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Effects of Cell Phone Radiofrequency Signal Exposure on Brain Glucose Metabolism

Nora D. Volkow, MD, Dardo Tomasi, PhD, Gene-Jack Wang, MD, Paul Vaska, PhD, Joanna S. Fowler, PhD, Frank Telang, MD, Dave Alexoff, BSE, Jean Logan, PhD, and Christopher Wong, MS

National Institute on Drug Abuse, Bethesda, Maryland (Dr Volkow); National Institute on Alcohol Abuse and Alcoholism, Bethesda (Drs Volkow, Tomasi, and Telang and Mr Wong); and Medical Department, Brookhaven National Laboratory, Upton, New York (Drs Wang, Vaska, Fowler, and Logan and Mr Alexoff).

Abstract

Context—The dramatic increase in use of cellular telephones has generated concern about possible negative effects of radiofrequency signals delivered to the brain. However, whether acute cell phone exposure affects the human brain is unclear.

Objective—To evaluate if acute cell phone exposure affects brain glucose metabolism, a marker of brain activity.

Design, Setting, and Participants—Randomized crossover study conducted between January 1 and December 31, 2009, at a single US laboratory among 47 healthy participants recruited from the community. Cell phones were placed on the left and right ears and positron emission tomography with (¹⁸F)fluorodeoxyglucose injection was used to measure brain glucose metabolism twice, once with the right cell phone activated (sound muted) for 50 minutes (“on” condition) and once with both cell phones deactivated (“off” condition). Statistical parametric mapping was used to compare metabolism between on and off conditions using paired *t* tests, and Pearson linear correlations were used to verify the association of metabolism and estimated

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Corresponding Author: Nora D. Volkow, MD, National Institute on Drug Abuse, 6001 Executive Blvd, Room 5274, Bethesda, MD 20892 (nvolkow@nida.nih.gov).

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Study concept and design: Volkow.

Acquisition of data: Wang, Vaska, Telang, Alexoff, Wong.

Analysis and interpretation of data: Volkow, Tomasi, Vaska, Fowler, Telang, Logan.

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amplitude of radiofrequency-modulated electromagnetic waves emitted by the cell phone. Clusters with at least 1000 voxels (volume >8 cm³) and $P < .05$ (corrected for multiple comparisons) were considered significant.

Main Outcome Measure—Brain glucose metabolism computed as absolute metabolism ($\mu\text{mol}/100$ g per minute) and as normalized metabolism (region/whole brain).

Results—Whole-brain metabolism did not differ between on and off conditions. In contrast, metabolism in the region closest to the antenna (orbitofrontal cortex and temporal pole) was significantly higher for on than off conditions (35.7 vs 33.3 $\mu\text{mol}/100$ g per minute; mean difference, 2.4 [95% confidence interval, 0.67–4.2]; $P = .004$). The increases were significantly correlated with the estimated electromagnetic field amplitudes both for absolute metabolism ($R = 0.95$, $P < .001$) and normalized metabolism ($R = 0.89$; $P < .001$).

Conclusions—In healthy participants and compared with no exposure, 50-minute cell phone exposure was associated with increased brain glucose metabolism in the region closest to the antenna. This finding is of unknown clinical significance.

The dramatic worldwide increase in use of cellular telephones has prompted concerns regarding potential harmful effects of exposure to radiofrequency-modulated electromagnetic fields (RF-EMFs). Of particular concern has been the potential carcinogenic effects from the RF-EMF emissions of cell phones. However, epidemiologic studies of the association between cell phone use and prevalence of brain tumors have been inconsistent (some, but not all, studies showed increased risk), and the issue remains unresolved.¹

RF-EMFs emitted by cell phones are absorbed in the brain² within a range that could influence neuronal activity.³ Although the intensity of RF-EMFs is very low, the oscillatory frequencies correspond to some of the oscillation frequencies recorded in neuronal tissue and could interfere with neuronal activity.⁴ Thermal effects from RF-EMFs have also been invoked as a mechanism that could affect neuronal activity, although temperature changes produced by current cell phone technology are likely minimal.⁵ Studies performed in humans to investigate the effects of RF-EMF exposures from cell phones have yielded variable results.⁶ For example, imaging studies that used positron emission tomography (PET) to measure changes in cerebral blood flow (CBF) with RF-EMF exposures from cell phones have reported increases,^{7,8} decreases and increases,^{9,10} or no changes¹¹ in CBF. The discrepancies among these imaging studies likely reflect their relatively small sample sizes (9–14 participants), and the potential confounding of CBF measures reflecting vascular rather than neuronal signals.^{12–14} This highlights the need for studies to document whether RF-EMFs from cell phone use affects brain function in humans.

