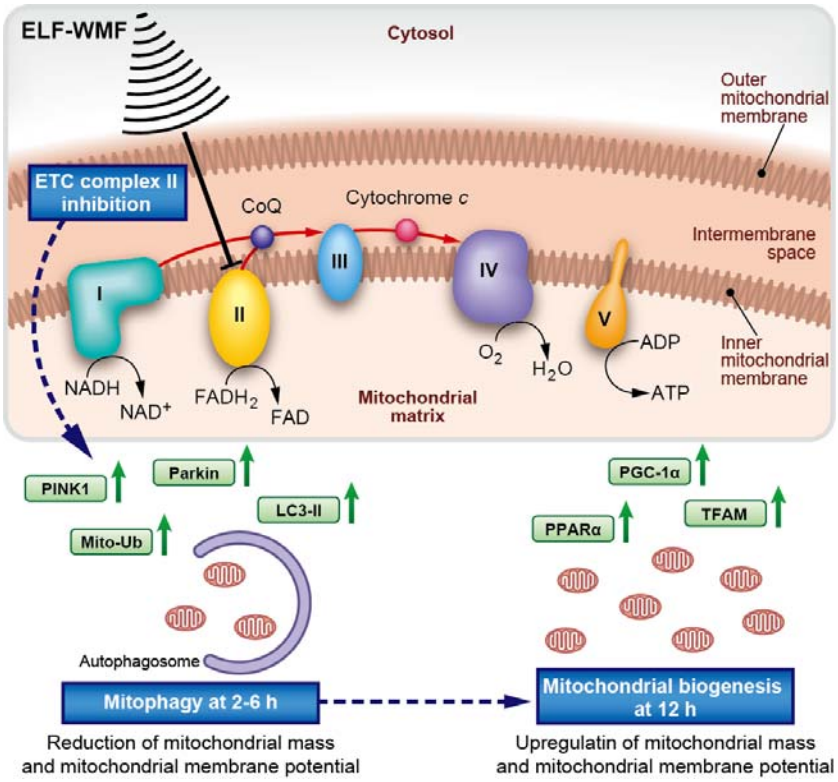
News Release

Title

Extremely low-frequency pulses of faint magnetic field rejuvenate mitochondria by inducing mitophagy

Key Points

- The biological effects of weak magnetic fields weaker than geomagnetism are scarcely known.
- Extremely low-frequency pulses of weak magnetic field (ELF-WMF) of 10 μT at 1-8 Hz suppressed the activity of mitochondrial electron transport chain complex II and induced mitophagy.
- Following mitophagy, mitochondrial neogenesis was activated to rejuvenate mitochondria.
- ELF-WMF is expected to be applied to the treatment of neuropsychiatric disorders and other diseases associated with mitochondrial dysfunction.



Summary

A group of Kinji Ohno (Professor), Takuro Toda (6th year undergraduate student at the time of research), and Mikako Ito (Lecturer) at the Graduate School of Medicine, Nagoya University, exposed cultured cells and wild-type mice to extremely low-frequency pulses of weak magnetic field (ELF-WMF), which was weaker than the geomagnetic field. They discovered that ELF-WMF induces mitophagy, which is a physiological mechanism to selectively eliminate damaged mitochondria, and then induces mitochondrial neogenesis to rejuvenate mitochondria.

We humans are daily exposed to weak static and fluctuating magnetic fields by the geomagnetism (~45 μT in Japan) and in environments where electricity is exploited. The biological effects of magnetic fields weaker than the geomagnetic field have been scarcely reported. Professor Ohno's group found that magnetic pulses of 10 μT at 1 to 8 Hz (Optimized ELF-WMF, Opti-ELF-WMF herein) suppressed the activity of mitochondrial electron transport chain complex II of mouse hepatocyte cell line AML12. Then Opti-ELF-

WMF induced mitophagy and reduced the amount of mitochondria to 70%. Twelve hours later, mitochondrial biogenesis was activated and the activity of mitochondrial membrane potential was increased. The increase of mitochondrial proteins and the activation of mitochondrial electron transport chain were also observed in hepatocytes in mice that were continuously exposed to Opti-ELF-WMF for 4 weeks. As mitophagy plays an important role in maintaining mitochondrial homeostasis, the induction of mitophagy by Opti-ELF-WMF is expected to ameliorate mitochondrial dysfunction in neuropsychiatric disorders, as well as other diseases that are causally associated with mitochondrial dysfunction.

The report was published online in "*Communications Biology*", a journal in the Nature Publishing Group, on May 12, 2022.

Research Background

In modern society, people are daily exposed to static and fluctuating magnetic fields originating from electrical appliances or factories in addition to geomagnetic field. The biological effects of extremely low-frequency weak magnetic field (ELF-WMF), which is defined as a weak magnetic field with a frequency of less than 300 Hz, on intracellular ROS and mitochondrial calcium concentration have been reported, but its underlying mechanisms remain to be elucidated. In this study, we investigated the biological effect of ELF-WMF of 10 μT, which was weaker than the geomagnetic field of 45 μT in Japan, and elucidated its underlying mechanisms.

