


# The Effect of a Portable Electrical Muscle Stimulation on Brain-Derived Neurotrophic Factor in Elderly People: Three Case Studies

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## Abstract

Brain-derived neurotrophic factor (BDNF), which plays an important role in cognitive and nerve function, is released from skeletal muscle cells into the blood by muscle contractions and/or electrical muscle stimulation (EMS). However, the influence of EMS administered by a portable device on BDNF is unclear. The purpose of this case report was to quantify the influence of EMS administered by a portable device on BDNF and physical function. Three elderly people (age,  $69.7 \pm 1.5$  years) were included in the present study. The participants used a portable EMS device to stimulate the bilateral quadriceps muscles for 8 weeks (23 min for 5 days/week). To determine the effects of EMS, the following parameters were assessed at baseline, 8 weeks, and 12 weeks (follow-up): knee extensor strength, muscle mass of the lower limb, Berg balance score, and blood BDNF level. All outcomes improved after the EMS intervention, but the improvements did not persist for 12 weeks. These findings suggest that portable EMS is potentially useful for improving the blood BDNF level and physical function.

## Keywords

aging, rehabilitation, therapy, prevention

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## Introduction

The Japanese population is aging rapidly. The number of elderly individuals aged  $\geq 65$  years is expected to reach 39.35 million by 2042 (Cabinet Office, 2016). Aging causes the progressive loss of muscle mass, which results in decreased muscle strength and physical performance. It is difficult for individuals whose levels of cognitive and/or physical function have deteriorated to maintain muscle mass and balance function. A previous study has reported that rehabilitation improves the quality of life and motivation to exercise in older adults with dementia (Sondell et al., 2018). However, a previous study reported that moderate-to high-intensity training programs do not improve the activities of daily living (ADL) or cognitive function of older adults with dementia (Lamb et al., 2018). Therefore, cognitive function is an important factor associated with the rehabilitation process and influences the effectiveness of physiotherapy.

Recently, it has been reported that brain-derived neurotrophic factor (BDNF), which plays an important role in cognitive and nerve function, is released from skeletal muscle cells into the blood during muscle contractions (Thoenen, 1995). A previous study has reported that exercise training

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increases blood BDNF (Fontanesi et al., 2016), but memory improvements induced through BDNF pathway activation are dependent on exercise intensity (Cefis et al., 2019). Electrical muscle stimulation (EMS) interventions have also been reported to increase blood BDNF (Miyamoto et al., 2018). However, many EMS-based studies require medical equipment and hospitalization or outpatient care to be applied, which can be difficult to perform in community-dwelling elderly people. On the other hand, portable EMS devices are inexpensive and convenient, as they can be used in the home. Although our previous study showed that a portable EMS device enhances muscle strength and muscle thickness in elderly people (Nishikawa et al., 2019), no studies have been performed to determine its effects on the blood BDNF level. Information on the influence of EMS administered with a portable device on the blood BDNF level and physical function may help improve the level of independence in ADL and/or quality of life of elderly people.

The purpose of this study was to examine the influence of an EMS intervention on the blood BDNF level and physical function in elderly people. This report is short due to the small number of patients.

## Methods

### Subjects

Three elderly people were included in this study: case (1) 68 years old, 55 kg, 158 cm, Mini-Mental State Examination = 29; case (2) 71 years old, 60 kg, 160 cm, Mini-Mental State Examination = 28; and case (3) 70 years old, 57 kg, 157 cm, Mini-Mental State Examination = 28. The inclusion criteria were independence in daily life, no history of orthopedic diseases, and the ability to walk without walking aids. The exclusion criteria were dementia, neuromuscular diseases, cardiovascular diseases, and diabetes mellitus. All procedures were performed in accordance with the Declaration of Helsinki and were approved by Hiroshima University's Committee on Ethics in Research (approval no. C-151). All participants signed an informed consent form and consented to the publication of this work. The following parameters were assessed at baseline, 8 weeks, and 12 weeks (follow-up) for all participants: for the primary outcome, serum BDNF level, and for the secondary outcome, knee extensor muscle strength, lower-limb muscle mass, and Berg balance scores. The intervention and each measurement in this study were conducted at Hiroshima University Hospital.

### EMS Intervention

The participants underwent EMS of the quadriceps muscle on both sides in a sitting position at home for 8 weeks. A portable EMS device (Sixpad Body fit; MTG Ltd, Nagoya, Japan) was used 5 days per week. The device was positioned at the midpoint of the femur. The muscles were stimulated at an

intensity of 4.85 mA (frequency = 20 Hz, pulse shape = square wave, pulse duration = 100  $\mu$ s, pulse period = 50 ms, size = 122 mm  $\times$  244 mm) for 23 min once per day (Nishikawa et al., 2019).