The objective of this study was to assess if acute cell phone exposure affected regional activity in the human brain. For this purpose we evaluated the effects in healthy participants ($N = 47$) of acute cell phone exposures on brain glucose metabolism, measured using PET with injection of (¹⁸F)fluorodeoxyglucose (¹⁸FDG). Brain glucose metabolic activity is a more proximal marker of neuronal activity than measures of CBF, which reflects vascular as well as neuronal components.¹⁵ Also, because brain glucose metabolic measures obtained with ¹⁸FDG reflect the averaged brain activity occurring over a 30-minute period,¹⁶ this method allowed assessment of the cumulative effects of cell phone exposure on resting brain metabolism. Because exposure to RF-EMFs from cell phones is well localized and is highest in brain regions closest to the antenna,² we hypothesized that the effects on brain metabolism would be greatest in inferior and anterior brain regions, the regions that would be exposed to the highest RF-EMF amplitude for the cell phone model used in this study.

METHODS

Participants

The study was conducted at Brookhaven National Laboratory from January 1, 2009, through December 31, 2009, and was approved by the local institutional review board (Committee on Research Involving Human Subjects, Stony Brook University). We enrolled 48 healthy participants recruited from advertisements in local newspapers and screened for absence of medical, psychiatric, or neurologic diseases. Special attention was given to ensure that participants did not abuse addictive substances (including alcohol and nicotine), and urine toxicology studies were performed prior to the imaging sessions to ensure lack of psychoactive drug use. For technical reasons, data from one of the participants could not be used (see below). Table 1 provides demographic characteristics and cell phone usage histories of the 47 participants whose data were used in the analysis. Participants each received \$250 for their participation in the study (\$200 for PET scans [\$100 per scan] plus \$50 for the physical examination and laboratory work). All participants provided written informed consent after receiving a complete description of the study.

Experimental Conditions

All participants had 2 scans performed on separate days using PET with ^{18}F FDG injection under resting conditions. For both scans 2 cell phones, one placed on the left ear and one on the right, were used to avoid confounding effects from the expectation of a signal from the side of the brain at which the cell phone was located. For one of the days both cell phones were deactivated (“off” condition). For the other day the right cell phone was on (activated but muted to avoid confounding from auditory stimulation) and the left cell phone was off (“on” condition). For the on condition the cell phone was receiving a call (from a recorded text), although the sound was muted. The order of conditions was randomly assigned, and participants were blinded to the condition. The mean time between the first and the second study was 5 (SD, 3) days.

Two Samsung model SCH-U310 cell phones, capable of transmitting at either cellular or personal communications service frequency bands with code division multiple access modulation, were used for each study. The maximum specific absorption rate in the head for this cell phone model corresponds to 0.901 W/kg. Cell phones were placed over each ear with microphones directed toward the participant’s mouth and were secured to the head using a muffler that did not interfere with the lower part of the cell phone, where the antenna is located. Activation of the right cell phone was started 20 minutes prior to ^{18}F FDG injection and maintained for 30 minutes afterward to correspond with the ^{18}F FDG uptake period. During the 50-minute period participants sat on a comfortable chair in a quiet, dimly lit room and with their eyes open, with a nurse present to ensure that they kept their eyes open and did not fall asleep.

The RF-EMF emissions were recorded once before the call (background) and every 5 minutes during the stimulation period to ensure that the call was not terminated. This was accomplished with a handheld spectrum analyzer (model FSH6; Rohde & Schwarz, Munich, Germany) connected to a cellular wide-band log periodic directional antenna (model 304411; Wilson Electronics, St. George, Utah) aimed at the head from a distance of 3 feet. The cellular band was active, with a frequency of 837.8 MHz. This frequency was monitored with a resolution bandwidth of 1 MHz. Activation of the cell phone for the experimental period was also corroborated with the records obtained from the cell phone company. For 1 participant the cell phone signal was interrupted at the time of ^{18}F FDG injection; this participant’s data were not included in the analysis.

