Your Brain On 9 Volts: The Specter and Hype of Electrical Brain Stimulation

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ABSTRACT

The potential of electricity to improve the brain has captivated many. Electrical gadgets attract the rich and the poor, the educated and uneducated, the scientist and the charlatan. Over hundreds of years, people have tried everything from shocking away headaches with live torpedo fish, to bombarding patients' brains with so much current that their bodies convulse. A more innocuous technology has since emerged: transcranial direct current stimulation, or tDCS. All it takes to build is a small battery, two wires, two electrodes, and salt water. The idea is that by priming the brain with a mild electrical current, an incoming stimulus would be easier to process. In other words: less mental effort to learn something new, like recovering from a stroke or improving ski jump performance. Three primary communities are interested in tDCS today: do-it-yourselfers, clinical researchers, and neurotechnology companies. They want it for different reasons, and yet they are still wary of one another. But tDCS, in all of its simplicity, is actually not so simple—and neither is the human brain. What makes it so appealing to so many people of so many different backgrounds? How does it work? And does it deliver?

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“Would you like to try it?” Dr. Elena Pavlova asked me. It was 3:00 PM in Stockholm, Sweden, and the sun was already starting to set.

I was nervous, but curious. “Yeah,” I replied, feigning confidence. “Sure.” With that, I followed Dr. Pavlova down to the basement of Danderyd Hospital. She led me into an examination room.

“Do you have any contraindications?” she asked, her accent thick with Russian and Swedish. “Nope,” I replied, no interfering medical problems.

She unlocked a metal cabinet, took out a heavy-duty briefcase, and lugged it to the examination table. She unclasped the case and assembled the contraption inside: an Oxford dictionary-sized gray box, which Dr. Pavlova hooked up to a red wire and a black wire. She opened a glass bottle labeled “0.9% NaCl” and poured some into a small dish. Finally, she soaked two teabag-sized sponges in this solution and fastened one to the end of each wire. All that was left was to measure my skull—so she could figure out where to put the sponge electrodes on my head.

Amid a flurry of cranial pencil prods, measuring tape, and muttered calculations, I started to wonder what it was going to feel like—or not feel like—to have my brain zapped. I was about to try a technology called transcranial direct current stimulation, or tDCS. It seemed simple enough: a mild electrical current will flow from the electrode under the red wire, through my brain, and exit through the black wire. The behavior of my brain cells depends on the direction of the electrical field above them. Those under the red, or positive, electrode would fire more easily. Those under the black, or negative, electrode would become less likely to fire. Or so it goes.

I first heard about this technology from companies boasting a way to stretch the limits of our mental potential, from becoming better athletes to getting more proficient at video games. And safely. The idea is that an incoming stimulus that excites the neurons under the positive electrode could be smaller. In other words: easier brain activation, less mental effort to learn something new. Plus, no serious side effects. It sounded incredibly ridiculous. But what if it actually worked? That would be ridiculously incredible.

When I looked more closely at the scientific literature, I saw tDCS was being tested on improving a myriad of other things—stroke recovery, memory retention, depression. The authors of these studies came from prestigious institutions, too, including Harvard and the Karolinska Institutet. Then there were people outside of the science research field, who were convinced that a cure to their Attention Deficit Hyperactivity Disorder, or ADHD, lay in the right combination of battery wirings. Then I wondered: What makes it so appealing to so many people of so many different backgrounds? And how does it even work, exactly?

Needless to say, there was a lot on my mind in the basement.

As Dr. Pavlova finished fastening the salty electrodes to my head with a few rubber straps, I shut out my remaining expectations of what to feel or not feel. She flicked the switch on the battery and slowly dialed up the current to one half of a milliamp, just under enough electricity to illuminate a Christmas tree light bulb. I felt the current ramping up: My scalp under the sponges tingled as if I were wearing cayenne plasters instead. I sat still.

Dr. Pavlova asked me questions. "Where are you from?"

I answered them. "Boston." Beyond shuttered shades, the sky was dimming to a rusted orange color. Some time later, I heard a beep. More scalp tingling—Dr. Pavlova dialed the current back down. All done. During the session, according to her, my talking slowed down and I appeared more sluggish. I did feel something. But there were too many confounding variables to point fingers at only one thing. The room was warm. Maybe its coziness was getting to me. There was also a belt strap under my chin, which made it harder to open my jaws and talk. Total, my session lasted eight minutes.

TDCS, in all of its simplicity, is actually not so simple—and neither is the human brain. This is where my mystery begins.

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The history of tDCS has roots within the story of electricity. Even before society understood electricity, people were stunned by a fish—literally. Electric fishes, namely within the *Torpedo* species, are capable of delivering thirty to 100 volts of electricity.

Ancient naturalists and philosophers were dumbfounded when describing the sensation of being shocked by a torpedo fish. Plato once compared Socrates' ability to electrify his audience to one, "who torpifies those who come near him with the touch." Others could only describe it as "poison."

These unpleasant experiences did not stop Scribonius Largus, an ancient Greek physician, from probing the fish's torpid nature. In 43 A.D., Scribonius recounted an incident in which a man suffering from gout accidentally stepped on a live black torpedo while walking on a beach. When the numbness of the shock faded, as the story goes, so did his gout pain. This experience prompted Scribonius to include the fish in his healing practices; he was the first to record using one for therapeutic purposes.

People from other parts of the world arrived at similar conclusions. Throughout the Middle Ages and into the Renaissance, a number of healers experimented with and used these fish to treat an excessive array of medical maladies, from headaches and vertigo to impotence and toothache. To them, the torpedo's powers were virtually magical.

These attitudes changed in the Enlightenment, when rational thinking came to prevail. Deists wondered whether the awesome power of electricity could bridge the gap between the natural world and mortality, thinking it might provide an explanation for animation.

Natural philosophers sought order in the physiological chaos of electricity that coursed through an electric fish's body, and they wondered if humans could contain this power. The Leyden jar, invented in 1745, was a step in this direction.

This glass container, with its metal foils, compartmentalized and increased the amount of stored electricity that could be used during experiments. In 1772, a scientist named John Walsh used the Leyden jar to demonstrate that torpedo fish not only have electrical tendencies, but that humans may possess them as well.

