First Congress

International Society of Diamagnetic Therapy

“Neuropsychiatric Aspects”

13th – 14th September 2024
Magna Graecia University - Catanzaro

Leonardo Palacios MD
Universidad del Rosario
Bogotá Colombia

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Dubium sapientiae initium

Spectrum of Neuropsychiatric Field

Neurology and psychiatry were born as the same specialty “diseases of the nervous system” in the second half of the 19th century.

The distinction between the two fields was initially conceived to offer a systematic method for comprehending and addressing problems of the neurological system.

K. Miyoshi et al. 2010, Taslim, Shadmani et al, 2024

Spectrum of Neuropsychiatric Aspects

Neurology, which concentrates on the biological and structural elements of the brain, seeks to decipher the enigmas of physical disorders that impact the neurological system.

Psychiatry, on the other hand, developed as a field focused on investigating mental and emotional illnesses, frequently linked to intricate behavioral expressions.

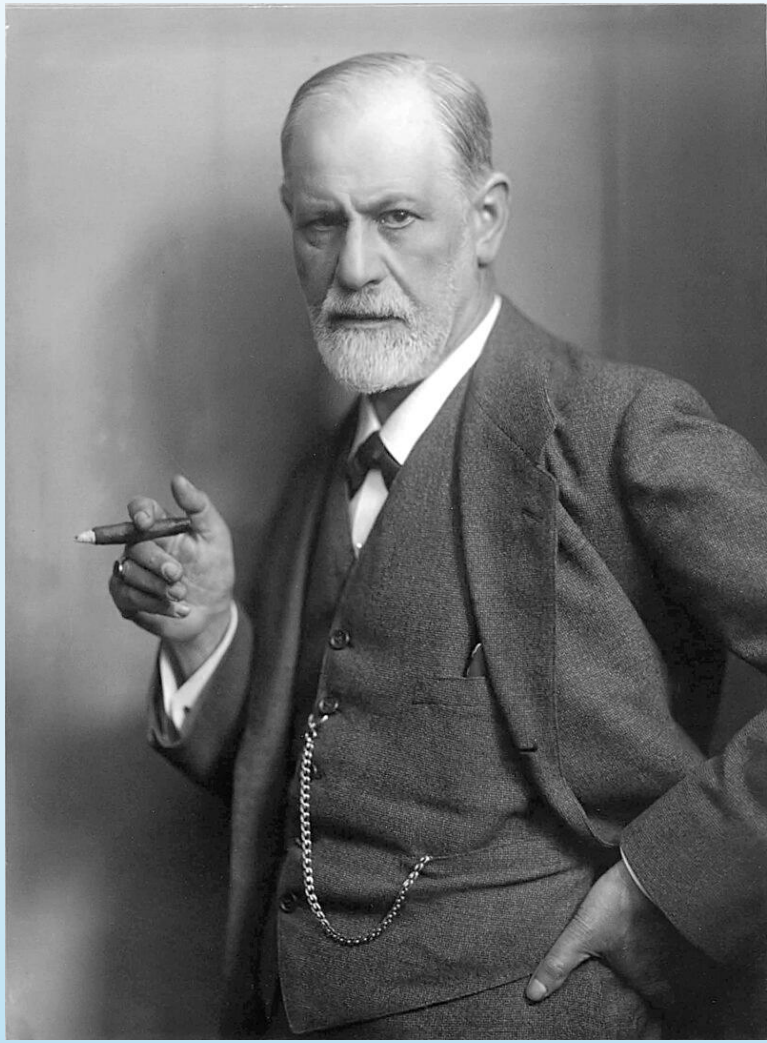
K. Miyoshi et al. 2010, Taslim, Shadmani et al, 2024

A Clinical Lesson at the Salpêtrière – André Brouilllet - 1887

Marie Wittman “Blanche”
Iconographie de la Salpêtrière

Jean-Martin Charcot and Sigmund Freud, were crucial in establishing clear distinctions between neurology and psychiatry.

Freud's psychoanalytic theories directed psychiatry toward investigating the subconscious mind and psychodynamic mechanisms. At the beginning of the 20th century, there was a significant change in how medical professionals thought about the relationship between neurology and psychiatry.



