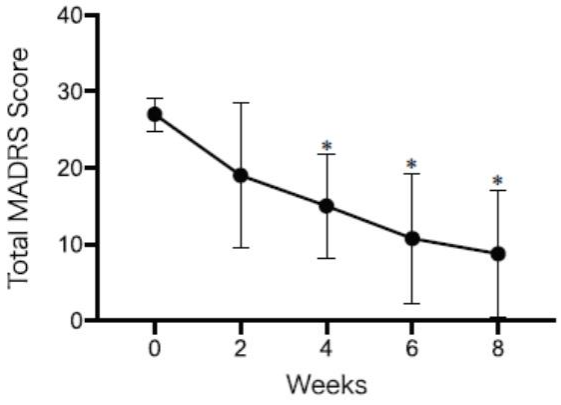
News Release

Title

Extremely Low Frequency, Extremely Low Magnetic Environment for Depression: An Open-Label Trial

Key Points

- Mitochondrial dysfunction is suggested to play a role in depression pathogenesis.
- Extremely Low Frequency, Extremely Low Magnetic Environment (ELF-ELME) has been shown to enhance the mitochondrial membrane potentials in cultured cells.
- Four depressive patients wore an ELF-ELME device for 2 hours a day for 8 consecutive weeks.
- Significant improvements were observed and no adverse events were reported.
- If the efficacy of ELF-ELME is confirmed in randomized controlled trials, it could be a potentially safe and effective therapy for depression.



Four depressive patients wore an ELF-ELME device for 2 hours a day for eight consecutive weeks. Significant improvements were observed and no adverse events were reported.

Summary

A group of Toshiya Inada (Professor), Masako Tachibana (Assistant professor), Mikako Ito (Lecturer), and Kinji Ohno (Professor Emeritus) at the Graduate School of Medicine, Nagoya University, has discovered that exposure of patients with depression to an Extremely Low Frequency, Extremely Low Magnetic Environment (ELF-ELME) weaker than geomagnetism for eight weeks improved depressive symptoms.

Mitochondrial dysfunction has been suggested to play a role in depression pathogenesis. Professor Inada's group conducted to evaluate whether depressive symptoms could be alleviated by ELF-ELME, which has been found in basic research studies to enhance the mitochondrial membrane potentials in cultured cells. Participants were exposed to the ELF-ELME via a head-mounted magnetic field device (10 μTesla, 4 msec, 1-8 Hz/ 8 sec) worn for 2 hours per day for 8 consecutive weeks. Four male patients with treatment-resistant depression were enrolled. Significant reductions from baseline in the average total Montgomery–Åsberg Depression Rating Scale (MADRS) score were observed at 4, 6, and 8 weeks. ELF-ELME appears to ameliorate depressive symptoms in patients with major depressive disorder safely and effectively, suggesting that it could be used as an alternative treatment for depressive patients who do not prefer to take antidepressants or as an additional treatment for patients who partially respond to pharmacotherapy.

The report was published online in *Asian Journal of Psychiatry*, a journal in the Elsevier Publishing Group, in March 2024.

Research Background

Major depressive disorder is a predominant cause of disability worldwide. Antidepressants are widely used for patients with depression; however, approximately 30% of patients do not improve with antidepressants. Although guidelines recommend treatments such as Electroconvulsive Therapy or repetitive Transcranial Magnetic Stimulation for patients with treatment-resistant depressive patients who do not respond to antidepressants therapy, these are not necessarily sufficient, and new treatments are being sought. The precise pathophysiology of depression remains elusive; however, a link between mitochondrial dysfunction in various brain regions and depression has been suggested. Addressing mitochondrial dysfunction and enhancing mitochondrial functions is a potential therapeutic option for depression. They have demonstrated that faint magnetic fields with extremely low-frequency pulses induce mitochondrial biogenesis and evoke the heat shock response. Professor Inada's group aimed to investigate whether exposure to an Extremely Low

Frequency, Extremely Low Magnetic Environment (ELF-ELME) could ameliorate depressive symptoms without adverse effects in patients with major depressive disorder in an open-label trial.

Research Results

Four participants were exposed to the ELF-ELME (10 μTesla, 4 msec, 1-8 Hz/ 8 sec) by wearing a head-mounted magnetic field device (Figure 1) for 2 hours per day for 8 consecutive weeks. Safety and efficacy were evaluated at baseline and 2-, 4-, 6-, and 8-weeks post-baseline. As a primary outcome, trained psychiatrists performed the efficacy assessment using the Japanese version of the MADRS. The Artificial Intelligence (AI)-MADRS was conducted as a secondary outcome measure at baseline and 8 weeks. The AI-MADRS includes nine structured interviews with modified question sentences from MADRS items 2–10, enabling a simple estimation of severity scores using a machine learning model. Participants' vocal responses to synthetic voice interview questions were analyzed using speech recognition and natural language processing model and automatically rated using machine-learning methods trained on previously accumulated MADRS interview data. Participants were instructed to maintain a logbook to record the time spent wearing the ELF-ELME device.

