Study on the Treatment of Bipolar Disorders Group Based on Neuroregulatory Techniques

Fengle Dong
Haidian International Highschool, Beijing, China
1607081019@stu.sqxy.edu.cn

Abstract. Bipolar disorder is a common mental illness in the 21st century. Bipolar disorder has caused great harm to patients due to its sudden, incurable and huge negative impact on patients' lives, such as inability to work and study normally and inability to take care of basic daily life. In the statistics, the number of suicides caused by bipolar disorder has reached 3% of the total patients, becoming a problem that cannot be ignored in today's society. At present, the treatment of bipolar disorder mainly relies on drug therapy and psychological counseling. Medication refers to the use of antidepressant drugs such as fluoxetine to treat depressive mood, while the use of depressant drugs to treat mania. While enjoying the effects of the drug, the patient's dependence on the drug cannot be ignored. In addition, the limitations of prescribing separate drugs for depression and mania still need to be addressed. Patients need a faster acting, more convenient, more integrated control of the treatment equipment for the overall control of bipolar disorder patients. BCI, as a new technology, has the ability to directly regulate brain activity and then affect human behavior. In the current database of papers, there are very few articles using BCI to treat bipolar disorder, or even other psychiatric disorders. By exploring the function of BMI, this paper hopes to understand the mechanism behind bipolar disorder and explore the possibility of using BMI to treat bipolar disorder.

Keywords: Bipolar disorder, mania, serotonin, brain-machine interface, electrodes.

1. Introduction

Bipolar disorders are a group of chronic but severe psychiatric disorders that includes bipolar I disorder and bipolar II disorder. Bipolar I disorder is defined by the presence of a syndromal manic episode, and bipolar II is defined by the presence of a symdromal hypomanic episode and a major depressive episode [1]. When mania take place, the bipolar disorder patient will be in euphoria, increse speech activity, be hightly excited, lack of sleep and be more acute in cognition. When depressive mood take place, the patient will drown into the bad mood, lack of appetite, avoid social interaction, even attempt to suicide. This recurrent episodes of elevated mood and depression, together with changes in activity levels caused by the bipolar disorder strongly affect the patient’s normal state of life.

As a intensive mental disease, bipolar disorders always cause their patients to lose ten to twenty years of life potential. Previous genetic studies have shown that 70% to 80% of bipolar disorder is related to genetic factors. Due to the complexity of bidirectional emotional disorders makes it difficult to establish animal disease models. Currently, most scientists seek to use the full range Genome Association Analysis wide association study (GWAS) method, utilizing large-scale comparative study of populations, analyzing the impact of common mutations on bipolar disorder, but only common mutations have been found can explain 100% to 20% of genetic factors. In addition, international research has also utilized whole exome sequencing technology to explore the rare pathogenic factors of bipolar disorder are mostly based on European populations or regional isolated populations, lack of understanding of the impact of rare mutations on bipolar disorder in the Chinese population [2].

The cause of bipolar disorder has not been fully determined, and the medical community generally believes that biological genetic factors and environmental factors lead to the production of this mental illness [3]. The two interact, leading to further progression of the disease. From an environmental perspective, negative social behaviors such as divorce, separation, and bankruptcy may be triggers for bipolar disorder. Due to the lack of unity between the social situation and their expectations, there is a gap in their emotional regulations. Adverse life events and environmental stress events can trigger the onset of bipolar disorder, such as unemployment, heartbreak, poor family relationships, and prolonged and highly stressful living conditions. Genetic factors may lead to a susceptibility trait in the onset of bipolar disorder, and people with this susceptibility trait will develop diseases under certain environmental factors [3]. At present, modification of the living environment is considered to be a more feasible way to prevent bipolar disorder than biological therapy. When the environment gradually adjusted, biologic treatment and prevention of bipolar disorder became the main topic.

