Suppression of drinking by exposure to a high-strength static magnetic field

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Abstract

High-strength static magnetic fields of 7 T and above have been shown to have both immediate and delayed effects on rodents, such as the induction of locomotor circling and the acquisition of conditioned taste aversions. In this study, the acute effects of magnet field exposure on drinking were examined. Exposure to a 14.1-T magnetic field for as little as 5 min significantly decreased the amount of a glucose and saccharin solution (G+S) consumed by water-deprived rats over 10 min. The decreased intake could be accounted for largely, but not entirely, by an increase in the latency of magnet-exposed rats to initiate drinking. When intake was measured for 10–60 min after the initiation of drinking, thus controlling for increased latency, magnet-exposed rats still consumed less G+S than sham-exposed rats. The increased latency was not due simply to an inability of magnet-exposed rats to reach the elevated sipper tube of the G+S bottle, providing rats with long tubes that could be reached without raising their heads normalized intake but latency was still increased. The increased latency and decreased intake appeared to be secondary to somatic effects of magnet exposure, however, because during intraoral infusions magnet-exposed rats consumed the same amount of G+S with the same latency to reject as sham-exposed rats. The suppression of drinking by magnetic field exposure is consistent with the acute effects of other aversive stimuli, such as whole-body rotation, on short-term ingestion. These results add to the evidence that high-static strength magnetic fields can have behavioral effects on rodents.

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1. Introduction

High-strength static magnetic fields from 2 T to 8.4 T are found in clinical and experiment magnetic resonance imaging (MRI) machines for use on humans, and up to 11.7 T in experimental MRI machines for in vivo animal imaging. While static magnetic fields are believed to be non-invasive and benign, there have been reports of vertigo and nausea in humans associated with exposure to 4 T and above [1,2].

Using superconducting NMR magnets and resistive magnets, we have characterized several effects of exposure to static magnetic fields of 7 T and above in rodents. These effects include: (1) The activation of neurons within the visceral (e.g. nucleus of the solitary tract and parabrachial nucleus) and vestibular (e.g. medial vestibular and prepositus nuclei) nuclei in the brainstem as measured by c-Fos immunoreactivity [3]. (2) The induction of tight locomotor circling (i.e. rapidly walking head-to-tail with a diameter of a body length or less) and suppression of rearing for several minutes after magnetic field exposure [4]. (3) The acquisition of a conditioned taste aversion (CTA) after the pairing of a sweet taste solution with magnetic field exposure [4,5].

These results indicate that the magnetic field may interact with the vestibular system of the rat; the induction of a CTA further suggests that magnetic field exposure is aversive to rats. While magnetic field exposure can act as the unconditioned stimulus in the acquisition of a CTA against a novel sweet solution, the expression of a CTA as seen days after exposure is an indirect measure of the magnetic field’s effect. A more direct measure of an aversive effect is the acute effect of stimulus pre-exposure on ingestion in the rat. Although there are exceptions [6–8], many agents that can serve as unconditioned stimuli for long-term CTA acquisition can also suppress ingestion acutely.
For example, relevant to the apparent interaction of magnetic fields and the vestibular system, whole-body rotation acutely suppresses drinking and feeding in rodents as well as inducing CTA [9–12].

Therefore, in this study, water-deprived rats were restrained within the bore of a 14.1 T superconducting NMR magnet, and intake of a palatable glucose–saccharin solution in the minutes immediately after exposure was measured. We found that a reduction in drinking was an unconditioned effect of magnetic field exposure on ingestion.

Furthermore, the results of the first three experiments suggested that magnetic field exposure decreased drinking by inhibiting the initiation of drinking, perhaps because of postural or locomotor after-effects of exposure. Therefore, in the fourth experiment, the G+S solution was delivered to rats through intraoral catheters to measure intraoral intake after magnet exposure. Because ingestion of an intraoral infusion depends only on the ability of the rat to swallow (or reject) the infusate, intraoral infusions are frequently used (e.g. [13,14]) to dissociate effects on ingestion that depend on the activity, orientation and approach of the whole animal (i.e. appetitive behaviors) from effects on reflex-like orofacial responses to the palatable stimuli (i.e. consummatory actions) [13,15,16]. We show below that intraoral intake is unaffected by magnetic field exposure, indicating that the reduction in drinking is mediated by appetitive effects (e.g. effects on locomotion, orienting or posture).