All participants were diagnosed with moderate major depressive disorder with recurrent episodes (DSM-5). One patient reported using the ELF-ELME device for only one hour due to dead batteries on days 5 and 47, and no other protocol deviations occurred. Thus, it can be inferred that all patients effectively adhered to the prescribed two-hour daily regimen of ELF-ELME device usage. No adverse events were reported in this study, demonstrating that the ELF-ELME therapy was well tolerated. All patients exhibited decreased total MADRS scores. The average improvement rates of the total MADRS score at weeks 2, 4, 6, and 8 post-baseline were 31%, 45%, 60%, and 68%, respectively. Figure 2 depicts the time course of the combined total MADRS score change in the four patients with depression. Significant reductions in the total MADRS score were observed at 4, 6, and 8 weeks compared with that at baseline. The average total AI-MADRS score significantly decreased from 32.8 at baseline to 12.5 at 8 weeks.

Figure 1.
The head-mounted extremely low frequency, extremely low magnetic environment (ELF-ELME) magnetic field device. a) Mock-up demonstrating how patients wear the device, b) Photograph of an ELF-ELME device.

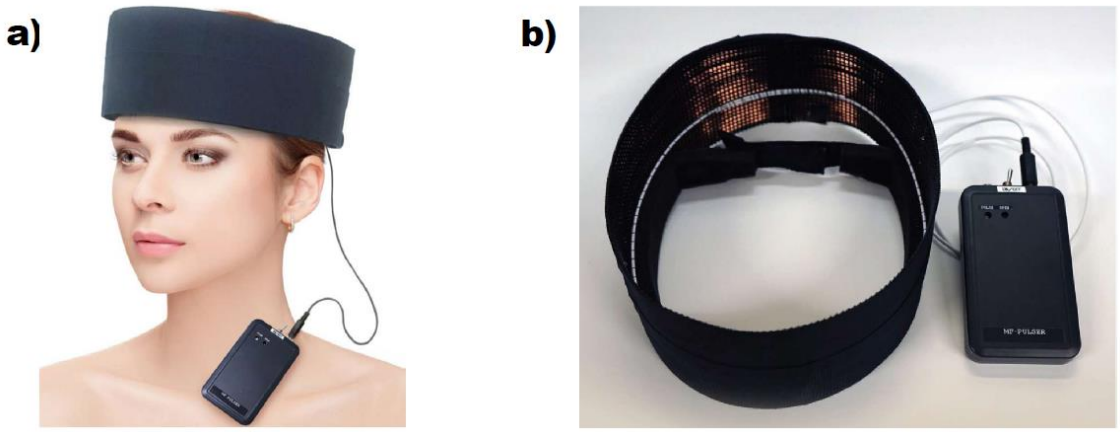
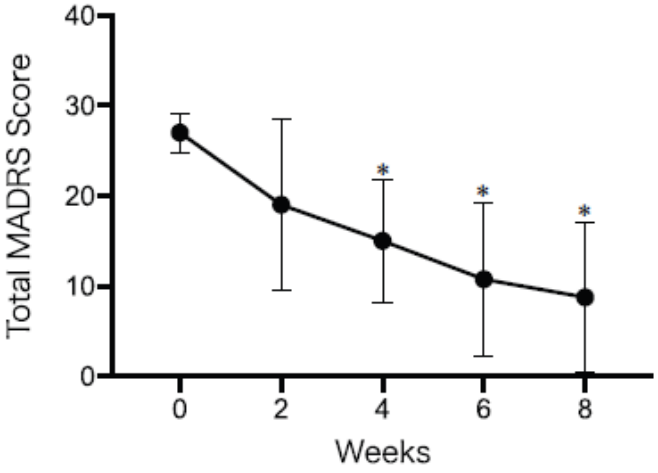


Figure 2.
Time course of the total MADRS score in patients with major depressive disorder (n = 4). Data are presented as the mean ± S.D.



Research Summary and Future Perspective

ELF-ELME appears to ameliorate depressive symptoms in patients with major depressive disorder safely and effectively, suggesting that it could be used as an alternative treatment for depressive patients who do not prefer to take antidepressants or as an additional treatment for patients who partially respond to pharmacotherapy.

An introductory video: https://youtu.be/T16rsP1ZJVY

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