Successful Treatment of Psychiatric Symptoms after Traumatic Brain Injury Using Deep Brain Stimulation to the Anterior Limb of Internal Capsule-Nucleus Accumbens

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Psychiatric symptoms are common after traumatic brain injury (TBI), and some patients have poor drug therapeutic efficacy. We report a successfully treated case of psychiatric symptoms after TBI using deep brain stimulation (DBS) to the anterior limb of internal capsule (ALIC)-nucleus accumbens (NAC) in a 76-year-old woman. The patient suffered from auditory hallucination, mood changes, and insomnia caused by TBI. Psychological test assessment showed the scores of Hamilton Anxiety Scale, Hamilton Depression Scale and Positive and Negative Syndrome Scale were 30, 35, and 96 respectively. Head magnetic resonance imaging scan showed right temporal lobe encephalomalacia. Head magnetic resonance spectroscopy (MRS) showed bilateral basal ganglia choline increased relatively. After DBS to the ALIC-NAC, the target parameters were adjusted. The psychiatric symptoms were completely improved and the result of head MRS was normal in the end. The current report declares that DBS is reversible, adjustable and safe in the treatment of psychiatric symptoms caused by TBI. DBS to the ALIC-NAC should be considered as a possible treatment choice once a patient showed psychiatric symptoms after TBI.

KEY WORDS: Deep brain stimulation; Traumatic brain injury; Psychiatry; Internal capsule; Nucleus accumbens.

INTRODUCTION

The mechanism of psychiatric symptoms after traumatic brain injury (TBI) is complicated [1]. The function of the brain tissue will be reduced or disappear due to direct organic damage [2]. So many factors such as brain edema, intracranial hypertension and cerebral vasospasm will result in brain ischemia and hypoxia after TBI [3]. Especially, the temporal lobe, frontal lobe, hippocampus, basal ganglion and limbic system which are related to mental activity are more sensitive to ischemia and hypoxia [4]. Their function and activities decrease gradually, and a series of psychiatric symptoms occur. Some researchers declared that antipsychotic drugs offered no satisfactory longterm benefit [5], which brought serious risks and burdens to society and families. Deep brain stimulation (DBS) has been reported repeatedly for refractory psychiatric treatment, such as attention deficit hyperactivity disorder [6] and obsessive-compulsive disorder [7]. However, there were no reports of DBS treatment on psychiatric symptoms after TBI. This study was the first time attempting to treat psychiatric symptoms after TBI using DBS to the anterior limb of internal capsule (ALIC)-nucleus accumbens (NAC). After 18 months of follow-up, the patients’ psychiatric symptoms had been alleviated significantly.
**CASE**

A 76-year-old retired woman was sent to the local hospital after falling from a height of about 2 meters on January 15, 2015. The head computerized tomography showed subarachnoid hemorrhage, cerebral falx hernia and fracture of the occipital bone (Fig. 1). She suffered from severe psychiatric symptoms during hospitalization, such as auditory hallucination, insomnia, anxiety, poor mood and suicidal behavior. She always heard strange voice of men and women, felt her inner thoughts could be expressed by someone else in her ears. Wechsler Adult Intelligence Scale-Revised (China) was 104, and Minimum Mental State Examination was 29. She was referred to our hospital after receiving numerous antipsychotic treatments (olanzapine 5 − 15 mg/d + sertraline 50 − 100 mg/d, ×3 month; quetiapine 50 mg − 0.4 g/d + citalopram 5 − 20 mg/d, ×3 month; aripiprazole 5 − 15 mg/d + mirtazapine 7.5 − 15 mg/d, ×2 month; risperidone 1 − 4 mg/d, ×2 month; amisulpride 0.1 − 0.4 mg/d, ×2 month) without any long-lasting relief of symptoms for 1 year. The patient was informed of the risks and benefits of DBS and underwent extensive multidisciplinary evaluation before surgery to ensure her suitability and compatibility for the treatment. The presurgery scores of the Hamilton Anxiety Scale (HAMA) [8], Hamilton Depression Scale (HAMD) [9] and Positive and Negative Syndrome Scale (PANSS) [10] were 30, 35, and 96 respectively (Table 1). Head magnetic resonance imaging showed encephalomalacia at right temporal lobe (Fig. 2A). Head magnetic resonance spectroscopy (MRS) showed bilateral basal ganglia choline (Cho) level increased relatively (Fig. 3A, 3B).

DBS electrodes (L302; PinChi, Beijing, China) were implanted into ALIC and NAc, each with 4 contact points 3 mm long and separated from adjacent contacts by 4 mm. Target coordinates for the electrode tip were 7 mm lateral

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**Table 1. Patient characteristics and stimulation settings**

| Time                  | Stimulator settings | Left                | Right               | HAMA | HAMD | PANSS |
|-----------------------|---------------------|---------------------|---------------------|------|------|-------|
| Preoperative          |                     |                     |                     |      |      |       |
| 1 month               | Points 1 (NAc)      | 240 μs, 150 Hz, 2.5 V| 240 μs, 150 Hz, 2.5 V| 30   | 35   | 96    |
| Postoperative 3 month | Points 3 (ALIC)     | 240 μs, 150 Hz, 2.5 V| 240 μs, 150 Hz, 2.5 V|      |      |       |
| 6 month               | Points 1            | 240 μs, 160 Hz, 3.0 V| 240 μs, 160 Hz, 3.0 V| 11   | 10   | 40    |
| Postoperative 8 month | Points 1            | 60 μs, 90 Hz, 1.0 V   | 60 μs, 90 Hz, 1.0 V   | 15   | 16   | 36    |
| Postoperative 12 month| Points 3            | 240 μs, 160 Hz, 2.5 V| 240 μs, 160 Hz, 2.5 V| 7    | 7    | 34    |

