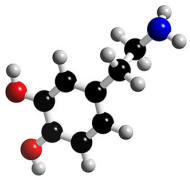
iPlant fiction

This is a novel-in-progress by Chris Harris. It describes the development of iPlants from the perspective of reserchers working a in the private brain surgery industry. The different segments of the story are not in chronological order.

In the novel, conditional rewarding brain stimulation (CRBS) has been introduced as a last-resort procedure to help morbidly obese patients exercise. The move was motivated by a worsening obesity-cardiovascular-neurodegeneration-aging epidemic, unsuccessful attempts to inhibit hunger in morbidly obese patients with traditional deep brain stimulation procedures (Hamani et al 2008), and several effective applications of CRBS to motivate exercise in rats (Burgess et al 1991, Garner et al 1991). Following success in several hospitals, the procedure is rapidly applied to a wide variety of patient groups and behaviours, including learning. As the effectiveness and safety of the implants improve, an increasing number of clinically healthy individuals choose to undergo the surgical procedure, and private clinics specializing in the procedure become increasingly lucrative. Ike, Meg, Lucy and the narrator Chris conduct R&D at such a clinic/company. Their research is necessarily self-experimental. The novel begins with the public launch of the 'iPlant' - an advanced CRBS implant aimed at a general market, which, unlike previous CRBS implants, targes dopamineand serotonin nuclei directly.



Chapter 1 - Program yourself

(written 2005-2007)

"Most people don't realize how common brain implants have become in the last couple of years. Every month thousands of patients all over the world have electronics surgically implanted into their heads to treat problems with hearing, movement and pain, and more recently with epilepsy, vision, paralysis, depression, compulsive behaviour and loss of consciousness (Schwalb & Hamani, 2008; Perlmutter & Mink, 2006;Lebedev & Licolelis, 2006; Kringelbach et al, 2007). The iPlant is just another implant, aimed at new regions in the brain."

Ike was addressing the press conference. Dark shirt, two deep blue wires running down the back of his head towards a console strapped to his chest. Two days ago he snapped Lucy's right index finger in three places when she tried to disconnect his dopaminergic nuclei. She's having problems not blaming him.

"It's eight implants really; each controlling a group of cells that supply the brain with dopamine or serotonin (the VTA, SNc, dorsal- and medial raphe nuclei, bilaterally). Electrical activity in these cells is at the core of our mental lives. Dopamine is the goal of behaviour and in large quantities it drives activity and growth in brain tissue. When a thought grabs you so you can't think of anything else it's because the neurons that make up that thought are being fed more than enough dopamine to keep on firing and connect to other neurons. When you're comparing two options, unable to decide, it's because they drum up the same amount of dopamine. Dopamine is motivation, its fluctuations describe where you direct your attention, what's important to you and what you remember (Cools & Robbins, 2004; Schultz, 2007). This is a gross oversimplification but it works - our implants control the flow of dopamine in the brain."

What began as a problem of mapping and reducing noise in the high power spectra of Ike's dopaminergic implants quickly became a problem of security, of preventing over-use. We knew we would have to 'tune' the implants, find the combination of electrodes and currents with the steadiest and most selective effect, with nothing but Ike's own words to guide us, but we didn't expect him to lie, and his eyes didn't reveal a thing. Then Lucy noticed his white knuckles, moved to disconnect and it took me and two of the software engineers to hold him down.

"The point is, there's no groundbreaking science here. This could have been done many years ago, probably was done in military labs somewhere, in Russia, the US or China, anywhere really; the regions in the brain where motivation and learning can be generated electrically were mapped in animals and humans more than half a century ago (Olds & Milner, 1954; Heath, 1963) and people immediately started thinking about realistic forms of mind control (Delgado, 1971). Only a few years ago the US army developed implants that allow them to remote control rats via normal laptops, 'for search-and-rescue missions' (Talwar et al, 2002)."

Ike could not have full access to the implants, so much was clear. Maybe it's a general rule that no one can control their own dopamine but in his case the problem had been exasperated - there was no way of knowing for sure how far he'd go to repeat that overflow. The security we put in place meant the computers had to be unlocked and operated from three points simultaneously: two in opposite corners of the lab, one in the library on the other side of campus. Whosever implants were being programmed could still

direct the work, but all uploading of compiled programs had to be cleared and confirmed by the others.