Sigmund Freud, 1856-1939

But we Continue to Interact Permanently

Major neurocognitive disorder

Alzheimer's disease

Parkinson's disease

Anxiety

Depression

Traumatic Brain Injury

Cerebrovascular disease

But we Continue to Interact Permanently

Bipolar disorder

Autism spectrum disorder

Autoimmune neurological disorders such multiple sclerosis, lupus erythematosus and autoimmune encephalopathies

Premi *et al. BMC Neurosci (2018) 19:34*
https://doi.org/10.1186/s12868-018-0434-z

BMC Neuroscience

RESEARCH ARTICLE

Open Access

Modulation of long-term potentiation-like cortical plasticity in the healthy brain with low frequency-pulsed electromagnetic fields

Enrico Premi[1,2*], Alberto Benussi[2], Antonio La Gatta[3], Stefano Visconti[4], Angelo Costa[1], Nicola Gilberti[1], Valentina Cantoni[2], Alessandro Padovani[2], Barbara Borroni[2] and Mauro Magoni[1]

Modulation of long-term potentiation-like cortical plasticity in the healthy brain with low frequency-pulsed electromagnetic fields

Enrico Premi, Alberto Benussi, Antonio La Gatta et al. 2018

Low Frequency-Pulsed Electromagnetic Fields, LF-PEMF have shown the potential to modulate living structures . These non-depolarizing approaches seem to influence synaptic activity and ion channels on cellular membranes.

LF-PEMF has been reported to influence brain glucose metabolism, thus affecting local brain activity.

Collectively, these studies indicate that LF-PEMF may be involved in neuroprotection.

The authors tested the hypothesis that LF PEMFs could modulate long-term corticospinal excitability in the healthy brain by applying transcranial pulsed magnetic fields with CTU Mega 20® (http://www.periso.ch/).

Fig. 1 CTU Mega 20 device. The original equipment used in the study, directly provided by PERISO SA (http://www.periso.ch/)

Modulation of long-term potentiation-like cortical plasticity in the healthy brain with low frequency-pulsed electromagnetic fields
Enrico Premi, Alberto Benussi, Antonio La Gatta et al. 2018

CONCLUSION

This proof-of-concept study in healthy subjects supports the idea that non-ionizing LF-PEMFs induced by the CTU Mega 20 diamagnetic acceleration system could represent a new approach for brain neuromodulation.

Further studies to optimize protocol parameters for different neurological and psychiatric conditions are warranted.

Modulation of long-term potentiation-like cortical plasticity in the healthy brain with low frequency-pulsed electromagnetic fields

Enrico Premi, Alberto Benussi, Antonio La Gatta et al. 2018

frontiers | Frontiers in Neuroscience

REVIEW
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Mechanotransduction: Exploring New Therapeutic Avenues in Central Nervous System Pathology

Daniela Nogueira Rocha[1,2], *Eva Daniela Carvalho*[1,2,3], *João Bettencourt Relvas*[2,4,5], *Maria José Oliveira*[1,2,6] *and Ana Paula Pêgo*[1,2,6]*

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Cells are continuously exposed to physical forces and the central nervous system (CNS) is no exception. Cells dynamically adapt their behavior and remodel the surrounding environment in response to forces. The importance of mechanotransduction in the CNS is illustrated by exploring its role in CNS pathology development and progression. The crosstalk between the biochemical and biophysical components of the extracellular matrix (ECM) are here described, considering the recent explosion of literature demonstrating the powerful influence of biophysical stimuli like density, rigidity and geometry of the ECM on cell behavior. This review aims at integrating mechanical properties into our understanding of the molecular basis of CNS disease. The mechanisms that mediate mechanotransduction events, like integrin, Rho/ROCK and matrix metalloproteinases signaling pathways are revised. Analysis of CNS pathologies in this context has revealed that a wide range of neurological diseases share as hallmarks alterations of the tissue mechanical properties. Therefore, it is our belief that the understanding of CNS mechanotransduction pathways may lead to the development of improved medical devices and diagnostic methods as well as new therapeutic targets and strategies for CNS repair.

