Shanghai Mental Health Center Scientific research project plan
(2018 Health Care Plan Edition)

Item Number: HKQ201813
Project Name: The efficacy of computerized cognitive remediation therapyand its molecular genetic mechanism
Project Category: Clinical Research
Starting and ending year: 2018.10.01—2021.03.31
Project leader: Hu Guoqin
Mobile number: 18817821826
Undertaking unit: Shanghai Huangpu District Mental Health Center
Date：2019.01.06

Study Protocol

In this study, a case-control study was conducted in which 154 patients with chronic schizophrenia were enrolled in our hospital. The patients were randomized into two groups using a random number table. The study group received antipsychotic drugs combined with computerized cognitive remediation therapy while the control group received psychiatric medication. No medical treatment, psychotherapy or physical therapy can be combined. BDNF and TRK-B genes were detected in both groups at baseline, and BDNF and TRK-B protein levels were measured in peripheral blood before and after treatment. Clinical symptoms and executive function evaluation were performed. Clinical evaluation included: positive and negative symptoms (PANSS), Clinical General Impression Scale (CGI), Side Effects Scale (TESS), and Extrapyramidal Side Effects Scale (RSESE) for assessment of psychotic symptoms and adverse events; cognitive function test (MCCB), The Webster's Memory Test (WMS), the Wechsler Smart Test (WAIS), the Wisconsin Card Sorting Test (WCST), and the Social Function Deficit Screening Scale (SDSS) for assessment of cognitive function and social function. To observe the correlation between CCRT and BDNF、TRK-B genes and proteins, exploring the molecular genetic mechanism of CCRT efficacy.

Statistical Analysis Plan

(1) Using t-test to analyze the functional dysfunction characteristics in patients with chronic schizophrenia;
(2) Using t-test to analyze the changes of executive dysfunction in patients with chronic schizophrenia before and after CCRT treatment;
(3) Detection of BDNF and its TRK-B receptor gene polymorphism using shesis software;
(4) Using t-test to analyze the changes of BDNF and its TRK-B protein expression levels before and after CCRT treatment;
(5) Correlation analysis was performed to investigate the correlation between changes in executive dysfunction and BDNF and TRK-B protein expression levels.

Results Information for Studies

（1）The scores of positive and negative symptoms (PANSS), Clinical General Impression Scale (CGI), Side Effects Scale (TESS), and Extrapyramidal Side Effects Scale (RSESE) for assessment of psychotic symptoms and adverse events; cognitive function test (MCCB), The Webster's Memory Test (WMS), the Wechsler Smart Test (WAIS), the Wisconsin Card Sorting Test (WCST), and the Social Function Deficit Screening Scale (SDSS) .

（2）The genotype of BDNF、TRK-B genes and the concentration of BDNF、TRK-B proteins.

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Informed consent

You will be invited to participate in a clinical study. This informed consent form provides you with information to help you decide whether to participate in this clinical study. Please read it carefully. If you have any questions, please ask the researcher responsible for the research. Your participation in this study is voluntary. This study has been reviewed by the ethics review committee of this research institution.

Research purposes: Among the cognitive disorders of chronic schizophrenia, the most reported is the executive dysfunction of the prefrontal lobe. There is increasing evidence that Computerized Cognitive Remediation Therapy (CCRT) has a significant improvement in the implementation of schizophrenia, but the specific mechanism is unknown. Therefore, this study plans to select 154 patients with chronic schizophrenia who were hospitalized for a long time. They were randomly divided into two groups. The study group received antipsychotic drugs combined with CCRT for 4 times/week for 45 minutes each time. The control group received antipsychotic drugs. For a total of 12 weeks. BDNF and TRK-B genes were detected in both groups at baseline, and BDNF and TRK-B protein levels were measured in peripheral blood before and after treatment. Clinical symptoms and executive function assessment were performed to observe CCRT and BDNF and TRK-B. The relevance of genes and their effects on downstream protein expression levels led to a molecular genetic mechanism for the efficacy of CCRT.

