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Research Report

Effects of 17 b-estradiol and extremely low-frequency electromagnetic fields on social recognition memory in female rats: A possible interaction?

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ARTICLE INFO

Article history:
Accepted 4 April 2006
Available online 30 May 2006

Keywords:
Estrogen
Social behavior
Olfactory memory
Short-term memory
Learning
Electromagnetic field

ABSTRACT

We have investigated a potential memory-enhancing effect of exposure to extremely low-frequency electromagnetic fields (ELF EMF) in female rats and its dependence on estrogen, using a social recognition task. A juvenile social recognition paradigm was used and memory retention tested at 30 and 300 min after an adult was exposed to a juvenile during two 4-min trials. Results showed that an intact social recognition memory was present at 30 min in both gonadally intact and ovariectomized rats with, or without, ELF-EMF. However, whereas gonadally intact control females failed to show retention of the recognition memory at 300 min, those additionally exposed to ELF EMF did. This shows that the enhanced duration effect of ELF EMF on social recognition memory occurs in gonadally intact females as well as in males. In addition, results showed that the ELF EMF facilitation of memory retention was prevented by ovariectomy but restored by exogenous treatment with estrogen. This suggests that this ELF EMF effect on social recognition memory is estrogen-dependent.

1. Introduction

Evidence from neuroanatomical, electrophysiological and behavioral studies supports a role for magnetic fields in learning and memory processes. Most of what is known about the functional impact of magnetic fields on the central nervous system is derived from studies of neurotransmitter release (Pesic et al., 2004; Zecca et al., 1991) and neural disorders (Poirrier et al., 2004) and behavioral studies (Lai, 2004; Saunders, 2005). Over the past few decades, emission of EMF by electronic devices and other systems has become relevant for its effects on neural mechanisms in humans and some vertebrates. Exposure to extremely low-frequency electromagnetic fields (ELF EMF) has apparently opposite effects on learning and memory processes probably affecting neurotransmitter function (Kavaliers et al., 1993; Kavaliers et al., 1996; Lai, 2004; Prato et al., 1995; Zecca et al., 1991). Thus, acquisition from behavioral task is modified by ELF EMF (Kavaliers et al., 1993; Kavaliers et al., 1996; Sienkiewicz et al., 1998; Sienkiewics et al., 2001).

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doi:10.1016/j.brainres.2006.04.020

We have recently demonstrated using a social recognition task that exposure to ELF EMF extended social memory duration to 300 min in adult male rats (Vázquez-García et al., 2004). However, the existence of recognized sex differences underlying mechanisms of social recognition (Ferguson et al., 2002) makes it important to evaluate the effects of ELF EMF on this social memory in female as well as in male rats.

Ovarian hormones have been shown to exert a powerful influence on learning and memory processes (Frye, 1995; Galea et al., 2001; O'Neal et al., 1996; Sánchez-Andrade et al., 2005; Tanabe et al., 2004; Warren and Juraska, 1997). Acquisition of spatial learning tasks appears to be impaired following replacement of estradiol (E_2) in ovariectomized voles (Galea et al., 2002). Indeed, it has been reported that high levels of E_2 in adult female rats are associated with impaired and low levels of E_2 with improved, spatial learning (Frye, 1995; Galea et al., 1995; Galea et al., 2001; Holmes et al., 2002; Luine et al., 1998; Warren and Juraska, 1997). However, Sandstrom and Williams (2001) reported that E_2 increases excitatory connectivity in the hippocampus and improves spatial memory retention in ovariectomized rats. Likewise, Woolley and McEwen (1993) reported a transient increase in dendritic spine density of CA1 pyramidal neurons that peaks approximately 48 h following a second injection of E_2 and which returns to baseline levels over the course of a week. Also, estrogen replacement increases the interest in social interaction in ovariectomized mice (Tang et al., 2005).

