	6.00(4.29)	1-16	53.00(10.68)	29-68	11 (73.3)
No Depressed Mood	29	3.10(2.86)	0-9	5.76(4.79)	0-18	35.97(9.73)	20-55	0 (0.0)
DASS Anxious Mood								
Anxious Mood	17	8.29(10.51)	0-35	10.65(3.00)	8-18	46.06(10.73)	33-68	2 (11.8)
No Anxious Mood	27	8.96(9.03)	0-30	2.81(2.13)	0-7	39.07(13.54)	20-67	9 (33.3)
DID Clinically-Defined Dep.								
Clinical Depression	11	22.00(8.46)	11-35	5.73(3.64)	1-14	54.91(11.77)	29-68	11 (100.0)
No Clinical Depression	33	4.27(4.27)	0-17	5.88(4.90)	0-18	37.39(10.00)	20-55	0 (0.0)
Total Sample	44	8.70(9.52)	0-35	5.84(4.58)	0-18	41.77(12.86)	20-68	11 (25.0)

Table 7

Summary of ANCOVAs included in Primary Analyses

Between-Subjects Variables	Within-Subjects Variables	Covariates
Dependent Variable: S-cone Sensitivity		
1. SSRI Medication Status (2) x DASS Depressed Mood (2) x DASS Anxious Mood (2)	Retinal Eccentricity (3)	Age
2. SSRI Medication Status (2) x DID Clinically-Defined Depression (2) x Trait Anxiety (2)	Retinal Eccentricity (3)	Age
3. SSRI Medication Status (2) x DASS Depressed Mood (2) x DASS Anxious Mood (2)	Hemiretina Section (5)	Age
4. SSRI Medication Status (2) x DID Clinically-Defined Depression (2) x Trait Anxiety (2)	Hemiretina Section (5)	Age
5. SSRI Medication Status (2) x DASS Depressed Mood (2) x DASS Anxious Mood (2)	Retinal Location (11)	Age
6. SSRI Medication Status (2) x DID Clinically-Defined Depression (2) x Trait Anxiety (2)	Retinal Location (11)	Age
Dependent Variable: Static Luminance CS		
1. SSRI Medication Status (2) x DASS Depressed Mood (2) x DASS Anxious Mood (2)	Spatial Frequency (10)	Age
2. SSRI Medication Status (2) x DID Clinically-Defined Depression (2)	Spatial Frequency (10)	Age, Trait Anxiety Score
3. Medication/Depression (4)	Spatial Frequency (10)	Age, Trait Anxiety Score
Dependent Variables: Separate ANCOVAs for (a) Luminance CS (static and dynamic); (b) R-G Chromatic CS; and (c) B-Y Chromatic CS		
1. SSRI Medication Status (2) x DASS Depressed Mood (2) x DASS Anxious Mood (2)	Temporal Freq. (2) x Spatial Freq. (3)	Age
2. SSRI Medication Status (2) x DID Clinically-Defined Depression (2)	Temporal Freq. (2) x Spatial Freq. (3)	Age, Trait Anxiety Score
3. Medication/Depression (4)	Temporal Freq. (2) x Spatial Freq. (3)	Age, Trait Anxiety Score

Table 8

Relative SSRI Dosage Scale and Actual SSRI Doses

	Relative SSRI Dosage Scale Score					
SSRI	1.00	4.00	5.50	7.00	7.75	8.50
citalopram	20 mg (n = 2)		40 mg (n = 1)			
fluoxetine	20 mg (n = 1)	40 mg (n = 1)				
paroxetine	20 mg (n = 1)				50 mg (n = 2)	
sertraline	50 mg (n = 1)	100 mg (n = 1)		150 mg (n = 2)		175 mg (n = 1)

Note. The relative SSRI dosage scale was based upon the following standard dose ranges for the SSRIs included in the present study: citalopram = 20 to 60 mg; fluoxetine = 20 to 80 mg; paroxetine = 20 to 60 mg; and sertraline = 50 to 200 mg. Scores for the relative dosage scale ranged from 1 to 10, with the lowest standard dose for each medication equaling 1 and the highest standard dose for each medication equaling 10. Intermediate doses were divided with equal spacing according to each medication's standard dose range.

Table 9

Log Unit Differences in Luminance Contrast Sensitivity Function Values between Variable Levels

	Spatial Frequency (cpd) at 0 Hz									
Variable Levels Comparisons	0.5	1.0	1.5	2.0	2.5	4.0	6.0	8.0	10.0	12.0
SSRI Medication Status										
No SSRI - SSRI	0.06	-0.07	0.02	0.05	0.03	0.02	0.03	0.05	**0.12•**	**0.19•**
DASS Depressed Mood										
No Depressed Mood - Depressed Mood	0.01	0.06	0.05	**0.11•**	**0.12•**	0.07	0.01	0.06	**0.10•**	0.00
DASS Anxious Mood										
No Anxious Mood - Anxious Mood	-0.02	-0.02	0.01	**-0.12•**	**-0.12•**	-0.02	-0.01	-0.02	0.00	0.02
DID Clinically-Defined Depression										
No Clinical Depression - Clinical	0.04	**0.10•**	0.07	0.05	**0.13•**	0.06	-0.01	0.06	0.03	-0.04
Medication/Depression										
HEALTHY - MEDONLY	0.02	-0.08	-0.01	0.06	-0.03	-0.01	-0.06	0.04	0.05	**0.20•**
HEALTHY - DEPONLY	-0.02	**0.11•**	0.03	0.06	0.06	0.02	**-0.11•**	0.05	-0.03	-0.05
HEALTHY - DEPMED	**0.16•**	0.03	**0.14•**	0.08	**0.27•**	**0.13•**	**0.17•**	**0.11•**	**0.21•**	**0.14•**
MEDONLY - DEPONLY	-0.03	**0.19•**	0.04	0.01	0.08	0.03	-0.05	0.00	-0.07	**-0.25•**
MEDONLY - DEPMED	**0.15•**	**0.12•**	**0.16•**	0.02	**0.30•**	**0.14•**	**0.23•**	0.07	**0.16•**	-0.07
DEPONLY - DEPMED	**0.18•**	-0.07	**0.12•**	0.02	**0.21•**	**0.11•**	**0.28•**	0.06	**0.24•**	**0.18•**

Note. Differences equal to or greater than 0.10 log units are indicated with a bullet (•) and in boldtype. They reflect contrast differences that are well beyond suprathreshold levels for discrimination, as generally defined by differences larger than 2% relative contrast.

Table 10

Log Unit Differences in Luminance Contrast Sensitivity (Static and Dynamic) between Variable Levels

	Spatial Frequency (cpd) at 0 Hz			Spatial Frequency (cpd) at 4 Hz		
Variable Levels Comparisons	0.5	1.5	4.0	0.5	1.5	4.0
SSRI Medication Status						
No SSRI - SSRI	0.06	0.02	0.02	-0.01	0.09	-0.07
DASS Depressed Mood						
No Dep. Mood – Dep. Mood	0.01	0.05	0.07	0.06	**0.10•**	0.05
DASS Anxious Mood						
No Anxious Mood - Anxious Mood	-0.02	0.01	-0.02	-0.05	0.00	-0.07
DID Clinically-Defined Depression						
No Clinical Dep. - Clinical Dep.	0.04	0.07	0.06	**0.11•**	**0.13•**	0.03
Medication/Depression						
HEALTHY - MEDONLY	0.02	-0.01	-0.01	-0.05	0.09	-0.08
HEALTHY - DEPONLY	-0.02	0.03	0.02	0.07	**0.14•**	0.02
HEALTHY - DEPMED	**0.16•**	**0.14•**	**0.13•**	**0.15•**	**0.18•**	-0.02
MEDONLY - DEPONLY	-0.03	0.04	0.03	**0.12•**	0.05	**0.10•**
MEDONLY - DEPMED	**0.15•**	**0.16•**	**0.14•**	**0.20•**	0.09	0.06
DEPONLY - DEPMED	**0.18•**	**0.12•**	**0.11•**	0.08	0.04	-0.04

Note. Differences equal to or greater than 0.10 log units are indicated with a bullet (•) and in boldtype. They reflect contrast differences that are well beyond suprathreshold levels for discrimination, as generally defined by differences larger than 2% relative contrast.

Table 11

Log Unit Differences in "Red-Green" Chromatic Contrast Sensitivity between Variable Levels

	Spatial Frequency (cpd) at 0 Hz			Spatial Frequency (cpd) at 4 Hz		
Variable Level Comparisons	0.5	1.5	4.0	0.5	1.5	4.0
SSRI Medication Status						
No SSRI - SSRI	0.04	-0.04	**0.11•**	-0.02	0.05	**0.15•**
DASS Depressed Mood						
No Dep. Mood – Dep. Mood	0.01	0.04	-0.05	-0.09	0.02	0.05
DASS Anxious Mood						
No Anxious Mood - Anxious Mood	0.03	0.01	0.05	-0.03	-0.04	-0.03
DID Clinical Depression						
No Clinical Dep. - Clinical Dep.	0.07	**0.10•**	-0.05	-0.03	0.01	0.05
Medication/Depression						
HEALTHY - MEDONLY	-0.02	**-0.12•**	0.08	-0.04	0.08	**0.19•**
HEALTHY - DEPONLY	-0.01	-0.01	-0.09	-0.06	0.04	0.08
HEALTHY - DEPMED	**0.21•**	**0.22•**	**0.10•**	-0.02	0.01	**0.13•**
MEDONLY - DEPONLY	0.01	**0.11•**	**-0.17•**	-0.02	-0.05	**-0.11•**
MEDONLY - DEPMED	**0.23•**	**0.35•**	0.02	0.02	-0.07	-0.06
DEPONLY - DEPMED	**0.22•**	**0.24•**	**0.18•**	0.04	-0.02	0.05

Note. Differences equal to or greater than 0.10 log units are indicated with a bullet (•) and in boldtype. They reflect contrast differences that are well beyond suprathreshold levels for discrimination, as generally defined by differences larger than 2% relative contrast.

Table 12

Log Unit Differences in "Blue-Yellow" Chromatic Contrast Sensitivity between Variable Levels

	Spatial Frequency (cpd) at 0 Hz			Spatial Frequency (cpd) at 4 Hz		
Variable Levels Comparisons	0.5	1.5	4.0	0.5	1.5	4.0
SSRI Medication Status						
No SSRI - SSRI	-0.02	-0.03	**0.13•**	0.03	0.04	0.01
DASS Depressed Mood						
No Dep. Mood – Dep. Mood	**0.15•**	**0.14•**	-0.02	0.04	0.05	-0.02
DASS Anxious Mood						
No Anxious Mood - Anxious Mood	0.01	-0.01	**-0.10•**	-0.09	-0.04	0.00
DID Clinical Depression						
No Clinical Dep. - Clinical Dep.	**0.20•**	**0.13•**	-0.02	0.09	0.08	0.05
Medication/Depression						
HEALTHY - MEDONLY	-0.07	-0.09	**0.15•**	0.00	0.00	-0.06
HEALTHY - DEPONLY	**0.14•**	0.05	-0.02	0.05	0.03	-0.03
HEALTHY - DEPMED	**0.28•**	**0.21•**	0.08	**0.17•**	**0.17•**	**0.16•**
MEDONLY - DEPONLY	**0.20•**	**0.14•**	**-0.17•**	0.05	0.03	0.03
MEDONLY - DEPMED	**0.35•**	**0.31•**	-0.07	**0.17•**	**0.17•**	**0.22•**
DEPONLY - DEPMED	**0.15•**	**0.17•**	**0.10•**	**0.12•**	**0.14•**	**0.19•**

Note. Differences equal to or greater than 0.10 log units are indicated with a bullet (•) and in boldtype. They reflect contrast differences that are well beyond suprathreshold levels for discrimination, as generally defined by differences larger than 2% relative contrast.

Table 13

Number of Participants tested each Month

Depression Variable	Month of Testing					Total
	February	March	April	May	June	
DASS Depressed Mood[a]						
Depressed Mood	7	0	4	1	3	15
No Depressed Mood	21	3	0	1	4	29
DID Clinically-Defined Dep.[b]						
Clinical Depression	3	0	4	1	3	11
No Clinical Depression	25	3	0	1	4	33
Total	28	3	4	2	7	44

[a] $\chi^2(4, N = 44) = 10.78, p = .029$

[b] $\chi^2(4, N = 44) = 17.91, p = .001$

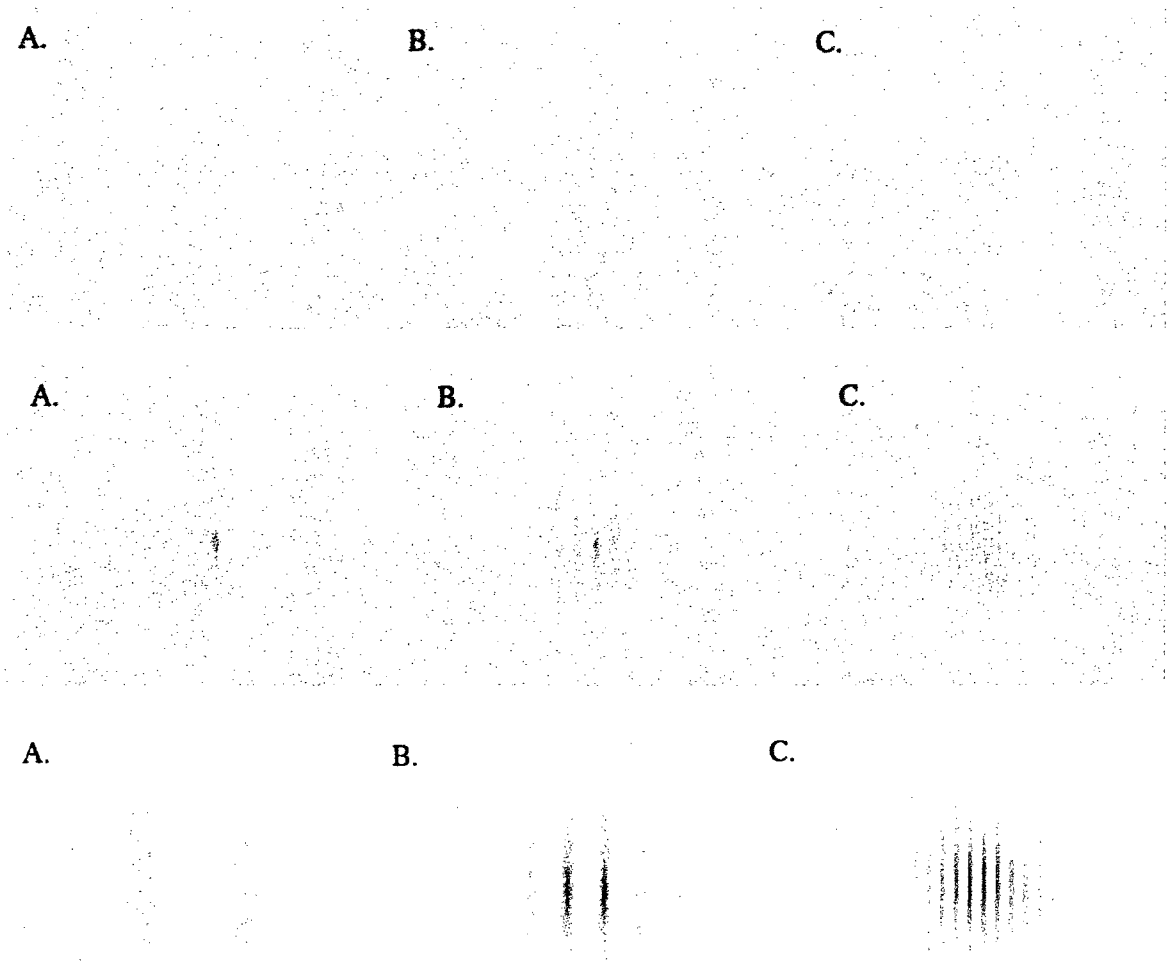


Figure 1. Examples of Gabor stimuli. Top and middle rows depict chromatic isoluminant "blue-yellow" and "red-green" Gabors, respectively. Bottom row depicts achromatic luminance Gabors. Panels A, B, and C illustrate Gabors with center spatial frequencies of 0.5, 1.5 and 4.0 cpd, respectively.

