EFFECT OF INTRACEREBRAL MAGNETOELECTRIC NANOPARTICLES ON BEHAVIORAL OUTCOMES

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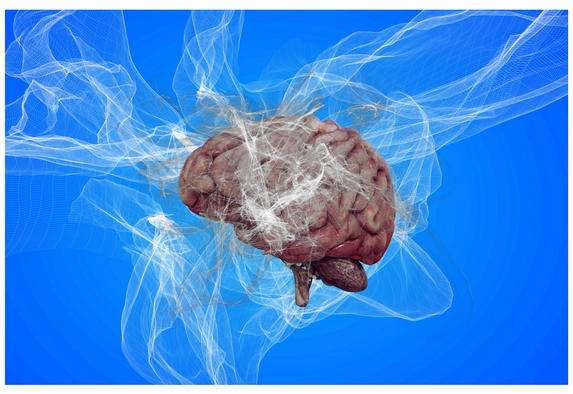
INTRODUCTION

Current neuromodulation technologies face significant limitations in terms of invasiveness, spatial precision, and long-term compatibility.

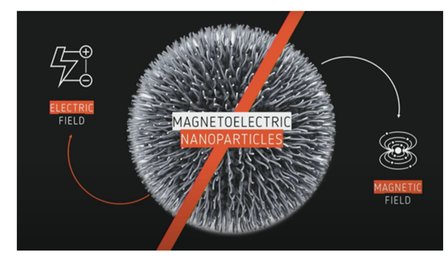
Brain stimulation has become a key therapeutic approach for conditions characterized by aberrant neural signaling, with techniques such as deep brain stimulation (DBS) and transcranial magnetic stimulation (TMS) showing clinical efficacy but still limited by their invasiveness or side effects.



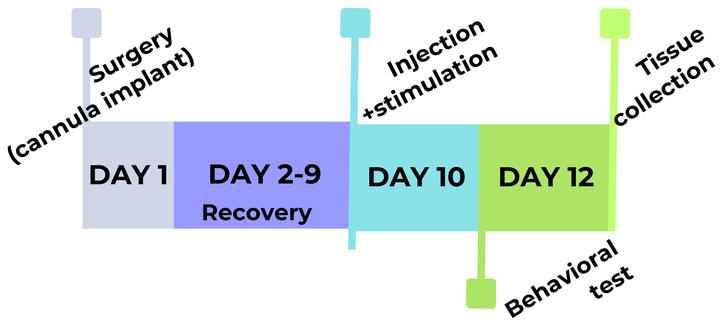
Recently developed magnetoelectric nanoparticles (MENPs) offer a promising alternative by enabling wireless and localized stimulation through external magnetic fields.
Our previous study (in preparation for publication) has demonstrated that a single 1 µg intracerebral dose of MENPs can induce motor activity and trigger intracellular calcium release, indicating neuronal activation. However, no evaluation post-anesthesia and stimulation was assessed.

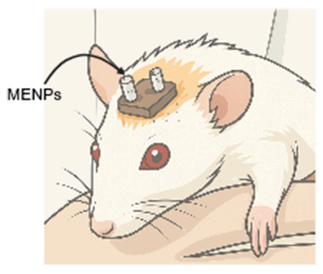
In the present study, we evaluated the behavioral and neurobiological effects of varying intracerebral doses of MENPs in a rat model.

METHODS



- $CoFe_2O_4$@$BaTiO_3$ core–shell nanoparticle (barium titanate ($BaTiO_3$) shell
- Intracerebral administration: Cannula placement on the targeted area Hippocampal Dentate Gyrus (DG)
- MENPs administration and estimulation: MENPs intracerebrally at doses 0,3, 6,12 µg dissolved in PBS, and subsequently exposed to magnetic stimulation (50 Hz freq, 20ms, 5V amplitude, 20% symmetry, 2s wait, 500 ms run, auto repeat 20 times800 Oe)
- Behavioral evaluation:
  - Locomotion: Open field (OF)
  - Anxiety: OF and Elevated plus maze (EPM)
  - Memory: Novel Object (short term 5 min & long term 24h)
- Inflammation: Microglia activation: ba1 staining: IHC 1:1000. FIJI (Image J) software

