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Leukocyte trafficking in response to magnetic resonance imaging

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Abstract. There were significant increases in total T cells and in T helper cells in blood samples collected immediately following magnetic resonance imaging (MRI) examinations of brains of male volunteers and patients. Percentages of total lymphocytes and suppressor/cytotoxic T cells decreased in these same samples. There were no significant changes in any leukocyte subpopulations in males undergoing lumbar MRI and females undergoing brain MRI. Thus, it is unlikely that stress from the procedure is the explanation for these changes. Our results show that MRI has specific effects on a brain system(s) that controls lymphocyte subpopulations.
Key words. Lymphocyte subpopulations; magnetic resonance imaging; leukocytes.

The potential carcinogenic effects of even simple EMFs[1–6] prompted us to investigate whether there are physiological consequences of acute exposure to the complex magnetic fields generated by magnetic resonance imaging (MRI), a widely used diagnostic procedure[7]. The EMFs associated with MRI consist of a static magnetic field, gradient magnetic fields that are cycled at frequencies of 0.5–1000 Hz, and electro-magnetic radiation having radio frequencies of 21–64 MHz.

We hypothesized that the various populations of leukocytes would serve as sensitive markers for effects on a central system of host defenses. Initially, the effect of MRI of the brains of males was studied to minimize the changes due to hormonal cycles. Studies were later extended to females to determine if they show similar changes. Controls consisted of males and females undergoing MRI of their lumbar regions which exposes them to similar procedural stresses.

Leukocytes (lymphocytes, granulocytes, and monocytes) and their subpopulations can be distinguished from each other by lineage-specific membrane proteins, termed cluster of differentiation (CD) antigens. Lymphocytes can be divided into two major subpopulations, T (thymus dependent, $CD3^+$) cells and B (bursal equivalent, $CD21^+$) cells. T cells can be further subdivided into T helper ($CD4^+$, T_h) cells and T suppressor/cytotoxic ($CD8^+$, $T_{s/c}$). The various subpopulations of leukocytes are often independently regulated[10]. We used flow cytometry to quantify the different populations of leukocytes based on cell size and on subpopulation specific CD markers. This provided us with a sensitive measure of the state of the immune system.

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Methods

Subjects. Blood samples were collected from patients undergoing a diagnostic MRI of the brain or lumbar region at the Medical College of Georgia. Only those patients having a negative MRI were included in the study. Patients ranged in age from 26 to 68. Blood samples were also collected from normal volunteers with an age range of 22 to 52. There was no population difference in leukocyte subpopulations between patients and normal subjects as determined by Student's t-test. All participants signed informed consent forms. Participants were divided into four groups: 1) males undergoing brain scans, 2) females undergoing brain scans, 3) males undergoing lumbar scans, 4) females undergoing lumbar scans. Multivariate analysis showed that initial values of leukocyte populations among subjects in the four groups were not statistically significantly different.

MRI. A 1.5 T Signa (GE Medical Systems, Milwaukee, WI) was used for the MRI. The brain MRI procedure consisted of sagittal T1 weighted localizers, axial T2 weighted images, and coronal T1 weighted images. The lumbar MRI procedures consisted of a sagittal multiplanar gradient recalled (MPGR) series, sagittal T1 weighted images, axial oblique T1 weighted images through the disc spaces, and axial oblique MPGR images through the disc spaces.

Blood. Two blood samples (one in a serum separation tube and one in EDTA) were collected via venipuncture immediately before and after the MRI procedure. To reduce the effect of diurnal variation, all samples were collected between 8:00 am and 10:00 am. The EDTA tube of each sample was immediately processed for flow

Table 1. Effect of MRI on leukocyte populations*.