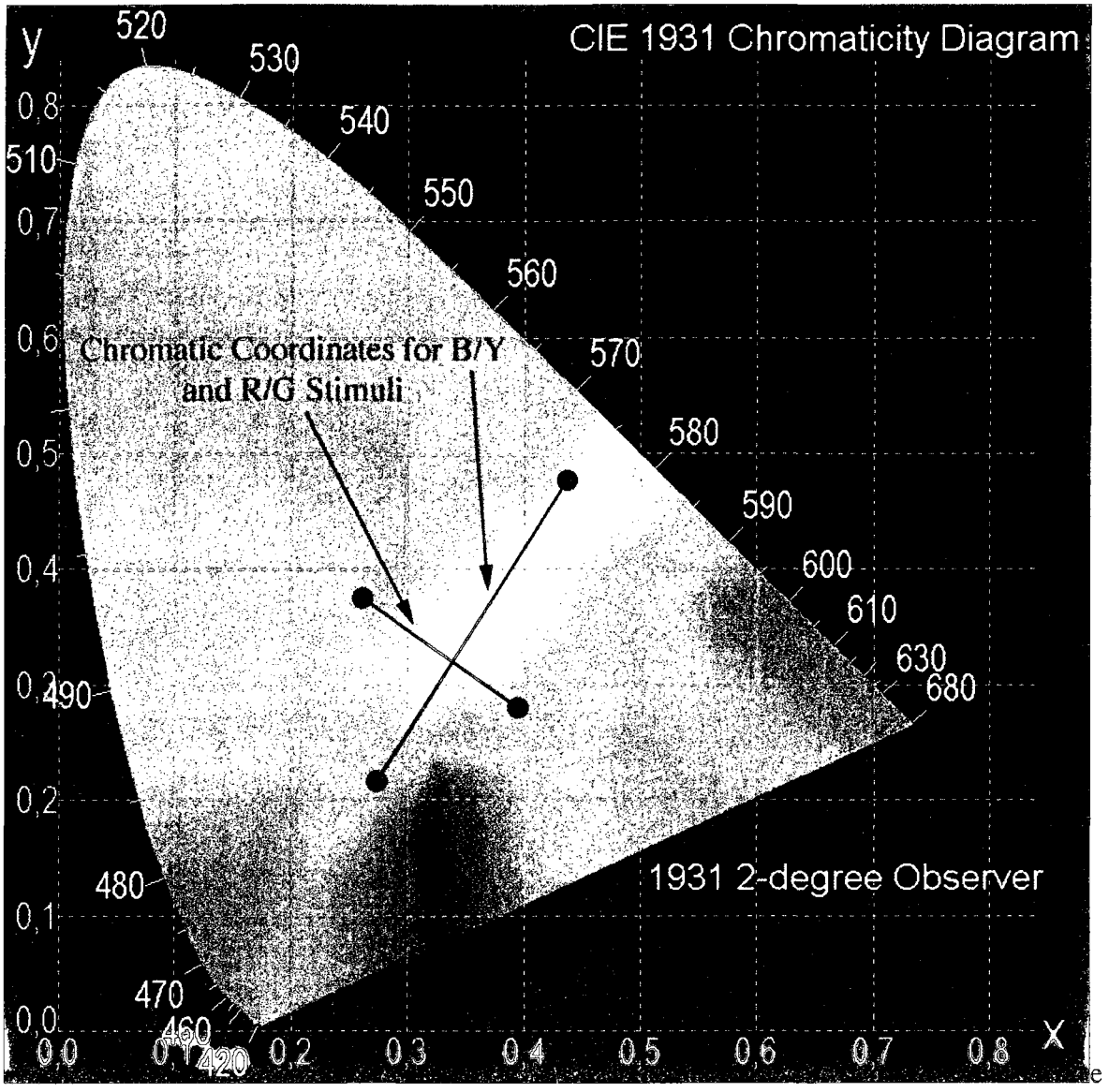


Figure 2. CIE (1931) Colour Space showing the "blue-yellow" (B-Y) and "red-green" (R-G) peak-to-trough chromatic Gabor modulations. B-Y endpoints were [(.2739, .2263), (.4280, .4976) and R-G endpoints were [(.3828, .2846), (.2639, .3722)]. Background chromaticities were halfway between the two endpoints.

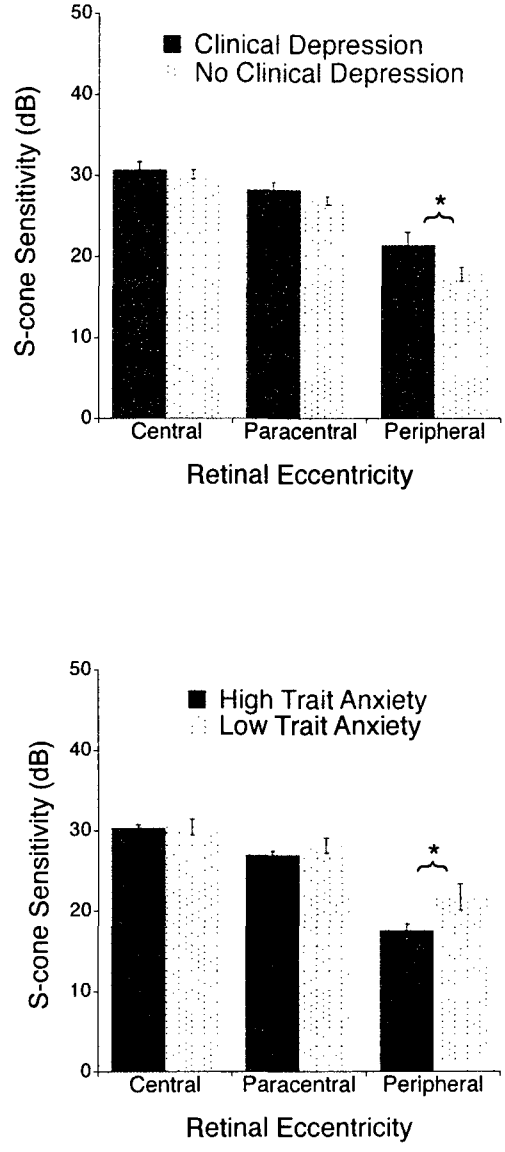
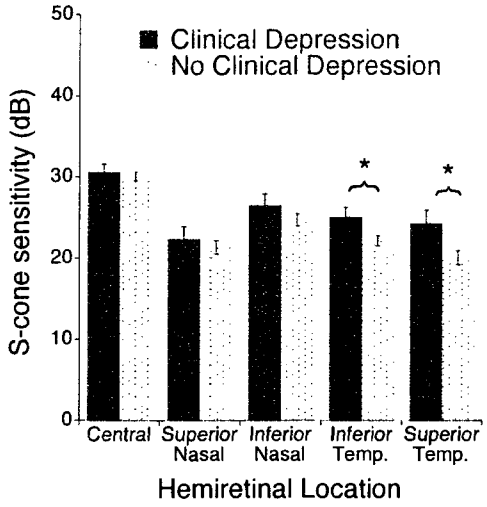


Figure 3. S-cone sensitivity (dB) by retinal eccentricity for DID Clinically-Defined Depression (top panel) and Trait Anxiety (bottom panel). In the top panel, solid blue bars represent the Clinical Depression group and open bars represent the No Clinical Depression group. In the bottom panel, solid red bars represent the High Trait Anxiety group and open bars represent the Low Trait Anxiety group. For retinal eccentricity, Central refers to 1-6°, Paracentral refers to 10-22°, and Peripheral refers to 30-50° of visual angle. For this figure and subsequent figures referring to S-cone sensitivity, mean values are adjusted for Age as a covariate (Age = 23.86) and error bars represent ± 1 SEM. $*p < .05$.



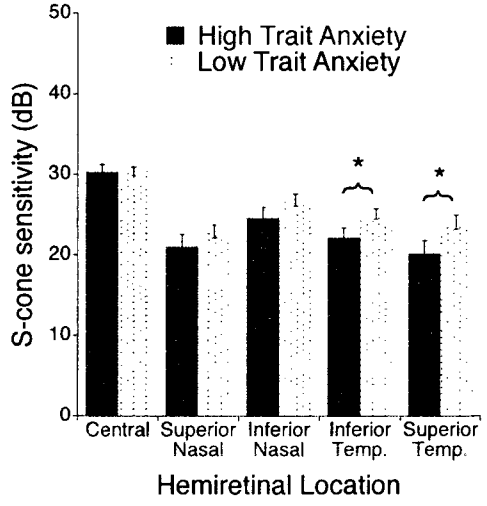


Figure 4. S-cone sensitivity (dB) by hemiretinal locations for DID Clinically-Defined Depression (top panel) and Trait Anxiety (bottom panel). In the top panel, solid blue bars represent the Clinical Depression group and open bars represent the No Clinical Depression group. In the bottom panel, solid red bars represent the High Trait Anxiety group and open bars represent the Low Trait Anxiety group. For hemiretinal locations, Central refers to 1-6° of visual angle, and the remaining quadrants of Superior Nasal, Inferior Nasal, Inferior Temporal, and Superior Temporal refer to the outer 10-50° of visual angle. $*p < .05$.

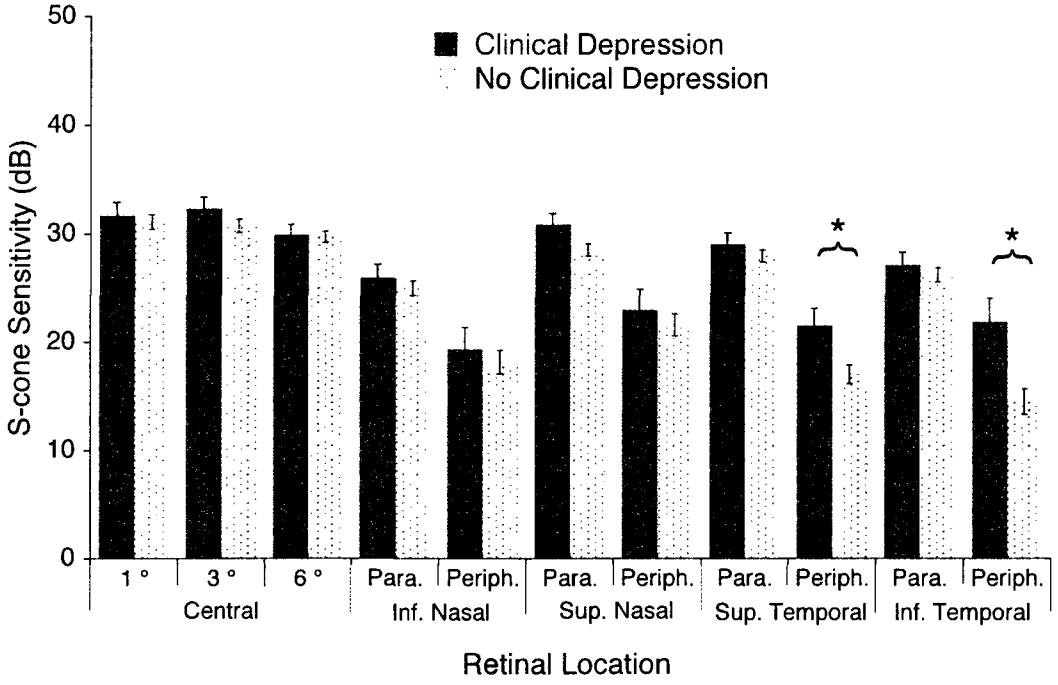


Figure 5. S-cone sensitivity by eleven retinal locations for DID Clinically-Defined Depression. Solid blue bars represent the Clinical Depression group and open bars represent the No Clinical Depression group. For retinal location, Central refers to 1-6°, Paracentral refers to 10-22°, and Peripheral refers to 30-50° of visual angle. $*p < .05$.

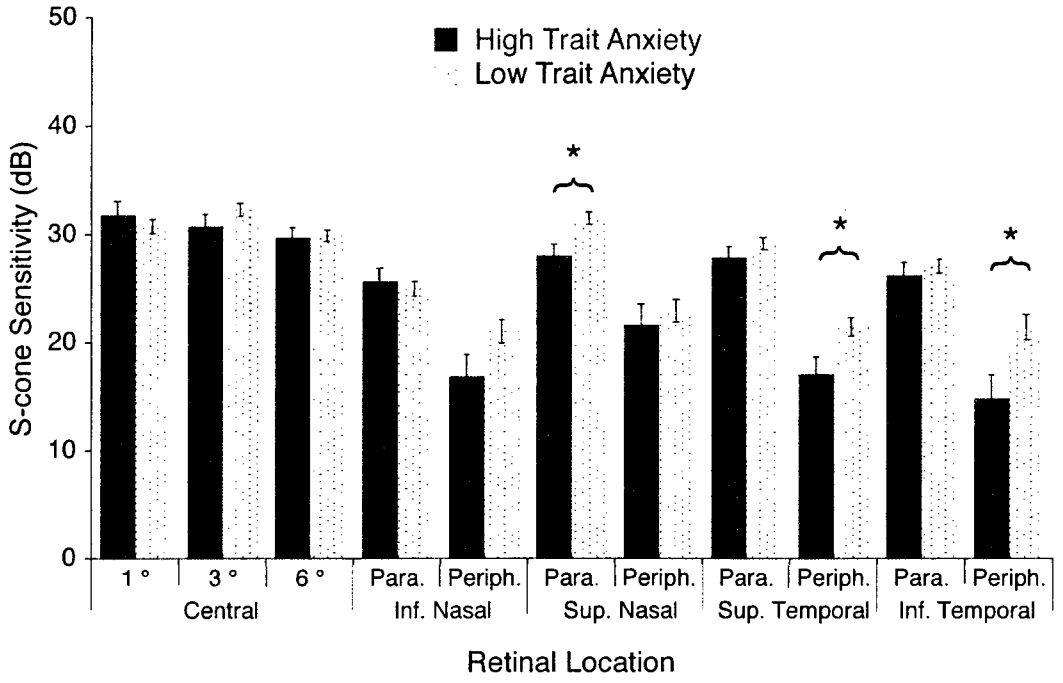


Figure 6. S-cone sensitivity by eleven retinal locations for Trait Anxiety (bottom panel). Solid red bars represent the High Trait Anxiety group and open bars represent the Low Trait Anxiety group. For retinal location, Central refers to 1-6°, Paracentral refers to 10-22°, and Peripheral refers to 30-50° of visual angle. *$p < .05$.