Neurotransmitters in the brain control people's behavior because they help carry chemical information from presynapses to postsynapses. In the treatment of bipolar disorder, adjusting the amount of neurotransmitter release is a topic worthy of discussion. Serotonin is a strong vasoconstrictor and smooth muscle contraction stimulator that exists specifically in the cerebral cortex and synapses. Serotonin produces pleasurable feelings and many antidepressant drugs, such as fluoxetine, increase Serotonin levels to achieve their antidepressant effects. Fluoxetine, as a reuptake inhibitor of serotonin, can effectively block the reuptake of 5-HT in the presynaptic membrane, thereby increasing the level and effect of 5-HT and exerting an antidepressant effect. However, there are certain shortcomings in using fluoxetine alone for treatment [4]. Central serotonin is synthesized in the brain, cannot cross the blood-brain barrier, and is metabolized in mitochondria. Serotonin deficiency is a diathesis marker for bipolar disorder. In addition to this there are neurotransmitters such as dopamine, norepinephrine, glutamate, acetylcholine, which may cause the brain to be less active and less stimulated, ultimately causing bipolar patients to switch between manic and depressive states. Today's treatment of bipolar disorder is largely dependent on medication. Lithium, for example, is commonly used to stabilize the mood of bipolar I patients. Lithium salt is an important medication for the treatment of manic patients with bipolar disorder, and it is effective for treating manic symptoms. The preventive effect of depression is very good. The main lithium salt used in clinical practice is lithium carbonate. from the therapeutic dose of lithium salt is very close to the toxic dose, so lithium salt poses a significant risk when used as the main drug for treating bipolar disorder [5]. The rest of the drugs, whether for manic states or antidepressants, aim to regulate the release of neurotransmitters in the brain. If we could visualize the activity of specific brain regions (the types and amounts of neurotransmitters released) and directly control the level of release of certain neurotransmitters, the treatment of bipolar disorder would be a leap forward.

2. Related Works

Brain-computer interface is a kind of human-computer interaction technology, which basically establishes the direct connection between the animal brain and the external device, and realizes the information exchange between the brain and the device. We can insert wires into a person's head, through the skull, directly to the brain; It can also connect with external transducers to reach electronic signals in certain areas of the brain and decode them to external actuators to form visual and easier to understand images. "The earliest application field in the future is definitely healthcare," said the author of an article. The application prospects of invasive brain computer interfaces in the medical field are broad. On the one hand, they can assist patients with stroke and ALS who have limited mobility to control peripheral devices through EEG signals from the motor cortex of the brain, improving their quality of life; On the other hand, it is also possible to release drugs stored on sensor scaffolds in a timely manner through real-time carrier emotional signals, helping assist patients with mental illnesses such as depression and bipolar disorder in controlling impulsive emotions that may occur irregularly [6]. The term brain-computer interface first appeared in a 1973 article from the University of California; The author of this article, Jacques Vidal, first proposed the concept of brain-computer interface, defining it as a system that bypassed the human muscles and limbs and the peripheral nervous system, and reached the direct communication mechanism between the human brain and the outside world [7]. Jacques Vidal used images from a screen to try to stimulate subjects' VEPs, or visual evoked potentials, and tried to capture this weak visual evoked potentials with brain-based brain-computer interface devices (non-invasive brain-computer interface EEG). Since this article, people have continued to streamline the equipment that captures electrical stimulation of the brain, and improve the accuracy of electrical signal capture.