2. Methods

2.1. Animals

Adult male Sprague–Dawley rats (175–200 g, Charles River) were individually housed at 25 °C under a 12:12 light/dark cycle with ad lib access to Purina rodent chow and water except as noted. All procedures were conducted in the first half of the lights-on period. Five days prior to the test day, the rats were placed on a water deprivation schedule under which they received daily water access in one drinking session. The initial session was 3 h in length and the session times were diminished each day so that the day before testing the rats received their water in a 10-min session. The water restriction schedule ensured that rats would show a reliable and robust drinking response even in the middle of the lights-on period after 30-min restraint, consistent with our previous studies [4,17].

2.2. Magnet exposure

The magnet exposures were done in a 14.1-T magnet was a 600 MHz Magnex Cryo magnet with a bore of 89 mm diameter and a fixed field strength of 14.1 T. The magnet contained shim magnets extending along the magnet bore for approximately ±15 cm from the magnet core, which were used to stabilize the magnetic field and to give a central core field of uniform strength. The magnetic field was orientated vertically so that the positive pole was at the top of the magnet. The magnet was operated without radiofrequency pulses, so rats were exposed to only static magnetic fields.

In order to expose the rats in the vertical bores of the magnet, rats were placed individually into a Plexiglas restraining tube that had an inside diameter of 56 mm and an outside diameter of 64 mm. A plug was inserted into the rostral end of the tube and held in position by nylon screws. The inside of this rostral plug was fabricated in a cone shape to accommodate the head of the rat. A 1-cm hole was bored in this plug at the apex of this cone to allow fresh breathing air. A second plug was inserted into the caudal end of the tube and could be adjusted to restrain the movement of the rat. A hole in the center of this plug accommodated the rat’s tail. When in the tube, the rat was almost completely immobilized. Individual restrained rats were carried from the animal facility to the superconducting magnet (~50 m distance). The restrained rat was inserted into the bottom of the vertical bore of the magnet and raised until the head of the rat was in the center of the magnetic field. Rats remained in the bore of the magnet for 1–30 min.

To control for restraint and handling, sham-exposed rats were inserted in identical restraining tubes. The sham-exposed rats were vertically inserted into an opaque PVC pipe with similar dimensions and conditions (sound, light and temperature) as the bore of the magnet. One magnet-exposed rat and one sham-exposed rat were conditioned at a time in parallel.

2.3. Experiment 1

To determine the acute effect of magnetic field exposure on drinking, rats were exposed to the 14.1-T magnet before being given access to a novel palatable solution. Rats (n=40) were placed on a water restriction schedule as above and reduced to 10-min daily access to water. Prior to their scheduled time of water access, rats were individually removed from their home cage and placed in the Plexiglas restraint tube as described above and raised to the core of the 14.1-T superconducting magnet. Rats were removed from the magnet after 0, 5, 10 or 30 min (n=8 per time point). A control group (n=8) was restrained and sham-exposed for 30 min. Immediately after being removed from the magnet or sham-exposure, rats were returned to their home cages and given 10-min access to a single bottle containing a solution of 30 g of glucose and 01.25 g of sodium saccharin mixed in 11 of deionized-distilled water (G+S). Intake of G+S was assessed to be consistent with our earlier studies on the effects of magnetic fields [4,17] and to ensure robust intake with a solution with greater palatability than water alone.

The G+S bottles were equipped with typical short sipper tubes (extending from the cage top 4.1 cm and ending about 13 cm above the cage floor). The latency of rats to begin licking was recorded to the nearest second. Consumption of the G+S was measured by weighing the G+S bottle before and after 10-min access.

2.4. Experiment 2

In order to determine if an increase in latency to begin drinking following magnet exposure accounted for decreased intake during 10-min access to fluid after magnetic field exposure, rats were given 60-min access to G+S beginning
behavior was suppressed in open field locomotor tests. In order to determine if a decreased tendency or ability to rear accounted for the increased latency to drink from spouts located near the top of the cage, rats were given access to G+S in bottles equipped with long spouts that projected nearly to the floor of the cage.

Rats (n=45) were placed on a water restriction schedule as above and reduced to 10-min daily access to water. Prior to their scheduled time of water access, rats were individually removed from their home cage and placed in the Plexiglas restraint tube as described above. Rats in the magnet-exposed groups were placed in the core of the 14.1-T magnet for 10 min, while rats in the control groups were sham-exposed for 10 min. Immediately after being removed from the magnet or sham-exposure, rats were returned to their home cages and given access to a single bottle of G+S.

