Brain Computer Interface Export Controls Conference

February 16-17, 2023

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Alan F. Estevez
Under Secretary of Commerce for Industry and Security

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Tongele Tongele

Bureau of Industry and Security -
Emerging Technology Division

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Patient Advocacy and the Need for BCI

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Jen French
Neurotech Network

Brain Computer Interface Export Controls Conference

February 16-17, 2023

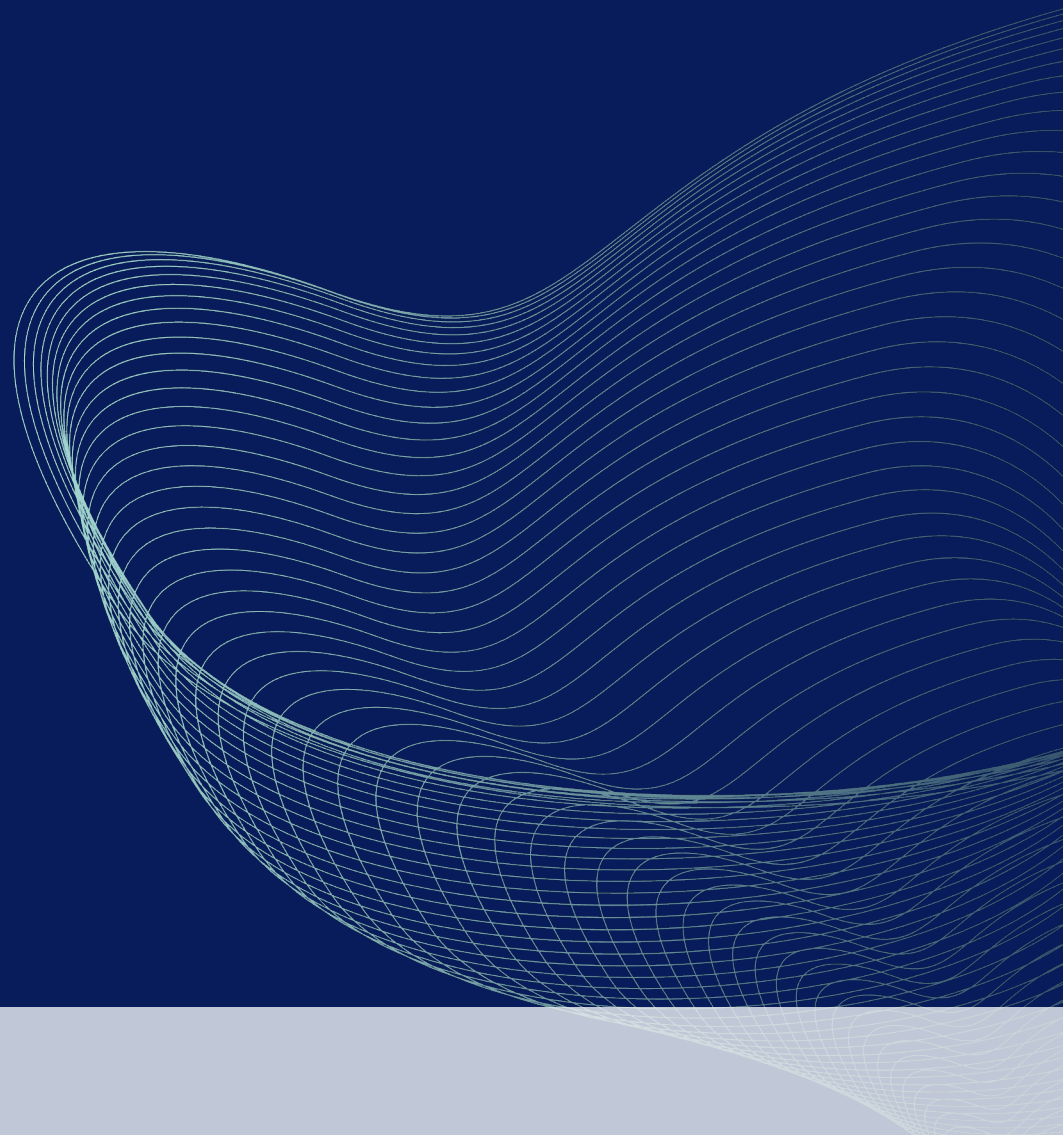
Ian Burkhart

Ian Burkhart Foundation and BCI Pioneers

Behind the BCI:

ALS Patients

By Zoe Lalji



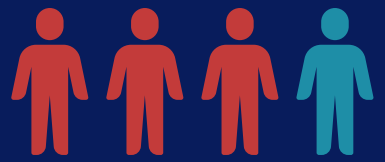
ALS HEROES

More than 150,000 people live with severe speech and motor paralysis.

End User Deep Dive: ALS Patients

Of all neurodegenerative diseases, ALS involves one of the most widespread and diverse losses of function.

ALS HEROES



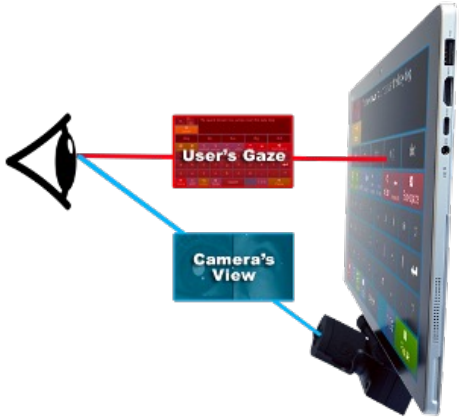
75%

of ALS patients ultimately require some form of Augmentative and Alternative Communication (AAC)

ALS HEROES

Current Assistive Communication

Eye



- Use the eyes as input
- About 10 words / min
- Most sustainable for ALS patients

Touch

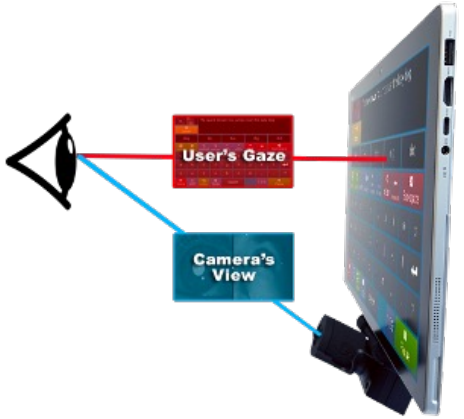
- Use touch as an input
- Not sustainable for limb onset ALS patients or as a long term solution for bulbar.

Switches

- Use different inputs
- Not sustainable for limb onset ALS patients or as a long term solution for bulbar.

Current Assistive Communication

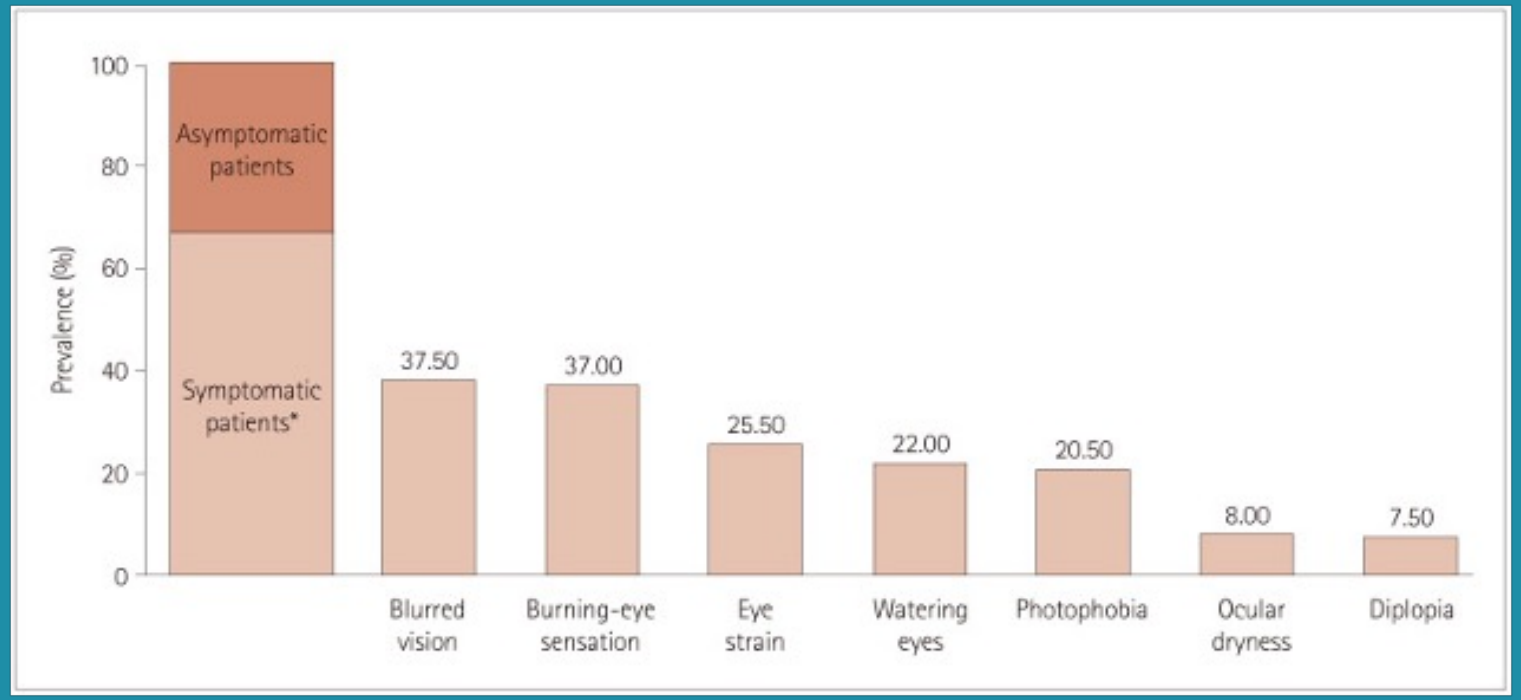
Eye



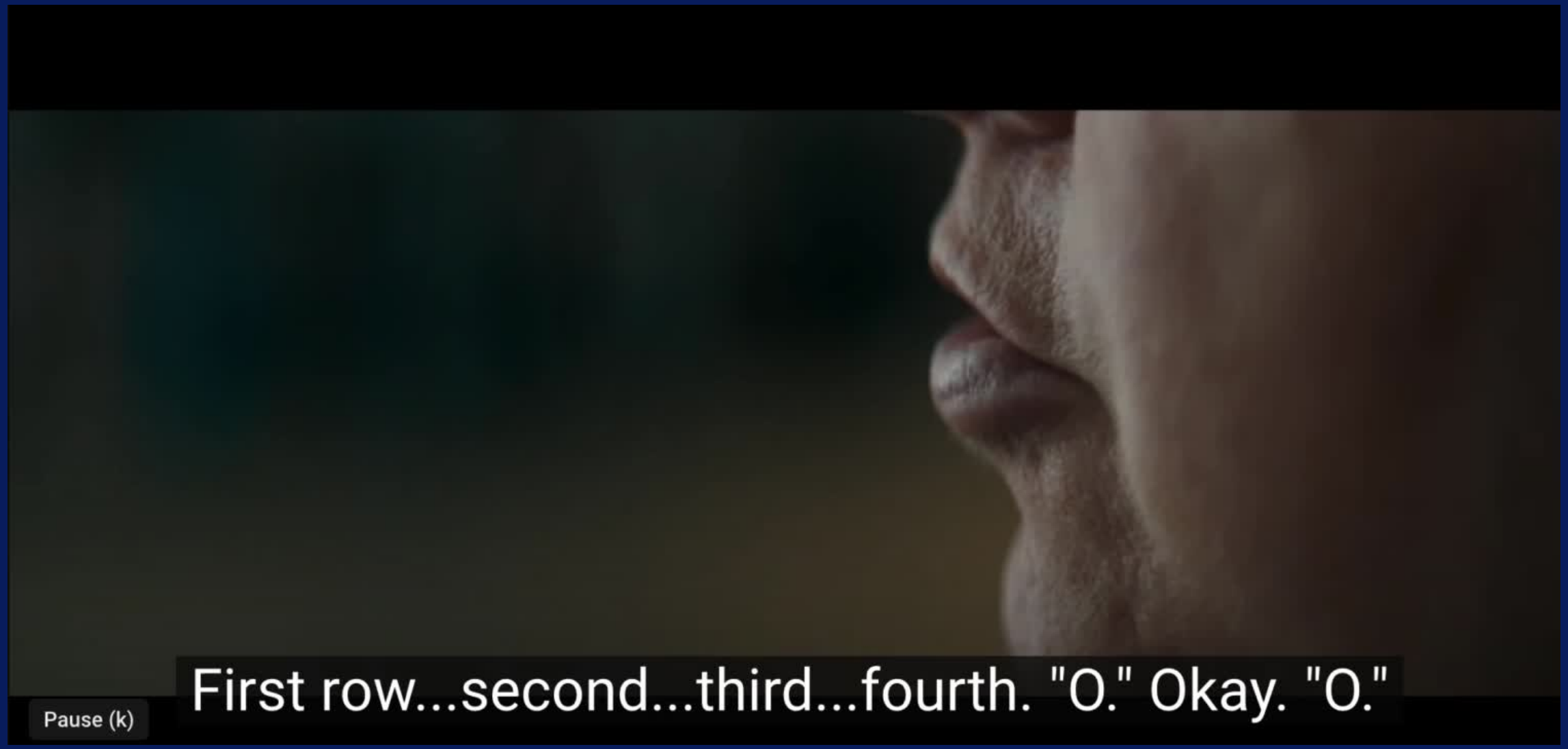
- Use the eyes as input
- About 10 words / min
- Most sustainable for ALS patients

Current Assistive Communication

Nearly 70% of the ALS patients in a study were found to have at least one ocular symptom as shown below



The Reality of ALS



We speak approximately
7,000 words in a day,
2.5 million words a year, and
200 million words a lifetime...

...but we never realize how precious those words are until they are taken from us.

Impact of BCI

on the patient and caregiver

Brain is completely intact

Near Normal Communication

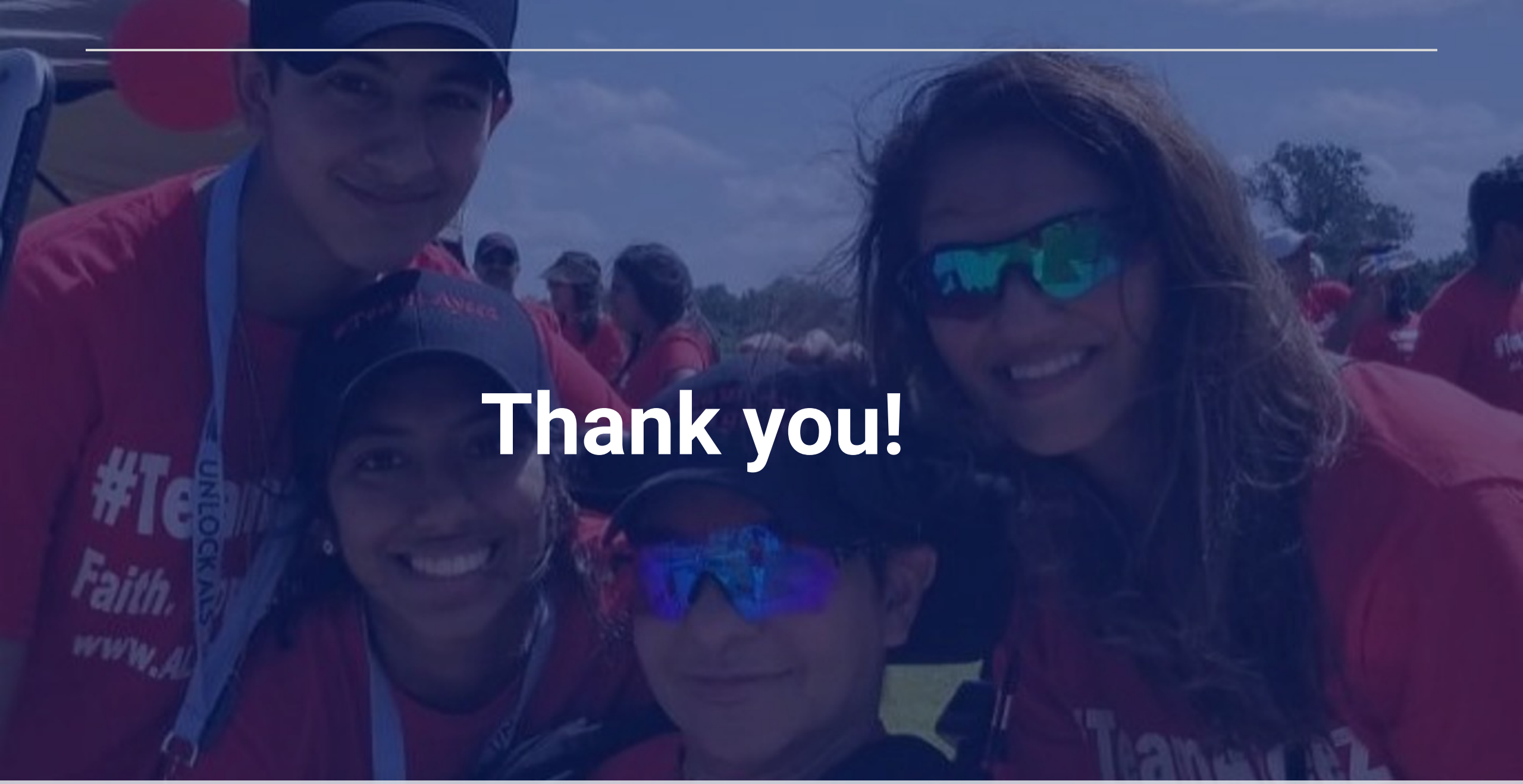
Increased Quality of life for patient and caregiver

”

Until there is a cure for ALS, technology is the cure.

- Steve Gleason

ALS HEROES



Thank you!

ALS HEROES

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Q&A

Jen French, Ian Burkhart, Zoe Lalji

Brain Computer Interface Export Controls Conference

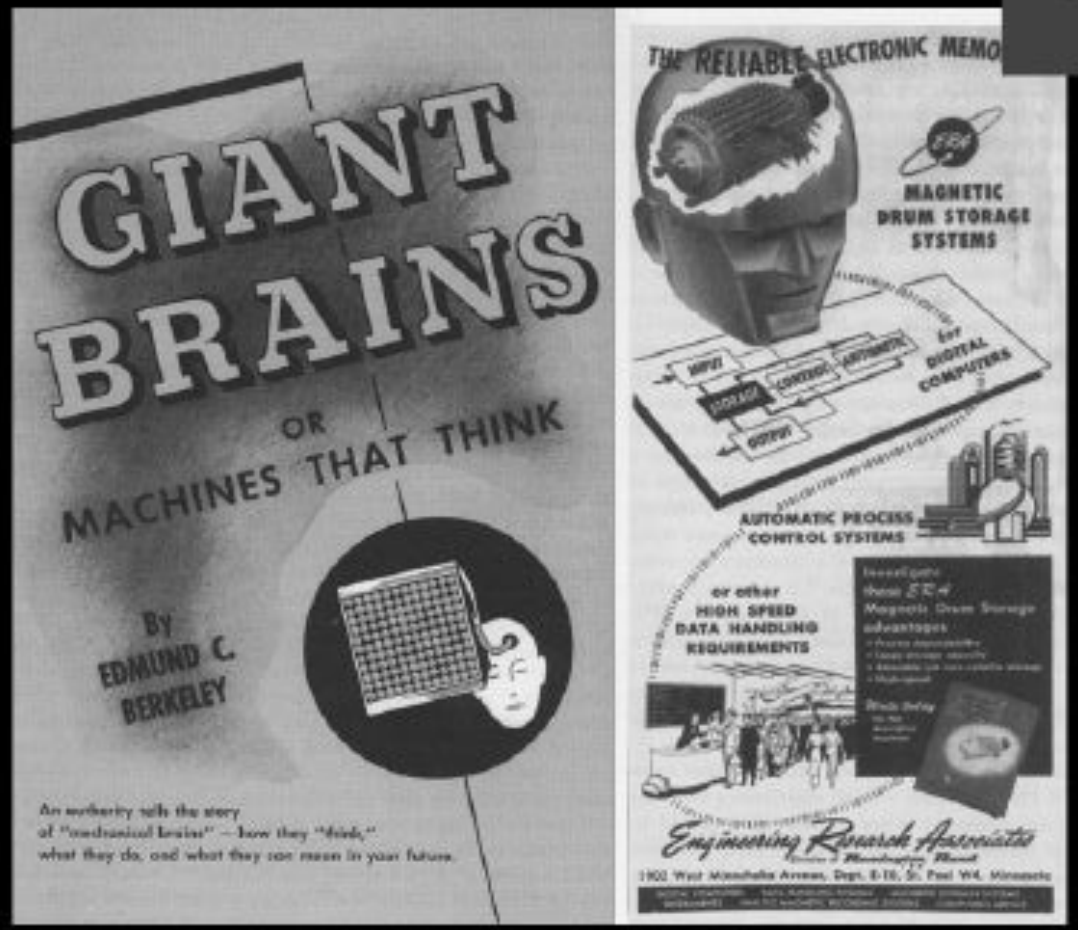
February 16-17, 2023

Government Investment & U.S Leadership in BCI

GOVERNMENT INVESTMENT & U.S LEADERSHIP IN BCI

Amy A Kruse, PhD

MAN-COMPUTER SYMBIOSIS



> The hope is that, in not too many years, human brains and computing machines will be coupled together very tightly and that the resulting partnership will think as no human brain has ever thought and process data in a way not approached by the information-handling machines we know today.
>
> —J.C.R. Licklider
> Man-Computer Symbiosis

IRE Transactions on Human Factors in Electronics (Volume: HFE-1, Issue: 1, March 1960)

CYBERNETICS TECHNOLOGY DIVISION

PROGRAM COMPLETION REPORT

Program Title: Close-Coupled Man/Machine Systems Research (Biocybernetics)

Program Element(s): 61101E, 62709E

ARPA Order No(s): 3053, 3294, 3306, 3330, 3510

DARPA Agent: ONR, Directorate of Research Programs, Psychological Sciences Division

DARPA Technical Agent Key Proj Manager and Phone Number: ONR - Don Woodward/696-4257

1. Direct man/machine communications through bio-electric signals, instead of traditional I/O or voice recognition and speech analysis for enhanced command and control.

   (a) Could the brain make advantageous use of order of magnitude or greater increase in rate of information flow?

   (b) To what extent can the brain act as time-shared or parallel processor?

   (c) How far can non-invasive interfaces lead? Research and end products presumably were to involve only intact humans.

   (d) Could same technology be applied to similar enhancement of man/man communications, perhaps by a central machine processor?

The Program's goal was to develop new communication links between man and computer-assisted systems. These links, it was hoped, would enhance a man-machine system ability to perform its goals. This effort was seen as complementary to the main thrust of the development of computer applications in man/machine systems. In the main the traditional goal has been the development of tools that can take over some of the operators' functions by providing substitutes that can perform a large variety of functions. This "prosthetic" approach includes a diversity of developments, from the development of power steering mechanisms for efficient control of mechanical devices to the implementation of sophisticated Artificial Intelligence. The Biocybernetics Program was based on the presumption that no matter how wide spread, and successful, the application of computer-based prosthetic devices the operator will not be eliminated. Therefore, in all such systems, success will ultimately depend on the interaction between man and the mechanical contrivances which surround him in the man/machine system.

Program Completion Report – 1980
Program Start – 1973/4

BCI: IT TAKES A VILLAGE

+ many others!