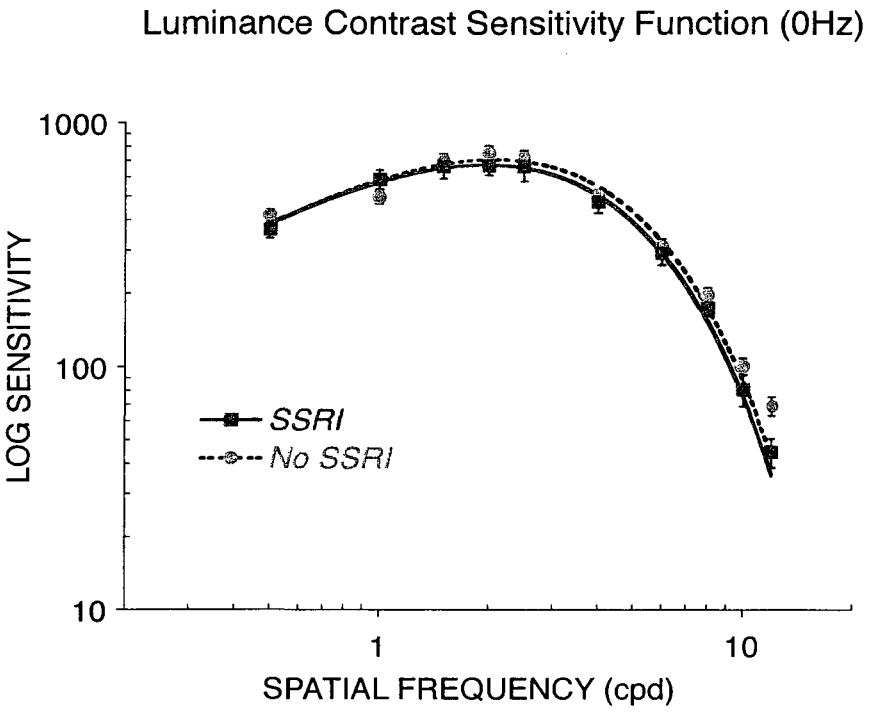


Figure 7. Spatiotemporal luminance contrast sensitivity functions for SSRI Medication Status (SSRI, No SSRI) variable. Luminance CS values for the SSRI group are indicated with purple squares. For clarity, the data are fit with a solid purple line based on a double exponential fitting function (Moshvon & Kiorpes, 1988). Luminance CS values for the No SSRI group are indicated with dark grey circles and a dashed line denoting curve fit. For this figure and all subsequent figures, values refer to unadjusted data and error bars represent ± 1 SEM. No apparent error bars indicates SEM less than the data symbol size.

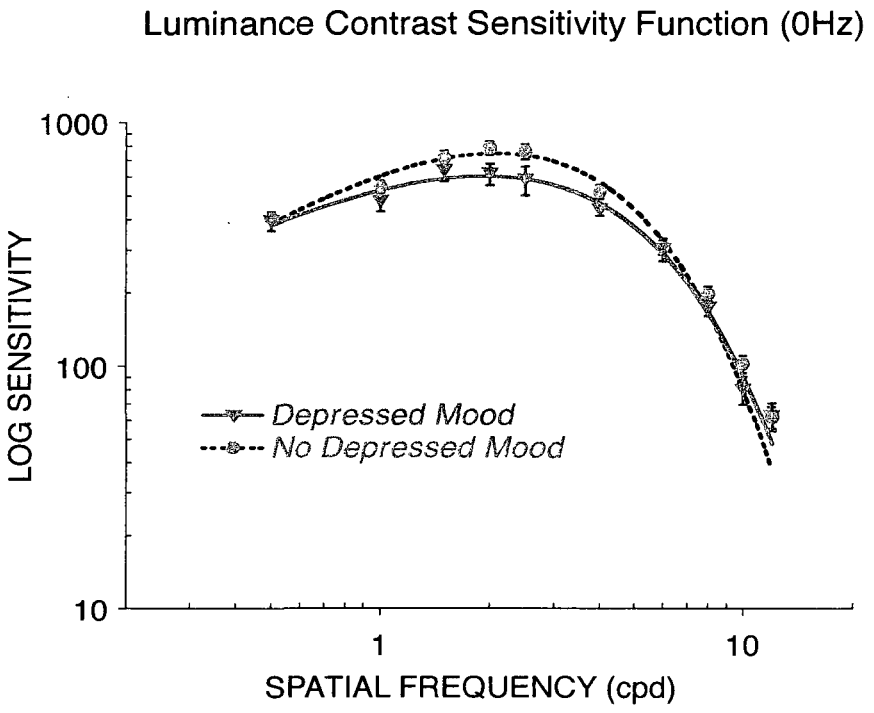


Figure 8. Spatiotemporal luminance contrast sensitivity functions for the DASS Depressed Mood (Depressed Mood, No Depressed Mood) variable. Luminance CS values for the Depressed Mood group are indicated with inverted blue triangles and a solid blue line denoting the double exponential curve fit (as described in Fig. 7). Luminance CS values for the No Depressed Mood group are indicated with dark grey circles and a dashed line denoting curve fit.

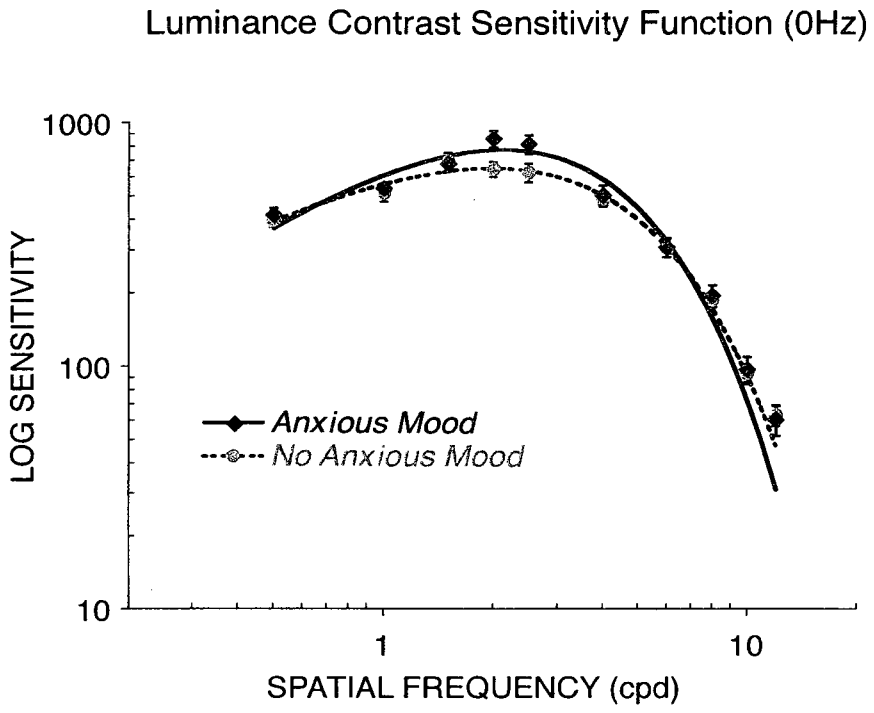


Figure 9. Spatiotemporal luminance contrast sensitivity functions for the DASS Anxious Mood variable (Anxious Mood, No Anxious Mood). Luminance CS values for the Anxious Mood group are indicated with red diamonds and a solid red line denoting the double exponential curve fit (as described in Fig. 7). Luminance CS values for the No Anxious Mood group are indicated with dark grey circles and a dashed line denoting curve fit.

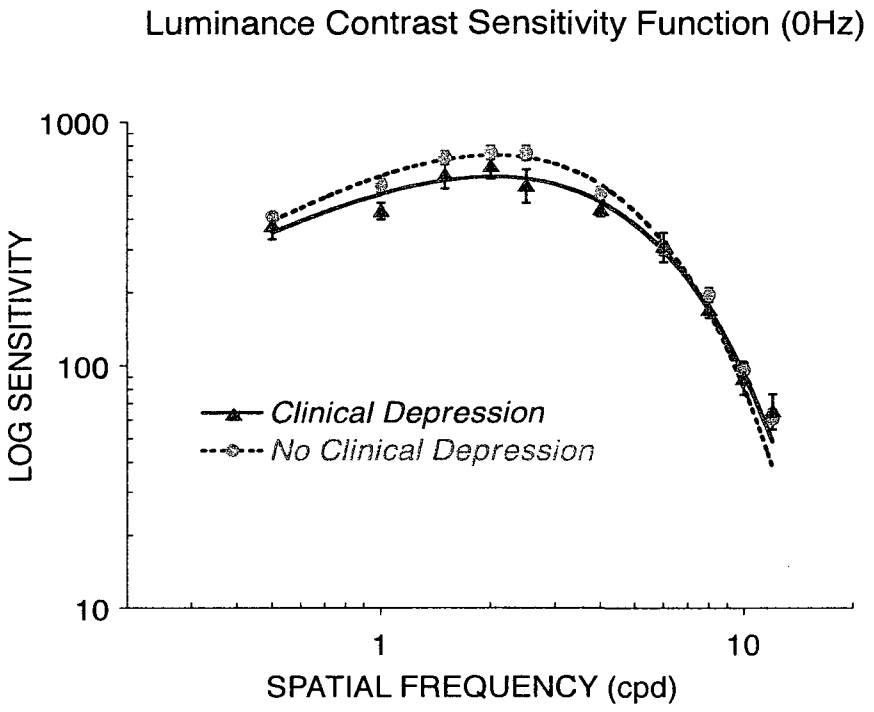


Figure 10. Spatiotemporal luminance contrast sensitivity functions for the DID Clinically-Defined Depression (Clinical Depression, No Clinical Depression) variable. Luminance CS values for the Clinical Depression group are indicated with blue triangles and a solid blue line denoting the double exponential curve fit (as described in Fig. 7). Luminance CS values for the No Clinical Depression group are indicated with dark grey circles and a dashed line denoting curve fit.

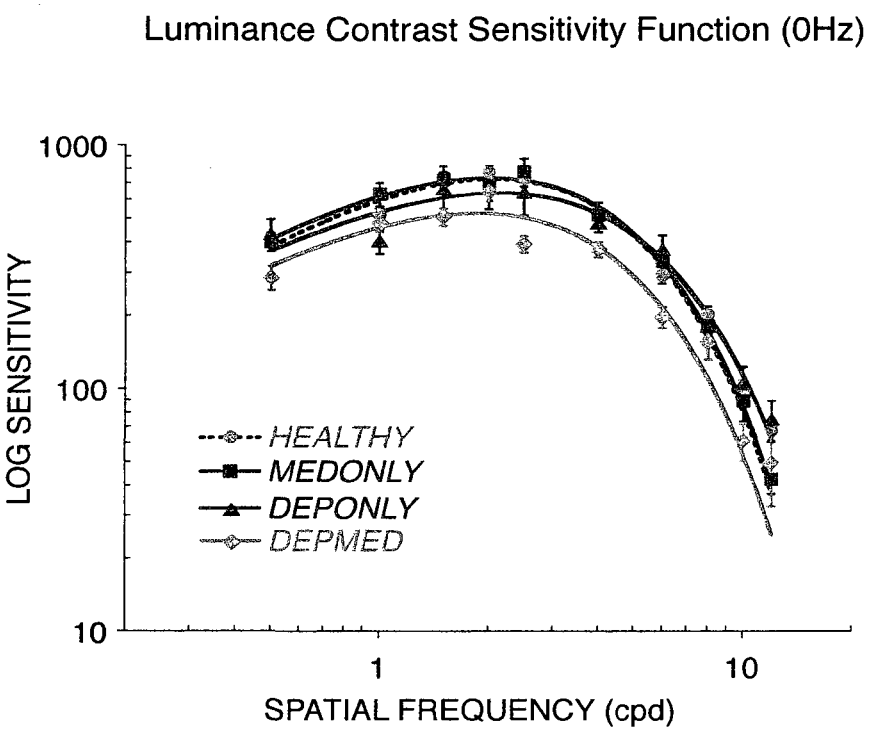


Figure 11. Spatiotemporal luminance contrast sensitivity functions for the Medication/ Depression variable. Luminance CS values are indicated by dark grey circles and a dashed line denoting the curve fit for the HEALTHY group; purple squares and a solid purple line for the MEDONLY group; blue triangles and a solid blue line for the DEPONLY group; and orange diamonds and a solid orange line for the DEPMED group.