Keywords: mechanobiology, extracellular matrix, mechanotransduction, central nervous system, neurodegenerative disorders

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Analysis of CNS pathologies in this context has revealed that a wide range of neurological diseases share as hallmarks alterations of the tissue mechanical properties. **Therefore, it is our belief that the understanding of CNS mechanotransduction pathways may lead to the development of improved medical devices and diagnostic methods as well as new therapeutic targets and strategies for CNS repair.**

RESEARCH ARTICLE

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Remote and Selective Control of Astrocytes by Magnetomechanical Stimulation

*Yichao Yu, Christopher Payne, Nephtali Marina, Alla Korsak, Paul Southern, Ana García-Prieto, Isabel N. Christie, Rebecca R. Baker, Elizabeth M. C. Fisher, Jack A. Wells, Tammy L. Kalber, Quentin A. Pankhurst, Alexander V. Gourine, and Mark F. Lythgoe**

Astrocytes play crucial and diverse roles in brain health and disease. The ability to selectively control astrocytes provides a valuable tool for understanding their function and has the therapeutic potential to correct dysfunction. Existing technologies such as optogenetics and chemogenetics require the introduction of foreign proteins, which adds a layer of complication and hinders their clinical translation. A novel technique, magnetomechanical stimulation (MMS), that enables remote and selective control of astrocytes without genetic modification is described here. MMS exploits the mechanosensitivity of astrocytes and triggers mechanogated Ca^{2+} and adenosine triphosphate (ATP) signaling by applying a magnetic field to antibody-functionalized magnetic particles that are targeted to astrocytes. Using purpose-built magnetic devices, the mechanosensory threshold of astrocytes is determined, a sub-micrometer particle for effective MMS is identified, the in vivo fate of the particles is established, and cardiovascular responses are induced in rats after particles are delivered to specific brainstem astrocytes. By eliminating the need for device implantation and genetic modification, MMS is a method for controlling astroglial activity with an improved prospect for clinical application than existing technologies.

1. Introduction

Astrocytes are a major type of glial cells in the central nervous system (CNS). They constitute an integral part of neural circuitry,[1] regulate a wide range of homeostatic processes,[2] and play key roles in the brain's defense against disease and injury.[3] Due to their extensive involvement in CNS function, astrocytes are implicated in many neurological disorders including neurodegenerative diseases,[4] epilepsy[4] and stroke.[5] In recent years, it has become possible to modulate astroglial activity with spatial, temporal and cell type specificity thanks to the advent of cell control methods such as optogenetics and chemogenetics.[6] These technological advances have not only provided better tools to study these important cells in health and disease,[4,6] but also opened new avenues for therapy development.[7–9] For example, optogenetics has been used to introduce a light-gated ion channel such as channelrhodopsin-2 (ChR2) into astrocytes and enable photostimulation of intracellular Ca^{2+} signaling and adenosine triphosphate (ATP) release, thereby helping researchers to elucidate how astrocytes regulate respiration[10] and pain sensitivity.[11] Chemogenetics involves using a designer drug to specifically activate an exogenous designer G protein-coupled receptor and it has been employed to demonstrate astroglial regulation of feeding

Journal of Neurology and Experimental Neural Science

Obando FT, et al. J Neurol Exp Neural Sci 4: 145.

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Research Article

The Effects of Low-Frequency High-Intensity Pulsed Electromagnetic Fields (Diamagnetic Therapy) in the Treatment of Rare Diseases: A Case Series Preliminary Study

Felipe Torres Obando[1,3], Pietro Romeo[2,3*], Diego Vergara[1], Federica di Pardo[3], Adriana Soto[1]

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Abstract

Rare and orphan diseases are a group of multiorgan disabilities that limit the life quality in young and adult patients, affecting the socio-economic burden for the families and the community. Despite the continuous attempts in research, no standardized and effective therapies are nowadays available. Orthosis supports and rehabilitation remain the unique possibilities to alleviate these challenging conditions. Among the emerging therapeutic odds, Pulsed Electromagnetic Fields (PEMFs) express anti-inflammatory and regenerative effects on musculoskeletal and parenchymal tissues. They have also shown intriguing properties to stimulate the central and peripheral nervous system either as Transcranial Magnetic Stimulation (TMS) and Low Frequency - High-Intensity -Pulsed electromagnetic Field (LF-HI-PEMFs) or Diamagnetic Therapy (Diamagneto-therapy). This last modulates brain plasticity and is effective in pain, reducing muscles contractures and tissue oedema. Our experience refers to the use of Diamagnetic Therapy to rare and orphan diseases and reports promising functional and behavioural results, opening the possibility of therapeutic applications integrated with conventional rehabilitative methods.