"The first programs we developed for the iPlant were exercise programs, originally for treating obesity. Take running: the soles of these trainers here contain sensors that punch out a bolt of dopamine with each step. Nothing like orgasm, but enough to make you want it like those few lucky people who really enjoy running want it, with a strict time limit of course. Implant-driven exercise programs have been available for rats for decades (Burgess et al, 1991; Gardner et al, 1991), now we've got them too. Learning programs work on a similar principle, dopamine for correct answers. The current version of the iPlant has about six thousand hours of training in French, German, Mandarin, Japanese and maths, but you can expect a lot more with each update. There are a few purely clinical programs as well, like DeTox and DePhobe. Dopamine-driven software lets you want what you want to want."

The rest of that day would have been a lot easier if he'd been genuinely affected by Lucy's finger, but the way he saw it him and the electrode arrays had malfunctioned, like an allergic reaction, not his fault. And who knows, who knows what it feels like to have pure dopamine filling up your frontal lobes with nothing to hold it back but... what? Only Ike. Rats given full access to their own dopamine self-stimulate until they collapse from starvation or lack of sleep.

"All eight implants also regulate baseline or so called 'tonic' electrical activity in their target cells. For dopamine we call this program Focus. People perform best when their dopamine concentrations are at an optimum level for the task at hand and most of us experience daily problems maintaining sufficient dopamine levels; maintaining concentration. Focus works similarly to the stimulants children are prescribed for ADHD, but it's cleaner and more flexible and can be turned off, which means fewer side effects. The analogous program for serotonin we call AntiDep because it works like SSRI antidepressants. If you're depressed or chronically anxious, chances are you were born with an underdeveloped serotonin system or its growth was stunted by stress (Jans et al, 2007). Like antidepressants, AntiDep prevents some of the more vicious long-term effects of not having enough serotonin, like overproduction of stress hormones, inhibited growth in the hippocampus, and, at least for some people, social isolation and despair (Dranovsky & Hen, 2006)."

I met Ike at UCL in 2008. In med school he'd done enough ecstasy to mentally cripple a rhesus monkey, but the damage MDMA does to humans is still not known. Ike wanted me to find out: to inject him with radioactive serotonin transporter ligands and PET scan his brain, then repeat the test yearly to check for regeneration. It didn't look good. The serotonergic branches perfusing his forebrain were down to 60% of normal thickness, and a mesh of regrowth had formed a fine, essentially useless cloud of axons around the serotonergic cell bodies back in the brainstem. This was ecstasy damage, same as in monkeys (Hatzidimitriou et al, 1999), and if the ligand had been approved for use in humans we might have been able to publish the scans. How much of the damage had been there before the pills and the powders - as the serotonergic vulnerability that surfaces as anxiety and compulsions - was not something we could know, and it didn't matter to Ike. I decided to introduce him to the team and to our research.

"All changes to your iPlant have to be uploaded and tuned here at our facilities using special surgical equipment: this means that no government satellites can turn you into mindless drones; no one can hack your brain and make you desperate to give them your money. No, the main challenge to the iPlant are those segments of society that will react to it with fear and try to demonize it. These people are often the ones who would benefit the least from an iPlant: they don't suffer the never-ending frustrations of a short attention span, excessive fatigue, addiction, depression or intense social anxiety; they are the ones whose

dopaminergic and serotonergic cell groups are working fine, and they'll say that you using an implant to reach your optimum is somehow wrong, as if you were cheating in some petty game. No, this is a 21st century class struggle - those born rich in dopamine and serotonin protecting their 'hard earned' privileges."

We pumped all the money generated by the iPlant into the development of new electronics and signal processing software for iPlant 2, a wireless comb of high-density electrode arrays for the corpus callosum and frontal lobes. Like the original BrainGate it was to enable direct neural control of a computer (Hochberg et al, 2006), but at a much much higher bandwidth than the mouse-and-keyboard interface. After five years we were at a stage where Meg could volunteer.

Some of us had thought she'd break the moment she connected. That her flow would rupture, her synchrony leaking out like in that book where a brain locked up in a lab aquarium gets hold of the wire of a security camera and almost manages to 'escape' (Jersild, 1988). The idea that the mind is ethereal is old, extremely old, but I don't think she doubted the hold of the body for a second, not really, I don't think she could.

The look on her face, it was the same smile Ike had had when he came back from his first three hours of running. She described the sensation as 'inward touch', as something like a blind person seeing shapes by touching and stroking. The link was largely one-way, brain to computer, the team relying on screens to structure her output, but from the start she had wanted 'primers' - faint feedback to the electrodes involved in any successfully executed command. It was no more than two hours before she turned the screens off and adjusted

the music in the lab using nothing but the direct link, flipping between tracks with a wide smile, holding back the laughter.

