

Mesopic Visual Contrast Sensitivity in Patients with Major Depression

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The present study evaluated the effects of major depression on visual contrast sensitivity (CS) at low mesopic luminance (.7 cd/m² mean luminance), a condition that has been little explored in the literature. We measured spatial visual CS in 20 male volunteers aged 20 - 30 years, including 10 healthy individuals and 10 medicated individuals with major depression, to linear sine-wave gratings of .25, 1.0, and 4.0 cycles per degree (cpd) of visual angle using the psychophysical staircase method with forced choice. The average spatial visual CS in the depressed group was approximately 1.7 lower than the average spatial visual CS in the control group. However, the post hoc test showed significant differences only at the spatial frequencies of .25 and 1.0 cpd ($p < .05$), which are likely processed by the magnocellular visual pathway. These results suggest that spatial visual CS to sine-wave gratings should be used to evaluate the responsiveness of the visual system in patients with major depression under conditions of low luminance.

Keywords: Visual Perception; Contrast Sensitivity; Depression; Spatial Frequency; Psychophysics

Introduction

Depression can be defined as a mental disorder presented by depressed mood, loss of pleasure and interest, feelings of guilt and low self-esteem, sleep and appetite disturbances, low energy, and poor concentration (WHO, 2012). The annual incidence of depression makes it one of the most important public health problems, with severe socioeconomic implications, high costs for health care, and a reduction of quality of life (Solomon, 2002). According to the World Health Organization (WHO, 2001), severe depression is the leading cause of disability and ranks fourth among the 10 leading causes of pathology worldwide. In fact, by 2020, depression is estimated to be the second leading cause of disability worldwide. Studying depression using different approaches can complement clinical research and contribute to the characterization of the basic cognitive, affective, and neurophysiological mechanisms of this disease. It may also reveal new theoretical, behavioral, and functional aspects of depression in general and highlight alternative means of diagnosis and prognosis. The present study used visual contrast sensitivity (CS) to assess the perception of patients with major depression.

Visual CS is one of the most widely used tools in the diagnosis and theoretical and clinical evaluation of changes in visual perception and alterations in the central nervous system (Wesner & Tan, 2006) caused by disorders or diseases, such as schizophrenia (Slaghuis & Thompson, 2003), amblyopia (Polat, Sagi, & Norcia, 1997), cataracts (Elliott & Situ, 1998), mercury

poisoning (Ventura et al., 2005), stroke (Santos & Andrade, 2012; Santos, Andrade, & Fernandez Calvo, 2013), and Alzheimer's and Parkinson's diseases (Polat et al., 1997; Akutsu & Legge, 1995; Bour & Apkarian, 1996; Vleugels et al., 1998).

Surveys related to visual CS and affective disorders are still sparse, with only a few studies performed under different conditions and for different purposes (Wesner & Tan, 2006; Cavalcanti & Santos, 2005; Szabó et al., 2004). For example, Szabó et al. (2004) measured visual CS in volunteers with and without seasonal affective disorder using static and dynamic sine-wave gratings with spatial frequencies from .5 to 14.4 cycles per degree (cpd) of visual angle. The aim of that study was to investigate the therapeutic effects of light therapy on seasonal depression. The results showed that light therapy significantly improved visual CS in patients at static spatial frequencies below 5.7 cpd.

In a pilot study, Cavalcanti e Santos (2005) measured contrast thresholds in adult volunteers with and without major depression under high photopic luminance conditions using non-Cartesian radial visual stimuli at spatial frequencies of .25, 1.0, and 4.0 cpd. The results showed that patients with major depression had a loss of or lower CS for all spatial frequencies compared with volunteers without neuropsychiatric disorders.

Wesner & Tan (Wesner & Tan, 2006) measured contrast thresholds in patients with seasonal depression and major depression and volunteers without depression using static and dynamic visual stimuli modulated by Gabor's function with spatial frequencies from .3 to 12 cpd under photopic luminance

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conditions. The results showed that participants with depression had higher visual CS than the group without depression at high static spatial frequencies of 6.0 and 12 cpd. The authors argued that depression can increase the CS to frequencies that are processed by the parvocellular visual pathway.

The present study evaluated the effects of major depression on spatial visual CS by measuring achromatic visual CS in adult volunteers with and without major depression using a psychophysical method. The present study was motivated by the assumption that depression alters the central nervous system and affects numerous sensory, cognitive, and emotional function to promote changes in visual pathways (Wesner & Tan, 2006). Visual CS is an objective tool, noninvasive, and widely used clinically to contribute to a greater understanding of the sensory mechanisms associated with symptoms of depression.