The G+S bottles were equipped with either the 4.1-cm short sipper tubes as above, or extended long sipper tubes (extending from the cage top 18.3 cm and ending about 5 cm from the cage floor). Because the snout of the typical rat when standing on all four paws was 4–5 cm above the cage floor, rats could reach the tip of the 18.3-cm long sipper tube without rearing or raising their heads. Thus, there were four groups of rats: magnet-

after their first lick. In other words, any effect of the magnet on the rats’ ability to initiate drinking was controlled for by waiting until each rat began to drink to start the 60-min drinking period.

Rats (n=16) were placed on a water restriction schedule as above and reduced to 10-min daily access to water. Prior to their scheduled time of water access, rats were individually removed from their home cage and placed in the Plexiglas restraint tube as described above. Rats were divided into two groups (n=8 per group): rats in the magnet-exposed group were placed in the core of the 14.1-T magnet for 30 min, while rats in the control group were sham-exposed for 30 min. Immediately after being removed from the magnet or sham-exposure, rats were returned to their home cages and given access to a single bottle of G+S with 4.1-cm sipper tubes as above. The latency of rats to begin licking was recorded to the nearest second. Ten minutes after a rat began licking, the G+S bottle was removed and weighed, then returned to the rat for an additional 50 min of access. Thus rats were allowed to consume the G+S for a total of 60 min after they initiated drinking.

2.5. Experiment 3

We have previously found that, after exposure to a high strength magnetic field, rats walked in circles and their rearing

Fig. 1. Latency to drink (A) and intake (B) during 10-min access to G+S by rats after 30-min sham-exposure (white bars) or 0-, 5-, 10- and 30-min exposure to 14.1-T magnetic field (black bars). Magnetic exposure of 5 min or more significantly increased the latency to begin drinking and decreased the amount consumed in the 10-min test. *p<0.05 vs. sham-exposed rats.

Fig. 2. Latency to drink (A) and intake (B) of G+S by rats after 30-min sham-exposure (white bars) or 30-min exposure to 14.1-T magnetic field (black bars). (A) Magnetic exposure significantly increased the latency to begin drinking. (B) Intake was measured for 10 min and 60 min after the first lick to compensate for the increased latency of magnet-exposed rats. Magnetic exposure decreased the amount consumed at 60 min but not 10 min. *p<0.05 vs. sham-exposed rats.
Intraoral catheters were flushed daily with water to maintain patency. Rats were placed on a water restriction schedule as above and reduced to 10-min daily access to water. For 3 consecutive days, rats were removed from their home cages prior to their scheduled time of water access and given intraoral infusions of deionized distilled water (10 ml over 10 min). For intraoral infusions, rats were weighed and placed in a glass aquarium subdivided into four individual compartments by Plexiglas sheets. Syringe pumps infused fluid into the mouth at a rate of 1 ml/min over 10 min. After the infusion, rats and any feces were weighed again as a measure of consumption.

On the fourth day, rats were removed from their home cage prior to their scheduled time of water access individually and placed in the Plexiglas restraint tube as described above. Rats were divided into two groups \( (n=8\) per group): rats in the magnet-exposed group were placed in the core of the 14.1-T magnet for 10 min, while rats in the control group were sham-exposed for 10 min. Immediately after being removed from the magnet or sham-exposure, rats were removed from the restraint tubes and given an intraoral infusion of G+S \((10 \text{ ml}/10 \text{ min})\). Rats were observed throughout the intraoral infusion. The time at which the rats first allowed the G+S to drip passively from their mouths was recorded to the nearest second as the latency to drip. Rats were also observed for the occurrence of two behaviors associated with active rejection, chin-rubbing and gaping \([18]\); however, no rats in either group were observed to express either chin-rubs or gapes, and so these behaviors were not quantified.

The first three experiments indicated that magnetic field exposure decreased intake by increasing latency, perhaps by suppressing rearing and other locomotor activity required for drinking from an elevated sipper tube. In order to further distinguish effects on the appetitive phase from effects on the consummatory phase of drinking, we tested the effects of magnetic field exposure on intraoral intake of G+S.

