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Synopsis

A DIALOGUE WITH THE CEREBRAL CORTEX:
CORTICAL FUNCTION AND INTERFACING

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THE ELECTRIC BRAIN:
A DIALOG FULL OF PROMISES

Breakthroughs in knowledge and technology mean we're seeing a boom in neuroscience. The prefix "neuro" has invaded nearly every area of our vocabulary, and society demands constantly updated information on developments in this field and their ever more widespread applications.

The brain mainly works through electricity, and this particularity allows us to alter how it works for our benefit. Surgically implanted electrodes can be used to control, for example, the symptoms of Parkinson, and scientists are looking into applying them in other, serious pathologies like cerebral infarctions. Moreover, part of the information emitted can be decoded using a computer. This is leading to the creation of interfaces that allow paralyzed patients to move robotic arms or control their own wheelchairs with their mind. For healthy people, electric stimulation seems to be able to boost skills like memory, but the middle and long-term side effects aren't yet known.

Some of the top global experts in the field presented their work at this B·Debate –an initiative of Biocat and the "la Caixa" Foundation to promote scientific debate– co-organized by IDIBAPS.

CONCLUSIONS:

- ✓ The field of neuroscience is in its best moment. One of the greatest possibilities it offers is to use electricity to manipulate the workings of the brain. This allows for the use of stimulation techniques and brain/computer interfaces in patients with specific conditions as well as in healthy people.
- ✓ Electric stimulation can treat the symptoms of Parkinson, epilepsy or resistant depression. For healthy people, it could improve memory or sleep quality, however most scientists are cautious in these cases due to the lack of long-term studies.
- ✓ The electric signals emitted by the brain can be partially decoded using a computer. This means they can be used to control a robotic arm, a wheelchair or even to write on a screen just with a person's thoughts. Scientists demand funding for more clinical trials and to find new applications.
- ✓ Researchers are looking into more new technology, like for example using graphene in different devices or optogenetics and optopharmaceuticals, which can control neuron behavior with light.

ELECTRIC BRAIN STIMULATION: A PANACEA … WITH CAVEATS

The brain is, in large part, a sort of black box: we know what goes in and what comes out but not what goes on inside. One advantage is that, in general, what goes on uses electric signals. The fact that these signals can be modified **opens up a whole range of possible applications**. This could be done in several different ways: by implanting electrodes into specific areas of the brain or by applying electricity or electromagnetic currents from the outside.

"The use of deep electric stimulation with electrodes in the brain is already an established, proven area for some medical applications"

Mavi Sánchez Vives
Scientific Leader of B·Debate and
ICREA research professor at IDIBAPS

The use of electric stimulation is most common in patients with Parkinson who have symptoms that can no longer be controlled using pharmacological treatments. But its applications don't end there: the FDA (US regulatory agency) has also approved it to treat certain types of epilepsy, depression and obsessive-compulsive disorder, as long as they don't respond to standard treatments. In Europe, these applications are starting to become more frequent in clinical trials. The FDA has also approved transcraneal magnetic stimulation, in which current is applied superficially and doesn't require surgery, for resistant depression and certain types of migraines.

Nevertheless, breakthroughs aren't coming as fast as experts would like. Jordi Rumiá, neurosurgeon at Hospital Clínic Barcelona, explains "Applications have spread but in essence, things haven't changed in the past twenty years." Moreover, regarding Parkinson, he said, "We know it works, but we still don't know why." Rumiá advocates for greater collaboration between basic and clinical scientists and believes the use of these applications shouldn't be put off just because we don't know exactly how they work, as long as they offer an acceptable level of safety. "It took one hundred years before we understood how aspirin works, but people didn't stop taking it," he says.

The use of electric stimulation in healthy patients sparks even more debate. Marom Bikson –co-director of the Translational Medical Device Development Program and Neural Engineering Group at the New York Center for Biomedical Engineering–

believes that **“Ten years from now most people will be wearing performance-enhancing devices on their heads.”** This is one thing not everyone agrees on. For Sánchez-Vives, although this is a possibility, **“We don’t know their true efficacy or middle and long-term effects.** Stimulation could interfere with normal neuronal activity and affect the brain’s plasticity, which isn’t always positive.”