Methods

Participants

Twenty 20- to 30-year-old male volunteers participated in the study. Ten of the participants had no neuropsychiatric diseases (mean age, 20.8 ± 1.2 years), determined by the Beck Depression Inventory, and 10 of the participants had a diagnosis of major depression (mean age, 23.9 ± 4.0 years) according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, text revision (American Psychiatric Association, 2000). The patients with major depression were selected and ranked by psychiatrists from the Centro de Atenção Psicossocial (CAPS; João Pessoa, Paraíba, Brazil) and were taken to the Laboratório de Percepção, Neurociências e Comportamento where the visual tests were conducted. Additional information about the patients with major depression is presented in **Table 1**.

All of the volunteers had normal visual acuity of 6/6 (inclusion criterion) tested with directional "E" Rasquin optotype cards (Xenônio, São Paulo, SP, Brazil) and were free of eye diseases and neurological disorders (exclusion criterion), with the exception of major depression or disorders related to major depression. The participation of the volunteers conformed to ethical aspects relevant to research that involves human subjects (National Health Council Resolution no. 196/96, Health Ministry, Brazil). The protocol was submitted to and approved by the Ethics Committee of the Health Sciences Center, Universidade Federal da Paraíba. The

participation of the volunteers was voluntary and occurred only after written informed consent was provided by them.

Visual Stimuli and Equipment

The test stimuli were achromatic linear sine-wave gratings ($.7 \text{ cd/m}^2$ mean luminance) with spatial frequencies of .25, 1.0, and 4.0 cpd. The non-test stimuli were gray and contained only the mean luminance. The diameter of the resulting patterns subtended approximately 7.2 degrees at a distance of 150 cm (i.e., the standardized distance between the monitor and volunteer). Contrast was defined according to Michelson's formula (Michelson, 1891):

$$C = \frac{L(x)_{max} - L(x)_{min}}{L(x)_{max} + L(x)_{min}}$$

$L(x)$ is the luminance at a given point on the sine wave, with x measured radially from the center. $L(x)_{max}$ and $L(x)_{min}$ are the maximum and minimum luminances of the pattern, respectively. C is the contrast. The spatial average luminance of the grating is given by $1/2[L(x)_{max} + L(x)_{min}]$.

The stimuli were presented on a 19-inch color cathode ray tube video monitor (1024×768 resolution, 70 Hz refresh rate). The stimuli were controlled by a computer through VGA and DVI video connectors. The dynamic range of the contrasts that the monitor could present was expanded more than 64 times by a BITS++ digital video processor (Cambridge Research Systems, Rochester, Kent, England, 2002), resulting in 14 bits per channel or 42 bits per pixel, allowing the presentation of more than 16,384 (or 2^{14}) grayscale levels. This allowed the testing of contrast thresholds while enabling high-contrast resolution. The BITS++ processor was controlled by C++ software developed by our research group. It generated and controlled the stimulus presentation and recorded the observer responses to calculate contrast threshold values.

The monitor was calibrated with LightScan software and an optical photometer (Cambridge Research Systems, Rochester, Kent, England, 2002). The monitor output was gamma-corrected using 48 points from 0 to 255 ($\gamma = 1.8$). The minimum and maximum luminance values of the screen were .5 and $.9 \text{ cd/m}^2$, respectively, and the background luminance was the minimum luminance itself. The laboratory room was 2.5×2.0 m, with one Philips 20W fluorescent lamp. The walls were gray to better control ambient lighting during the experiment.

Table 1.
Characterization of the experimental group.

Patient*	Age (Years)	Beck Depression Inventory	Time of Disease (Years)	Sex	Drug	Education
P1	23	Moderate depression	2	Female	Fluoxetine	Graduate
P2	20	Moderate depression	2	Female	Fluoxetine	Academic
P3	26	Moderate depression	2	Male	Fluoxetine	Academic
P4	22	Moderate depression	1	Female	Fluoxetine	Academic
P5	30	Severe depression	2	Female	Fluoxetine	Academic
P6	19	Mild depression	1	Female	Risperidone	Academic
P7	28	Severe depression	2	Female	Venlafaxine, Clonazepam, Zolpidem	Academic
P8	29	Moderate depression	2	Female	Floral de Bach	Graduate
P9	22	Moderate depression	1	Female	No drug	Academic
P10	20	Mild depression	1	Male	No drug	Graduate

*The characteristics of the participants in the control group (i.e., age, sex, and education level) were similar to the experimental group. See the average ages of the two groups in the Participants section.

Procedure

The participants viewed the stimuli binocularly with natural pupils at a distance of 150 cm. A fixed chair and forehead-chin support were used to control the viewing distance. The visual CS of all of the participants was estimated using a temporal two-alternative forced-choice staircase method (Wetherill & Levitt, 1965). The procedure for measuring the threshold for each frequency consisted of presenting successive pairs of simple stimuli, one of which was the test stimulus that should be identified by the participant (i.e., the first or second stimulus of each pair). The order of the presentation of the stimuli and frequencies was randomized by the software. The criterion used to alternate the contrast during the experimental session was three consecutive hits to reduce contrast by 20%, and one error to increase contrast by the same percentage.