### Measures of Knee Extension Strength

All participants performed maximal voluntary isometric contractions (MVCs) during isometric knee extension at baseline, 8 weeks, and 12 weeks (follow-up) for their dominant side. The dominant leg was defined as the leg used to kick a ball. Isometric knee extension was performed using a Biodex system (Biodex system 4; Biodex Medical Systems, Shirley, NY, USA). The subjects were seated on a Biodex seat with the hip and knee extension angles fixed at 90° (180°, full extension) during the measurement. For the MVC trials, the participants gradually increased the knee extension torque exerted by the knee extensor muscles from 0 to maximum over 3 s, holding the maximum torque for 2 s (Nishikawa et al., 2019). The participants performed two MVC trials with > 120 s of rest between trials, and before the MVC trials, they performed a warm-up session for 10 min that included indoor walking and lower-limb stretching. The highest MVC torque was recorded.

### Measures of Muscle Mass

Lower limb muscle mass was measured using direct segmental multifrequency bioelectrical impedance analysis (InBody S 10, InBody Japan, Tokyo, Japan). It is a method that has been validated for estimating skeletal muscle mass with respect to dual-energy X-ray absorptiometry. Electrodes were placed bilaterally on the thumbs, middle fingers, and ankles. The participants were asked to lie down in a supine position and instructed to lie as still as possible during the measurements. The measurements were performed 5 hours before meals.

### Measures Using the Berg Balance Scale

The balance function of the subjects was assessed with the Berg balance scale (BBS). The BBS is rated on a 5-point scale from 0 (cannot perform) to 4 (normal performance) and consists of 14 different tasks including the ability to sit, stand, reach, turn, and step. The BBS has been reported to exhibit high interrater reliability (intraclass correlation coefficient = 0.96) (Berg et al., 1989).

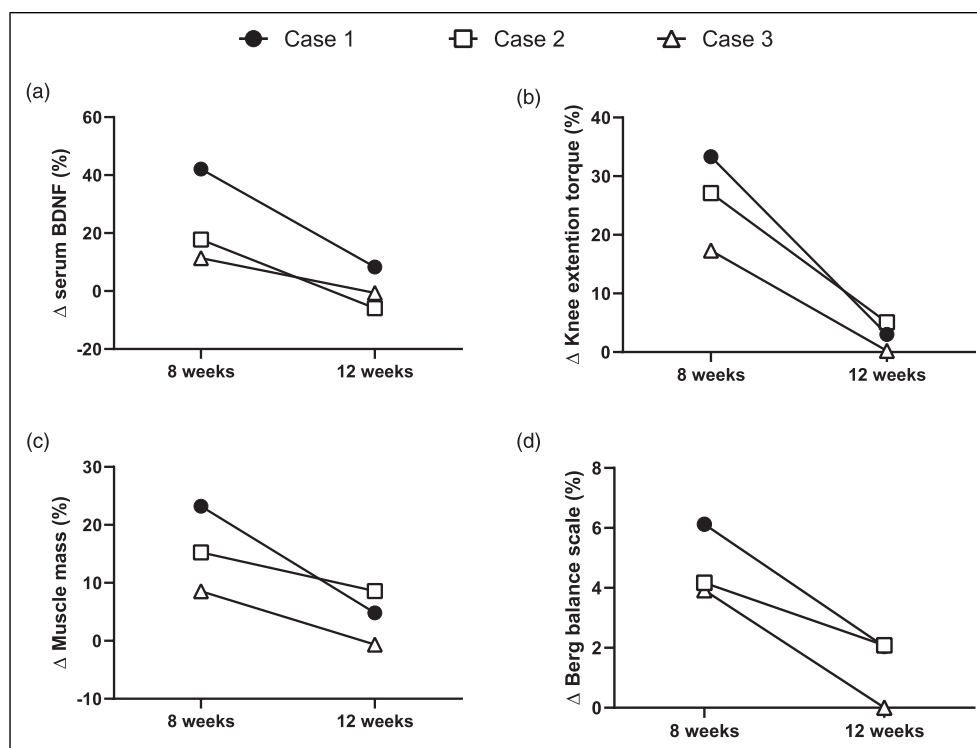
### Measures of Blood BDNF

Blood was sampled from an antecubital vein into vacuum tubes for the determination of the BDNF level. The serum samples for BDNF were frozen and stored at  $-80^{\circ}\text{C}$  until quantification by enzyme-linked immunosorbent assays (ELISA) according to the manufacturer's instructions (BDNF ELISA kit, KE00096, Proteintech, Chicago, IL, USA).