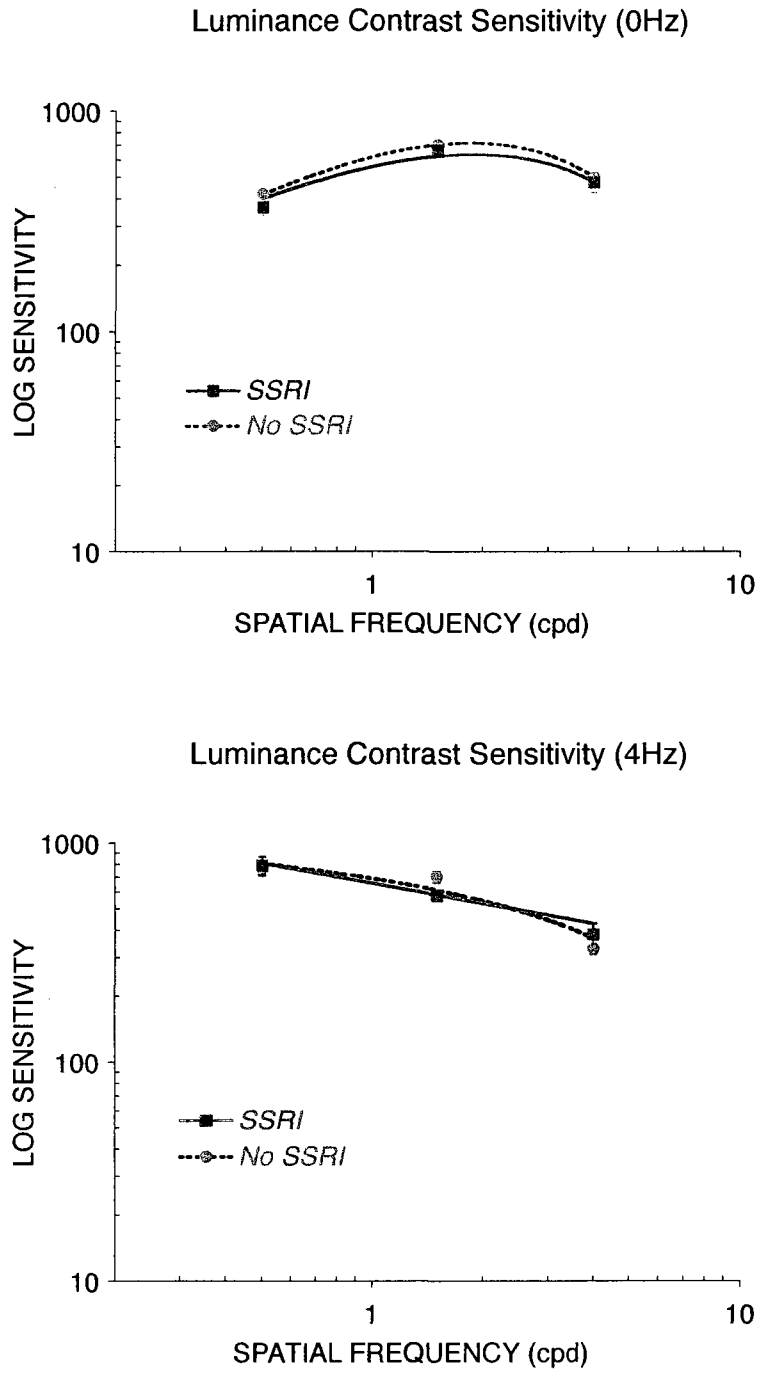


Figure 12. Spatiotemporal luminance contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the SSRI Medication Status (SSRI, No SSRI) variable. Luminance CS values for the SSRI group are indicated with purple squares and a solid purple line denoting the curve fit. Luminance CS values for the No SSRI group are indicated with dark grey circles and a dashed line denoting curve fit.

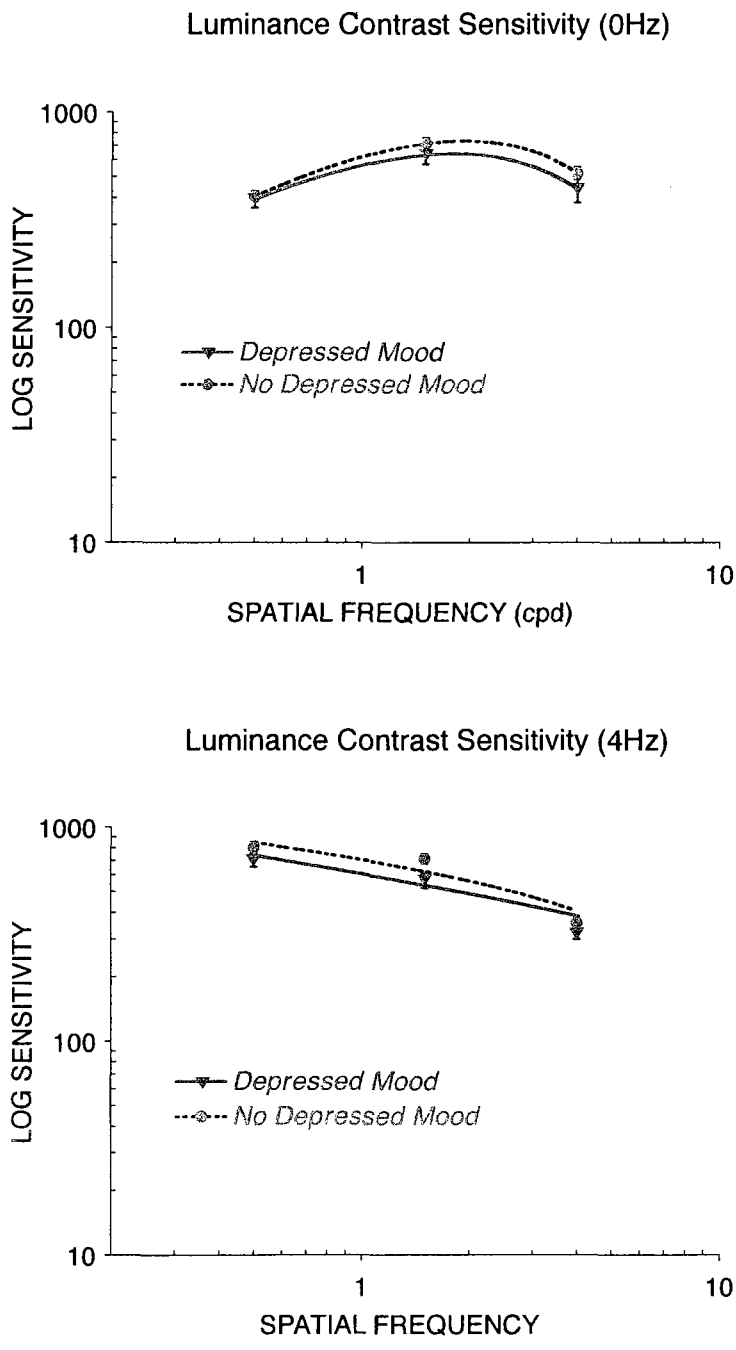


Figure 13. Spatiotemporal luminance contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DASS Depressed Mood (Depressed Mood, No Depressed Mood) variable. Luminance CS values for the Depressed Mood group are indicated with inverted blue triangles and a solid blue line denoting the curve fit. Luminance CS values for the No Depressed Mood group are indicated with dark grey circles and a dashed line denoting curve fit.

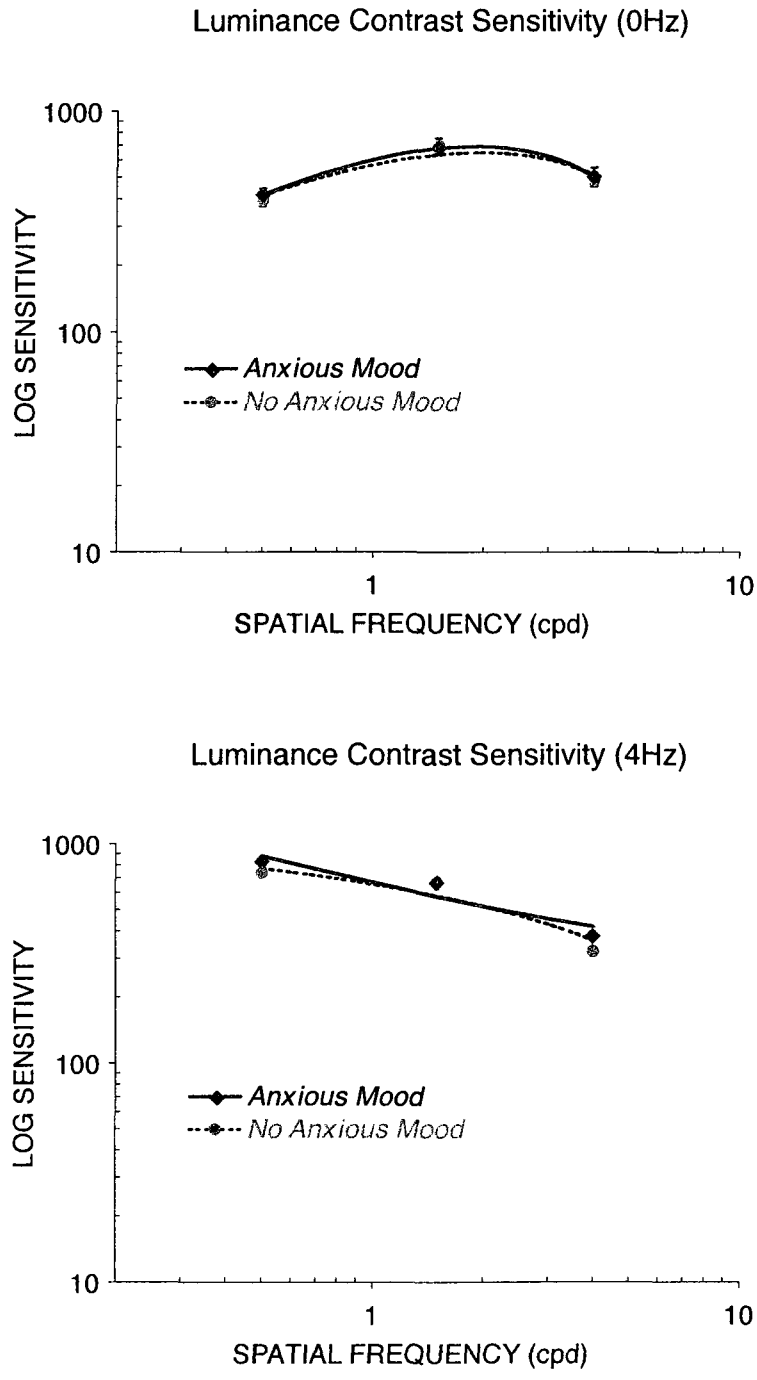


Figure 14. Spatiotemporal luminance contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DASS Anxious Mood (Anxious Mood, No Anxious Mood) variable. Luminance CS values for the Anxious Mood group are indicated with red diamonds and a solid red line denoting the curve fit. Luminance CS values for the No Anxious Mood group are indicated with dark grey circles and a dashed line denoting curve fit.

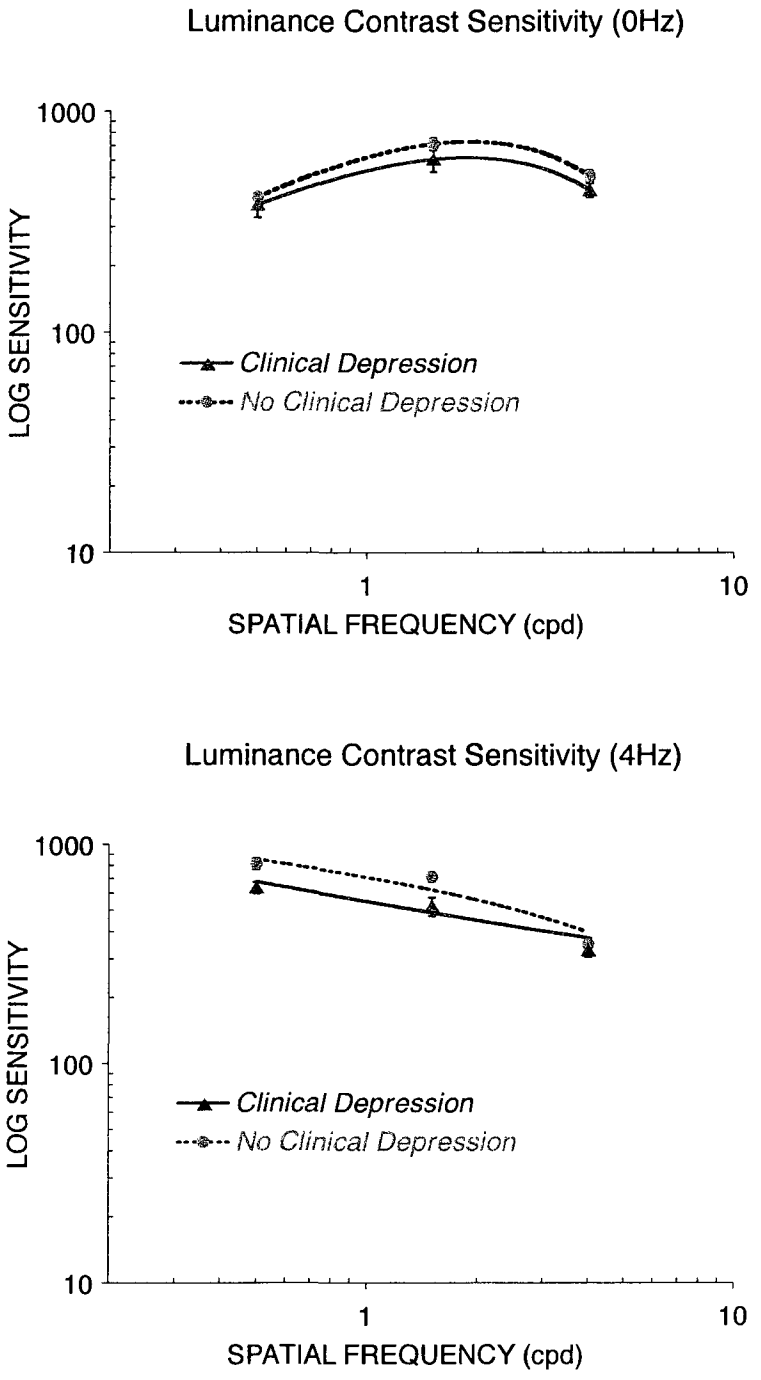


Figure 15. Spatiotemporal luminance contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DID Clinically-Defined Depression (Clinical Depression, No Clinical Depression) variable. Luminance CS values for the Clinical Depression group are indicated with blue triangles and a solid blue line denoting the curve fit. Luminance CS values for the No Clinical Depression group are indicated with dark grey circles and a dashed line denoting curve fit.