Under halothane anesthesia, rats \((n=16)\) were implanted with intraoral catheters made of PE-90 tubing that entered the mouth through the lateral cheek and were externalized on the dorsal surface between the scapulae, as described previously.

![Fig. 3. Latency to drink (A) and intake (B) of G+S after 10-min sham-exposure (white bars) or 10-min exposure to 14.1-T magnetic field (black bars) in rats with access to bottles with short or long sipper tubes. (A) Magnet exposure significantly increased the latency to begin drinking regardless of tube length. (B) Intake was measured for 10 min after the first lick. Magnet exposure decreased the amount consumed in rats with access to short sipper tubes but not long sipper tubes. *\(p<0.05\) vs. sham-exposed rats.](image)

![Fig. 4. Latency to drip (A) and intake (B) of G+S during a 10-min intraoral infusion (1 ml/min) by rats after 10-min sham-exposure (white bars) or 10-min exposure to 14.1-T magnetic field (black bars). Magnet exposure had no effect on intraoral intake.](image)
2.7. Statistical analysis

Significant treatment effects were detected by ANOVA or t-test (Statview). Post hoc comparisons were made by orthogonal comparison (Experiment 1) or by Fisher’s least significant difference test. Data are presented in all figures as mean±standard error of the mean.

3. Results

3.1. Experiment 1

One-way ANOVA showed a significant effect of treatment for both latency ($F[4,35]=4.3$, $p<0.01$; see Fig. 1A) and intake ($F[4,35]=14.6$, $p<0.001$; see Fig. 1B). Restraint within the 14.1-T magnet for 5–30 min immediately before a 10-min single bottle test significantly increased the latency of rats to start drinking and decreased the amount of G+S consumed compared to rats sham-exposed for 30 min. Placing rats in the core of the 14.1-T magnet and immediately removing them (0-min exposure) did not increase latency or decrease intake.

3.2. Experiment 2

As in Experiment 1, 30-min restraint within the 14.1-T magnet significantly increased the latency to drink compared to 30-min sham-exposure ($t[14]=3.5$, $p<0.005$; see Fig. 2A). When both groups of rats were allowed 60-min access to G+S after they initiated drinking, there was no difference in intake over the first 10 min; over 60 min, the magnet-exposed rats drank significantly less G+S than did sham-exposed rats ($t[14]=-1.9$, $p<0.05$; see Fig. 2B). The decrease in drinking over 60 min (~80% of sham) was not as large, however, as the decrease seen over 10 min in Experiment 1 (~60% of sham).

3.3. Experiment 3

After 10-min restraint with the 14.1-T magnet or sham-exposure, rats were given access to G+S in bottles with short sipper tubes or long sipper tubes. A two-way ANOVA revealed a significant effect of magnet treatment on latency to begin licking ($F[1,42]=10.7$, $p<0.005$; see Fig. 3A). There was no significant effect of tube length on latency to lick, although several rats with access to long tubes after magnet exposure showed very short latencies comparable to the latencies of sham-exposed rats. A two-way ANOVA on the intake of rats in the 10 min after their first lick showed a significant interaction of magnet and tube length for intake ($F[1,41]=6.5$, $p<0.05$; see Fig. 3B). While magnet exposure decreased intake significantly in rats that drank from short sipper tubes compared to sham controls, there was no difference between the intakes of magnet- and sham-exposed rats that drank from long sipper tubes.

3.4. Experiment 4

Both magnet-exposed rats and sham-exposed rats drank nearly all G+S that was delivered by intraoral catheter. Both groups of rats did not allow any G+S to drip from their mouths (either actively or passively) until close to the end of the 10-min infusion period (see Fig. 4). There was no significant difference between the groups in latency to drip or consumption of G+S.

4. Discussion

Exposure to a 14.1-T magnetic field for as little as 5 min significantly decreased the amount of G+S consumed by water-deprived rats over 10 min (Experiment 1). The decrease in intake could be accounted for largely, but not entirely, by an increase in the latency of magnet-exposed rats to initiate drinking. Even when intake was measured for 10–60 min after the initiation of drinking, thus controlling for increased latency, magnet-exposed rats still consumed less G+S than sham-exposed rats (Experiment 2). The increased latency was not due simply to an inability of magnet-exposed rats to reach the elevated sipper tube of the G+S bottle; providing rats with long tubes that could be reached without raising their heads normalized intake but latency was still increased (Experiment 3). The increased latency and decreased intake appeared to be secondary to the effects of magnet exposure on appetitive behaviors, however, because magnet-exposed rats consumed the same amount of G+S with the same latency to reject as sham-exposed rats when G+S was delivered directly into the mouth by intraoral infusion (Experiment 4).