Neuron
Review

Traumatic Brain Injury and the Neuronal Microenvironment: A Potential Role for Neuropathological Mechanotransduction

Matthew A. Hemphill,[1] Stephanie Dauth,[1] Chung Jong Yu,[1] Borna E. Dabiri,[1] and Kevin Kit Parker[1,*]
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http://dx.doi.org/10.1016/j.neuron.2015.02.041

Traumatic brain injury (TBI) is linked to several pathologies for which there is a lack of understanding of disease mechanisms and therapeutic strategies. To elucidate injury mechanisms, it is important to consider how physical forces are transmitted and transduced across all spatial scales of the brain. Although the mechanical response of the brain is typically characterized by its material properties and biological structure, cellular mechanotransduction mechanisms also exist. Such mechanisms can affect physiological processes by responding to exogenous mechanical forces directed through sub-cellular components, such as extracellular matrix and cell adhesion molecules, to mechanosensitive intracellular structures that regulate mechanochemical signaling pathways. We suggest that cellular mechanotransduction may be an important mechanism underlying the initiation of cell and sub-cellular injuries ultimately responsible for the diffuse pathological damage and clinical symptoms observed in TBI, thereby providing potential therapeutic opportunities not previously explored in TBI.

PSYCHOLOGIC STRESS


CellPress

Cell Metabolism
Previews

The Link between Stress and IL-6 Is Heating Up

Justin Darcy[1] and Yu-Hua Tseng[1,2,*]

Neuroinflammation

Anxiety, Stress Disorder, Depression

PNEI

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The psycho-endocrine-neuro connection…