	Monocytes			Granulocytes			Lymphocytes		
	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ
Male brain									
Avg	5.70	5.17	−0.53	51.8	52.1	0.30	28.6	26.2	−2.40
SEM	0.2	0.2	0.45	0.89	1.15	1.28	0.40	0.45	0.57
p			0.27			0.82			**0.001**
n	11	11	11	11	11	11	16	16	16
Female brain									
Avg	5.4	4.7	0.7	57.9	59.9	1.93	24.1	22.7	−1.43
SEM	0.7	0.6	0.40	3.53	2.29	2.09	2.67	2.39	1.06
p			0.13			0.39			0.22
n	9	9	9	9	9	9	9	9	9
Male lumbar									
Avg	5.34	5.02	−0.30	57.2	56.4	−0.70	25.9	26	0.14
SEM	1.4	1.2	0.34	5.74	4.51	1.41	4.75	4.76	0.93
p			0.40			0.67			0.82
n	10	10	10	10	10	10	10	10	10
Female lumbar									
Avg	6.1	5.9	−0.2	57.3	57.6	0.28	25.2	23.5	−1.71
SEM	0.5	0.7	0.24	2.73	2.96	1.16	1.51	1.56	0.77
p			0.42			0.81			**0.05**
n	13	13	13	13	13	13	16	16	16

*Monocytes, granulocytes, and lymphocytes shown as a percentage of total leukocytes before and immediately following MRI of the brains (top half) or lumbar regions (bottom half) of males and females. Percentages were determined by analyzing duplicate samples via flow cytometry. Δ = Differences between percentages of pre- and post-MRI.

cytometry analysis of granulocytes, monocytes, lymphocytes, and the lymphocyte subsets marked by $CD3^+$, $CD4^+$, $CD8^+$, and $CD21^+$.

Values for monocytes, granulocytes, and lymphocytes are expressed as the percentage for each subpopulation of the total leukocyte population. Values for the lymphocyte subpopulations are shown as a percentage of total lymphocytes.

Statistics. Significance of differences between leukocyte subpopulations and of neurohormones due to MRI was determined using a paired Student's t-test. Significance of differences in initial values for the leukocyte subpopulations was determined using Student's t-test for differences between populations.

Results

Initial values for percentages of the various leukocyte subpopulations were not significantly different between those having brain scans compared to those having lumbar scans. Similarly there were no gender based differences in initial values of the subpopulations, except that women had significantly lower initial percentage of lymphocytes than men (29.5% vs 24.8%, $p = 0.04$).

Circulating lymphocytes as a percentage of leukocytes decreased significantly ($p < 0.001$) in men immediately following MRI of the brain and in women after MRI of the lumbar region (table 1, last column). They were unchanged in the other groups. Monocytes and granulocytes were not affected by MRI treatment in any group (table 1).

The percentages of several lymphocyte subpopulations changed in *males* following MRI of their brains. Circulating T ($CD3^+$) cells and T_h cells ($CD4^+$) as a percentage of total lymphocytes both increased significantly ($p < 0.04$ and $p < 0.03$ respectively; table 2, columns 3 and 6). In contrast, the percentage of circulating $T_{s/c}$ ($CD8^+$) cells decreased significantly ($p < 0.03$; table 2, column 9). *Women* undergoing lumbar scans also showed significant decreases in lymphocytes (bottom of table 1, column 9) and $T_{s/c}$ cells but also had an increase in B cells (bottom of table 2, columns 9 and 12). MRI of brains of females and of the lumbar region of males had no effect on any of the leukocyte (middle of table 1) or lymphocyte subpopulations (middle of table 2).

Correlations of changes between various leukocyte subpopulations were observed within the different treatment groups, but there was no consistent pattern (not shown).

Discussion

These results indicate that magnetic fields and EMFs generated by MRI have an acute effect on a major physiological system. This effect is most evident in men undergoing brain examinations but was also seen in women having scans of their lumbar regions. The com-

Table 2. Effect of MRI on lymphocyte subpopulations*.