PET Scanning

In preparation for the study, participants had 2 venous catheters placed, one in the antecubital vein for radiotracer injection and the other in a superficial vein on the dorsal surface of the hand for sampling of arterialized blood. Arterialization was achieved by warming the hand to 44°C. The participants were injected with ^{18}F FDG (148–222 MBq [to convert to millicuries, divide by 37]) and asked to refrain from moving or speaking during the 30-minute ^{18}F FDG uptake period. At the end of the sessions, the cell phones were removed and the participants were positioned in the PET scanner as previously described.¹⁷ Participants were scanned with a whole-body tomograph (ECAT HR+; Siemens/CTI, Munich, Germany), with a resolution of $4.6 \times 4.6 \times 4.2 \text{ mm}^3$ as measured by National Electrical Manufacturers Association protocols. Emission scans were started 35 minutes after ^{18}F FDG injection and lasted 20 minutes. Transmission scans were performed simultaneously.

Radiofrequency Field

The average position of the antenna in the stereotactic space of the Montreal Neurological Institute (\mathbf{r}_0) ($\mathbf{r}_0 = 21$ [SD, 10] mm for x [left to right], 30 [SD, 11] mm for y [anterior to posterior], -160 [SD, 7] mm for z [superior to inferior]) was determined for 21 participants using calibrated orthogonal photography that registered orthogonal views (front and sides) of the cell phone positions on the participant's head. The positions of the eyes were used as landmarks to determine \mathbf{r}_0 with the aid of the standard brain template (ch2.nii) provided in MRI-cron (available at <http://www.sph.sc.edu/comd/rorden/mricron/>). The relative amplitude of the cell phone's electric field, $E(\mathbf{r})$, at every position in the brain, \mathbf{r} , was computed in Interactive Data Language version 6.0 (ITT Visual Information Solutions, Boulder, Colorado) using the far-field approximation, $E(\mathbf{r}) \sim \|\mathbf{r} - \mathbf{r}_0\|^{-3}$, of a dipole field (Figure 1).

Image Analysis

The data were analyzed using statistical parametric mapping (SPM) in the SPM2 mapping package (Wellcome Department of Cognitive Neurology, London, United Kingdom).¹⁸ The SPM analyses were performed on the absolute as well as the normalized (to whole-brain metabolism) metabolic images. For this purpose, the images were spatially normalized using the SPM2 PET template and a $2\text{-mm}^3 \times 2\text{-mm}^3 \times 2\text{-mm}^3$ voxel size and were subsequently smoothed with an 8-mm isotropic Gaussian kernel. Voxel-wise paired t tests were used to assess regional changes in glucose metabolism.

Because the electric field, $E(\mathbf{r})$, produced by the cell phone decreases rapidly with distance to the antenna, we hypothesized that the effects of cell phones on glucose metabolism would occur in regions close to the antenna and that the regions far from the antenna would show no effects. Therefore, the corrections for multiple comparisons were restricted to brain regions in which $E(\mathbf{r})$ was higher than 50% of the maximum field value, E_0 , in the brain ($E_0/2 < E(\mathbf{r}) < E_0$) (Figure 1). Thus, the Bonferroni method with a searching volume (S_v) of 201.3 cm^3 ($S_v = 25 \text{ } 161$ voxels) was used to correct cluster-level P values for multiple comparisons as a function of the cluster volume (C_v) ($P_{\text{corr}} = P \times S_v/C_v$). Clusters with at least 1000 voxels ($C_v > 8 \text{ cm}^3$) and $P < .05$ (corrected for multiple comparisons) were considered significant.

A simple model assuming a linear relationship between cell phone-related increases in metabolism ($\Delta^{18}\text{F}$ FDG; average across participants) and E was used. The paired values ($\Delta^{18}\text{F}$ FDG _{i} , E_i) from all voxels that were statistically significant in the SPM2 t test analyses contrasting on vs off conditions within S_v were sorted by E , clustered in groups of 50 voxels, and averaged. These clusters were treated as independent. The Pearson linear

correlation factor, R , was used to assess the linear relationship between $\Delta^{18}\text{FDG}$ and E in Interactive Data Language version 6.0.

The sample-size calculation was based on our preliminary study of the effect of low-frequency magnetic field gradients in glucose metabolism,¹⁹ which demonstrated metabolic differences between stimulation and sham conditions with effect size (ratio between the mean difference and the pooled standard deviation) between 0.65 and 0.80. The minimal important difference in glucose metabolism used to determine the sample size was 1 $\mu\text{mol}/100$ g per minute. For such effect sizes, to achieve a power of at least 80% using the independent-samples t test with a significance level of .05, at least 40 participants were needed.

