A Deep Brain Stimulation System with Low Power Consumption and Wide Output Range

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Abstract— Deep brain stimulation (DBS) therapy has been widely used in clinical practice for the treatment of neurological diseases and has achieved significant therapeutic effect. In this paper, aiming at the social problem of drug addiction, we design an electrical stimulation system which can be used in animal experiments, carry out the memory extinction experiment of addiction in rats, and explore the effective electrical stimulation parameters. The DBS system consists of a rechargeable battery and a PCB stimulation circuit composed of discrete devices. In animal experiments, the power consumption of the circuit is 0.36mW in the electrical stimulation stage. Theoretically, the circuit can work continuously for more than 100 days with a 3.7V 250mAh lithium battery. The stimulation circuit is highly programmable and the output stimulation current ranges from 100μA to 5000μA with a 20μA current resolution.

I. INTRODUCTION

Nerve electrical stimulation is to stimulate specific nerve targets by implanting a certain frequency and amplitude of electrical stimulation signal into the body to regulate the activity of neurons to achieve the purpose of treatment. The device that uses electrical signals to regulate the nervous system is called neural electrical stimulator. According to the different stimulation regions, nerve stimulators can be divided into the following categories: spinal cord stimulation (SCS), deep brain stimulation (DBS), sacral nerve stimulation (SNS), vagus nerve stimulation (VNS) and cochlear implant [1].

Compared with the traditional drug therapy or surgical damage therapy, DBS therapy has the advantages of accuracy and less side effects, and can bring less pain to patients [2]. The core of the DBS therapy is the stimulation output circuit. At present, the energy optimization of the stimulation output circuit is very important, which will determine the working time of the stimulation system and affect the heat emission during stimulation. On the other hand, the stimulation parameters for DBS are quite different [3][4][5][6][7], so it is necessary to adjust the parameters flexibly to find the most suitable parameters.

In order to solve the problem of energy consumption and uncertain output stimulation parameters, this paper presents a DBS system for the treatment of drug addiction in rats. This system includes rechargeable battery and stimulation circuit,

which achieves low energy consumption to meet the needs of long-term use in animal experiments, and the highly programmable stimulation circuit can meet the stimulation needs of different currents and frequencies in animal experiments.

This paper also introduces the experiment of electrical nerve stimulation in rats, which is designed and completed in cooperation with National Institute on Drug Dependence, Peking University. All experimental operations on experimental animals comply with the ethics regulations of experimental animals and follow the regulations promulgated by the National and Peking University Institutional Animal Care and Use Committee. The DBS system designed in this paper is used to treat drug addiction in rats. The stimulation regions were substantial nigra pars recitulata (SNr) and dorsal raphe. The relapse rate of experimental rats with different stimulation regions and frequencies was tested and compared with other work. The stimulation parameters for electrical nerve stimulation in rats were explored.

This paper is organized as follows: Section II introduces the design constraints of DBS system in order to meet the needs of animal experiments. Section III presents the stimulation circuit design and the circuit improvement to meet the different needs of animal experiments. Section IV introduces the process and results of the experiments on the treatment of drug addiction in rats by using the designed DBS system. Section V generalizes the current design and experiment results of DBS treatment for rats.

II. DESIGN CONSIDERATIONS AND CONSTRAINTS

A. Power Consumption

It can be seen from Fig. 3 that the DBS device needs to work for 8 days in animal experiments to treat rats with DBS. If the DBS device is implanted into the human body, the non rechargeable battery needs to supply power for several years. In [8], the rechargeable battery needs to be able to last for four weeks.

Low energy consumption can prolong the working life of DBS equipment. For the device with rechargeable battery, the charging frequency can be reduced, which is more convenient in animal experiments and clinical applications, and brings less pain to patients

B. Wide Range of Stimulation Parameters

It can be seen from Table I that in the previous study of DBS treatment in animal experiments, the stimulation parameters used are greatly different due to different stimulation regions and the performance of stimulators.

Because the research on DBS parameters is not clear, and the stimulation parameters required for stimulating different

brain regions are also different, the DBS system proposed in this paper needs to provide a wide range of stimulation parameters to adapt to different needs.

