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Research Report

Behavioral changes with brief exposures to weak magnetic fields patterned to stimulate long-term potentiation

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ABSTRACT

Brief whole body exposures of rats to weak (1 μT) complex magnetic fields whose patterns induce long term potential (LTP) when applied as electric current to hippocampal slices produced powerful behavioral changes. Rats exposed for 30 min before but not 30 min after hourly training sessions for spatial memory displayed impairments comparable to those elicited by complete electrode-induced saturation of hippocampal activity. Exposure to the same LTP-patterned magnetic fields after weaning during the induction of limbic seizures produced diminished learning of conditioned contextual fear during adulthood. However exposure to magnetic fields designed to simulate a "virtual" hippocampal state during acquisition of a timed inhibitory task (DRL) facilitated performance. These results show that physiologically-patterned magnetic fields can produce dramatic changes in behavior when they are applied during states associated with marked synaptic plasticity.

1. Introduction

Recent elegant experiments by Ahmed and Wieraszko (2008) showed that application of 3 s on–3 s off 15 mT magnetic fields to hippocampal slices increased the amplitude of population spikes and induced seizure-like activity. The pulsed-magnetic field (PMF)-induced amplification of population spikes involved electrical synapses and neurochemical processes in addition to those which normally mediate long term potentiation (LTP). Ahmed and Wieraszko (2008) concluded that the PMF-induced balance between different hippocampal networks might resonant differently with the applied magnetic fields. In the present series of experiments we demonstrated that whole body exposure to weak (1 μT) magnetic fields patterned after LTP-evoking stimuli for hippocampal slices (Rose et al., 1988) produced conspicuous changes in learning and memory.

One important prediction of the hypothesis that activity-dependent synaptic plasticity occurs in the hippocampus is that physiological saturation of this process should disrupt encoding of new memories (Bliss and Collingridge 1993; Chen et al., 1999; Liao et al., 1995; Lynch and Baudry 1984; McNaughton 1983; McNaughton and Morris 1987; Mellor et al., 2002; Teyler and DiScenna 1987). Repeated tetanization of a single site in the perforant pathway within the hippocampal formation can affect spatial learning; however, the direction has been variable (Castro et al., 1989; Korol et al., 1993; McNaughton et al., 1986).

During the last 15 years we have found that whole body exposures for 30 min to microTesla (μT), physiologically-patterned PMFs as "theta bursts" to induce intrinsic LTP by magnetic pulses delivered through computer software produced powerful disruptions in olfactory memory traces (Stewart, 2000), fear-conditioned analgesia (Stewart and Per-

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singer, 2000), conditioned fear to context (McKay et al., 2000) and spatial association (Delparte and Persinger, 2007).

The hippocampus contributes significantly to all of these behaviors. In the McKay et al. (2000) experiments that measured the strength of contextual fear conditioning, rats exposed to intensity-matched 7 Hz or 20 Hz sine wave magnetic fields did not differ from sham field controls. Only exposure to LTP-patterned magnetic fields resulted in marked attenuation of these behaviors. This treatment accommodated 75% of the variance in the scores for "freezing" (immobility) to contextual stimuli.

Whole body exposures of rats to appropriately-patterned 1 μT magnetic fields elicited analgesia (Fleming et al., 1994; Martin and Persinger, 2003; Martin et al., 2004a,b), comparable to 4 to 5 mg/kg of morphine. The effect was attenuated with naloxone (Martin et al., 2004b), synergized by agmatine, or enhanced by the alpha-2 agonist clonidine in a dose-dependent manner (McKay and Persinger, 2003). The analgesic effects emerged only after 15 min of exposure and were clearly evident after 30 min of exposure (Martin et al., 2004b). Similar patterns applied within the mT range produced analgesia in snails that was diminished by mu-receptor antagonists (Thomas et al., 1997). Del Seppia et al. (2007) have recently published a thorough review of that literature.

In unpublished molecular signaling experiments Buckner et al. (2008) showed that the same frequency-modulated magnetic field pattern that produced analgesia in rats (Martin et al., 2004a,b) and snails (Thomas et al., 1997) and induced "spontaneous" seizures in limbic epileptic rats (Persinger and Belanger-Chellew, 1999) affected cAMP and inhibited cell growth in various cell cultures after 3 daily exposures to 1 μT intensities. The effect was conspicuous when the daily exposures were 30 min but not 15 min and approached asymptote when daily exposures were 60 min. The temporally-reversed presentation of the same magnetic field pattern did not produce this effect. Similar anisotropic temporal effects were noted for the complex cognitive experiences reported by human subjects when these fields with similar intensities were applied transcerebrally across the temporal lobes of human volunteers (St-Pierre and Persinger, 2006).

