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Interveners

J.K. GRAYSON
Radiation exposure, socioeconomic status, and brain tumor risk in the US Air Force: A nested case-control study.
Am J Epidemiol 1996; 143:480-6. http://aje.oxfordjournals.org/content/143/5/480.full.pdf .

This study found an association between exposure to ELF and RF/MW radiation and brain tumors.

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Exhibit SE-AQLPA-7 - Document 14
J.K. GRAYSON, Radiation exposure, socioeconomic status, and brain tumor risk in the US Air Force: A nested case-control study
Attachment to the Expert Report of David O. Carpenter
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Radiation Exposure, Socioeconomic Status, and Brain Tumor Risk in the US Air Force: A Nested Case-Control Study

J. Kevin Grayson[1]

A nested case-control study was used to investigate the relation between a range of electromagnetic field exposures and brain tumor risk in the US Air Force. Cumulative extremely low frequency and radiofrequency/microwave electromagnetic field potential exposures were estimated from a job-exposure matrix developed for this study. Ionizing radiation exposures were obtained from personal dosimetry records. Men who were exposed to nonionizing electromagnetic fields had a small excess risk for developing brain tumors, with the extremely low frequency and radiofrequency/microwave age-race-senior military rank-adjusted odds ratios being 1.28 (95% confidence interval (CI) 0.95–1.74) and 1.39 (95% CI 1.01–1.90), respectively. By contrast, men who were exposed to ionizing radiation had an age-race-senior military rank-adjusted odds ratio of 0.58 (95% CI 0.22–1.52). These results support a small association between extremely low frequency and radiofrequency/microwave electromagnetic field exposure and no association between ionizing radiation exposure and brain tumors in the US Air Force population. Military rank was consistently associated with brain tumor risk. Officers were more likely than enlisted men to develop brain tumors (age-race-adjusted odds ratio (OR) = 2.11, 95% CI 1.48–3.01), and senior officers were at increased risk compared with all other US Air Force members (age-race-adjusted OR = 3.30, 95% CI 1.99–5.45). *Am J Epidemiol* 1996;143:480–6.

brain neoplasms; case-control studies; electromagnetic fields; military personnel; occupational exposure; socioeconomic status

Considerable interest in the relation between cancer and several sources of extremely low frequency (30–300 Hz) electromagnetic radiation, including high-voltage power transmission lines and video display terminals, has been expressed by members of the US Air Force. Apprehension about exposures from cellular telephones and other electronic equipment which operate in the radiofrequency/microwave region (>3,000 Hz) of the electromagnetic spectrum has also arisen. To help address these concerns, the relations between potential exposures to different regions of the electromagnetic spectrum and brain tumor risk were explored in a population of male members of the US Air Force. Given the small brain tumor excesses reported in other occupational studies, it was deemed important to quantify the associations between different potential workplace hazards. Confounding might

account for a significant proportion of the small estimated brain tumor risk attributed to extremely low frequency electromagnetic field (EMF) exposures in previous investigations. In addition, evidence that extremely low frequency EMFs act as brain tumor promoters in concert with either radiofrequency/microwave or ionizing radiation was sought by examining joint effects between these potential exposures.

Experimental evidence that nonionizing EMFs play a significant role in carcinogenesis has been difficult to obtain. Easterly (1) proposed in 1981 that alterations in mitotic processes of EMF-exposed cells might provide a proliferative stimulus to latent tumor cells, followed by progression. His thinking was amplified by Adey (2), who proposed that extremely low frequency EMFs may act as tumor promoters by altering intercellular communications. Most investigators suggest that extremely low frequency EMFs do not act as initiators in the classic multistage model of carcinogenesis. Rather, a promoting role has been suggested (3). On the other hand, Balcer-Kubiczec and Harrison (4, 5) have observed that microwaves may either act alone as tumor initiators or as cocarcinogens with ionizing radiation in transforming cultured cells, and the ability of ionizing radiation alone to affect all phases of tumorigenesis is well recognized.

Many occupational studies of the association between occupational exposures to extremely low frequency EMFs and brain tumor risk have been reported in the literature (see references 3 and 6 for reviews). Contemporary reports have tended to use the nested case-control study design to examine cohorts of electrical workers (7–9), although a population-based study has been recently reported (10). In general, the results from these investigations have been negative, in contrast to the findings from earlier decedent case-control studies, which suggested a small excess risk (11–16).