TABLE I.   STIMULATION PARAMETERS FOR DBS ON RATS

Authors	Current[μA]	Pulse width[μs]	Frequency[Hz]
[3]	200	500	10/100
[4]	0-150	100	130
[5]	50-200	N/A	20/160
[6]	100-200k	100	20/130
[7]	150	100	13/130
This work	100-150	70-100	20/130

III. DESIGN OF STIMULATION CIRCUIT

The stimulation circuit consists of the following modules: MCU, switch control array, current detection amplifier, DC-DC converter, as is shown in Fig. 1.

The MCU controls the switch array to change the direction of stimulating current. The ADC in the MCU receives the stimulating current information amplified by the current detection amplifier. After being processed by MCU, the output voltage of DC-DC converter is controlled by the DAC in the MCU to ensure the stability of stimulating current. The output stimulating current is sampled by current detection amplifier, amplified and transmitted to the MCU. The output voltage of DCDC is adjusted by MCU control signal.The pulse width, interval delay and pulse cycle timing of stimulation are controlled by timer in the MCU. The start and end timing control of stimulation is completed by real-time clock in the MCU.
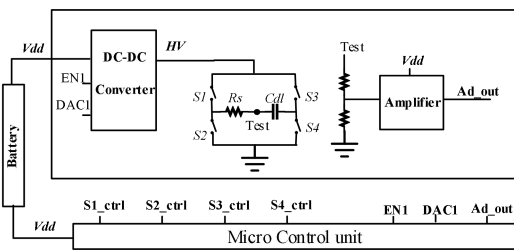

Figure 1.   Block diagram of stimulation circuit.

Fig. 2 shows the PCB stimulation circuit composed of discrete devices. Depending on the stimulation current signal collected by the current detection amplifier, the MCU can accurately control the output voltage of the DC-DC converter to ensure stable output stimulation current and avoid power consumption caused by high output voltage of DC-DC converter. In the typical case of DBS treatment of addiction in rats, the current consumed by rechargeable lithium battery was 98μA with a 250mAh rechargeable lithium battery. Therefore, in an ideal situation, it can work for more than 100 days after fully charged, which is enough to meet the needs of animal

experiments, and it is more convenient in the clinical situation, bringing less pain to patients.

Table II shows the adjustable range of output current amplitude, frequency and pulse width. The wide range of stimulation parameters enables the stimulation circuit proposed in this paper to meet the various needs of different animal experiments and different stimulation regions.
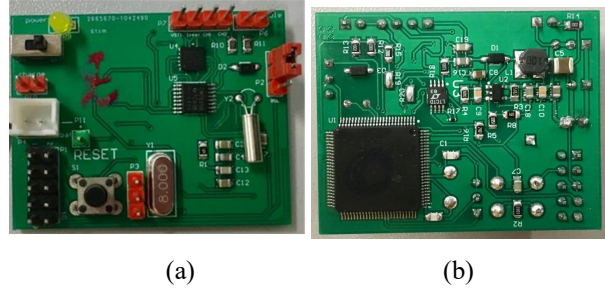

(a)   (b)

Figure 2.   Front (a) and back (b) of the print circuit board.

TABLE II.   ADJUSTABLE RANGE OF STIMULATION PARAMETERS

	Current[μA]	Pulse width[μs]	Frequency[Hz]
This work	100-5000	60-300	0-1000

IV. ANIMAL EXPERIMENT PROCESS AND RESULTS

In order to study the effect of SNr and dorsal raphe in addictive memory and test the function of DBS system, the experiment of electrical nerve stimulation in rats was conducted in cooperation with National Institute on Drug Dependence, Peking University. In this experiment, the stimulation circuit proposed in this article was chosen to explore suitable stimulation parameters in a wide range, while at the same time minimizing power consumption to reduce the number of charging times, and to avoid additional impacts on experimental animals caused by battery replacement.

This experiment mainly studied the change of Conditioned Place Preference (CPP) score [9] and relapse of addictive drugs after DBS treatment of different frequencies on trained addictive rats with implanted electrodes. The timeline of the experiment process is shown in Fig. 3. In the experiment, the rats were implanted with electrodes, and CPP addiction training was carried out after recovery. The rats were then treated with DBS at different frequencies. After the DBS treatment, the CPP score was tested.
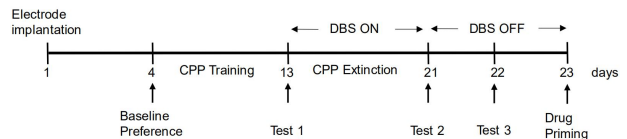

Figure 3.   The timeline of the experiment process.

