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EFFECTS OF LOW POWER MICROWAVES ON THE LOCAL CEREBRAL BLOOD FLO--ETC(U)  
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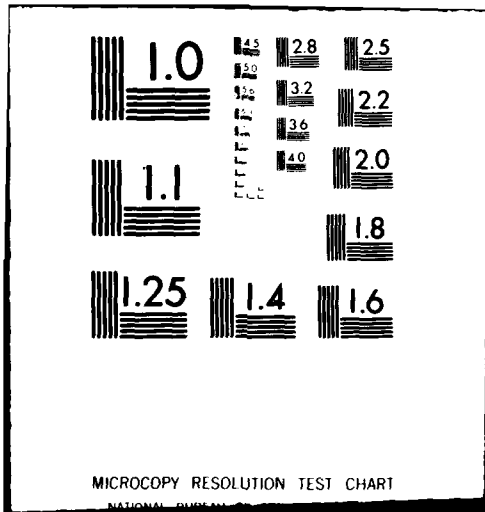
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(6) EFFECTS OF LOW POWER MICROWAVES ON THE LOCAL CEREBRAL BLOOD FLOW OF CONSCIOUS RATS

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Background

Camouflage, decoy and deception techniques can play a decisive role on the modern battlefield. The rapid advance of surveillance, targeting and weapons homing sensor technology now makes every element which is detected almost assured of being destroyed. Camouflage, decoy and deception equipment and techniques are a low cost way to increase survivability and shift this balance by reducing the signature of targets (camouflage), increasing the signature level of the background (clutter), creating false targets (decoy), and distorting the perceived target value (disguise).

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~~One~~ decoy and deception concept presently being considered is to remotely create the perception of noise in the heads of personnel by exposing them to low power, pulsed microwaves. When people are illuminated with properly modulated low power microwaves the sensation is reported as a buzzing, clicking, or hissing which seems to originate (regardless of the person's position in the field) within or just behind the head (12). The phenomena occurs at average power densities as low as microwatts per square centimeter with carrier frequencies from 0.4 to 3.0 GHz. By proper choice of pulse characteristics, intelligible speech may be created. Before this technique may be extended and used for military applications, an understanding of the basic principles must be developed. Such an understanding is not only required to optimize the use of the concept for camouflage, decoy and deception operations but is required to properly assess safety factors of such microwave exposure.

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Under MERADCOM's In-House Laboratory Independent Research (ILIR) Program an experimental effort to explore the basic interaction between microwaves and brain function has been conducted. In a joint program with MERADCOM, Stanford Research Institute (SRI) and Walter Reed Army Institute of Research (WRAIR), it was shown for the first time that lethality, seizures and behavioral performance decrements were strongly frequency and polarization dependent (2,3). A later collaboration between MERADCOM and WRAIR demonstrated for the first time increases in the differential uptake of saccharides to water in several brain regions of rats when exposed to low power microwaves of the same characteristics which can create the perception of noise in people (4). These increases could be caused by alterations of the blood-brain barrier, brain blood volume, cerebral blood flow, or some combination of the above. In order to better define and understand these results a joint program was undertaken with MERADCOM, Naval Medical Research Institute (NMRI) and the National Institutes of Health (NIH) to measure local cerebral blood flow in conscious rats when exposed to low power, pulsed microwaves. It is these experiments which will be reported here.

#### Introduction

Recent experiments indicating that low power microwaves may affect brain activity and possibly alter central nervous system function have caused wide spread concern regarding the safety of such exposure. Seemingly conflicting experimental results, difficulties in extrapolating animal findings to humans, problems of dosimetry, and misunderstanding over what constitutes an effect versus a hazard have created a controversy in the area of microwave safety (5). Of particular concern have been recent reports, from several different laboratories (4, 6-9), that low power microwaves may alter the permeability of the blood-brain barrier (BBB). Several of the techniques (10,11) used to measure BBB permeability depend on constant blood flow during the experiment. We now report for the first time that microwave exposure increases local cerebral blood flow (LCBF) in the conscious rat and suggest that previously reported BBB permeability changes (4), may be less in magnitude than originally indicated.

