Low Field Magnetic Stimulation (LFMS) on Proliferation and Differentiation of Oligodendrocyte Progenitor Cells

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INTRODUCTION

Low Field Magnetic Stimulation (LFMS), a neuromodulation and non-invasive therapy, has shown to produce rapid mood improvement in patients with major depressive disorder⁽¹⁾. Research showed that static magnetic field stimulation enhances oligodendrocyte differentiation by secreting neurotrophic factors⁽²⁾. Studies showed that increased levels of brain-derived neurotrophic factor and NT-3 are critical for cell proliferation^(3,4). Transforming growth factor β , TGF- β , known as a multi functional growth factor⁽⁵⁾, participates in many essential functions, including cell cycle control, regulation of early development and differentiation, neuron survival and glial differentiation. The underlying molecular mechanisms by which LFMS exerts are remained unclear. Our present data showed that LFMS increased TGF- β 1 secretion and together with the enhanced differentiation of progenitor cells to oligodendrocytes.

RESULTS

OBJECTIVES

1) Determine effects of LFMS on proliferation and differentiation of CG4 cells, a bi-potential oligodendrocyte-type-2 astrocyte (O-2A) progenitor cell line, capable of differentiating into either oligodendrocytes or type 2-astrocytes. 2) Investigate mechanisms to explain the differentiation promoting properties of LFMS.

MATERIALS AND METHODS

1. Cell culture and treatment: **LFMS**: 20 min/day at RT with 40Hz daily; **Sham**: 20 min/day at RT with no magnetic daily; 2. MTT and WST to measure cell proliferation; 3. ICC to locate the cell lineage markers; 4. ELISA to measure the cytokine levels in culture medium; 5. Western blot to show the expression levels of cell lineage markers.

Upper Figure: MTT and WST results showed the CG4 cell proliferation in growth medium (GM, proliferation status) treated with or w/o LFMS. Western blots showed changes of signaling molecules and cell lineage markers. * $p < 0.05$, *** $p < 0.001$ vs corresponding controls. ICC staining showed CG4 cells in proliferation status treated with or w/o LFMS for 48 hrs. The percentage of Ki-67 (red), GFAP (red), and Olig2 (green) positive cells vs DAPI were counted. * $p < 0.05$ vs corresponding control group.

Lower Figure: Western blots showed the early increased GFAP and later increased Olig2 expressions with LFMS treatment in CG4 cells in differentiation medium (DM). ICC showed the increased O4 positive cell number with LFMS on Day 3 and 5. * $p < 0.05$, *** $p < 0.001$ vs controls. ELISA showed the increased TGF- β 1 levels in CG4 culture medium treated with LFMS on day 1, *** $p < 0.001$, however decreased on Day 5, ### $p < 0.001$ vs corresponding controls.

Conclusions:

The present data suggested that: 1) LFMS could preferentially promote differentiation of CG4 (OPCs) cells into oligodendrocyte lineage; 2) LFMS increased TGF- β 1 secretion, when most cells were in astrocyte lineage; TGF- β 1 secretion was decreased, when cells differentiated to oligodendrocyte lineage. Further work will explore the involvement of TGF- β Smad or non-Smad pathways with LFMS treatment.

References

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