Walsh's work paved the way for two characters vital to the story of electricity and tDCS: Luigi Galvani and Alessandro Volta. Galvani, a physician, touched an arc of two metals to the nerve of a frog's legs and spinal cord at the same time. The legs contracted. He concluded that animals made electricity in their brains and stored it throughout their body. Volta, a physicist who repeated Galvani's experiments himself, was convinced that the electricity driving bodily functions in animals arose externally—from the contact of two dissimilar metals to nerves.

Volta's observation was the basis for one of the world's most important inventions: the electric battery. This pile of metal, which trumped the Leyden jar with its great electric potential, harnessed the power of Galvani's animal electricity—minus the animal.

Despite their differing viewpoints, Galvani and Volta were both right. Nerve cells possess electric potential, and dissimilar metals provide a way to excite nerves and drive the flow of electricity. Volta, somewhat graciously, coined the term "galvanism" for the application of an electric current in this way. Galvanism is the basis of tDCS, which sends a direct electrical current through the brain with two oppositely charged electrodes.

In the early 1800s, physicist Giovanni Aldini ambitiously picked up where Galvani, his late uncle, left off. Aldini tested galvanism on humans and was determined to convince people of its therapeutic usefulness, including treatment for melancholia—today known as depression—and reviving the dead. While he reported success with the former, the latter engrossed and repulsed many. Aldini had used galvanism to stimulate the corpse of a young criminal in 1803. Dramatic and showy experiments like this one likely drove interest away from galvanism. Noninvasive brain stimulation, at least within the scientific community, was largely ignored for over 100 years.

Neuroscience discoveries blossomed in the late 1800s, including Santiago Ramon y Cajal's connectionist theory. He proposed that the nervous system is a complex network of circuitry wherein individual neurons communicate. Yet still only a few researchers were active in electrotherapy at this time. Guillaume Duchenne de Boulogne systematically studied electricity in diagnosing and treating disease. In 1855, he also introduced the method of using electrodes on wet skin to apply galvanism, which stimulated muscles without damaging the skin. Physician Julius Althaus advocated for a gentler galvanic current in treating patients, convinced it was safer and posed less side effects. The methods of both these scientists are in use today.

Unfortunately, these new techniques were overshadowed by the showiness of electricity spectacles during the Industrial Revolution. At international exhibitions like the 1893 Columbian Exposition in Chicago, laypeople watched with wonder at spectacular possibilities in applying electricity for medical conditions. Treatments arose for real and fake disorders: shell shock, "sexual neurasthenia," and irregular menstruation, to name a few.

Whether or not they actually worked, the results of these noninvasive electrical treatments were chiefly anecdotal and became associated with quackery. The inconsistent evidence, along with the invention of a new electrotherapy called electroconvulsive therapy, or ECT, steered these early forms of tDCS out of the spotlight by 1936.

ECT was aggressive. Doctors bombarded the brain of their patients with a current 800 times greater than what is usually used in tDCS. Their neurons fired uncontrollably, inducing seizures. This was on purpose. Patients convulsed so violently that they broke bones, sometimes even their spines, unless restrained by a team of nurses. Possibly the most tragic side effect of ECT is memory loss. And yet, ECT was—and still is—effective in treating severe mental illnesses, namely depression. Even though the FDA grandfathered it in as a pre-amendment device, scientists still are unclear on how exactly it works.

In 1949, psychologist Donald Hebb made a vital prediction toward understanding how neurons work at the cellular level. Where Cajal's work advanced the idea that different areas of the brain communicate in a sort of cellular circuitry, Hebb's research enabled us to understand how neurons within this circuitry communicate. Hebb coined the phrase, "Neurons that fire together, wire together," which describes the basic mechanism underlying synaptic plasticity. The most studied forms of synaptic plasticity are long-term potentiation, or strengthening of neural connections, and long-term depression, or weakening of these connections. Plasticity would become key to understanding how neurons adapt in the learning process, as well as how tDCS might influence this process.

Electrotherapy research did not regain popularity until the 1960s. Still scarred from ECT and then learning that psychiatric drugs had their limitations, scientists began seeking alternatives. They wanted to know how *mild* electricity affected the brain. Indeed, they found that low magnitudes of electrical current could influence whether or not neurons fired in brain tissue of animals.

In 1966, psychologist Daniel J. Albert published two studies that hinted at how tDCS worked. By changing polarity—that is, the direction of the electric field—of a specific part of the brain, he changed how well rats retained learning a task. Anodal current, which passes through the positive electrode, seemed to speed up retention. Cathodal current contrarily blocked or reversed retention. Incredibly, while subject to an anodal current, Albert found that his rats learned a task in nearly half as many trials compared to the rats that did not. Even more astonishing: the effects of tDCS lasted long after the few minutes it was implemented—this period of retention lengthened from several hours to several days. These lasting effects, or so-called "after-effects," would become a heated

topic of discussion in future research. A number of pharmacological studies concluded that these after-effects seemed to be driven by changes in synaptic strength and plasticity—effects similar to Hebb's long-term potentiation and depression. TDCS appeared to be affecting the sensitivity of neurons to firing or not firing, while not making them react as intensely as with ECT. Yet, despite these advances, tDCS research once again declined in the following decades, probably due to the improvement of psychiatric drugs and the rise of magnetic brain stimulation and imaging techniques, including transcranial magnetic stimulation (TMS) and magnetic resonance imaging (MRI).

In the 1980s, though, researchers P.A. Merton and H.B. Morton showed that TMS can noninvasively provoke muscle twitching. Instead of a nine-volt battery, TMS involves a large, donut-shaped magnet positioned over a patient's head. And unlike tDCS, TMS makes neurons fire (but not as strongly as with ECT). When Merton and Morton magnetically stimulated someone's part of the brain that corresponded with arm movement, their fingers twitched. On a read-out of electrical activity, these twitches look like tall, sharp spikes. The higher the spike, which is recorded with surface electrodes, the higher the excitability of the motor, or muscular, system. An individual spike is something called a motor evoked potential, or MEP, and it would become the most common way to quantify the effects of tDCS.