Research process: we will collect

1) Age 18-45 years old, Han nationality, male or female;

2) Comply with the American Diagnostic Criteria for Mental Disorder (DSM-V) diagnostic criteria for "schizophrenia";

3) The course of the disease and continued treatment with antipsychotic drugs for > 2 years, stable for at least one month;

4) PANSS < 70 points;

5) IQ>80;

6) Cultural, social and educational backgrounds are sufficient to understand informed consent and research content.

A total of 154 cases were collected and their demographic data and clinical data were evaluated. Each person will receive 5 ml of venous blood for biochemical testing. The relationship between BDNF gene polymorphism and chronic schizophrenia and clinical features will be analyzed based on the results.

The scales were measured before treatment and at the end of the 12th week of treatment, including:(1) Positive and Negative Symptom Scale (PANSS); (2) Clinical General Impression Scale (CGI); (3) Side Effects Scale (TESS); (4) Extrapyramidal Side Effects Scale (RSESE); (5) Cognitive Function Test (MCCB); (6) Wisconsin Card Sorting Test (WCST); (7) Webster's Memory Test (WMS); (8) Webster's Smart Test (WAIS); (9) Social Function Defect Screening Scale (SDSS).

If you agree to participate in this study, we will communicate with you or your family in detail, to inform you about the study, and to provide information about the disease, including the onset, family history, and previous visits. And have done some inspection results. We will

number each participant to create a medical record file. During the course of the study we need to collect some of your specimens, and a professional will take 5 ml of venous blood from your arm. In addition, if you need to participate in the study of drug intervention, we will take 5 ml of venous blood from your arm again on the 12th week after treatment.
Risk and discomfort:
Blood draw may have adverse reactions: 1 dizziness; 2 palpitation; 3 heart rate acceleration; 4 low blood pressure.
If you experience symptoms or conditions during your study, please contact your doctor to decide what to do.
Contact and phone number are as follows:
Unit contact phone
Shanghai Huangpu District Mental Health Center Hu Guoqin 02154010724
Shanghai Huangpu District Mental Health Center Shen Tao 02154010724
For you, communicating and talking with us may be psychologically uncomfortable. Your sample collection will be performed in strict accordance with the sterility requirements. Specimen collection may have some very small risks, including short-term pain, local bruising, a few people with mild dizziness, or extremely rare needle infections. All your information will be kept confidential.
Benefits: Provide the necessary advice for your treatment by testing your specimens, providing scientific evidence and useful information for genetic diagnosis, clinical treatment and new drug development of schizophrenia. For each selected person, we will give each person a transportation fee of RMB 50 per person. In addition, we will provide you with an assessment of olanzapine treatment and scale during the follow-up period.
As a research subject, you have the following responsibilities: to provide information about your medical history and current physical condition: Tell the research doctor about any discomfort that occurred during the study: Do not take restricted medications, food, etc.: Tell the study Whether the doctor himself has recently participated in other research or is currently participating in other research.
Privacy Issues: If you decide to participate in this study, your participation in the trial and the personal data in the trial are confidential. Responsible for research awareness and other researchers will use your medical information for research. This information may include your name, address, phone number, medical history, and information obtained during your research visit. Your blood sample will be identified by the study number number instead of your name. Information that identifies you will not be disclosed to members outside the research team unless you have permission. All research members and research sponsors are required to keep your identity confidential. Your files will be kept in a locked filing cabinet for researcher only. In order to ensure that the research is carried out in accordance with the regulations, if necessary, members of the government administration or the ethics review committee can check your personal data in the research unit as required. When the results of this study are published, you will not disclose any of your personal information.
You may choose not to participate in this study, or notify the investigator to withdraw from the study at any time, your data will not be included in the research results, and any medical treatment and benefits will not be affected.
If you need additional treatment, or if you do not follow the research plan, or if there is a research-related injury or any other reason, the study physician may terminate your participation in the study.
You can keep track of the information and research progress related to this research. If you have any questions related to this research, or if you have any discomfort or injury during the research, please contact Hu Guoqin, the main researcher, at 18818821826; For questions about the participants' rights and interests in this study, you can contact Shen Tao__ at _54010724.