Review

The review of cellular effects of a static magnetic field

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Received 30 November 2005; received in revised form 6 January 2006; accepted 7 January 2006
Available online 4 May 2006

Abstract

The effects of static magnetic fields at the cellular level are reviewed. Past studies have shown that a static magnetic field alone does not have a lethal effect on the basic properties of cell growth and survival under normal culture conditions, regardless of its magnetic density. It has also been shown that cell cycle distribution is not influenced by extremely strong static magnetic fields (up to a maximum of 10 tesla (T)). A further area of interest is whether static magnetic fields cause DNA damage, which can be evaluated by determination of the frequency of micronucleus formation. The presence or absence of such micronuclei can confirm whether a particular treatment damages cellular DNA. This method has been used to confirm that a static magnetic field alone has no such effect. However, the frequency of micronucleus formation changes significantly when certain treatments (for example, X-irradiation and mitomycin C) are given during exposure to a strong static magnetic field. It has also been reported that treatment with trace amounts of ferrous ions in the cell culture medium and exposure to a static magnetic field increases DNA damage, which is detected using the comet assay. Several reports suggest that a strong static magnetic field may affect the ion transport and the gene expression. In addition, many studies have found a strong magnetic field can induce orientation phenomena in cell culture.

Keywords: Static magnetic field; Cultured cells; Genotoxicity; Gene expression; Orientation

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1. Cell proliferation and cell cycle distribution

Clonogenic activity, DNA synthesis, cell cycle, and proliferation kinetics were not altered by exposure to the magnetic field and repetitive exposure to a static magnetic field up to 10 T exerted no effects on proliferation of human fetal lung fibroblast cells [1,2]. Cell cycle analysis of synchronized and nonsynchronized human fetal lung fibroblasts (HFLFs) cells did not reveal statistically significant differences between the cells exposed to 0.2, 1.0, or 1.5 T for 1 h/day for 5 consecutive days and control cells [3].

On the other hand, prolonged exposure to a 7 T field appeared to inhibit growth of three human tumor cell lines in vitro [4]. Alterations in cell growth cycle and gross fragmentation of DNA were excluded as possible contributory factors. These reports suggest that the effect of exposure to static magnetic fields varies depending on the cell type.
2. Genotoxic effects

2.1. Mutation

No mutagenic effect of static magnetic fields up to 5 T (1 T = 10,000 G) was detected using four strains of Salmonella typhimurium (TA98, TA100, TA1535 and TA1537) and Escherichia coli (E. coli) WP2 uvrA [5]. The mutation rate in the exposed group was significantly higher than in the non-exposed group when cells were treated with N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG), N-methyl-N'-nitro-N-nitrosoguanidine (MNNG), ethylmethanesulfonate (EMS), 4-nitroquinoline-N-oxide (4-NQO), 2-amino-3-methyl-3H-imidazo [4,5-f]quinoline (IQ) or 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide (AF-2). The expression of the soxS::lacZ fusion gene strain GC4468 and its derivatives defective in DNA repair enzymes or redox-regulating enzymes showed no effect to exposure [6]. On the other hand, the mutation frequency was reached approximately 20%. Exposure of the cells to static magnetic field of 9 T in soxR and sodAsodB mutants, which are defective in defense mechanisms against oxidative stress.

2.2. Micronucleus formation

Long-term exposure to a static magnetic field alone did not affect micronucleus formation [2]. In X-ray-irradiated cells, exposure to a 1-T static magnetic field also did not affect micronucleus formation, but exposure to a 10-T static magnetic field resulted in a significant (p < 0.05) increase in micro-nucleus formation induced after a 4-Gy exposure.

Exposure to the static magnetic field of 4.7 T for 6 h significantly decreased the frequency of mitomycin C-induced micronucleus formation after culture periods of 18, 42, 54 and 66 h [7]. These results suggested that a 4.7 T static magnetic field might have exerted an influence on the DNA damage stage produced by mitomycin C rather than on the formation of micronuclei during the stage following mitomycin C-induced DNA damage.

2.3. DNA strand breaks

Lymphocyte exposure to a static magnetic field of 7 mT did not affect the number of cells with DNA damage in the comet assay [8]. However, when the lymphocytes were simultaneously exposed to FeCl₂ and a 7 mT static magnetic field, the number of damaged cells increased significantly and reached approximately 20%. Exposure of the cells to static magnetic fields and simultaneous treatment with a known oxidant, ferrous chloride, may therefore produce oxidative damage of DNA molecules.

3. Ion transport

Human lymphocytes were simultaneously exposed to 4.75 T for static component and 0.7 mT for the pulsed component at 500 MHz generated by an NMR apparatus for 1 h. This exposure increased the Ca²⁺ influx without any proliferative, or proinflammatory effect on either unstimulated or PHA-stimulated lymphocytes [9].