It wasn't until 2000 that attention snapped back to the field of mild electrical stimulation of the brain. Neuropsychologists Michael Nitsche and Walter Paulus showed that weak direct-current stimulation, now known as tDCS, could influence brain function in *humans* as well as rats. MEPs increased by forty percent after five minutes of anodal tDCS on motor cortex, while they decreased by thirty percent for cathodal tDCS. Further, they did not detect any brain cell or tissue damage in their test participants. Their landmark study helped nudge tDCS into a more promising spotlight. It had clearer potential to be a cheap, noninvasive, nonpharmacological method of treating brain disorders—one without harmful side effects. It sounded too good to be true.

Indeed, tDCS's accessibility, as well as its potential and versatility to treat different parts of the brain, made it gain ground. Twenty tDCS studies were published in 2004. In 2015, 531 were published. Charting the growth since Nitsche and Paulus first published their seminal work, the pattern of interest has grown exponentially.

The potential of electricity to improve the brain has captivated many. Electrical gadgets attract the rich and the poor, the educated and uneducated, the scientist and the charlatan. The three communities that are interested in this particular technology today are the do-it-yourselfers, clinical researchers, and neurotechnology companies. They want it for different reasons, and yet they are still wary of one another. The do-it-yourselfers or DIYers are interested in manipulating tDCS devices in order to understand how the science and technology works, and some in these circles—for better or worse—are interested in using it for self-improvement. Laboratory scientists and clinicians in response worry whether or not the do-it-yourselfers will contribute to fringe perceptions of their field of research, like the charlatans of years past. And then tDCS companies

claiming to adhere to high standards of the research process are under scrutiny by both the laboratory scientists and DIYers, who think the field is still in its early stages and should not yet sell any products they have made to the public.

Possibly because of its simply designed technology, tDCS has progressed quickly. As concerned advocates reveal, lurking underneath a promising technology, dangers of the science research process abound. Recent developments of and attitudes toward tDCS are paralleling that time in past history when electricity was still novel. As Nitsche and Paulus hinted in the end of their study, there is much we have to learn. By understanding the ecosystem of communities working with tDCS today, I sought to tease apart this mystery. My first stop: another basement in Sweden. But instead of a clinic, it was in search of a homemade laboratory.

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TDCS has gained a following with people outside of the lab, from curious laypeople on YouTube and Reddit to engineers with little or no background in the life sciences. The Reddit forum on tDCS began in April 2011. It had 7,882 subscribed readers in February 2016. That number went up to 8,553 six months later. The autism forum on Reddit, for comparison, has been around for twice as long as the tDCS forum but with 10,851 subscribers. When I typed "DIY tDCS" into YouTube's search bar, 612 individual videos appeared in the results. When I tacked on the word "tutorial" with my original search terms, 535 videos came up. From just the first page of the top results, it is clear to see that people from all over the world—young and old, engineering students and non-scientists—are demonstrating how to build circuits and make these devices from their desk at home.

With tDCS's simple design and its potential to help with certain medical issues, it is easy to see the allure of tinkering with this technology, whether it is for learning science or for self-enhancement. As long as someone has access to an electrical power source, a bit of wire and metal, and a way to stick it all on the head, she can crudely craft a way to polarize the brain. Or as some parts of the do-it-yourself community like to put it, hack the brain.

One of the most prominent DIY subcultures working with tDCS is the biohackers. They are the clandestine cowboys of science: ex-researchers seeking freedom beyond the bureaucracy of their laboratories, building underground maker spaces, and reaching out to like-minded people. Their goal? To democratize science and technology, and to provide a space for people to teach and learn about it.

Nearly seventy cities across the world are home to biohacking groups, from Boston to Auckland. I was particularly interested in investigating the biohacking scene in Sweden. Stockholm—home to Spotify, Sony Ericsson and AstraZeneca—is a city at the forefront of technology and medicine. The Karolinska Institutet and Danderyd Hospital, two of Europe's leading medical research institutions, carry out tDCS research. So, it seemed natural for Stockholm to incubate an off-the-grid tDCS industry. I not only met members

of the biohacking community here, but I also met the man who carried the weight of Sweden's biohacking future on his shoulders. His name is Sina Amoor Pour.

A graduate school dropout, Amoor Pour stumbled into biohacking by accident. He grew tired of working with DNA every day for five months in his biology program at the Royal Institute of Technology (KTH). So, he quit and searched for other ways to pursue science. Before long, three men in other areas of science contacted him. They were working together as biohackers, and they wanted Amoor Pour for his technological skills. Together, they founded BioNyfiken, Stockholm's first biohacking organization. KTH let them have a space in the basement of their general-purpose building, where Amoor Pour created a laboratory. Today, ten people head the board of BioNyfiken.

Beyond his day job in IT, which allows him to pay the bills, Amoor Pour considers his voluntary biohacking gig a good fit. "I'm more free to do whatever I want," he said. "Say I want to do PCR or CRISPR-*Cas9* on some crazy gene somewhere, nobody can tell me, 'That's not working' or 'You're wasting your time; you have your protein to focus on.'" Working in BioNyfiken granted him and his colleagues the freedom to experiment with projects, no matter how far-fetched they may seem to outsiders. "We've been under the radar for a long time," Amoor Pour told me, "but now I think the authorities are becoming suspicious of what we're doing." SÄPO, Sweden's secret police, is not too thrilled over one of BioNyfiken's recent projects: injecting radio-frequency identification chips into human hands.

In 2014, though, Amoor Pour learned from his colleagues of a technology that was simpler to build: a tDCS device. He documented his efforts on his blog Biohacking.se. When I visited him in the basement of KTH one night in January 2016, he showed me his device.

He set it before me on the white tabletop. The first feature that stood out was how much smaller the battery was compared to the Oxford dictionary-sized one from Danderyd Hospital. It was, quite literally, a black box—one about the size of a computer mouse. A red wire and a black wire sprouted from one side of the box. Each snaked to an alligator clip clamping onto a thin blue sponge slightly smaller than a Post-It note. A small sheet of aluminum, which conducts electricity coursing through the anode and cathode, glinted in between each sponge.

Amoor Pour flipped a switch. An orange LED light turned on, indicating the nine-volt battery—the black box—was on. He showed me a knob on the top of the battery: a current regulator. This is how he is able to ramp up and ramp down current, which goes no higher than what Nitsche and Paulus established: two milliamps. As curious as I was to try his device, I decided against it.