DARPA Funding for BCI over the decades

Most programs are in the USD 50-100 Million USD range, and overall funding for invasive interfaces has been higher than non-invasive ones

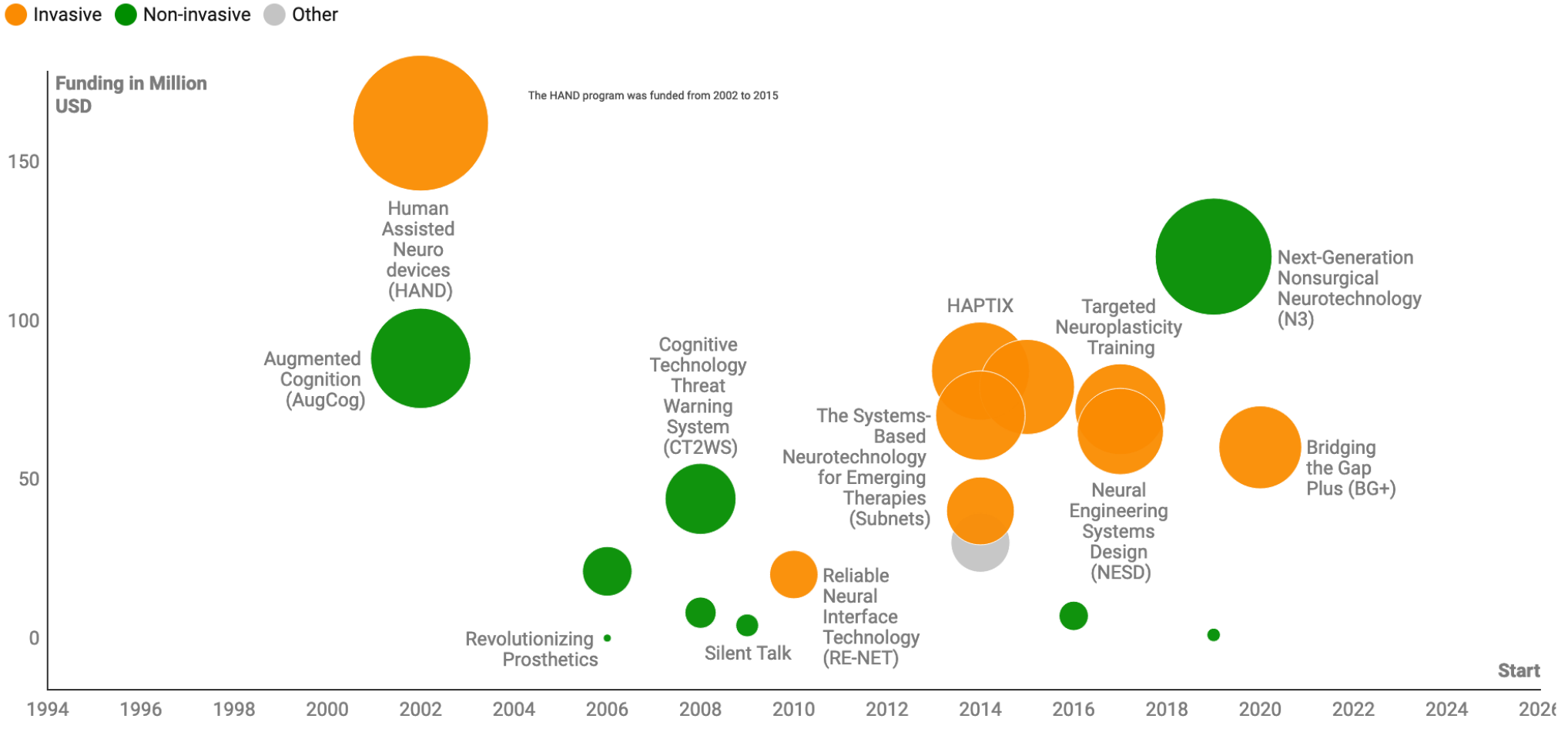


Chart: Pooja Rao • Source: News reports and DARPA's website • Created with Datawrapper

DARPA's Brain-Computer Interface Programs

On average, DARPA has funded a new multi-million dollar neural interface R&D program every year for the last two decades

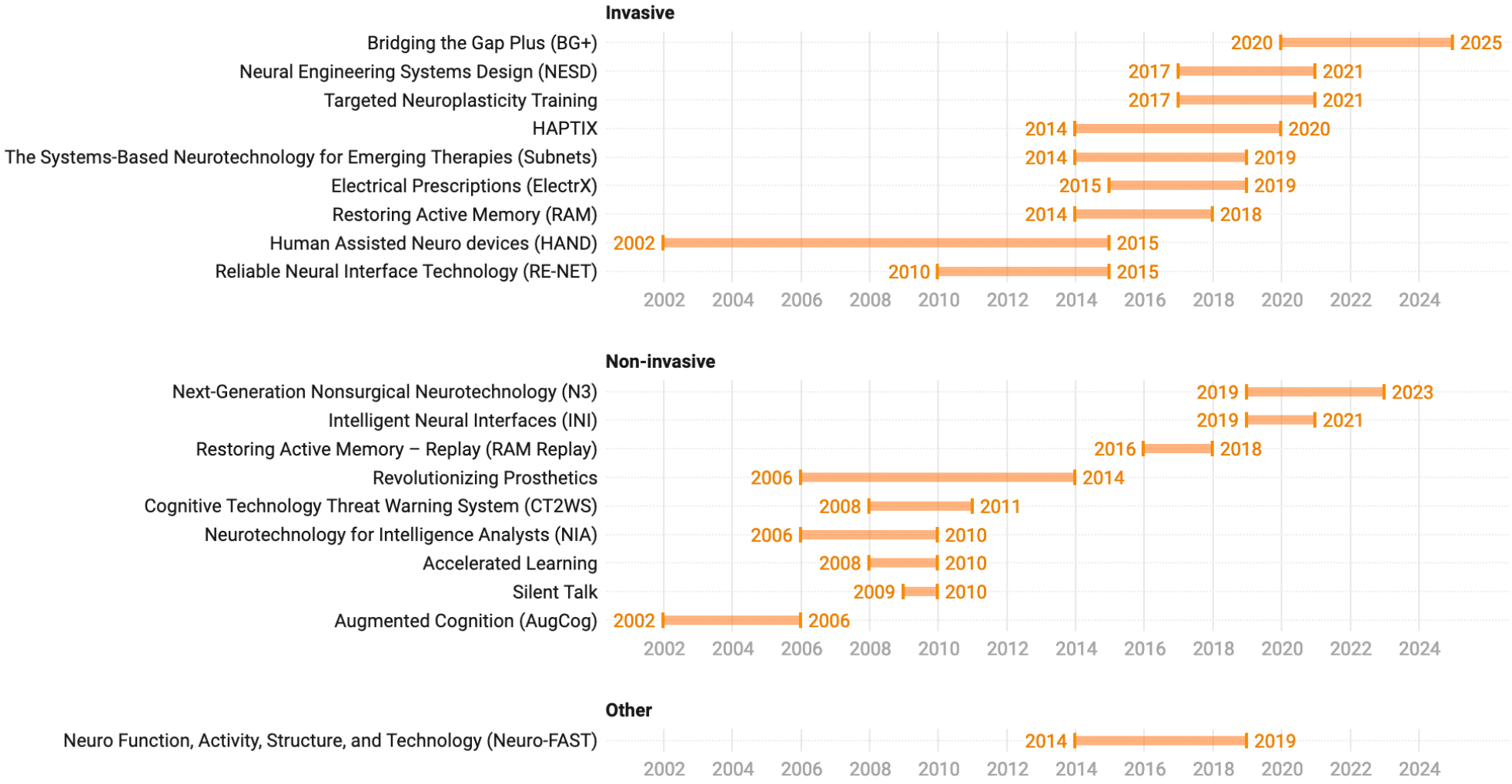
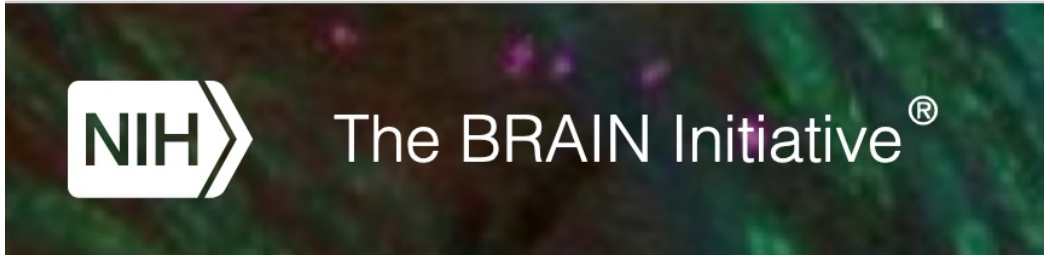


Chart: Pooja Rao • Source: News reports and DARPA's website • Created with Datawrapper

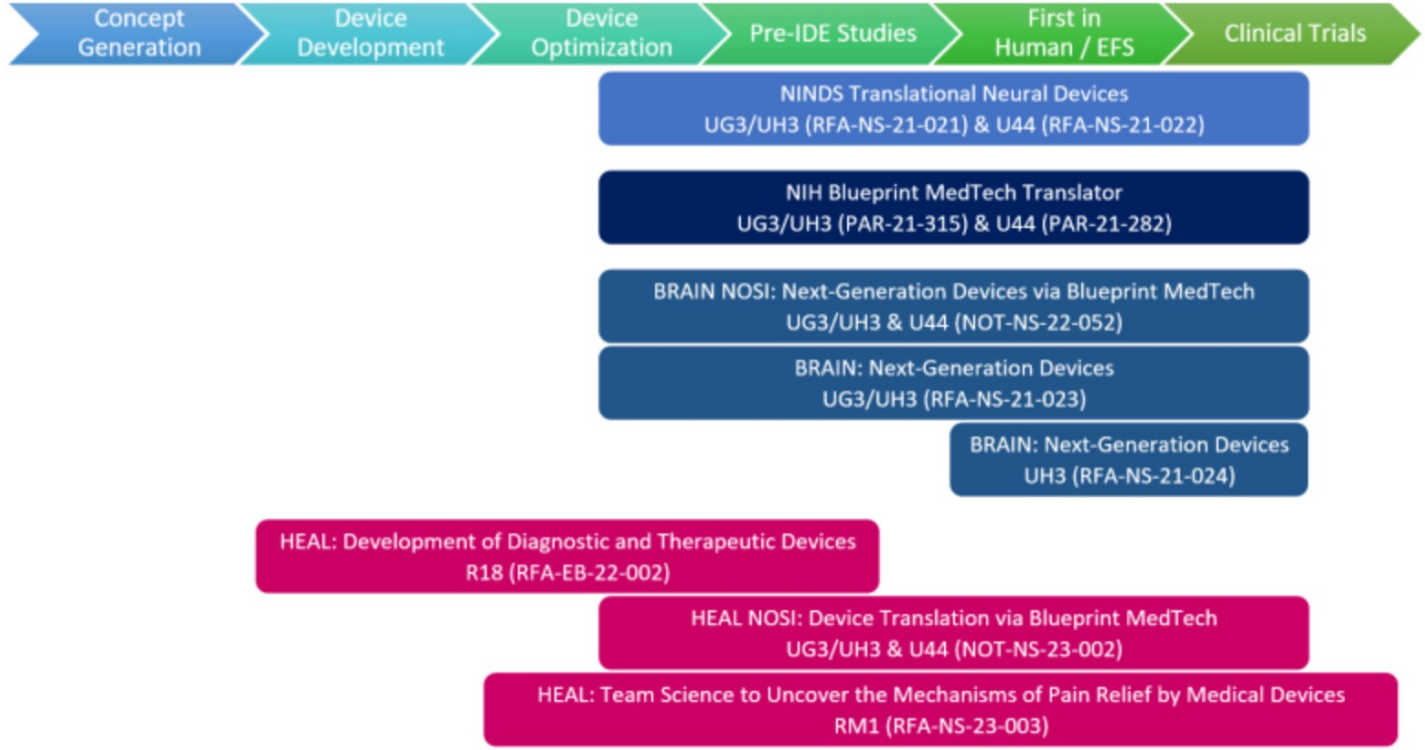
Program end dates aren't quite accurate, but it's a reasonable estimate

NIH INVESTMENTS

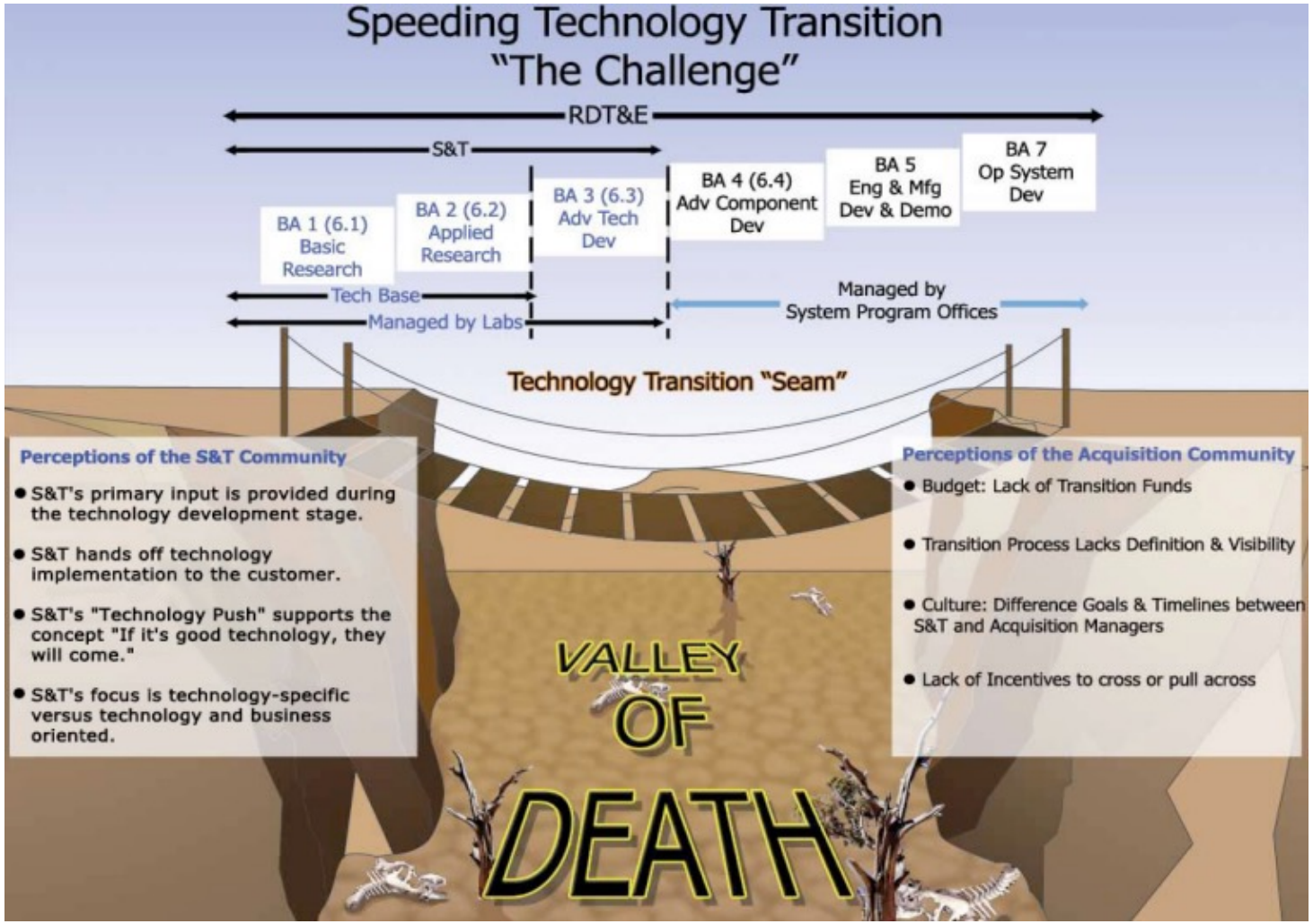


National Institute of Neurological Disorders and Stroke

Initiated 2013: Estimated over $3B allocated; 2022 Appropriations ~$620 Million



HOWEVER: THE VALLEY OF DEATH



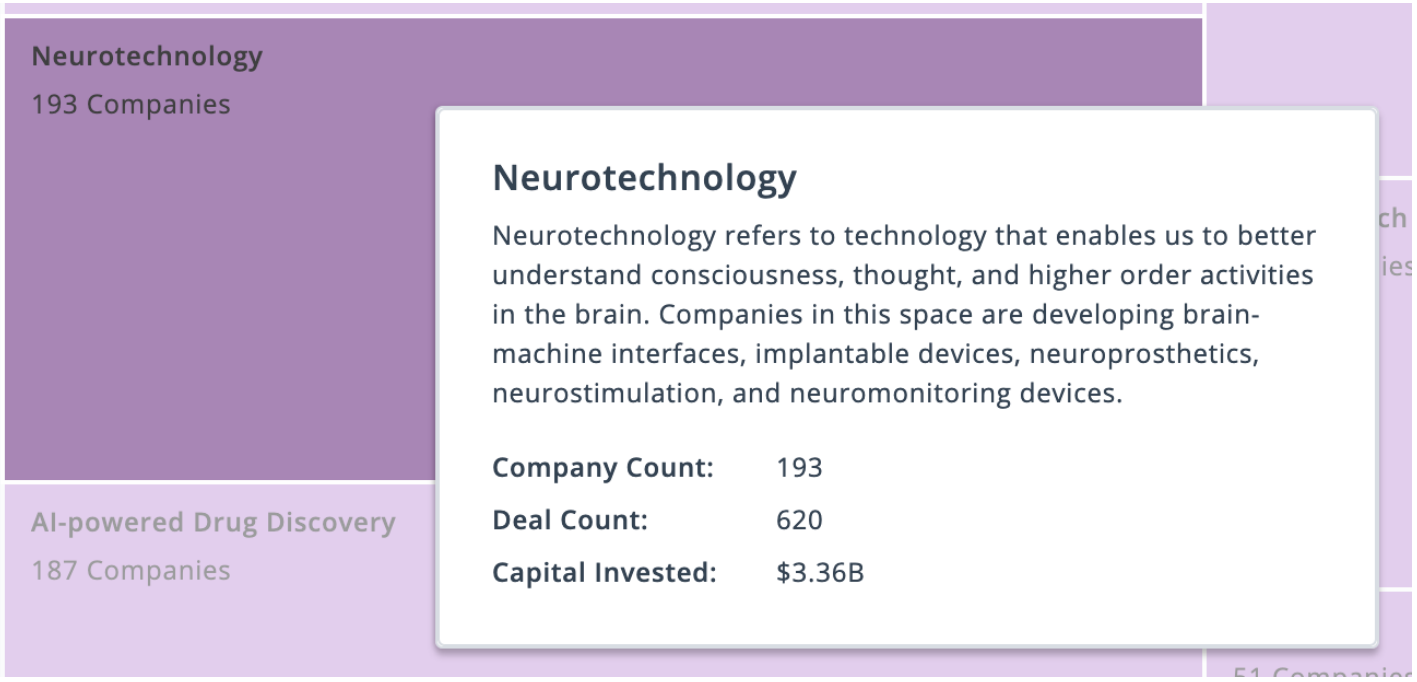
VALLEY OR BLACK HOLE?

BCI: REMEMBER IT TAKES A VILLAGE

DARPA NSF NIH DEPARTMENT OF VETERANS AFFAIRS UNITED STATES OF AMERICA

+ And others!

AND VC INVESTMENT: ESCAPE VELOCITY?



Pitchbook Data: 2018-2023

Brain Computer Interface Export Controls Conference

February 16-17, 2023

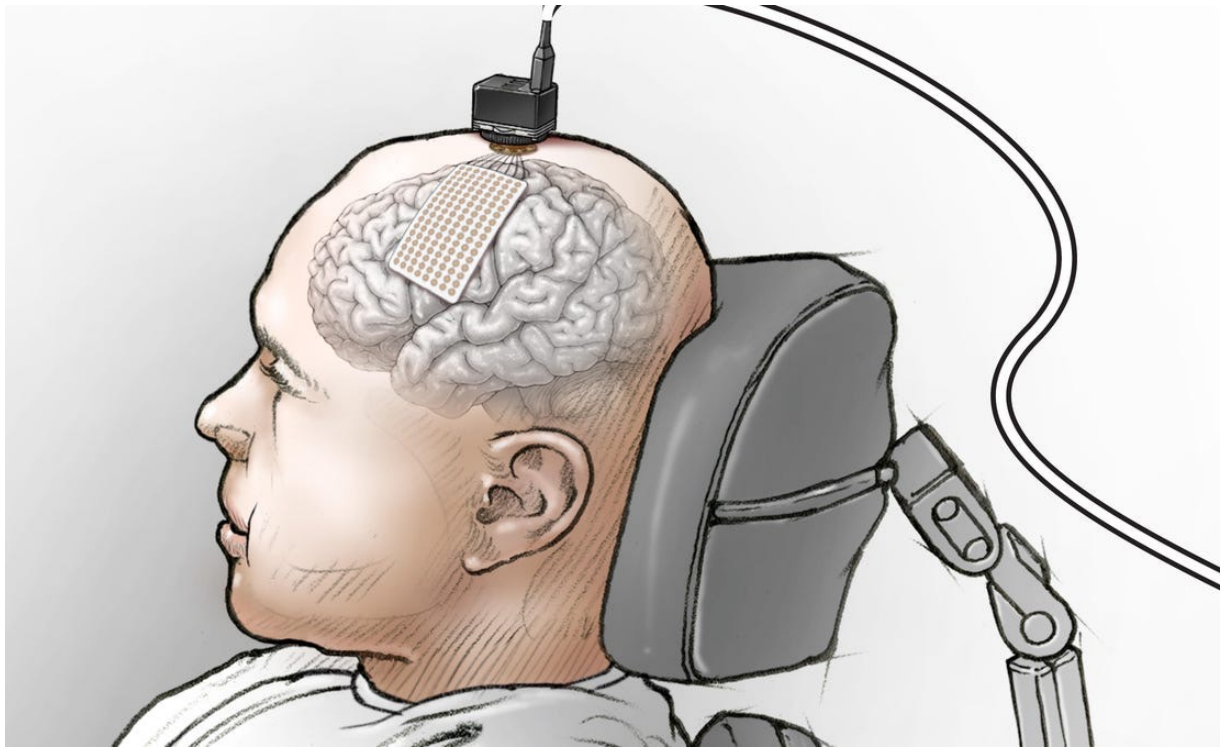
State of the Art & Applications

Landscape of current and near-future noninvasive BCIs

February 16, 2023

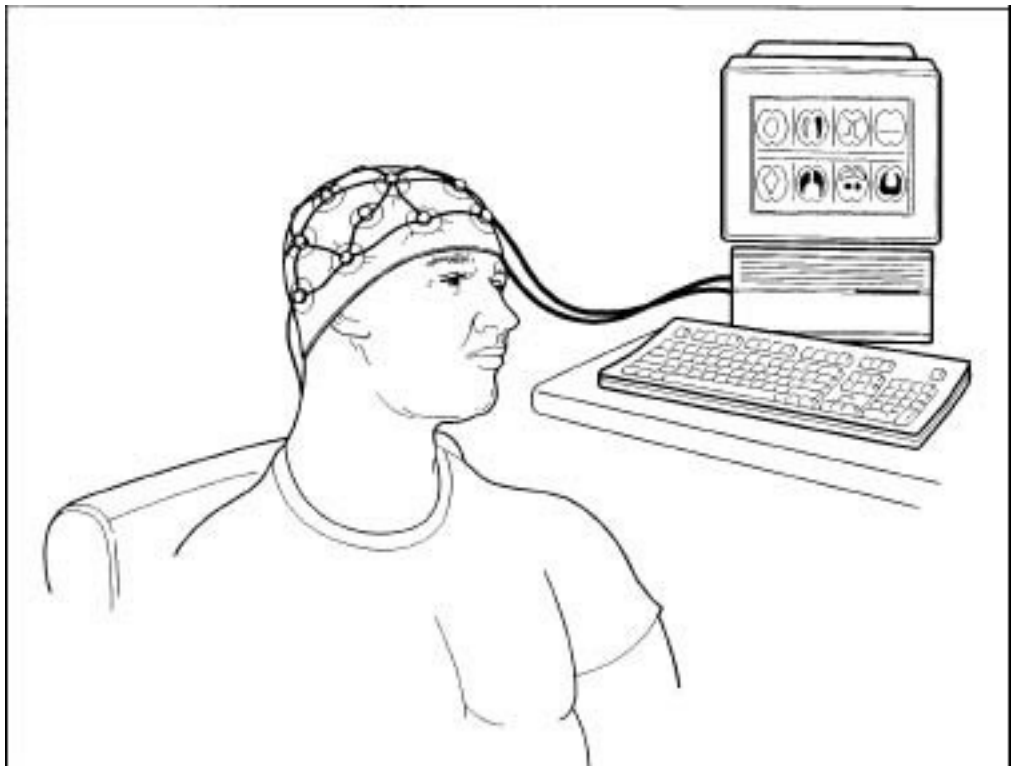
Anna Wexler
Assistant Professor, Department of Medical Ethics & Health Policy,
University of Pennsylvania Perelman School of Medicine

Invasive

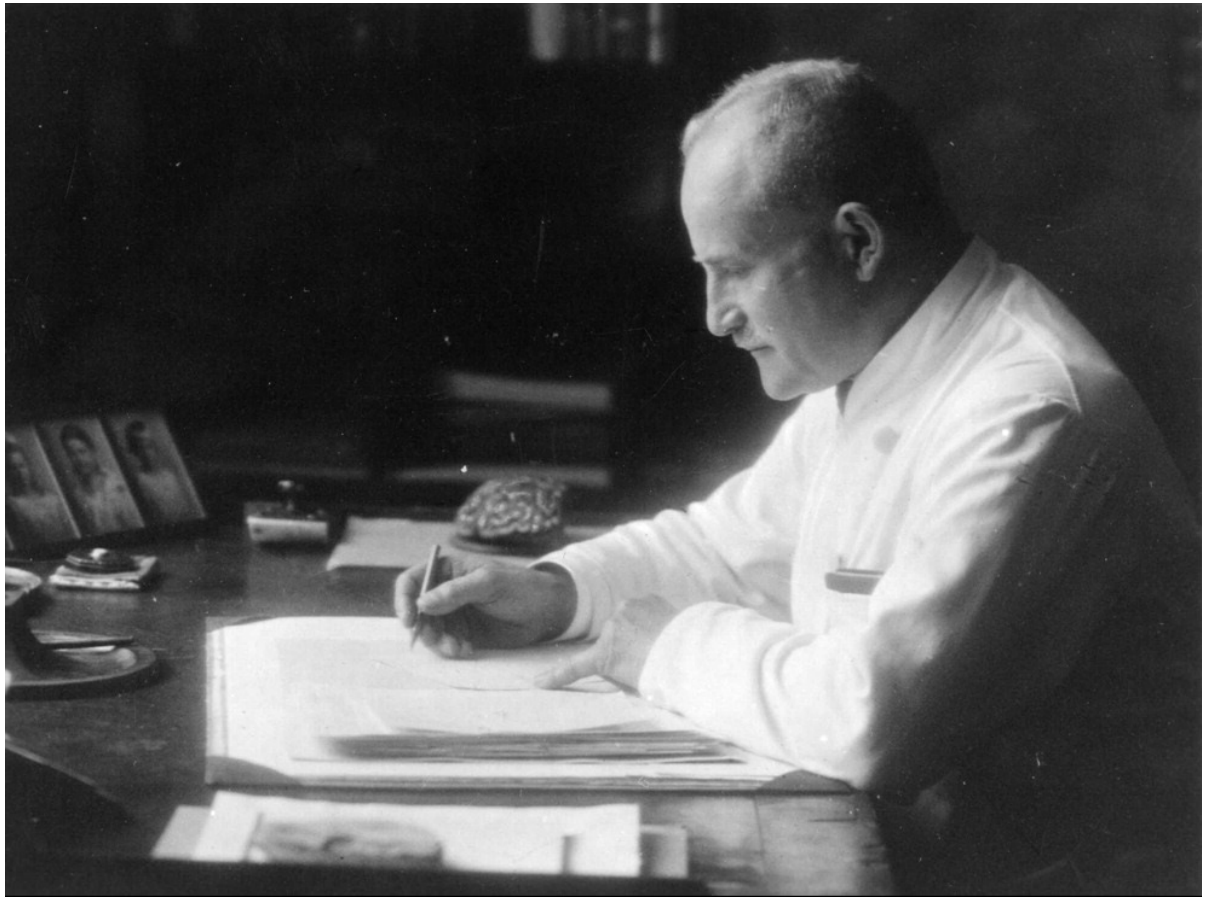


Ken Probst/UCSF

Noninvasive



Brainwave recording technology is nearly 100 years old



Über das Elektrenkephalogramm des Menschen.

