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Clinical Study

Treatment with escitalopram improves the attentional bias toward negative facial expressions in patients with major depressive disorders

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ABSTRACT

We hypothesized that treatment with escitalopram would improve cognitive bias and contribute to the recovery process for patients with major depressive disorder (MDD). Many previous studies have established that patients with MDD tend to pay selective attention to negative stimuli. The assessment of the level of cognitive bias is regarded as a crucial dimension of treatment outcomes for MDD. To our knowledge, no prior studies have been reported on the effects of treatment with escitalopram on attentional bias in MDD, employing a dot probe task of facial expression. We studied 25 patients with MDD and 25 controls, and used a dot probe task of facial expression to measure cognitive bias. The patients' psychopathologies were rated using the Hamilton Depression Scale (HAMD) at baseline and after 8 weeks of treatment with escitalopram. All participants performed the facial expression dot probe task. The results revealed that the 8 week escitalopram treatment decreased the HAMD scores. The patients with MDD at baseline exhibited an attentional bias towards negative faces, however, no significant bias toward either negative or happy faces were observed in the controls. After the 8 week escitalopram treatment, no significant bias toward negative faces was observed in the patient group. In conclusion, patients with MDD pay more attention to negative facial expressions, and treatment with escitalopram improves this attentional bias toward negative facial expressions. This is the first study, to our knowledge, on the effects of treatment with escitalopram on attentional bias in patients with MDD that has employed a dot probe task of facial expression.

1. Introduction

Major depressive disorder (MDD) is a type of mental disorder that is characterized by a persistent low mood, accompanied by low self-evaluation and a loss of interest or pleasure in normally enjoyable activities. MDD is a disabling condition that adversely affects individuals' social lives, eating and sleeping habits, and general health. Understanding the cognitive symptoms of MDD, including attention and memory deficits, is a high priority for MDD research. Currently, the general interest in MDD research is focused on the relationship between attentional bias and mood-related psychopathology [1]. Attentional bias is an automatic process that does not require conscious processing of stimuli [2]. Due to attentional bias, some stimuli are given priority and are amplified while others are inhibited. As one important factor of cognitive bias, attentional bias in information processing plays important roles in the etiologies and maintenance of emotional disorders [3]. Previous studies have indicated that attentional bias toward negatively valenced information supports and sustains the maladaptive patterns of information processing that are characteristic of depressive disorders, and that patients with MDD tend to pay selective attention to negative stimuli [4–6]. Based on the above findings, individual differences in attentional bias should constitute an important state marker for individuals with depressive disorders.

The clinical symptoms of MDD are paralleled by typical cognitive dysfunction, including deficits in verbal memory, attention processing and executive function [7]. Cognitive dysfunction is a core syndrome but is also correlated with functional impairment in MDD. The decision making process is one important factor related to cognitive function. Because attentional bias can dramatically affect decision making processes and cause people to make poor or inaccurate choices [8], the assessment of the level of attentional bias is a crucial dimension for the assessment of treatment outcomes in MDD.

Cognitive reaction time (RT) tasks, such as the modified Stroop and probe detection tasks, are commonly used tools for research

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into attentional biases in clinical populations due to their ability to indirectly measure selective attention. The classic paradigm for the probe detection task originated in a report by Posner et al. [9]. This task presents pairs of emotionally toned and neutral words for a brief period of time. The subjects are asked to respond as quickly as possible to a dot probe that appears in one of the two locations that were formerly occupied by the words. Shorter response latencies indicate that the dot probe appeared in the attended region of the visual field. A modified dot probe task that features pictures instead of words has been used in several studies of attentional bias in anxiety disorders and bipolar disorder [10–12]. In the modified dot probe task, following the 500 ms (millisecond) presentation of a pair of pictures, a probe is presented for 1000 ms in a location that was formerly occupied by one of the pictures. The subjects are asked to press one of two response buttons as quickly as possible to indicate the location of the probe. The RT for correct responses are employed as a measure of attentional bias. The dot probe task is widely employed to study attentional biases in MDD [13,14]. Facial expressions are stimuli with strong arousal effects, therefore, a dot probe task that utilizes facial expression stimuli is a useful tool for the study of attentional bias in MDD.

The most common clinical treatments for MDD are psychotherapy and medication therapy. The effects of antidepressants are superior to those of psychotherapy, particularly in patients with chronic major depression [15,16]. Escitalopram is a member of the selective serotonin reuptake inhibitor (SSRI) class of drugs and is used clinically as a first line agent for the treatment of depression. Escitalopram is the therapeutically active S-enantiomer of RS-citalopram, which is a commonly prescribed SSRI. In a previous study which assessed the efficacy, acceptability, and tolerability of escitalopram compared to tricyclics, other selective serotonin reuptake inhibitors, heterocyclics, and newer agents in the acute phase of treatment of major depression [17], escitalopram scored better than the other antidepressants in terms of efficacy and acceptability. To our knowledge, there are still no reports on the effects of treatment with SSRI, such as escitalopram, on attentional bias in MDD.