Though he works on other projects, Amoor Pour's DIY blog followers are especially interested in his tDCS device. "Every single month, people email me asking to buy it," he said. He even gets requests from medical students. "You know they find out about it somehow. The word is out there about tDCS."

With BioNyfiken, Amoor Pour and his colleagues have arranged demonstrations and events for lay people who are interested in "future technologies" such as tDCS. He has tested tDCS on around two hundred people, many of whom expect to feel something right away. Getting the device to work properly in the first place can be difficult. Hair gets in the way of the electrodes, Amour Poor only gets fifteen minutes to work with a person, and he only has three or four devices for double-digit attendance. His solution to this is using a simple, albeit crude, electrode placement: both on the forehead, with one over each eye. This is the easiest arrangement, given time and resources. However, this electrode placement has neither been extensively studied nor used in clinical settings.

With all of these circumstances in place at a session, his participants may be experiencing placebo effects at best. Others want to take tDCS into their own hands. "When it comes to this tDCS movement, there really isn't anyone else wanting to build tDCS [devices]. They just want to try it out," Amoor Pour said. People contact him asking to buy a kit. And yet, to date, not a single person has asked him how to build one.

Amoor Pour's devices are not for sale. At least, not now. One encounter with a blog follower, which exemplifies one of the dangers of experimental tDCS, has made him uneasy about handing his work over to amateur users.

A man diagnosed with ADHD wanted to buy a tDCS device thinking it would help control his condition better than his prescribed medication could. Amoor Pour sold him two of his prototypes. Some time later, he began to think it was not such a good idea. "Maybe he gets results that are worse than in his condition and start blaming me for it." Amoor Pour lamented. A soft-spoken man, his voice grew in intensity. "How would I be responsible for his condition? Because I'm not a doctor, I don't have a company. So if I get sued, it's on me." For these reasons, Amour Poor has stopped selling them. Before he builds his second version of his device, he wants to find the answers to these ethical questions—if something happens, who is responsible?

Further, the more tDCS literature Amoor Pour read, the more skeptical he grew of whether or not the technology actually works. "Like fifty percent say there is an effect and fifty percent say there is no effect," Amoor Pour told me. "We can't have fifty-fifty. There must be consensus on the subject."

I was surprised to hear this. Was fifty percent an exaggeration? I asked Amoor Pour what he meant. He cited inconsistent stimulation parameters, using electrode size and distance as an example. An experiment may follow the same procedure, but these two experiment characteristics can drastically alter the results. Differing choices of electrode size and positioning can affect current density, or how far it spreads out over the skull, and whether or not the current will actually spread. To Amoor Pour, the research does not seem to currently agree on what is best. "That's the big thing I think in the do-it-yourself and biohacking community," he concluded. "I don't think we know enough to make these decisions."

The Do-It-Yourself community depends on the research to drive what they do, and some researchers and physicians I later met expressed concern that the DIYers might be invalidating their work. And yet, as seen with Amoor Pour's experiences, tDCS is simple enough to learn to build. His colleagues (some of which are biology Ph.D. students at Karolinska) firmly believe in its utility for self-enhancement—so much so that Amoor Pour fears if he voices his skepticism, he will be ostracized from the place that lets him pursue science as he wishes. For now, as the only one in his group that knows how to build these devices, he works with a cautious enthusiasm. As I forayed into the precarious confines of institutional research, I would learn that Amoor Pour's "fifty-fifty" observation was not so far-fetched.

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After visiting BioNyfiken, I wanted to know if tDCS was good for something beyond just playing around with and showing people its novelty at biohacking meetups. Why does Amoor Pour not feel confident in the current state of tDCS research, yet wants to resolve whether or not the technology has a meaningful effect?

The exponential growth in published papers over the past sixteen years reveals how researchers are interested in tDCS for a number of different reasons. Early research on animals and humans sparked an interest in the potential therapeutic benefits of tDCS. What would happen if we used tDCS to improve stroke rehabilitation, memory performance, or depression symptoms? From what neuroimaging and pharmacological studies can tell, all three of these associated conditions—stroke, impaired memory, and depression—seem to have one thing in common: deficiencies in plasticity. That is, weakened communication between neurons and other areas in the brain, which can lead to damaged brain tissue.

Could tDCS, then, help speed up recovery in these injured areas? Does it work just as well as—or better than—existing interventions, such as physical rehabilitation, cognitive training, or taking anti-depressant medications? I investigated in three places. Two were hospitals in Stockholm, Sweden: the Danderyd Rehabilitation Center and the Center for Aging Research. Both are in the prestigious Karolinska Institutet system, Sweden's equivalent of the Mayo Clinic. The third was Harvard Medical School's Spaulding Rehabilitation Clinic in Cambridge, Massachusetts.

Danderyd Hospital has the largest rehabilitation center in Greater Stockholm, where hundreds of patients are recovering from limb paralysis in stroke. Unfortunately, due to abnormal communication between neural networks, usually one hemisphere of the brain is damaged after a stroke. The excitability of the damaged hemisphere goes down relative to the unaffected hemisphere. Thanks to plasticity, though, these neural networks are able to reorganize and reroute themselves in the aftermath of a stroke. The key in making recovery work, though, is painstakingly relearning how to move the affected limb. Many of the patients at Danderyd are elderly, and some have been in rehabilitation for over a year.

The cumbersome recovery process from a stroke is where researchers see potential with tDCS as a therapy: as a way to even out the imbalance of communication between hemispheres. By reducing neural activity of the unaffected hemisphere with cathodal stimulation and enhancing excitability—and plasticity—in the injured hemisphere with anodal current, researchers think that tDCS could help expedite physical therapy sessions.

This is where Dr. Elena Pavlova and Dr. Jörgen Borg come in. Both are Danderyd clinicians who research the effectiveness of stroke therapies. The typical rehabilitation program here begins with setting up stroke patients with intensive training as soon after the incident as possible. They wondered if combining physical training with tDCS could help patients recover muscle function faster than physical training alone.

Dr. Pavlova's interest in tDCS was personal: After her sister had a stroke, Dr. Pavlova researched alternative therapies to help her. She thought tDCS looked promising. And so, in 2014, she teamed up with Dr. Borg and Dr. Nitsche. (Recall that Dr. Nitsche co-authored the first tDCS study applied on people in 2000.) Together they investigated the effects of tDCS on hand dexterity, a fine motor skill considered to be a major predictor for how well patients recover from a stroke.