She could write, of course, but we never understood how she learned to read, not with the screens off. It seemed impossible. Her control of the computers were at the coding-level of mouse and keyboard and there was no way of re-routing the screen-output to the implant. We thought maybe she'd found a way to locate text and somehow 'check' each letter or object against output of her own, using some difference in the primer-feedback for correct and incorrect trials to determine a letter sequence. But the software for that kind of checking, however simple, wasn't installed. She said it was a matter of 'jumping', said it felt like skipping stone. She'd stopped smiling.

She wasn't there in the morning. Her body I mean, she wasn't there at all. We'd all stayed at the compound overnight, in case of emergency, sleeping right there along the walls. She sat by the desk with the software-people for hours asking questions, more about computer science it seemed then about the implant or the decoding software. Then she went to sit on the operating table, drawing beautiful flowers in photoshop, with edges that looked smooth and soft and razor-sharp at once, and had layers of coloured shadows hanging under them. Why didn't I make her tell me more about it? She explained 'jumping' in some detail, like it was a matter of getting through a series of commands so quickly the computer had to catch up, which gave you a half-second glimpse of your own serial trace at deeper levels of coding. Then you took that output and repeated it with minor changes and eventually you learned how to get behind the surface of programs. She said the internet was beautiful.

She wrote her parents a 32 page letter, all hand, which they won't let us read. Her dad quit his job and moved to France within a week. We still haven't heard from her. I think it'll take us between three and five months to assemble another implant. Ike and I flipped a coin and I'm next. I've agreed to keep the doors locked this time.

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Chapter 2 - iPlant-driven research

(written in 2008)

Science is about money. Scientific facts are not so much discovered by intellectual curiosity as they are constructed by cash investments. Science is objective but also directed. Research equipment has a cost, as do scientists. Our initial large source of funding, the one that carried the first one hundred iPlants through clinical trials demonstrating their capacity to treat morbid obesity, was unexpected.

We arranged to meet Aubrey de Grey in a pub in Cambridge in 2009. He surprised me by bringing chips to the table - I'd thought he would at the very least avoid saturated fats.

"And you are confident patients undergoing this new form of deep brain stimulation therapy would willingly volunteer some of their free time to become conditioned to conduct biomedical research?" Aubrey asked.

"Maybe initially they would be people from the obesity trials." Lucy said, "Initially. But we're convinced a lot of people with no clinical problems will want iPlants once we get them past clinical trials. And if we can show in concrete terms, in research hours and actual findings, just how much a single iPlant can contribute to medical science... It would be exactly what we need to generate public support and get a foot in the door on government funding. We considered a climate change oriented approach - iPlant-driven research into renewable energy - but that kind of science is unstructured and abstract; it's engineering, not lab work, takes years of training. SENS is different; you've worked out in detail what needs to be done, even for cancer (de Grey, 2005; de Grey et al, 2004). What you need is an army of motivated scientists to do it. This is that army."

"Bunch of fat people in lab coats addicted to exercise and arbitrary research protocols" Ike said and sipped his pint.

"Nooo..." Lucy said, "Let's say four hours of iPlant-driven research per week per participant, one hundred participants in the stage II trials and one year of actual trials. That's over twenty thousand research hours; something like £250.000 in saved research funding at a typical UK payrate. And that's from the clinical trials alone. You've estimated the full cost of SENS at $100 million per year. That's roughly twenty thousand volunteers working four hours a week. That's a lot of people, but say we advertise it as a Manhattan Project to cure cancer - you really think finding volunteers would be a serious problem? If it's safe and the initial clinical trials show how effective it is? If it requires no effort whatsoever?"

"Mind control on a mass scale, ain't nothing like it" Ike said.

"Ike! Fuck! What's wrong with you?" Meg punched Ike's shoulder.

"Just sparing dr de Grey the trouble of listing reasons why he wouldn't want his reputable foundation associated with an existential bomb-shell like this one."

"I'm not sure I accept your calculations." Aubrey said. "But apart from that, how would you organize tens of thousands of unskilled researchers? How exactly would you train them? What about laboratories and equipment and logistics?"

"We're not sure" Lucy said. "We have a detailed plan for how to organize up to two hundred

researchers across four universities. Basic molecular biology mostly, building on old protocols. It's tempting to go further and try and to model the Human Genome Project but we'd like to avoid having the Chinese play the role of Celera in all this. You know what their demographics look like. We also feel there's an event horizon shortly after a few hundred."

"Things won't exactly stay the same after Hu gets his hands on this implant." Ike said.

Aubrey coughed. He was looking out the window. "How far away from clinical trials are you?"

"That depends on how much you want to invest."

