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## Dysregulation of visual motion inhibition in major depression

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## ABSTRACT

Individuals with depression show depleted concentrations of the inhibitory neurotransmitter GABA in occipital (visual) cortex, predicting weakened inhibition within their visual systems. Yet, visual inhibition in depression remains largely unexplored. To fill this gap, we examined the inhibitory process of center-surround suppression (CSS) of visual motion in depressed individuals. Perceptual performance in discriminating the direction of motion was measured as a function of stimulus presentation time and contrast in depressed individuals ( $n=27$ ) and controls ( $n=22$ ). CSS was operationalized as the accuracy difference between conditions using large ( $7.5^\circ$ ) and small ( $1.5^\circ$ ) grating stimuli. Both depressed and control participants displayed the expected advantage in accuracy for small stimuli at high contrast. A significant interaction emerged between subject group, contrast level and presentation time, indicating that alterations of CSS in depression were modulated by stimulus conditions. At high contrast, depressed individuals showed significantly greater CSS than controls at the 66 ms presentation time (where the effect peaked in both groups). The results' specificity and dependence on stimulus features such as contrast, size and presentation time suggest that they arise from changes in early visual processing, and are not the results of a generalized deficit or cognitive bias.

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## 1. Introduction

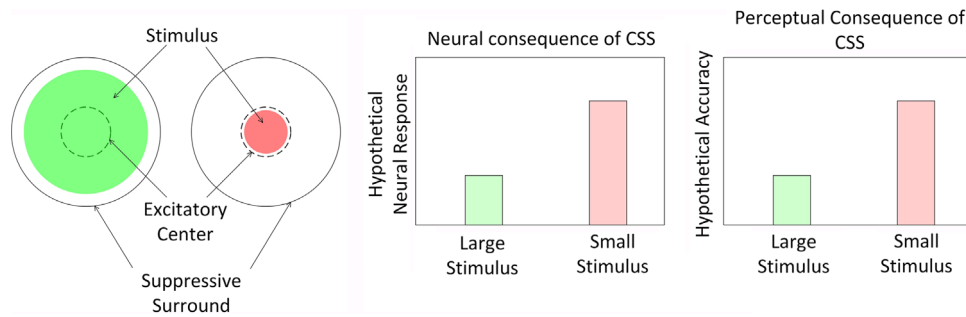
Perceptual changes in depression represent an understudied and promising area, one that lends itself to addressing a major shortcoming of research on this mood disorder. While progress has been made in understanding major depression at both biological and psychological levels (Sanacora et al., 1999; Kircanski et al., 2012; Belzung et al., 2014; Treadway and Pizzagalli, 2014) there is often a disconnect between biological and behavioral levels of analysis—in part due to the complexity of the phenomena being studied. From a neurobiological perspective, perceptual changes are simpler, and better understood. The visual system in particular may be used as a model to study altered brain function in depression at both levels. Basic perceptual processing deficits, including non-affective stimuli, have been shown in currently and formerly depressed individuals (Golomb et al., 2009; Bubl et al., 2010). In addition, perceptual changes may be important factors in the etiology and maintenance of major depression. For example, depressed individuals gaze disproportionately more at dysphoric

stimuli and less at positive stimuli during free viewing or search tasks (Armstrong & Olatunji, 2012).

The present study represents an effort to understand functional consequences of brain changes in depression at a perceptual level. We studied a basic visual process in depression, specifically, an inhibitory process within the visual motion system called center surround suppression (CSS). CSS was chosen because depressed individuals, as well as those who have recovered from depression, show reduced concentrations of gamma-aminobutyric acid (GABA) – the main inhibitory neurotransmitter – in the occipital cortex (Sanacora et al., 1999; Bhagwagar et al., 2008). The established GABA deficit in depression suggests that inhibitory processing within the visual system might be altered, and perhaps more specifically, weakened. Indeed, a previous study on CSS in recovered depressed individuals showed reduced CSS of visual motion in these individuals despite a lack of depressive symptoms (Golomb et al., 2009), but data on currently depressed individuals are not available. CSS is well understood at both the neurobiological and perceptual levels (Born, 2000; Tadin et al., 2003), and holds promise to shed light on how depression-associated brain changes manifest at a perceptual level.