Threshold measurements began with the test stimulus contrast set at a suprathreshold level (contrast = 1). Each time the volunteer gave a correct answer, the contrast was decreased successively until he made an error. The software recorded the last perceived contrast value. The contrast was then raised until the volunteer could perceive the stimulus again. In this case, the software recorded the first perceived contrast value. The experimental session automatically ended after the software recorded six staircase contrast values. Each threshold measurement was repeated for each spatial frequency. The contrast threshold calculated for each volunteer was the mean of the 12 contrast values (six at the test and six at the retest).

A stimulus sequence was presented during each experimental session, starting with a beep and followed immediately by the presentation of the first stimulus for 2 s. A 1 s interval elapsed between stimuli, followed by the presentation of the second stimulus for 2 s and the volunteer's response. All of the participants responded within the 3-s interval. A correct response was followed by another beep. The interval between trials was 3 s, regardless of a correct or incorrect response (or choice). The beeps that indicated the beginning of the stimulus pair presentation and correct choice were different.

All of the participants received the following instructions: "Pairs of circles will appear on the screen, one after the other. One of them will be totally gray, whereas the other will contain light and dark gratings (bars) inside it. When the circle with light and dark gratings (bars) appears first, you must press the left mouse button (button 1); when the circle with light and dark gratings (bars) appears second, you should press the right mouse button (button 2)."

The experiments began only when the experimenter was confident that the participants understood and responded according to the directions. In this context, instructions were repeated in a training and familiarization session with the experimental conditions.

After each experimental session, the software produced a record sheet with the 12 staircase contrast values from each participant, six in the test and six in the retest. Values were grouped according to mental condition (i.e., participants without major depression [control group] and participants with major depression [experimental group]). All of the staircase contrast threshold values were converted into CS values (1/threshold).

All 240 staircase contrast values (12 from each volunteer) for each spatial frequency were used to conduct a Tukey Two-Sided Outlier Test. The 3, 4, and 8 outlier values for .5, 1.0, and

4.0 cpd, respectively, identified by the Tukey test were set to equal the group mean calculated in the absence of the outlier. After the Tukey Outlier Test, the means of the staircase contrast values were used to calculate their individual linear CS values.

Results

A one-way analysis of variance (ANOVA) applied to CS revealed significant differences between groups ($F_{3,396} = 80.5$, $p < .05$) and a significant interaction ($F_{3,396} = 905.2$, $p < .05$). Thus, the control and experimental groups had different contrast sensitivity ($p < .05$).

The Tukey Honestly Significant Difference *post hoc* test showed significant differences between the groups only at low spatial frequencies of .25 and 1.0 cpd ($p < .05$). The differences between groups at the spatial frequency of 4.0 cpd were not significantly different ($p > .05$). The participants with major depression generally required higher contrast to detect the spatial frequencies of .25 and 1.0 cpd than the participants without any neuropsychiatric disease.

The results showed that the maximum CS in the control group occurred at frequencies of .25 and 1.0 cpd, whereas the maximum CS in the experimental group occurred at the frequency of .25 cpd (Figure 1). The data also showed that the participants without any neuropsychiatric disease were 1.57-, 2.14-, and 1.28-times more sensitive to spatial frequencies of .25, 1.0, and 4.0 cpd, respectively, than the patients with major depression.

Discussion

The present study measured visual CS using a psychophysical staircase method, with forced choice between two temporal alternatives under mesopic luminance conditions. The research hypothesis was that major depression would alter the response of the visual system or the basic sensory mechanisms involved in processing visual patterns, altering contrast sensitivity to sine-wave gratings with spatial frequencies of .25, 1.0, and 4.0 cpd.

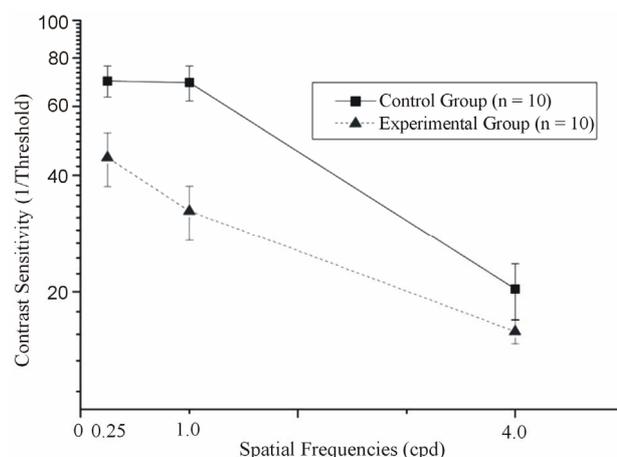


Figure 1. The estimated contrast sensitivity in adult volunteers is presented as a spatial frequency function of .25, 1.0, and 4.0 cpd. The continuous curve (—■—) represents the control group (without major depression), and the dotted curve (---▲---) represents the experimental group (with major depression). The error bars indicate standard errors of the mean ($p = .05$).