Few epidemiologists have attempted to examine the association between exposure to higher frequency electromagnetic fields and brain tumor risk. A massive cohort study of radar operators and repairers in the US Navy reported by Robinette et al. (17) found no association between brain tumor risk and exposure to radar waves (17). In contrast to these findings, later work reported by Thomas et al. (12) found a significant excess of brain tumors among electronics workers who were presumably exposed to high frequency EMFs.

An association between ionizing radiation exposure and brain tumor excesses has been demonstrated in several populations, including persons who received high-dose radiation therapy (18, 19). Among occupational groups exposed to low levels of ionizing radiation, the situation is less clear. While studies of medical workers (20, 21), uranium miners (22), and military personnel exposed to nuclear weapons tests (23) do not support an association, follow-up of nuclear materials workers in the United States suggests that a slight excess of brain tumors may be present in this cohort (24), although similar findings have not been observed in the United Kingdom (25, 26).

Male members of the US Air Force proved to be a useful population for study of the health effects of EMF exposure. The technical nature of their activities meant that the potential for exposures to extremely low frequency and radiofrequency/microwave EMFs, and ionizing radiation, singly and in combination were common, increasing the power of this study to detect weak associations and to discern potential joint effects. In addition, several sources of historical exposure data were available, case ascertainment was believed to be 100 percent, and computerized personnel records allowed complete reconstruction of occupational histories as well as acquisition of accurate demographic data.

MATERIALS AND METHODS

Subject selection

This case-control study was nested within a cohort composed of all male members of the US Air Force who had completed at least one full year of service between January 1, 1970 and December 31, 1989. The study was restricted to males, because there were too few female brain tumor cases to allow detailed analyses by gender. Incident cases were obtained by screening hospital discharge records for individuals diagnosed with a primary malignant brain tumor (*International Classification of Diseases*, 9th revision, code 191 (27)) who were serving in the US Air Force during the study period. Follow-up of individuals who had separated from the US Air Force was not attempted. Financial accounting procedures ensured that patients treated outside of US Air Force institutions, for example in Army or Navy facilities, were registered, so case ascertainment was believed to be complete. Initially, 246 cases were identified. Sixteen cases were later dropped from the study when incomplete data were found, or when there was a lack of agreement between hospitalization and master personnel records.

The basis for each brain tumor diagnosis could not be determined from existing records. However, the nosologic schemes used to classify brain tumors are specific. Primary malignant, metastatic, and benign tumors are each coded differently. Comparison of death certificates with autopsy data in one study suggested that diagnostic inaccuracies for brain tumor registrations were not a significant concern (28). Therefore, misclassification, which might have appeared due to the presence of benign or metastatic tumors in the case series, should not have been an important factor in this investigation.

Using US Air Force personnel records, four controls were randomly selected from each case's "risk set," which was composed of all individuals in the cohort who exactly matched the case on year of birth and race, and who were present in the US Air Force cohort at the time the case was diagnosed (8). Potential controls were not eligible if they had been diagnosed with leukemia, breast cancer, or malignant melanoma, because excess risks for these tumors have been associated with EMF exposures in other studies (3).

Occupational histories

Complete occupational histories were obtained from Air Force personnel records for each study subject. For each assignment held, these histories included the job title and starting and ending dates. Additional abstracted data included the subject's age, race, military rank, and duration of military service, all at the time that the index case was diagnosed. Control histories were censored at the index case's diagnosis date to ensure that case and control person-time coincided. All subsequent control history was ignored.

Military rank at the time of index case diagnosis was included as a surrogate for socioeconomic status. These data were subsequently stratified into six categories according to a scheme commonly used in the US Air Force: airman basic to senior airman, *airman*; sergeant to technical sergeant, *noncommissioned officer*; master sergeant to chief master sergeant, *senior noncommissioned officer*; second lieutenant to captain, *company grade officer*; major to colonel, *field grade officer*; brigadier general to lieutenant general, *general officer*. Airmen, noncommissioned officers, and senior noncommissioned officers were further classified as *enlisted men*, while all others were categorized as *officers*.

Exposure estimation

A job title-time-exposure matrix utilizing potential intensity scores for both extremely low frequency and radiofrequency/microwave EMFs was developed as a basis for exposure estimation. This matrix ultimately contained over 1,950 entries, indexing 552 different job titles over a time period covering 1953 to 1992. A temporal component was needed in the matrix because the exposure scores assigned to a given job-title shifted over time—driven by changes in technology and by arbitrary personnel reclassifications.

