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Difference in the binocular rivalry rate between depressive episodes and remission

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HIGHLIGHTS

- Binocular rivalry rate is slow in patients with depression.
- Rivalry rate during depressive episodes was slower than during remission.
- No significant correlation between the changes of HAMD scores and the rivalry rates.

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ABSTRACT

Binocular rivalry refers to a phenomenon in which, when different images are presented to each eye simultaneously, perception alternates spontaneously between monocular views rather than being a superposition of the two images. Recently, the involvement of serotonin systems has been reported to be related to the phenomenon. There is abundant evidence for abnormalities of the serotonin systems in depression and the antidepressants that enhance 5-HT transmission, which in turn improves mood and behavior. However, the available data with respect to rivalry rates in depression are less clear. Therefore, we aimed to explore whether perceptual rivalry was affected by a dysfunctional serotonin system in patients with depression and whether there was a rivalry rate difference between episode and remission states in depression patients. Twenty-eight patients with depression and 30 healthy controls were recruited in the study. We assessed the rivalry rate and the 17-item Hamilton Depression Rating Scale (HAMD) in patients with depression during clinical episode and remission states. The results suggested that alternation rates for patients during episodes were significantly slower than during remission and than in healthy controls. Also, alternation rates for patients during remission were slower than in healthy controls. These results may provide further clues to serotonergic neural systems contributing to the dynamics of perception rivalry and may foster enlightenment regarding the field of binocular rivalry in psychiatric disorders other than bipolar disorder.

1. Introduction

Binocular rivalry refers to a phenomenon in which, when different images are presented to each eye simultaneously, perception alternates spontaneously between monocular views rather than being a superposition of the two images. This fascinating phenomenon provides an effective tool for investigating the neural bases of consciousness and has intrigued neuroscientists for centuries [1–3]. Numerous neuroimaging [4–6] and neurophysiologic [7–9] studies of rivalry have occurred, recently, and researchers have also begun to focus on pharmacologic studies to examine the phenomenon from a neurochemical perspective [10–12].

The relationship between serotonergic (5-hydroxytryptamine; 5-HT) neural systems and binocular rivalry has been the subject of investigation. A suggestive psychopharmacologic study [10] has shown that the administration of psilocybin, a 5-HT1A and 5-HT2A agonist that can inhibit serotonin release from the raphe nucleus decreased the rate of perceptual switching in binocular rivalry. This study suggests the involvement of serotonin pathways in neural processing related to binocular rivalry. Subsequently, Nagamine et al. [13] have explored the rivalry rate in subjects with various degrees of anxious temperament. Anxiety is a state thought to be associated with dysfunctional

Abbreviations: ED, episode state depression; RD, remission state depression; HC1, the first test of healthy controls; HC2, the second test of healthy controls.

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serotonergic neural activity [14]. Nagamine et al. have demonstrated that the rivalry alternation rate was accelerated in subjects with higher degrees of trait anxiety, and suggested that anxiety and perceptual rivalry may have overlapping serotonergic neural substrates. In accordance with previous studies, Nagamine et al. [12] have measured the binocular rivalry rate under the influence of tandospirone, a highly selective 5-HT1A agonist. This study confirmed that tandospirone decreased the binocular rivalry rate, suggesting that the 5-HT1A neural pathway is involved in this phenomenon. There is also evidence from a recent genetic study indicating that serotonin receptor genes are involved in visual bistable perception [15]. All these findings support the involvement of serotonergic neural systems in binocular rivalry. Indeed, the serotonin system is the largest brain neurotransmitter system, comprising a widespread and extremely complicated innervation system of most cortical and subcortical structures in the brain [16].

Depression is a debilitating and highly recurrent mental disease that has a lifetime prevalence of up to 20% in the community, which is among the highest for psychiatric disorders [17]. Despite years of research on depression, its underlying pathogenesis remains poorly understood. However, at the neurochemical level, the dysfunction of serotonergic neural systems is widely accepted [18]. An aberrant serotonin system has been hypothesized to play a crucial role in the pathogenesis of depression. The serotonin hypothesis suggests that a deficiency of serotonin neural activity increases individual vulnerability to depression [19]. Also, there have been many studies that have reported a decreased 5-HT transporter level in depression or depression-related suicide [20–22]. Indeed, selective serotonin reuptake inhibitors (SSRIs) and other 'newer antidepressants' such as serotonin–norepinephrine re-uptake inhibitors (SNRIs) or norepinephrine and specificity serotonergic antidepressants (NASSAs), which enhance 5-HT transmission, are the first choice for pharmacotherapy [23].