Twenty-four adults in good health took part. Since they were being tested on a motor skill, they were each set up with an electrode arrangement to the corresponding part of the brain: the motor cortex. Here, the anode goes on the right side of the head, while the cathode sits symmetrically on the left. They line up where a headband would go. In fact, the nickname for this electrode arrangement, which goes by "M1" in the literature, is also known as "the headband."

Each person had one goal: to squeeze a tiny spring between her thumb and index finger as much as possible and without dropping it. The patients were unaware that they didn't always get stimulated with an active current. For at least one of the trials, each received a fake current. By the end of the experiment, Dr. Pavlova found that the people who received active tDCS compressed the spring fourteen percent greater during active stimulation compared to fake stimulation. Fourteen percent did not seem like very much to me, even though her analysis found it to be a statistically meaningful amount of change.

What struck me as unusual, though, was that everyone in the experiment received active tDCS at some point. They did not put together a group that received only fake stimulation, or a control group. Why was this? How would they assess the effectiveness of receiving tDCS to none at all? To account for learning differences, Dr. Pavlova told she had everyone practice the spring test before the actual trials took place. But was this enough? I would soon learn that this experiment was not the only one to lack a control group.

Next thing I knew, I was following Dr. Pavlova to the basement examination room of the hospital, where I voluntarily took part in that one under-the-table session of tDCS. She fitted the cathode above my right eye, while she centered the anode on the left side of my

head, slightly behind my ear. It was not until after this session and visiting the next Karolinska lab did I learn what kind of electrode position she tried on me. It was called the "dlPFC," which corresponds to the dorsolateral prefrontal cortex of the brain.

Clinically, we know the prefrontal cortex is involved with regulating working memory. As we age, brain matter shrinks, which can lead to cognitive deficits. For these reasons, researchers are interested in stimulating the dlPFC to enhance memory and learning performance. Using tDCS to help improve the brain's malleability made sense.

Martin Lövdén, a neurologist at the Aging Research Center, compared cognitive aging to driving a car with the brakes on. In a series of experiments called the REBOOT Project, he is presently seeking ways to remove these brakes. He and his colleagues Jonna Nillson and Andre Rydstrom are researching the effectiveness of different interventions on improving memory. Among them: giving participants drugs or making them do physical exercises prior to having them undergo cognitive training.

When I visited their lab this past winter, though, they were experimenting with another potential therapy: tDCS. Lövdén had never worked with it before. "It was just one of those alternatives that could maybe work," he said with a shrug. In an experiment last December, they experimented with the effects of tDCS on memory performance in older adults. The researchers recruited thirty people and made them do something called an n-back task, a well-established method of measuring working memory performance. It works by testing someone's ability to remember a particular image in a series of other images—the "n" represents how far back in the series the researchers want someone to recall an image. So, if you were to undergo a 3-back test, you would have to recall what you saw three images ago. Similar to Dr. Pavlova's experiment, everyone also received tDCS at two different current strengths, as well as fake stimulation, in random order.

Nillson was surprised to find that their results were not statistically meaningful. For all three stimulation types, including the fake type, tDCS did not seem to make a difference on accuracy or response times during or after stimulation. Lövdén, on another hand, was not terribly shocked by these findings. His first impression of reading literature from the field of tDCS? "Oh my god, so many bad studies are in this field." This was not exactly news to me at this point, but his explanation of why made me sit up in my seat: "I think this field is an example of the publication bias," he told me. "You only publish if you get significant results, then for that reason, the effects are overinflated."

Looking back, they would not have had everyone do each kind of stimulation. The participants were able to guess the order they received each type of stimulation—more than the researchers expected than by random chance alone. Next time, the Karolinska researchers plan to assign one type of stimulation per group, including a control group with fake stimulation.

The excitement I had harbored toward tDCS was turning into skepticism—not just as an effective technology, but also as a fraught symbol of faulty research. By the time I

arrived at Spaulding, I did not know what to expect. Here I visited Dr. Felipe Fregni, who researches tDCS and its effects on depression.

According to the World Health Organization, depression is the leading cause of disability worldwide. Neuroimaging studies reveal that depression impacts more than one area of the brain, but most notably with impaired dorsolateral prefrontal cortex activity. About thirty percent of patients with major depression do not respond to anti-depressant medications or experience intolerable side effects from them. Once again, I could see why this technology entices tDCS researchers, as well as why they would consider using the dlPFC arrangement on patents or test subjects.

Dr. Fregni was in one of the first research groups in developing tDCS as a therapy. So I was intrigued when he told me, "I was super skeptical at the beginning." Originally from Brazil, Dr. Fregni travelled to Germany in 2003 to research new neurotherapies with colleagues. At that point, only four tDCS papers were published. Upon seeing the results of the pilot study that he and his German colleagues conducted, though, he became convinced otherwise. The study involved ten depression patients, and Dr. Fregni found that the symptoms of the group that received active stimulation showed five times greater improvement than the group that received fake stimulation and their counterparts on the placebo. He was amazed by this difference. When Dr. Fregni repeated the experiment with eighteen patients, he got similar results: nearly sixty percent improvement for active stimulation, compared to thirteen percent via fake stimulation. Then he went to Cambridge, Massachusetts, and has been researching tDCS ever since.

Dr. Fregni thinks that depression is more than an imbalance in serotonin that can be restored with a pill. "If you increase serotonin, it will help, but it has transmission in different areas of your brain," he told me. "It's basically using a very big gun to get a small target."

Indeed, in the largest controlled study of its kind, Fregni demonstrated that combining tDCS (over the dlPFC) with either medication or cognition psychotherapy improved depression symptoms better than each alone. 120 depression patients were evenly split into four treatment groups. One received an antidepressant medication and tDCS. The second got tDCS only and the third got medication only. Finally, the fourth was a placebo, which got fake stimulation. He found that the patients receiving only tDCS and only the medication had significantly improved depression ratings, and to a similar magnitude. But, when the two therapies were combined, they had even larger effects than each intervention alone—more than two times better, in fact. "So now, the question is, which one primed the other?" Dr. Fregni wondered. "Was it antidepressant priming the effects of tDCS? Or tDCS priming the effects of the antidepressant?" From only thirty people, it is hard to say.