Research Results

The research group applied 4-ms pulses of 10-μT magnetic field at 1-8 Hz repeatedly to wild-type mice for 4 weeks (Fig. 1). In the mouse liver, the mitochondrial membrane potential, the mitochondrial basal respiration, and the mitochondrial electron transport chain complex proteins were increased. Next, when the mouse hepatocyte cell line AML12 was exposed to Opti-ELF-WMF (Fig. 1), the mitochondrial mass was decreased to 70% in 3 hours and the mitochondrial membrane potential was increased to 110% in 12 hours (Fig. 2). Next, they investigated the expression levels of PINK1 and LC3-II, which are mitophagy-related proteins. Mitophagy is one of the autophagy in the mitochondrial quality control system that selectively eliminates damaged mitochondria. PINK1 was increased up to 90 minutes and LC3-II was increased up to 2 hours after Opti-ELF-WMF exposure. The mitochondrial fraction of AML12 cells exposed to Opti-ELF-WMF for 2 hours showed an increase in PINK1, Parkin, and ubiquitinated protein levels, indicating that mitophagy was activated. Furthermore, the staining with the fluorescent probe Mtphagy Dye for detecting mitophagy showed that mitophagy was most strongly induced in 2.5 hours after Opti-ELF-WMF exposure (Fig. 2). Twelve hours after ELF-WMF exposure, PGC-1α, PPARα, and TFAM proteins were elevated in AML12 cells, indicating that mitochondrial biogenesis was induced.

Research Summary and Future Perspective

The Opti-ELF-WMF, which induces mitophagy and rejuvenate mitochondria, is expected to ameliorate neuropsychiatric disorders and other diseases associated with mitochondrial dysfunction, including Parkinson’s disease, Alzheimer’s disease, cardiovascular disease, depression, and aging. In addition, repetitive transcranial magnetic stimulation (rTMS) is currently applied to treat depression, migraine, obsessive-

compulsive disorder, and Parkinson's disease, but ~ 3-T intensity of rTMS has potential adverse effects. We expect that Opti-ELF-WMF may serve as a safer alternative for rTMS.

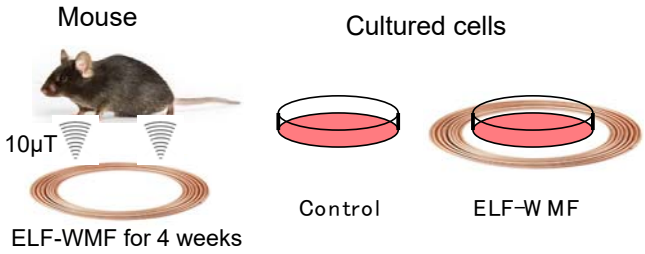


Fig. 1. Opti-ELF-WMF was applied to wild-type mice and cultured cells.

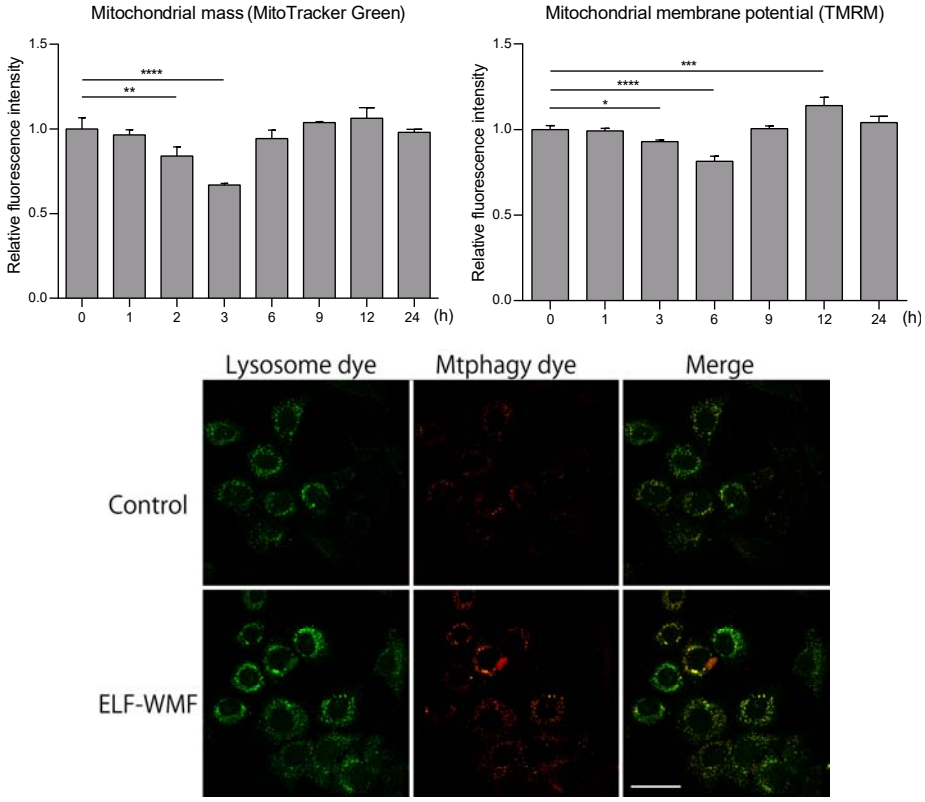


Fig. 2. Opti-ELF-WMF induced mitophagy and decreased mitochondria mass in 3 hours. Then, Opti-ELF-WMF increased mitochondria membrane potential in 12 hours.

Publication

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