Numerous studies have demonstrated slow binocular rivalry in patients with bipolar disorder [24–26] and suggested slow binocular rivalry as a potential trait marker for this disorder [27]. However, the available data with respect to binocular rivalry rates in depression are limited and no previous studies have measured the rate of binocular rivalry in different clinical states of the same patients with depression. Because there is a deficiency of serotonin neural activity in depression and the 5-HT1A agonists can inhibit serotonin release and cause a decrease in binocular rivalry, we hypothesized that patients with depression might show a slower binocular rivalry rate than healthy individuals. We further hypothesized that patients who received antidepressants which enhance 5-HT transmission could exhibit faster switching rates. Therefore, we assessed binocular rivalry rates in episode state depression (ED) and remission state depression (RD) in 28 patients with a history of depression, to investigate these hypotheses.

2. Methods

2.1. Participants

Patients with depression were recruited from the Anhui Mental Health Center. The diagnoses of depression were established on the basis of Diagnostic and Statistical Manual of Mental Disorders—IV criteria [28]. All the patients with depression in this study were diagnosed by at least two chief physicians. Specifically, they were asked in detail if they had any past episodes of mania or hypomanic, both of which served as exclusion criteria. The general exclusion criteria were as follows: (i) visual dysfunction such as amblyopia, strabismus or diplopia; (ii) decimal visual acuity less than 0.8 either unaided or with correction; (iii) history of brain trauma or neurologic disorders; (iv) drug abuse such as hallucinogens or alcohol; and (v) age over 60 years. We excluded patients who received physical therapy, such as transcranial magnetic stimulation or electroconvulsive therapy, to prevent it from interfering with the results. In addition, the absence of GABAergic medication was confirmed in these patients because a recent study showed that gamma-aminobutyric acid (GABA) is involved in perceptual dynamics [29]. Patients who received GABAergic medication during the subsequent antidepressant treatment had stopped taking the drugs for more than a week by the time of the second testing. Final enrollment in the study was 28 patients with depression. Regarding the duration of antidepressant treatment before testing, of the 28 patients, 15 were antidepressant-naive individuals and 13 had received less than a week of antidepressant treatment. All 28 were included in this work due to small sample size (the mean duration of treatment was 3.46 ± 1.27 days).

We recruited 30 healthy control participants matched as a group for age, gender and education who met the same exclusion criteria as the patients with depression. In particular, the absence of a personal or familial history of psychiatric disorders was confirmed for all healthy subjects. All participants were asked to abstain from ingesting alcohol, tea, coffee, cola and cigarette for 4 h before testing, as these substances may affect a subject's rivalry rate [30]. All participants were naive to the purpose of the study.

Regarding antidepressant medication, of the 28 patients, 23 were administered SSRIs (11 were on paroxetine; 7 were on escitalopram; and 5 were on sertraline), and five were receiving SNRIs (4 were on venlafaxine; 1 was on duloxetine). Of 23 patients who received SSRI treatment, 7 were in combination NASSAs (all were on mirtazapine). The mean dosages of the antidepressants are reported in Table 1.

Written informed consent was obtained from all participants after a detailed description of the study. This study was approved by the Anhui Medical University Ethics Committee.

2.2. Clinical measures

The 17-item Hamilton Depression Rating Scale (HAMD) [31] was used to assess the participants' depression symptoms. Healthy controls were excluded from the study if their HAMD total scores were >7. Clinical remission in patients with depression was defined as having a HAMD total score of ≤ 7, which is the current widely accepted cut-off value [32]. All assessments were conducted in the afternoon to avoid the effects of diurnal fluctuations in cortisol levels and mood. All assessments were performed by the same trained rater.

2.3. Binocular rivalry test

The test was conducted in a darkened room. Rivalry stimuli were presented on a 15.6 inch monitor with a resolution of 1366×768 pixels and a refreshment rate of 60 Hz controlled by a personal computer. Subjects viewed the stimuli at a distance of 100 cm from the monitor, yielding a viewing angle of 2°. Stimulus presentations and trial timing were controlled using the Matlab software package with the PsychToolbox [33,34]. Binocular rivalry was established by having participants view overlapping color-filtered images on the monitor screen through red–green anaglyph glasses; a green radial grating and a red circular grating were presented to the subject's left and right eyes, respectively (spatial frequency, angular grating, 8 cycles/degree and radial grating, 4 cycles/degree; luminance, 135 cd/m^2; contrast, 0.9; waveform, sinusoidal). To ensure clarity of the test, detailed instructions were given while a practice screen was presented to the participant. Subjects were asked to press the appropriate button once each time their perception switched. They were instructed to press the left key when perceiving the red circular grating and the right key when perceiving the green radial grating. Specifically, subjects were instructed to press neither button if they experienced either a mixed percept or a fused figure. Following the practice session, participants viewed the dichoptic stimulus through red–green anaglyph glasses.

Each testing session consisted of three blocks, with each block consisting of three 30-s trials, separated by a 15-s break in which a catch trial appeared. The catch trial consisted of a 15-s movie of simulated rivalry to check whether the participant understood the