CSS refers to the organization of a neuron's receptive field, or the area of visual space which, when stimulated, causes the

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**Fig. 1.** Illustration of center-surround suppression. The inhibitory process occurs for a variety of stimuli processed in various parts of the visual system. Note that a larger stimulus generates a smaller neural response and lower performance accuracy (i.e., perceptual response).

neuron to respond. If the center portion of the receptive field is stimulated with light, the neuron's firing rate increases, and if the area immediately surrounding this center portion is stimulated, the neuron's firing rate decreases (Hubel and Wiesel, 1959; Born, 2000; Born and Bradley, 2005) (Fig. 1). This visual organization has been well-studied at the cellular level in animals, and at the population level in humans using transcranial magnetic stimulation (TMS) and functional magnetic resonance imaging (fMRI) (Hubel and Wiesel, 1968; Williams et al., 2003; Born and Bradley, 2005; Sincich and Horton, 2005; Moutsiana et al., 2011; Tadin et al., 2011). CSS has also been demonstrated psychophysically: as predicted by the neurobiological mechanisms at work, individuals determine the direction of motion in a small object more easily than in a large one, when both have high contrast (Tadin et al., 2003).

CSS is hypothesized to be sensitive to GABA dysfunction, for several reasons. First, GABA is the primary inhibitory neurotransmitter in the brain, and is thought to play a role in surround suppression (Betts et al., 2005), which is an intrinsically inhibitory process as described above. Second, administration of GABA antagonists has been shown to modulate the size of the surround portion of the receptive field (Pernberg et al., 1998; Murthy and Humphrey, 1999). Third, individuals who have recovered from depression, as well as individuals with schizophrenia, show both depleted GABA levels in occipital cortex, and abnormalities in CSS (Bhagwagar et al., 2008; Golomb et al., 2009; Yoon et al., 2010).

We investigated CSS within the motion processing system, where GABA has been shown to play a key role in making cells selective to direction of motion (Barlow et al., 1964; Grzywacz, 1997), in depression. We aimed to determine whether and how depression is associated with altered inhibitory processing (operationalized using CSS) within the visual system. Based on a previous study in recovered-depressed individuals (Golomb et al., 2009) and findings of diminished GABA levels in occipital cortex in depression (Sanacora et al., 1999), we hypothesized that CSS would be weakened in depressed individuals. Based on prior reports (Churan et al., 2009), we further anticipated that CSS itself would be present in both subject groups only at brief presentation times.

## 2. Methods

### 2.1. Participants

Twenty-seven individuals with depression and 22 normal controls participated in the study. Demographic and clinical characteristics of the sample are provided in Table 1. Depressed participants were diagnosed using the Structured Clinical Interview for DSM Disorders, 4th edition, (SCID-IV; First et al., (2002)), and control participants were screened for Axis I disorders using the non-patient version of the SCID (First et al., 2002). Twenty-two

**Table 1**  
Demographic and clinical information of the sample.

	Control (n=22)	Depressed (n=27)	Test statistic (DF)	p
Age	34.5 (14.8)	40.3 (12.4)	T (47)=1.49	0.14
Education	15.9 (2.1)	16.07 (2.2)	T (47)=0.23	0.82
Gender (M/F)	10/12	11/16	$\chi^2$ (1)=0.11	0.74
WRAT*	49.3 (4.9)	50.4 (2.9)	T (40)=0.95	0.35
BDI-II**	0.59 (0.85)	29.6 (10.3)	T (47)=13.12	< 0.001

\* Wide Range Achievement Test Word Reading Score.

\*\* Beck Depression Inventory – 2.

of the depressed individuals met full criteria for a major depressive episode at the time of the study, and five met criteria for a major depressive episode in the last year and were in a state of partial remission with significant residual clinical symptoms. Depression levels at the time of testing were assessed using the Quick Inventory of Depressive Symptomatology (QIDS) and Beck Depression Inventory (BDI-II) (Beck et al., 1996; Rush et al., 2003). QIDS data were missing for one depressed individual, and four controls, to whom it was not administered.

None of the depressed participants had a co-morbid diagnosis of any psychotic disorder. There was also no immediate family history of psychotic disorders such as schizophrenia or bipolar disorder with psychosis. Twelve of the depressed participants had co-morbid Axis I disorders (eight anxiety disorders, three eating disorders not including anorexia, and one PTSD), but depression was their primary diagnosis. Eleven of the depressed participants had a past but not current history of alcohol or substance abuse or dependence. Thirteen of them were unmedicated, while 14 were taking antidepressant medications. Of these, 6 were also taking an anxiolytic, and 3 were taking an antipsychotic (aripiprazole) along with a typical antidepressant to achieve autoreceptor activation. The Wide Range Achievement Test (WRAT; Wilkinson (1993)) was administered as a proxy of premorbid intellectual ability, though this score was missing for 7 control subjects who were tested prior to its adoption in the study protocol.

Twenty-two depressed individuals were recruited from McLean Hospital outpatient and partial hospital clinics, while five depressed individuals – as well as all control participants – were recruited via advertisements in the greater Boston community. All participants were fluent English speakers, with no history of neurological diseases or head injuries with loss of consciousness for more than one minute.

### 2.2. Stimulus and procedures

The stimulus was a drifting Gabor patch shown along with its parameters in Fig. 2. Size and contrast of the stimulus remained constant within a testing block; there were four blocks

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