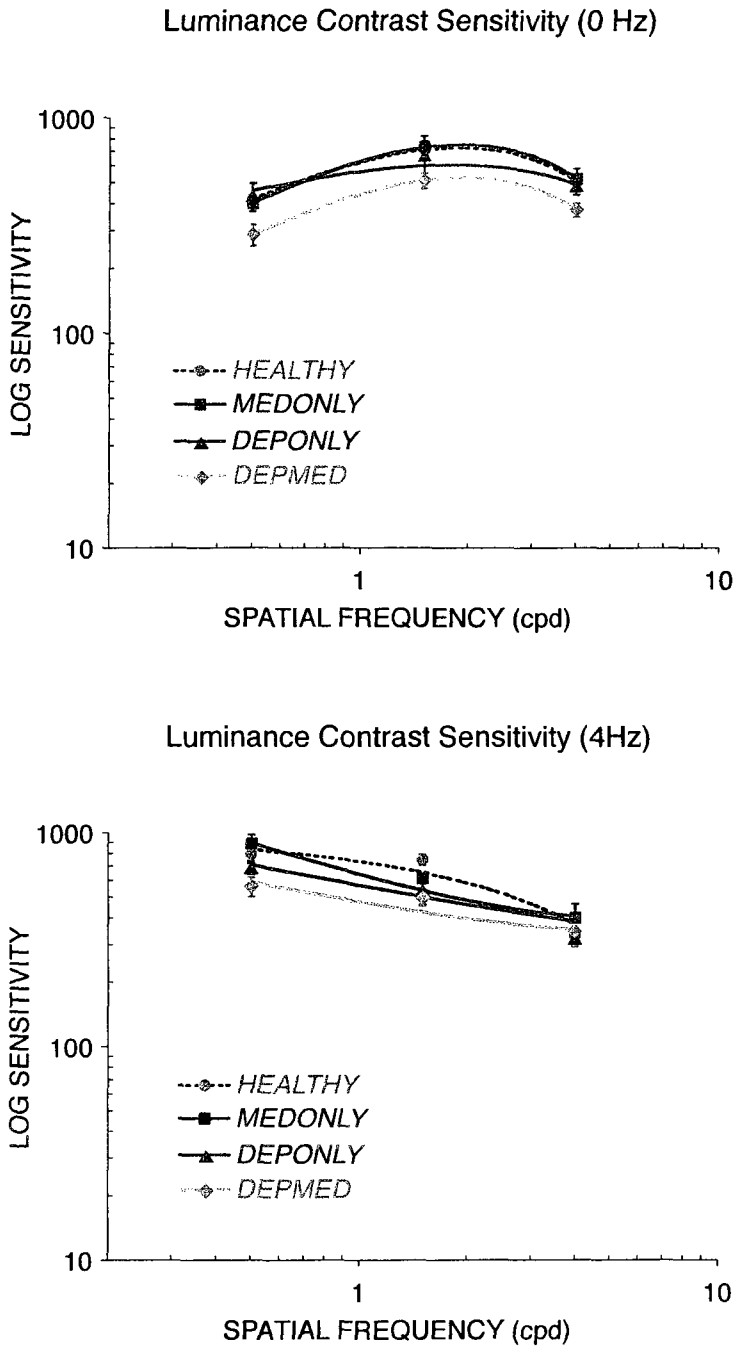


Figure 16. Spatiotemporal luminance contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the combined Medication/Depression variable. Luminance CS values are indicated by dark grey circles and a dashed line denoting curve fit for the HEALTHY group; purple squares and a solid purple line for the MEDONLY group; blue triangles and a blue line for the DEPONLY group; and orange diamonds and an orange line for the DEPMED group.

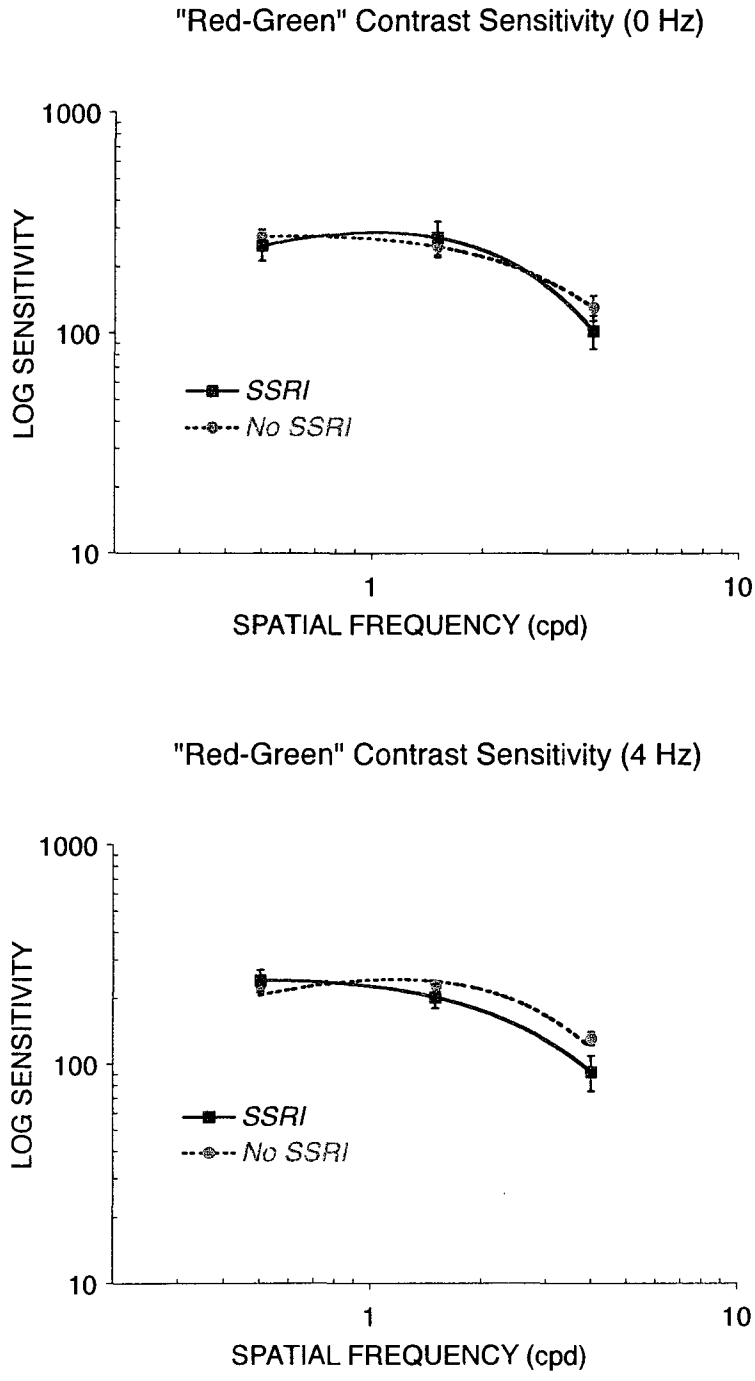


Figure 17. Isoluminant "red-green" (R-G) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the SSRI Medication Status (SSRI, No SSRI) variable. R-G chromatic CS values for the SSRI group are indicated with purple squares and a solid purple line denoting the curve fit. R-G chromatic CS values for the No SSRI group are indicated with dark grey circles and a dashed line denoting curve fit.

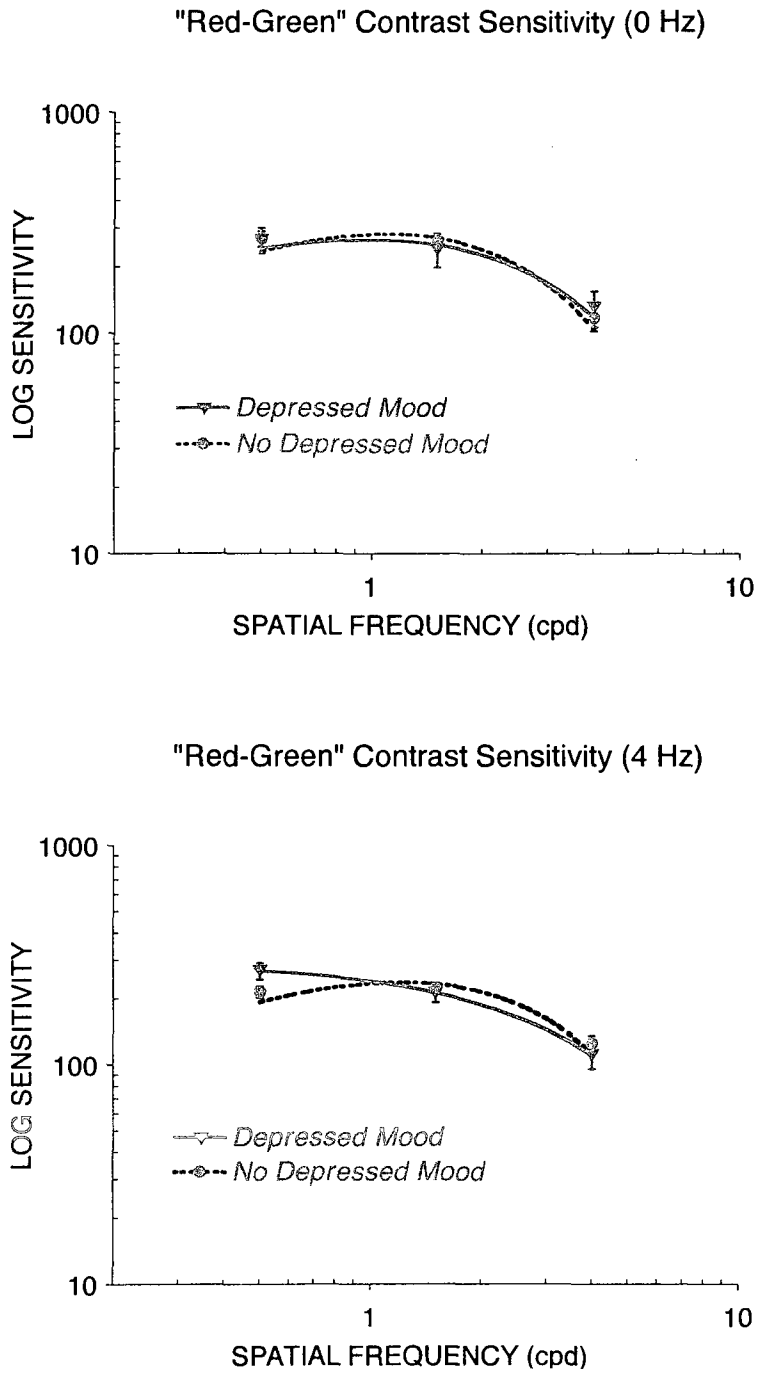


Figure 18. Isoluminant "red-green" (R-G) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DASS Depressed Mood (Depressed Mood, No Depressed Mood) variable. R-G chromatic CS values for the Depressed Mood group are indicated with inverted blue triangles and a blue line denoting curve fit. R-G chromatic CS values for the No Depressed group are indicated with dark grey circles and a dashed line denoting curve fit.

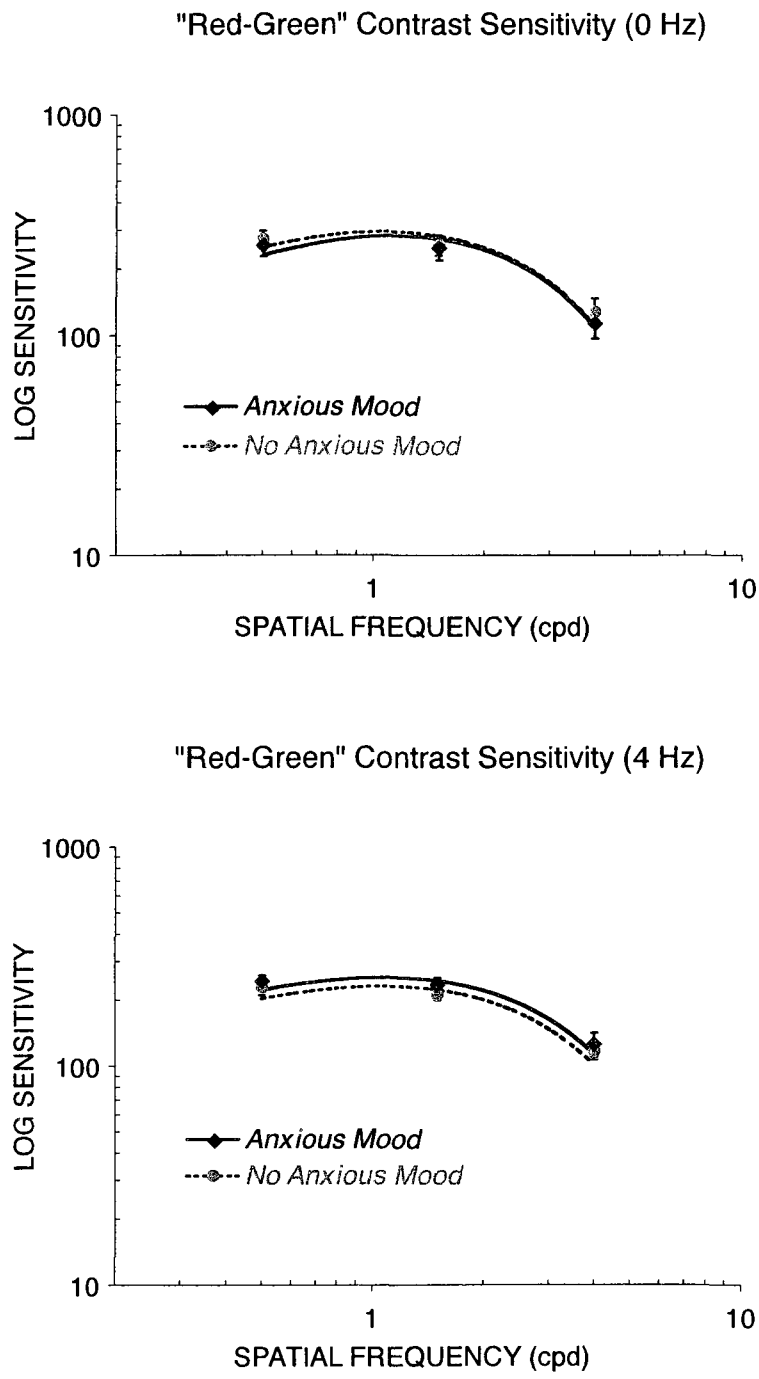


Figure 19. Isoluminant "red-green" (R-G) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DASS Anxious Mood (Anxious Mood, No Anxious Mood) variable. R-G chromatic CS values for the Anxious Mood group are indicated with red diamonds and a solid red line denoting the curve fit. R-G chromatic CS values for the No Anxious Mood group are indicated with dark grey circles and a dashed line denoting curve fit.