RESULTS

Whole-brain glucose metabolism did not differ between conditions, which for the off condition corresponded to 41.2 $\mu\text{mol}/100$ g per minute (95% confidence interval [CI], 39.5–42.8) and for the on condition to 41.7 $\mu\text{mol}/100$ g per minute (95% CI, 40.1–43.3). However, there were significant regional effects. Specifically, the SPM comparisons¹⁴ on the absolute metabolic measures showed significant increases (35.7 vs 33.3 $\mu\text{mol}/100$ g per minute for the on vs off conditions, respectively; mean difference, 2.4 [95% CI, 0.67–4.2]; $P = .004$) in a region that included the right orbitofrontal cortex (BA11/47) and the lower part of the right superior temporal gyrus (BA 38) (Figure 2 and Table 2). No areas showed decreases. Similar results were obtained for the SPM analysis of the normalized metabolic images (normalized to whole-brain glucose metabolism), which also showed significant increases (1.048 vs 0.997 for the on vs off conditions, respectively; mean difference, 0.051 [95% CI, 0.017–0.091]; $P < .001$) in a region that included right orbitofrontal cortex and right superior temporal gyrus (BA 38) (Figure 2).

The regression analysis between cell phone–related increases in metabolism ($\Delta^{18}\text{FDG}$) and E revealed a significant positive correlation both for the absolute metabolic measures ($R = 0.95$, $P < .001$) and the normalized metabolic measures ($R = 0.89$, $P < .001$) (Figure 3). This indicates that the regions expected to have the greater absorption of RF-EMFs from the cell phone exposure were the ones that showed the larger increases in glucose metabolism.

CONCLUSIONS

These results provide evidence that the human brain is sensitive to the effects of RF-EMFs from acute cell phone exposures. The findings of increased metabolism in regions closest to the antenna during acute cell phone exposure suggest that brain absorption of RF-EMFs may enhance the excitability of brain tissue. This interpretation is supported by a report of enhanced cortical excitability to short transcranial magnetic stimulation pulses (1 msec) following 40-minute RF-EMF exposures.²⁰

Although increases in frontal CBF during acute cell phone exposure had been previously reported by 2 independent PET laboratories, such increases did not occur in brain regions with the highest RF-EMF exposures.^{7–10} Moreover, one of these studies reported CBF decreases in the region with maximal RF-EMF exposure.¹⁰ These discrepancies are likely to reflect, among others, the methods used, particularly because the ^{18}FDG method is optimal for detecting long-lasting effects (30 minutes) in brain activity, whereas CBF measures reflect activity over 60 seconds. In this respect, this study is an example of the value of the ^{18}FDG method for detecting cumulative effects in brain activity that may not be observed when using more transient measures of activity. Discrepancies also could reflect uncoupling between CBF and metabolism.^{12–14} Moreover, the relatively large sample size

($n = 47$) improved our ability to detect small effects that may have been missed in prior studies with smaller sample sizes.¹¹

The experimental setup also differed from prior studies that used cell phones for which the antenna was closest to superior and middle temporal cortices.²¹ However, this is unlikely to have accounted for the differences in results, because the findings in this study show increases in the region with maximal RF-EMF exposure, whereas findings from other studies have shown decreases in regions with the highest RF-EMF exposures, increases in regions far from the antenna, or both. However, the increases in frontal CBF previously reported with acute cell phone exposure possibly could reflect a downstream effect of connections with the regions that had the highest RF-EMF exposures.

The linear association between cell phone–related increases in metabolism ($\Delta^{18}\text{FDG}$) and E suggests that the metabolic increases are secondary to the absorption of RF-EMFs from cell phone exposures. The mechanisms by which RF-EMFs from cell phones could affect brain glucose metabolism are unclear. However, based on findings from in vivo animal and in vitro experiments, it has been hypothesized that this could reflect effects of RF-EMF exposure on neuronal activity mediated by changes in cell membrane permeability, calcium efflux, cell excitability, and/or neurotransmitter release.⁴ Athermal effect of cell phones on the brain has also been proposed,²² but this is unlikely to contribute to functional brain changes.⁵ Disruption of the blood-brain barrier has also been invoked as a potential mechanism by which RF-EMFs from cell phone exposure could affect brain activity.²³ A recent clinical study reported alterations in a peripheral biomarker of blood-brain barrier integrity (transferrin) after cell phone exposure, but the significance of this finding is unclear.²⁴