Major depression likely does not equally interfere with the anatomical and physiological mechanisms related to the processing of the tested visual spatial frequencies. The decrease observed in visual spatial CS in patients with major depression was statistically significant only at the low spatial frequencies (.25 and 1.0 cpd), which are probably processed preferentially by the magnocellular visual pathway, especially when considering low luminance used in the study (Lee, Martin, & Valberg, 1989; Livingstone & Hubel, 1987; Murray, Parry, & Carden, 1987; Valberg & Rudvin, 1997; Vassilev, Stomonyakov, & Manahilov, 1994). According to Souza et al. (2007), at low spatial frequencies of .4 - .8 cpd, only the magnocellular visual pathway appears to be relevant for the cortical response. No significant differences in CS were found between the control group and experimental group at the highest spatial frequency tested (4.0 cpd). Therefore, major depression may preferentially damage the magnocellular visual pathway rather than affect the mechanisms that process high spatial frequencies, which may involve the parvocellular visual pathway. This hypothesis relies on the possibility that magnocellular channels are activated by spatial frequencies below 2.0 cpd, whereas parvocellular channels are activated by spatial frequencies above 4.0 cpd (Adams & Courage, 2010; Burbeck & Kelly, 1981). Importantly, however, the levels of scotopic and photopic contrast appear to be the dominant factor for the functional activity of the magnocellular and parvocellular pathways, respectively, rather than the spatial frequency itself (Skottun & Skoyles, 2011).

We cannot definitively state that the alterations found in visual perception or CS solely resulted from changes in the central nervous system produced by major depression. Other factors are likely involved. For example, antidepressants, such as fluoxetine, venlafaxine, and others, act by modulating the function of the central nervous system. The present study did not seek to control the effects of antidepressants on visual CS measures. Typical and atypical antipsychotic medications can also differentially change perceived contrast (Chen et al., 2003).

Changes in visual CS caused by major depression were expected in the present study, based on studies that reported that neuropsychiatric disorders affect cognition and central nervous system function (Bubl et al., 2010; Duman, Heninger, & Nestler, 1997; O'Donnell et al., 2002; Slaghuis, 1998; Wolman & Stricker, 1990). Some studies used electrooculography (EOG) (Lam et al., 1991; Fountoulakis, Foutiou, Iacovides, & Kaprinis, 2005) and flash electroretinography (ERG) (Fountoulakis et al., 2005; Hébert et al., 2004; Lavoie et al., 2009) to evaluate patients with seasonal depression and reported the presence of changes in the retina at the photoreceptor level, which resulted in decreased light sensitivity in depressive patients compared with the control group. Both EOG and ERG are useful tools, the results of which indirectly reflect dopamine activity in the retina. Several studies have related decreased dopamine activity with specific depressive symptoms. For example, Harris, Calvert, Leendertz e Phillipson (1990) suggested that lower dopamine levels in the brain in depressed patients result in a decrease in visual CS. Bodis-Wollner e Tzelepi (1998) proposed that dopamine D₂ receptors affect the ability to visually detect high spatial frequencies, whereas D₁ receptors affect the ability to visually detect low spatial frequencies. These authors argued that decreased dopamine levels could attenuate the inhibition modulated by horizontal cells, which are involved with the perception of visual CS, thus resulting in a reduction of this visual function.

Szabó et al. (2004) reinforced the hypothesis that major depression damages the magnocellular visual pathway. These authors found a decrease in CS at a low spatial frequency (.5 cpd). However, these results are different from the results reported by Wesner e Tan (2006), who found no losses in visual CS in patients with depression but greater CS to higher spatial frequencies. The authors argued that depression can increase the CS to spatial frequencies processed by the parvocellular visual pathway. However, Wesner e Tan (2006) used different stimuli (i.e., a gabor patch) and luminance, rendering direct comparisons between their results and the present study difficult.

The present study investigated whether major depression alters visual CS at low levels of luminance. The results showed a reduction of CS in patients with major depression compared with healthy volunteers who were matched for age, sex, and educational level. However, unclear is whether the changes observed were caused by depression itself, medications, or a combination of both. Only three of the 10 participants in the experimental group did not use medications. Finding patients with major depression who use only a single medication is difficult, but new research needs to systematically investigate the effect of medication on visual spatial CS. Overall, the present data suggest that major depression caused changes in the magnocellular pathway, a pathway that is important in the processing of spatial frequencies under low luminance conditions.

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