Von

Professor Dr. **Hans Berger**, Jena.

(Mit 17 Textabbildungen.)

(Eingegangen am 22. April 1929.)

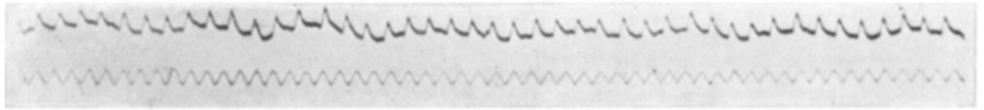
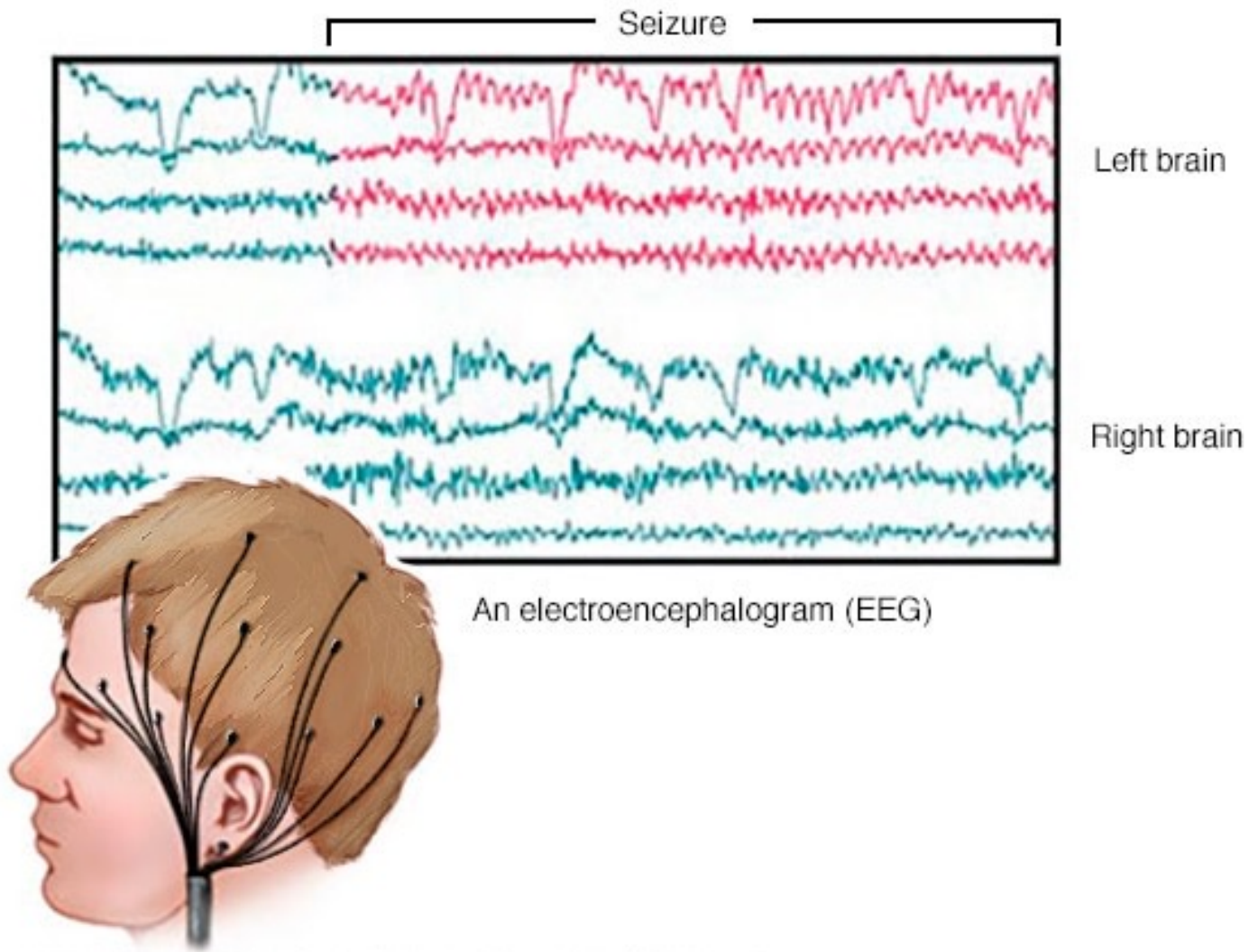


Abb. 4. 40jähriger Mann. Große linksseitige, von der Stirn bis in die Parietalgegend reichende Knochenlücke. Doppelspulengalvanometer. Kondensation. Nadelelektroden subcutan im Bereich der Knochenlücke, 4,5 cm voneinander entfernt. Oben Schwankungen der epidural abgeleiteten Kurve, unten Zeit in $^1/_{10}$ Sekunden.

EEGs are part of standard medical care, used to monitor sleep and localize seizures.



An electroencephalogram (EEG)

EEG is the most common technology used in noninvasive BCIs, though it is possible to use other brain imaging or recording techniques.

MEG

fMRI

fNIRS

Noninvasive electrical stimulation techniques are over 100 years old

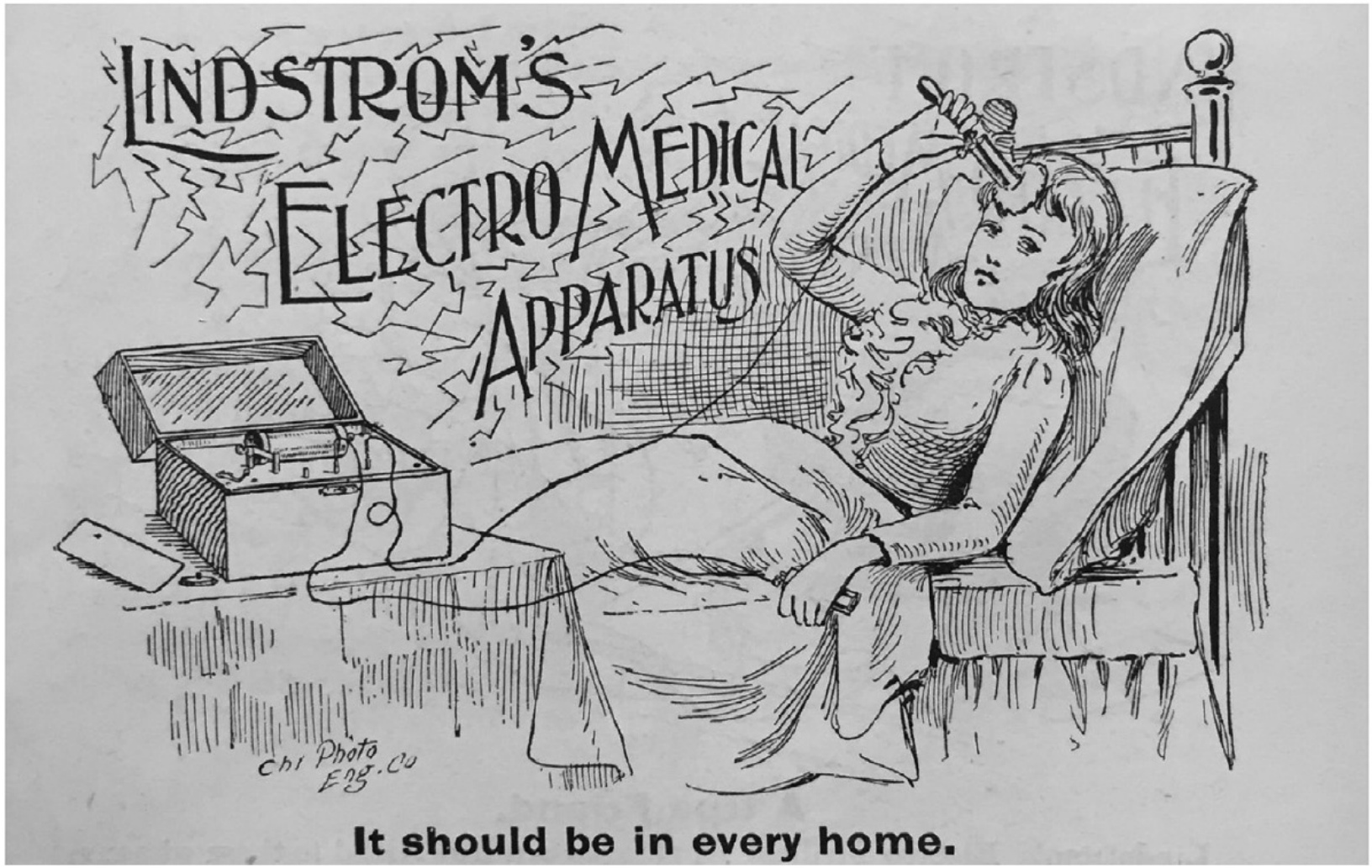
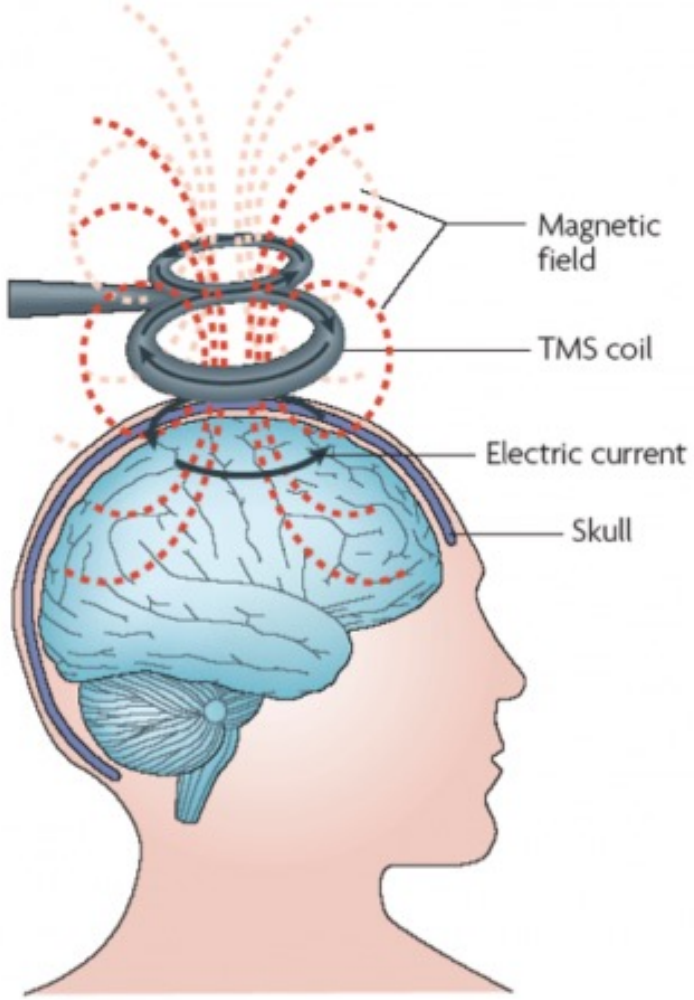


Fig. 4. Lindstrom's Electro-Medical Apparatus (ca. 1895, Bakken Library Collection.)

(Wexler 2016)

Noninvasive neurostimulation techniques are used to treat indications like depression, migraine, and obsessive-compulsive disorder (OCD).

Electro-convulsive therapy (ECT)



Transcranial magnetic stimulation (TMS)

Forbes

Soon, Facebook Will Know What You're Thinking

The Brain Implants That Could Change Humanity

Brains are talking to computers, and computers to brains. Are our daydreams safe?

VICE

How Hackers Could Get Inside Your Head With 'Brain Malware'

Brain-computer interfaces offer new applications for our brain signals—and a new vector for security and privacy violations.

The Washington Post
Democracy Dies in Darkness

INNOVATIONS

Your tech devices want to read your brain. What could go wrong?

Neurable, NextMind, Facebook and other tech firms are championing brain-controlled gadgets as the next big thing

OBSERVER BUSINESS | ARTS | ENTERTAINMENT

BUSINESS

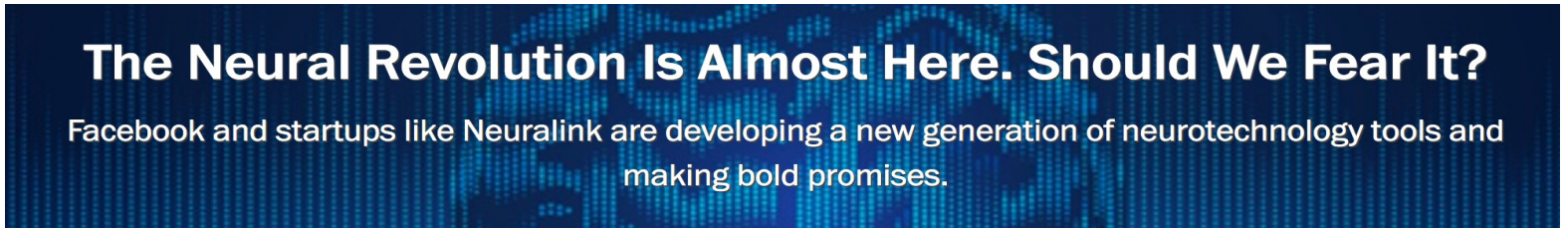
Mind-Reading Tech Is Dangerously Close to Becoming a Reality

Thanks to Facebook and Elon Musk, our brains and thoughts may no longer be private anymore.

FUTURE TENSE

Elon Musk Wants to Hack Your Brain

How will the FDA manage that?



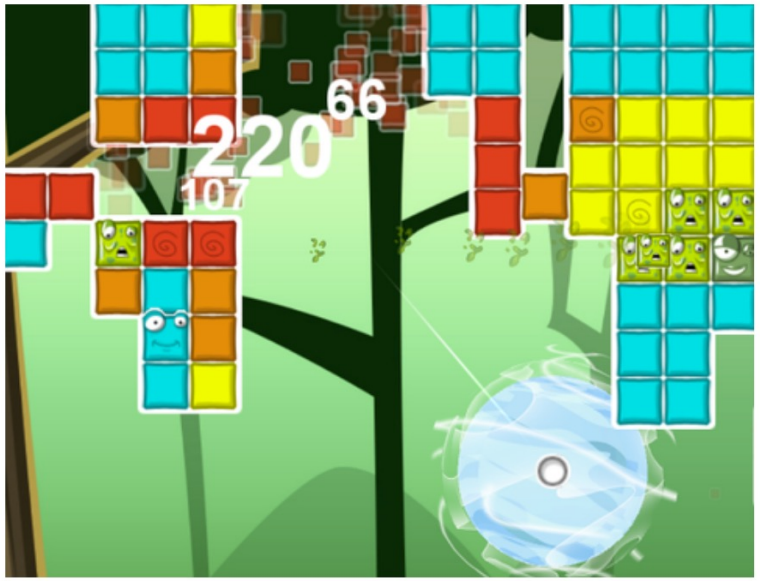
What is unique to the present moment?

- Unprecedented private investment in neurotechnology
- Fast-paced technological developments
- Development and marketing of neurotechnology for consumer applications beyond medicine

Early 2000s: first consumer EEG devices come to market.

Early applications of consumer EEG devices focused on object control.

Novelty cat ears

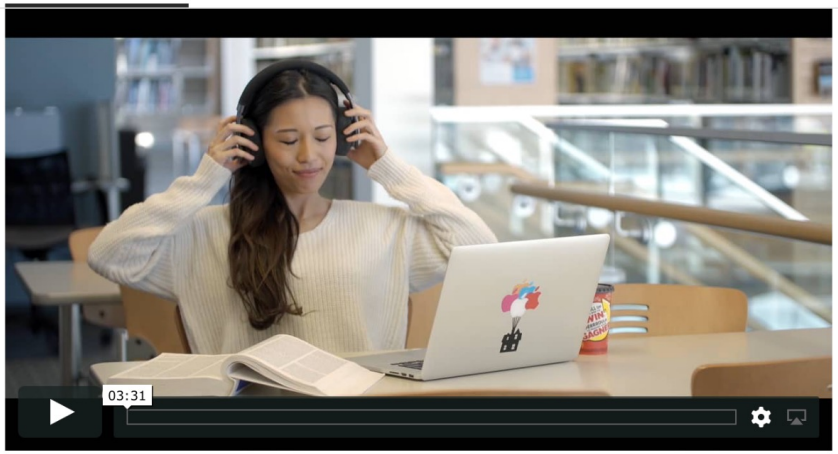


Video game

Toy helicopter

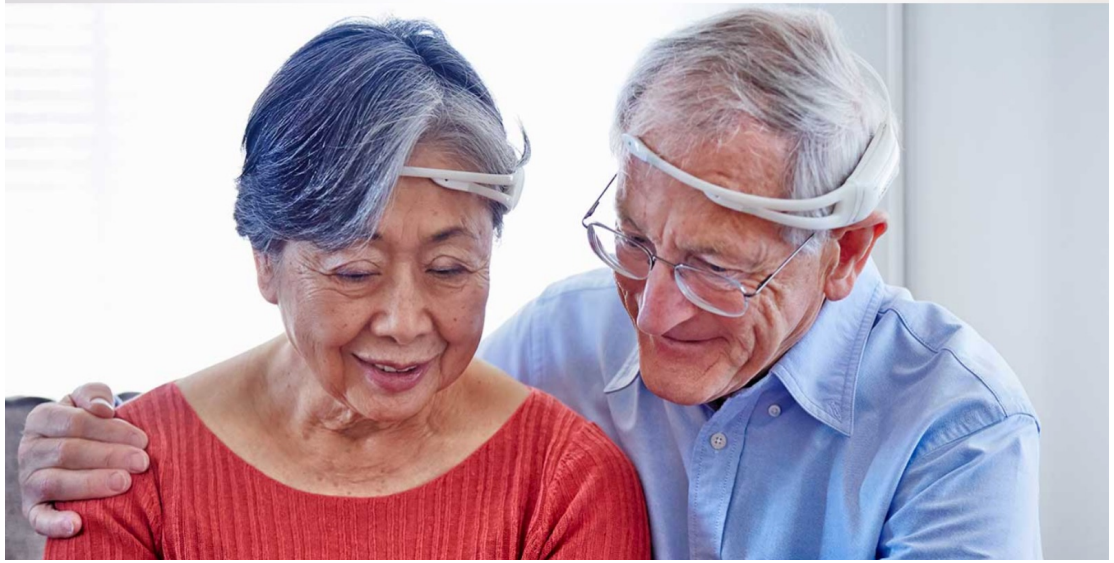
Mid-2010s: consumer EEG devices marketed for “wellness.”

Relax thanks to science



Focus like never before

For health and wellbeing



Suitable for Children

Today: the next generation of EEG devices are being developed for applications such as control, wellness, and focus.

Other kinds of brain recording devices are being developed…

Kernel Flow Live Stream

10,420 views • Streamed live on Oct 22, 2020

366 7 SHARE SAVE ...

… and abandoned.

Facebook Announces "Typing-by-Brain" Project

Facebook promises 100 words per minute, but doesn't detail the technology that can pull that off

By **Eliza Strickland**

Photo: Stephen Lam/Reuters

April 2017 (IEEE Spectrum)

Facebook is ditching plans to make an interface that reads the brain

The company's research into a consumer mind-reading device is over, for now. Some scientists said it was never possible anyway.

By Antonio Regalado

July 14, 2021

A prototype of Facebook's optical device for reading brain signals.

FACEBOOK

July 2021 (MIT Tech Review)

Early 2010s: consumer brain stimulation “kits” come to market.

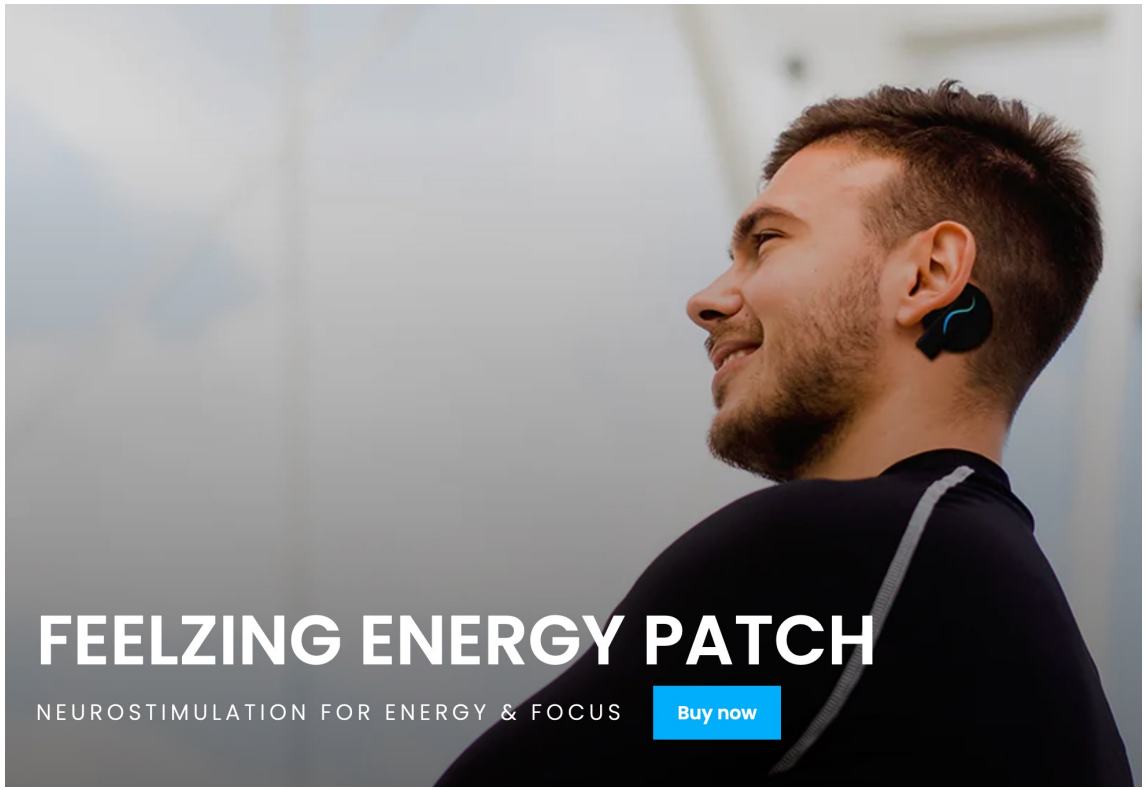
Power Your Mind!

tDCS allows you to unlock your brain’s true potential!

RECHARGE YOUR BRAIN

Mid-2010s: the first wearable consumer brain stimulation devices come to market.

Today: the next generation of consumer brain stimulation devices are being developed for wellness and enhancement.



LIFTiD tDCS Device for Improving Focus, Attention, Memory, and Productivity

In the U.S., consumer neurotechnology falls into a regulatory grey zone.

SCIENCE AND REGULATION

Oversight of direct-to-consumer neurotechnologies

Efficacy of products is far from clear

U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

FEDERAL TRADE COMMISSION
PROTECTING AMERICA'S CONSUMERS

UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION

(Wexler & Reiner, 2019)

Companies around the world are developing noninvasive neurotechnology.

Austria/g.tec

Australia/SmartCap

Serbia/MBT

In the consumer neurotechnology space, companies' claims have largely outpaced the science.

Mind-Reading or Misleading? Assessing Direct-to-Consumer Electroencephalography (EEG) Devices Marketed for Wellness and Their Ethical and Regulatory Implications

Anna Wexler [1] · Robert Thibault [2,3]

Received: 19 June 2018 / Accepted: 30 August 2018

Abstract

The market for direct-to-consumer brain health products—including brain-training games, neurostimulation devices, and consumer electroencephalography (EEG) devices—is expected to top $3 billion by 2020. While many direct-to-consumer neurotechnology products have come under scrutiny from scientists and regulators, one set of products—consumer EEG devices—have largely escaped scholarly and regulatory critique. While these products do not present overt safety risks, by claiming to provide individuals with "snapshots" of their own mental states, they present a subtle, and arguably more complex, set of ethical issues. In addition, consumer EEG companies often explicitly or implicitly rely on studies conducted in the field of neurofeedback, a domain in which almost all adequately controlled studies point to little more than an interesting placebo effect. This paper presents an initial critique of consumer EEG devices, focusing only on devices that are marketed directly to consumers for improving their well-being. We categorize the behavioral and wellness-related marketing claims made by consumer EEG companies, analyze the evidence base for such claims, and argue that the ethical and legal issues wrought by these devices deserve greater attention.

