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Static magnetic field as biological modifier: A study on temperature dependent influence

A L Bhatia*

Zoology Department, University of Rajasthan, Jaipur 302 004

Magnetic fields seemingly alter a number of physiological indicators in intact animals and influence cellular metabolism. We have studied the magnetic field effects on the membrane and receptors of the reticulo-endothelial cells of bone marrow which are mainly responsible for the phagocytic activity of nanocolloid particles of human serum albumin tagged with Tc99m. A series of experiments carried out on immobilisied mice exposed to a static 1.4 T SMF for 60 min at 27°C or 37°C body temperature showed an increased phagocytic activity at 37°C and decreased activity at 27°C.

The effects of magnetic fields on physiological processes in living organisms were demonstrated and investigated as early as 1888. However, no damage to either organs or cells has been clearly identified in the mammalian organisms as a result of high stationary magnetic fields. In recent years, the study of the interaction of living systems with non-ionizing electromagnetic fields has focussed on physicochemical events associated with the cell membrane[1]. Strong stationary magnetic field is opposed by thermal kinetic energy so that small diamagnetic molecules hardly respond to stationary magnetic field of an intensity of 1 Tesla (T) at room temperature. However, when many small diamagnetic molecules are linked within the membranes formed by double layers of fatty acids. The function and organization of the membranes can be influenced by the magnetic field. For example, it has been reported that synthetic membranes, (membrane vesicles or liposomes) undergo structural changes due to the effects of a homogeneous stationary magnetic field. These changes depend on the temperature. The clinical applications of magnetic fields in medical magnetic resonance imaging (MRI) and spectroscopy have dramatically increased the number of individuals exposed to high magnetic fields. In MRI studies the whole body is immersed in fields of up to 2.0 T.

Strong static magnetic fields (SMF) have been proposed to alter membrane fluidity. The steady magnetic fields can directly affect the activity of biologically important macromolecules[2,3]. Chiles *et al.*[4] investigated the effects of strong magnetic field of 2.0 T on neurotransmitter receptors and reported that the amount of binding of the neurotoxin, alpha-bungarotoxin, to nicotine acetylcholine receptors was significantly reduced. A significant body temperature-dependent difference in the erythropoietic activities in male and female mice has been reported. The strong homogeneous magnetic field (of 1.4 Tesla) influenced the action of the erythropoietin depending on the temperature of the body, sex of animal as well as possibly the age of the animal[5]. In order to ascertain further whether a strong SMF influences the receptor molecules and thus membrane function *in vivo*, an attempt has been made to study the effect of SMF on the receptors responsible for phagocytosis.

Materials and Methods

For phagocytic receptors, female NMRI mice (Charles River Wiga, Sulzfeld, FRG), 8-10 weeks old, were acclimatized in the laboratory and were provided with SNIFF diet (Sniff. Soest, FRG) and water *ad libitum*. Tc99m-nanocolloid marked nanoparticles from human serum albumin (9 SOLOCO NANOCOLL, Basel, Switzerland) with a particle size ranging 95%<85 nm, a radioactive compound with gamma energy 144 keV and physical half life 6.2 h was used for the application. The mice were immobilised and this is necessary for the action of a strong magnetic field[2]. These animals were anaesthetised by intravenous injection of 0.08 g sodium pentobarbital per kg body wt (Nembutal from Ceva, Paris, France) through catheters after fixing them into the caudal vein. About 40 min after its administration, till nembutal metabolized and the body temperature attained the desired level, the animals were placed in an electromagnet, type B-E, 25 v (Bruker GmbH. Karlsruhe, FRG), in such a way that they were immobilized transaxially to the poles in the SMF. Three mice were placed between the poles in a lucite chamber in which body