Today, there are two main types of brain-computer interfaces. The first type is non-invasive brain-computer interfaces, most of which are called EEG. The EEG is a "cap" worn on the human head that contains a large number of EEG collectors, which collect electrical stimulation or certain signals from the brain around the scalp. We do not need to implant electrodes into the brain to collect a large number of brain waves and electrical brain stimulation. However, due to the problem of loose adhesion between the dry electrode and the scalp, the collected signal is unstable, and the signal noise generated by the friction between the electrode and the skin has a significant impact. Currently, research in this area focuses on how to make the electrode tightly adhere to the scalp, stabilize the signal acquisition channel, and improve the quality of signal acquisition [8]. These EEG signals collected by EEG are susceptible to external factors, such as the surrounding magnetic field, other people's brain signals, etc. Even some behaviors of the subjects can affect the collection of electrical signals in the brain, such as blinking, breathing, and racing heart. In order to collect more accurate data about the human brain, scientists have developed invasive brain-computer interfaces, which insert electrodes directly into designated areas of the brain (of course, some damage to the skull is required to open the window for the electrodes to be inserted). Invasive brain-computer interfaces can accurately capture electrical signals from the brain and efficiently decode them into the actuator. Inevitably, due to its involvement in craniotomy, implantation of probes into the gray matter, and other operations, it inevitably leads to the necrosis of some neuronal cells, which has certain harmfulness. Therefore, ethical issues often arise when implanting probes into human subjects. In addition, although implantable electrodes can collect the highest quality EEG signals, over time, the accumulation of scar tissue around them can easily lead to a weakened or even no signal being collected [9]. In between is eCoG, where electrodes are implanted into the cortex of the brain to capture electrical signals. eCoG's accuracy and vulnerability fall somewhere between invasive and non-invasive BCI.

In the case of bipolar disorder, invasive brain-computer interfaces may be more suitable for treating the condition. This is because invasive BCI not only enables the capture of weak electrical signals in the brain but also allows for implantation in specific brain regions and subsequent stimulation through electrodes to regulate neural activity. Brain-computer interfaces can be classified into sensory (input) and motor (output) types, similar to nerve classification. Sensory BCI are primarily used for capturing and decoding brain electrical signals, while motor BCI are employed to stimulate targeted brain areas for achieving control over bodily functions. Considering the significant role of biological factors, particularly neurotransmitters, in bipolar disorder pathogenesis; if invasive BCI could be directly implanted into regions involved in neurotransmitter release and modulate their release patterns artificially, it might offer a means of controlling bipolar disorder.

Serotonin is a good example of a brain-computer interface that regulates neurotransmitter levels in the brain to control the depressive side of bipolar disorder. As mentioned above, serotonin produces pleasurable feelings, and central serotonin synthesized in the brain cannot cross the blood-brain barrier, and is metabolized in mitochondria. Serotonin deficiency is a diathesis marker for bipolar disorder. Serotonin is found in about two per cent of the brain and is mostly stored in raphe nuclei in the hindbrain. Different types of serotonin receptors are widely located on different types of neurons in the brain, mainly divided into 5-HT1A receptor, 5-HT2A receptor and 5-HT2C receptor. 5-HT1A receptors are concentrated on the synaptic membranes of the serotonergic neurons themselves, on glutamate neurons in the frontal/parietal cortex and hippocampus, and on dopaminergic/noradrenergic/acetylcholinergic neurons in the striatum and midbrain. When activated, it inhibits the release of serotonin itself. 5-HT2A receptors are mainly located on glutamate neurons in the frontal/parietal cortex and hippocampus, and 5-HT2C receptors are mainly located on dopaminergic neurons and noradrenergic neurons in the striatum and hypothalamus [10]. Once we know where the serotonin receptor is, we can implant the electrode at the receptor site (usually an area with a concentration of receptor sites, because there will be not one or fewer but thousands of receptor sites) and provide electrical stimulation to the area of the brain where the electrode is implanted. The transmission of neurotransmitters in the brain depends on the action potential of the presynaptic nerve, which means that sodium channels on the axon open, allowing sodium ions to enter the axon and causing a change in the potential difference between the axon and the axon-a reaction called depolarization. When the potential peaks, potassium channels also open, allowing potassium to move from inside the axon into regions outside the axon-a reaction called epolarization. This causes the axon external and axon external and internal potential differences to return to their original state. Finally, sodium and potassium ions swap positions and wait for the next action potential; The information is then relayed by this circular relay of action potentials to the nerves below, releasing specific neurotransmitters such as serotonin. If we can use the electrode implanted at the serotonin release site to promote the action potential of the nerve to achieve the purpose of releasing more serotonin, the arousal of pleasant emotions in humans will become more frequent, and then effectively control the depressive state of bipolar disorder.