The increases in regional metabolism induced by RF-EMFs (approximately 7%) are similar in magnitude to those reported after suprathreshold transcranial magnetic stimulation of the sensorimotor cortex (7%–8%).²⁵ However, these increases are much smaller than the increases after visual stimulation reported by most studies (range, 6%–51%).²⁶ The large difference in the magnitude of regional glucose metabolic increases is likely to reflect multiple factors, including differences in glycolytic rate between brain regions,²⁷ the duration of the stimulation (transient stimulation increases glucose metabolism more than continuous stimulation²⁶), and the characteristics of the stimulation used.²⁸ Indeed, whereas resting glucose metabolism is predominantly supported by glucose oxidation (>90%), with acute visual stimulation the large increases in glucose metabolism appear to reflect predominantly aerobic glycolysis,²⁹ which is used for purposes other than energy expenditures, and actual energy utilization is estimated to be 8% at most.¹³

Concern has been raised by the possibility that RF-EMFs emitted by cell phones may induce brain cancer.³⁰ Epidemiologic studies assessing the relationship between cell phone use and rates of brain cancers are inconclusive; some report an association,^{31–33} whereas others do not.^{34–36} Results of this study provide evidence that acute cell phone exposure affects brain metabolic activity. However, these results provide no information as to their relevance regarding potential carcinogenic effects (or lack of such effects) from chronic cell phone use.

Limitations of this study include that it is not possible to ascertain whether the findings pertain to potential harmful effects of RF-EMF exposures or only document that the brain is affected by these exposures. Also, this study does not provide an understanding of the mechanism(s) by which RF-EMF exposures increase brain metabolism, and although we interpret these exposures as indicators of neuronal excitation, further studies are necessary to corroborate this. Lastly, this model assumes a linear relationship between the amplitude of

the radiofrequency field and its effects in neuronal tissue, but we cannot rule out the possibility that this relationship could be nonlinear.

In summary, this study provides evidence that in humans RF-EMF exposure from cell phone use affects brain function, as shown by the regional increases in metabolic activity. It also documents that the observed effects were greatest in brain regions that had the highest amplitude of RF-EMF emissions (for the specific cell phones used in this study and their position relative to the head when in use), which suggests that the metabolic increases are secondary to the absorption of RF-EMF energy emitted by the cell phone. Further studies are needed to assess if these effects could have potential long-term harmful consequences.

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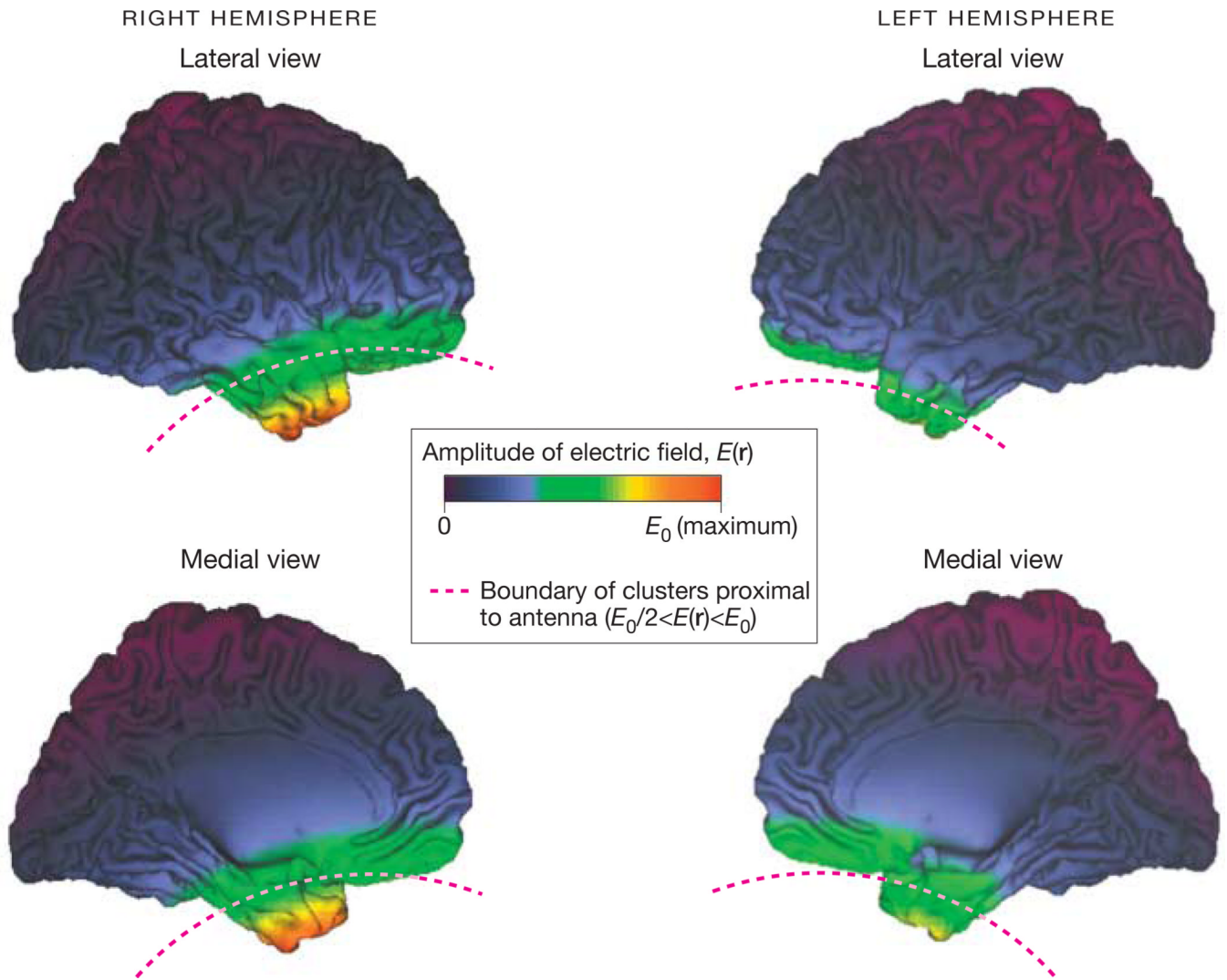