Capabilities of neurotechnology are often overstated by the media.

SCIENTIFIC AMERICAN

Mind Reading and Mind Control Technologies Are Coming

We need to figure out the ethical implications before they arrive

Facebook is building tech to read your mind. The ethical implications are staggering.

Our brains are perhaps the final privacy frontier.

POLITICO

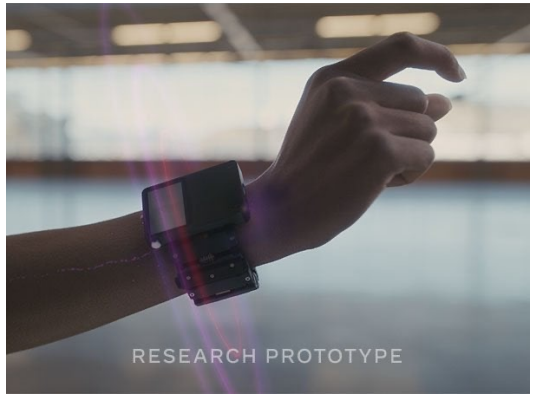
Machines can read your brain. There's little that can stop them.

Technology is giving access to the inner workings of the brain, and policymakers are scrambling to regulate it.

It is not clear what value brain data will have for the average consumer.

The question of definitions is not trivial.

- What technologies count as brain-computer interfaces?



- Should we use terms like invasive and noninvasive?

AJOB NEUROSCIENCE
2023, VOL. 14, NO. 01, 13–15
https://doi.org/10.1080/21507740.2022.2150708

OPEN PEER COMMENTARIES

Invasiveness is Inevitable in Psychiatric Neurointerventions

Nick J. Davis[a]

- Where is the line between treatment and enhancement?

Protection of neural data is part of a larger data privacy challenge.

The Guardian/Greedy Hen, 11/6/21

The Machine that Reads Minds

"Today they are still secret signs, tomorrow they may perhaps reveal mental and brain illnesses, and the day after tomorrow, one may even be exchanging personal correspondence in brain script."

Die Maschine, die Gedanken lieſt . . .

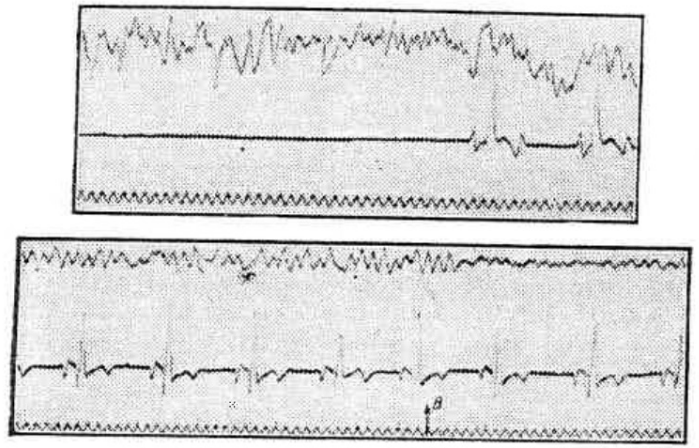
Die ſenſationelle Entdeckung eines deutſchen Pſychiaters.

Elektriſche Hirnſchrift.

Von Walter Finkler.

Dunkelkammer der Pſychiatriſchen Klinik in Jena. Doppeltüren ſchließen den Raum ſchalldicht von der Umwelt ab. Eine bahnbrechende Entdeckung ſoll ausprobiert werden, die Profeſſor Dr. Hans Berger, dem Direktor der Pſychiatriſchen Univerſitätsklinik in Jena, gelungen iſt. Es handelt ſich um die Aufzeichnung der Gedanken in Geſtalt einer Zickzack-Kurve, um die elektriſche Schrift des Menſchenhirns.

Das Verſuchskaninchen iſt ein Aſſiſtenzarzt der Klinik. An Arm und Bein des Arztes wird eine Silberplatte



Das Elektrenkephalogramm einer vierjährigen Hündin (oben) ſowie das eines dreißigjährigen Mannes (unten).

als das Zickzack, das ein Zeiger auf einem Papierſtreifen aufzeichnet, und doch weiß man genau, wann der Mann im Nebenzimmer zu rechnen begonnen hat, ob ihn die Arbeit ſehr anſtrengt und wann er mit der Rechnung zu Ende iſt.

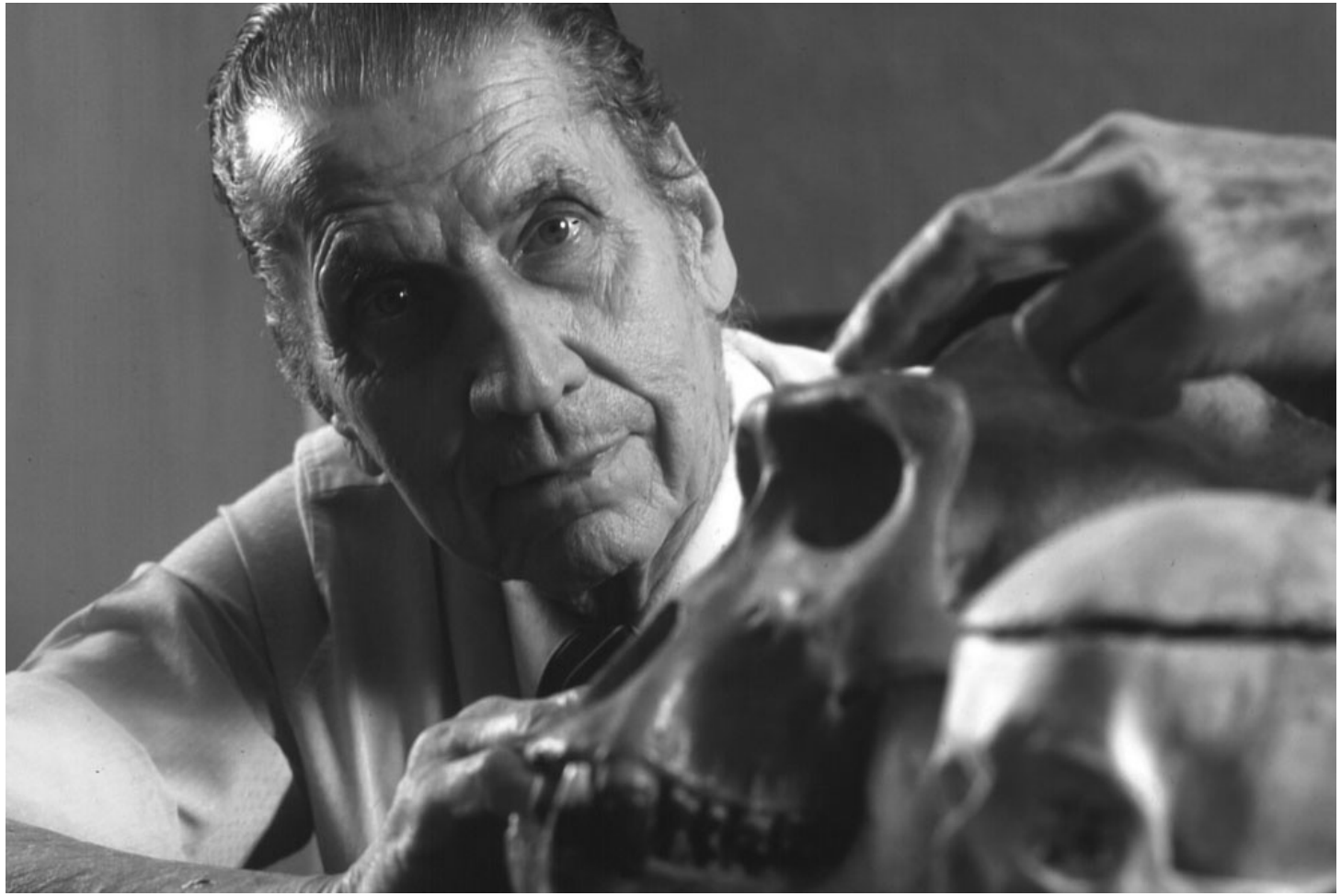
*

Man hat bisher ſchon wiederholt verſucht, die elektriſchen Ströme des tätigen Gehirns nachzuweiſen und glaubte auch poſitive Ergebniſſe erzielt zu haben. Aber bei Nachprüfungen ſtellte es ſich ſtets heraus, daß der elektriſche Strom nicht der Lebenstätigkeit der Hirnzellen entſtammte, ſondern auf andere Vorgänge zurückzuführen war. Vor allem auf die elektriſche Entladung, die durch die Reibung des Blutes an den Wänden der kleinen Blutgefäße entſteht, auf einen rein phyſikaliſchen Vorgang alſo, der mit den Hirnzellen und überhaupt mit Leben nichts zu tun hat. Oder der elektriſche Strom rührte von Aktionsſtrömen der Blutgefäße her, bei deren Muskeltätigkeit ja auch elektriſcher Strom frei wird.

Sorgſame Kontrollverſuche haben ergeben, daß die elektriſche Hirnſchrift des Profeſſors Berger mit allen dieſen Erſcheinungen nichts zu tun hat, denn die Kurven bleiben auch dann erhalten, wenn Herz und Atmung ausgeſchaltet ſind, wenn alſo gar kein Blutkreislauf im Gehirn ſtattfindet. Charakteriſtiſch iſt ferner, daß die Kurven während des Tiefſchlafs abnehmen, ohne jedoch zu verſchwinden. Damit iſt ein experimenteller Beweis für die Lehren der modernen Seelenkunde erbracht, die annimmt, daß die Hirntätigkeit im Schlafe nie völlig aufhört.

Auf Grund von Tierverſuchen und Beobachtungen an Menſchen mit geöffneten Schädelknochen ſchloß man, daß dieſe Ströme in der Hirnrinde entſtehen, jenem Teil des Gehirns, der als Sitz der höheren geiſtigen und ſeeliſchen

Stadt-Anzeiger, Dusseldorf, 8/6/1930
courtesy of Cornelius Borck, as noted in *Brainwaves: A Cultural History of Electroencephalography*

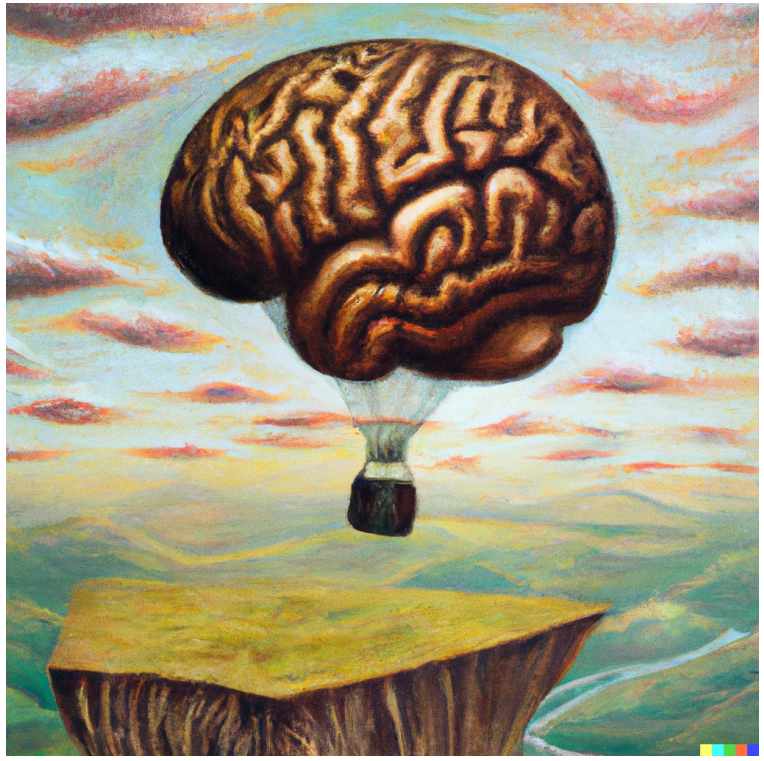


“Could drives, desires and thoughts be placed under the artificial command of electronics?”

“Fears have been expressed that this new technology brings with it the threat of possible unwanted and unethical remote control of the cerebral activities of man by other men.”

– Jose Delgado, 1969, *Physical Control of the Mind*

Perelman School of Medicine
University of Pennsylvania



Thank you!

awex@pennmedicine.upenn.edu

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Q&A

Amy Kruse, Leigh Hochberg, Anna Wexler

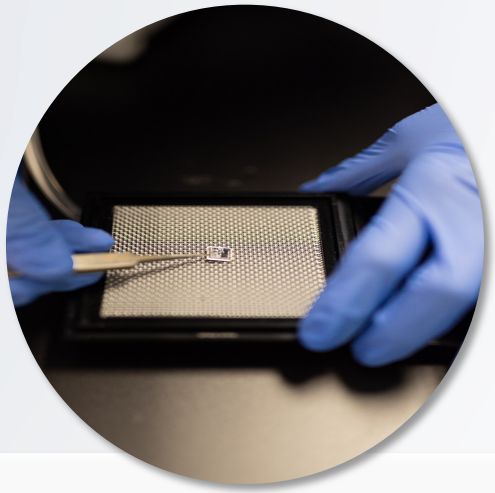
Brain Computer Interface Export Controls Conference

February 16-17, 2023

BCI Commercialization

Paradromics

Paradromics is building a **direct data interface** with the brain to enable technology solutions to unmet medical needs

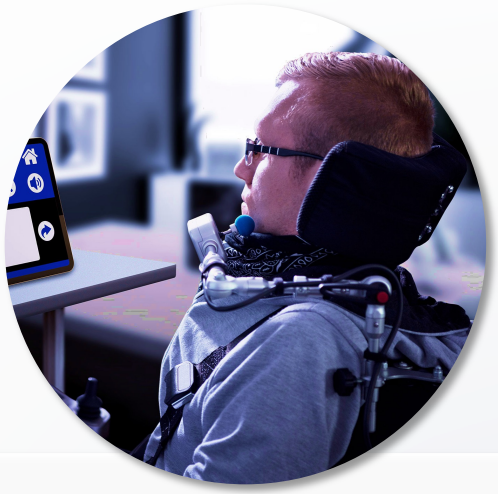


About

- Founded in 2015
- Located in Austin, Texas
- $18M public funding (DARPA and NIH)
- $47 venture funding
- First-in-human expected Q1/2024

Team

- Experts in neuroscience, microelectronics, computation, and advanced materials
- Experienced go-to-market medical device team with deep clinical and regulatory experience



Technology

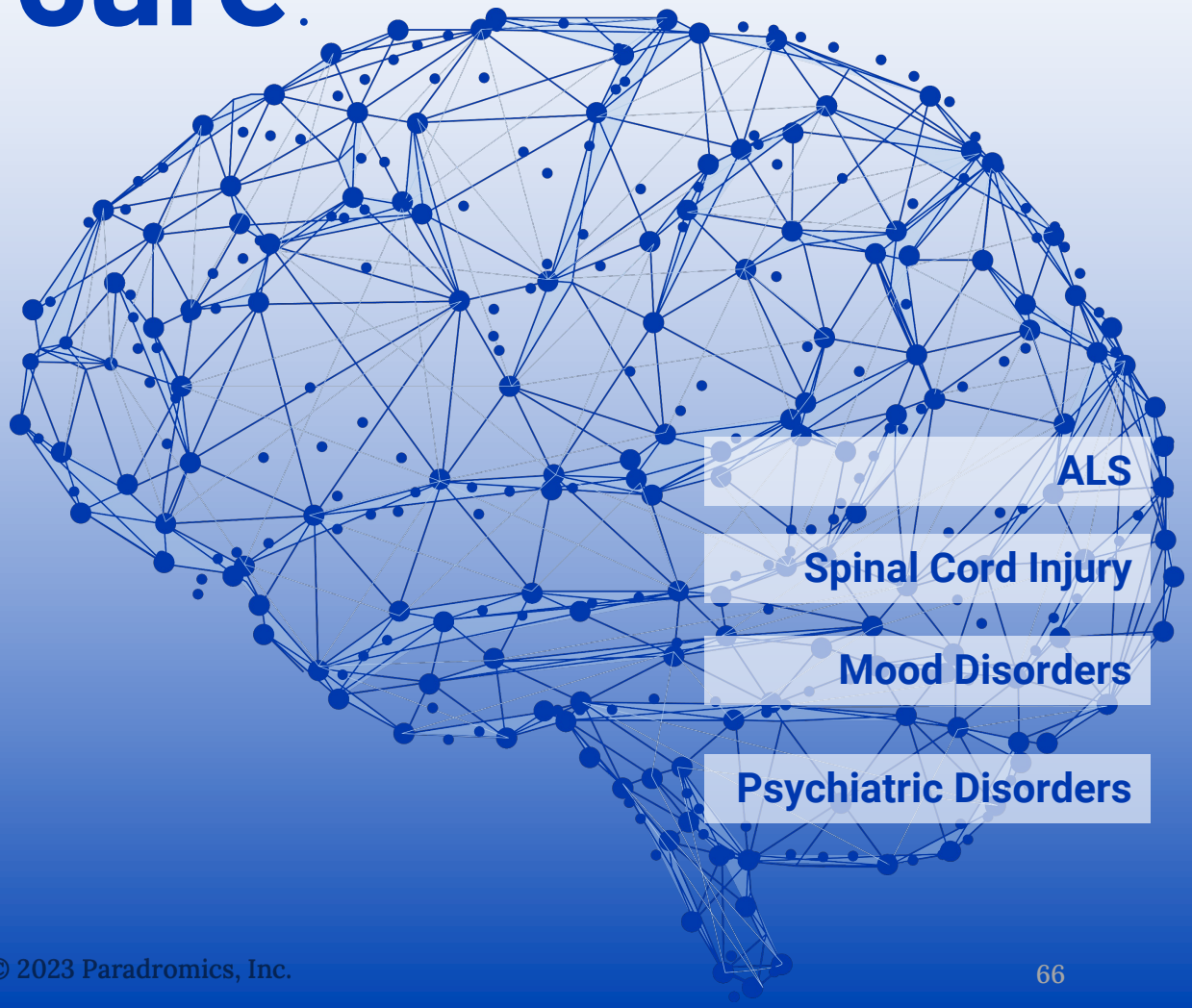
- Direct data interface - high data rate BCI
- 1600+ intracortical microelectrodes
- Wireless data and power transfer
- Long-term, everyday use

“Until there is a cure, **technology is the cure**.”

-Steve Gleason

Biological treatments for many conditions are nonexistent or insufficient.

Cures may be decades away.



Our first product will help people to communicate

For patients with severe speech-motor impairment

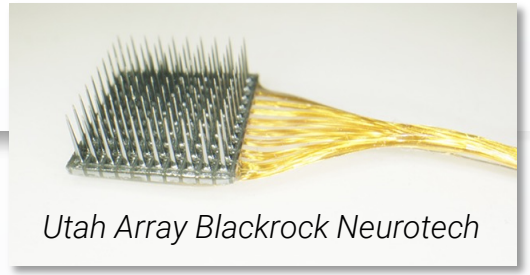
Connexus® Direct Data Interface

BCI-enabled

- typing
- cursor control
- speech generation

Assistive communication rates today

BCIs can help people communicate through a computer



Utah Array Blackrock Neurotech

Speech decoding: 62
2 Utah Arrays with 124 intracortical microelectrodes (Willett, et al., 2023)

Two-handed typing: 40

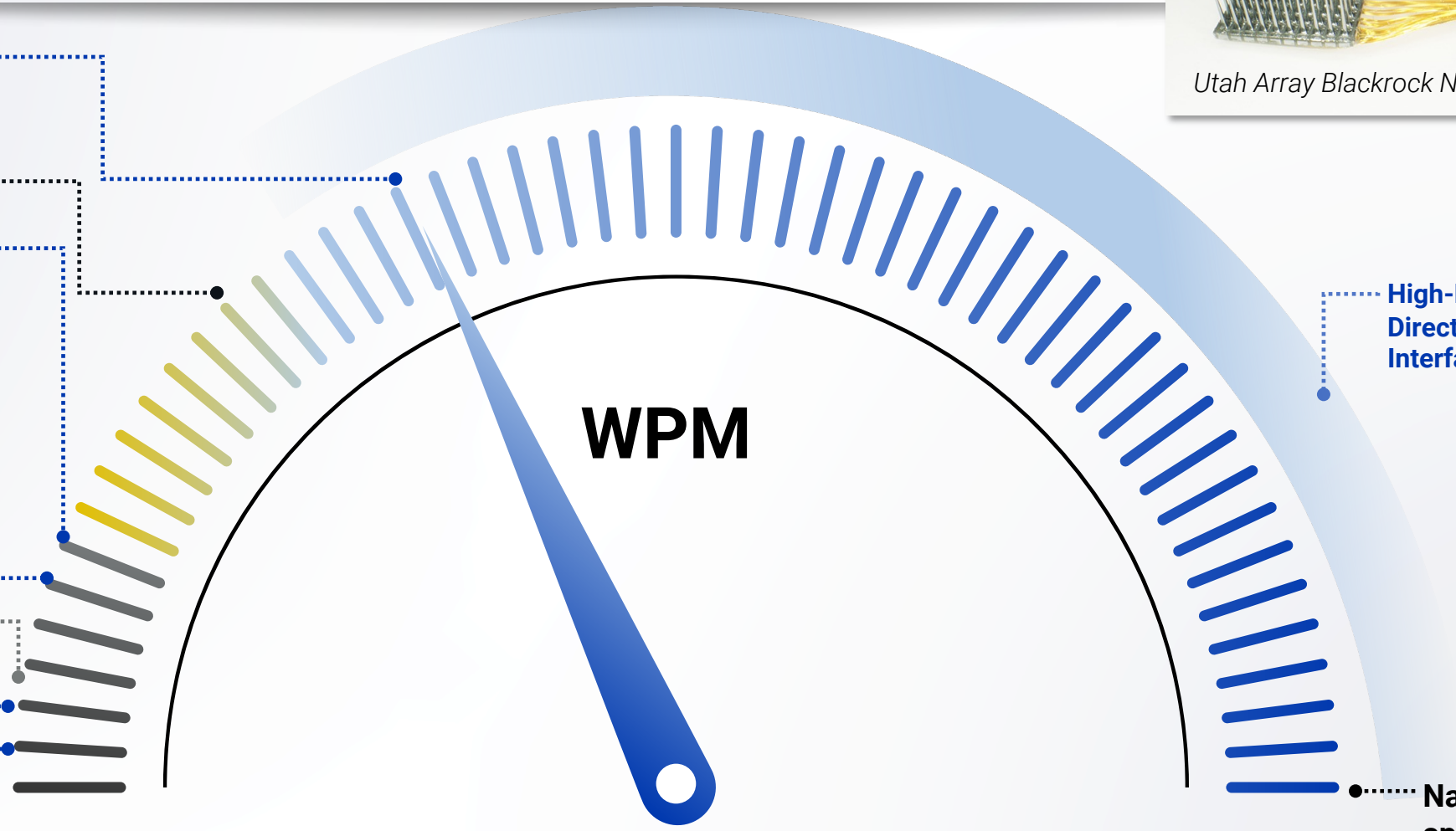
Imagined handwriting: 18
2 Utah Arrays with 192 intracortical microelectrodes (Willett, et al., 2021)

Speech decoding: 15.2
128-electrode ECoG mesh on brain's surface; 50-word corpus (Moses, et al., 2021)

Gaze tracking (no BCI): 9.51
Cascading dwell gaze typing (no BCI) by ALS patients (Mott, et al., 2017)

Cursor Control BCI: 5.6-7.8
1 Utah Array with 96 intracortical microelectrodes (Pandarinath, et al., 2017)

Cursor Control BCI: 2.7-4.02
16-electrode Stentrode + **gaze tracking** in ALS patients (Oxley, et al., 2021)



words/minute (WPM) ≈ 5 characters/minute (CPM)

Conversational speech though BCI communication

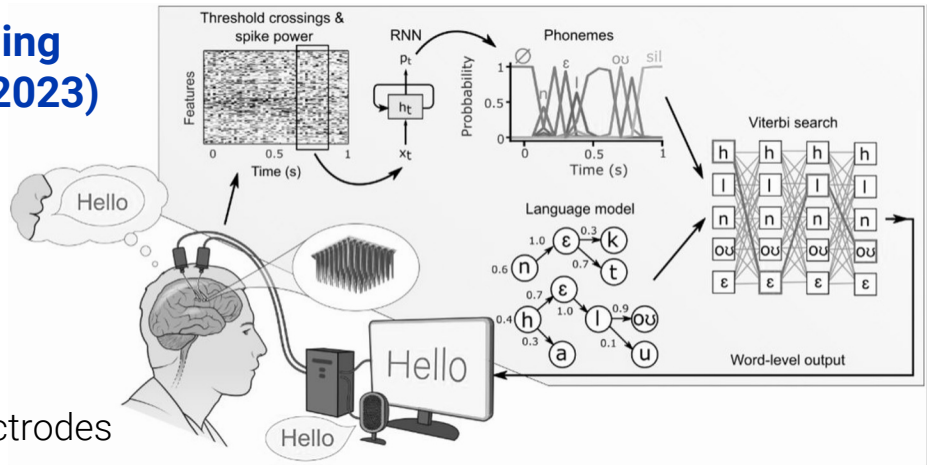
Even better with higher channel-count **intracortical electrodes**