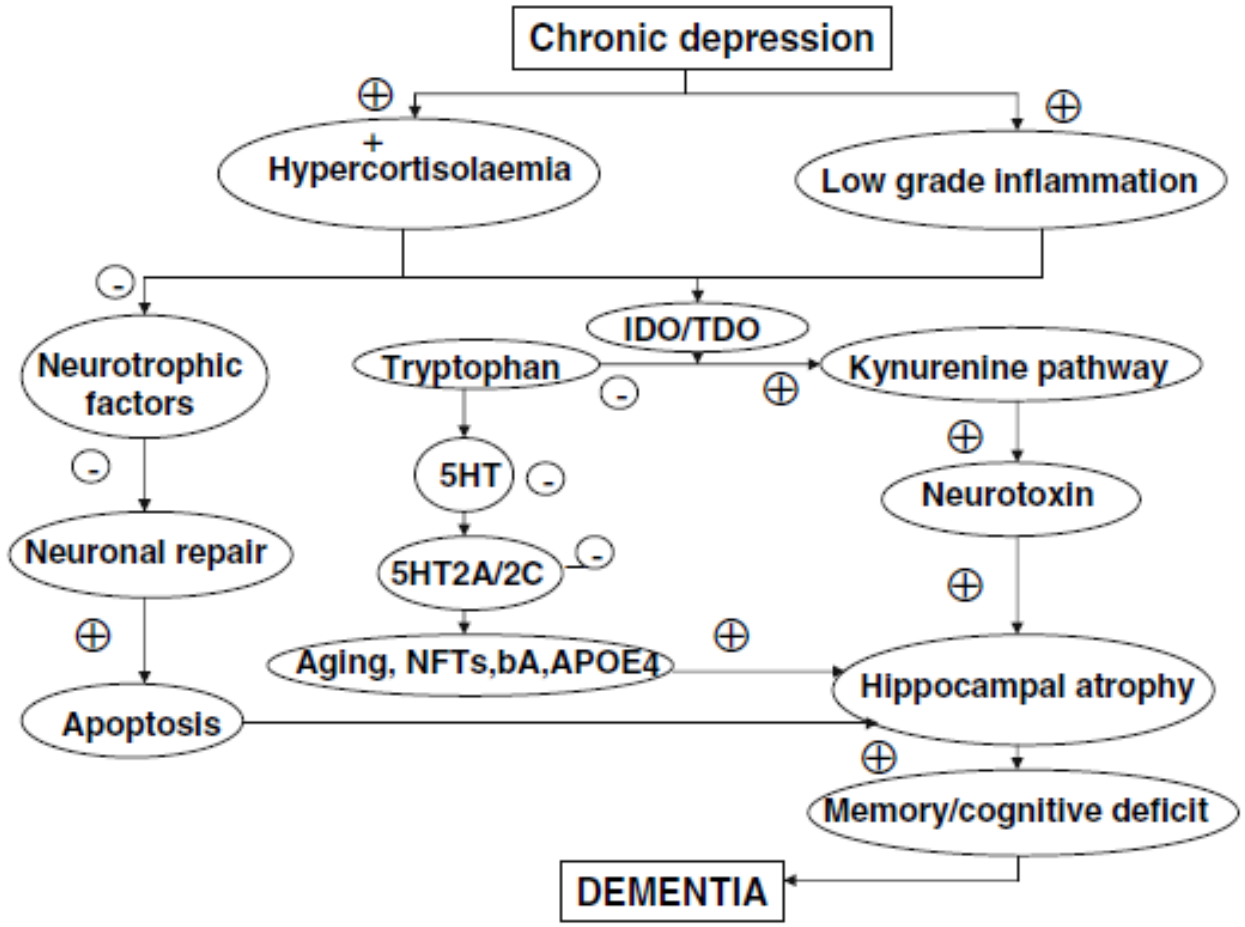

Fig. 1 Possible links between chronic depression and dementia.NFT's = neurofibrillary tangles, bA = beta amyloid, APOE 4 = apolipoprotein E4 (+) = increase; (–) = decrease

Stanford MEDICINE | News Center

Menu

Stanford Medicine / News / Study: New depression treatment effective

Experimental depression treatment is nearly 80% effective in controlled study

In a double-blind controlled study, high doses of magnetic brain stimulation, given on an accelerated timeline and individually targeted, caused remission in 79% of trial participants with severe depression.

October 28, 2021 - By Mandy Erickson

Autism Spectrum Disorder

Persistent deficiencies in social communication and social interaction in various contexts, manifested by deficiencies in socio-emotional reciprocity, in non-verbal communicative behaviors, in the development, maintenance and understanding of relationships, movements, use of stereotyped or repetitive objects or speech monotony, excessive inflexibility of routines or ritualized patterns of behavior and very restricted and fixed interests that are abnormal in terms of their intensity or focus of interest.

DSMV

Autism Spectrum Disorder

Epidemiology

2010: Autism rate was estimated at around 1-2 autistic people per 1000 people worldwide and occurred four to five times more frequently in boys than in girls.

2014: one in 68 people in the United States

2023: Approximately 1 in 100 children in the world has ASD (WHO, 2023

ETIOPATHOGENESIS

1. Inheritance
2. Psychoneuroimmunological dysfunction (oxytocin deficiency)
3. Metabolic disorders (hyperoxidation)
4. Toxic (mercury, other heavy metals¿?)
5. Dysbiosis (candida – clostridium)
6. Perivascular inflammatory process in the brain

Major Cognitive Disorder*

55 to 60 million cases in the world

60 to 70% of them correspond to Alzheimer's disease

2 to 4% hereditary family form

96 to 98% sporadic form

Three fundamental characteristics

Amyloid beta protein deposits

TAU protein deposits

Astrocyte activation-Chronic inflammation

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*Previously called dementia (DSMV)