In spite of the mixed results from these labs, each researcher agreed on one thing: combining motor or cognitive therapy with stimulation can enhance the effectiveness of tDCS and the after-effects, as well as improve symptoms. But, these same researchers had their doubts and suspicions about the medical efficacy of tDCS, too. Collectively,

they warned me about three main concerns: electrode placement, how effects are measured, and how an experiment is designed. I dove into the literature.

Beyond inconsistent perceptions of what constitutes a control group, I sensed issues with electrode placement illustrated with the stroke research at Danderyd. Following the results of their hand dexterity study, Borg thinks electrode placement may not be so simple as putting the anode over the injured part of the brain. He suspects anodal stimulation could have a *worse* effect over cathodal when treating brain lesions in different people, and he would like to see more research on the effects of stimulating the injured side of the head versus the non-injured side. Why would *suppressing* excitability help?

I did see considerably more studies carrying out anodal tDCS over the affected hemisphere in the headband region than the unaffected hemisphere. This made sense to me, since excitability is supposed to maximize plasticity and help heal an affected limb. But, the deeper I looked, the more I saw what Borg was talking about. I came across studies that claimed *cathodal* tDCS over the affected hemisphere increased cortical excitability, as evidenced by higher MEPs. And then I found a meta-analysis of twenty-five studies whose authors concluded cathodal tDCS enhanced cognitive and motor performance in healthy older adults.

I then learned of two reasons that influence why researchers choose anodal over cathodal stimulation: some think that suppressing brain activity in the uninjured hemisphere (with cathodal stimulation) ensures it does not overshadow recovery in the injured hemisphere. Others assert it is better to excite the uninjured hemisphere (with anodal stimulation), which would help compensate the impaired functions of the injured hemisphere. In either case, experimental results are inconsistent and mixed. Some patients improved after "suppression" of the uninjured motor cortex, others did not.

Two experiments examined changes in MEPs tDCS. They used the same current level and put the anode in the same area over the motor cortex. Priori found that anodal stimulation significantly *depressed* the excitability of the motor cortex. Nitsche and Paulus, on another hand, found that *enhanced* excitability. The only difference between the two experiments was the placement of the cathode: under the chin in the former, and over the eye in the latter.

While it's relatively easy to measure the effects of tDCS on motor function, it's more difficult to assess its effects on cognition. Researchers measure working memory performance in different ways. The n-back test, which is what Lövdén used, is only one way. But even within this test, researchers can assess different parameters. They can choose to look at factors like total accuracy, misses, or recall time. Lauren Mancuso, a neuroethicist at the University of Pennsylvania, suspects that "researchers can be lured by chance differences to focus on the measure with the biggest effect, believing that it shows the enhancement effect 'most clearly.'"

Of all the researchers I spoke with, only Fregni's experiments had dedicated control groups. One of the four groups of patients received no treatment whatsoever. Both labs at Karolinska, on another hand, did not. Each of their subjects experienced live and fake stimulation at some point in the experiments. How can scientists reconcile these differences and determine whether or not tDCS had an improvement over no stimulation at all?

In 2014, neurologist Jared Horvath found something shocking: Of 117 tDCS studies he screened for control groups, 92 of them did not include one. In another paper, he analyzed 80 studies that explored the effect of M1, the headband arrangement, on MEPs. Only ten compared results to a control condition. The effects of tDCS on motor skill learning have been extensively researched, and the M1 electrode arrangement is the most studied in the literature. "This means 87.5% of the studies examining the foundational claim upon which the modern tDCS field is built have not utilized a proper control condition," he concluded.

I turned to other meta-analyses. The further out I zoomed, the more frustrated I became: Results seemed more and more conclusive. Meta-analyses examining results of motor function with the headband electrodes seemed to be overall positive. Still, others are not statistically meaningful. Meta-analyses for cognition studies are precarious. One author reviewed 61 studies of applying tDCS over the dlPFC and found the outcomes so inconsistent that he had difficulty "making causal conclusions between dlPFC stimulation and a particular cognitive function." Meta-analyses about depression seem to cancel out one another. One found improvement; another didn't. The former considered depression classification scores as a measure of success, the latter on rates of remission. The list goes on. Amoor Pour's lament of a "fifty-fifty" consensus echoed in my head, and I realized he was right.

As if that wasn't enough, Mancuso took another step back. In May 2016, she reviewed three meta-analyses examined the effects of tDCS over dlPFC on working memory. A *meta*-meta-analysis. She replicated and analyzed the selection criteria, and she adjusted for publication bias. Her results? Inconclusive. When discussing the three different studies – Horvath's among them – she called the effects of left DLPFC anodal stimulation reliable "though small, partial, or nonexistent." Her frustrations echoed mine: Why is it so difficult to get an answer from the literature? This was not how science was supposed to work. At an individual level, depending on where I chose to look, I could find plenty of studies that looked promising on their own. But the farther I stepped back to take in everything as a whole, the muddier my view of the field got. For such a simple technology, there is still so much we do not know.

But, ready or not, companies have packaged this technology for the public to buy and use. Feeling more cautious, I got ready for my last visit: to a company founded by a Stanford-trained neuroscientist.

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For some companies, transcranial electrical stimulation has progressed enough to be commercialized to the masses. Companies have come and gone, but three are still standing today: Foc.us, Thync, and Halo Neuroscience. I will concentrate on Halo, which was how I first heard about the technology of tDCS.

Before founding Halo, CEO Dr. Daniel Chao and CTO Brett Wingeier worked with NeuroPace, a brain stimulation company specializing in implantable electrodes for epileptic patients. Ten years and nine digits-worth of money later, their electrodes reached FDA approval. Even though they were shown to help eligible patients, Chao said, most patients declined the surgery required to implant it – even for very dire needs. "I felt like we could do better." They wanted to make something that could help people noninvasively. In October 2013, Chao and Wingeier quit NeuroPace and founded Halo.

From their research, the entrepreneurs became attracted for tDCS over other noninvasive treatments. Their reasons echo those of a number of clinical researchers. Similar to Dr. Fregni, Dr. Chao feels pills are "too messy;" they go places in the body where they should and should not go. TDCS is capable of applying treatment in a more focused fashion: over the brain area of interest.

