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BRAIN RESEARCH

Research Report

Short-term low intensity PMF does not improve functional or histological outcomes in a rat model of transient focal cerebral ischemia

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ABSTRACT

Stimulation with pulsed magnetic fields (PMF) is a non-invasive technique that can modulate neural activity and has the potential to facilitate functional recovery and tissue preservation/repair following brain injury. The effect of low intensity (8 mT) PMF on functional recovery and infarct tissue volume was assessed in a middle cerebral artery occlusion model of transient focal ischemia in Spontaneously Hypertensive rats. Rats received a combination of PMF protocols, including high and low frequencies and recovery was monitored over eight days. PMF treatment had no effect on functional recovery or infarct volume. Infarcted tissue accounted for ≈8% of total brain volume, encompassing both cortical and subcortical structures. The microglial and astrocytic response to PMF treatment was monitored and there was no change in glial scarring, however there was increased macrophage infiltration in animals that received chronic high (6–9 Hz) and low (1 Hz) stimulation. There was no effect of PMF on the degree of cell death observed within the ischemic core, with no TUNEL positive cells observed in the non-infarcted tissue. No detrimental side-effects of PMF were observed, indicating that low-intensity PMF may have limited safety concerns for future human and animal studies.

1. Introduction

Stroke is a cerebrovascular disorder affecting approximately 15 million individuals annually world-wide. Studies in humans and animal models have indicated an increase in brain activation in the early stages (as early as one to two weeks post-stroke in humans) following ischemic injury (Cicinelli et al., 2003; Liepert et al., 2004; Manganotti et al., 2002), potentially facilitating plastic change and remodelling to allow for functional recovery. However, the concomitant increase in inhibitory signals from the intact hemisphere may negatively influence recovery (Duque et al., 2005).

Electrical stimulation of the brain by magnetic induction has emerged as a powerful non-invasive treatment option for

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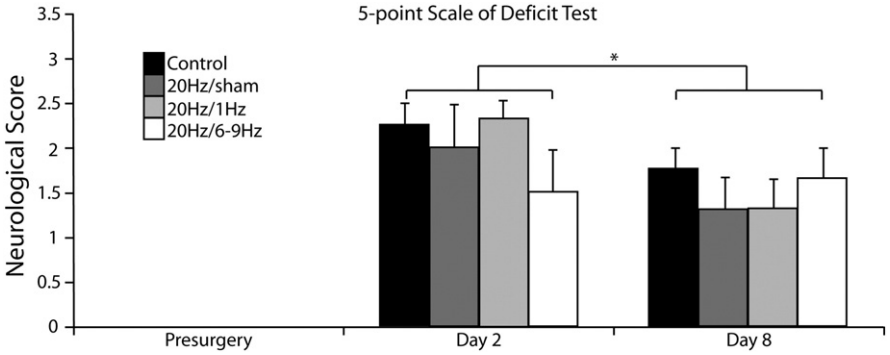

Fig. 1 – 5-point scale of deficit test. There was no significant improvement in neurological score following PMF treatment for any of the experimental groups. All groups improved over time (*p < 0.0001, repeated-measures ANOVA, data presented as mean ± SEM).

a wide variety of nervous system disorders. The most common procedure is repetitive transcranial magnetic stimulation (rTMS), which uses a strong magnetic field pulsed at determined frequencies to modify excitability of the cortex (Pell et al., 2011) In general, high frequency rTMS (≥5 Hz) has excitatory effects, whereas low frequency rTMS (≤1 Hz) reduces cortical excitability (Pell et al., 2011). Delivery of both high (Khedr and Fetoh, 2010; Khedr et al., 2010) and low (Takeuchi et al., 2008a, 2008b) frequency rTMS have been shown to improve functional outcomes following stroke, however the strength of the electrical currents induced by rTMS is close to the threshold required to induce action potentials, and thus may increase the risk of stroke patients suffering seizures and other side effects (Fauth et al., 1992; Hu et al., 2011; Rossi et al., 2008) although strict guidelines and training protocols have made them rare (Green et al., 1997; Hummel and Cohen, 2006).

Recent studies have demonstrated safety and efficacy of *low intensity* pulsed magnetic fields (PMF) in treating chronic conditions such as treatment-resistant depression (Martiny et al., 2010) and in repairing congenitally abnormal circuitry (Rodger et al., 2012). In addition, low intensity PMF is effective

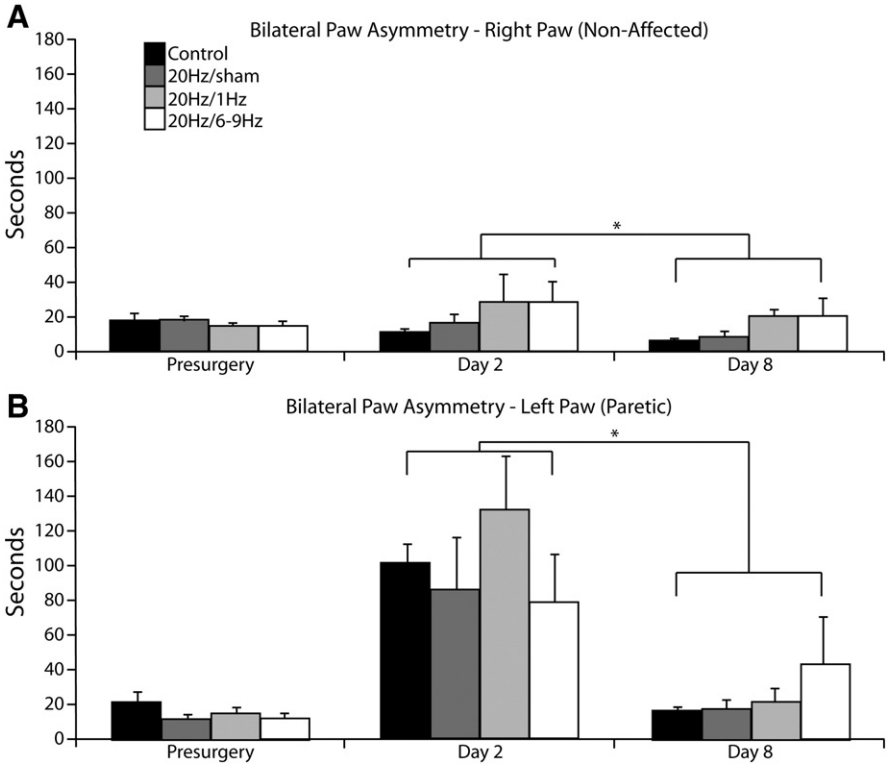

Fig. 2 – Bilateral paw asymmetry test. Both the right (A non-affected) and left (B paretic) front paws were tested. A) There was no effect of PMF treatment on performance for the right (unaffected) paw and all groups improved over time. B) The data for the left paw show a large increase in the time taken to remove the sticky label following surgery. There was no significant effect of PMF treatment found between Day 2 to Day 8, however, all groups improved over time in removing the label by Day 8 (*p < 0.0001, repeated-measures ANOVA, mean ± SEM).