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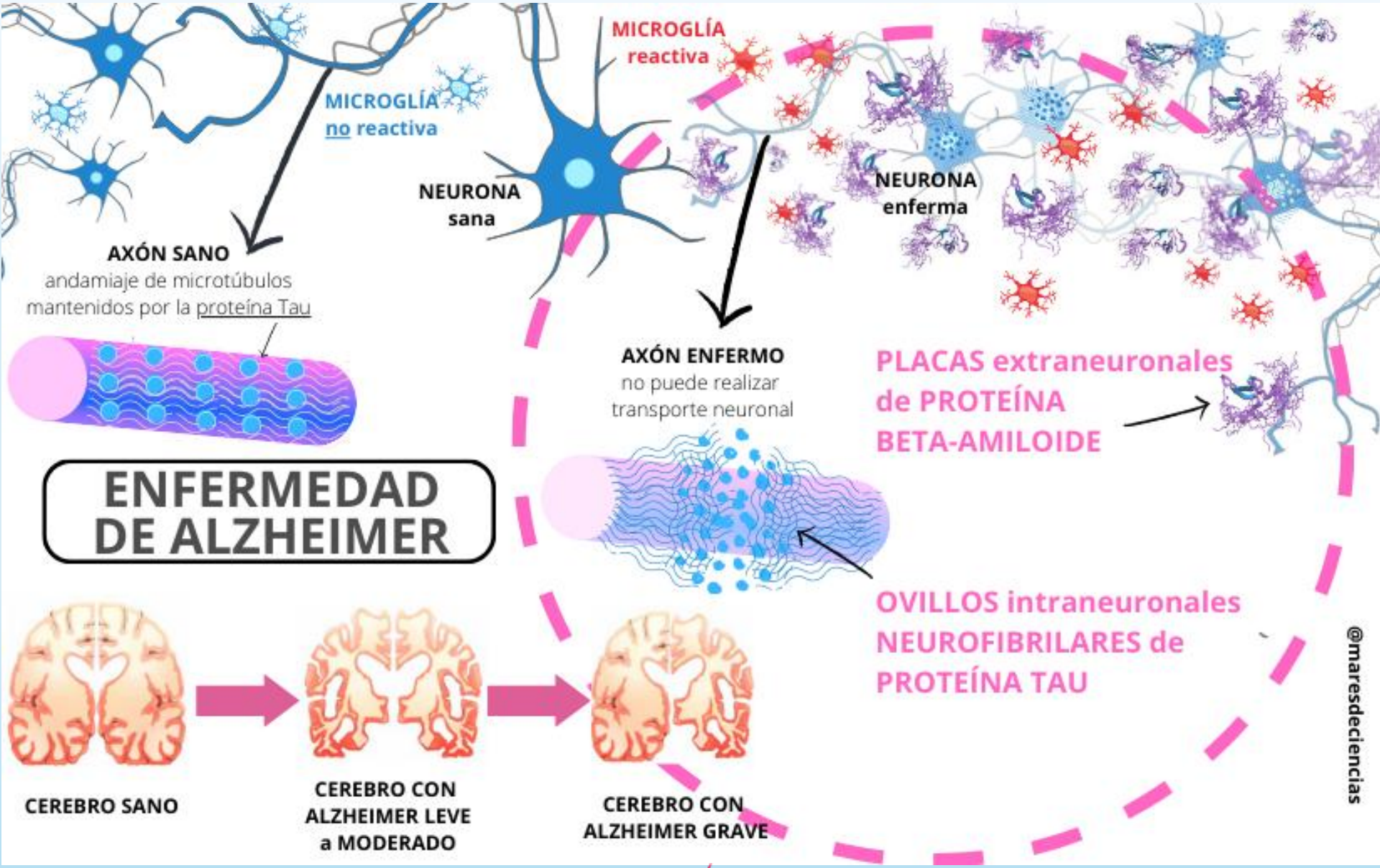
MICROGLÍA
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MICROGLÍA
reactiva
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NEURONA
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Clinical Neurophysiology

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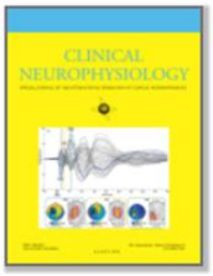


Review

Diagnostic contribution and therapeutic perspectives of transcranial magnetic stimulation in dementia

Vincenzo Di Lazzaro [a], Rita Bella [b], Alberto Benussi [c], Matteo Bologna [d, e], Barbara Borroni [c], Fioravante Capone [a], Kai-Hsiang S. Chen [f], Robert Chen [g, h], Andrei V. Chistyakov [i], Joseph Classen [j], Matthew C. Kiernan [k], Giacomo Koch [l, m], Giuseppe Lanza [n, o], Jean-Pascal Lefaucheur [p, q], Hideyuki Matsumoto [r], Jean-Paul Nguyen [s], Michael Orth [t, u], Alvaro Pascual-Leone [v, w, x], Irena Rektorova [y, z], Patrik Simko [y, aa], John-Paul Taylor [ab], Sara Tremblay [ac, ad], Yoshikazu Ugawa [ae], Raffaele Dubbioso [af, 1], Federico Ranieri [ag, 1]

Alzheimer´s Disease
In vitro and Mouse Model

Guo et al. *Zool. Res.* 2024, 45(4): 924–936
https://doi.org/10.24272/j.issn.2095-8137.2024.034

ZR | Zoological Research

Article Open Access

Rotating magnetic field inhibits Aβ protein aggregation and alleviates cognitive impairment in Alzheimer's disease mice

Ruo-Wen Guo[1,2], Wen-Jing Xie[1,3], Biao Yu[1], Chao Song[1], Xin-Miao Ji[1], Xin-Yu Wang[1,3], Mei Zhang[4], Xin Zhang[1,2,3,*]

[1] *High Magnetic Field Laboratory, CAS Key Laboratory of High Magnetic Field and Ion Beam Physical Biology, Hefei Institutes of Physical Science, Chinese Academy of Sciences, Hefei, Anhui* 230031, *China*

Animals

APP/PS1 mice are double transgenic mice expressing a chimeric mouse/human amyloid precursor protein (Mo/HuAPP695swe) and a mutant human presenilin 1 (PS1 dE9).