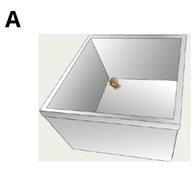


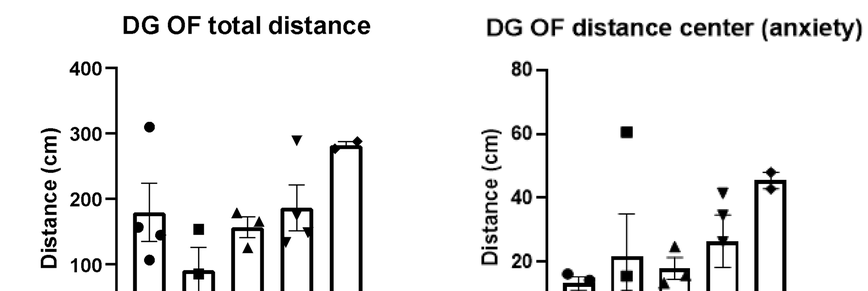


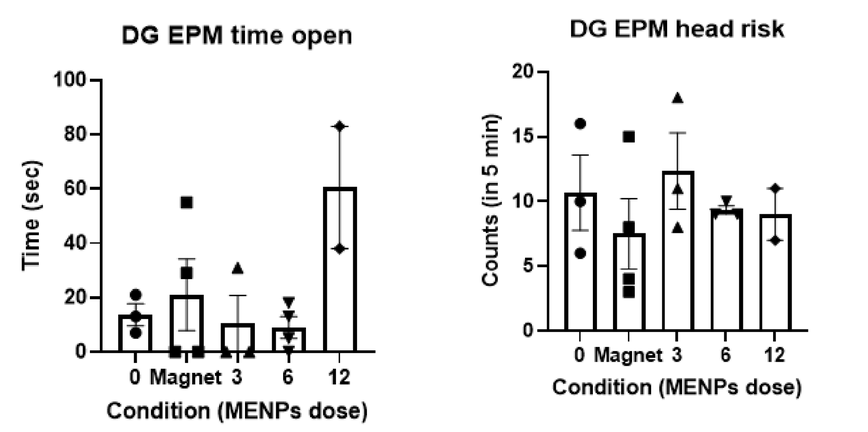
RESULTS

1. EFFECTS OF MENPS ON BEHAVIORAL PERFORMANCE

MENPs (3–12 µg) do not produce detrimental behavioral outcomes







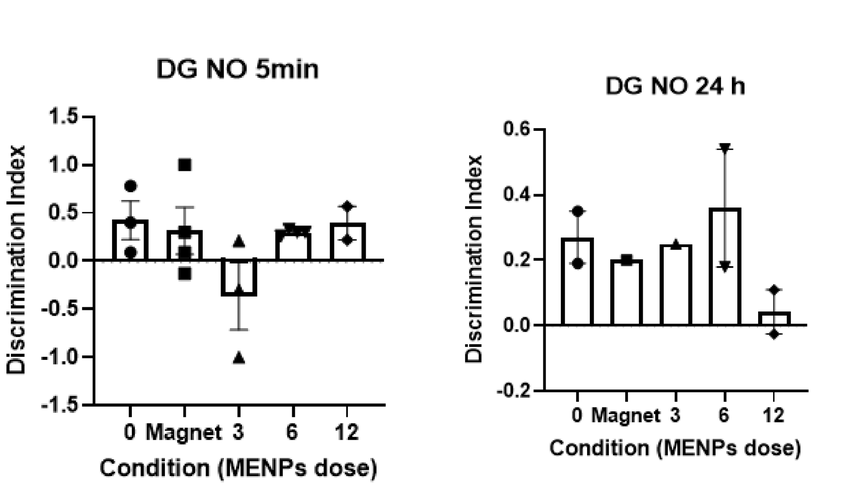
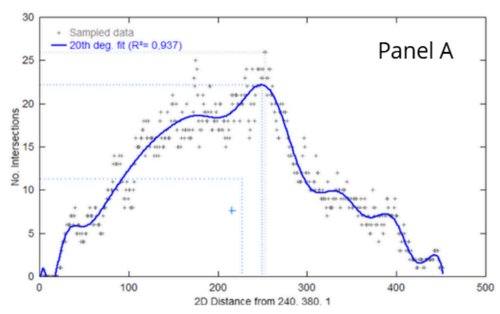