Figure 1. Amplitude of the Electric Field Emitted by the Right Cellular Telephone Antenna Rendered on the Surface of the Human Brain
 E_0 indicates maximal field value. Clusters proximal to the antenna are inferior to the red dashed line. Images created using the freeware Computerized Anatomical Reconstruction and Editing Toolkit (CARET) version 5.0 (<http://brainvis.wustl.edu/wiki/index.php/Caret:About>).

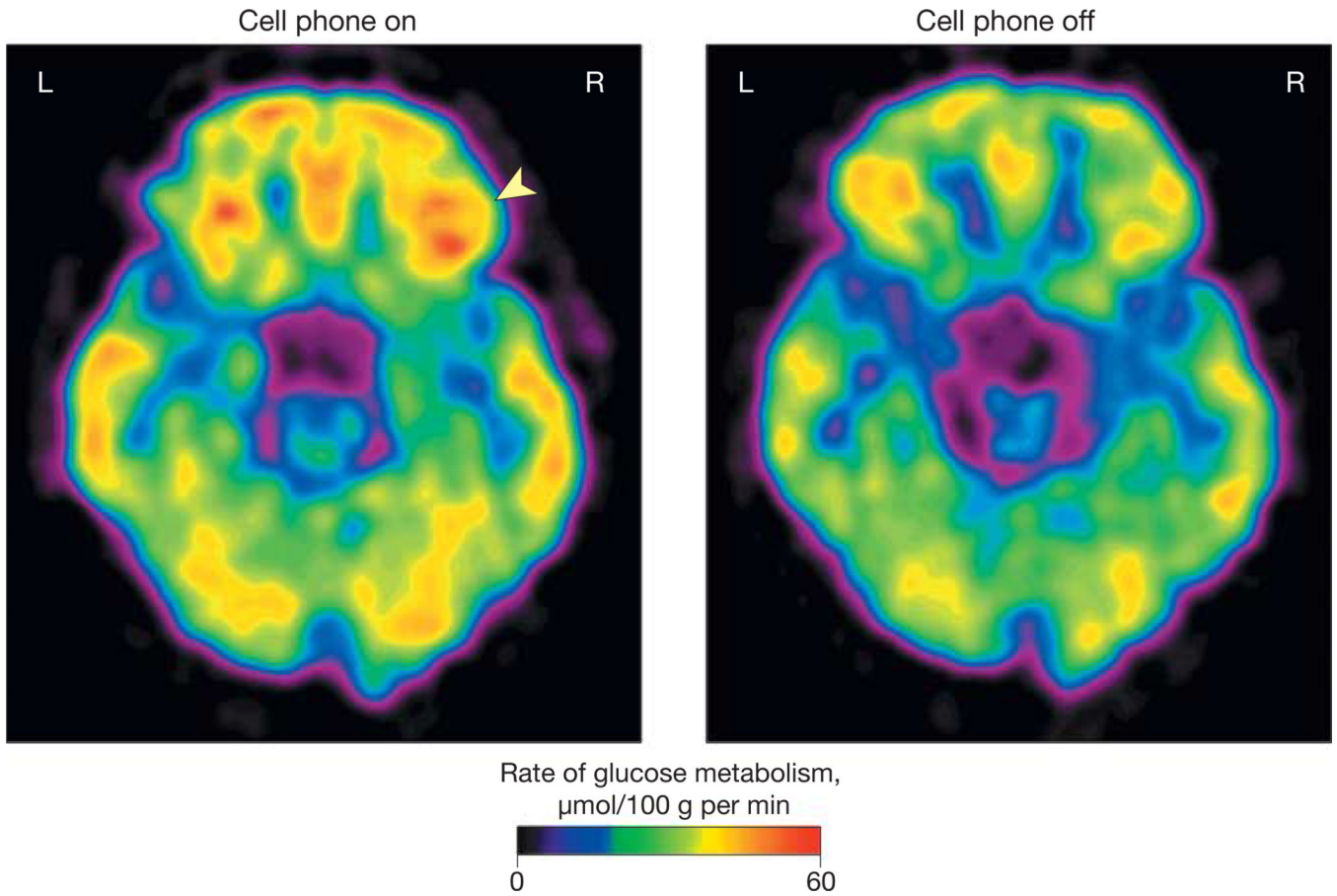


Figure 2. Brain Glucose Metabolic Images Showing Axial Planes at the Level of the Orbitofrontal Cortex

Images are from a single participant representative of the study population. Glucose metabolism in right orbitofrontal cortex (arrowhead) was higher for the “on” than for the “off” condition (see “Methods” for description of conditions).