A. Experimental grouping and electrode implantation

The experiment was carried out in two rounds. The first round of stimulation part was dorsal raphe, and the second round of stimulation part was SNr. Two rounds of experiments were carried out in strict accordance with the experimental

process timeline. In each round of experiment, rats were divided into high frequency stimulation group, low frequency stimulation group and sham stimulation group (the electrodes were implanted normally without electrical stimulation). The number of rats in each group was 8.

The rats were anesthetized with isoflurane and fixed on a stereotaxic device. According to the stereo-tactic map of rat brain [10], the electrode was implanted into the SNr region or the dorsal raphe region and fixed on the top of skull with denture cement, which is shown in Fig. 4. After the denture cement was solidified, the rats were removed and waiting for resuscitation, and then each rat was raised in a separate cage for 5 days to recover.
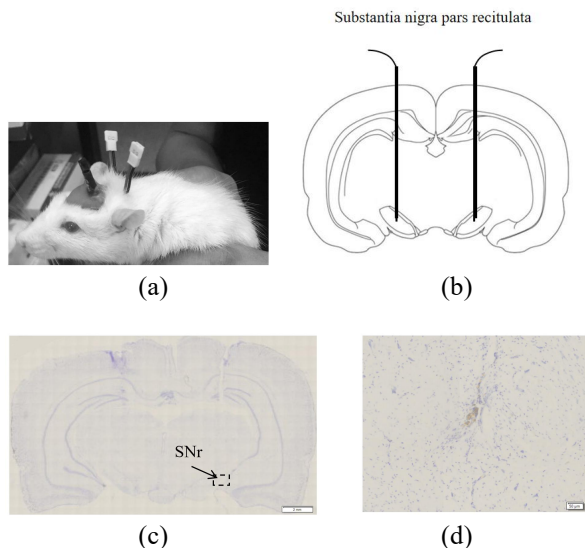

Figure 4. (a) A rat implanted with electrodes, (b) a sketch map of rat brain implanted with two electrodes in both sides, (c) a diagram shows the SNr region, (d) a diagram shows the implanted electrode.

B. CPP training and CPP extinction

After 5 days of recovery, the CPP score of methamphetamine was tested and recorded. Then the CPP training was conducted to the rats to make them addicted to methamphetamine. CPP score was tested and recorded again after the CPP training. The CPP score results in the SNr experiment are shown in Fig. 5(a) and Fig. 6(a).

During the CPP extinction, the DBS system designed in this paper was used to treat the rats in each group for 8 days, stimulating for 1 hour every day. The stimulation current was 0.1mA. The stimulation frequency was 130Hz in high frequency group and 20Hz in low frequency group. The CPP score results in the SNr experiment are shown in Fig. 5(b) and Fig. 6(b).

After the CPP extinction, the CPP score of the rats was tested, and methamphetamine was given at the end of the experimental process to test whether they relapsed. The final CPP score results in the SNr experiment are shown in Fig. 5(c) and Fig. 6(c).

C. Experiment results

It can be seen from Fig. 5(c) that after high-frequency electrical stimulation of the SNr region, the CPP score of high

frequency stimulation group was significantly lower than that of sham stimulation group.

After low-frequency electrical stimulation of the SNR region, the CPP score of low frequency stimulation group was higher than that of sham stimulation group, which is shown in Fig. 6(c).

Therefore, it can be concluded from Fig. 5 and Fig. 6 that high-frequency stimulation of SNr region can effectively promote the extinction of addictive memory, while low-frequency stimulation can inhibit the extinction of addictive memory.