For mania, we can reduce the release of neurotransmitters such as serotonin to achieve the purpose of control. The authors speculate that the length of the refractory period between nerve impulses can be controlled, or the neuroplasticity of specific brain regions can be adjusted to reduce the level of certain neurotransmitters released at specific times. But based on a review of current technology and the possibility of further unnecessary damage to the brain, these ideas are currently speculative - and it seems more feasible to control the release of some inhibitory neurotransmitters, such as GABA, in order to suppress mania in patients. Gamma-aminobutyric acid (GABA) is the most important inhibitory neurotransmitter in the nervous system of mammals, crustaceans, and insects.

In animals, GABA is almost exclusively present in nervous tissue, with the amount in brain tissue being about 0.1-0.6mg/g. Studies have shown that 30%-40% of central neurons use GABA as an inhibitory neurotransmitter to regulate brain activity [11]. Some experts have proposed the release of non-neuronal cell derived GABA vesicles as the source of GABA activity. The amount of GABA released into the extracellular form constitutes the GABA activity state and regulates synaptic transmission and cognitive function by inducing tonic GABA currents. Due to the variable equilibrium potential of the local intracellular chloride ion (Cl^-) concentration [Cl^-] and Cl^- (E_{Cl}), tonic GABA currents can hyperpolarize or depolarize the membrane potential of the cell body. GABA can bind and activate anti-anxiety brain receptors, and then cooperate with other substances to prevent anxiety-related information from reaching the brain indicator center, thereby fundamentally calming nerves and relieving anxiety [12]. Studies have shown that after taking 100mg of GABA orally for 60 minutes, GABA significantly increased alpha waves and reduced beta waves in the brain compared with the control group, indicating that GABA can promote relaxation and reduce anxiety [13]. We can regulate brain activity and anxiety by implanting electrodes in the brain region where GABA receptors are located and stimulating the brain to release GABA in a similar way to regulating serotonin.

The use of brain-computer interface control to treat bipolar disorder was inspired by successful experiments using brain-computer interface to treat depression. In 2023, Shanghai Ruijin Hospital successfully used deep brain stimulation (DBS) controlled by brain computer interface for the first time to regulate nerves; The first 26 patients had a brain pacemaker implanted in the heart, using brain-computer interface technology to manipulate two electrodes implanted in the brain to stimulate brain nuclei that regulate emotions. Results Patients treated with DBS improved by more than 60% on average, and some people have begun to report their positive recovery after treatment [14]. At present, the treatment of bipolar disorder is limited to drug therapy and emotional supervision, and there are few articles on BCI therapy for bipolar disorder, the use of BCI therapy has considerable prospects.

3. Discussion

The current treatment for bipolar disorder is very limited, roughly divided into two types of treatment: medication and psychological counseling. The way of drug treatment has been mentioned above, mainly divided into drugs to control mania mood and depression mood. Most drugs can only control the different ranges of mood fluctuation in bipolar disorder separately, not the fluctuation of mood as a whole. Devices that can control mania or depression at any time according to the patient's condition through overall control of the brain mood have not been mentioned much in the current medical devices. As a new type of device, brain-computer interface can regulate the different emotional states of patients with bipolar disorder. If the electrodes were placed at sites that regulate the release of different neurotransmitters, patients could activate different electrodes depending on whether they were depressed or mania. In this way, patients themselves can be targeted to regulate their own bipolar disorder, to minimize its impact on normal life. In addition, the limitations of the drug itself in the field of treatment cannot be ignored. First, the drugs themselves are toxic and harmful to the body. Such as fluoxetine for depression, bipolar disorder and bulimia nervosa; Although the side effects are relatively low in the current observation, they can still cause insomnia, nausea, headache, increased anxiety, nervousness, and tremors in the early days of the drug. If the drug is used for a long time, the appetite and sexual function of the drug taker will be reduced. Three percent of those who took the drug experienced a rash, while one percent experienced a manic mood. For people with bipolar disorder who are allergic to fluoxetine, fluoxetine is not appropriate to regulate their condition. If brain-computer interfaces are used to manage the condition in people with bipolar disorder, these concerns will be dispelled. The use of BCI can minimize the use of specific neurotransmitter sites in the brain region of the drug, and achieve the purpose of rapid control of the disease. Also, because BCI uses electrodes to self-regulate brain activity and human emotions, the risk of drug addiction is minimized. In summary, brain-computer interface, as a device that can rapidly regulate bipolar disorder, has a relatively fast effective speed and small side effects, and has a broad development prospect.