Development of the in vivo  $^{14}\text{C}$ -2- deoxyglucose technique (12, 13) as a measure of glucose consumption and the in vivo  $^{14}\text{C}$ - iodoantipyrine technique (14) as a measure of LCBF have resulted in experiments (15) yielding convincing evidence that local blood flow is regulated by the metabolic activity of that region. Further experiments (16,17) have led to the demonstration that brain functional activity, sensory stimulation, cerebral temperature, biochemical

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balance, blood volume, metabolism, BBB permeability, and blood flow are coupled. Microwave exposure has been experimentally shown to affect all of these parameters except LCBF. Humans and small animals can perceive microwaves as auditory sensations (18). Microwave and very high frequency (VHF) energy have influenced spontaneous and conditioned electroencephalographic patterns in cats, rabbits, and rats (19-21). Low-level pulsed and continuous wave (CW) microwaves have altered glucose consumption in the auditory structures of rat brain (22). Low intensity microwaves have caused thyroid suppression and adrenomedullary activation (23). Microwaves have also been reported to affect behavior (24-28), neurotransmitter levels (29), BBB permeability (4,6-9) cerebral calcium efflux (30,31) and behavioral baselines to pharmacological agents (32). It seemed a reasonable hypothesis then that microwaves would alter brain blood flow. If so, the measurement of LCBF in the conscious animal would provide a valuable technique to map the regional influence of microwaves and lead to a better understanding of microwave safety factors and general brain function.

### Materials and Methods

In 1955 the first method (33,34) for quantitative determination of the rates of blood flow in discrete brain structures was reported; the method employed the radioactive gas tracer  $^{131}\text{I}$ -trifluoriodomethane along with the principles of inert gas exchange. This radioactive gas was chosen because diffusional equilibrium between brain and blood is established almost instantaneously when it is administered. Two technical problems are encountered in the use of this technique of a volatile gas tracer: short half life and difficult assay. To overcome these problems, investigators have used  $^{14}\text{C}$ -antipyrine as a nongaseous tracer; however, it provides values of local cerebral blood flow that are considerably below those obtained with radioactive gases (35,26). In addition, transfer of antipyrine from blood to brain is limited by its comparatively low diffusion at the cerebral vasculature. Recently, a new method has been developed that uses  $^{14}\text{C}$ -iodoantipyrine and an audioradiographic assay (37). The  $^{14}\text{C}$ -iodoantipyrine has a higher oil/water partition coefficient than  $^{14}\text{C}$ -antipyrine, is more permeable at the cerebrovasculature, and provides values of local cerebral blood flow that are comparable to those obtained with  $^{131}\text{I}$ -trifluoriodomethane.

The present blood flow experiments were performed with  $^{14}\text{C}$ -iodoantipyrine measured by brain homogenization and liquid scintillation counting (38). Although scintillation counting does not give the structural resolution of audioradiography and densitometry, it is repeatable, fast, quantitative, and technically easier. Male Wistar

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rats from the Walter Reed colony were provided food and water ad libitum until they had grown to a body weight of 250-320g. All animals were prepared for the experiments by insertion of polyethylene catheters into one femoral artery and vein under sodium pentobarbital (35 mg/Kg, i.p.) anesthesia. After surgical preparation, the hindquarters were wrapped in a loose-fitting plaster cast and secured to a styrofoam block. The animals were allowed to recover from anesthesia for 4 hours or more before the experiment. Conscious rats could freely move their forequarters, head and neck, and appeared comfortable.

The rats were selected randomly and individually exposed for 5, 30, or 60 minutes to sham irradiation (controls) or for 5, 15, 30, 45, or 60 minutes to pulsed microwaves of  $15\text{mW/cm}^2$  average power density. A microwave anechoic chamber (2m wide by 3m high by 3m long) maintained at  $23 \pm 2^\circ\text{C}$  was used for exposure. This chamber also aided in the reduction and standardization of possible background noise stimulation. All microwave exposures were at a frequency of 2.8 GHz, a pulse rate of 500 pps, and a pulse width  $2\mu$  sec. Exposures were produced by a 40KW pulsed microwave generator (Applied Microwave Lab., PH40) coupled to a standard gain horn. The field intensity was measured with a field intensity meter (National Bureau of Standards) and an isotropic radiation monitor (Narda Model-8300). Overall accuracy of reported average power density measurements is estimated to be better than  $\pm 25\%$ .