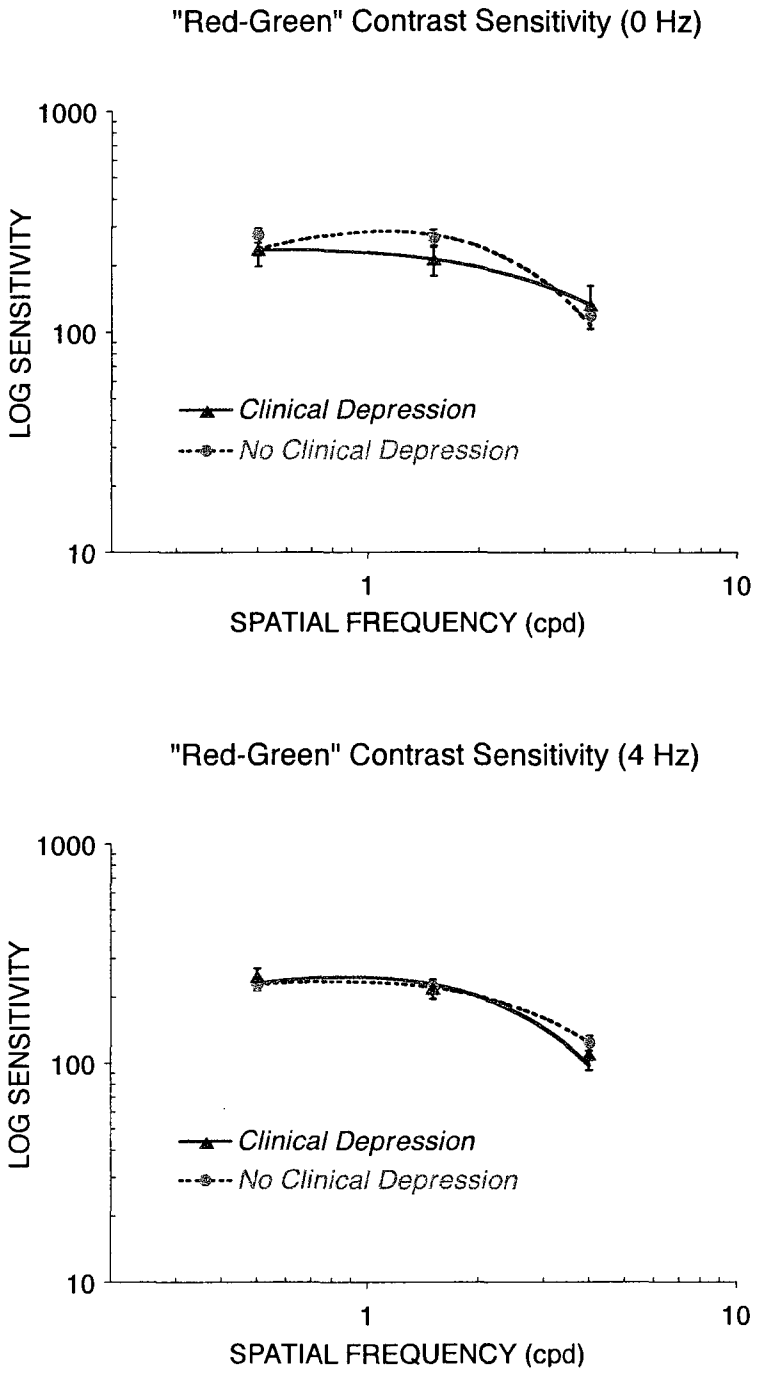


Figure 20. Isoluminant "red-green" (R-G) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DID Clinically-Defined Depression (Depressed Mood, No Depressed Mood) variable. R-G chromatic CS values for the Clinical Depression group are indicated with blue triangles and a blue line denoting curve fit. R-G CS values for the No Clinical Depression group are indicated with dark grey circles and a dashed line denoting curve fit.

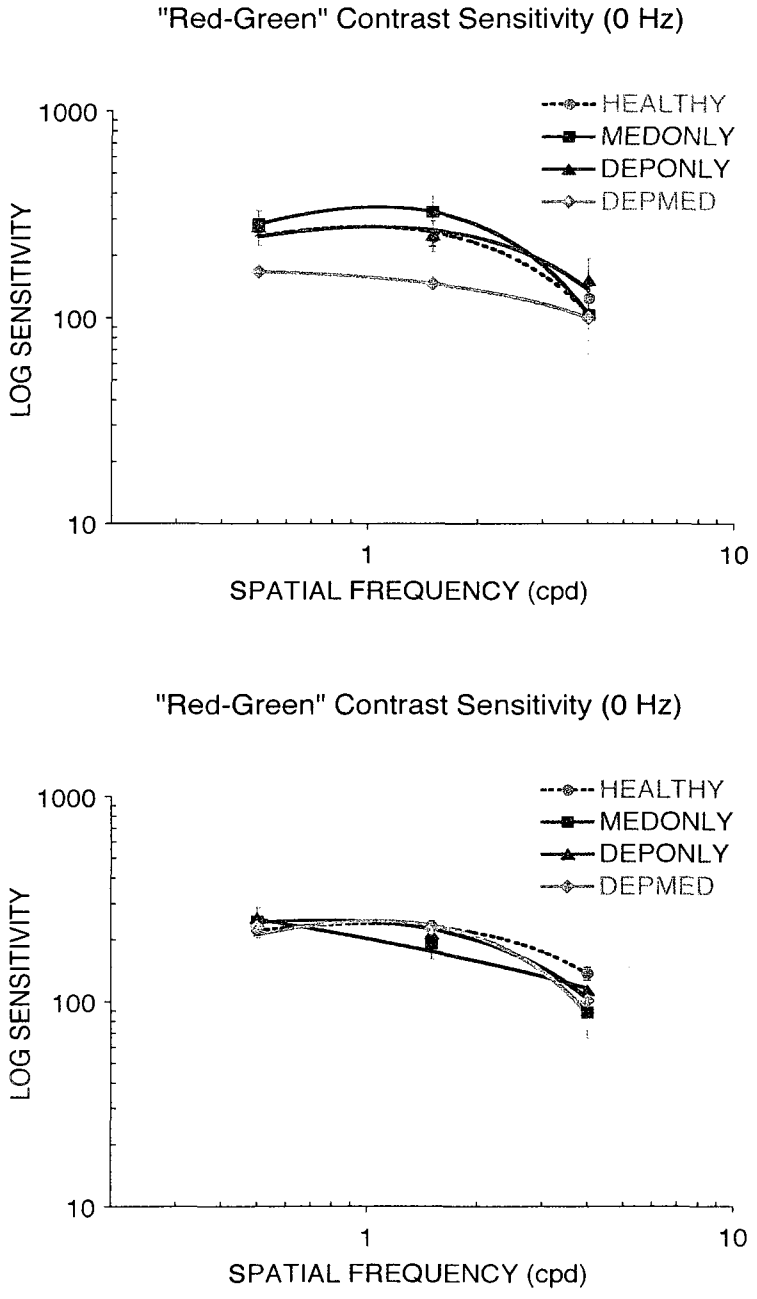


Figure 21. Isoluminant "red-green" (R-G) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the Medication/Depression variable. R-G chromatic CS values are indicated by dark grey circles and a dashed line denoting curve fit for the HEALTHY group; purple squares and a solid purple line for the MEDONLY group; blue triangles and a blue line for the DEPONLY group; and orange diamonds and a solid orange line for the DEPMED group.

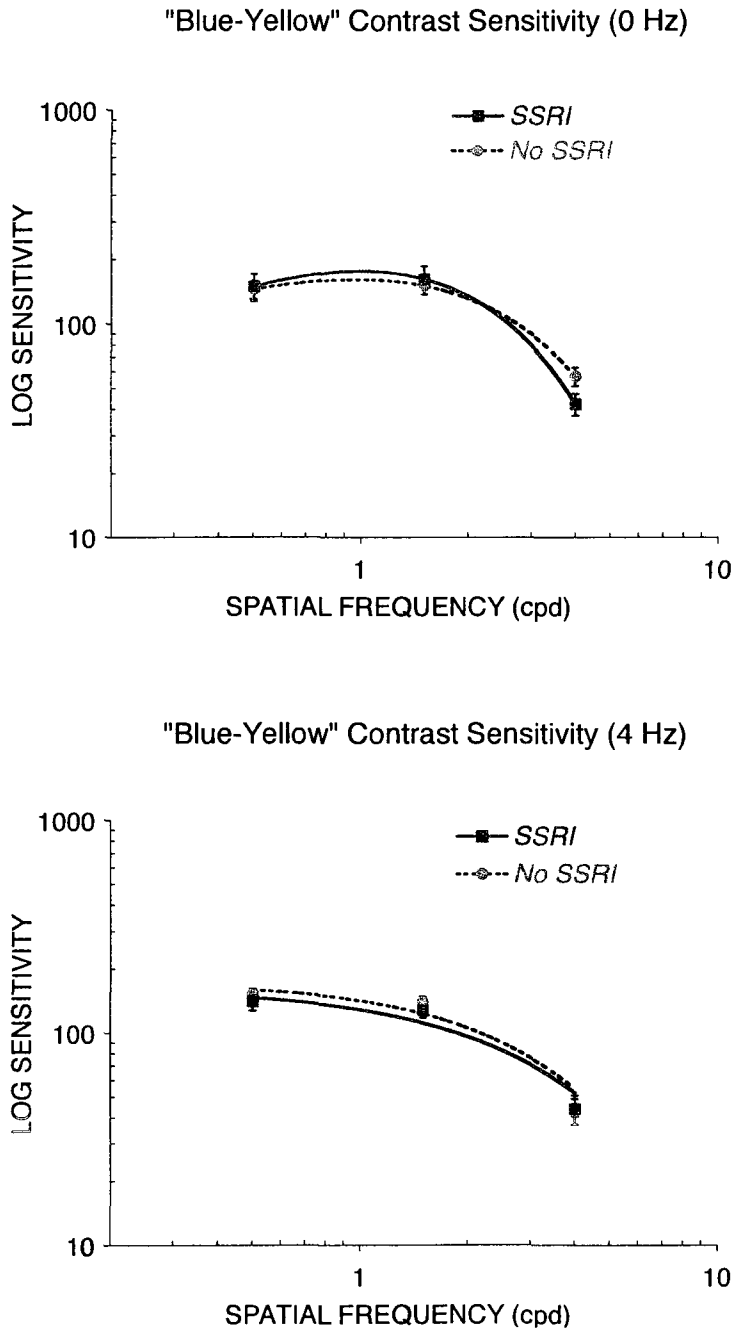


Figure 22. Isoluminant "blue-yellow" (B-Y) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the SSRI Medication Status (SSRI, No SSRI) variable. B-Y chromatic CS values for the SSRI group are indicated with purple squares and a solid purple line denoting the curve fit. B-Y chromatic CS values for the No SSRI group are indicated with dark grey circles and a dashed line denoting curve fit.

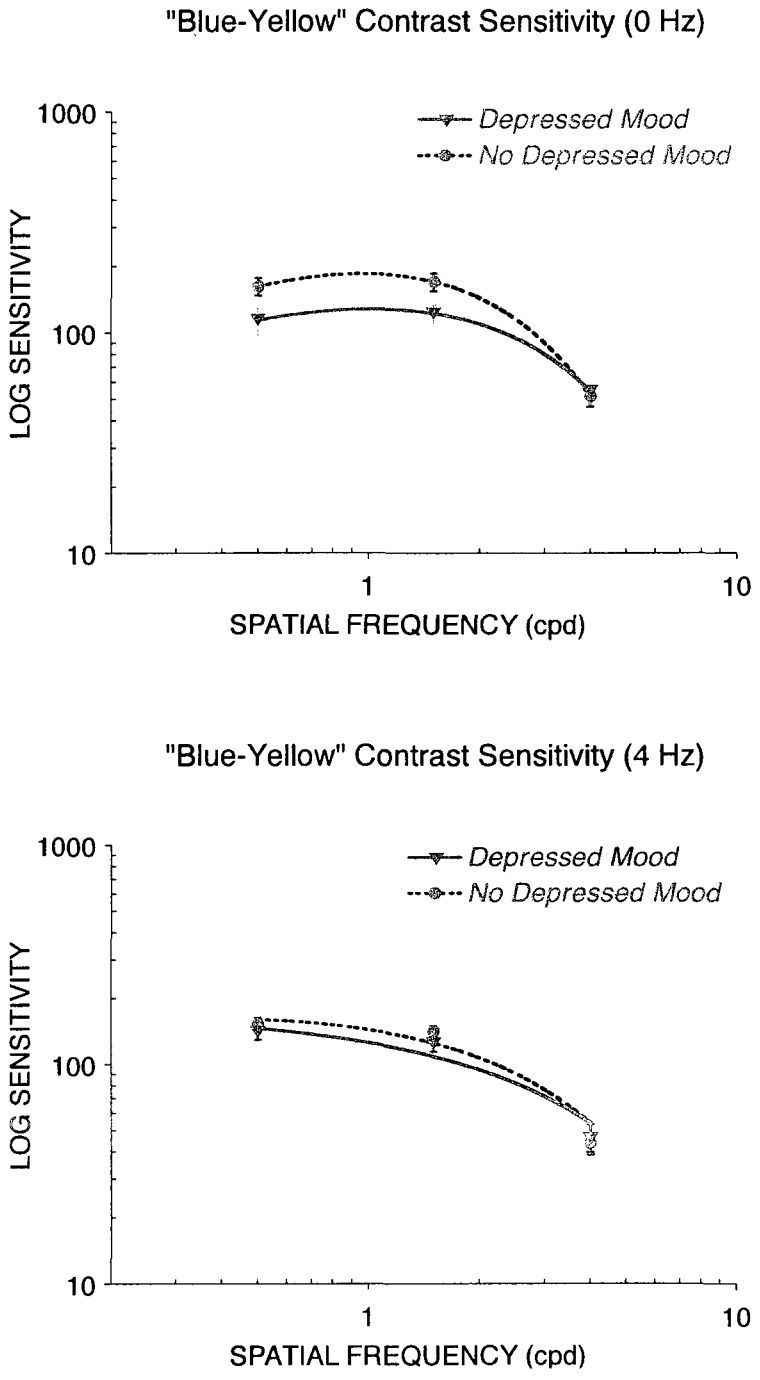


Figure 23. Isoluminant "blue-yellow" (B-Y) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DASS Depressed Mood (Depressed Mood, No Depressed Mood) variable. B-Y chromatic CS values for the Depressed Mood group are indicated with inverted blue triangles and a blue line denoting the curve fit. B-Y chromatic CS values for the No Depressed group are indicated with dark grey circles and a dashed line denoting curve fit.

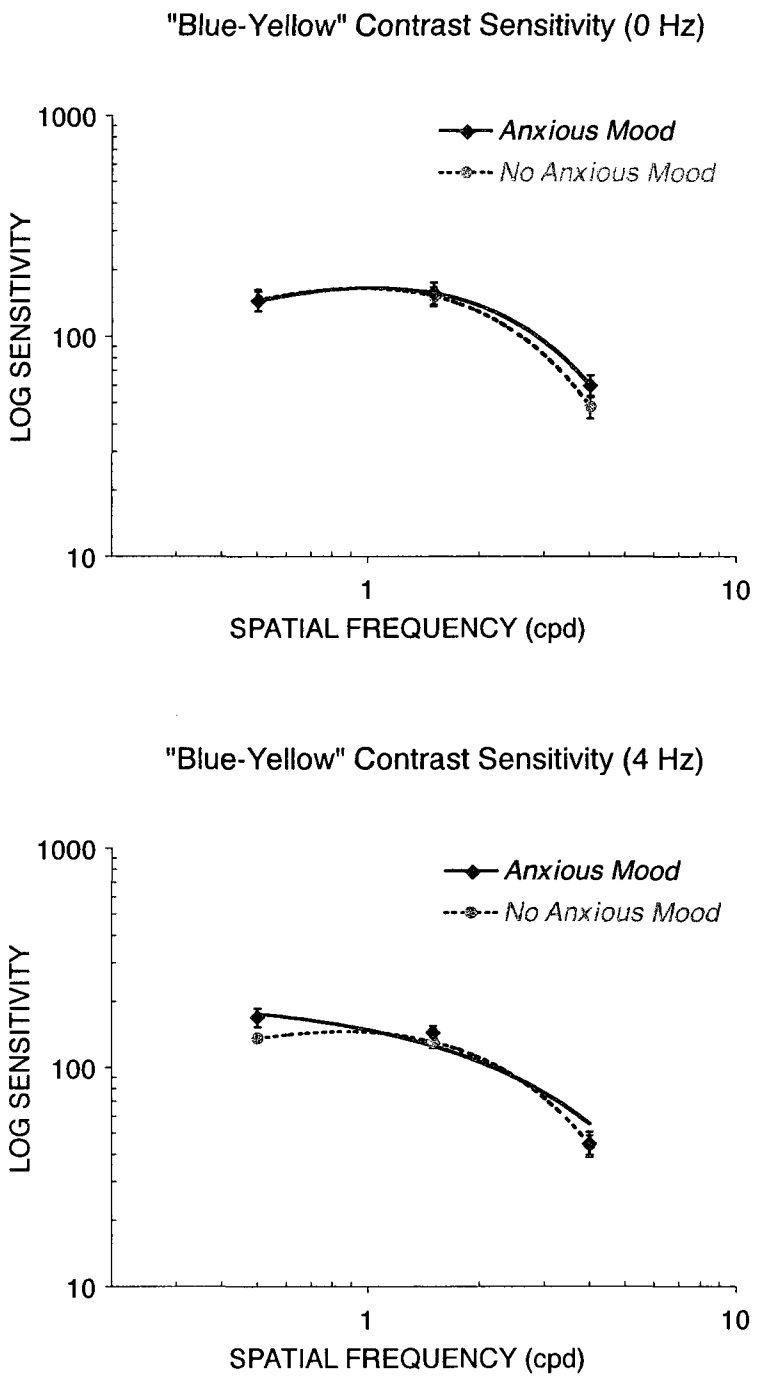


Figure 24. Isoluminant "blue-yellow" (B-Y) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DASS Anxious Mood (Anxious Mood, No Anxious Mood) variable. B-Y chromatic CS values for the Anxious Mood group are indicated with red diamonds and a solid red line denoting the curve fit. B-Y chromatic CS values for the No Anxious Mood group are indicated with dark grey circles and a dashed line denoting curve fit.