temperature was maintained by means of a thermostatically controlled warm water device which elevated the air temperature in the chamber. The body temperature of the anaesthetized animals were monitored constantly by a rectalthermometer. After the desired body temperatures had been attained and maintenance was assured, the magnetic was switched on. Temperature control continued during SMF exposure. Control mice were treated identically in every respect except that MF was turned off. Therefore stress situation was identical for control and treated groups. During magnetic field exposure just 30 min after initiation/switching on the field a dose of 3 νCi/g body wt (10 νCi or 9370 kBq) of Tc99m-NNC was very gently administered in each mouse through already fixed catheters in both the groups. Thirty min after Tc99m-NNC administration (60 min of MF exposure, the magnetic field was turned off and the animals were removed from the plates and left in the cages. The whole body activity of Tc99m-NNC was measured with the help of a whole body counter by which it could be reaffirmed that each mouse received the same dose and activity. Thirty min after switching off the magnet/turning off the magnetic field (60 min after Tc99m-NNC administration or 90 min after switching on the magnetic field), the animals were killed and the femur, empty femur and bone marrow were examined. The schematic diagram Fig. 1 depicts the materials and methods.

Results and Discussion

A temperature-dependent influence of magnetic field has been observed. About 49.65% ($0.1<p<0.05$: paired T test) higher uptake of nanocolloid as compared to control in bone marrow cells and 23.04% ($(0.001<p<0.01)$ by empty femur as well as 15.28% ($p>0.05$) by full femur of anaesthetised mice at 37°C have been recorded. This indicates possibly a stimulation of phagocytic process mediated through the activation of receptors on the membrane. Side by side about 18% ($p>0.05$: paired T test) lesser uptake in blood is noticed. Whereas at 27°C, a relatively 20% less uptake by the bone marrow cells ($p>0.05$) as compared to respective controls has been observed. This represents a depressed phagocytic activity. A 18.31% higher uptake by the blood ($p>0.05$) has been marked which may be unconsummated or the left over portion of Tc 99 m-NNC. Full femur and empty femur also show a reduced uptake of nanocolloid by 5% and 8% ($p>0.05$), respectively. The order in the magnitude of increase has been. bone marrow>empty femur>femur (Table 1).

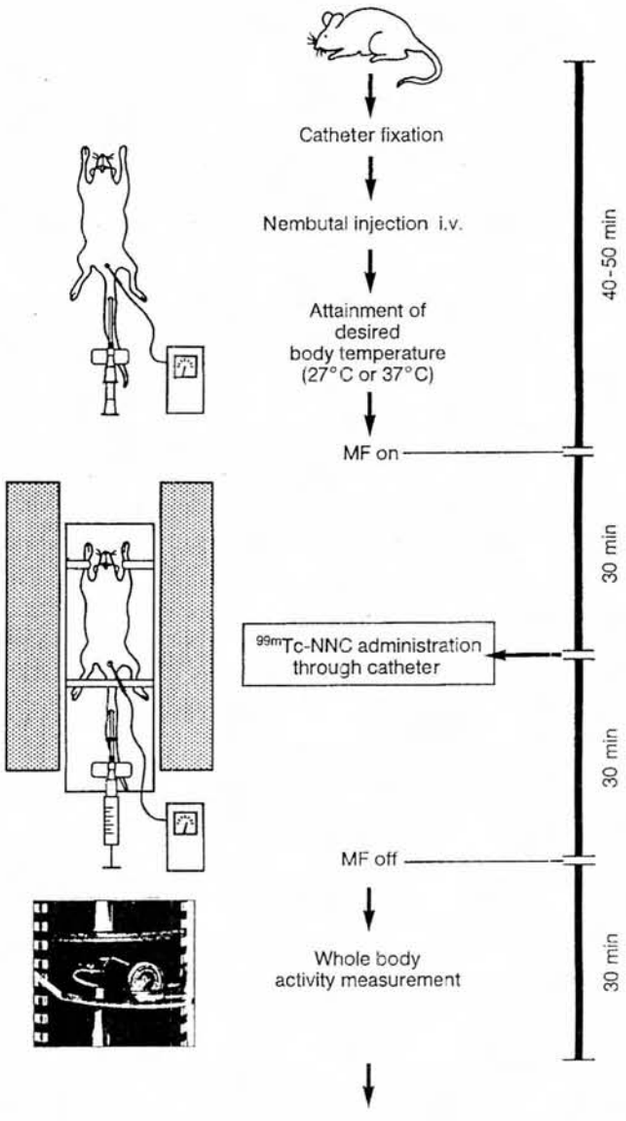

Fig. 1—Schematic diagram showing the protocol and design of the experiment

The reticulo-endothelial system is involved in a variety of biological processes. Along the phagocytosis and transfer of antigen, its functions include clearance of bacteria, fibrin, and foreign particles from blood stream, detoxification of toxic substances, neutralization of enzyme etc. In the phagocytic processes both the free and fixed cells are involved. The clearance of particulate matter artificially brought into the blood stream, its accumulation in the different organs and further fate in the body are generally employed as an available model of phagocytic function.

