

NO EVIDENCE OF CEREBROMETABOLIC EFFECTS OF NON-IONIZING RADIATION

*ALBERT GJEDDE, CHRISTOPHER BAILEY,
PAUL CUMMING, KIM VANG HANSEN, ARNE MØLLER*

In 2004, the present researchers at the PET-center, Aarhus University Hospitals, were funded to conduct, first, a pilot study and, second, a definitive study of the metabolic reactions of the brain to potential effects of non-ionizing radiation from cellular telephones. The researchers entertained the working (“null”) hypothesis that radiation emitted by cellular telephones would not be able to deposit sufficient energy in adjacent areas of brain tissue to raise measurably the temperature and hence energy metabolism of the tissue.

Unphysiological increases of brain energy metabolism, if present, would give rise to so-called excitotoxic lesions, caused by abnormally intense release of the excitatory amino acid neurotransmitter glutamate to the extracellular space and subsequent action at ionotropic receptors of cortical neurons. Evidence of locally mismatched changes of cerebral blood flow and glucose consumption on one hand and oxygen consumption on the other, consistent with elevated oxygen extraction fractions and impaired delivery of oxygen upon reception of the radiofrequency radiation would be evidence against this “null” hypothesis, which would justify further attempts to reject the hypothesis.

In the pilot study, as well as in all subsequent studies, three healthy volunteers in two sessions underwent three applications of Positron Emission Tomography (PET) in a randomized design of cellular telephones on or off with an experimental cellular telephone fixed to the right ear. The researchers three tracers, ^{15}O -water, ^{15}O -oxygen, and ^{18}F -fluorodeoxyglucose (glucose analogue) to determine, respectively, regional cerebral blood flow, oxygen consumption, and glucose consumption. Dynamic emission recordings with arterial sampling were obtained with the ECAT Exact HR47 positron emission tomograph, and individual PET scans were co-registered to individual MR images.

In the first three subjects, substantial (25-55 %) increases of oxygen extraction fractions (OEF) were noted by simple inspection in the region of the right medial temporal lobes in the PET images of the subjects, at approximately the same distance from the antenna. Due to the small number of subjects included at this time, no statistical analysis was completed at this time, but the project was funded in 2005 to include additionally eleven subjects.

In the subsequent preliminary analysis of the first ten subjects, anatomical masks of whole brain, hippocampus, and temporal lobes, were used to co-register individual MR and PET images to a standard template. Individual PET images were co-registered to individual MR images with a 6-parameter linear fit, and individual MRI images were then co-registered to the standard template with a 12-parameter linear fit. Masks of the standard template were applied to each dynamic PET images separately and used to extract time-activity curves of tracer uptake. The curves were fitted with standard kinetic models of the brain uptake to determine the cerebral blood flow (CBF), cerebral metabolic rate of oxygen (CMRO₂), cerebral metabolic rate for glucose (CMR_{glc}), and OEF. In the 10 subjects, small but significant increases of the variables CMRO₂ and OEF were calculated for the right temporal lobe mask when the on- and off-radiation conditions were compared. No significant changes happened for the CBF, nor were any other significant changes recorded in any other brain region. These observations were presented at the 7th International Conference on Brain Energy Metabolism in Lausanne in 2006.

For the same 10 subjects, Aalborg University undertook a complementary study of the individual three-dimensional numerical dosimetry fields emanating from the cellular telephone used with the PET sessions (see report of O. Franek, J.B. Andersen & G.F. Pedersen), including 1) Specific Absorption Rate (SAR) averaged over 10 g of brain tissue [W/kg], 2) electric field intensity E [V/m], 3) magnetic field intensity H [A/m], and 4) current density J [A/m²]. When masks prepared from the individual SAR fields were applied to these 10 subjects, no significant changes of CBF, CMRO₂, CMR_{glc}, or OEF were calculated in the regional extent of the SAR masks.

Part of the “null” hypothesis ruled out the possibility that glutamate release would intensify to an extent sufficient to increase glutamate occupancy at any of the many glutamate receptors. To specifically examine the presence of intensified glutamate release under the influence of radiofrequency radiation, this group received 4

additional funding to test a novel PET tracer of glutamate release in the form of a labeled ligand of the AMPA receptor, which would react by displacement to any increase of glutamate occupancy at these receptors. In the past, radioligands of the glutamate receptors have tended to be water-soluble and hence to have difficulty crossing the blood-brain barrier, at least in larger mammals. However, the ligand we had in mind had shown promising properties in preliminary experiments on rodent behavior, but no direct evidence of brain uptake existed prior to the proposed studies. We successfully completed the labeling of this very specific AMPA receptor antagonist, but in vivo determination of uptake in rodent and porcine brains revealed no binding or uptake in either species.

To obtain a normal material of a sufficient size with which to compare the results of volunteers on and off radiofrequency radiation, we collected regional cerebral blood flow rates in 82 normal volunteers in the age range 20 to 80 years, and matching regional cerebral metabolic rates for oxygen in 49 of these volunteers, one of the largest such materials in the world. This material was designed to become the standard basis for comparison with materials associated with specific physiological or pathological states. Because the normal material revealed a very large interindividual variability of measures of CBF and CMRO₂, for which there are now wide-reaching explanations, we developed a novel approach to the normalization of individual statistical parametric maps to a common but non-biased average. We also revised the laboratory's standard procedures of statistical parametric mapping, BRAINSTAT, developed by Professor Keith Worsley in collaboration with the Montreal Neurological Institute, with which this laboratory has a long very long-standing relationship.

The definitive analysis of all 14 subjects employed these updated and improved procedures. Statistical parametric maps of the main variables, CBF, CMRO₂, CMR_{glc}, and OEF, were prepared as described above. The maps were compared on and off the radiofrequency radiation, as well as with the standard maps of the large normal population. These procedures upheld no statistically significant change of any of the variables anywhere in the brain in the presence of the radiofrequency radiation, nor any differences between the maps of the 14 subjects and the maps of the same variables in the normal population. In conclusion, there is no evidence that indicates that the "null" hypothesis of no influence of the non-ionizing radiation on variables of brain circulation and metabolism in vivo must be abandoned.