There are studies that link the use of electric stimulation (in this case using a helmet, without the need for surgically implanted electrodes) to improve memory, motor abilities, reading and math skills... even to boost feelings of compassion. Sánchez-Vives believes these studies don’t always isolate the possible placebo effect and, furthermore, many more that don’t yield positive results are never published. Bikson accepts that there are many doubtful applications: “When someone says that something is a cure-all, the natural reaction is to say it really cures nothing.” But, even though there may be a placebo effect, she defends the use of this technology with the following comparison: “It’s like wondering why weights work for so many sports: because they allow for specific types of training.” For Bikson, electrically stimulating the right area after working it intensely would help reinforce the activity, because ”it specifically works on the neurons that are already active.” However this is one thing Arthur Konnerth, team leader at the Munich Excellence Clusters CIPSM and SyNergy, doesn’t fully agree with. “These results have been achieved in laboratory experiments, but they may not be able to be repeated in vivo, under normal conditions,” he warns.

Identifying consciousness after a coma

Some coma patients “emerge” from their condition and go into what is called a “vegetative state”. They open their eyes but don’t seem to recover real consciousness or respond to external stimuli. Nevertheless, they may have traces of perception and desires that are hidden, unexplorable.

In 2006, a study showed that when some patients were asked to think about a tennis match or move through their homes mentally, the areas of their brains responsible for these activities were activated. Meaning that they heard the orders, understood them and executed them. They still take in what goes on around them. Now a new experimental method has used transcranial magnetic stimulation to improve these states. It sends a powerful stimulus and then measures the complexity with which the brain responds, which can be quantified and broken down into different degrees and states of consciousness. In the words of Marcello Massimini, professor of physiology at the University of Milan and head of the study, “it’s like calling the brain and listening to the echo.”

BRAIN/COMPUTER INTERFACES: TOWARDS A BRAIN-MACHINE RELATIONSHIP

The electric signals produced by the brain can also be interpreted to a certain extent. By decoding these signals, patients who are paralyzed, for example, can move robotic hands and arms with their thoughts, or even guide their own wheelchairs.

When Jean-Dominique Bauby woke up after a massive stroke, he could only move his left eyelid. The former editor-in-chief of Elle magazine managed to write, with the help of an assistant, his book “The Diving-Bell and the Butterfly” by blinking when the assistant said the next letter to be written. But to do so, she had to say the alphabet over and over again.

Now, **brain/machine interfaces allow patients to write directly with their thoughts**. The speed record is currently at 0.8 seconds per word and there are already applications like Intendix that allow patients who are totally paralyzed to write and send e-mail.

José del R. Millán, professor at the Ecole Polytechnique Fedérale de Lausanne, is working to perfect interfaces to control wheelchairs, which isn’t an easy task. “There are unavoidable errors,” he says, “but these can be minimized by incorporating automatic learning techniques into computers to help them learn from the mistakes.” To do this, they introduce mechanisms that give feedback on how the movement is going. And it could even help in therapy, for example, for patients who have had a stroke, as the brain could improve its plasticity by receiving the feedback and adapting to the new mechanism. “The goal is to combine function replacement and rehabilitation into one device,” explains Millán. This is why he calls for increased funding for clinical trials, which are “the only way to make sure these advances become a reality.”

We can’t discard the possibility that, in the future, **paralytic patients may walk again with an exoskeleton**. This is the goal, for example, of the Walk Again Project, launched at the inauguration of the Football World Cup in Brazil in 2014. For Mikhail Lebedev, researcher at Duke University, “This is something we will surely see very soon.”

New techniques, new knowledge, new possibilities

Technological breakthroughs lead to new knowledge and applications. For example, voltage-sensitive colorants allow us to see how the neurons in the brain are activated in real time. This allows us to identify what are called "**slow brain waves**", which are activated and spread through the brain periodically and while we are asleep and help consolidate memory. "They are essential," says Sánchez-Vives, "because the brain can't be inactive. They are the compromise solution, allowing it to rest without suffering any negative consequences."

Other new techniques include **optogenetics** and **optopharmaceuticals**, which control neuron activity using specific types of light. The first uses algae genes introduced into neuron cells through viruses. This could lead to safety problems in humans. Pau Gorostiza, ICREA research professor at the Institute for Bioengineering of Catalonia (IBEC), is working to develop drugs that attach to neurons and make them light sensitive. "If effective, they could be regulated like any other sort of drug," he says.

Researchers are also developing new materials to improve electric devices implanted in the brain. One of the most promising materials is graphene, which has highly unique properties, as explains Gemma Gabriel-Buguña, researcher at the Barcelona Microelectronics Institute, "It is flexible, transparent and biocompatible. And even harder than diamonds."