Title:

Chronic pulsed magnetic field (PMF) stimulation in mice

Species:

Mouse (Mus musculus)

Purpose:

Pulsed magnetic field stimulation (PMF) is a non-invasive technique that utilises magnetic fields to modulate the electrical activity of the brain. For these experiments, a pulse generator is used to deliver PMF (i.e. the PMF device). The PMF device emits a rapidly changing magnetic field that induces electric fields in brain tissue that are proportional to the strength of the emitted magnetic field. This in turn can cause activity in specific or general parts of the brain. This procedure outlines the protocol for conducting PMF at any waveform (to be determined by each user and programmed into the pulse generator as described below), for the purpose of delivering chronic PMF treatment. This PMF treatment can be delivered once daily for longer than two days and is therefore termed “chronic”. Magnetic stimulation is applied at a short distance above the head and no direct physical contact between the stimulating coil and the animal is required.

Linked SOPs:

UWA ACS approved SOP: Handling of the mouse

Definitions:

Hz- Hertz, the SI (International System of Units) unit of frequency defined as the number of cycles per second of a periodic phenomenon i.e. magnetic pulses, such that 1Hz is equivalent to 1 cycle per second.

PMF- pulsed magnetic field
**Description of Procedure:**

**Animals must be habituated to handling and to the coil at least 4 days prior to the onset of PMF**

1. The appropriate smart card, programmed to deliver the desired waveform is inserted into the pulse generator.
2. The pulse generator is switched on and a final function check is conducted by placing the coil in front of an Ultrasonic Detector, which converts magnetic pulses into audible pulses that can be heard from the speaker, verifying the presence of the magnetic field.
3. The animal is removed from its home cage, as per techniques outlined in the *Handling of the mouse* SOPs.
4. The experimenter holds their forearm flat over a bench surface in parallel with the floor or bench surface.
5. The animal is placed on the forearm of the experimenter, facing towards the elbow, with the base of the tail held firmly between the fingers by the same hand to prevent the animal from falling off the arm. The pressure should be firm, but gentle enough to allow the animal to explore the experimenter’s arm (i.e. small movement, sniffing etc.), whilst providing enough of a grip to prevent falls.
6. The stimulation coil attached to the pulse generator is held over the head of the mouse, immediately above the target eye or brain structure (will depend on the experiment). Magnetic stimulation is delivered over a period of 10 minutes.
7. The animal is returned to its home cage, as per techniques outlined in the *Handling of the mouse* SOPs.
8. The experimenter removes gloves and is to use a fresh pair for each animal to be handled.
9. After the last animal has been stimulated, a final function test of the coil is performed, the coil is wiped clean with facial tissue lightly sprayed with 70% ethanol and the pulse generator is switched off.

**Sham/control animals**

1. Sham/control animals are handled and ‘stimulated’ in the same fashion as treatment animals except that the stimulating coil does not produce the magnetic field. This is achieved by either using a sham coil (coils configured such that no magnetic field is produced) or by having the pulse generator switched off.

**Precautions - Health and Safety Considerations**

- Animals must be handled by trained personnel to avoid injury to both the animal and handler.
- Facility zone specific equipment must be worn
- Care must be taken when working with electrical equipment
- Current “Permission to use animals (PUA) authority at The University of Western Australia
- Valid tetanus immunisation
- Current AEC approval for research involving animals
Animal Welfare Risks:

There are no obvious behavioural responses to PMF stimulation in mice. The main welfare concern is that animals are appropriately handled and habituated to handling during stimulation. Potential negative effects of PMF stimulation on mice can be extrapolated from human studies. The safety of PMFs is supported by over a decade of research in human clinical trials. The intensity of the PMFs delivered is quoted either in terms of Tesla (magnetic field strength) or by the motor threshold (intensity required to elicit a motor response). Based on human studies and intensities commonly used in animal studies, the safe upper limit for stimulus intensity is 2T and the upper limit for frequency 20Hz (Gao et al. 2010; Gersner et al. 2011). However, if stimulation is delivered at an intensity below motor threshold (lower than approximately 500mT), there is no recommended upper limit to the frequencies that can be delivered. We therefore propose the following safety limits in mice that may be revised as further research is carried out:

<table>
<thead>
<tr>
<th>Intensity range</th>
<th>Maximum frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5-2T</td>
<td>20Hz</td>
</tr>
<tr>
<td>&lt;0.5T</td>
<td>unlimited</td>
</tr>
</tbody>
</table>


Equipment:

- Pulse generator with programmable card
- Ultrasonic Detector
- Coil
- Timer
- 70% ethanol
- Facial tissue

Substances to be administered, if relevant:

<table>
<thead>
<tr>
<th>Drug name (generic name, not trade name)</th>
<th>Dose rate (mg/kg body weight)</th>
<th>Route</th>
<th>Timing of administration and frequency (eg. 90 minutes pre-operative, to induce anaesthesia, during procedure, at specific intervals during the procedures)</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td></td>
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</tbody>
</table>
**References:**

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Title</th>
<th>Year</th>
</tr>
</thead>
</table>

**Applicant’s Name: Title, First name, Last name**

| A/Prof Jenny Rodger and A/Prof Kristyn Bates |

| I give permission for this SOP to be made available for general use | YES [X ] | NO [ ] |

| Applicants Signature: | Date: |