Extremely low frequency electromagnetic fields. An expert panel composed of a radiation physicist, occupational health specialist, and an industrial hygienist was utilized to score all US Air Force job titles by potential for exposure to extremely low frequency EMFs. Each panelist was provided detailed listings of US Air Force job titles, along with a short job description and the starting and stopping dates for each particular job title. Raters independently assigned no, possible, probable, and definite scores to each job title-time couplet. These approximated the rating system developed by Lin et al. (11). For the most part, typical Air Force occupations were readily classified using their system, although some US Air Force-specific vocations, such as electronic warfare countermeasures specialist, presented challenges to the panelists. In general, those classified as definitely exposed were believed to have a potential for exposure to high intensity extremely low frequency EMFs, such as power generation specialists and telecommunications equipment repairers. Probable exposure assignments were given to most electronics equipment operators, while the possible designation was used for pilots and related technical occupations. All others were classified as non-exposed. A composite rating was assigned to a job title-time couplet if at least two raters awarded the same score. Such was the case in 92.8 percent of the couplets reviewed. Where no agreement occurred,

i.e., each rater awarded a different score, a rounded average of the three scores was used. This method was needed for only 7.2 percent of the couplets.

Radiofrequency/microwave electromagnetic fields. Data were available to quantitate potential historical exposures to radiofrequency/microwave EMFs in the US Air Force population. Since 1972, all incidents in which Air Force workers were believed to be exposed to radiofrequency/microwave EMFs above permissible exposure limits (10 mW/cm^2) have been reported to a central registry. Based on data in this registry, a job exposure matrix was developed by the author which categorized US Air Force job titles over time as having no, possible, or probable potential for exposure to radiofrequency/microwave EMFs. Probable intensity scores were assigned to occupations that had been reported to have been overexposed to radiofrequency/microwave EMFs in the past, as well as closely related job titles. Essentially, this included all occupations involved in the maintenance and repair of radiofrequency and microwave emitters. The possible intensity score was assigned to occupations requiring the operation of radiofrequency or microwave emitters for which excessive exposures had not been reported. All other job titles were assigned to the non-exposed category.

For each study subject, estimates of cumulative potential career exposure for extremely low frequency and radiofrequency/microwave EMFs were developed by summing the product of exposure score and months spent in a particular occupation for all job titles held during each individual's career. Outcomes for extremely low frequency EMF-exposed individuals ranged from 1 to 885 extremely low frequency intensity-months in 48 percent of the study subjects, while for radiofrequency/microwave EMF exposure, 30 percent had exposures ranging from 8 to 610 radiofrequency/microwave intensity-months.

Ionizing radiation. Personal dosimetry data were obtained from a centralized US Air Force ionizing radiation exposure registry. Primarily, these records consisted of thermoluminescent dosimeter data, from which lifetime deep, superficial, extremity, and neutron exposures were available, although only the superficial doses were used in this study. Three percent of the study subjects had ionizing radiation dosimetry records. The rest were assigned zero lifetime occupational ionizing radiation exposures.

Analysis

Matching on year of birth and race was maintained in the analyses. Odds ratios and confidence intervals were obtained from conditional logistic regression models using a commercial software package (29).

Analyses were first performed with dichotomous exposure variables for extremely low frequency and radiofrequency/microwave EMFs, and ionizing radiation, where subjects who had any potential exposure were considered exposed and compared with individuals who had no potential for exposure. Study subjects were also allocated to increasing potential cumulative exposure strata for both extremely low frequency and radiofrequency/microwave by calculating arithmetic quartiles of positive scores among the controls. These were then compared with those individuals who had never been occupationally exposed to EMFs and had zero scores. Potential dose-response relations were examined by observing stratified data for departures from linear models (30).

Joint effects between extremely low frequency and radiofrequency/microwave EMFs, extremely low frequency EMFs and ionizing radiation, and radiofrequency/microwave EMFs and ionizing radiation were assessed by the addition of interaction terms to main effects models. Assessment of joint effects under this circumstance was model-dependent—in this instance, a multiplicative model of independent effects was assumed.

RESULTS

The study base consisted of approximately 880,000 US Air Force members, who contributed 11,174,248 person-years to the cohort between 1970 and 1989. From this population, 230 cases and 920 matched controls were ultimately selected for study. Demographic characteristics of these subjects are presented in table 1.