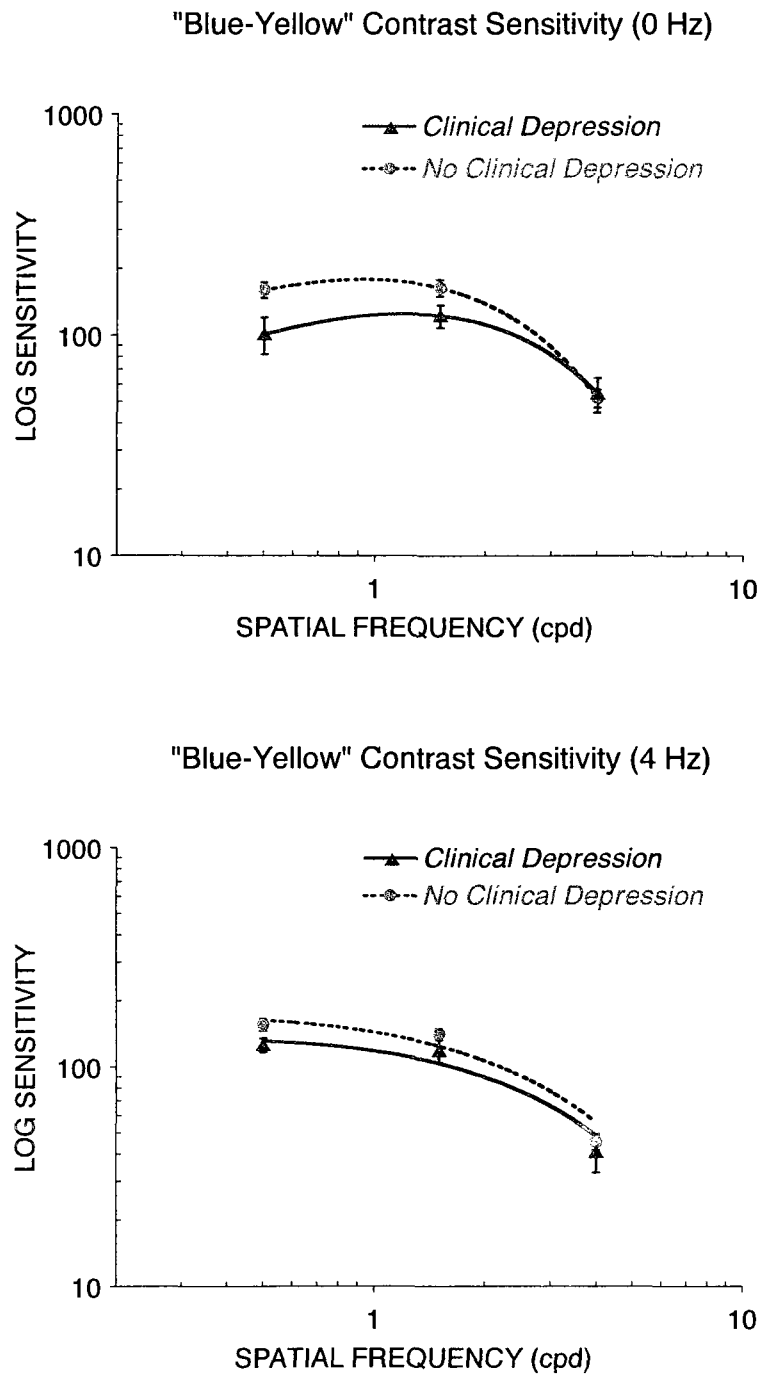


Figure 25. Isoluminant "blue-yellow" (B-Y) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the DID Clinically-Defined Depression (Depressed Mood, No Depressed Mood) variable. B-Y chromatic CS values for the Clinical Depression group are indicated with blue triangles and a blue line denoting curve fit. B-Y CS values for the No Clinical Depression group are indicated with dark grey circles and a dashed line denoting curve fit.

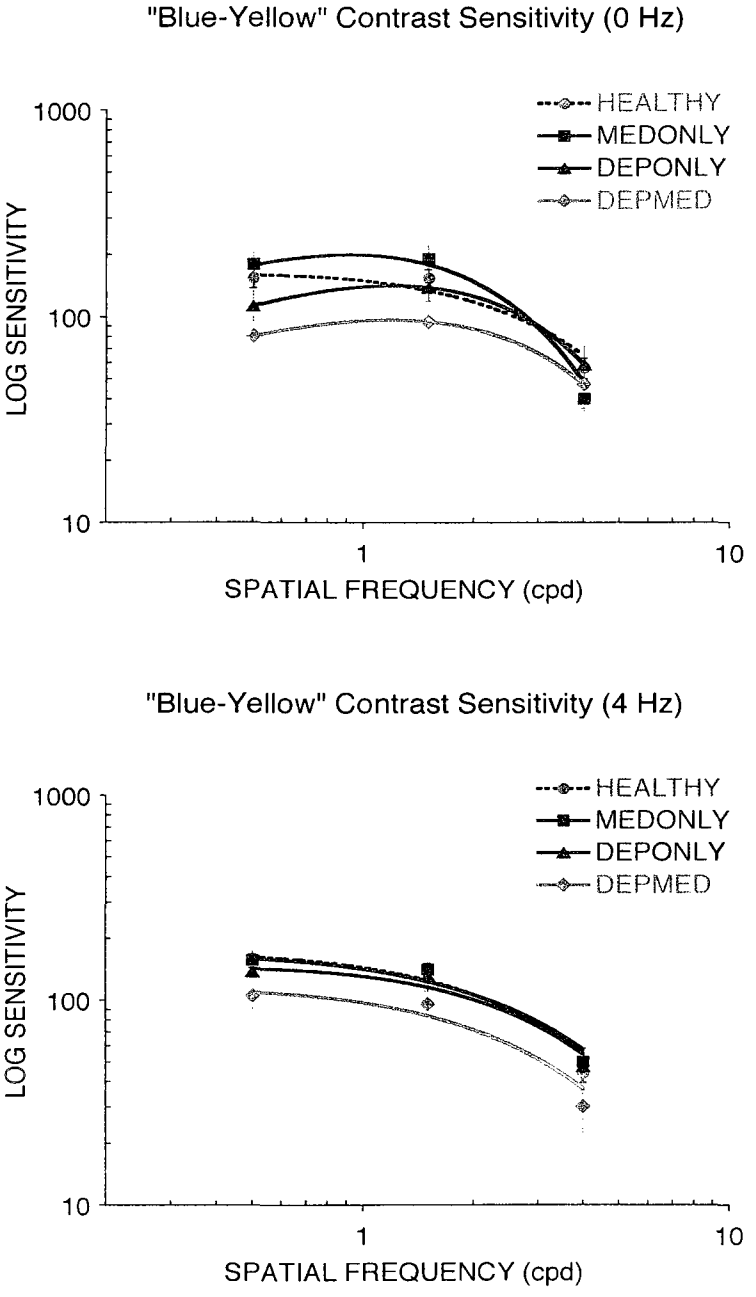


Figure 26. Isoluminant "blue-yellow" (B-Y) chromatic contrast sensitivity in the static (0 Hz; top panel) and dynamic (4 Hz, counterphase flickered; bottom panel) conditions for the Medication/Depression variable. B-Y chromatic CS values are indicated by dark grey circles and a dashed line denoting curve fit for the HEALTHY group; purple squares and a solid purple line for the MEDONLY group; blue triangles and a blue line for the DEPONLY group; and orange diamonds and a solid orange line for the DEPMED group.

Appendix A

Cover Letter, Contact Information and Informed Consent

[Letterhead]

Dear Potential Participant,

We are conducting a study that examines the effect of certain medications on visual functioning. Specifically, we are interested in comparing the visual performance of people who are taking antidepressant medication with those who are not. You are invited to be a participant in this research.

If you choose to participate, you will be asked to complete a number of non-invasive, automated vision tests. These involve viewing a screen and indicating when you see a dot appear, which side of the screen a pattern is presented, or which direction a shape is facing. Additionally, participants will be asked to fill out a series of questionnaires regarding general medical information and measures of mood. The vision tests and questionnaires will be completed in one research session, lasting approximately 2 hours. There are no physical or psychological risks associated with participation in any part of this research.

If you choose to participate, your involvement and the information you provide will remain strictly confidential and only shared amongst the researchers. Your name will not be associated with your responses to the questionnaires or the vision tests. Instead, your data will be assigned a random identification number. All the data collected for this study will be securely stored at Lakehead University for a period of 7 years, after which it will be destroyed.

The information you provide will not be analyzed separately or individually, but will be combined with the data provided by all other research participants and analyzed in aggregate, as a group. This means that the results of this study will not include information on any individual participant. This also means that participants will not be given individual feedback on their test performance or questionnaire responses. Potential participants will be given information on how to contact a health care professional for any concerns they might have regarding their vision or their mental health.

Participation in this study is completely voluntary. If you agree to participate, you will be able to withdraw at any point during the research session without explanation. You will also not be obligated to answer every question on the questionnaires. However, because each of the questions was chosen for a specific research purpose, we do encourage participants to be as complete as possible. Incomplete questionnaires may affect the validity of the results and might not be able to be included for analysis.

Because you have taken the time to meet with the researcher to discuss this study, you will be given the opportunity to enter your name in a draw for $50, even if you do not participate in the research session. Additionally, if you are a Lakehead University student enrolled in an Introductory Psychology class you may choose to have your participation counted toward course bonus marks. These are the only direct benefits to yourself as a potential participant.

Please feel free to ask questions at any time. We have provided our contact information if you wish to contact us outside of the research session. We have also provided contact information for Lakehead University's Research Ethics Board, if you have any concerns. Additionally, if you wish to receive a summary report of the results of this study, there is a space for you to provide your mailing information on the following pages. Thank you for your interest in this research.

Sincerely,

Joy Harrison, M.A. Michael Wesner, Ph.D.

Research Contact Information

Project Title: "The Impact of Depression and Antidepressant Medication on the Visual Functioning of the Magno-, Parvo-, and Koniocellular Pathways"

Joy Harrison, Researcher .....346-1272; jjharrison@shaw.ca
Dr. Michael Wesner, Supervising Researcher .....343-8457; mwesner@lakeheadu.ca

Mail can be directed to either researcher at the following address:

Psychology Department
Lakehead University
955 Oliver Road
Thunder Bay, ON
P7B 5E1

Lakehead University Research Ethics Board 343-8283

Counselling and Mental Health Resources

- A number of mental health services in Thunder Bay are available free of charge to individuals with a physician referral. These services include individual counseling, support groups, or education workshops. After you are referred by a physician, you will meet with a mental health worker to determine what services and resources would best meet your needs.

- Additionally, you may contact the following not-for-profit agencies directly:
  Thunder Bay Counselling Centre .....684-1880 (www.tbaycounselling.com)
  Catholic Family Development Centre ..... 345-7323 (www.catholicfamilycentre.ca)

- Lakehead University students are eligible for free counselling services by contacting:
  LU Health and Counselling Services 343-8361

- Counselling services may also be available to you if your employer participates in an Employee Assistance Program (EAP). Check your terms of employment for details. Importantly, your involvement with any services provided through an EAP is kept confidential from your employer.

- Therapists in private practice can be found in the Yellow Pages under *Psychologists and Psychological Associates; Psychotherapy; or Marriage, Family & Individual Counsellor*. Fees are set by therapists independently.

- The Thunder Bay Branch of the Canadian Mental Health Association provides a 24-hour crisis phoneline, as well as crisis responses services:
  Thunder Bay Crisis Response Phoneline .....346-8282 (toll free: 1-888-269-3100)

- Emergency services are also available at the Thunder Bay Regional Health Sciences Centre.

Eye Care and Vision Resources

- Optometrists can be contacted directly for an appointment. Check the Yellow Pages under *Optometrists* for contact information. There is usually a fee, although OHIP may cover costs for clients with certain conditions.

Informed Consent to Participate

Title of Research: "The Impact of Depression and Antidepressant Pharmacotherapy on Visual Functioning of the Magno-, Parvo, and Koniocellular Pathways"

Researchers: Joy Harrison and Dr. Michael Wesner (Supervising Researcher)

PARTICIPANT CONSENT:

I have read the preceding cover letter and am aware of the nature and procedures of research as described therein. In particular, I am aware that:

- My participation is voluntary. I am able to withdraw at any time, without explanation. I am also not obligated to answer every item on the questionnaires.
- My participation and the responses I provide will be kept confidential. My name or identifying information will not be included in the results of the study. My responses will be securely stored at Lakehead University for 7 years, and will then be destroyed.
- I am free to ask questions or raise concerns at any time. I have been given contact information for the researchers and the Research Ethics Board of Lakehead University.
- As a potential participant, I have the opportunity to enter my name in a draw for $50. If I am enrolled in an Introductory Psychology class, I may also have my participation counted toward bonus marks. Otherwise, there are no direct benefits to my participation in this study. There are also no physical or psychological risks associated with participation.

I agree to volunteer as a participant in this study, according to the terms outlined above and in the cover letter.