Speech Decoding (Willet, et al., 2023)

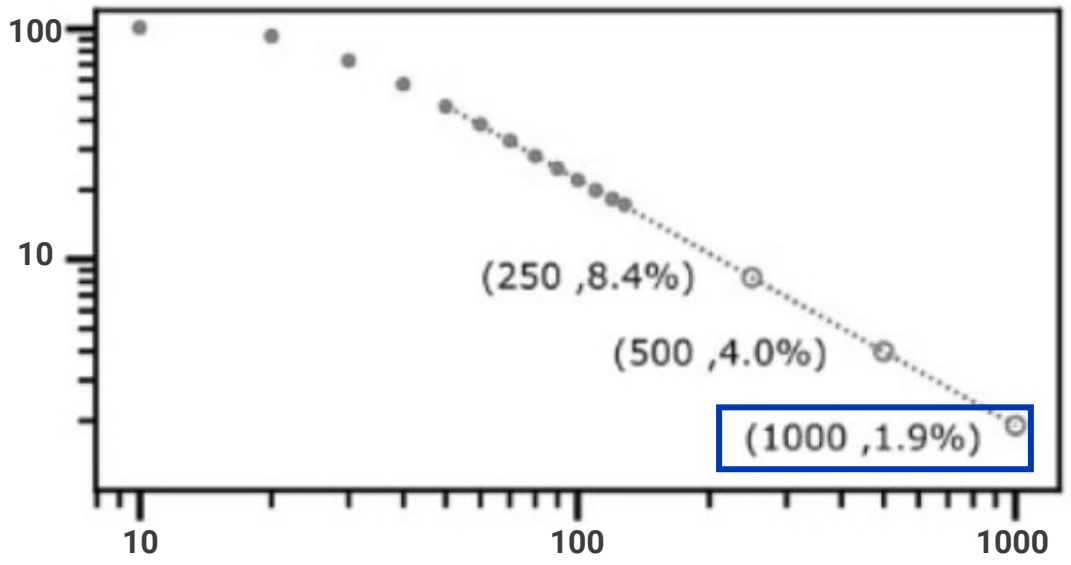
62
WPM

23%
word-error rate

124
Intracortical electrodes



Word-error rate vs. # of intracortical electrodes

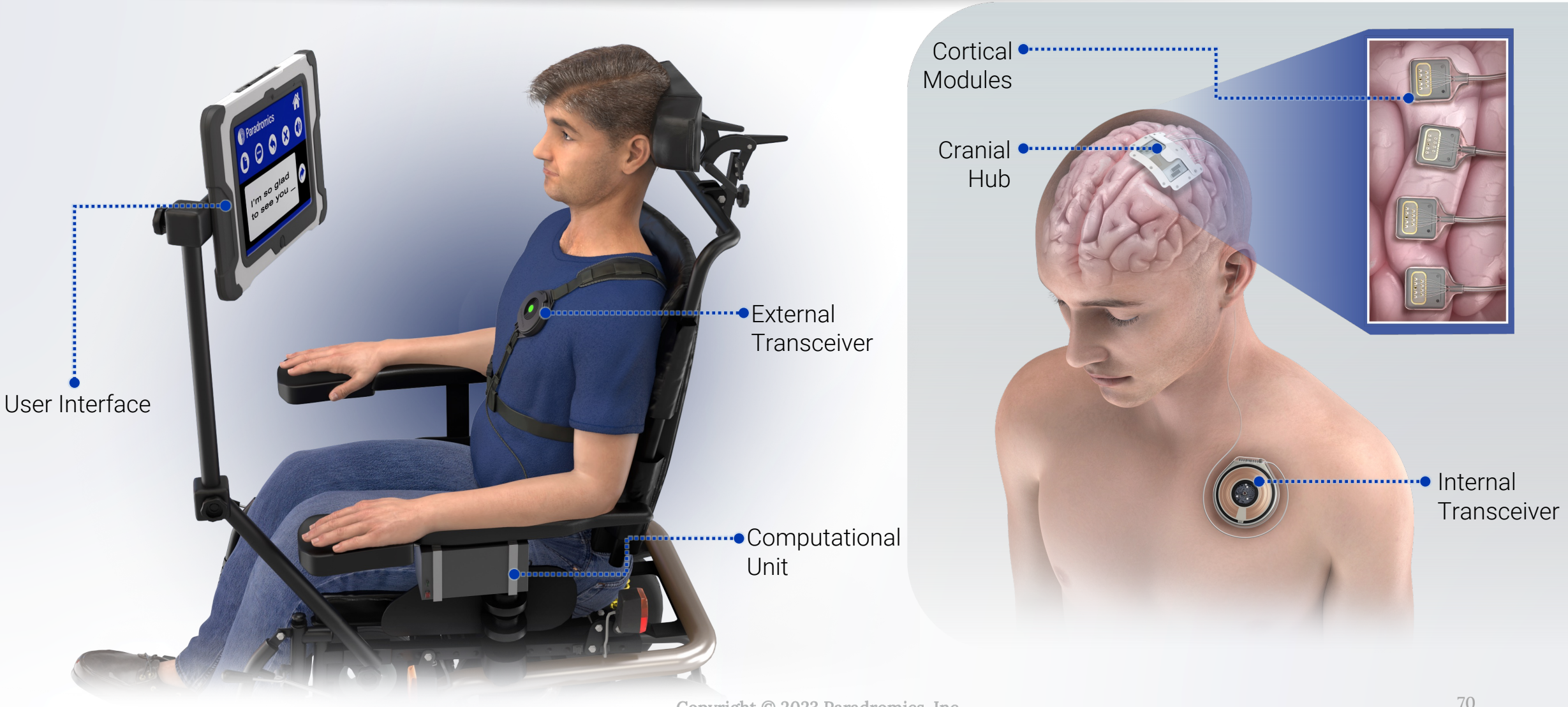


"a higher channel count system that records from only a small area of [the motor cortex] is a feasible path forward towards a device that can **restore communication at conversational speeds to people with paralysis**."

1600+ intracortical electrodes → **> 62 WMP**
< 1.9% error

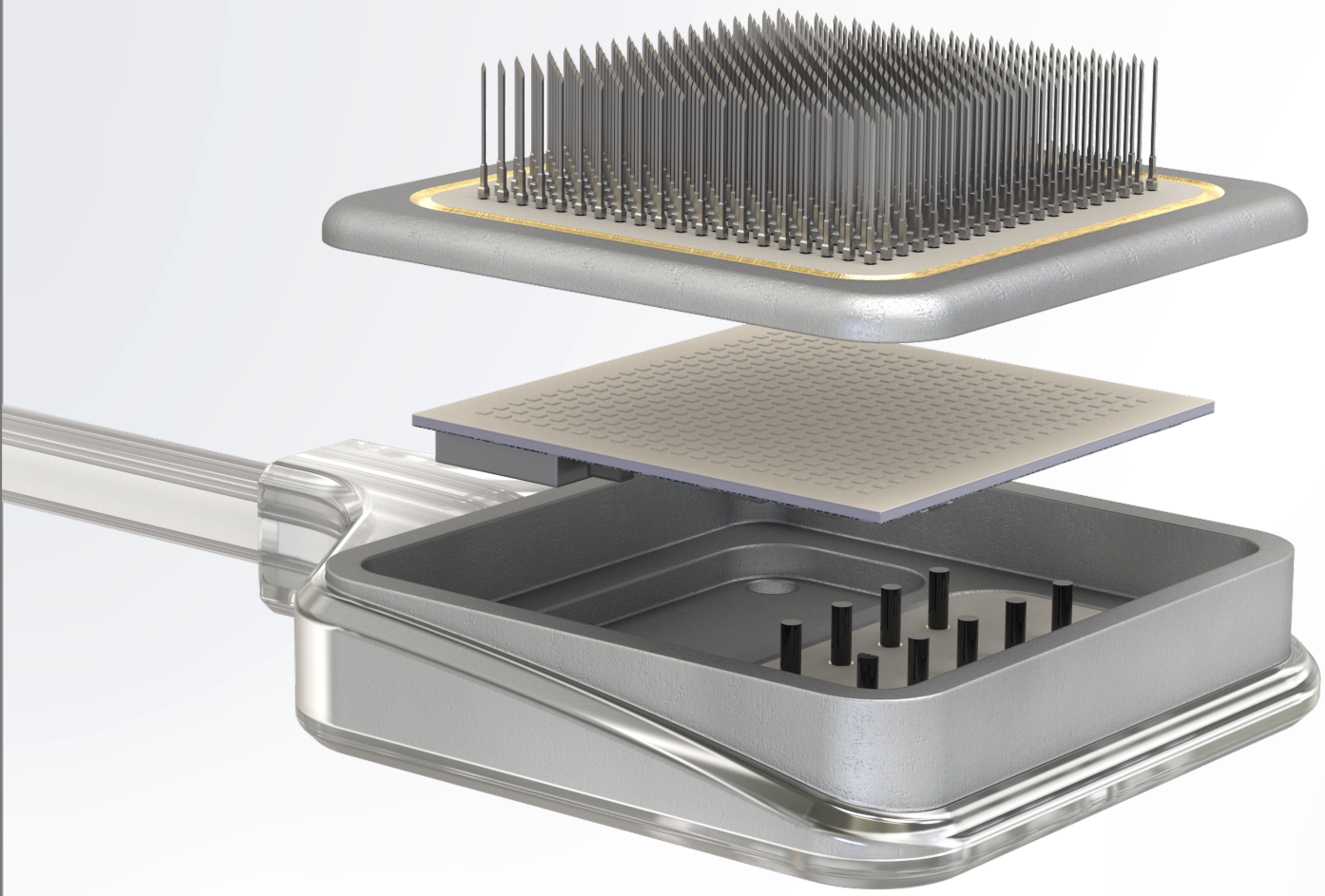
Connexus® Direct Data Interface System

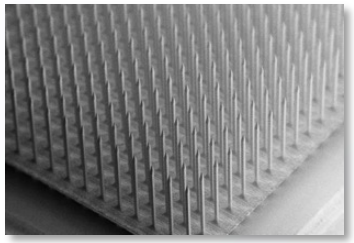
BCI-enabled **medical device** supporting advanced applications



Connexus® Cortical Module

Leveling up the microelectrode array

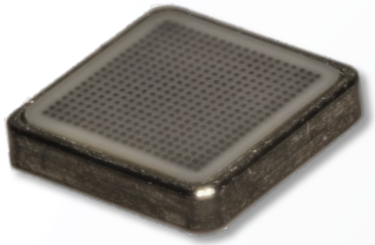




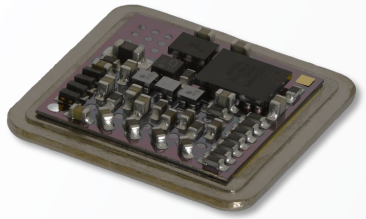
400+ electrodes per module for **higher data rate**

< 40-µm diameter PtIr microwires for improved **reduced tissue impact**

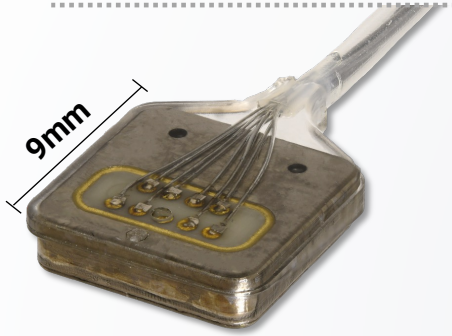
Durable ceramic coating for **biostability**



Hermetic metal-ceramic feedthroughs for **long-term reliability**



Patented on-chip processing for dramatically **reduced power consumption**



Active ASIC multiplexes high channel count array to a **surgeon-friendly flexible, 8-wire lead**

Compatible with **standard medical device connectors**

More cortical coverage. More data. More capabilities

Scalability to support up to 4 cortical modules and 1600+ electrodes

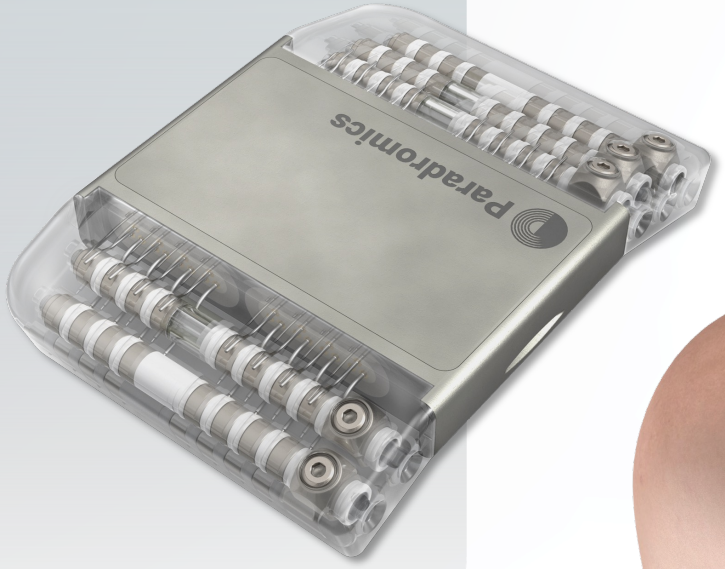
Cranial Hub

Housed in the **cranioplasty**

Multiplexes **4 cortical modules** onto one easy-to-manage lead

Zero suppression **data compression** for sparse output

Moves processing power away from the brain for improved **thermal management**



1600+ intracortical electrodes

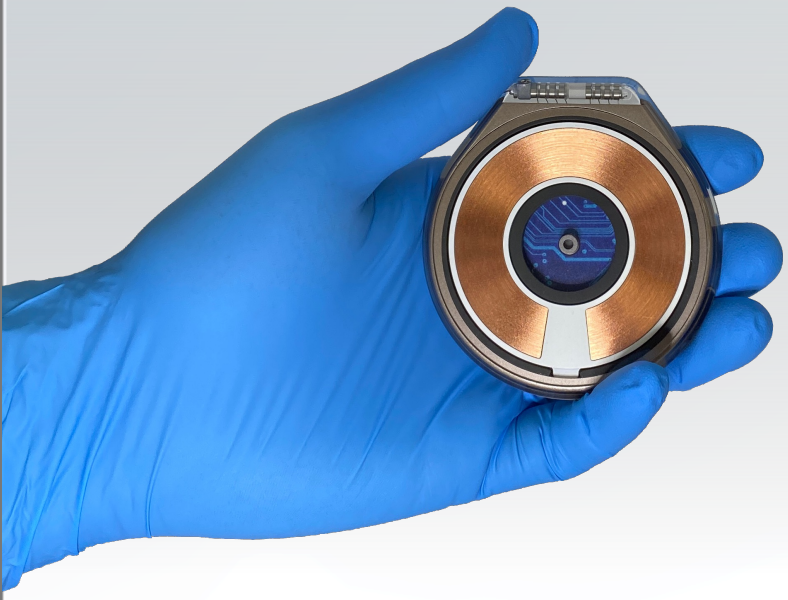
Connexus® Transceiver wireless coupling

No through-skin ports or wires

Internal Transceiver

Implantable pulse generator (IPG) form factor is **familiar to neurosurgeons**

Data transmission **up to 100 Mbps** with 850 nm near-infrared optical link



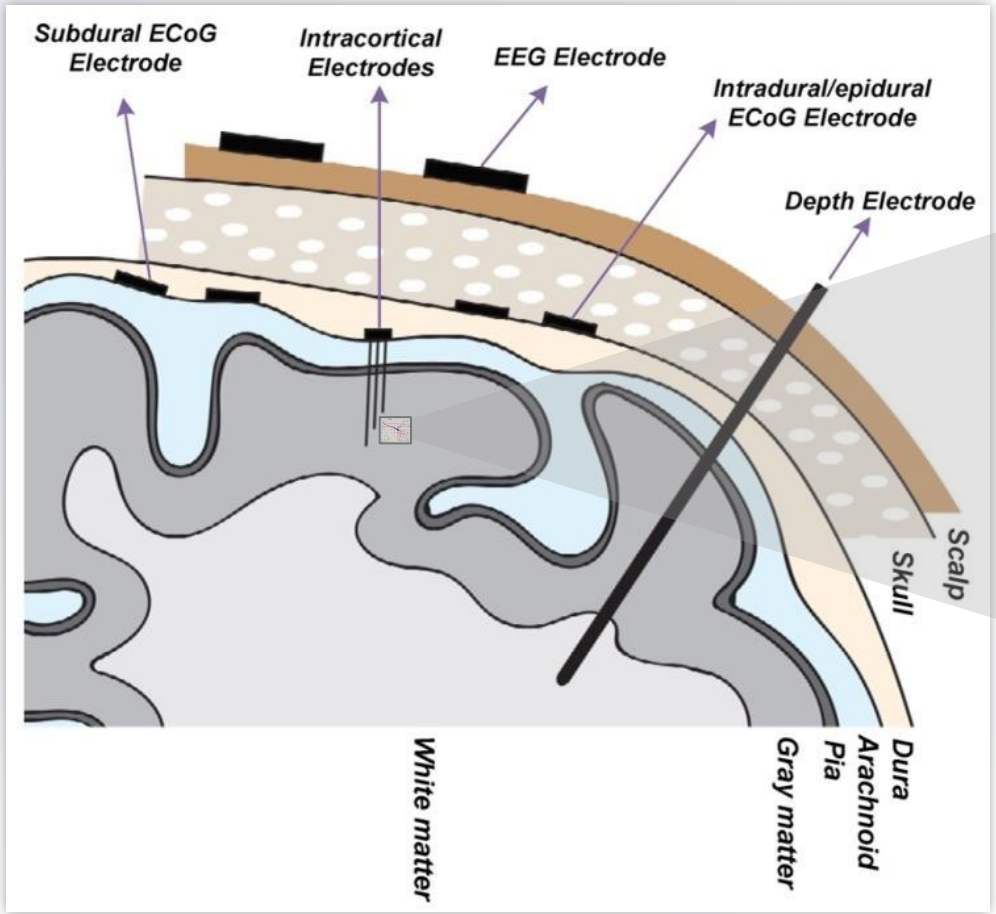
External Transceiver

Lightweight wearable

Inductive power transfer up to **500 mW**

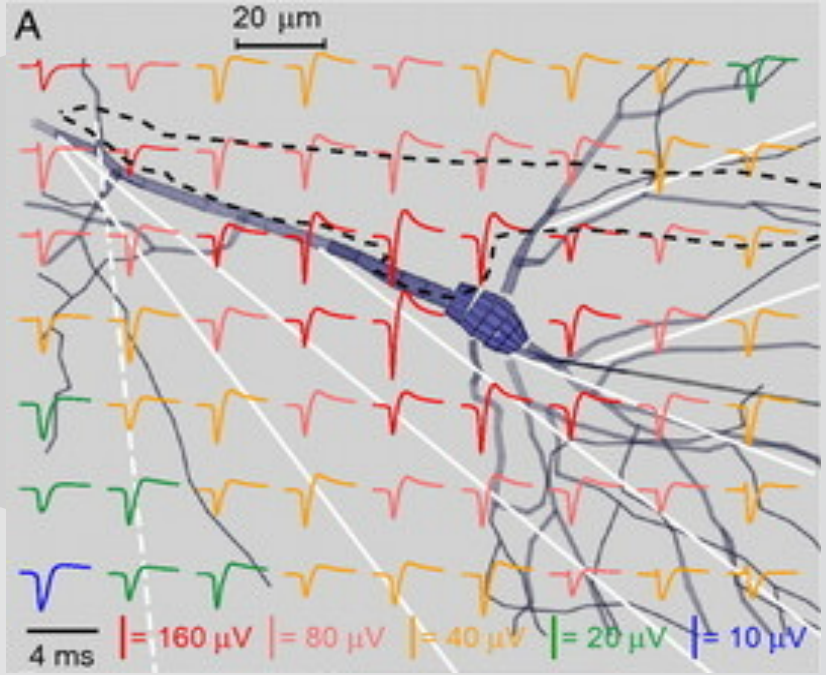
Why do we need microelectrodes "in" the brain?

Design rationale for Connexus® Direct Data Interface



Ranjandish and Schmid, *Sensors*. 2020; 20(19):5716.

Only **intracortical** electrodes can gather signals from **single neurons**



Gold, et al., J Neurophysiology 2006 95:5, 3113-3128

- Signal amplitude decreases as distance from the neuron increases *(Gold, et al., J Neurophysiology, 2006)*
- Increasing intracortical electrode density increases signal recovery
- Increasing surface electrode density yields diminishing returns

Thickness of one sheet of paper

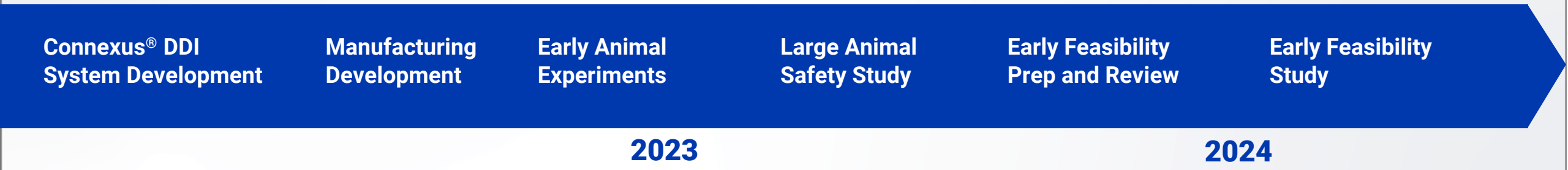
Path to first-in-human use

Key Milestones

Q2/2023 Begin pre-clinical Large Animal Safety Study

Q4/2023 Approval of Early Feasibility Study

Q1/2024 First patient enrolled in Early Feasibility Study



Bringing the Connexus® Direct Data Interface to market

Worldwide expertise, partnerships, and collaboration

Current and past employees from over 12 countries

Manufacturing partners from 3 countries

Paradromics

www.paradromics.com

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Blackrock Neurotech

Marcus Gerhardt

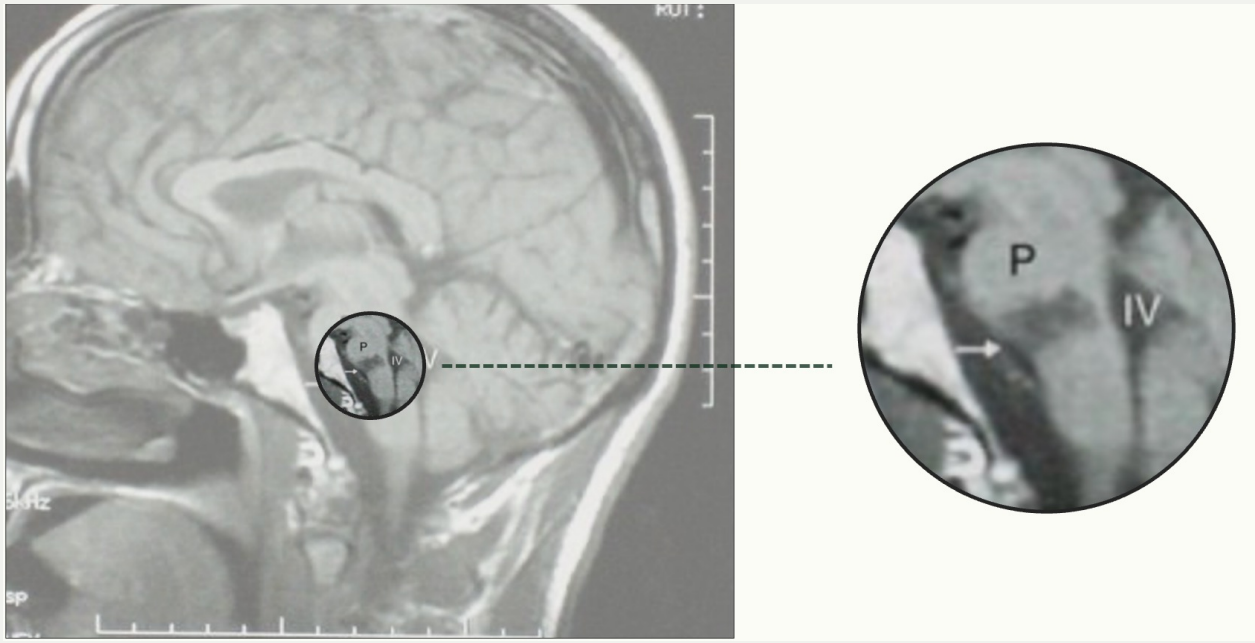
synchron

Brain Computer Interface for Paralysis

Tom Oxley MD PhD
CEO Synchron
Faculty of Neurosurgery, Mount Sinai Hospital, New York City
Associate Professor of Neuroscience, University of Melbourne, Australia