Fig. 7 shows the dorsal raphe experiment results. Both the high frequency group and the low frequency group have lower CPP score than the sham stimulation group, which concludes that both high-frequency and low-frequency stimulation of dorsal raphe region can promote the extinction of addictive memory. By comparison, the inhibitory effect of high frequency stimulation was more significant. From the results of high-frequency stimulation, stimulating the SNr region is better than stimulating the dorsal raphe region in promoting the w\extinction of addictive memory.
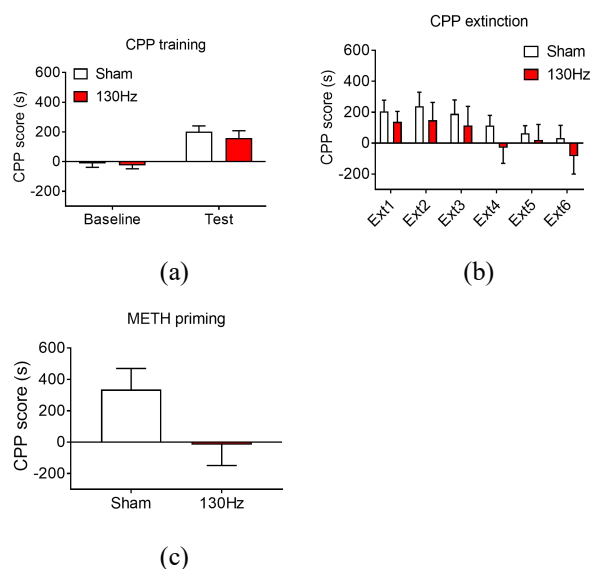

Figure 5. CPP score results of high frequency (130Hz) group in the SNr experiment. (a) CPP training results, (b) CPP extinction results, (c) CPP score(s) with methamphetamine priming.

CPP training

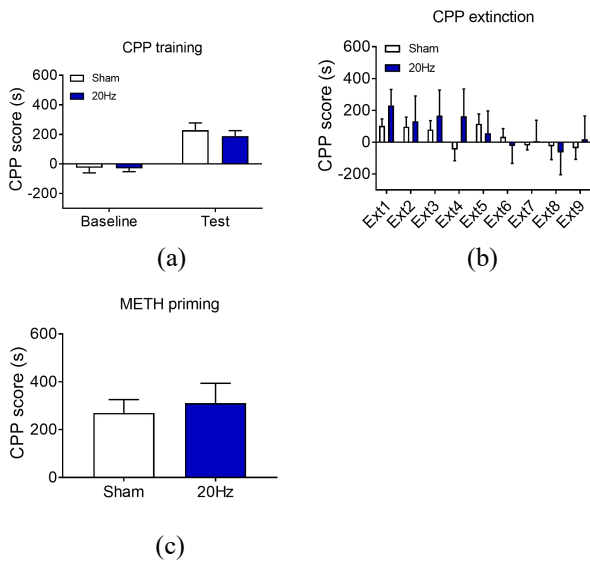(a)

CPP extinction

(b)

METH priming

(c)

Figure 6. CPP score results of low frequency (20Hz) group in the SNr experiment. (a) CPP training results, (b) CPP extinction results, (c) CPP score(s) with methamphetamine priming.

CPP extinction
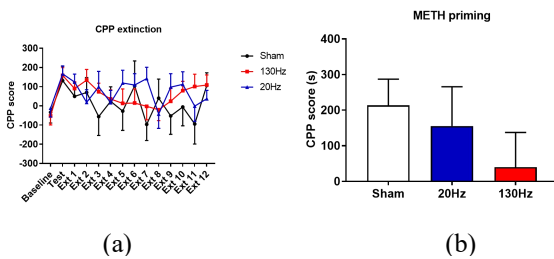
(a)

METH priming

(b)

Figure 7. CPP score results of the dorsal raphe experiment. (a) CPP extinction results, (b) CPP score(s) with methamphetamine priming.

V. CONCLUSION

This paper presents a DBS system that has low power consumption and can provide a wide range of stimulation parameters suitable for different needs in DBS animal experiment. The current consumption of the stimulation circuit is 98μA under typical conditions, and it can work for more than 100 days under ideal conditions.

In the experiment of DBS treatment for methamphetamine addiction in rats, this paper verified the function of the proposed DBS system, and studied the effect of the SNr region and dorsal raphe region in the formation and extinction of addiction memory in rats with the system proposed.

ACKNOWLEDGMENT

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