Images of Conflict: MEG vs. EEG

The father of a new brain-imaging method has become its severest critic—producing controversy in an emerging field

New technologies frequently promise the moon—but they don't always deliver. Initially a new technology may appear to be a miracle tool, but as it works its way toward practical application, the luster often dims. The real advantages—and disadvantages—of the method become clearer, and finally it takes its place in the scientific toolbox as one among many useful instruments, all having different benefits and drawbacks. By the end of this summer, magnetoencephalography (MEG), which only 2 years ago was the center of very high hopes indeed, may turn out to be an example of this scenario. Then, again, it may not.

MEG is a method of determining electrical activity in the brain noninvasively by detecting the magnetic fields associated with electric currents produced by neuronal activity. Hopes for it have been extravagant because MEGs offered to localize brain activity more precisely and more easily than electroencephalography (EEG)—the standard method—or high-tech methods such as positron emission tomography (PET) scanning. Researchers from fields as diverse as epilepsy and cognitive psychology have been experimenting with the new technique and several companies have developed and are now selling complex MEG systems costing millions of dollars. But recently, MIT physicist David Cohen has been arguing that the claims for MEGs—particularly the notion that they are superior to EEGs—are overblown.

The proponents of MEG aren't taking Cohen's charges lying down: They fault him for using outdated equipment, doing sloppy work, and coming to erroneous conclusions. This week, at a meeting in Toronto, Cohen and his critics will square off in public for the first time; that face-off coincides with a printed debate in the pages of a neurology journal. What's perhaps most ironic about this controversy is that Cohen himself is the inventor of the field—and if his work is correct, it could tarnish the promise of MEGs, cut research funding, and deter companies from investing more money in the extremely expensive devices. By the end of the summer it may become clearer whether Cohen is a cool observer trying to quash inflated claims or a frustrated father attempting to strangle a child who's outgrown him. Cohen didn't begin his scientific career thinking about the brain's magnetic fields. He began as a high-energy physicist, but found it frustrating to be a "small cog in a big machine" as a member of a large collaboration. In 1965 he switched fields and began applying his talent to measuring the magnetic fields of the brain, coining the term "magnetoencephalography" in the process (*Science*, 23 August 1968). The

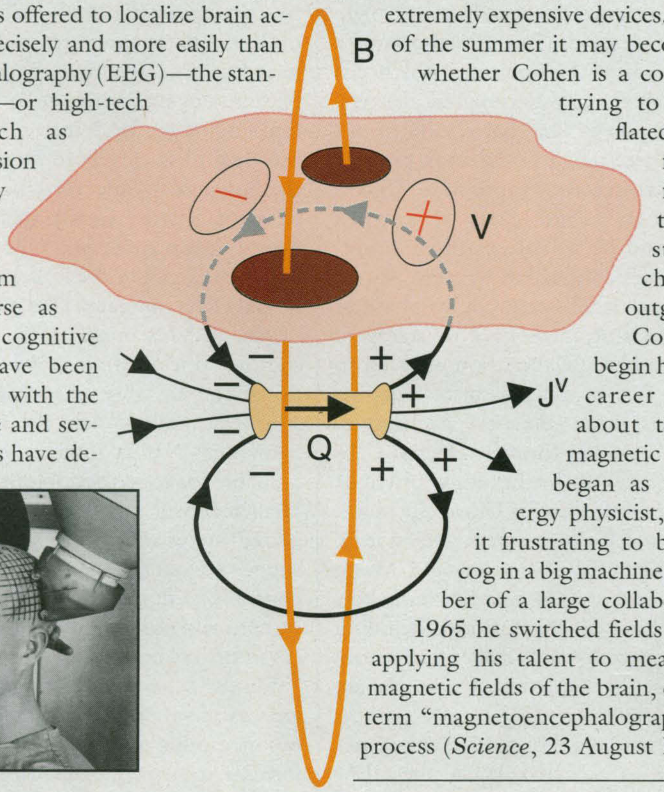


Photo: MIT; Illustration Source: Samuel Williamson

Magnetic moment. *Neuronal activity in a small segment of brain tissue produces a net intracellular electric current* (Q). *Accompanying this current is a magnetic field* (B) *that emerges from a patch of scalp (pink) and re-enters it nearby. MEG records changes in this field. The current also produces a charge imbalance that creates an electric field with a current density* (J)*, which diffuses to reach the scalp. EEG measures the electric potential* (V) *associated with the current at the scalp.*

field took off 2 years later when Cohen encountered Superconducting Quantum Interference Devices (SQUIDs): extremely sensitive detectors of magnetic fields, developed for other purposes, that were hundreds of times more sensitive than the bulky coils Cohen had been using.