THE INSPIRATION FOR SYNCHRON

synchron



synchron

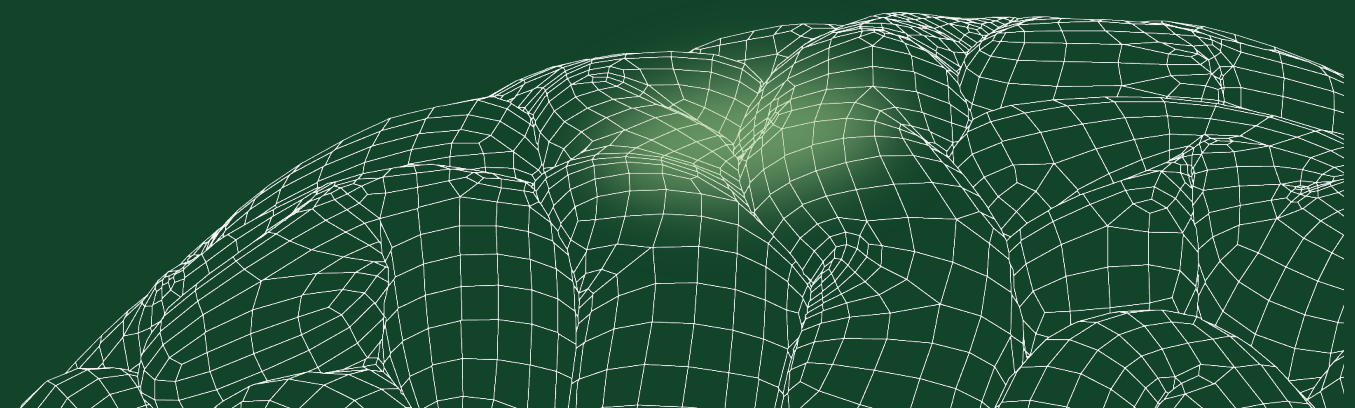
Patients with severe paralysis

>5 million people with severe paralysis due to ALS, stroke, spinal cord injury and many other conditions

↓ Autonomy

↓ Functional independence

↓ Ability to access health care when needed



A return to autonomy - connection to the digital world

24 hours a day

Simple to use

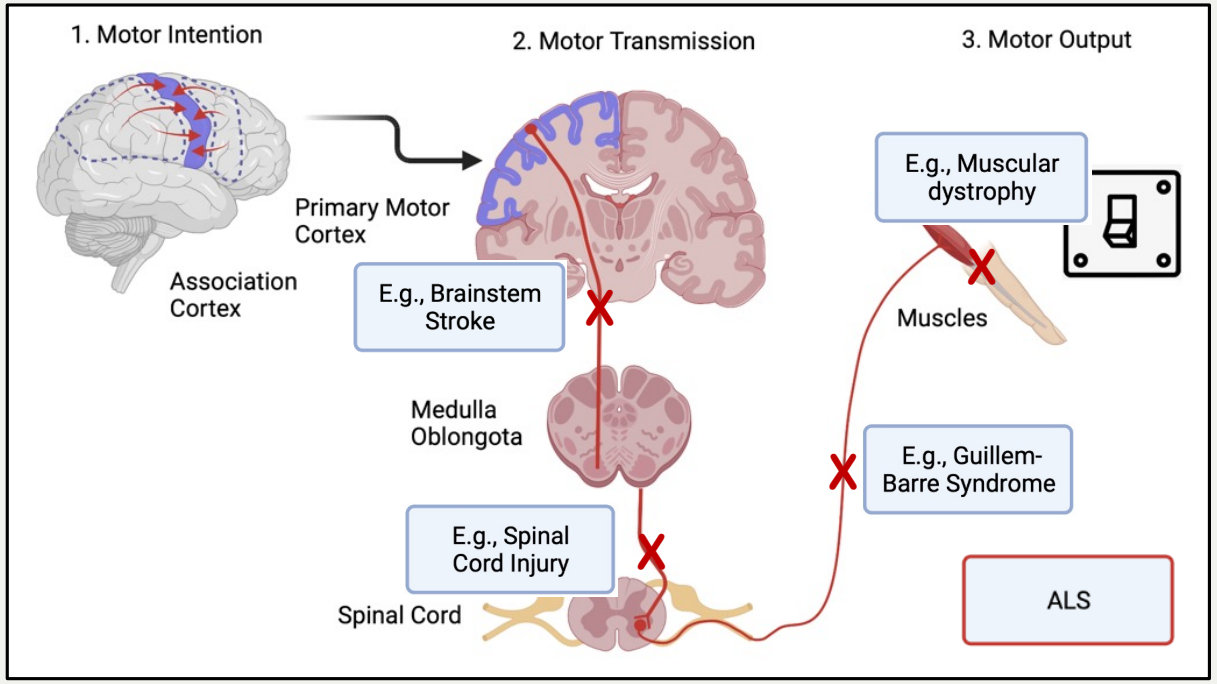
No delay in system turn on

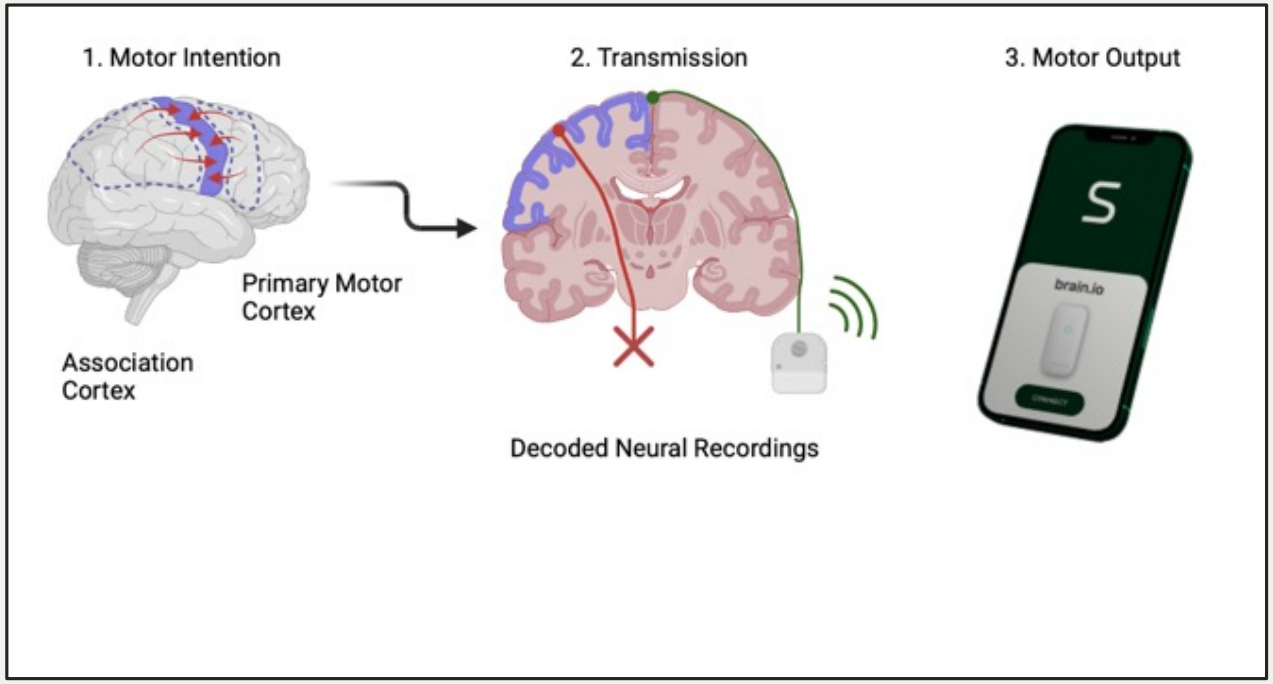
No calibration

With no assistance from a caregiver

PARALYSIS & BCI AS A POTENTIAL SOLUTION

synchron






synchron

Mission:

Delivering endovascular BCI, at scale, unlocking thought-enabled control of digital devices for people with disability to reconnect with the world.

Team:

US company headquartered in Brooklyn, New York, with a subsidiary in Australia.

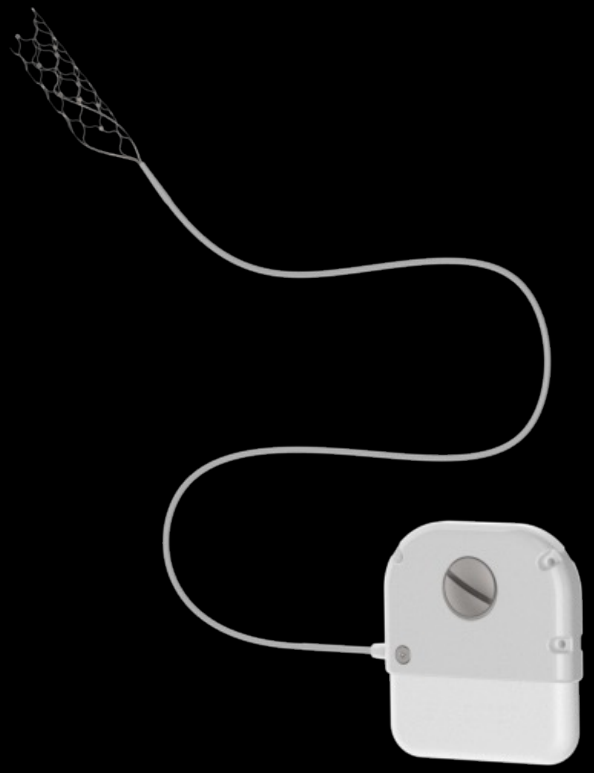
Funding:

Recently closed a $75M Series C round led by Arch Ventures. Total funding $130M.

synchron

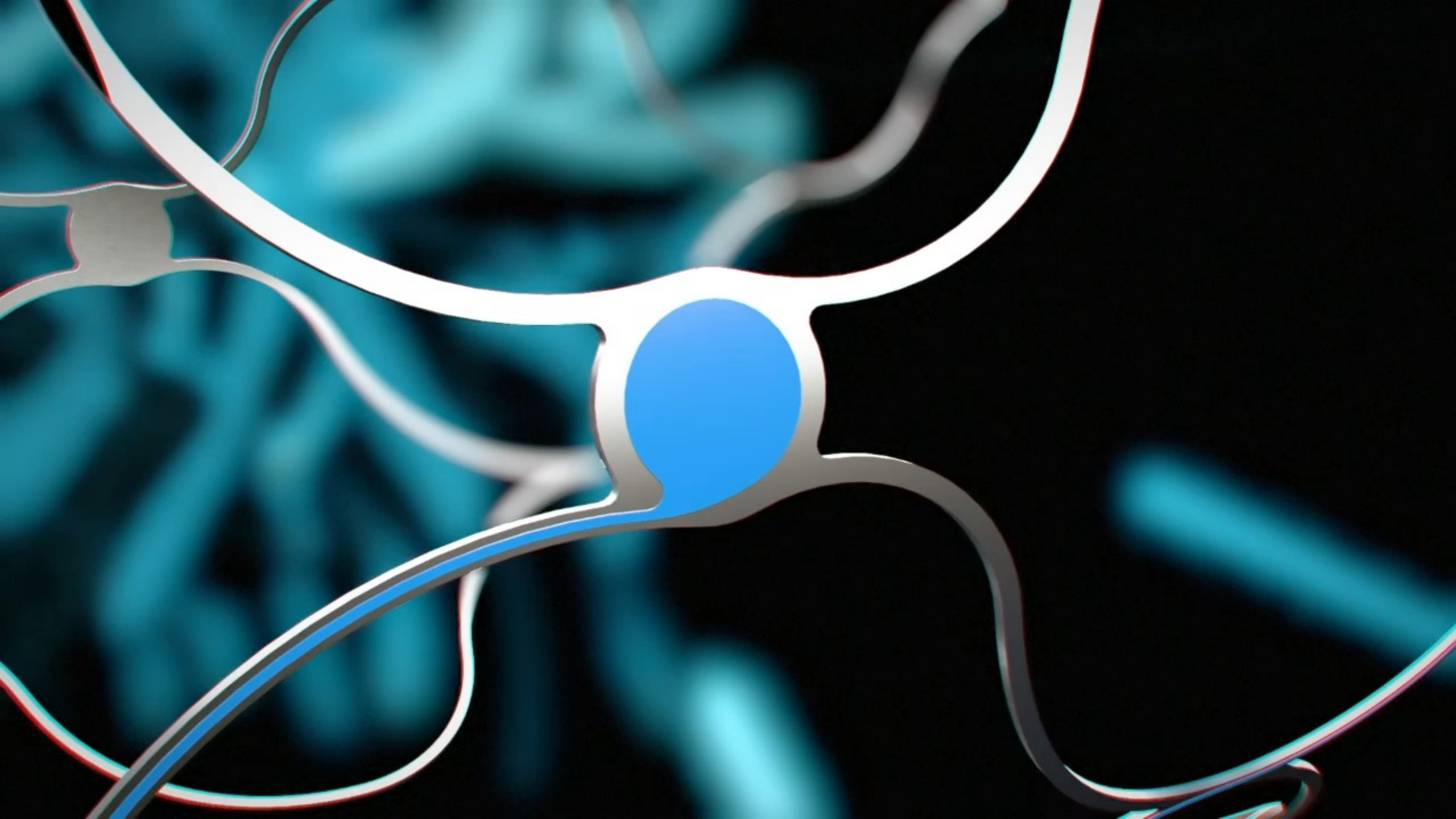
Our MVP product is a motor neuro-prosthesis BCI that enables hands-free control of digital devices using Bluetooth. The system is designed for people who can no longer use their hands to control a digital device.

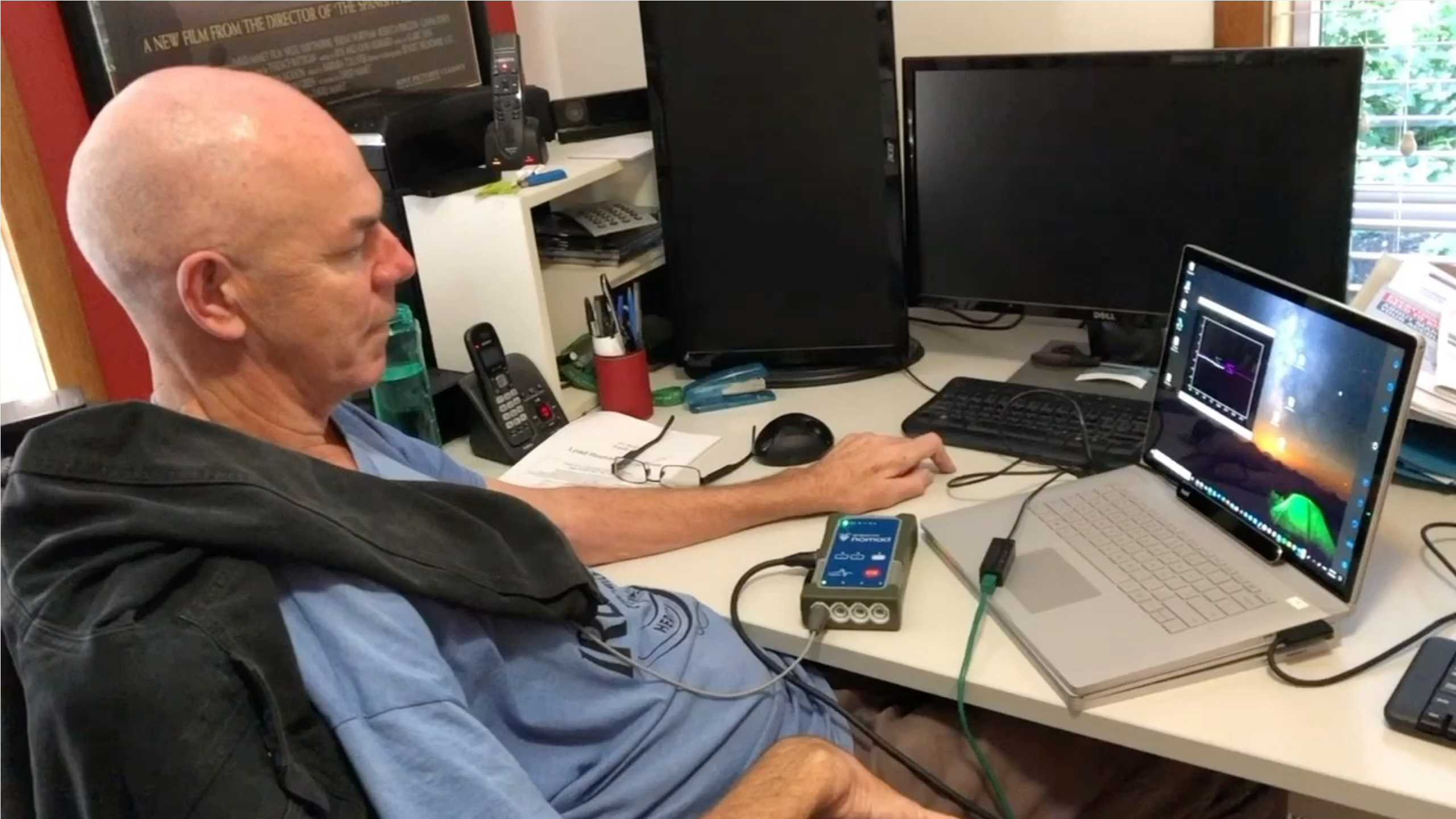
- Communication: Emailing, texting, messaging, long-form writing
- Online tasks: Financing, shopping
- Digital healthcare access: Telehealth, medication management

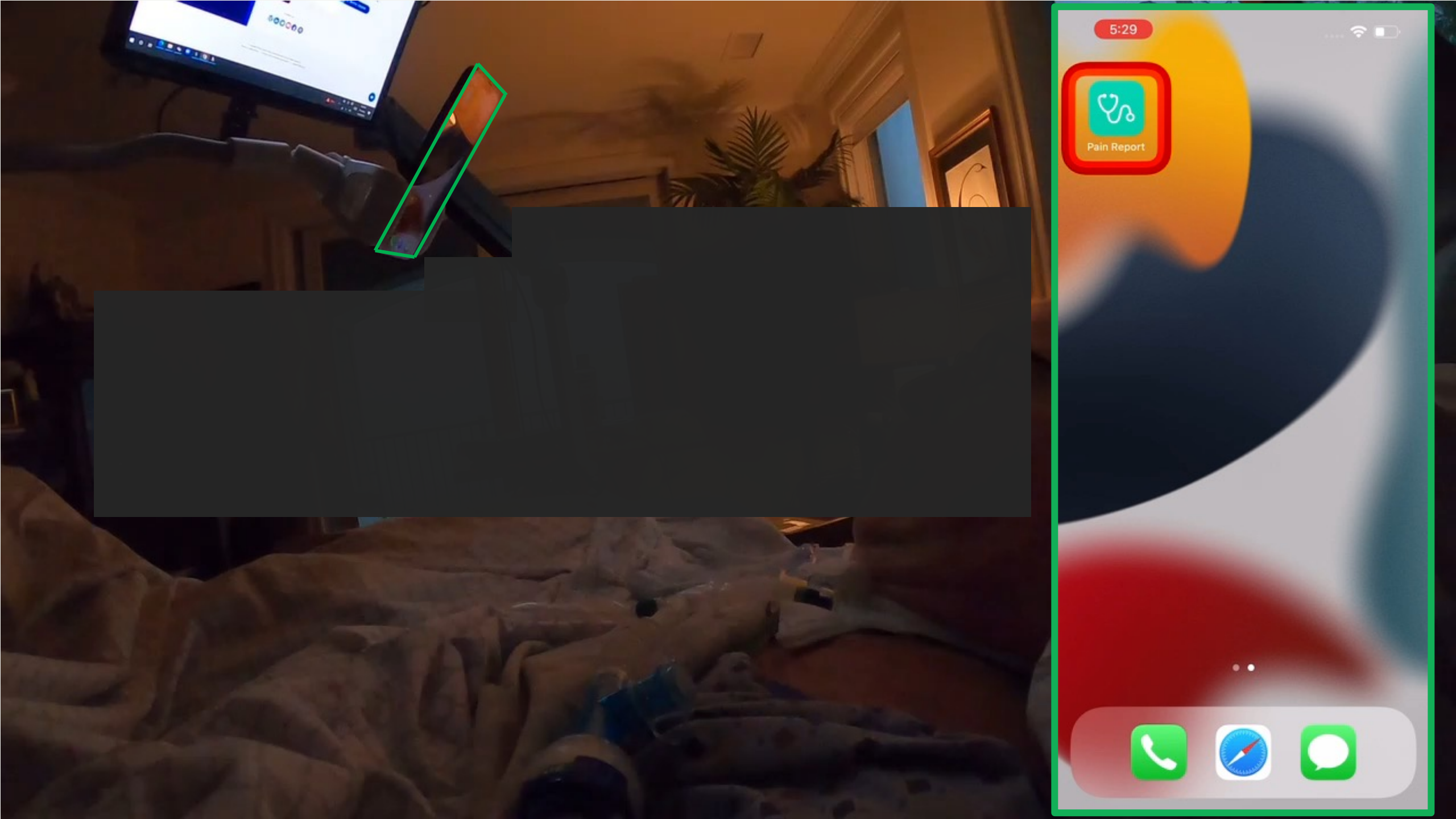


IMPLANTED

EXTERNAL




A NEW FILM FROM THE DIRECTOR OF


5:29
Pain Report

GUIDANCE DOCUMENT

Implanted Brain-Computer Interface (BCI) Devices for Patients with Paralysis or Amputation - Non-clinical Testing and Clinical Considerations

Guidance for Industry and Food and Drug Administration Staff

MAY 2021

First-in-Human Study → Feasibility Study → Pivotal Study

SWITCH Trial

2019

COMMAND Trial

2021

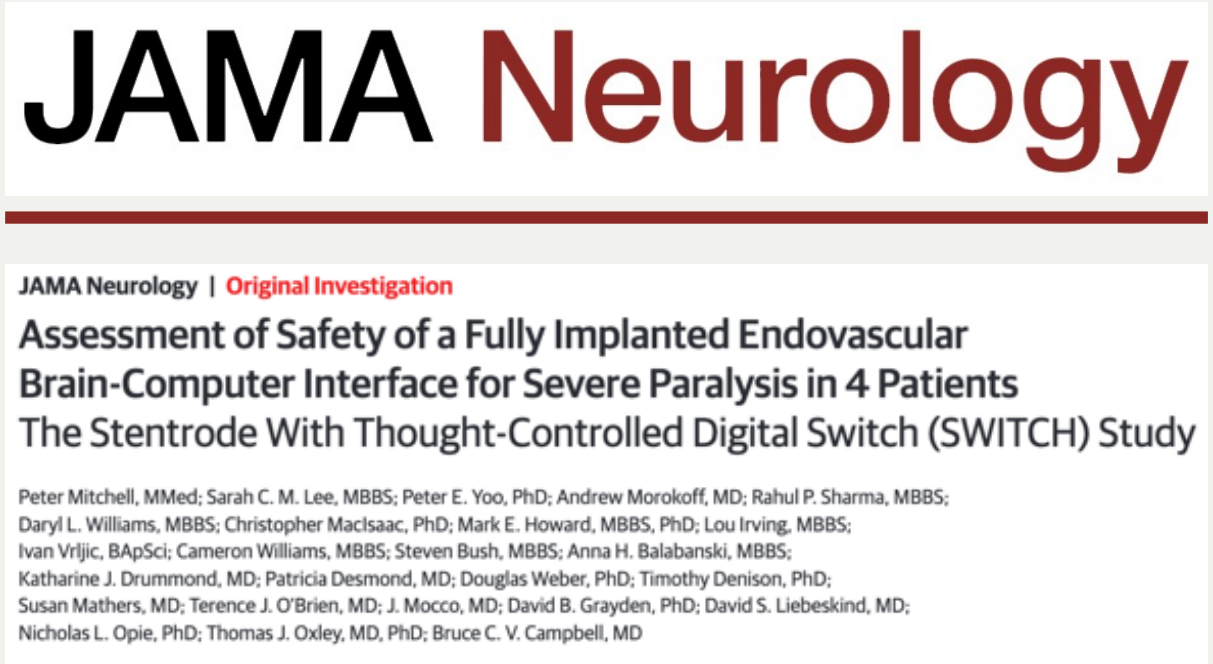
EMPOWER Trial

2024

4 patients with ALS implanted with device

12 months of follow-up showed:

- ↗ No serious adverse events
- ↗ Used independently at home
- ↗ Clinical improvements in instrumental activities of daily living (IADLs): texting, emailing, online shopping, banking



JAMA Neurology

JAMA Neurology | Original Investigation

Assessment of Safety of a Fully Implanted Endovascular Brain-Computer Interface for Severe Paralysis in 4 Patients
The Stentrode With Thought-Controlled Digital Switch (SWITCH) Study

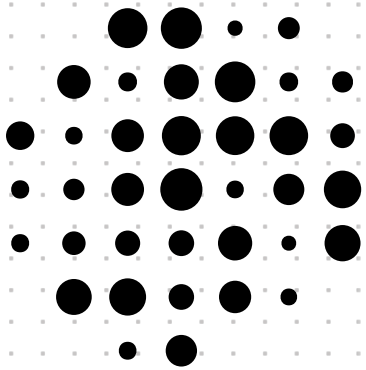
Peter Mitchell, MMed; Sarah C. M. Lee, MBBS; Peter E. Yoo, PhD; Andrew Morokoff, MD; Rahul P. Sharma, MBBS; Daryl L. Williams, MBBS; Christopher MacIsaac, PhD; Mark E. Howard, MBBS, PhD; Lou Irving, MBBS; Ivan Vrljic, BApSci; Cameron Williams, MBBS; Steven Bush, MBBS; Anna H. Balabanski, MBBS; Katharine J. Drummond, MD; Patricia Desmond, MD; Douglas Weber, PhD; Timothy Denison, PhD; Susan Mathers, MD; Terence J. O'Brien, MD; J. Mocco, MD; David B. Grayden, PhD; David S. Liebeskind, MD; Nicholas L. Opie, PhD; Thomas J. Oxley, MD, PhD; Bruce C. V. Campbell, MD

First-in-Human Study → Feasibility Studies → Pivotal Study

The Economist

When the device was implanted, I was still working part-time. I could do some of my online work with the device. I could go onto my company's portal and update information and produce reports.


synchron
Brain Computer Interface



Precision

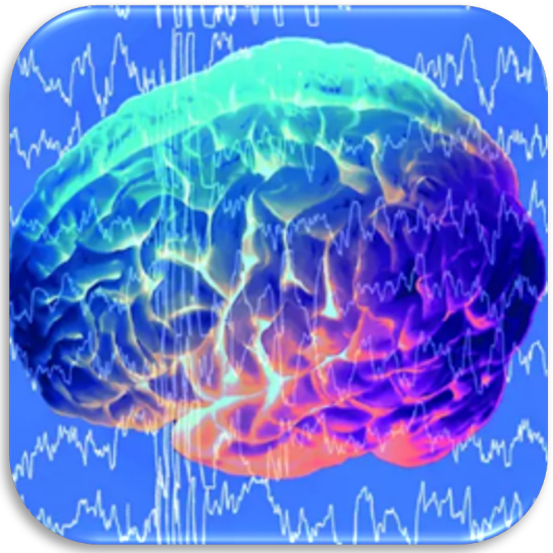
U.S. Department of Commerce

February 27, 2023

1. Precision Neuroscience is a medical device company developing a brain implant.
2. Devices like ours are focused on changing the lives of people with neurological disorders… with potential defense applications likely many years away.
3. Creating a successful company developing a Class III medical device is extremely challenging.
4. The U.S. Government can support American companies' efforts, rather than constrain market access and increase regulatory burden through *premature* policy action.