The APP/PS1 mice were divided into sham and 0.4 T RMF groups, with age-matched C57 mice used as wild-type (WT) controls. Starting at 2 months of age, the APP/PS1 mice were exposed to 0.4 T RMF or sham treatment for 3–6 h/day, 5 days/week (Monday–Friday, 2–11 months old, 3 h/day; 11–14 months old, 6 h/day) over a period of 12 months

Cognitive Tasks

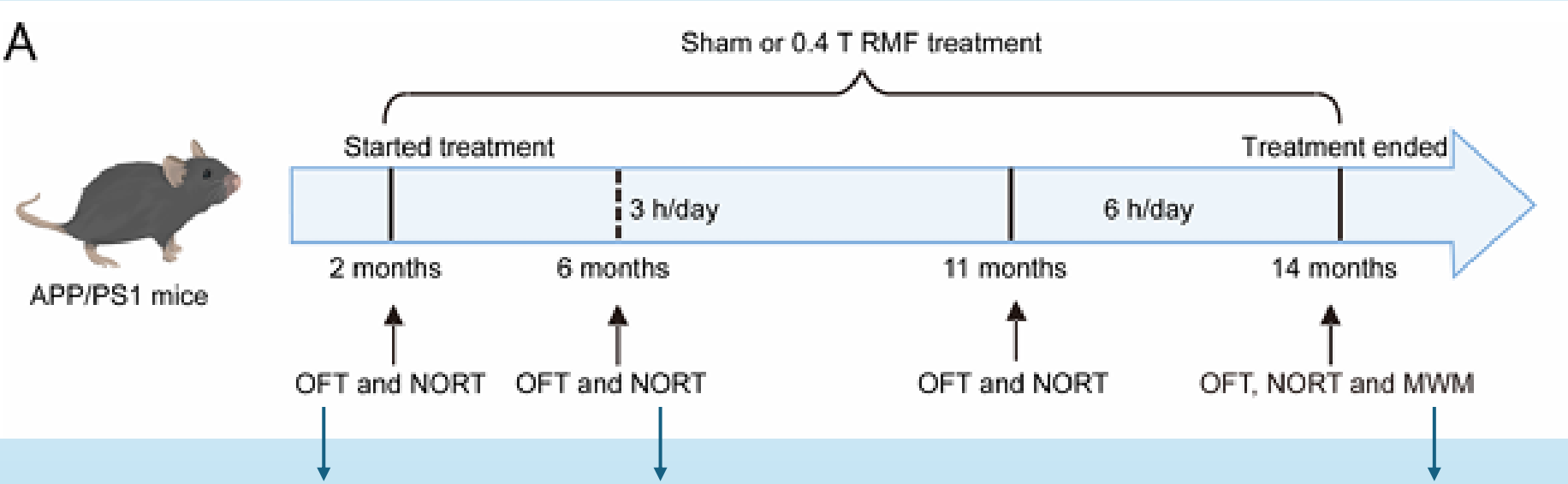
Animals were exposed to different tasks

Open field test

Novel object recognition test

Morris Water maze experiment

Timeline



Open Field Test Novel object recognition test Morris water maze (MWM) experiment

Alzheimer´s Disease
In vitro and Mouse Model

Tissue examinations demonstrated that RMF reduced amyloid plaque accumulation, attenuated microglial activation, and reduced oxidative stress in the APP/PS1 mouse brain.

These findings suggest that RMF holds considerable potential as a non-invasive, high-penetration physical approach for AD treatment.

Guo RW, Xie WJ, et al. Rotating magnetic field inhibits Aβ protein aggregation and alleviates cognitive impairment in Alzheimer's disease mice. Zool Res. 2024 Jul 18;45(4):924-936

