Physiology & Behavior 92 (2007) 741–747

Rats avoid high magnetic fields: Dependence on an intact vestibular system

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Received 30 September 2006; received in revised form 22 May 2007; accepted 23 May 2007

Abstract

High strength static magnetic fields are thought to be benign and largely undetectable by mammals. As magnetic resonance imaging (MRI) machines increase in strength, however, potential aversive effects may become clinically relevant. Here we report that rats find entry into a 14.1 T magnet aversive, and that they can detect and avoid entry into the magnet at a point where the magnetic field is 2 T or lower. Rats were trained to climb a ladder through the bore of a 14.1 T superconducting magnet. After their first climb into 14.1 T, most rats refused to re-enter the magnet or climb past the 2 T field line. This result was confirmed in a resistive magnet in which the magnetic field was varied from 1 to 14 T. Detection and avoidance required the vestibular apparatus of the inner ear, because labyrinthectomized rats readily traversed the magnet. The inner ear is a novel site for magnetic field transduction in mammals, but perturbation of the vestibular apparatus would be consistent with human reports of vertigo and nausea around high strength MRI machines.

Keywords: Inner ear; Labyrinthectomy; Magnetic resonance imaging

1. Introduction

Increased resolution in magnetic resonance imaging (MRI) requires the use of high strength static magnetic fields (MFs): MRI machines with 8 tesla (T) magnets are now in use for human imaging [1], and up to 11.7 T has been employed for experimental animal imaging [2]. While it has been reported that many vertebrates can detect or orient to earth-strength MFs of ~50 μT, the sensory effects of high MF on mammals are largely unknown. As the MFs used in clinical and experimental MRI get stronger, the possibility of aversive sensory effects becomes more relevant. Indeed, engineers working with 4 T magnets reported a significant occurrence of nausea and vertigo in the vicinity of the magnets [3], and vertigo has been reported after head movements within 7 and 8 T magnets [1].

There has been little evidence that rodents are affected by 2 T or lower MFs [4–9]. We have previously found, however, that exposure to MFs of 7 T and above induced clear behavioral and neural effects. Immediately after restraint for 10 min or longer within high field magnets, rearing in an open field was suppressed and the rats walked in tight circles for up to 2 min; the direction of circling was dependent on the orientation of the rat within the magnet field [10]. When rats drank a novel sweet solution prior to MF exposure, they acquired a conditioned taste aversion such that they subsequently avoided drinking the solution [10,11]. At the neural level, MF exposure induced c-Fos, an immediate-early gene product frequently used as a marker of neuronal activity, in vestibular and visceral relays of the brainstem [12]. Taken together, these results suggested that MF exposure was an aversive stimulus, possibly akin to motion sickness due to vestibular perturbation.

Although rats show effects of high MF exposure in the minutes and days after restraint within magnets, it is not clear if rats can immediately perceive a high MF during exposure and alter their voluntary behavior based on MF detection. To determine if rats acutely perceive a MF as an aversive stimulus, we trained rats on a task that required voluntary entry and traversal of a 14.1 T MF.

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0031-9384/$ - see front matter
doi:10.1016/j.physbeh.2007.05.062

Our approach was similar to that of Weiss et al. (1992), who observed that rats avoided entering the arm of a T-maze which extended into the horizontal bore of a 4.5 T electromagnet.

Here we confirm and extend the observations of Weiss et al. by showing that rats trained to ascend a vertical “ladder” will avoid entering the bore of either a 14.1 T superconducting magnet or a large resistive electromagnet ramped up to 14 T. We also demonstrate using chemical labyrinthectomy that the inner ear is required for rats to learn an avoidance of the high MF. These results suggest that the mechanism of MF detection and avoidance requires an interaction of the MF and the peripheral vestibular apparatus.

2. Materials and methods

Two magnets located at the US National High Magnetic Field Laboratory (NHMFL) were used in this study: a superconducting 14.1 T NMR magnet and a resistive 20 T magnet.