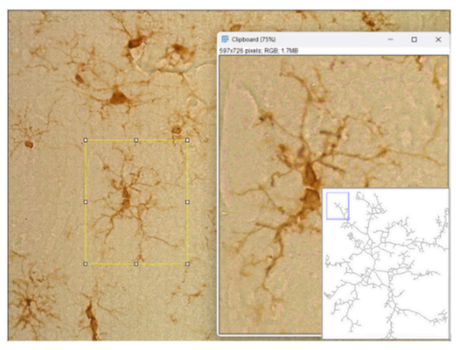
Figure 1. Behavioral performence on A) Open field (distance traveled in the total field and in the center, B) Elevated Plus Maze (EPM, time in open arms, and head risks), C) Novel Object Recognition (NO, short term and long term 24h)

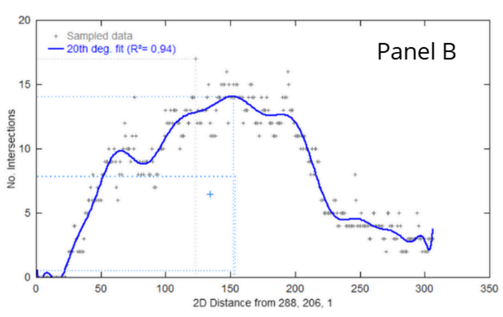
2. IMPACT OF MENPS ON INFLAMMATION (MICROGLIA STATE)

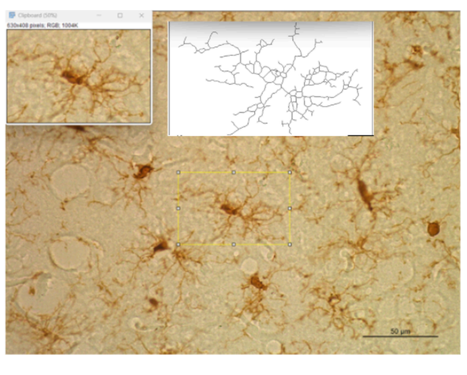
Reduced microglial activation or less neuroinflammation in the MENPs-treated group

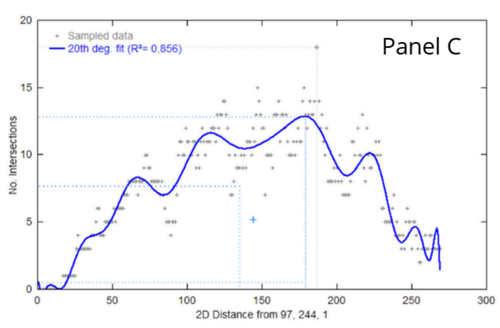
The more branched, extended morphology (increased intersections and ramification) suggests that the microglia are in a less activated state, which often correlates with lower levels of neuroinflammation.











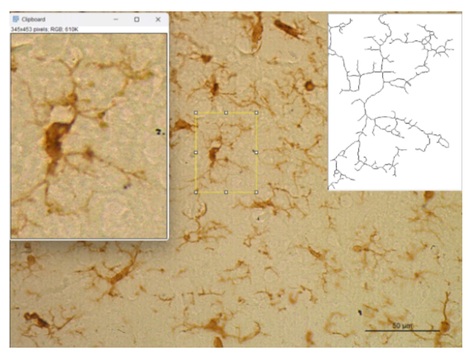


Figure 2. Representative IBA1 immunostaining and Sholl analysis data from the 12 ug (Panel A), 6 µg MENPs-treated (Panel B), 6ug and control (PBS, Panel C) condition.
The microglial cell selected for further analysis is highlighted with a yellow square. Representative quantification was performed on this cell. Sholl analysis represents the number of dendritic intersections at increasing radial distances from the cell nucleus.

CONCLUSIONS

Behavioral assays revealed no detrimental effects on locomotor activity, anxiety-like behavior, or cognitive function following MENP administration. Histological analyses showed no apoptotic cell death, suggesting excellent biocompatibility.

These results support the safety profile of MENPs and underscore their potential for future applications in non-invasive neuromodulation therapies.

MENPs may offer a novel, targeted approach for modulating brain circuits implicated in conditions such as depression, Parkinson's disease, and Alzheimer's disease (Given the role of dysregulated neural activity in psychiatric and neurodegenerative disorders)

These findings are essential for validating MENPs as a clinically viable platform for future therapeutic applications.
-->substantial translational promise, particularly in addressing dysregulated neural circuits implicated in psychiatric and neurodegenerative disorders.

MENPs enable focal modulation without requiring chronically implanted hardware or systemic pharmacological agents.

Our findings open the door to next-generation, non-pharmacological interventions with high spatial precision

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