Within 5 min after sham or microwave exposure, the catheter in the femoral vein was connected to a 5-ml syringe, which was mounted in a constant-flow pump (model 341, Sage Instruments) and set to deliver at a rate of  $0.78\text{ ml min}^{-1}$ . The femoral vein was then infused for 50 s with isotonic saline containing  $5\mu\text{C/ml}$  of  $^{14}\text{C}$ -iodoantipyrine (New England Nuclear, specific activity =  $50\text{ mC/mmol}$ ). Periodically during infusion,  $20\mu\text{l}$  samples of arterial blood were collected into heparinized vials. The rats were decapitated 50 seconds after infusion. Brain regions were dissected out according to the method of Chiueh *et al.*, (39,40) placed in tared scintillation vials, and weighed. The tissue and whole blood samples were dissolved and subjected to routine liquid scintillation counting (Beckman, LS-9000).

Local cerebral blood flow,  $F$ , was calculated from the equation first derived by Kety (33,34):

$$C_{\text{brain}}(T) = mF \int_0^T C_{\text{blood}}(t) e^{-mF(T-t)} dt$$

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where  $C_{\text{brain}}(T)$  equals the tracer concentration (dpm/g) in the brain parenchyma (excluding intravascular concentration) at time  $T$ ;  $m$  is a constant between 0 and 1 that represents the extent to which diffusional equilibrium between the tissue and blood is reached (for iodoantipyrine  $m=1$ );  $C_{\text{blood}}(t)$  equals the tracer concentration (dpm/ml) in the arterial blood as a function of time;  $\lambda$  equals the steady state, tissue: blood partition co-efficient (0.8 for iodoantipyrine);  $t$  equals the variable time; and  $T$  equals the time from initial infusion to decapitation.  $C_{\text{brain}}(t)$ , which represents intraparenchymal brain concentration of tracer, was obtained by subtracting intravascular from net regional radioactivity when the former quantity was taken as the product of regional blood volume and blood concentration at time  $T$ .

### Results and Discussion

The results of the present study indicate that low-power pulsed microwave exposure increases the LCBF in the conscious rat. By 60 minutes of exposure, the blood flow in all 17 brain regions sampled increased a minimum of 39% with many increasing well over 100%. The calculated values of blood flow for all exposures are presented in Table 1. The LCBF values for the control animals subjected to either 5, 30 or 60 minutes of sham exposure were unchanged and are combined in the table. In six regions both the left and right brain structures were individually sampled. No left right differences were observed, and after statistical testing these data were pooled and denoted as "P" in the table. The first brain region affected, after only 5 minutes of microwave exposure, was the inferior colliculus. The largest blood flow increases occurred after 60 minutes of microwave exposure and were in the pineal, pituitary, temporal cortex, inferior colliculus, lateral geniculate, medial geniculate.

The LCBF values of the control animals varied from 0.86 to  $1.84 \text{ cm}^3 \text{ g}^{-1} \text{ min}^{-1}$  and are in close agreement with those in the recent literature. In the conscious rat, the values of LCBF are higher in the visual, auditory, and sensorimotor areas due to normal external stimulation of these systems. The increased LCBF values after short time microwave exposure, 5 to 30 minutes, occurred in these same sensory regions and suggest along with experiments of Wislon *et al* (22) indicating microwave induced glucose consumption changes in these regions, that microwaves are increasing the metabolic activity through direct or indirect excitation of brain tissue. After longer microwave exposure, 60 minutes, all the sampled brain regions displayed large LCBF increases of a magnitude which suggest a gross alteration of

Table 1 Effect of Microwave Exposure on Local Cerebral Blood Flow in the Conscious Rat