"It just had all the right connotations," Wingeier said about their company's name. "It implies the head, and implies good things."

Brain training programs, like Lumosity, promised to strengthen cognitive skills like memory retention. But Chao did not see promise in this realm of noninvasive—and ostensibly selective—treatment, either. In January 2015 conference for healthcare entrepreneurs, he said he thought these games were too slow, require months of training, and have controversial outcomes. Indeed, in January 2016, Lumosity came under fire in a $2 million lawsuit for deceptive advertising. The Federal Trade Commission (FTC) raised these charges. "Lumosity preyed on consumers' fears about age-related cognitive decline, suggesting their games could stave off memory loss, dementia, and even Alzheimer's disease," said FTC Director Jessica Rich in a press statement. "But Lumosity simply did not have the science to back up its ads."

My next question, then, was whether or not Halo's science backed them up. Even though Halo's device was ready to be released by the time I visited them, the company was still testing its effects on people in their lab. By the time I came, they had already experimented with 1200 participants. The average size of an experiment was around thirty people—not a lot, but still more than average for a neuroscience experiment. They can fill participation slots every day. I managed to squeeze in the last morning slot on a particular morning, one month in advance.

One morning in late January 2016, I sat in a small, gray, windowless room at a desk. I was ushered here from a sunlit lobby in downtown San Francisco. A young man with a gray sweater and a mop of brown hair walked in. "Ready to start?" I nodded, handing

him a fat packet I signed just before he entered. In one pass, I gave Halo Neuroscience permission to experiment with my brain.

The man who collected my packet, Danny Holtzman, sat down on the other side of the room from me. “All right,” he said, opening a drawer next to him. “Today we will be testing hand strength.” He took out a gray plastic bar the size of a chalkboard eraser, and gave me my instructions: Every minute or so, I would hear a series of beeps. On the fourth beep, I was told to squeeze the bar as hard as I could and hold it until the beep silenced, which was about two seconds. The bar was hooked up to a computer, which was measuring my strength output. We began.

On the graphing program Holtzman set up before me, I watched a red line climb up the y-axis on the computer screen. This signaled each time I heard the beep and squeezed the bar. Another few minutes passed. Then beeps. Then squeezing, then relaxing. And so on.

My hand ached. I could not drop the bar, though, or else the computer would pick up on the grip difference and make my data useless. When I couldn’t take it anymore, Holtzman said it was time for a break and I could put the probe on the table. Five minutes later, we were back to the trial. I was to do the same task again, except while undergoing tDCS.

Holtzman set a pair of headphones out on his tray. He popped out two gray, nubby squares the size of a teabag from underneath the headband. The headphones looked skeletal – the earpieces and headband were hollow. As Holtzman spritzed the nubby squares with a bottle of salt water, I realized those were the electrodes and the skeleton headphones would hold them to my head – literally a headband. The M1 arrangement.

Holtzman fastened the electrodes back on the device, combed them through my thick hair, and pushed a button on his phone through the companion app. I felt a familiar tingling and prickling underneath the headband. The current was ramping up, but I knew it could go either stay steady or decline imperceptibly. The catch with this trial was, neither Holtzman nor I knew if I was getting real or fake stimulation. So the current could go either way.

It turned out I received fake stimulation. I asked to try active current, and Holtzman brought out the device version to be sold to the public: Halo Sport. If not for the yellow and turquoise circle logo on the earpieces, I would have guessed they were a pair of Dr. Dre headphones. “It’s not enough anymore that your medical device is a beige box with cords sitting on the table,” Wingeier told me. One of his and Dan’s biggest challenges in designing their device was going beyond a beige box both into something people would be familiar using and get the stimulation to the right place. While Halo is interested in eventually working with tDCS and improving cognitive abilities, motor skills was the most feasible starting point. Not just for the reliability of measuring MEPs in the literature, but also for the ease of finding the headband region. Unlike Dr. Pavlova’s lab, where she poked and prodded my head for several minutes to find the dlPFC; or Amoor Pour’s impromptu electrode placement, which is easy to apply but not in the literature. All I had to do was simply put on a pair of headphones.

When I set them on my head, the app beeped—it would not let me start because of poor contact between the device and my scalp. This impedance check allows the app to know when to start or stop stimulation. When the connection was good enough, the app let me press the Start button. The current ramped from 1.1 milliamps to 2 milliamps, the standard amount in the literature. Aside from the familiar prickling on my scalp, I did not feel much differently than the squeeze trial. I did not even feel much different from before and after the session. Holtzman said the effect would not be so instantaneous—a number of sessions over time, and paired with physical activity, I would reportedly get the intended effect.

For Halo, that effect is better athletic performance: to have the ability to practice a skill and be primed to master it sooner. By making neural tissue more plastic and for more often, the founders—who have both studied neuroscience at Stanford—reason that these neural pathways will strengthen more easily and sooner.

Priming is the effect of a stimulus influencing a response to a later stimulus. For instance, if you were to read a list of words including the word "table," and then you were later asked to complete a word starting with "tab," you are more likely to answer "table" than if you were not primed to—that is, if you had not read the list.

Their reasoning has some merit. The process of plasticity is how we are able to strengthen connections, no matter if we are learning how to ride a bike at five years of age or learn how to speak a third language at fifty-five. Learning a new skill, at the neural level, is like figuring out how to deliver a message to the other side of an overgrown forest. With steady footing, and possibly some circumventing, you will find another way across. Practice, at the neural level, is what happens when you tread out a steadier path. As a result, you are more confident in getting to the other side of the forest.

The ability to help make for a more meaningful practice session is what makes tDCS so appealing in clinical settings, like for stroke patients, people struggling with working memory, or depression patients. Halo's device, on another hand, targets athletes: healthy people in peak performance. A month after I left San Francisco, Halo unveiled their device to the public. But there was more: They released four research papers on their website, one of which boasted the successful results of a case study with the U.S. Ski Team. The ski jumping team had been secretly training with Halo's headphones in the gym before hitting the slopes.