NAc, nucleus accumbens; ALIC, anterior limb of internal capsule; HAMA, Hamilton Anxiety Scale; HAMD, Hamilton Depression Scale; PANSS, Positive and Negative Syndrome Scale.
to the AC/PC line, 3 mm anterior to the anterior border of the anterior commissure, and 4 mm inferior to the intercommissural line, with the trajectory of implantation through the ALIC (Fig. 2B). Stimulation contacts were shown in Figure 2C. Stimulation parameters of contact points 1 and 3 were set 1 month after operation, with a pulse width of 240 μs, a frequency of 150 Hz, and a voltage of 2.5 V (Table 1). The patient still had auditory hallucination 6 months after operation, with improved mood and no suicidal thoughts. The scores of HAMA, HAMD,
and PANSS were 11, 10 and 40 respectively. The parameters of the contact point 1 were adjusted to 240 μs, 160 Hz and 3.0 V for considering that she still had auditory hallucination. Unfortunately, the symptom of auditory hallucination went worse, so the contact point 1 was given down to 60 μs, 90 Hz and 1.0 V. The auditory hallucination was alleviated, but anxiety and depression were aggravated 12 months after operation. The scores of HAMA, HAMD, and PANSS were 15, 16, and 36 respectively. Therefore, the parameters of the contact point 3 were adjusted to 240 μs, 160 Hz and 2.5 V. The patient’s condition was stable 18 months after operation. All the psychiatric symptoms were improved, including auditory hallucination, anxiety, and depression. The scores of HAMA, HAMD, and PANSS were 7, 7 and 34 respectively. Head MRS showed levels of Cho, creatine (Cr), Cr2 and N-acetyl aspartate were normal (Fig. 3C, 3D).

This study was approved by the ethics committee of Brain Hospital of Hunan Province (NO. K2017012). A written informed consent was obtained from the patients for the publication of this case report.

DISCUSSION

The patient suffered from auditory hallucination, insomnia, anxiety, poor mood and suicidal behavior after TBI. She tried a variety of antipsychotic drugs but they didn’t work, so the DBS operation was adopted. Shin et al. [11] declared DBS could ameliorate motor, cognitive and emotional disorders after TBI, but they didn’t discuss how to choose the target if psychiatric symptoms occurred. The patient had hallucination and emotional changes. Mikell et al. [12] considered that chronic, high-frequency electrical stimulation to the hippocampus or NAc may improve positive symptoms of schizophrenia via stabilizing the dopamine release in the striatum. The human NAc locates among the caudate nucleus, ventral side of the forelimb of the internal capsule and uncinate fasciculus. The NAc and the olfactory tubercle collectively form the ventral striatum, and it’s also a part of the basal nucleus. We performed a head MRS scan to the patient and found elevated choline in the bilateral basal ganglia. It has been reported that abnormal choline metabolism was associated with illusion in schizophrenia; dopamine and choline may affect each other in the pathogenesis of mental disorders [13]. The M receptor agonists could induce dopamine release [14]. It can be explained that the abnormal choline metabolism of the NAc and the ALIC may be related to the mental abnormality of the patient.

Right now, more and more DBS operations are targeting ALIC-NAc in mental disorders, such as addiction, obsessive and depression [15-17]. Scholars evaluated the effects of DBS in the NAc core on the extracellular concentration of monoaminergic neurotransmitters in the medial prefrontal cortex and orbitofrontal cortex, and found rapid increases in the release of dopamine, serotonin and noradrenaline [18]. Thus we assumed perhaps stimulation to ALIC-NAc will improve hallucinations. This patient’s mood symptoms were more serious than psychiatric symptoms, so the ALIC and NAc were selected to be the DBS stimulation targets.

In this case, the patient had both emotional symptoms and hallucination, so the settings of target stimulation parameters were of great importance. Rauch et al. [19] believed that low-frequency stimulation of the nucleus played a similar role in activating the nucleus, while high-frequency stimulation above 100 Hz inhibited or blockaded the related nerve conduction pathways. Therefore, we used high frequency to stimulate the ALIC and NAc at the very beginning and found that the patient’s mood improved but the auditory hallucination still existed. The stimulation frequency had to be modified. The final results demonstrated that the frequency above 150 Hz aggravated auditory hallucination, while the frequency below 100 Hz improved it. Auditory hallucination improvement was mainly related to adjusting the stimulation frequency to NAc, and emotional relief required high-frequency stimulation to the ALIC. Only one patient was included, which was the shortcoming of this study. Moreover, the patient is too old to carry out more examinations. The exact mechanism of TBI-induced psychiatric symptoms remains unclear and requires further study.

In conclusion, we declare that DBS is reversible, adjustable and safe in the treatment of TBI-induced psychiatric symptoms. DBS to the ALIC-NAc should be considered as a possible treatment choice once a patient showed psychiatric symptoms after TBI.

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### Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

### Author Contributions

Design: Liang Li. Data collection: Ping Yang. Operation: Weiping Kuang, Hongxing Huang. Postoperative follow-up: Yong Zhu, Xiaofeng Chen. Writing—original draft: Bin Zhou. Writing—review & editing: Ping Yang.

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