**Table 1.** Outcome changes in participants.

	Serum BDNF, pg/mL	Knee Extension Torque, Nm	Muscle Mass, kg	Berg Balance Scale
Case 1				
Baseline	11,843	66	12.5	49
8 weeks	16,828	88	15.4	52
12 weeks	12,826	68	13.1	50
Case 2				
Baseline	12,891	59	10.5	48
8 weeks	15,183	75	12.1	50
12 weeks	12,134	62	11.4	49
Case 3				
Baseline	16,182	88	15.2	51
8 weeks	18,017	103	16.5	53
12 weeks	16,081	88	15.1	51

BDNF, brain-derived neurotrophic factor.



**Figure 1.** Comparison of changes in (a) serum BDNF, (b) knee extension torque, (c) muscle mass, and (d) Berg balance score from 8 weeks to 12 weeks.

## Results

All outcomes showed improvement after 8 weeks compared with the baseline, but a decline was observed after 12 weeks, confirming the lack of a sustained effect of the EMS intervention (Table 1). All outcomes were calculated as the percent change from baseline. All subjects showed improvement at 8 weeks compared with the baseline, but decreased to values similar to baseline at 12 weeks (Figure 1).

The degree of change in BDNF tended to correlate with the degree of change in other outcomes.

## Discussion

We assessed the effects of an EMS intervention on physical function and neurotrophic factor in locomotive syndrome subjects. In addition to improvements in physical function, the serum BDNF level increased from baseline to the end of

the EMS intervention, but the improvements did not persist after the EMS intervention.

It is widely known that EMS can improve muscle performance. Several previous studies have also reported that improvements in muscle strength and thickness occurred after EMS interventions (Nishikawa et al., 2019, 2020). Our previous study also showed that EMS enhances muscle strength and muscle thickness in elderly people (Nishikawa et al., 2019). These previous findings are in accordance with the results of the present report, in which the EMS intervention led to increases in muscle strength, muscle mass, and physical performance. In addition to analyzing physical function, we examined the influence of the EMS intervention on the neurotrophic factor (e.g., BDNF) level. The results of the present study showed that the serum BDNF level was increased by the EMS intervention after 8 weeks. Neurotrophic factors (such as BDNF) contribute to the process of axonal regeneration (Gordon, 2010). BDNF is the predominant molecule involved in axonal regeneration (Zhang et al., 2000), and its expression has been demonstrated to be upregulated after EMS (Miyamoto et al., 2018; Willand et al., 2016). EMS accelerates axonal outgrowth and the reinnervation process at the neuromuscular junction and is mediated by BDNF through the tropomyosin-related kinase receptor B and its downstream pathways (Guo et al., 2021). In addition to neural adaptation, BDNF contributes to morphological change and physical function. An increase in BDNF stimulates the fast-twitch muscle type gene program, whereas a decrease in BDNF reduces the volume of the motor endplate (Delezie et al., 2019). Furthermore, administration of BDNF improves the exercise capacity in a mouse model (Matsumoto et al., 2018). Our results support the findings of these previous studies. In general, research using EMS often involves expensive medical equipment that has a high output and many frequency settings, but this equipment is difficult to introduce into the home. Therefore, it is necessary to go to the hospital and/or clinic to perform these EMS interventions. In the present study, we demonstrated the efficacy using a small portable EMS device in the home in improving BDNF and physical function levels. Portable EMS devices are inexpensive and convenient as they can be used in the home. Our results suggest that a portable EMS device is a useful and effective tool for improving physical function and neurotrophic factor levels.

This report has several limitations. First, number of the participants was limited. Second, this report included only an intervention group. Third, we recruited only participants with noncognitive dysfunction. Future studies (e.g., large-sample studies with a control group and studies including participants who have cognitive dysfunction and higher-order brain function evaluations (e.g., Paced Auditory Serial Addition Tests)) are needed to clarify the influence of EMS on physical function, neurotrophic factor, and cognitive function.

## Conclusion

We investigated the influence of EMS on the blood BDNF level and physical function using a portable EMS device. The present study showed that EMS improves physical function and increases the serum BDNF level, but these results were not sustained without the EMS intervention. These results suggest that a portable EMS device enhances blood BDNF and physical function levels in elderly people.

## Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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