Increasing military rank was found to be associated with age-race-adjusted brain tumor risk, as shown in table 2. Officers appeared to have an excess age-race-adjusted brain tumor risk when compared with enlisted men. Senior (field grade and general) officers had an even higher age-race-adjusted brain tumor risk in contrast to all other US Air Force members. Recoding military rank as officer vs. enlisted and senior officer vs. all others increased precision and yielded the statistically significant odds ratios shown in table 3. Consequently, presence or absence in the senior officer ranks at the time of index case diagnosis was used as a covariate in subsequent analyses.

In table 4, age-race-senior military rank-adjusted analyses of the brain tumor risk for those ever potentially exposed to extremely low frequency and radiofrequency/microwave EMFs, and to ionizing radiation, in comparison to those never exposed are presented. Odds ratios for ever vs. never potential exposure to extremely low frequency EMFs were slightly elevated following adjustment for age, race, and senior military

TABLE 1. Distribution of US Air Force study subjects, by age, race, military rank, and months of military service, 1970-1989

Variable	No. of cases	No. of controls
Age group (years)		
≤24	53	211
25–34	78	310
35–44	81	325
45–54	15	62
≥55	3	12
Race		
White	203	812
Black	23	92
Other	4	16
Military rank		
Airmen	34	111
Non-commissioned officers	100	466
Senior non-commissioned officers	35	205
Company grade officers	24	76
Field grade officers	35	60
General officers	2	2
Months of service, mean (SD*)	148 (99)	151 (94)

* SD, standard deviation.

rank. Similar results were observed in the analyses for radiofrequency/microwave EMFs. In contrast to the outcomes for nonionizing radiation, the ionizing radiation age-race-senior military rank-adjusted odds ratios were not elevated.

No clear potential exposure-response patterns emerged from the data presented in tables 5 and 6, where brain tumor risks are reported by potential cumulative exposure level for extremely low frequency and radiofrequency/microwave EMFs, respectively. The data for ionizing radiation exposure were not subjected to stratified analyses, because there were too few study subjects with nonzero exposures to yield precise point estimates. Months of military service was dropped from the analysis when it proved to be colinear ($r = 0.82$) with age, a matching variable.

Assessment of joint effects between the exposures relied on the use of dichotomous coding, since the analyses with polychotomous variables suggested that excess brain tumor risk was not dose-dependent for extremely low frequency and radiofrequency/microwave EMFs. Joint effects were examined for the following exposure combinations: extremely low frequency and radiofrequency/microwave EMFs, extremely low frequency EMFs and ionizing radiation, and radiofrequency/microwave EMFs and ionizing radiation, where main effects models were composed of these variables and senior military rank. None of the interaction terms resulted in significant decreases in deviance from the main effects model when they were

TABLE 2. Age-race-adjusted odds ratios and 95% confidence intervals (CI) for brain tumors among US Air Force workers, by military rank category, 1970–1989

Military rank category	No. of cases	No. of controls	Odds ratio	95% CI*
Enlisted				
Airmen	34	111	1.00†	
Non-commissioned officers	100	466	0.55	0.29–1.03
Senior non-commissioned officers	35	205	0.52	0.23–1.18
Officers				
Company grade officers	24	76	0.79	0.37–1.70
Field grade officers	35	60	1.76	0.74–4.14
General officers	2	2	5.47	0.42–71.2

* Test-based confidence intervals.
† Reference group.

TABLE 3. Age-race-adjusted odds ratios and 95% confidence intervals (CI) for brain tumors among US Air Force workers, by main military rank category, 1970–1989

Main military rank category	No. of cases	No. of controls	Odds ratio	95% CI*
Officer vs. enlisted				
Enlisted	169	782	1.00†	
Officers	61	138	2.11	1.48–3.01
Senior officers vs. all others				
All others	193	858	1.00†	
Senior officers	37	62	3.30	1.99–5.45

* Test-based confidence intervals.
† Reference group.

TABLE 4. Age-race-senior military rank-adjusted odds ratios and 95% confidence intervals (CI) for brain tumors among US Air Force workers ever exposed to extremely low frequency or radiofrequency/microwave electromagnetic fields or ionizing radiation compared with those never exposed, 1970–1989

Exposure	No. of cases	No. of controls	Odds ratio	95% CI*
Extremely low frequency				
Ever exposed	129	441		
Never exposed	101	479	1.28	0.95–1.74
Radiofrequency/microwave				
Ever exposed	94	281		
Never exposed	136	639	1.39	1.01–1.90
Ionizing radiation				
Ever exposed	5	30		
Never exposed	225	890	0.58	0.22–1.52

* Test-based confidence intervals.

added (data not shown), indicating that statistical interaction at least was not present.