2.1. Superconducting 14.1 T NMR magnet

A 600 MHz high resolution superconducting NMR magnet (Magnex Scientific, Ltd, Abingdon, England) was used in experiments 1 and 3. The magnet had an 89 mm bore and a fixed maximum field strength of 14.1 T at its center (B_0). The magnet contained shim magnets extending along the bore for approximately ±15 cm from the core, which were used to stabilize the MF and to give a central core field of uniform strength. The MF was orientated vertically with the positive pole at the top of the magnet. The magnets were operated without radiofrequency pulses, exposing rats to only static MFs.

To map the gradient of the magnet field along the vertical axis of the bore, a copper coil was pulled through the magnet at a constant speed [13]. As it ascended through the bore of the magnet, the current induced in the coil by the MF was recorded every 1 mm. The current measurements were integrated and calibrated with the peak field strength of the magnet to calculate the MF at all vertical positions (see Fig. 1B).

2.2. Resistive 20 T magnet

A large resistive magnet at the NHMFL was used in experiment 2 to test ladder-climbing at increasing field strengths (0–14 T) within a single magnet [15]. Direct current of up to 40 kA at 500 V (20 MW) is passed through copper coils, resulting in vertically-oriented, static MFs of up to 20 T. The field strength falls off rapidly with distance, so that when the field is 20 T in the center of the magnet, the field is near 0 T at 2 m distance from the center. The distribution of the MF produced by this resistive magnet is very similar to the field produced by the 14.1 T superconducting magnet [14].

2.3. Ladder

A ladder was constructed out of a 1.25 cm^2 plastic mesh rolled into a vertical cylinder 8 cm in diameter and 2.2 m in height. Two plastic boxes (30 cm wide × 15 cm deep × 20 cm tall) were connected to the bottom and top ends of the cylinder: a start box at the bottom and a goal box at the top. Sliding plastic doors at the juncture of the boxes with the ladder controlled access to the ladder.

2.4. Animals and training

Adult female Sprague–Dawley rats (175–200 g; Charles River, Wilmington, DE) were individually housed in polycarbonate, solid-bottom cages under a 12-h light, 12-h dark cycle in the temperature-controlled animal facility of the NHMFL. Rats had *ad libitum* access to water but were maintained on a food restriction schedule at 85% of their starting body weight.

Rats were trained early in the light period prior to their daily feeding time. The rats were trained to exit the start box at the bottom of the ladder, climb the ladder, and enter the goal box, which contained a palatable food reward (a mash of 70 g powdered rodent chow mixed with 14 g sucrose, 40 g chocolate syrup and 70 ml distilled water). Each day at the start of training, rats were placed for 1 min in the goal box at the top of the ladder and allowed to eat the food reward. They were then removed from the goal box and placed in the start box at the base of the ladder. Most rats climbed the ladder spontaneously; rats that did not start to climb the ladder within 1 min were given access to the food reward in the goal box again before returning to the start box. After rats reached the goal box, they were allowed to consume the food reward for 1 min before beginning the next trial.

Rats were given 5 climbing trials each day for 10–14 days, until all rats reached the goal box on all 5 trials within 1 min or less after exiting the start box. Rats that refused to climb to the goal box on all 5 trials by the fifth day of training were excluded. On the last few days of training, a 2-m long cardboard tube (the “sham-magnet”) was placed around the mid-section of the ladder to simulate the passage through the darkened bore of the superconducting NMR magnet. Rats readily climbed the ladder, and after several days would complete 5 consecutive trials with climb times of 10–60 s.

2.5. Experiment 1. Climbing a ladder through a 14.1 T magnet

Rats ($n = 8$) were trained to climb the ladder as above; 4 other rats failed to climb consistently on 5 consecutive trials per day and so were excluded from the study. The rats were tested on 3 consecutive days. On each day, rats ran 5 trials (each 3 min or less) and their climb time was recorded. Rats were run in 5 trials to be consistent with their training protocol, and to observe any differences in climb time across trials. If a rat did not leave the start box or if it started to climb the ladder but did not reach the goal box within 3 min, the trial was terminated and assigned a climb time of 180 s.

On the first day (pre-sham), the ladder was extended through the cardboard “sham-magnet” tube. On the second day, the ladder was inserted through the vertical bore of the 14.1 T superconducting magnet (see Fig. 1A). The rats began climbing from the start box at floor level, where the fringe field was 0.05 T. Rats were given 5 trials to reach the goal box above the magnet