As a new technology, brain-computer interface brings many possibilities for human beings. One of the closest to society is the use of brain-computer interfaces to treat psychiatric disorders. The causes of many mental illnesses have not been fully understood until now; If we could use a brain-computer interface to fully reveal the activity of a patient's brain and stimulate treatment with electrodes, more than bipolar disorder could be erased from human history.

As a new kind of technical equipment, brain-computer interface still has many shortcomings that need to be solved. First, the safety and effectiveness of BCI cannot be met simultaneously. As mentioned above, brain computer interfaces are mainly divided into two types, one is non-invasive brain computer interface, and the other is invasive brain computer interface. The advantages and disadvantages of the two types of BCI have been mentioned above. Non-invasive BCI has less damage to the brain, but little function of direct regulation of the brain and detection of electrical signals in specific brain areas. Invasive BCI is very accurate for the exploration of electronic signals in specific areas of the brain, but the destruction of the skull will directly expose the brain tissue, and if it is infected by viruses or bacteria, it will directly inflame and supersurate, causing irreversible effects on many human functions (such as movement, language, etc.). This paper hypothesized that BCI has not been widely used in the treatment of psychiatric diseases because it is as safe and effective as a fish and a bear's paw. In addition, current scientists do not fully understand the number of electrodes that need to be inserted into specific brain regions to collect electrical signals from the brain (or to provide effective stimulation to promote an increase in the release of certain neurotransmitters). Testing with mice or primates is ultimately different from humans, and the question is still being explored.

The most widespread and important concern about BCI in society today is ethical. Brain-computer interfaces, devices that can be inserted directly into specific brain regions to control certain behaviors in the human body, can be directly used to manipulate human movements and even thoughts. The medical community will not be able to use BCI on a large scale until the complete safety of BCI as a therapeutic device for the human body is ensured. As the intermediary between people and the objective world, brain-computer interface is not impeccable, but also has the risk of being invaded or even taken over by opponents, which objectively increases the complexity and uncertainty of people's decision-making and increases the risk of decision-making. Bci has great potential but also great uncertainty, and it may need feasible ethical support and a lot of practice before BCI can be used in large numbers.

4. Conclusion

As a new technology, brain-computer interface (BCI) has important application value in the treatment of mental diseases such as bipolar disorder. Bci provides a new therapeutic approach - we can directly use BCI to monitor the functional evolution of the patient's brain, and even directly insert electrodes into specific brain regions to mimic action potentials, improve the release of certain neurotransmitters (such as GABA and serotonin) by increasing the action potential and the plasticity of the brain nerve, and directly control the brain. Achieve direct overall regulation of two emotions in bipolar disorder (mania and depression). This new treatment not only overcomes the limitations of drug therapy and dependence on drugs, but also improves the efficiency of treating this disease. But while the possibility of a cure for bipolar disorder has greatly improved, the risks of brain infections and the ethical issues raised by BCS still need to be addressed. In addition, the technical difficulties of the brain-computer interface make this type of treatment not efficient enough to completely replace medication and psychological therapy at present. All in all, brain-computer interfaces have great potential in the treatment of bipolar disorder. In the near future, brain-computer interfaces will be more widely used not only in the treatment of bipolar disorder, but also in the treatment of many mental illnesses, bringing a bright future for patients.

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