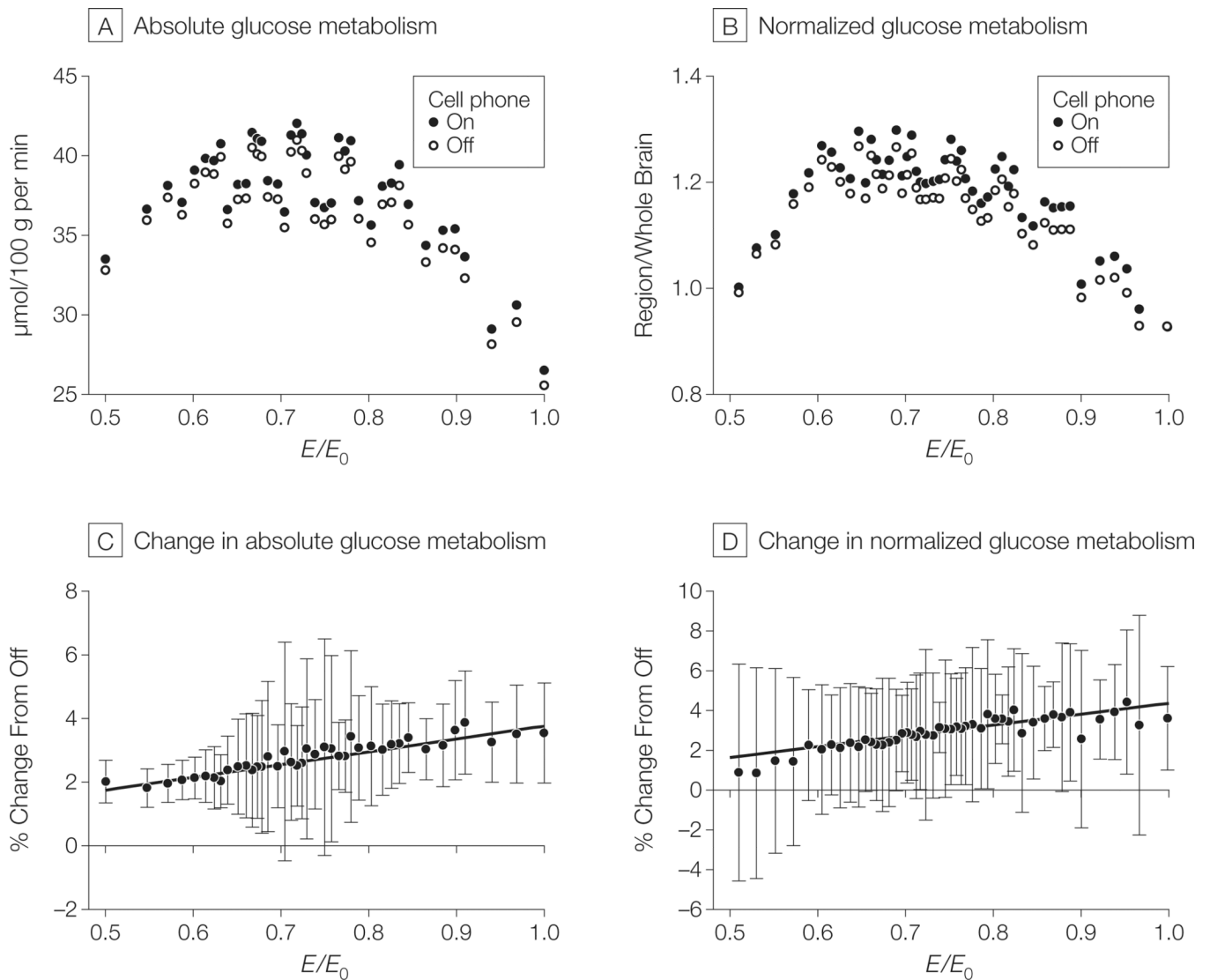


Figure 3. Measures of Absolute and Normalized Glucose Metabolism and Correlation Between Estimated Electromagnetic Field Amplitudes and Increases in Measures (N = 47 Participants)
 A and B, Mean measures of absolute glucose metabolism (µmol/100 g per minute) and normalized glucose metabolism (region/whole brain; units cancel) in regions with increased metabolism during “on” vs “off” conditions (see “Methods” for description of conditions) in the brain area within the spherical constraint, $E_0/2 < E(\mathbf{r}) < E_0$ (where E_0 indicates maximal field value and $E(\mathbf{r})$ indicates amplitude of the theoretical electromagnetic field) and the $E(r)$ emitted by the antenna of the right cellular telephone. Absolute = 40 clusters; 2000 voxels were activated within searching volume and grouped into clusters of 50 voxels each; normalized = 48 clusters; 2400 voxels were activated within searching volume and grouped into clusters of 50 voxels each. Range of variability (95% confidence interval [CI]): 9–21 µmol/100 g per minute (panel A) and 0.29–0.57 (panel B). C and D, Regression lines between cell phone–related increases in absolute and normalized glucose metabolism (both expressed as % change from the off condition) in brain regions within the spherical constraint, $E_0/2 < E(\mathbf{r}) < E_0$, and the theoretical electric field, $E(\mathbf{r})$, emitted by the antenna of the right cell phone. Increases significantly correlated with estimated electromagnetic field amplitudes (absolute: $R = 0.95$, $P < .001$; normalized: $R = 0.89$, $P < .001$). Data