Escitalopram is an effective and well tolerated first line treatment option for the management of MDD. Therefore, we hypothesized that treatment with escitalopram would improve cognitive bias and contribute to the recovery process. In the present study, we investigated whether patients with MDD exhibited cognitive bias toward unhappiness-related facial expressions compared with healthy controls, and whether treatment with escitalopram affected attentional bias in MDD using a facial expression dot probe task.

2. Subjects and methods

2.1. Study design and setting

We performed a case-controlled observational experiment in the Department of Psychiatry at the Wuxi Mental Health Center of Nanjing Medical University, China from October 2012 to April 2014. All research procedures were approved by the Ethics Committee on Human Studies of the Wuxi Mental Health Center of Nanjing Medical University, China, and were conducted in accordance with the Declaration of Helsinki. All patients and controls provided written informed consent to participate. For the patients who had compromised capacities to consent, we provided their next of kin, care takers or guardians with the written informed consent forms and all research procedures, all of whom consented on the behalf of the participants.

2.2. Diagnostic approaches and subjects

According to the admission order, we selected 25 patients who met the Diagnostic and Statistical Manual of Mental Disorders (fourth edition, DSM-IV) diagnostic criteria for MDD, and 25 age and sex-matched controls with no personal or family histories of depressive disorders. The patients with MDD were recruited from the Wuxi Mental Health Center of Nanjing Medical University. The controls were recruited from local advertisements to citizens of Wuxi City, Jiangsu Province, China. Exclusion criteria were a diagnosis of alcohol or substance dependence, neurological disorder, or any type of head injury or if they had received electroconvulsive therapy within the last 6 months. All participants were Chinese.

2.3. Clinical assessments

All participants underwent a clinical assessment by a psychiatric resident to collect information about their medications and socio-demographic data, and to confirm/exclude the DSM-IV diagnosis. At baseline, all patients were antidepressant naive. After 2 weeks of follow-up, the patients received escitalopram (10–20 mg/day; mean 16.00 mg ± a standard deviation of 3.50). To detect the effects of the treatment on attentional bias in MDD, all patients perform the facial expression dot probe task at baseline and after 8 weeks of escitalopram treatment. All controls performed the facial expression dot probe task once. The severity of MDD was rated in all patients with the 17 item version of the Hamilton Depression Scale (HAMD) [18].

2.4. Experimental procedure

2.4.1. The dot probe task

E-Prime software (edition 2.0; Psychology Software Tools, Sharpsburg, PA, USA) was used for the trial procedure. The dot probe task was adapted from Elder et al. [19]. A gray plus sign (2×2 cm) was designated as the fixation display and presented in the center of the screen. The face stimuli included 36 pictures that consisted of 12 unhappy, 12 happy and 12 neutral facial expressions that were taken from the Chinese affective picture system [20]. Each displayed face was presented at equal distances from the subject on the left and right sides of the screen (center to center distance of 16.5 cm) and in the upper visual field. There were three types of face pairs that included unhappy–neutral, happy–neutral, and neutral–neutral (for a total of 36 different pairs). The target display included two dots (5 mm center to center). Each dot subtended 2 mm in diameter. The dot pair was oriented either horizontally or vertically and appeared at the location of the center of either the left or the right photograph in each face pair. The types of face pairs composed the three emotional conditions and were presented in separate blocks. The order of the block presentation was counterbalanced across the participants. Within the unhappy–neutral and happy–neutral blocks, the emotional face (unhappy or happy) was equally likely to be on the left or right side of the screen, the target was equally likely to appear at the location of the emotional or the neutral face, and the dot orientation was equally likely to be horizontal or vertical. These variables were fully counterbalanced within each block. In the neutral–neutral block, the target location and target orientation were counterbalanced.

Each trial began with a 500 ms fixation display followed by the face display for 500 ms, which was immediately replaced by the target display for 200 ms. Following the target display, the screen went blank for an intertrial interval of 1300 ms, after which, a new trial began. The patients and controls were required to determine the orientation of the dots by pressing one of two buttons (Fig. 1).

2.4.2. Calculations of the attentional bias scores

For the unhappy–neutral and happy–neutral conditions, the attentional bias scores were calculated by subtracting the mean