Cellular metabolism is partly controlled by K⁺ influx. Rb⁺ is used in place of K⁺ in the cellular experiment. Exposure to strong homogeneous magnetic fields with various magnetic flux densities of less than 1.6 T had no significant effect on either active or passive Rb⁺ influxes into HeLa cells [10]. The patch-clamp method was used to measure transmembrane Na⁺ and K⁺ currents in SH-Sy5Y neuroblastoma cells exposed to static magnetic fields of 0.1, 0.5, and 7.5 mT [11]. Application of the magnetic fields did not result in detectable changes in any of the action potential parameters chosen in this study.

There was a slight shift in the current–voltage relationship and a less than a 5% reduction in peak current during magnetic field exposure to 125 mT in voltage activated Na⁺ channels in proliferating GH3 cells [12].

4. Morphology

Human skin fibroblast cell morphology was modified with a concomitant decrease in the expression of some sugar residues of glycoconjugates after 1h exposure to a 0.2 T static magnetic field [13]. However, cell viability, assessed by the colony-forming assay, was unaffected.

Gradient magnetic fields of 6 T with 60 T/m affected the convection of floating cell aggregations in the cell culture flask, and reversibly changed the direction of convective flow [14]. HeLa cells exhibited streamlike-cell distribution patterns in the direction of the applied magnetic field gradient.

The extent of neurite elongation from chick embryo dorsal root ganglia neurons into the rods was found to be substantially greater than that observed in controls and increased with magnetic field strength, as did the collagen gel rod birefringence, indicative of collagen fibril alignment along the rod axis [15]. These results may translate into an improved method of entubulation repair of transected peripheral nerves by directing and stimulating axonal growth through a tube filled with magnetically aligned collagen gel.

5. Gene expression

We used a static magnetic field exposure system, to expose cells to a spatially inhomogeneous 6 T with a strong magnetic field gradient (41.7 T/m) or to a spatially homogeneous 10 T [16]. The protein of some early response genes, such as c-Myc, c-Fos, and c-Jun, is known to have a strong relation to the cellular growth condition. HL-60 cells exposed to either a 6 or 10 T static magnetic field for periods of 1 to 48 h did not exhibit significant differences in the levels of c-Myc and c-Fos protein expression, as compared to sham-exposed cells. In contrast, c-Jun protein expression increased in HL-60 cells after exposure to the 6 T static magnetic field for 24, 36, 48, and 72 h. Exposure to a strong magnetic field gradient induced c-Jun expression, which suggested that strong magnetic field gradients may have significant biological effects, particularly
regarding processes related to an elevation of c-jun gene expression.

Brief exposure (15 min) to a static magnetic field of 100 mT led to a marked but transient potentiation of binding of a radiolabeled probe for activator protein-1 (AP-1) in immature cultured rat hippocampal neurons with high expression of growth-associated protein-43 [17]. Exposure to the static magnetic field increased AP-1 DNA binding through expression of Fra-2, c-Jun and Jun-D proteins in immature cultured hippocampal neurons.

6. Orientation

It was firstly reported that the sickled erythrocytes were oriented perpendicular to the magnetic field at 0.35 T [18]. The erythrocytes were oriented with their disk planes parallel to the magnetic field direction [19]. This effect on erythrocytes was detectable at 1 T and almost 100% of the cells were oriented when exposed to 4 T. It has been reported that exposure to strong static magnetic fields on the order of 1 T can result in the orientation of macromolecules such as collagen [20] and of animal cells in vitro. Human foreskin fibroblasts were also oriented using the magnetic orientation of collagen with static magnetic fields of 4.0 and 4.7 T [21]. Furthermore, osteoblast cells have been shown to be oriented under exposure to a strong static magnetic field of 8 T in the absence of collagen [22].

Human glioblastoma A172 cells embedded in collagen gels were oriented perpendicular to the direction of the static magnetic field at 10 T [23]. A172 cells cultured in the absence of collagen did not exhibit any specific orientation pattern after 7 days of exposure to the static magnetic field.

The morphological effects of strong static magnetic fields on adherent cells are less well understood than the effects of magnetic fields on red blood cells. A high-intensity magnetic field of 14 T affected the morphology of smooth muscle cell assemblies by extending the cell colonies along the direction of the magnetic flux [24]. The speculated mechanism was that a diamagnetic torque force acts on cytoskeleton fibers, which are dynamically polymerizing and depolymerizing during cell division and cell migration.

7. Conclusions

Considering many articles comprehensively, the conclusions are as follows: exposure to static magnetic fields alone has no or extremely small effects on cell growth and genetic toxicity regardless of the magnetic density. However, in combination with other external factors such as ionizing radiation and some chemicals, there is evidence to strongly suggest that a static magnetic field modifies their effects. A static magnetic field may have effects on intracellular ion control, especially Ca$^{2+}$. Regarding gene expression, although not a consistent view, static magnetic fields and strong magnetic field gradients have an effect on c-Jun expression. Many studies report orientation by high magnetic flux densities on cells and collagen fibers, which have been confirmed as effects of static magnetic fields. However, these effects often depend on the tested cell type and were not found in all types of cells. Since, magnetic resonance imaging (MRI) has gained widespread use for diagnostic purposes and since the magnetic flux densities used are increasing, studies of the effects of static magnetic fields at the cellular level should continue.

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