markers indicate mean metabolic measures; error bars, 95% CIs. Linear regression lines were fitted to the data using Interactive Data Language version 6.0.

Table 1

Characteristics and Cellular Telephone Histories of Participants (N = 47)

Characteristic	No. (%)
Age, mean (SD), y	31 (9)
Sex	
Men	23 (48.9)
Women	24 (51.1)
Body mass index, mean (SD) ^a	26 (3)
Handedness	
Right-handed	43 (91.5)
Left-handed	4 (8.5)
Education mean (SD), y	14 (2)
Cell phone use, mean (SD) [range], min/mo	1500 (1850) [15–9000]
Ear favored for use	
Right	38 (80.9)
Left	9 (19.1)

^aCalculated as weight in kilograms divided by height in meters squared.

Table 2
 Statistical Parametric Mapping For Brain Regions Showing Higher Glucose Metabolism With Cellular Telephone On Than Off

Brain Region	Volume ^a	Brodmann Area	Region Coordinates, mm ^b			Z Score, On vs Off	P _{corr} ^c	On vs Off, Mean Difference (95% CI)
			x	y	z			
Absolute glucose metabolism								
Right inferior frontal	2649	47	18	23	-18	2.7	.05	2.4 (0.67-4.2) ^d
Right superior temporal			24	12	-37	2.6		
Right middle frontal			23	38	-15	2.6		
Normalized glucose metabolism								
Right superior temporal	2910	47	27	2	-35	3.1	.05	7.8 (2.7-12.9) ^d
Right inferior frontal			16	27	-16	3.1		
Right middle frontal			23	38	-15	3.1		

Abbreviation: CI, confidence interval.

^aNo. of voxels. One voxel = 0.008 mm³.

^bCoordinates on the Montreal Neurological Institute stereotactic space corresponding to distance (in mm) for x (left to right), y (anterior to posterior), and z (superior to inferior).

^cSee "Methods" for details of calculation of Bonferroni-corrected *P* value.

^dValues for absolute metabolism reported in μmol/100 g per minute; those for normalized metabolism reported as percentages.