With the addition of SQUIDs, the promise of MEGs seemed to soar far beyond that of EEGs. For example, EEGs measure the sum total of all electrical currents reaching the scalp. Researchers would like to be able to localize the source of a particular current, but that task is made more difficult by the fact that the electrical conductivity of brain tissue varies from region to region. MEGs, however, measure the magnetic fields produced by those same electrical currents, and since the brain is essentially transparent to magnetic fields, using them to localize the electrical source is simpler and more sensitive. MEG proponents claimed neuronal activity could be pinpointed to within millimeters.

Lured by the bait of MEG's simplicity and precision, researchers pounced. Epilepsy researchers were interested in a method of localizing sources of seizures that did not involve cutting open the head and lacing it with wires. Psychologists and physiologists were interested in knowing which parts of the brain are activated when a person is engaged in using language, visualizing, dreaming, and so on. Major interdisciplinary collaborations using MEGs quickly sprang up at the Helsinki University of Technology and at New York University (NYU), the latter group headed by physicist Samuel J. Williamson and psychologist Lloyd Kaufman. The exciting prospects for extensive applications in medicine and basic physiology led Rudolfo Llinas, chair of NYU's department of physiology and biophysics, to set up a complementary MEG lab.

Despite the field's promise, an inhibiting factor was instrumentation, which was expensive and in a relatively primitive state of development. Cohen's SQUID had a lone detector in a cryostat that measured magnetic field strength at a single point. But several companies, including Biomagnetic Technologies (BTI), Siemens, CTF, and Phillips, began developing commercially available SQUIDs not only for basic researchers but also for possible clinical use. Soon multichannel instruments appeared, with several detectors in each cryostat, that were able to measure the magnetic field pattern at a number of points simultaneously. Today, 37-channel SQUIDs have been built by BTI and Siemens, costing some $3 million apiece; a 128-channel system is on the drawing board.

The interest in MEGs reached a high-water mark 2 years ago at a meeting organized by Williamson and Kaufman: the Seventh International Conference on Biomagnetism at NYU (*Science*, 8 September 1989). Attendees at the meeting spoke of the prospect of doctors using MEGs for "annual brain checks." But even in the midst of that enthusiasm, says Cohen, he had preliminary results that ran counter to the prevalent euphoric spirit (though he kept mum at the meeting because his experiment, begun in 1988, was only half-complete).

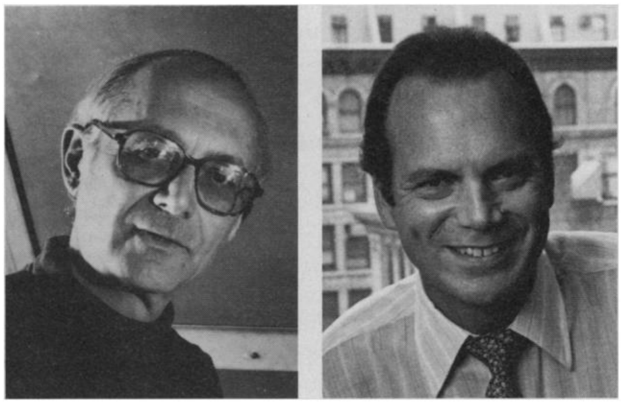
Cohen claims that his spirit-dampening research is more realistic than most of the work that's fueled the high hopes for MEGs. "Most statements in the literature about the localization potential of MEGs and EEGs," he says, "are based on measurements made with model glass heads or skulls filled with goo. We thought the fairest comparison would be an experiment with a live head—but one in which you knew exactly where the source was."

That wasn't an easy thing to do, but Cohen finally managed it. Four severely epileptic patients from Boston's Beth Israel hospital whose heads had been wired with electrodes for therapy were refitted with specially designed platinum electrodes (ordinary electrodes are magnetic and would swamp the measurements) and transferred to Cohen's magnetically shielded room at MIT's Francis Bitter National Magnet Laboratory. The MIT team passed currents through the patients' electrodes while monitoring them from the outside with EEGs and MEGs; simultaneous head x-rays established the precise location of the electrodes.