	Total T cells			T helper cells			T suppressor			B cells		
	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ	Pre	Post	Δ
Male brain												
Avg	69.5	71.8	2.27	42.1	43.7	1.58	27.4	26.4	−1.38	9.7	9.3	−0.45
SEM	0.5	0.57	0.97	0.5	0.55	0.67	0.47	0.46	0.57	0.4	0.4	0.9
p			**0.04**			**0.03**			**0.03**			0.62
n	18	18	18	18	18	18	18	18	18	13	13	13
Female brain												
Avg	71.7	74.1	2.4	44.0	44.9	0.9	30.1	31.7	1.66	10.8	10.4	−0.4
SEM	2.3	1.91	1.41	2.73	2.43	0.66	1.87	1.39	1.55	1.2	1.3	1.11
p			0.14			0.20			0.30			0.63
n	9	9	9	10	10	10	10	10	10	10	10	10
Male lumbar												
Avg	73.2	69.2	−4.0	45.6	43.1	−2.5	32.5	31.1	−1.0	10.0	10.2	−0.2
SEM	2.17	4.57	2.91	2.2	2.82	1.9	2.27	2.78	1.18	0.9	1.0	0.3
p			0.20			0.22			0.59			0.52
n	10	10	10	10	10	10	10	10	10	10	10	10
Female lumbar												
Avg	70.9	72.1	1.23	45.0	45.9	0.96	27.9	26.7	−1.16	9.6	11.0	0.97
SEM	2.2	1.94	1.16	2.12	1.70	0.93	1.62	1.73	0.41	1.30	1.50	0.45
p			0.30			0.22			**0.01**			**0.05**
n	16	16	16	16	16	16	16	16	16	13	13	13

*Lymphocyte subpopulations shown as a percentage of total lymphocytes before and immediately following MRI of the brains (top half) or lumbar regions (bottom) of males and females. Percentages were determined by analyzing duplicate samples via flow cytometry.

plex of changes, although not large, is very consistent and statistically significant. The increase in T_h cells and concomitant decrease in $T_{s/c}$ cells in men following brain scans could potentiate the immune system for response. Similarly, decreased $T_{s/c}$ cells coupled with increased B cells in women following lumbar MRIs could result in an enhanced antibody response. Thus, rather than being detrimental as might be expected from some results of chronic exposure to environmental EMFs, any physiological effects resulting from MRI would either have no measured effect or could be such as to temporarily enhance the patient's ability to respond to environmental threats.

The enclosure in which the subjects are placed (potential claustrophobia), noise, restricted movement, etc., are all similar for both experimental and control groups. Lack of any detectable effect of MRI in men undergoing lumbar scans and women having brain scans shows that the alterations are not due simply to the stress of the procedure. The only differences are the area on which the magnetic fields are focused and the subject's gender. Men and women may respond to this stress differently, but there is no overt evidence for that. In addition, the changes in the cell percentages described above are the opposite of stress-induced changes, since stress is known to depress immune responses[11,12,13].

Cox[14] postulated that electromagnetic fields could act as a trigger for a physiological system that would amplify the effect of the relatively minor currents induced. The neuroendocrine system serves that function since it is known to influence the proportions of circulating leukocyte subsets[15] by controlling differential expression of various adhesion molecules and their receptors on vascular endothelium and leukocytes respectively[16]. In fact, the communication is two-way in that lymphocytes and macrophages have receptors for various neurohormones and also secrete the neurohormones[17]. MRI could have direct effects on pituitaries of men undergoing brain scans. For women undergoing lumbar scans, the effects could be indirect due to the large concentrations of lymphocytes in the abdomen exposed the the induced EMFs. However, in preliminary studies on two potential regulators in cell trafficking, we have been unable to demonstrate consistent changes in prolactin or vasoactive intestinal peptide induced by MRI in any of the subject populations (not shown).

The physical mechanisms that may elicit the changes we observed in the immune system are yet to be identified. MRI examinations involve exposure to static magnetic fields, time-varying gradient magnetic fields, and radio frequency EMF. The static magnetic field is probably not strongly involved, or subjects would have shown similar responses for lumbar and brain exams since the body is exposed to essentially the same static magnetic field during exams of both areas. The time-varying gradient magnetic fields and EMF are applied differently in brain exams compared to lumbar exams. Our

data cannot definitely identify EMF or time-varying gradient magnetic fields as the agent that affected the lymphocyte subsets. It is likely that the immune system reacts to time-varying magnetic fields (in contrast to time-varying electric fields), since the EMF used in MRI procedures does not have a significant electric field component.

EMF exposure during MFI is significantly different from EMF exposure near high voltage transmission lines where time-varying electric fields constitute a large component. The time-varying gradient magnetic fields used in MRI are cycled at frequencies similar to those of extremely low frequency EMF that has been studied for carcinogenic effects. Thus extrapolation of our results to the effects of chronic exposure to high voltage transmission lines must be very tentative. However, it does indicate that it may be worthwhile studying the lymphocyte subpopulations and neurohormone concentrations in people subjected to such exposure.

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