Halo's study claimed that the team members who used the headphones while training improved their "jump force" by thirty-one percent, while the control group improved by eighteen percent. I remain cautious of their research, even though they had a control group. Additionally, none of their studies are peer-reviewed, and they do not account for all 1200 participants they reportedly screened. While I await they day they are, I wonder how many tDCS peer-reviewed studies—including the ones I investigated in the three labs and on my own in the literature—have reliable results. And more importantly, who is building upon these results, and how do they decide on doing this?

The story of Halo set in motion many motivations for researchers in wanting to pursue tDCS, but it also highlighted some of the allures and dangers of working in a promising field still in its infancy. For such an innocuous name, Halo is still cloaked in mystery.

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We have come a long way since slapping on an electrical fish wherever we hoped to take away pain. But, in other ways, we are still in that place: tDCS is at a relatively young stage. The first reliable experiment on humans took place in 2001, and the number of experiments since than has grown to over 2000 papers. Researchers agree that tDCS has the potential to be an inexpensive, nonpharmacological way of augmenting training without any known adverse side effects. They agree on what happens when a direct current is applied through the head – that it affects cortical excitability and can make neurons more or less likely to fire. And they agree that the effects of stimulation depend on how the brain interacts with what is being trained or practiced.

Clearly, this technology holds promise and appeals to a wide breadth of neuroscience expertise. And yet, no one in either of the three communities—researchers, DIYers, or companies—fully understands the cellular and molecular processes that give rise to the lasting after-effects or what happens long term in the brain as a result of them. We also do not understand enough about all of the different stimulation parameters. Wan-Yu Hsu, an occupational therapist who researches noninvasive brain stimulation techniques at the University of California, San Francisco, agrees: One of the biggest unanswered questions in whether or not tDCS works is agreeing on appropriate parameters. “Everyone is different,” she told me, “so what is uniform?” Hsu is uninvolved with researching tDCS.

The burning question among all three communities, though, is what happens in the long term. No one knows how much stimulation over how much time is enough – or too much. For these reasons, it is easy to sense the tenuousness of the clinical researchers and Amoor Pour toward democratizing this technology: there are too many unanswered questions. Even still, companies have compartmentalized it into a form that is not meant to be altered. Can we trust the safety and security measures within these devices, which are not meant to be broken apart and toyed with? And more importantly, can we trust the results that tDCS is currently building upon?

“That’s the problem,” Dr. Fregni told me. “It’s not about results. It’s about predicting one thing and finding something else. The value is not running a study and finding a result. The value is understanding why that thing happens.”

Researchers are realizing that tDCS is focal, but not necessarily in the same way for everyone. While researching optimal electrode placement and size may help resolve these related problems, it does not get to the level of understanding how our neurons are individually wired. Dr. Fregni and other researchers I visited think that we should be using tDCS to understand more of our brain circuitry—more specifically, how our brain responds to different diseases. In depression, we know the headband and dlPFC regions

have clear links with the pain network. By using tDCS to study the connection between these areas, researchers think we can further understand the neurosignatures of diseases that can injure the brain.

The accessibility of this technology raises some bioethics concerns: How should tDCS be regulated? Of course, it is impossible to regulate a device a layperson made by himself or herself. Physicians and companies, though, should take responsibility for how they present and administer the technology to the lay public. The U.S. Food and Drug Administration (FDA) does not approve the use of tDCS devices for medical use. Instead, they fall into the category of a general wellness device, which are not marketed or intended to cure, diagnose, or treat any medical disease. The Apple watch, which can track blood pressure and other health data, falls in this same category.

Considering tDCS through a bioethics lens gets even more interesting when applied to professional sports, like the case of Halo working with the US Ski Team. When I asked Wingeier if this would be considered neurodoping, I sensed he was uneasy. "The administrative agencies that decide what is doping, they will decide what they decide at some point in the future," he said. He insisted that tDCS is safe and consistent with the spirit of sport, which are two criteria that doping violates. "You are still putting in the work," he went on, "and you still have the obligation to train smart, and to train the right way." If the US Ski Team is one of few teams—or the only team—that has access to this elite technology, does this give them an unfair advantage?

The situation gets more tenuous when we consider that doping changes an athlete's physiology and biochemistry. In an open letter to the public in *Nature*, neurologists warned the tDCS is not a plaything. "Meddling with the tDCS dose is potentially as dangerous as tampering with a drug's chemical composition," wrote Dr. Roi Cohen Kadosh, the primary author of the letter. "Painstaking efforts by researchers to understand the risks and benefits of tDCS should never be interpreted as encouraging such practices." There is no reliable way to reliably detect whether or not someone has received brain stimulation

Neurodoping would be undetectable. "The changes in brain chemistry are on the order of 10% in metabolite concentration," according to neuroscientist Nick Davis. "They require carefully controlled conditions to pick out the signal from the noise."

The neurobiological effects of tDCS cannot be simplified to just one mechanism or neurotransmitter. Many appear to be involved. NMDA receptors, for one, are involved with changes in neuroplasticity and MEP size, and a number of studies suggest they may enhance the degree of after-effects from tDCS. So, should brain stimulation—and effectively neurodoping—be considered the same as taking a drug for enhancement? I do not think we will know for sure until we know what happens at the biochemical level. And for that, the DIYers, researchers, and companies acknowledge that we still have a long way to do.

In May 2016, I spoke with Paulus, one of the two pioneers of this technology. I asked if he had any misconceptions he wished would be cleared up about tDCS. He paused. “1817,” he finally said. “Do you know what happened in 1817?” No, I said. “That was the year *Frankenstein* was published.”

Then I understood. *Frankenstein* set the expectation that we could rescue dead people and shock away pain, through the trough of disillusionment. “This was the peak of inflated expectations,” Paulus concluded, “and we are at peak hype.”

The field of tDCS reveals how we desire to improve our brains and take our health and wellbeing into our own hands. We may understand how the technology works, as well as how it can help us overcome our limits in strength and disability. But, among the blossoming literature in the field, we see that we have yet to understand what we are trying to change with this technology. Even though tDCS is very simple, the complexity comes from how our brain reacts to it.

## People Interviewed

Dr. Jorgen Börg
Daniel Chao
Dr. Felipe Fregni
Danny Holtzman
Martin Lövdén
Jonna Nillson
Michael Nitsche
Walter Paulus
Dr. Elena Pavlova
Sina Amoor Pour
Andre Rydstrom

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