

Effects of Transcranial Weak Ultrasonic Stimulation on Parkinson's Symptoms

- Consideration Focused on Cognitive Function Tests -

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Abstract

We investigated the effect of weak ultrasound stimulation combined with drugs on the behavioral and psychological symptoms of dementia (BPSD) in a patient with cognitive impairment from a psycho-cognitive evaluation perspective. Here, we report the case of a patient in whom a marked improvement in motor symptoms was observed.

Keywords: weak ultrasonic stimulation, behavioral and psychological symptoms, psycho-cognitive evaluation, motor symptoms

Introduction

In the midst of global super-aging, pandemics, and rapid changes, we are required to respond to several situations that involve small units, such as individuals and families. Furthermore, the demand for caregivers for older adults (such as parents) is rapidly increasing in Japan, which emphasizes the importance of maintaining the ability of an individual to have a will, think, and act for as long as possible. This study, which started in 2017, looked into dementia prevention and reported the efficacy of ultrasound equipment in patients who presented motor symptom improvement. In recent years, there have been global reports of the use of ultrasound stimulation for Parkinson's disease¹⁻³⁾, and ultrasound stimulation of the brain has been found to promote dopamine release³⁾ and protect dopamine neurons²⁾. The Mini-Mental State Examination (MMSE) was used to assess cognitive function, and the Neuropsychiatric Inventory Questionnaire (NPI-Q) was used to assess patient severity and caregiver burden. Physician evaluations, such as the classification of Hoehn-Yahr severity, have not been performed. The subjects were patients with dementia with Parkinson's symptoms who were already receiving drug therapy, with insufficient effects, and psychological testing was possible⁴⁻⁶⁾. The implementation period was set to 12 weeks, during which we used a weak ultrasonic stimulator without changing the oral medication^{7,8)}.

Materials and methods

1. Equipment

As an ultrasonic stimulator, we used a weak long-wave ultrasonic device with 4 transducers (a hair band type equipped with a total of 4 transducers in the left and right frontal and temporal regions) (Ueyama Seisakusho Co., Ltd., Chiba)⁹⁾ (Fig. 1).

2. Methods

The participant and their family received an explanation about the handling of the above equipment from a doctor at the hospital, and after confirming a sufficient understanding of the operation, consent was obtained. The equipment was used at home. The maximum ultrasound intensity volume was fixed, and the subject used the device continuously for 12 weeks (3 months from February 2018) for 20 minutes/time, 2 times/day; morning and afternoon⁸⁾. The medications were to be maintained for six months prior to the commencement of the use of the device, after confirming the symptoms and progress, without changing the type and dose⁷⁾.

3. Assessment

The participant returned at 0, 4, 8, and 12 weeks and were interviewed by a physician using the MMSE (minimum 0 points, maximum 30 points), to assess cognitive impairment, and the NPI-Q to assess BPSD (patient severity-minimum 0 points, maximum 30 points, caregiver burden-minimum 0 points, maximum 50 points).

4. Subject

The participant was male and 68 years old at the start of the device use (February 2018).

Medication status: Madopar 3T/day

Reminyl OD tablet 8 mg 2T/day

Medical History

Since his late 50s, the patient presented with symptoms of visual hallucinations, REM sleep behavior disorder, and depression; and had visited a nearby doctor. At that time, he was suspected of having Parkinson's disease (PD), was referred to a nearby specialized hospital for examination, and was diagnosed PD at 61 years of age. Subsequently, he changed hospitals several times, but returned to the same hospital for regular treatment. At the age of 62, he was diagnosed with PD dementia (PDD) and was referred to our clinic. A strong tremor was noted from the patient's first visit, and he had a low voice, poor mouth opening, and a tendency to look down (downward eyes). With the assistance of his wife, he was able to take his first step and constantly received walking assistance. His Parkinson's symptoms worsened gradually, and at the age of 68, he used a wheelchair, had difficulty maintaining a sitting position, and was often silent and expressionless, with his eyes kept closed.

Medical history: none

Family history: none

This study was approved on February 13, 2017 by the Folkmore Clinic Ethics Review Board.

Results

The patient who had strong symptoms of PD before using the equipment could walk with guidance from week four. He was subsequently able to maintain an upright sitting position, even after lying down and leaning back, and could hold a fork when eating. From week 4 to 12, the patient's improvements were even more dramatic. His NPI-Q severity improved from 5 points to 0 points (-5) at eight weeks, and his caregiver burden score improved from 8 points to 0 points (-8) at four weeks (Table 1). Regarding the MMSE, while the diurnal fluctuations and wearing off conditions were reduced from weeks 0 to eight, he had a poor physical condition (catching a cold, week 4, 15 points) that destabilized the results. However, his score did not fall below 20 after week eight. Furthermore, the patient showed clear improvements in MMSE spontaneous writing and graphic copying (Figure 2).

Considerations

The patient had tremors, rigidity, immobility, and postural reflexes prior to device use. However, an improvement in his symptoms was observed after use of the device.

In this study, the subject used four ultrasound transducers, and although his symptoms were severe, both his NPI-Q and MMSE tended to improve, as early as week four. In addition, the improvement continued. In contrast, although the MMSE fluctuated from 24 points at week 0, 15 points at week 4, 22 points at week 4, and 20 points at week 12, an effect on Parkinson's symptoms was observed (Figure 2). At the beginning (week 0), the patient could not write or draw anything and could only place a pencil on the paper. By week eight, he could write a little and began to show a desire to improve. Subsequently, he could write by week 12, and at the week 20 follow-up, he could write about how he felt on the day of the test. He also showed improvements in drawing two overlapping pentagons clearly, though they were small in size.