Quantitative measurements of reticuloendothelial activity apply solely to its phagocytic function. These are usually made by injecting a suitable colloid intravenously and subsequently measuring its rate of dis-

Table 1—Uptake of nannocolloids (percentage values) of the different tissues with and without MF exposure at different temperature

Body temp.	Tissue	% Values (mean±SD)		p Value
		Control	MF-exposed	
37°C	Femur	100 ± 9.74 (18)	115.28 ± 14.02(16)	<0.05
	Empty femur	100 ± 8.42 (16)	128.04 ± 15.71 (16)	<0.05
	Bone marrow	100 ± 14.6 (16)	148.04 ± 16.83 (17)	>0.05
	Blood	100 ± 12.21 (18)	82.41 ± 16.16 (17)	>0.05
27°C	Femur	100 ± 8.87 (8)	95.1 ± 12.48 (8)	>0.05
	Empty femur	100 ± 8.94 (7)	91.91 ± 9.09 (6)	>0.05
	Bone marrow	100 ± 20.5 (9)	81.65 ± 15.60 (10)	>0.05
	Blood	100 ± 14.34 (9)	118.31 ± 23.09	>0.05

(in parentheses are numbers of animals)

appearance from the blood. The interaction of such particles with macrophage in tissue culture has been characterized as a three-staged process: (a) attachment at the receptor of the macrophage membrane, (b) phagocytosis, and (c) intralysosomal degradation of the engulfed material. In such model experiments, the homeostatic importance of the macrophage has demonstrated their permanent functional phagocytic state and high metabolic activity.

There have been few studies on the high sensitivity of the immunogenic potentiality to non-ionizing fields. The stationary magnetic field exerts a protective effect in rodents against Trypanosoma infection[7], and both stationary and 50 Hz magnetic fields have an antiinflammatory influence in rodents[8,9]. It has been stated that SMF may influence cellular metabolism, enzyme activity and growth[10]. Effect with respect to orientation in bilayer lipid membrane have been demonstrated *in vitro*[11-14] and were observed as functional changes in membranes, i.e. in diffusion or transport processes[15] of uptake of oxygen radicals by membranes *in vitro*[16].

In one of the parallel previous studies the strong homogeneous magnetic field (of 1.4 Tesla) was found to influence the action of the erythropoietin depending on temperature of the body, sex of animal as well as possibly the age of animal. The SMF exposure suppressed the EPO-induced stimulus of erythropoietic differentiation in the male mice whereas no effect was seen in female mice. SMF reduced radioiron[^{59}Fe] activity in whole blood at 37°C and in femora at 27°C in male mice whereas no statistically significant effect was observed in female mice, at either temperatures. Significant differences had also been noted between normal male and female rats with regard to radioiron incorporation. Female femora had significantly higher mean incorporation of radioiron than from male femora. The body temperature determined the activity of radioiron retained. In all cases, greater radioiron activity was retained at the normal body temperature of 37°C than at 27°C. At 27°C, in male blood, the activity of radioiron reduced by 51% and in female blood by 26% that of 37°C[5].

The authors had also reported earlier[17] an *in vitro* study on the binding of the hormone erythropoietin to murine bone marrow cells to show that SMF can change the specific binding of EPO to its receptor on murine bone marrow cells in a sex-specific manner, perhaps by different membrane characteristics. At 37°C marrow cells of male mice showed depression of specific binding by 24% (p 0.01) whereas no effect was reported at 27°C. Female marrow cells showed depression of specific binding by 23% (p 0.01) at 27°C in the same time interval. No significant effect was reported at 37°C[17]. Though present study does not show any age and sex dependent effects on the phagocytic receptors, a temperature dependent influence of the magnetic field is quite obvious. However, the possibility of sex dependent response of the phagocytic receptors in *in vitro* bone marrow cells to magnetic freld can not be ruled out and is under study.

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