These results are consistent with the unconditioned anorectic effect of other stimuli that can mediate CTA acquisition. In particular, the effects of the magnetic field on drinking parallel the effects of vestibular perturbation due to whole-body rotation previously reported [9–11]. For example, intermittent whole-body rotation for 5 min at 70 rpm increased the latency to initiate drinking by 2.5 min [9], almost exactly the amount seen in Experiment 1 after 5 min of magnet exposure. The suppression of water intake immediately after rotation is proportional to the duration of rotation [9] and to the angle of tilt away from the horizontal plane during rotation [11]; in humans, increased angle of tilt is associated with increased ratings of motion sickness [11]. Unlike the behavioral effects of LiCl, the reduction of drinking induced by rotation (and the acquisition of CTA after rotation) does not require an intact area postrema [10,19]. Both rotation-induced suppression of drinking and locomotor activity, and the acquisition of CTA after rotation, however, require an intact peripheral vestibular apparatus [9,20,21].

The results of intraoral infusions indicate that magnetic field exposure did not appear to alter consummation of the act of drinking. While not all orofacial responses were scored, all rats were observed to consume the G+S readily, and they did not passively or actively reject the infusate within the first 8–9 min of the 10-min infusion. The persistent consumption we observed is consistent with the long latency to drip and high intraoral intake we recorded. Therefore, the magnetic field does not alter satiety or induce avoidance or aversion as expressed by orofacial motor behaviors of passive drip or active rejections as seen after administration of satiety factors [22], conditioned avoidance stimuli [23] or conditioned aversive stimuli [24]. To
date, the unconditioned effects of vestibular stimulation on intraoral drinking have not been examined, although pairing rotation with a novel saccharin solution was shown to cause conditioned rejection of intraoral infusions of saccharin with active rejection behaviors [20,25].

The finding that exposure to a magnetic field does not acutely induce aversive responses to a novel taste is not inconsistent with the ability of high magnetic fields to induce a robust CTA after rodents ingest a novel taste. In fact, it has been demonstrated that many potent satiating or anorexic compounds (e.g. cholecystokinin or bombesin) are not very potent at inducing CTA; conversely, other compounds that are potent at inducing CTA are not potent anorexic agents [6]. For example, LiCl can induce a CTA when administered after ingestion of a novel taste. When administered prior to ingestion, however, the same doses of LiCl do not cause a short-term decrease in chow intake [6] or intraoral intake of sucrose [26], nor does LiCl immediately alter orofacial responses to the intraoral infusion of saccharin [27].

Because ad libitum drinking from bottles was disrupted (even with long spouts) while intraoral intake was not altered, the appetitive phase of ingestion (i.e. orientation and approach to the bottle) must be disrupted by magnetic field exposure. Because magnetic field exposure [4], like vestibular perturbation [21], causes acute decreases in both locomotor activity and rearing behavior, the decrease in drinking may be due to lower mobility and a reflexively lowered posture.

It is also possible that disruption of the appetitive phase of ingestion could be an indirect effect of stimulation mediated by other induced behavioral states. For example, vestibular stimulation by whole-body rotation can induce anxiety-related behaviors in rodents such as increased defecation [28] and increased head-dipping within the elevated-plus maze [29]. Anxiety also shows high comorbidity with balance disorders in humans [30]. Increased anxiety levels, or other indirect effects of magnetic field exposure on forebrain limbic systems, could potentially modulate drinking by increasing the latency for the rat to approach the spout.

In conclusion, exposure to a high-strength static magnetic field caused an acute decrease in consumption of a palatable solution by water-deprived rats. The decreased intake was due to an increased latency to initiate drinking and a decreased appetitive phase during ad lib intake from bottles. The consummatory phase of ingestion was unaffected by magnet exposure, because intraoral intake was not different between magnet- and sham-exposed rats. This effect of magnetic field exposure is consistent with the acute effects of other aversive stimuli, such as whole-body rotation, on short-term ingestion. These results add to the evidence that high-strength static magnetic fields can have behavioral effects on rodents.

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References