Friday. Me, Ike and Meg are in the new proteomics lab in Reading, tuning the reinforcement system. At least that's what we keep telling ourselves. Why we're really doing it... well that's the big question. Ike is still in the protein factory. Meg finished purification a few hours ago and said she'd give microarray imprinting another try even though it looks too complex for a protocol. I'm doing quality control.

Proteomics is the ever-expanding region between cell biology and genetics. The science of proteins. The Reading facility is a high-throughput unit developing antibodies towards short, specific segments of protein (compare Nilsson et al, 2005; Uhlen et al, 2005). The segments are isolated in the protein factory and sent to a farm in Cardiff where they're used to immunize rabbits. The serum is returned to us and the antibodies are extracted by washing the diluted yellowish fluid through columns containing the target protein segments. The end product is a transparent liquid of pure, polyclonal antibody. I'm not sure how many thousand pounds they get for each millilitre.

Quality control means taking a sample of the finished product, pipetting it onto glass microarrays containing twenty different sets of protein fragments, incubating and washing the slides, running them through a scanner and going through the resulting images to make sure the antibody sticks to the right fragment and the right fragment only.

Maybe it sounds difficult but it's not. It's about two hundred separate behaviours, none of which require knowledge of what a protein or an antibody is. It's surprising how much of science consists of these monotonous construction lines; so called 'protocols', and how much money is spent getting people to do them. The reinforcement system I've developed

this week adds rewarding dopamine pulses at thirty-two points along the protocol.

Another round. One more. Then I'm probably done. It's not gonna get much better than this. Picking up the vials from the freezers and carrying them over to the bench. You can tell which ones are Ike's from the labelling. OK. Four at a time. I plug in and carefully read the labels, entering the letters slowly on the computer as I go along. One. Yea, just right. Makes you wonder how you just did that. Makes you think about the motion of your arm, the fingers on the keyboard, the muscles in your fingers. Mindfulness meditation comes to mind but of course it's nothing like it. Two. What is it this experience, what is it? It's a pulse of dopamine of course, mostly prefrontal cortex, and a weak tail of serotonin, which, if the scans are any good, seems to be better... work better... if it's focused along the ventral branches. But that's not it, there's something to this. Three. Summers from when I was twelve years old or so visualize quite a lot these days. I was happy in a very different way back then, unrestrained. Plastic? Remembering learning to do somersaults in a field or a garden. Four. Ouch. Ooouch. Not right. Way too hard. Ike's right: you can't do more than three in a row if they're identical, even though you want to. I tell the computer to randomize the dopamine outwards on the last pulse next time; to push it more towards the edges. Next time... hah... This segment might be a bit too good, despite that last one. I make a note of it, put the music back on and start diluting PBS for the first microarray.

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Chapter 3

(written in 2009)

- "Every time, every time we meet she's late"
Lucy and Ike stood waiting outside D's assistant's office. The glass door was shut and the room inside in semi-darkness. The assistant was almost twenty minutes late.
- "Dopamine deficiency, swear to God", Lucy said.
- "Which one?", Ike said.
- "Midbrain insufficiency. Plain cell numbers, not enough dopamine."
- "Not a receptor problem? D1, D2? Unresponsive adrenal glands?"
- "Adrenal problems don't cause chronic lateness, she *relies* on her adrenal stress response to get her ass off the couch in the morning, but that doesn't kick in until she's critically late and then there's terrible traffic or some shit and we end up loosing our fucking morning staring at her door.."
- "Never heard you curse before", Ike said.
- "Period", Lucy said, holding her elbow and stepping restlessly on the spot.
- "D1 then? D2? Receptors not growing the way they should?"
- "Midbrain insufficiency"
- "How do you know? How would you know without scanning her? You got her *scans*??"
- "No. I just know."
- "Bullshit"
- "Fuck you"
They glared at each other for a brief moment.
"It's not D1", Lucy said, "because she's not inattentive and certainly not impulsive. And it's not D2 because she's a vicious learner, not just memoranda but procedure as well, that's why D hired her."
  - "When was that?"
- "Same as me, for a while I thought we'd work together - her background is biotech and biomedical patents - but she's all administration now and real close to D."
- "Balanced D1 and D2 deficienciencies then? Hyperactive dopamine transporter?"
- "Knew you'd say that"
- "Well?"
- "You're pretty obvious Ike, as a person"
- "You're stalling"
- "Midbrain insufficiency. Not enough dopamine neurons."
- "How could you possibly know that without looking at her scans?!"
- "Calm down", Lucy said and lowered her voice as a small group of people emerged from the elevator at the end of the corridor and disappeared around a corner. "Look, first of all Meg and I agree on it and that's rare and I trust her judgement when it comes to guessing phenotypes and so should you. Second, Marlena is unstable, not in a way that really impacts her work but she's *selectively* anhedonic, severely - sometimes she truly doesn't see the point or doesn't care unless she's told and I bet you she's a lot less polished at home. But it's a *partial* problem and if you don't look for it you might not notice: and that's the point, receptor deficiencies have a smooth psychological profile, transporter deficiencies doubly so. Marlena's problem comes in patches. Third, look at her forehead! I'm not saying she's got a small midbrain, I'm saying her forebrain is oversized and sometimes she doesn't have the dopamine to keep all her units running, especially in the morning, which is why we're standing here wasting time."
Ike watched her speak.
- "Don't you ever tell anyone what I just said", Lucy said and suddenly looked nervous.
- "Course not"