DISCUSSION

A small association between both extremely low frequency and radiofrequency/microwave EMF exposure and brain tumor risk was detected in this study of men who were serving in the US Air Force at the time of index case diagnosis. Interaction between exposures at different frequencies was not present, which calls into question the role of extremely low frequency EMFs as a tumor promoter.

The most important outcome of this investigation was the association between senior military rank and brain tumor risk in the US Air Force cohort. A concern might be that age and months of Air Force service would be expected to increase with military rank. However, conditional logistic models using age, months of service, and military rank showed no evidence for confounding or joint effects between senior military rank and age or months of service in the US

TABLE 5. Age–race–senior military rank-adjusted odds ratios and 95% confidence intervals (CI) for brain tumors among US Air Force workers ever exposed to increasing levels of extremely low frequency electromagnetic fields compared with those never exposed, 1970–1989

Exposure*	No. of cases	No. of controls	Odds ratio	95% CI†
None	101	479	1.00‡	
1–59	39	118	1.31	0.81–2.14
60–134	33	97	0.93	0.56–1.53
135–270	44	113	1.60	1.00–2.55
271–885	13	113	1.44	0.88–2.34

* Produce of potential exposure score and duration in months summed for every occupation.
† Test-based confidence intervals.
‡ Reference group.

TABLE 6. Age–race–senior military rank-adjusted odds ratios and 95% confidence intervals (CI) for brain tumors among US Air Force workers exposed to increasing levels of radiofrequency/microwave electromagnetic fields compared with those never exposed, 1970–1989

Exposure*	No. of cases	No. of controls	Odds ratio	95% CI†
None	136	639	1.00‡	
2–48	15	62	1.26	0.71–2.24
49–127	29	71	1.50	0.90–2.52
128–235	25	68	1.26	0.71–2.22
236–610	25	80	1.51	0.90–2.51

* Product of potential exposure score and duration in months summed for every occupation.
† Test-based confidence intervals.
‡ Reference group.

Air Force. The latter finding suggests that the association between brain tumors and military rank was not influenced by these factors (data not shown). In all phases of this study, military rank was positively associated with brain tumor risk. The highest age-race-adjusted odds ratio for brain tumor risk was found for senior officers above the rank of major, although all officers had a significantly elevated brain tumor risk when compared with enlisted personnel. Socioeconomic status can encompass many factors, including education, income, power, life-style, and prestige. Military rank is believed to be an accurate indicator of socioeconomic status in the US Air Force cohort, because it correctly represents income and also reflects status and power within the US Air Force community.

Among occupational studies, only that of Thériault et al. (8) reported socioeconomic status to be strongly associated with brain tumor risk. Sahl et al. (7) considered socioeconomic status to be a weak confounder which would be likely to bias their results downward, and therefore they did not adjust for socioeconomic status in their analyses. Other population-based studies have investigated the role of socioeconomic status as a risk factor for brain tumors. Preston-Martin (31) used census tract residence as a surrogate for social class in her study of central nervous system tumors among residents of Los Angeles, California. She found a positive trend for glioma risk among males by social

class when all races were combined. Demers et al. (32) obtained similar results in their analysis of brain tumor mortality among men in Washington state, where socioeconomic status was coded using the usual occupation listed on death certificates and a socioeconomic index derived from the US Census classification of occupations. Statistically significant trends in brain tumor risk by social class were also reported by Preston-Martin et al. (33) from their descriptive study of data from the New Zealand Cancer Registry. The results of this investigation are in agreement with their findings.

Several investigators have speculated that the positive association between brain tumors and increasing socioeconomic status might have arisen because of a greater likelihood of diagnostic confirmation, whether clinically or postmortem (32, 34). In the US Air Force, however, medical care is provided free to all members and differences in health care availability by military rank would not be expected, at least for serious conditions. Therefore, diagnostic (selection) bias should not have influenced the outcomes reported here. Similar conclusions have been reported by Preston-Martin et al. (33) from studies in New Zealand, which has a nationalized health care system.

Although the present study has its limitations, particularly in exposure estimation, it does suggest that there is a small association between potential EMF

exposures and brain tumor risk among Air Force members, especially for personnel potentially exposed to radiofrequency/microwave EMFs. There was no evidence in this investigation that extremely low frequency EMFs acted as brain tumor promoters following radiofrequency/microwave EMF or ionizing radiation exposures. Senior military rank, as a surrogate for socioeconomic status, was the factor most strongly associated with age-race-adjusted brain tumor risk in this study.

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