The discrepancies in the literature concerning the effect of estradiol on cognition may reflect the differential involvement of brain regions recruited during the various types of tasks utilized. Consequently, E_2 may differentially affect various cognitive processes and the corresponding brain regions that mediate behaviors associated with these. Performance in the Morris Water Maze task and the spatial working-reference memory version of the radial arm maze both rely on the integrity of the hippocampus (Jarrard, 1993; Morris et al., 1982; O' Keefe et al., 1975). However, there is evidence that estradiol may affect other types of memory that are mediated by brain regions independent of the hippocampal formation. For example, in ovariectomized rats treated with E_2, social recognition behavior that depends of the integrity of the olfactory bulbs was improved, suggesting that estradiol plays an important role in social recognition (Hlinak, 1993). Several lines of evidence also suggest that E_2 mediates socially motivated behaviors in rodents (Imwalle et al., 2002). Mice lacking a fully functional estrogen receptor α or β showed reduced chemo-investigatory behavior (Choleris et al., 2003; Imwalle et al., 2002; Rissman et al., 1997; Rissman et al., 2002).

It has been shown that short-term social memory is mainly dependent upon olfactory cues (Dluzen et al., 1998; Ferguson et al., 2002; Sawyer et al., 1984; Thor and Holloway, 1982; Young, 2002), and that sexual dimorphism may reflect differential dependence of the sexes on oxytocinergic (female) and vasopressinergic (male) inervation of limbic brain areas (Engelmann et al., 1998; Ferguson et al., 2001; Ferguson et al., 2002). Furthermore, oxytocin effects in female rats are mediated, al least in part, by estrogens (Choleris et al., 2003; Tang et al., 2005).

The aim of the present study was therefore to investigate whether ELF EMF would also affect the duration of short-term social memory in female rats and whether this action was estrogen-dependent.

2. Results

All 48 OVX-female rats were in anestrus (diestrous stage) based upon cytology from vaginal smears. In 16 out of the 48 OVX-female rats, the effectiveness of estrogen replacement was demonstrated by changes in the stage of estrous cycle, from diestrous to estrus.

Fig. 1 shows the mean duration in investigation at IEI of 30 min by the 32 adult female rats tested. Fig. 1A depicts the mean time spent in social investigation by the non-ELF EMF-stimulated group (left panel) and by the ELF EMF-stimulated group (right panel). In both the non-ELF EMF-stimulated group (t test, $P = 0.0008$, $n = 8$) and ELF-stimulated one (t test, $P = 0.002$, $n = 8$) the investigation

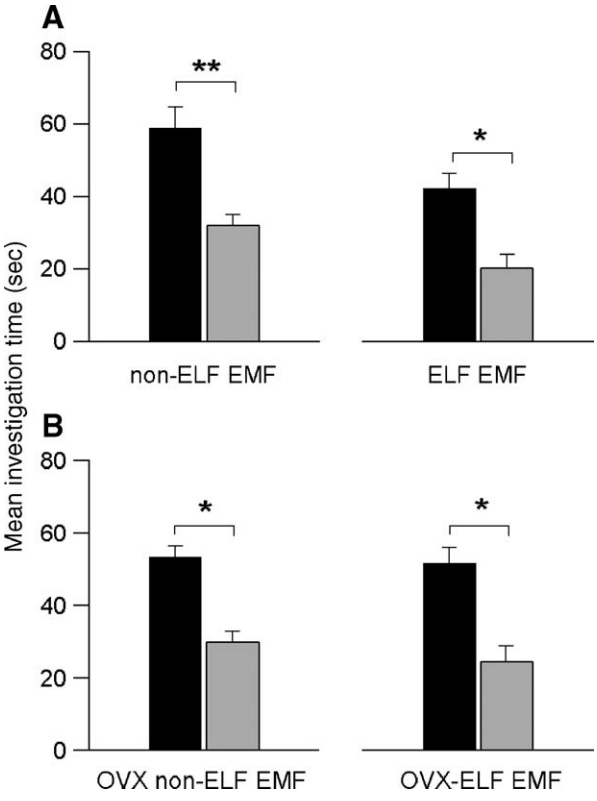

Fig. 1 – Mean investigation time (x ± SEM) during first (solid bars) and second (grey bars) encounters of social recognition responses of adult female rats tested at 30-min IEI. Non-ELF EMF-stimulated animals (A, left panel) and ELF EMF-stimulated animals (A, right panel) show significant differences between first and second encounters, t test, $P = 0.0008$ and $P = 0.002$, respectively, $n = 8$. In panel (B) the ovariectomized non-ELF EMF-stimulated rats (left panel) and the ovariectomized plus ELF EMF-stimulated rats (right panel), also show significant differences between both encounters, respectively. t tests, $P = 0.001$ and $P = 0.004$ respectively.