Tissue	15 mW/Cm <sup>2</sup> Microwave Exposure					
	Sham Exposure (7)	5 min(5)	15 min(8)	30 min(3)	45 min(7)	60 min(7)
Pineal	1.33±0.16	1.35±0.48	2.01±0.28	2.51±0.38 <sup>‡</sup>	3.65±0.53*	5.21±0.30*
Pit	1.16±0.15	1.27±0.09	1.50±0.10 <sup>‡</sup>	1.75±0.33 <sup>‡</sup>	1.70±0.10 <sup>‡</sup>	2.06±0.24*
Hypo	1.40±0.18	1.28±0.09	1.41±0.08	1.61±0.05	1.54±0.07	2.00±0.08*
Temp,P	1.84±0.16	1.78±0.14	1.96±0.14	2.52±0.34 <sup>‡</sup>	2.92±0.20*	3.26±0.36*
Cereb	1.27±0.15	1.32±0.13	1.21±0.06	1.31±0.09	1.29±0.05	1.76±0.08 <sup>‡</sup>
White	0.86±0.07	1.00±0.04	0.91±0.06	0.90±0.15	1.02±0.06	1.58±0.15*
Visual, P	1.80±0.13	1.95±0.09	2.04±0.12	2.07±0.23	2.13±0.12 <sup>‡</sup>	3.42±0.23*
SC,P	1.64±0.18	1.69±0.07	1.75±0.08	1.90±0.18	1.90±0.08	2.82±0.21*
IC,P	1.82±0.09	2.23±0.10*	2.43±0.16*	2.65±0.25*	2.64±0.05*	4.37±0.30*
LG,P	1.39±0.13	1.41±0.10	1.55±0.13	1.69±0.10	1.83±0.07*	3.79±0.43*
MG,P	1.47±0.15	1.35±0.09	1.75±0.11	1.68±0.10	1.84±0.09 <sup>‡</sup>	3.24±0.29*

Local cerebral blood flow values are the means ±S.E.M. in cm<sup>3</sup>g<sup>-1</sup>min<sup>-1</sup> from the measurements made on the number of animals in parenthesis. The LCBF values for the control animals subjected to either 5, 30, or 60 minutes of sham exposure were unchanged and after statistical testing are combined in the table. In several cases both left and right brain regions were individually measured yielding double the number of samples as indicated in the parenthesis. After statistical testing these data were pooled and denoted in the table as "p". Statistical significance was calculated first by brain region for all exposure conditions with a one way analysis of variance then for individual exposure conditions by a student's t-test. (Differs significantly from sham mean <sup>‡</sup>p<0.05, <sup>\*</sup>p<0.01, and <sup>\*</sup>p<0.005). Pit is pituitary, Hypo is hypothalamus, temp is grey matter in the temporal region, SC is the superior colliculus, IC is the inferior colliculus, LG is lateral geniculate, and MG is medial geniculate.

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brain function due possibly to stress from microwave induced temperature rise, fatigue, brain stimulation, biochemical imbalance, neurotransmitter release, etc.

One area impacted by these results is the selection of techniques to quantitatively measure the affects of microwaves on BBB permeability. The dual indicator techniques of Oldendorf or Crone use either highly diffusible or relatively non diffusible internal standards and rely on constant circulatory flux during the experiment. Most previous studies reporting BBB permeability changes due to microwave exposure used protein bound markers and observation with optical, fluorescent, or electron microscopy. The one study, (4), reporting quantitative measurement of microwave induced BBB permeability increases used the Oldendorf technique with tritiated water as the internal standard. It has been subsequently found that water does not freely equilibrate in the brain, and as cerebral blood flow increases, water's diffusion is lowered, (44). Since the Oldendorf technique measures the ratio of a test substance to the internal standard, as blood flow increases and causes the brain tissue level of water to decrease, the reported ratio measurements of BBB permeability may be overly high. The small BBB permeability increases which do seem to exist from microwave exposure, as evidenced by microscopy studies, may be a secondary effect caused by microwave alterations of blood flow, blood pressure, and/or blood vessel area.

Our present experiments demonstrating microwave induced LCBF increases indicate an alteration of brain activity. The mechanism of this, and other mentioned microwave effects on brain function are unclear; direct or indirect stimulation of central or peripheral receptors by microwave induced thermal, mechanical or electrical disturbances are possibilities.

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41. The opinions and assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Department of Defense. The experiments reported herein were conducted according to the principles set forth in the "Guide for the care and use of laboratory animals", Institute of Laboratory Resources, National Research Council, DHEW, Pub. No (NIH) 78-23.