_____ _____ _____

Print name here Sign name here Date here

Do you wish to be entered into a random draw for $50? YES / NO

Do you with to receive a summary of the results? YES / NO

Participant Contact Information:

Phone: _____

E-mail: _____

Mailing address: _____

_____

_____

_____

Appendix B

Research Questionnaire

Age: _____ Birth Month: _____ Current Month: _____

Sex: _____

Section A. Vision Information

1. Eye colour: _____

2. Do you currently wear glasses or contact lenses? YES / NO

3. Have you ever been diagnosed with any of the following eye conditions?

YES	NO	
		optic neuritis
		retinopathy
		macular degeneration
		glaucoma
		cataracts
		retinitis pigmentosa
		neovascularization of the eye
		detached retina
		cornea dystrophy
		amblyopia (lazy eye)
		scleritis
		keratitis
		uveitis
		Other. Please specify: _____

4. Have you ever had eye surgery? YES / NO

5. If yes, please provide the following details:

Date	Type of Eye Surgery	Reason for Eye Surgery

6. Have you ever had bright light therapy? YES / NO

7. If yes, when was the last time you had the light therapy? _____

Section B. Medical Information

1. Have you been diagnosed with any of the following medical conditions?

YES	NO	
		Diabetes
		Epilepsy
		Multiple Sclerosis
		Parkinson's Disease
		Lupus Erythematosis
		Rheumatoid Arthritis
		Hyperthyroidism or Grave's Disease
		Other Thyroid conditions. Please specify: _____
		Pituitary or other Endocrine disorders. Please specify: _____

2. Do you currently have any chronic medical condition not listed above? If so, please specify:

_____

_____

_____

3. Do you have high blood pressure / hypertension? YES / NO

4. Do you get migraine headaches? YES / NO
5. If yes, do you ever see auras or have other visual disturbances when you get a migraine? YES / NO

6. When was the first day of your most recent period? _____

7. Do you take birth control pills? YES / NO

8. Are you receiving any type of hormonal therapy? YES / NO
9. If yes, please indicate the type of hormone medication or treatment you are receiving.

_____

_____

_____

10. Please indicate with a check mark if any of your biological relatives have been diagnosed with the following conditions.

	Sibling	Parent	Grandparent, Aunt or Uncle
Diabetes			
Epilepsy			
Multiple Sclerosis			
Parkinson's Disease			
Alzheimer's Disease			

Section C. Mental Health Information

1. Have you ever been diagnosed by a health care professional with any of the following conditions?

YES	NO	
		Depression
		Seasonal Affective Disorder (SAD); Seasonal Depression
		Bipolar Disorder
		Premenstrual Dysphoric Disorder
		Anxiety Disorder; Generalized Anxiety Disorder
		Social Anxiety Disorder
		Post-traumatic Stress Disorder
		Obsessive-Compulsive Disorder
		Eating Disorder; Bulimia; Anorexia; Binge Eating Disorder
		Schizophrenia
		Schizoaffective Disorder
		Personality Disorder
		Bipolar Disorder
		Alcohol or Substance Abuse or Dependence
		Other Psychiatric or Psychological Disorder. Please specify: _____

2. If you answered "YES" to any of the above:

   a. How old were you when you first experienced symptoms? _____

   b. Were you ever hospitalized for any of the above conditions? YES / NO

   c. Have you ever received treatment for any of the above conditions? YES / NO

3. If you answered "YES" to having being diagnosed with depression, how many separate episodes have you experienced in your lifetime? _____

4. Please indicate with a check mark if you know of any biological family member who has been diagnosed with or treated for any of the following conditions.

	Sibling	Parent	Grandparent, Aunt or Uncle
Depression			
Bipolar Disorder, Manic Depression			
Anxiety Disorder			
Obsessive-Compulsive Disorder (OCD)			
Eating Disorder, Bulimia, Anorexia			
Schizophrenia			
Schizoaffective Disorder			
Alcohol or substance abuse/dependence			

Section D. Drug Information

1. Have you consumed alcohol in the last 24 hours? YES / NO
   a. How much did you drink? _____
   b. How many hours ago did you last drink? _____

2. Have you used marijuana in the last 24 hours? YES / NO
   a. How many hours ago did you last use marijuana? _____

3. Have you used any other mood-altering drugs in the last 24 hours? YES / NO

4. Do you smoke cigarettes? YES / NO
   a. If yes, how many cigarettes do you smoke per day on average? _____

5. Please list any over-the-counter medications you have used in the last 24 hours, including cold medicine, pain relievers, allergy medications, and supplements.

Name of medication	Amount used	How many hours ago?

5. Please list any prescription medication you are currently taking.

Name of medication	How long have you been taking this medication?	How many hours ago did you take your last dose?

Appendix C

Medication Questionnaire

Section A. Prescription Information (To be filled out by the researcher.)

1. Current Prescription #1

a. Label Information

Month/Year Filled: _____

Name of medication: _____

_____

Size of single dose: _____

Number of doses per day (protocol): _____

b. When was the medication started (month/year)? _____

2. Current Prescription #2

a. Label Information

Month/Year Filled: _____

Name of medication: _____

_____

Size of single dose: _____

Number of doses per day (protocol): _____

b. When was the medication started (month/year)? _____

3. Other Antidepressant Prescriptions in the Last Year

a. If the current medication was started less than one year ago, was the participant being treated with other antidepressant medications in the last year? YES / NO

b. If so, what were they and when were they started? _____

_____

_____

_____

_____

Section B. Reason for Antidepressant Medication

Medications that fall under the broad classification of antidepressants are prescribed for a variety of reasons other than depression, such as anxiety, eating disorders, sleep difficulties, chronic pain, and quitting smoking, for example. This section is meant to determine the reasons for your prescription.

Part 1. What is the reason that you are currently taking antidepressant medication?

_____

_____

_____

_____

_____

Part 2. The following questions ask about possible symptoms, conditions, or issues that may have led you to seek the medical treatment resulting in your prescription. When responding to these questions, please think back to the few months before you were initially prescribed antidepressant medication for the reason you are currently taking it. **Specifically, think back to the last 6-month time period when you were not taking antidepressant medication.**

Module A. During the last 6-month time period when you were not taking antidepressant medication:

	YES	NO
1. Did you often feel that you couldn't control what or how much you ate?		
2. Did you often eat, within any 2-hour period, what most people would regard as an unusually large amount of food?		
3. Did either of these usually happen at least twice a week for 3 months?		
*If "No" to all of the above, skip to the next Module.		
4. During those 3 months, did you usually do any of the following at least twice a week in order to avoid gaining weight?		
a. make yourself vomit?		
b. take more than twice the recommended dose of laxatives?		
c. fasted, not eating anything at all for at least 24 hours?		
d. exercised for more than an hour specifically to avoid gaining weight after binge eating?		

Module B. During the last 6-month time period when you were not taking antidepressant medication:

	YES	NO
1. Was there a period of at least 2 weeks when you had any of the following experiences nearly every day?		
a. Little interest or pleasure in doing things you normally enjoyed?		
b. Feeling down, depressed, or hopeless?		
c. Trouble falling asleep, trouble staying asleep, or sleeping too much?		
d. Feeling tired or having little energy?		
e. Poor appetite or else over-eating?		
f. Feeling bad about yourself or worthless, feeling like a failure, or feeling that you had let yourself or others down?		
g. Trouble concentrating on things?		
h. Thoughts that you would be better off dead or of hurting yourself in some way?		
i. Moving or speaking so slowly that other people could have noticed? Or the opposite, being so fidgety or restless that you were moving around a lot more than usual?		
*If "NO" to all of the above, skip to the next Module.		
2. If you experienced any of these symptoms, did it make it hard for you to do your work, take care of things at home, or get along with other people?		
3. If you experienced any of these symptoms, was it because		
a. you were physically ill or had a general medical condition?		
b. you were taking medication?		
c. you were drinking alcohol or using recreational drugs?		
d. someone close to you had died?		

Module C. During the last 6-month time period when you were not taking antidepressant medication:

	YES	NO
1. Did you have a period of time lasting at least 1 week when you were feeling so good, high, excited, or hyper that other people thought you were not your normal self or you got into trouble?		
2. Did you ever have a period of time lasting at least 1 week when you were so irritable that you found yourself shouting at people or starting fights or arguments?		
If so, did you find yourself yelling at people you didn't really know?		
*If "NO" to all of the above, skip to the next Module.		
3. During the period of at least 1 week, did you experience any of the following:		
a. feeling more self-confident than usual?		
b. feeling that you had special abilities or powers?		
c. needing less sleep than usual in order to feel rested?		
d. being much more talkative than usual?		
e. having your thoughts racing through your head?		
f. being so easily distracted that you had trouble concentrating or staying on track?		
g. feeling physically restless?		
h. focusing more time than usual on any specific goals?		
3. If you experienced any of these symptoms, was it because		
a. you were physically ill or had a general medical condition?		
b. you were taking medication?		
c. you were drinking alcohol or using recreational drugs?		

Module D. During the last 6-month time period when you were not taking antidepressant medication:

	YES	NO
1. Did you have any panic attacks when you suddenly felt frightened or anxious?		
*If "NO", skip to the next Module.		
2. Did these attacks ever come on out of the blue, in situations where you did not expect to be nervous or uncomfortable?		
3. Did you have more than one of these attacks?		
4. For at least one month following any of these attacks:		
a. did you worry that there might have been something very wrong with you?		
b. did you worry a lot about having another one?		
c. did you do anything differently because of the attacks, like avoid certain places or situations, or not go out alone?		
5. During these attacks:		
a. did the symptoms come on quickly and take less than 10 minutes to get really bad?		
b. did your heart race, pound, or skip?		
c. were you short of breath?		
d. did you sweat?		
e. did you have chest pain or pressure?		
f. did you tremble or shake?		
g. did you have nausea or an upset stomach?		
e. did you feel as if you were choking?		
f. did you have hot flashes or chills?		
g. did you feel dizzy, unsteady, or faint?		
h. did you have tingling or numbness in parts of your body?		
i. were you afraid you might die?		
j. were you afraid you were going crazy or might lose control?		
k. did things around you seem unreal or did you feel detached from things around you or detached from parts of your body?		
6. Did you have these attacks because		
a. you were physically ill or had a general medical condition?		
b. you were taking medications?		
c. you were drinking alcohol or using recreational drugs?		

Module E. During the last 6-month time period when you were not taking antidepressant medication:

	YES	NO
1. Was there a period of at least 4 weeks that you felt nervous, anxious, on edge, or worried a lot, nearly every day?		
*If "NO", skip to the next Module.		
2. Did you experience any of the following symptoms nearly every day for at least 4 weeks?		
a. feeling restless so that it was hard to sit still		
b. getting tired very easily		
c. muscle tension, aches, or soreness		
d. trouble falling asleep or staying asleep		
e. trouble concentrating on things		
f. becoming easily annoyed or irritable		

Module F. During the last 6-month time period when you were not taking antidepressant medication:

	YES	NO
1. Were you ever afraid of going out of the house alone, being alone, being in a crowd, standing in a line, or traveling on buses or trains?		
2. Is there anything that you have been afraid to do or felt uncomfortable doing in front of other people, such as speaking, eating, or writing?		
3. If yes to either #1 or #2, did these behaviours or feelings interfere with your work or your social activities and relationships?		

Module G. During the last 6-month time period when you were not taking antidepressant medication:

	YES	NO
1. Was there ever anything that you had to do over and over again and could not resist doing, such as washing your hands again and again, counting up to a certain number, or checking something several times to make sure you had done it right?		
a. Did you engage in these behaviours because you felt you had to prevent something terrible from happening or in order to not feel distressed?		
b. Would you spend more than an hour a day engaged in these behaviours?		
2. Were you bothered by thoughts that kept coming back to you even when you tried not to have them?		
a. Were these reasonable worries about real-life problems?		
b. Were these your own thoughts?		
c. Were these thoughts inserted into your mind from elsewhere?		
*If "NO" to #1 or #2, skip to the next Module.		
3. Do you feel that these thoughts and/or behaviours were reasonable or appropriate?		
4. Did these thoughts and/or behaviours interfere with your work, social activities, or relationships?		
5. Did you have these thoughts and/or behaviours because		
a. you were drinking alcohol or using recreational drugs?		
b. you were taking medication?		
c. you were physically ill or had a general medical condition?		

Module H. During the last 6-month time period when you were not taking antidepressant medication:

	YES	NO
1. Were you bothered by a traumatic event that had occurred at some point in the past and that had involved you experiencing or witnessing actual or threatened injury or death to someone else or yourself?		
*If "NO", skip to the next section.		
2. Did you experience any of the following for at least 4 weeks?		
a. thinking about the prior traumatic event when you did not want to?		
b. dreaming about the traumatic event?		
c. acting or feeling the traumatic event were happening again?		
d. getting very upset when something reminded you of the event?		
e. physical reactions when you were reminded of the event, including sweating, irregular breathing, or your heart racing or pounding?		
3. Did any of the following occur for at least 4 weeks?		
a. did you make a special effort to avoid thinking or talking about the traumatic event?		
b. did you stay away from things or people that reminded you of the traumatic event?		
c. were you ever unable to remember some important part of what had happened during the traumatic event?		
d. did you have much less interest in doing things that used to be important to you?		
e. did you feel distant or cut off from others?		
f. did you feel numb or as if you no longer had strong feelings about anything?		
g. did you change the way you thought about or planned for your future?		
4. Did you experience any of the following for at least 4 weeks?		
a. difficulty falling or staying asleep?		
b. unusual irritability or outbursts of anger?		
c. trouble concentrating?		
d. being watchful or on guard even when there was no reason to be?		
e. being jumpy or easily startled?		

Part 3. Please indicate what you were prescribed antidepressant medication for.

Please check the boxes for all the categories that apply. If you check more than one box, please circle which category is the main or primary reason.

Depression; Major Depressive Disorder; Dysthymia

Premenstrual Dysphoric Disorder; Premenstrual symptoms

Bipolar Disorder; Cyclothymia; Manic Depression

Panic Attacks; Panic Disorder with or without Agoraphobia

Anxiety; Generalized Anxiety Disorder; Social Anxiety Disorder

Obsessive Compulsive Disorder (OCD)

Eating Disorder; Bulimia

Attention Deficit-Hyperactivity Disorder (ADHD)

Chronic Pain; Neuropathic Pain; Fibromyalgia

Sleeping Difficulties; Insomnia

Smoking Cessation

Other (please specify). _____

Section C. Medication and Vision

1. Did you notice any changes in your vision after you started taking your medication? **YES / NO**

2. If yes, please describe those changes. _____

_____

_____

_____

3. If yes, please circle the number on the rating scales below that best describes your visual experience after starting to take your medication.

Colour appearance

1	2	3	4	5
Faded colour Washed out, Dim		No change		Deeper colour Brighter, Richer

Light/dark contrast

1	2	3	4	5
Low contrast Less detail, Hazy		No change		High contrast More detail, Sharp