In our research we have assumed that the effectiveness of these weak physiologically-patterned magnetic fields is increased within biological systems during heterostasis such as learning or seizure induction. We consider periods of marked synaptic activity and plasticity as manifestations of heterostasis. Wallenstein and Hasselmo (1997) have shown functional transitions between epileptiform-like activity and associative memory in the CA3 region of the hippocampus. The model of Sandblom and Galvanovski (2000) indicates that stochastic cellular systems absorb weak low frequency magnetic fields resulting in enhanced signal detection in ion channels and calcium oscillators. Voltage-gated calcium channels in cell cultures have been affected by the brief application of extremely low frequency magnetic fields (Morgan-Valle et al., 1998).

We report here that whole body exposure to a physiologically-patterned magnetic field, known to induce LTP in hippocampal slices when applied as electric currents (Rose et al., 1988), interfered with the acquisition of a water maze with the same magnitude of effectiveness as direct, current-induced depolarization (Moser et al., 1998). Simultaneous exposure to this field during post-weaning seizure induction also resulted in long-term deficits in contextual fear learning. LTP is necessary for this form of associational learning. However, rats acquiring an operant task requiring timed-inhibition of responding displayed enhanced performance when the field was applied *during* this behavior.

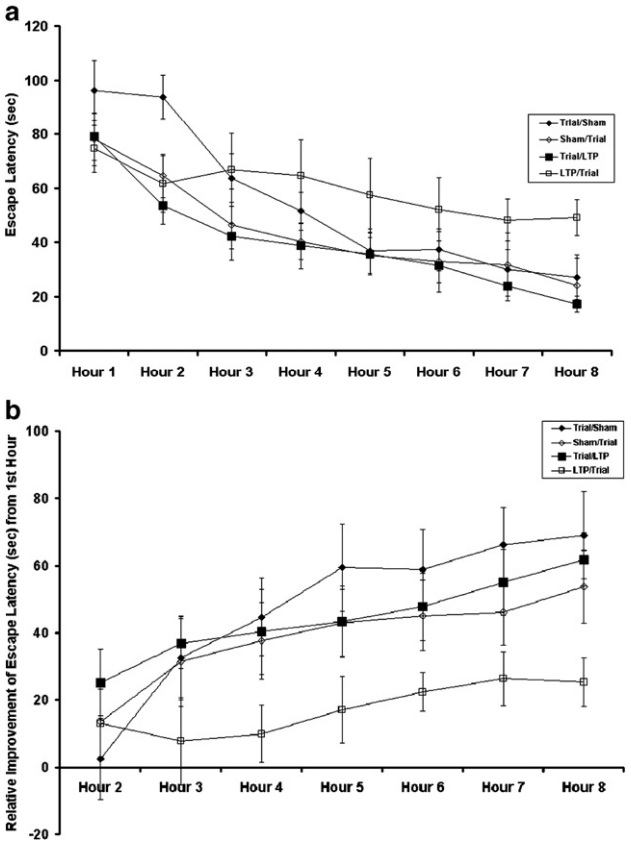

Fig. 1 – Latencies in seconds over hourly trials for rats to escape from a water maze as a function of exposure for 30 min before or after the trials to a LTP-patterned magnetic field or to a sham condition for the same periods. (a) Raw score escape latency for the four groups ($n=36$; 9/group) for each of the 8 trials, (b) The relative time of improvement (in seconds) over the subsequent 7 h compared to the first hour (trial) for rats from the four conditions. The rats receiving the LTP-patterned magnetic field before each trial (dark square, Trial/LTP) effectively did not learn as indicated by the flat slope. Vertical bars indicate standard errors of the mean.

2. Results

2.1. *Simulation of interference of maze learning by electrode saturation with whole body LTP-patterned magnetic fields*

We replicated the exact behavioral testing of Moser et al. (1998) except that we substituted the direct current-induced saturation by electrodes with whole body (non-invasive) exposure to