The result, announced in "MEG versus EEG Localization Test Using Implanted Sources in the Human Brain" (*Annals of Neurology* 28:6, December 1990), was that "the MEG offers no significant advantage over the EEG in localizing a focal source." Says Cohen: "We weren't saying the MEG was useless." He argues, however, that "its principal use is not in localization but in its ability to see more specific information than EEGs can." For reasons that have to do with the physics of electromagnetism and the shape of the skull, MEGs are sensitive only to magnetic fields coming from sources where the current flow is tangent to the skull, whereas EEGs pick up a superposition of all electrical sources to reach the scalp, swamping weak signals. MEGs thus get less—but more specific—information than EEGs can. "Identifying those tangential sources, rather than localization, is the real use of the MEG," says Cohen. "There is no 'localization magic.'"

Cohen's critics—including Williamson, Llinas, and Kaufman of the NYU group and Riitta Hari of the Helsinki group—don't accept this criticism. They say that Cohen, an ex-physicist, lacks understanding of brain anatomy. Furthermore, they say, he used inadequate measuring techniques. Many of these limitations, they say, are due to the fact that he still works with a 1-channel SQUID system—which in the day of the 37-channel SQUID, they say, is like trying to compete in the Indianapolis 500 in a Model T.

What's happened, say the critics, is that the field has simply passed by its progenitor. "David played a key role in discovering a variety of biomagnetic fields," says Williamson, "and his work was state-of-the-art at that time. But the field has evolved. It's now strongly interdisciplinary, and there have been dramatic changes in technology and methods of interpretation. It's essential to keep up with these changes to do acceptable work, and we find his paper is inappropriate by present standards." Others hint that Cohen became a spoiler in part because he resents losing his original preeminence in the field.



Oedipal conflict. *David Cohen* (left) *is the father of MEG; Samuel Williamson is a high-tech practitioner of the art.*

But whether Cohen is correct or not—and whatever his motivation—the controversy also highlights a less personal issue having to do with the sociology of the field (which is coming to be called "MSI," for Magnetic Source Imaging). Like many relatively young fields, this one does not yet have standard practices, instruments, or training programs. And in the uncertainty produced by the existence of different techniques, instruments, and ways of interpreting results, the emergence of controversies such as the one sparked by Cohen is no surprise. Until the field achieves a stabilization of standards, such controversies are likely to persist in one form or another.

And for the moment, this particular controversy is the chief topic of interest in the field—not only among brain imaging researchers, but also among those who fund them and those who build the equipment they use. Says Llinas, "If Cohen's claim were correct, a $50,000-EEG machine would do essentially the work of a $3-million MEG device. It would then be ridiculous to buy the latter, or put in work to develop more of them. But this is not the case—as we and others have demonstrated." And Williamson has recently received worried calls from individuals at funding agencies asking just how serious the controversy is.

The controversy will reach a peak this week with publication of the August issue of *Annals of Neurology* containing two letters critical of Cohen's 1990 article, one by Williamson and the other by Hari and other members of the Finnish group, as well as a reply by Cohen. At the same time, the second annual meeting of the International Society for Brain Electromagnetic Tomography (ISBET) will be going on in Toronto. On Tuesday, 30 July, there will be a symposium titled, "Functional Localization: Comparative Aspects of MEG and EEG." At the symposium Cohen will not only describe his experimental work but will also present for the first time theoretical arguments that his MIT group has developed against any significant superiority of MEGs over EEGs.

When he makes his presentation at the symposium, Cohen may well cite two pieces of research that he claims support his iconoclastic contentions regarding MEG. The first is a Ph.D. thesis done in 1987 by Cees J. Stok at Twente University of Technology in Holland. The other is a paper published last week in the July *Neurology*, "Localization of Implanted Dipoles by Magnetoencephalography," by a team of four researchers led by epileptologist S. Sato using a 7-channel system at NIH in Bethesda, Maryland. Although this last paper did not do an EEG comparison, its conclusion regarding MEG localization is even less charitable than Cohen's own. But MEG researchers, including Williamson, will be on hand at the symposium to challenge these results and to argue that the distortion Cohen sees as limiting the MEG's localization potential is a second-order effect for which compensations can be made.

Scientists and clinicians outside the MEG community but involved in brain imaging methods will be following the proceedings with keen interest—since what is at stake is a more precise look into the works of that most intriguing of organs: the human brain. All sides are anticipating a wide-open discussion that could be a first step toward achieving agreement in a field that, for the moment, lacks anything resembling consensus. ■ ROBERT P. CREASE