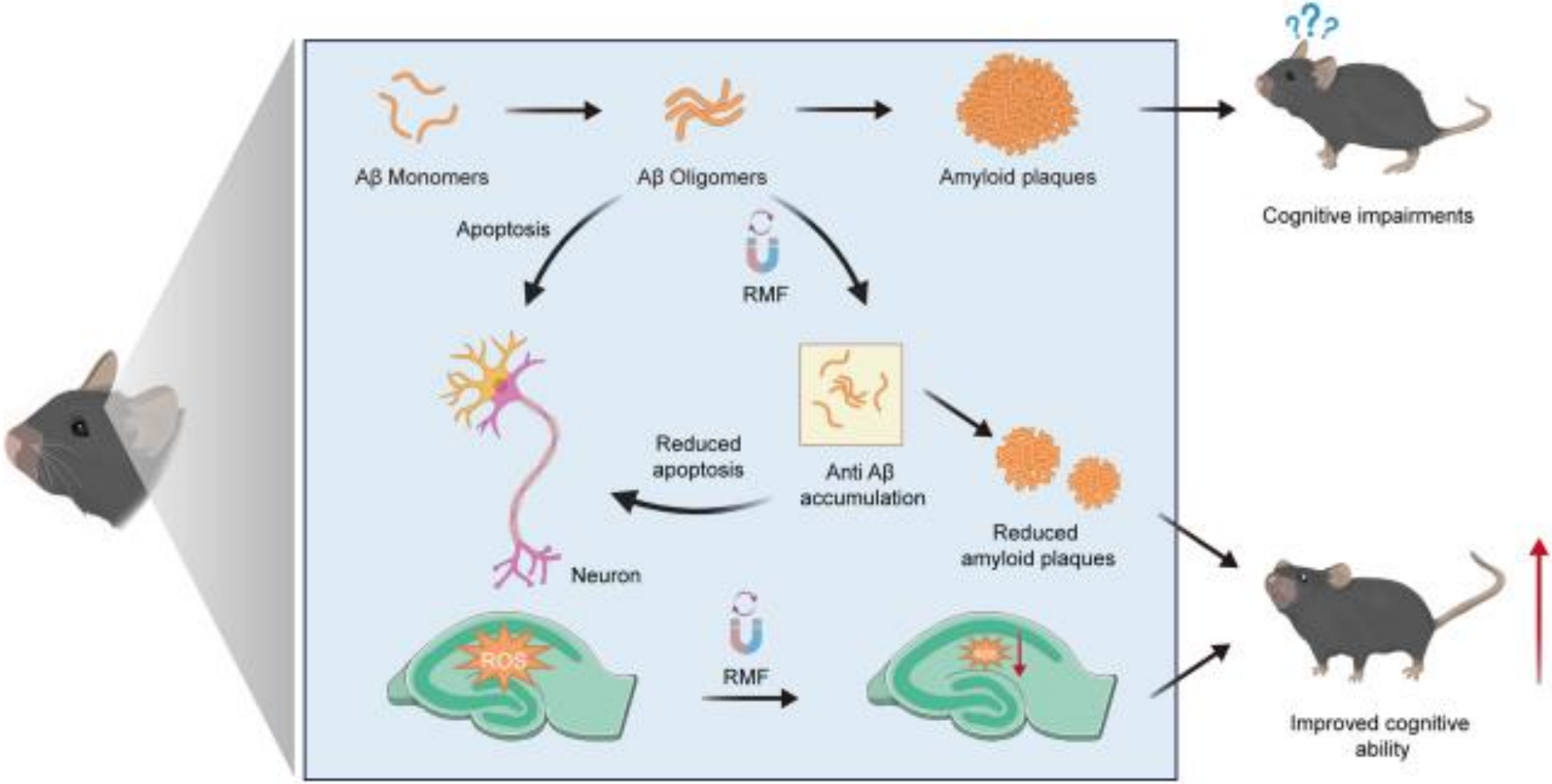


Figure 7 RMF reduces Aβ protein aggregation and alleviates cognitive impairment in AD mice

Guo RW, Xie WJ, et al. Rotating magnetic field inhibits Aβ protein aggregation and alleviates cognitive impairment in Alzheimer's disease mice. Zool Res. 2024 Jul 18;45(4):924-936

Alzheimer´s Disease
In vitro and Mouse Model

Results indicated that the RMF directly inhibited Aβ amyloid fibril formation and reduced Aβ-induced cytotoxicity in neural cells in vitro.

The mouse model APP/PS1, RMF restored motor abilities to healthy control levels and significantly alleviated cognitive impairments, including exploration and spatial and non-spatial memory abilities.

Guo RW, Xie WJ, et al. Rotating magnetic field inhibits Aβ protein aggregation and alleviates cognitive impairment in Alzheimer's disease mice. Zool Res. 2024 Jul 18;45(4):924-936

CONCLUSIONS

Diamagnetic therapy has a very important place in the treatment of different neuropsychiatric conditions.

There is a broad panorama of basic and clinical research that allows us to expand our horizons for the benefit of our patients.

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