- "I shouldn't have said all that"
- "I'm not telling, why would I tell?"
- "Shouldn't have said that"
- "Look, we're not gonna work well together if you keep distrusting me"
- "'Keep'?"

Ike paused, unsure.

- "Meg", he said finally, "You're trying to protect her from me"

Lucy burst into a high laugh.

- "Don't wanna sound cliché or theatrical but I'm more concerned about what she'll do to *you*, if you step on her feet. Do whatever you want, just don't fuck up so you can't work together."
- "How about some pointers then? What do you mean 'what she'll do' to me? She 'unstable' too?"
- "Oh no, I've gossiped more than enough"

They were silent for a while.

- "How about you tell *me* something?", Lucy said after a while, "How about you tell me where you got that scar?" She stroked the left side of her jaw, indicating a thick scar on his.
- "Stepped on someone's feet", Ike mumbled.

Marlena suddenly appeared from the elevator at the end of the hallway and hurried towards them.

- "I'm *so* sorry I'm late", she said, "Traffic's terrible and it's raining. Please come along."

Lucy and Ike looked with surprise at eachother as they followed Marlena down the corridor towards D's office, which she opened with a metal key.

- "We need Ike fully installed by the end of the day", Marlena said. She sat down behind D's large black desk, roused his computer with a quick mouse shake, typed out a long string of characters and hit enter unnecessarily hard. The computer logged in, showing the company logo against a dark background. She gestured for them to sit down in two easy chairs opposite the desk. "Water?" She fished up a bottle of sparkling mineral water from a drawer.
- "No thanks", they both said, attentive.

Marlena paused and looked at them.

- "You've been hired", she finally said to Ike, "I thought you knew."

Ike beamed.

- "D wants you installed and ready to work by the end of the day, you're going with the others to Brussels tomorrow."
- "That's excellent!", Ike exclaimed.
- "You need to bring your scans, we need you to discuss them with some people from the council"

There was a pause.

- "The *brain* scans", Marlena continued, looking steadily at him "You and Chris used his new ligands to make scans of *your brain*. You imaged your serotonin system a week ago in the PET scanner. You found substantial changes."
- "Chris told you?", Ike said, "He told D? He said I'd get him *fired* if I told anyone. So did you.", he turned to Lucy.
- "I don't know anything about this", Lucy said and held up her hands "don't particularly want to know"
- "You're going to Brussels to determine the council's true limits on experimental and commercial deep brain stimulation", Marlena said, "You want to work here because, one day, you want to undergo such surgery *yourself* - sooner rather than later I understand"
- "I want an iPlant", Ike said.
- "The iPlant is a theoretical construct as far as human application is concerned", Marlena said. "We need a battery of permissions and suspicions cleared before we can proceed with surgery. You're going to Brussels to test the European medical law authorities on that particular point. You'll pursue the argument that our implants and surgical procedure are

worth the risks of surgery to customers who have never been hospitalized but who might nevertheless consider themselves neurologically handicapped. Your scans will provide a vivid example of such a case."
- "Do we really want to use one unauthorized procedure to get permission for another?", Lucy asked.
- "You're not going there to get permisison, just to test the waters..", Marlena began.
- "I know", Lucy said, "And to be frank we'll probably proceed with the iPlant either way. I'm asking whether these scans might do more harm than good."
- "D tells me they are quite convincing", Marlena said and looked at Ike.
The three fell silent for a moment.
- "Jeez Ike", Lucy finally said, "How much ecstasy did you have?"
- "It makes sense", Ike said, "I'm in"
- "Brilliant", Marlena said and began filling out a form she'd pulled up on the screen.
- "How much did you have?", Lucy asked again.
- "Enough", Ike said.
- "If you'll come with me over here..", Marlena said and led Ike over to an eye and finger-scanner beside a small safe in the far corner of the room, next to a large liquor cabinet. "Just place your fingertips here please.. and look at the white dot there.. and again.. excellent."