The results of the NPI-Q showed that the patient's motor function improved, and he could

keep moving for a longer time than before, which led to a reduction in the burden on caregivers. Notably, he was now able to bathe and wear and remove clothes on his own. Furthermore, the patient could feel an improvement his in Parkinson's symptoms through the changes in his body movements.

The above results confirmed that weak ultrasonic stimulation with four transducers improved Parkinson's symptoms and motor disorders peculiar to PD. In addition, since the end of the trial (March 2018 to December 2021), the patient has been using this device while continuing appropriate treatment, mainly drug therapy, under the supervision of a specialist. Notably, he can now walk independently, change direction, and maintain a sitting position. These findings show that that ultrasound stimulation can improve several symptoms associated with dementia by activating cerebral blood flow and reduce side effects, while increasing drug efficacy. Furthermore, this device has been confirmed to be safe¹²⁾, with no adverse events^{10,11)} among existing ultrasonic stimulations. As such, the burden on the patient is small and the likelihood of activity of daily living improvements is high.

Conclusion

According to this study, the combination of weak ultrasonic stimulation to the head in combination with therapeutic drugs is effective for treating cognitive impairment and Parkinson's symptoms, has a high immediate effect, and can reduce the burden on caregivers. The ultrasound device with four transducers used in this study enabled a wheelchair-bound patient with strong Parkinson's symptoms to walk independently or with assistance through 12 weeks of continuous use. This result can be expected to provide a new treatment method related to motor symptoms.

In the future, it is necessary to confirm these results in a larger study population, the degree of cognitive symptom improvement, and the durability of the effect, including patient tolerance due to long-term use. For Parkinson's symptoms, in addition to the Hoehn-Yahr, a unified scale, we would like to collect and analyze more accurate data, consider the position of the oscillator for each symptom from the role of the brain, and translate the device into a new treatment method that is founded on accurate evidence.

Sponsor

Ueyama Seisakusho Co., Ltd.

Conflict of interest

No conflict of interest to report.

Acknowledgments

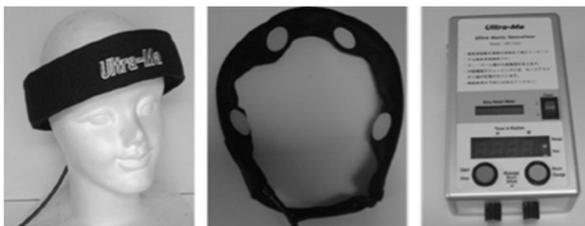
We would like to thank Ueyama Seisakusho Co., Ltd. for providing the sonography device.

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Table 1. Rating Score Data for a Patient with Parkinsonism NPI-Q, MMSE.

						N P I - Q
Test items and test week	Week 0	Week 4	Week 8	Week 12	Amount of change (Week 12-Week 0)	Remarks
Patient Severity	5	3	0	0	-5	Severe Parkinson's symptoms improved and caregiver's burden decreased
Burden on caregiver	8	0	0	0	-8	
						M M S E
	24	15	22	20	-4	This cognitive function test showed an on/off effect, but the score did not fall below 20 after week 8.



A B C

Figure 1. Weak long-wave ultrasonic device.

A: Attachment, B: Layout of ultrasonic transducer, C: Control device

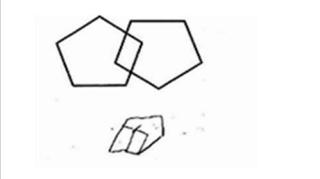
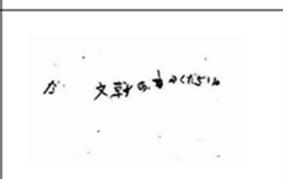
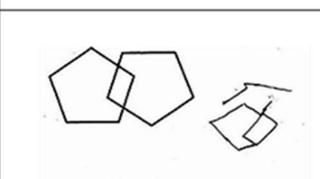
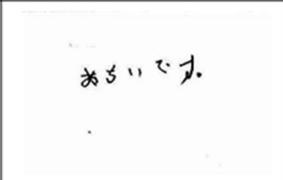
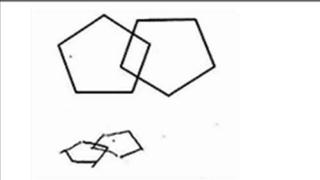
臨床経過	MMSE① 何か文章を書いてください。	MMSE② ここに図形を正確にそのまま書き写してください。
0 w		
	点のみ 何も書けない	点のみ 何も描けない
8w		
	私は・・・書く意欲が出た。	描く意欲が出ている。
12w		
	文章を書く意欲が見える。	片側の5角形が描けた。
20w		
	あちいです。暑い意味。	5角形の重ね明確に描けた

Figure 2 MMSE spontaneous writing and figure copying

Abstract

Behavioral and psychological symptoms were examined via psychiatric and cognitive functional evaluation in a patient with cognitive dysfunction who received weak ultrasound stimulation and drugs. We found a great improving in the motor symptoms of the patient, for the first time, in this study.

Key words:

weak ultrasound stimulation, behavioral and psychological symptoms of dementia, psychiatric and cognitive functional evaluation, motor symptoms