Precision Neuroscience is a medical device company developing a brain implant.

Brain–computer interfaces are beginning to treat “untreatable” diseases



TRAUMATIC BRAIN INJURY

4M Patient Population (US)

1.4M	Treatable by BCI

SPINAL CORD INJURY

2.6M Patient Population (US)

1.7M	Treatable by BCI

STROKE

7.8M Patient Population (US)

5.2M	Treatable by BCI

NEURODENERATIVE DISEASE (ALS, MS)

1M Patient Population (US)

650K	Treatable by BCI

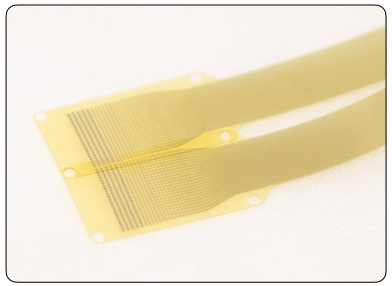
1. Common Conditions Requiring Rehabilitation in the US, 2. The Lancet , 3. US Pharmacist.com, Stroke Prevalence, 4. National MS Society.org, 5. ALS.org

Our Mission

Precision Neuroscience's goal is to provide breakthrough treatments for the **one billion people** worldwide suffering from neurological illnesses.

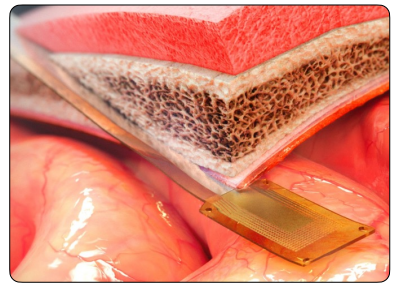
Precision’s platform is built on cortical arrays and minimally-invasive implantation

Precision has pioneered a new approach to brain-computer interfaces that is designed to scale to millions of electrodes and millions of patients.

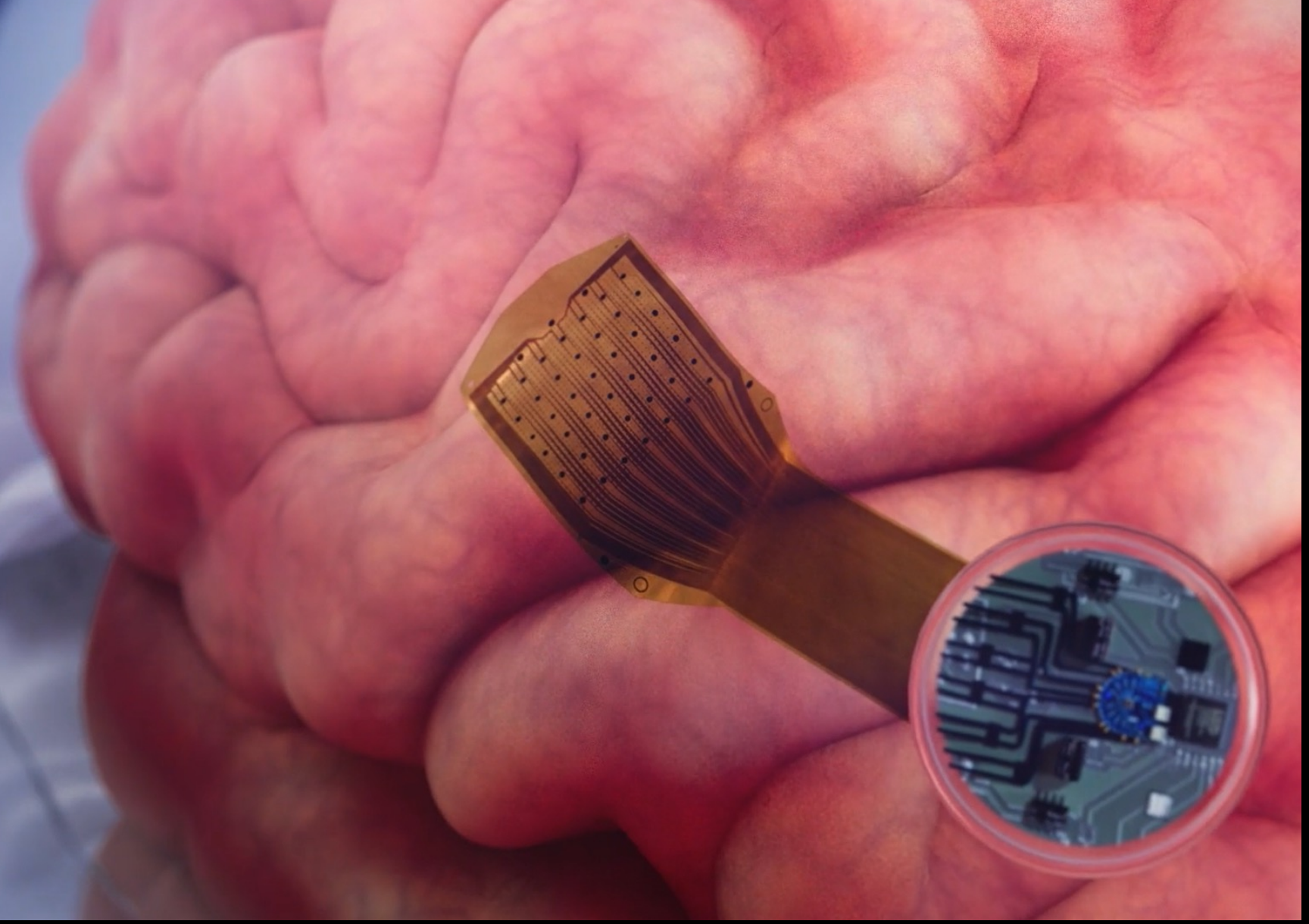


High-density thin-film electrode array that is designed to safely conform to the cortical surface

2 KEY INNOVATIONS



Patented minimally invasive insertion technique



Precision's implant is a full-stack system

- Microfabricated electrode array
- In-house designed microelectronics
- Machine-learning software

Our Team

Specialized expertise from 6 countries and counting. Disciplines include mechanical engineering, electrical engineering, microfabrication, ASIC design, software, and business operations.

BEN RAPOPORT
CSO

Neurosurgeon
Neuralink Co-founder
Harvard/MIT MD/PhD

CRAIG MERMEL
CPO

Senior leader at Apple, Google
Harvard MD/PhD

MICHAEL MAGER
CEO

Business builder
and investor
Harvard/Univ. of Cambridge
AB/MPhil

KEY ADVISORS

Tim Hanson
Co-founder, Neuralink

Vanessa Tolosa
Co-founder, Neuralink

Alan Levy
Co-founder, Northstar Neuroscience

KEY EMPLOYEES

D. Papageorgiou
VP of R+D, ex-Neuralink

M. Hettick
Head of Microfabrication, ex-Neuralink

M. Monge
Head of ASIC Design, ex-Neuralink

A. Poole
Head of Mech. Engineering, ex-Neuralink

K. Hatzianestis
Head of Wireless, ex-Cochlear and Neuralink

D. Trietsch
Principal Software Architect, ex-Apple

E. Ho
Senior Neural Engineer, ex-Stanford Post Doc

H. Melville
Head of People Operations, ex-Paige AI

K. Takahashi
Senior Data Scientist, ex-Univ of Chicago

L. Widdicombe
Head of Communications, ex-The New Yorker

A. Pillai
VP of Program Management, ex-Thermo Fisher

L. Nevulis
Embedded Systems Engineer, ex-Microsoft

K. Reed
Senior Software Engineer, ex-Apple

M. LaMarca
Senior Biomedical Engineer, ex-Neuralink

Devices like ours will change lives.


“I'm a C6 incomplete quadriplegic… I have a son—he's almost 11 years old—and **I would love to get out of this wheelchair and into his life!**

There's nothing I wouldn't do to get my independence back! ”

“I am 25 years old… I was in a car wreck… I suffered… a spinal cord injury….

I would desperately love to be a part of this trial. The things I miss the most are bartending & walking in the woods with my dogs**. I have fought so hard to get to where I am & I assure you that I will do whatever needs to be done to make this work.”**

"I'm a 29-year-old quadriplegic! I was injured in an… accident in… 2016 leaving me a C5 complete quad. **I would love to participate in your program**."

Implantable Brain–Computer Interface Uses

Today

Medical Necessity

Back to Work

People suffering from paralysis, stroke, traumatic brain injury, neurodegenerative disease seeking to regain function

Everyday Enhancement

Enhancing Work

Able-bodied people seeking to increase efficiency and performance

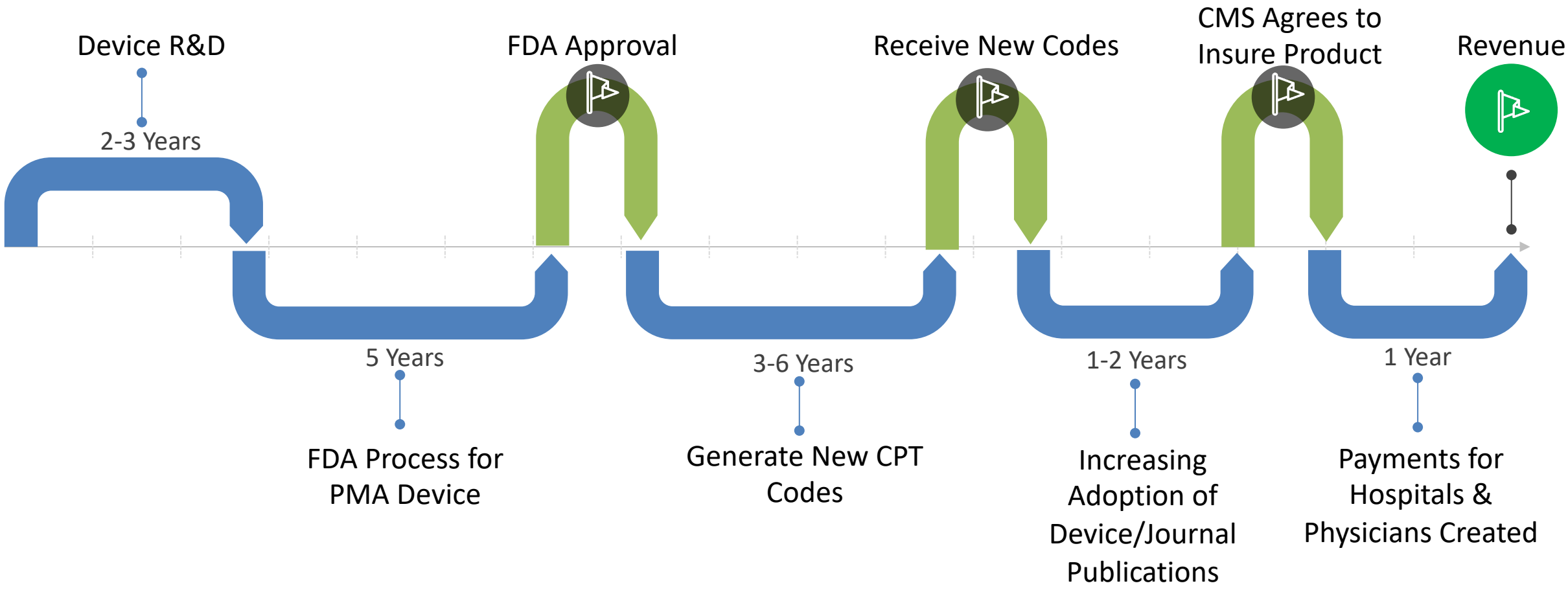
Military Augmentation

Potential Military Uses

Augmented decision-making, integration with military technology systems, control of unmanned aerial vehicles

Creating a successful company developing a Class III medical device is extremely challenging.

Implantable device roadmap: 12 - 17 years



Source: Stanford Biodesign Textbook

The process favors established players

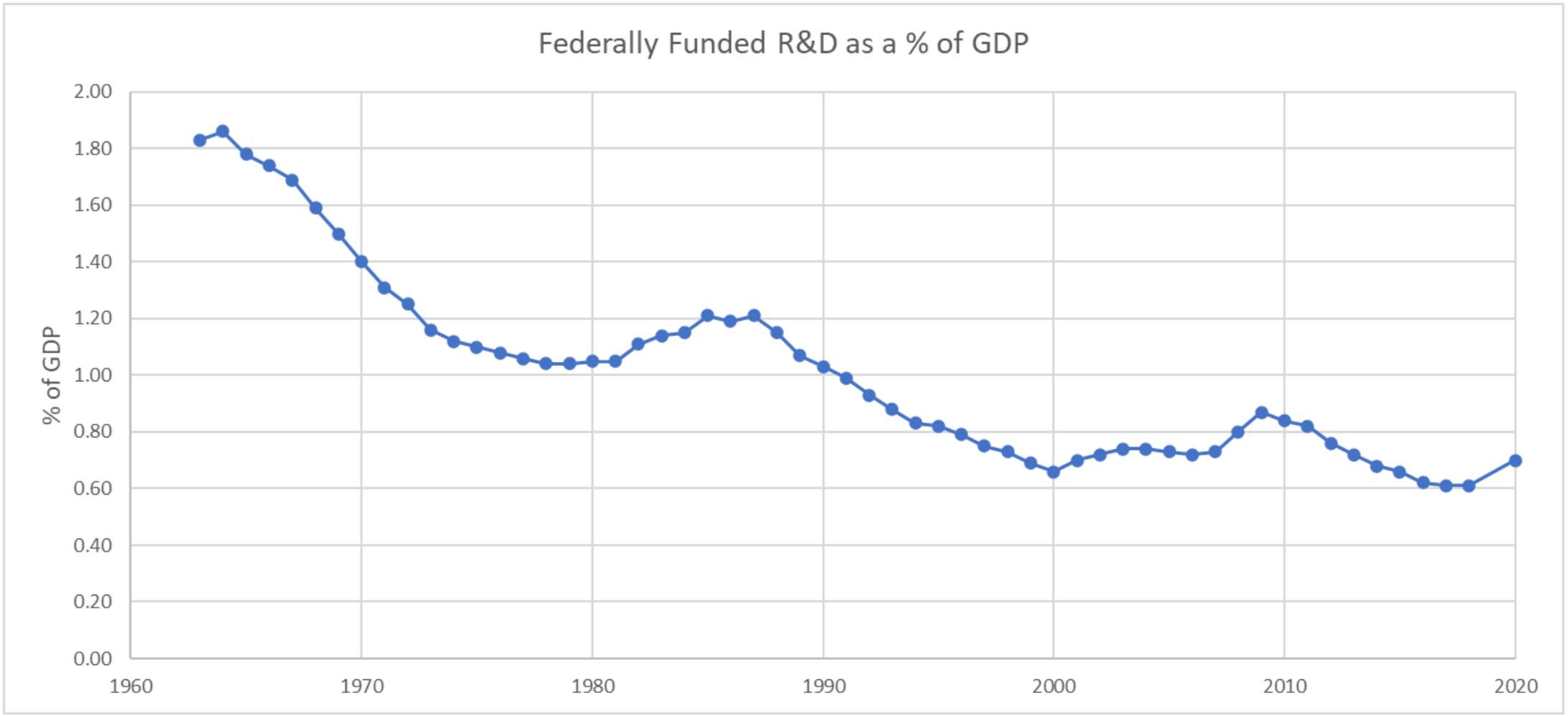
In the last 40 years, only 20 new implantable neurotechnology devices have been cleared for sale in the U.S. Of these, just 12 were developed by startups or small companies.

- 1981 Cordis spinal stimulator (pain)
- 1982 EBI, L.P. Scolitron Stimulator (Scoliosis)
- 1984 Medtronic Intrel(R) spinal stimulator (pain)
- 1994 Sigmedics Parastep 1 functional neuromuscular stimulation (walking)
- 1995 Biocontrol Technology Neurocontrol Freehand System (hand function)
- 1997 LivaNova VNS (vagus nerve stimulator) system (epilepsy)
- 1997 Medtronic Activa Tremor System (Parkinson's Tremor)
- 2001 Abbott/Advanced Bionics Genesis and Eon Neurostimulator (pain)
- 2004 Boston Scientific Precision Spinal Stimulator (pain)
- 2012 Codman MedStream Infusion System (spasticity)
- 2013 NeuroPace RNS System (epilepsy)
- 2015 Abbott Brio DBS System (Parkinson's)
- 2015 Nuvectra/Greatbatch Algovita Spinal Stimulator (pain)
- 2015 Nevro Senza Spinal Stimulator system (pain)
- 2017 Boston Scientific Vercise DBS (Parkinson's)
- 2018 Medtronic DBS System (epilepsy)
- 2019 Saluda Medical Evoke Spinal Stimulator (pain)
- 2020 Medtronic Percept (brain recording)
- 2020 Mainstay Reactiv8 Spinal Stimulator (pain)

Companies in red denote small companies/startups.

The U.S. Government can support American neurotechnology companies to help them compete globally. Export controls would do the opposite.

U.S. Government support is dwindling



Source: Sino-American Tech Trap, Project Syndicate

Meanwhile, China has made developing BCI a national priority

Excerpt from the "14th Five-Year Plan for National Information," published in 2021 by China's Central Commission for Cybersecurity and Informatization

布局战略性前沿性技术。瞄准可能引发信息化领域范式变革的重要方向，前瞻布局战略性、前沿性、原创性、颠覆性技术。加强人工智能、量子信息、集成电路、空天信息、类脑计算、神经芯片、DNA 存储、脑机接口、数字孪生、新型非易失性存储、硅基光电子、非硅基半导体等关键前沿领域的战略研究布局和技术融通创新。

Deploy strategic advanced technologies. Aim at important directions that may trigger changes in informatization areas and forms; arrange strategic, forefront, originally created and disruptive technologies in a forward-looking manner. Strengthen strategic research deployments and scalable technological innovation in critical and advanced areas such as artificial intelligence, quantum information, integrated circuits, aerial information, neuromorphic computing, neural chips, DNA storage, **brain–machine interfaces**, digital twinning, novel non-volatile storage, silicon electrons, non-silicon semiconductors…

China's efforts are paying off, attracting American investors

Chinese BCI Startup NeuroXess Bags Tens of Millions of US Dollars in Fundraiser Led by Zhongping

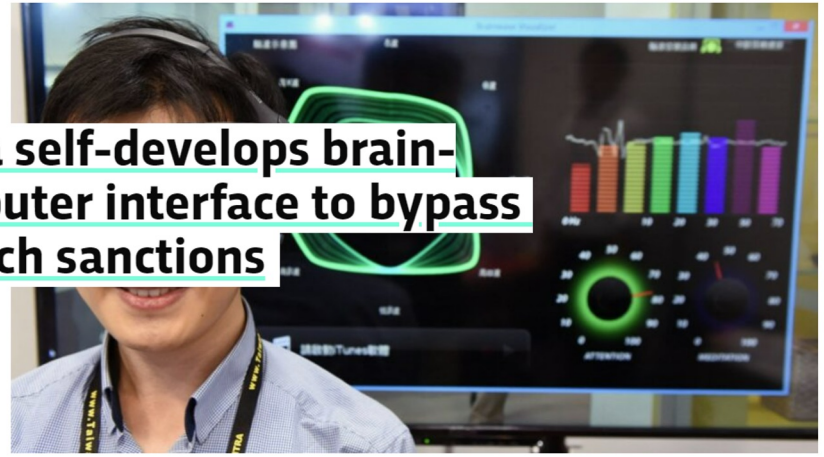
TANG SHIHUA

DATE: DEC 28 2022 / SOURCE: YICAI

In January, the Chinese BCI start-up said it has raised 97 million yuan ($15.2 million) in funding from major investors Shanda Group and Sequoia Capital.

Shanghai Hongqiao International CBD
@shhqcbd

NeuroXess is a brain computer interface (#BCI) company based in #Shanghai #Hongqiao Intl CBD. "Our main competitor is @neuralink, run by @elonmusk," said Phoenix Peng, Founder and CEO of NeuroXess. Watch the preview and stay tuned on @shhqcbd for more! @sinoprise @InvestShanghai



China self-develops brain-computer interface to bypass US tech sanctions

Chinese researchers have had to be innovative to develop working BCI applications, despite tech supply chain limitations in recent years. (Photo by SAM YEH / AFP)

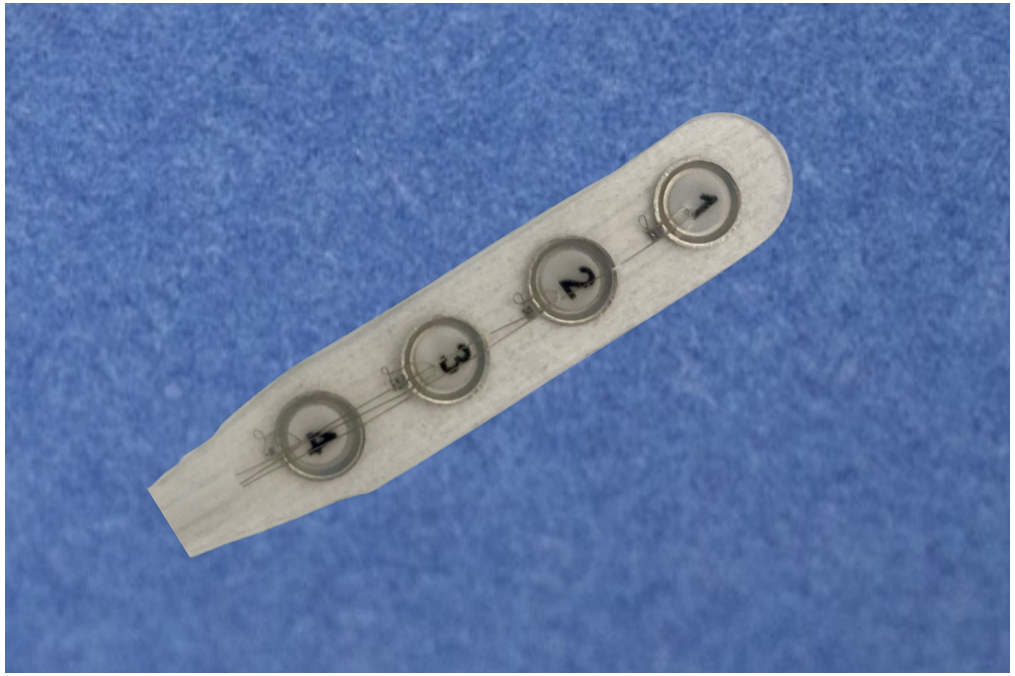
Export controls would limit the ability of American BCI companies to do the following:

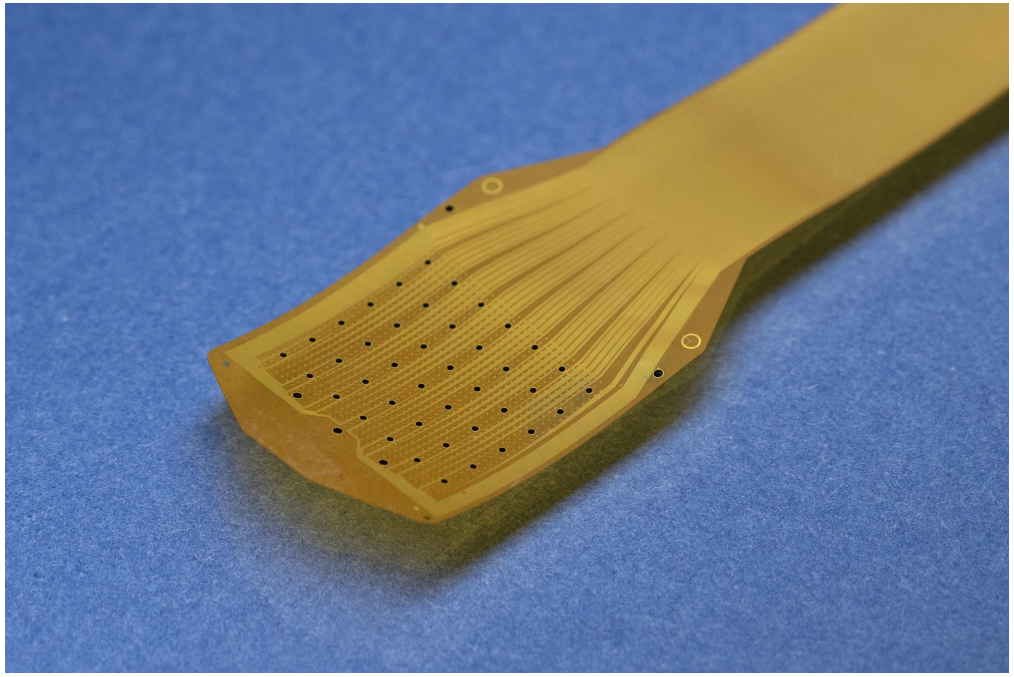
X Hire specialized talent from overseas

X Access global capital

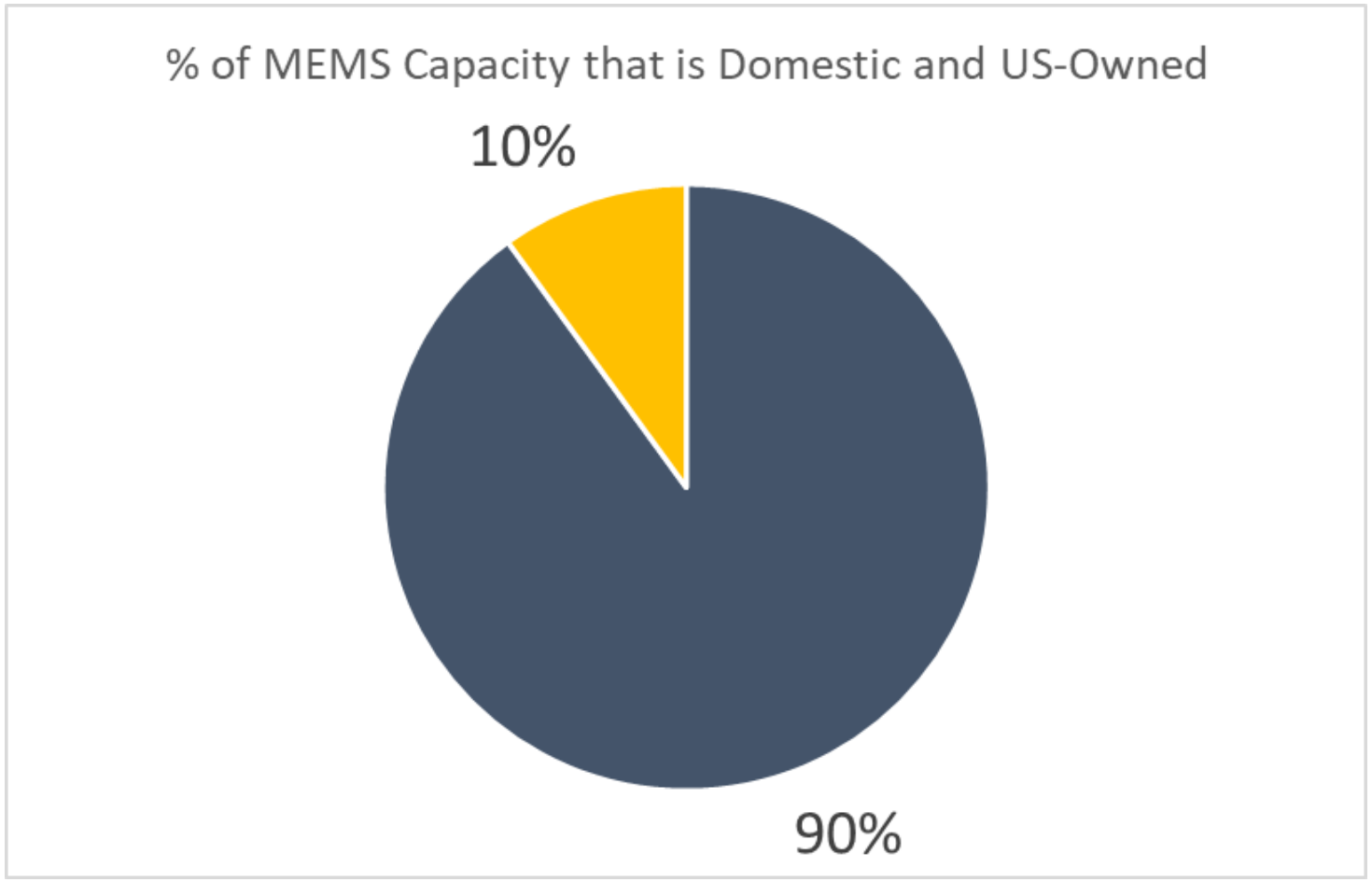
X Access global supply chains and critical manufacturing facilities

The days of handmade medical devices are ending. Manufacturing for devices such as ours must be done with high-precision machining called MEMS (microelectromechanical systems)





The vast majority of MEMS capacity is overseas and/or foreign owned

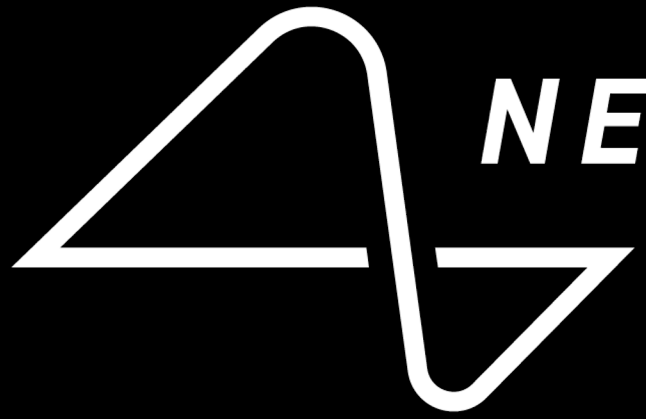


Source: Yole Development, Status of the MEMS Industry 2021, Internal Estimates

Ways that the U.S. Government can support the emerging American BCI industry:

- ✓ Expedite the typical timelines for FDA approval and insurance reimbursement.
- ✓ Facilitate the American BCI industry's access to global talent and capital.
- ✓ Enable BCI technologies to qualify for CHIPS Act and other grant and incentive programs.
- ✓ Encourage the adoption of technologies produced by American companies at U.S. Government medical facilities.

1. Precision Neuroscience is a medical device company developing a brain implant.
2. Devices like ours are focused on changing the lives of people with neurological disorders… with potential defense applications likely many years away.
3. Creating a successful company developing a Class III medical device is extremely challenging.
4. The U.S. Government can support American companies' efforts, rather than constrain market access and increase regulatory burden through *premature* policy action.



NEURALINK

2023 BIS BCI Conference

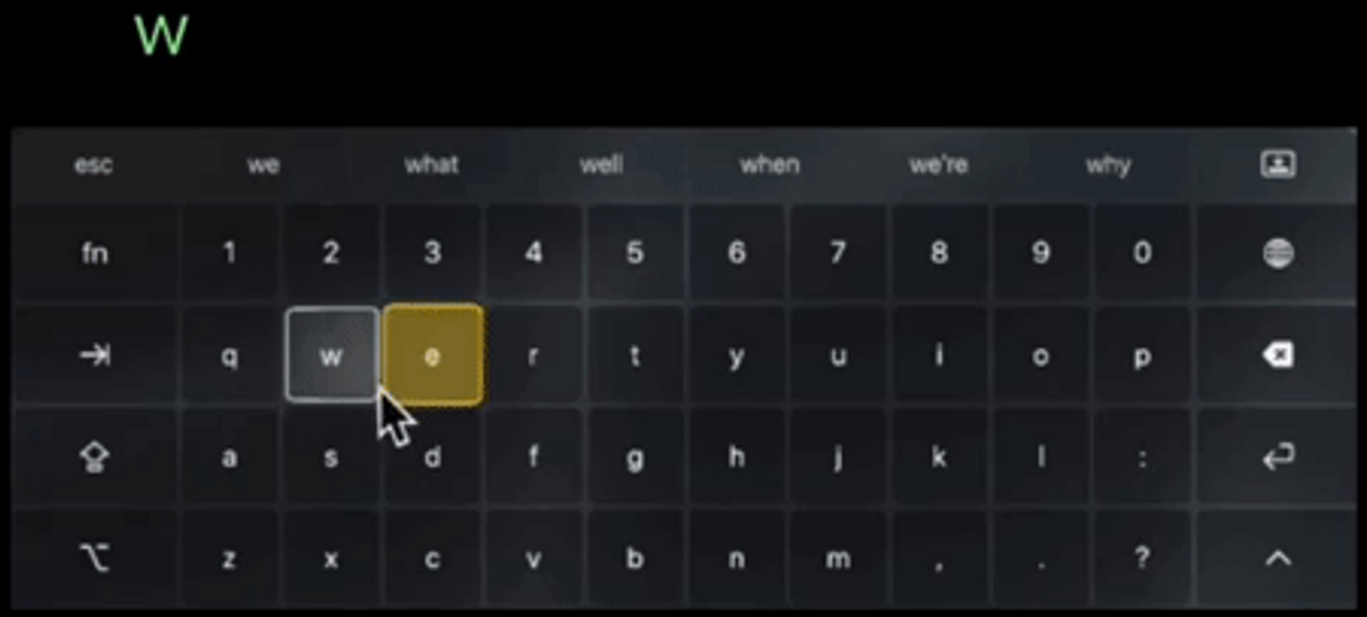
DJ Seo | Member of the Founding Team & VP

Solve important brain & spine problems with a seamlessly implanted device

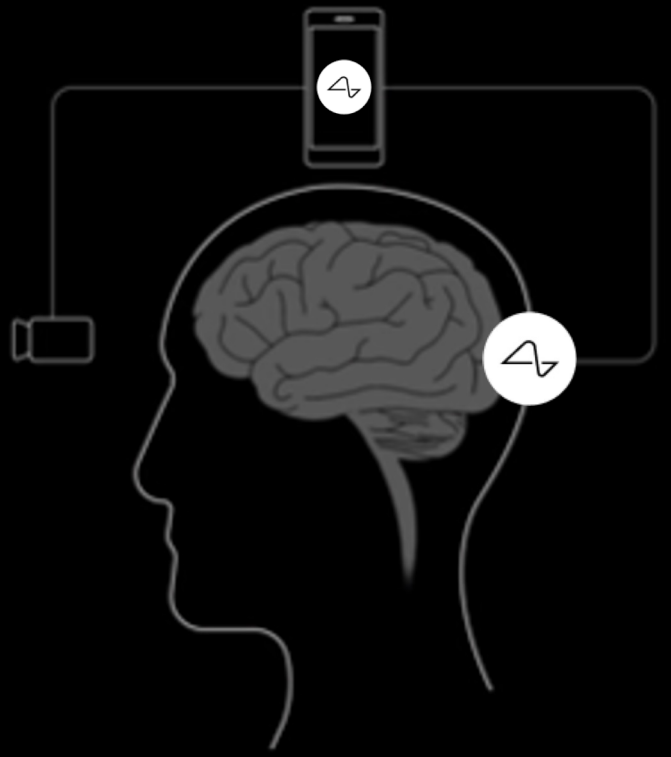
Almost everyone has neurological problems over time, so we need a generalized brain device that is reliable and affordable for patients

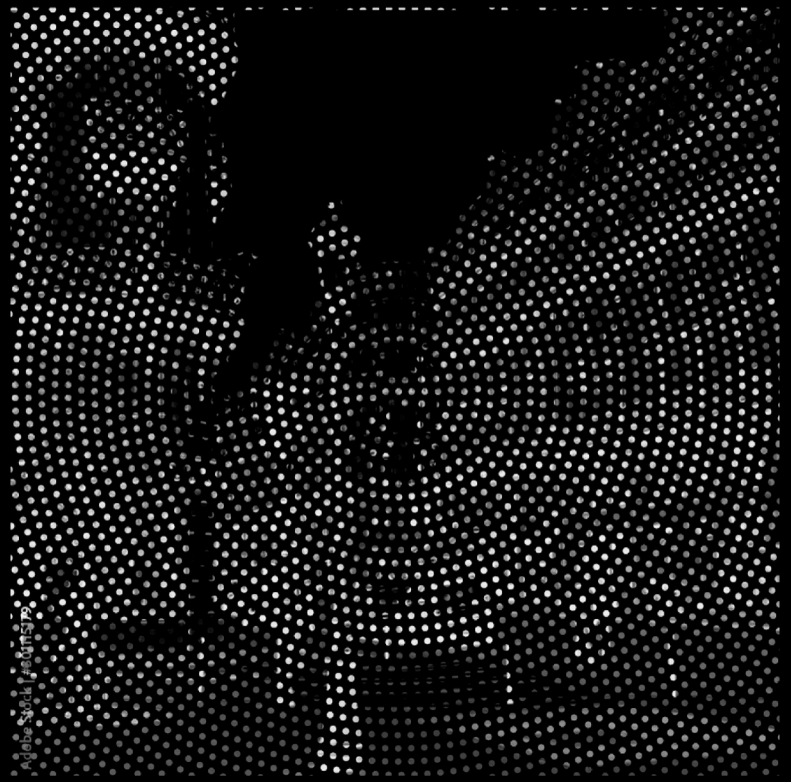
Chronic Pain	Blindness	Depression
Insomnia	Paralysis	Anxiety
Addiction	Stroke	Seizure

FIRST INDICATION: CURSOR CONTROL

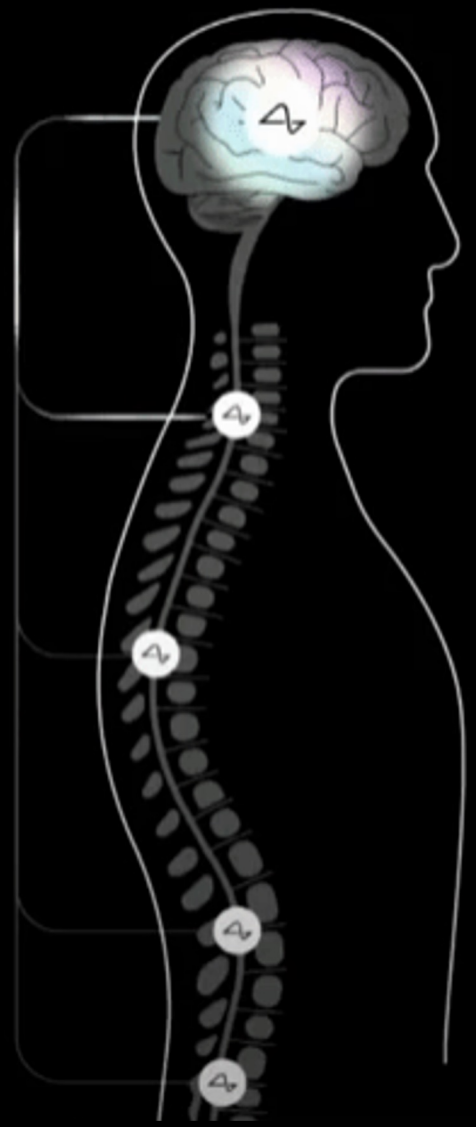


FUTURE INDICATIONS: VISION RESTORATION





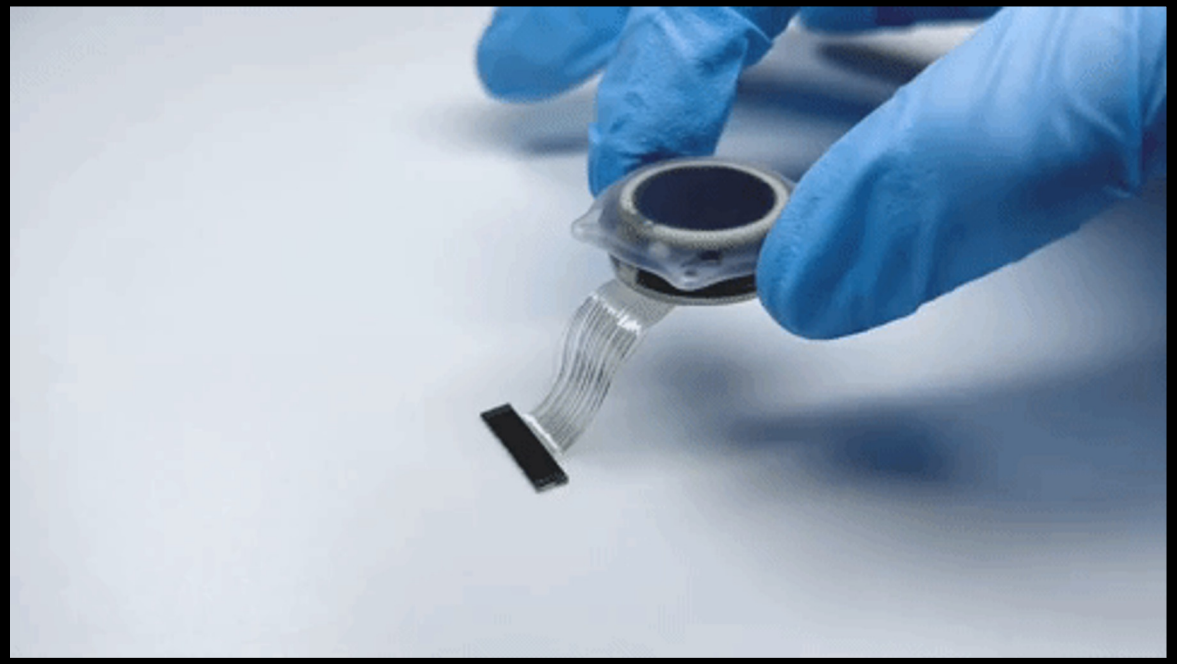
FUTURE INDICATIONS: MOTOR RESTORATION



POTENTIAL IMPACT

Millions of Americans currently live with traumatic brain & spinal cord injuries and uncorrectable vision impairment

OUR APPROACH: IMPLANTABLE BRAIN-COMPUTER INTERFACE



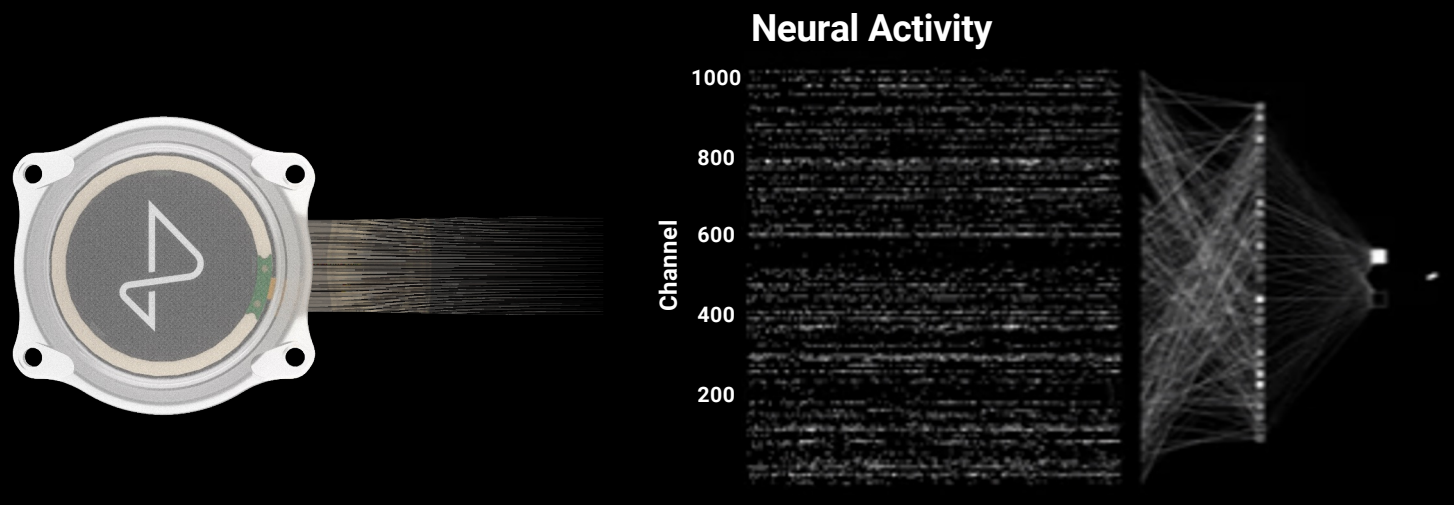
1024 channels

Flexible electrodes

Wireless

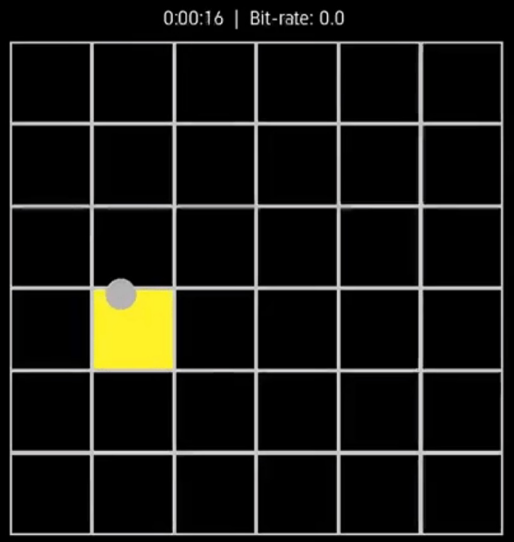
Usable at home

DECODING NEURAL SIGNALS

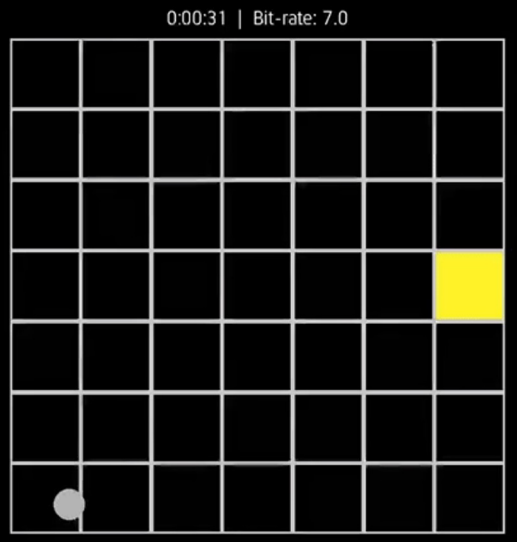


STATE-OF-THE-ART PERFORMANCE

2021



2022



CONSUMER ADVISORY BOARD (CAB)

Our CAB, composed of people with tetraparesis/tetraplegia, offers guidance at every stage of our development process to maximize usefulness of our device for end-users

2021 SCI Community Survey Results

Preferences for the future applications below were equally distributed among respondents:

Physical therapy	*Environmental controls*	*Bed/mattress control*
Health & safety	*Biometric monitoring*	*Car*
Robotic arm	*Wheelchair*	*Entertainment*

Other Example Areas of Guidance

- Expectations and preferences around device charging
- Requirements for the BCI application user interface
- The current market for assistive technology for people with SCI

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Q&A

BCI Commercialization Part I

ONWARD®

EMPOWERING MOVEMENT

Export Controls for BCI Conference
February 16-17, 2023

Erika Ross Ellison, PhD
VP, Global Clinical & Regulatory

ONWARD at a Glance

Key Facts

- Founded in 2015
- 100+ FTEs[1]
- HQ in Eindhoven, the Netherlands
- Science and Engineering Center in Lausanne, Switzerland
- Growing US presence centered in Boston, Massachusetts
- IPO 2021, Euronext Brussels and Amsterdam; $150M+ raised since inception

- Technology - 2 purpose-built investigational neuromodulation platforms that stimulate the spinal cord with implantable (ARC^{IM}) or external (ARC^{EX}) technologies
- Innovation - 7 FDA Breakthrough Device Designations and 330+ issued or pending patents
- Clinical Validation - One pivotal trial complete with positive top line results reported for ARC^{EX}; positive interim outcomes also reported for ARC^{IM} blood pressure indication
- Commercialization - Large Total Available Market ($20B+); first commercial sale expected in H2 2023; favorable reimbursement for ARC^{IM} in the US; strategic relationship with Christopher Reeve Foundation

[1] *As of 01 December 2022*

Large unmet need:
There is no cure for Spinal Cord Injury (SCI)

Problem

Devastating

Not only paralysis & loss of sensation; frequently also infection, incontinence, loss of sexual function, and other challenges

Assistance required to support activities of daily life

Quality of life changes

Prevalent

US & Europe[1,2]
Prevalence ~650,000
Incidence ~50,000

Global[2]
Prevalence ~7,000,000
Incidence ~768,000

Costly

Avg Lifetime Cost (paraplegic)
$2.5M

Avg Lifetime Cost (tetraplegic)
$5.0M

[1] *NSCISC Annual Report, US and Europe only – with 25 years old patients, World Health Organization Fact Sheet, November 2013, estimate 40-80 cases per million.*
[2] *Kumar et al. 2018, Traumatic Spinal Injury: Global Epidemiology and Worldwide Volume – Traumatic spinal injury may be broader than traumatic spinal cord injury.*

Our Solutions

ONWARD ARC™ Investigational Therapies

ARC EX™

Non-Invasive Platform

External system for non-invasive, programmed stimulation of the spinal cord

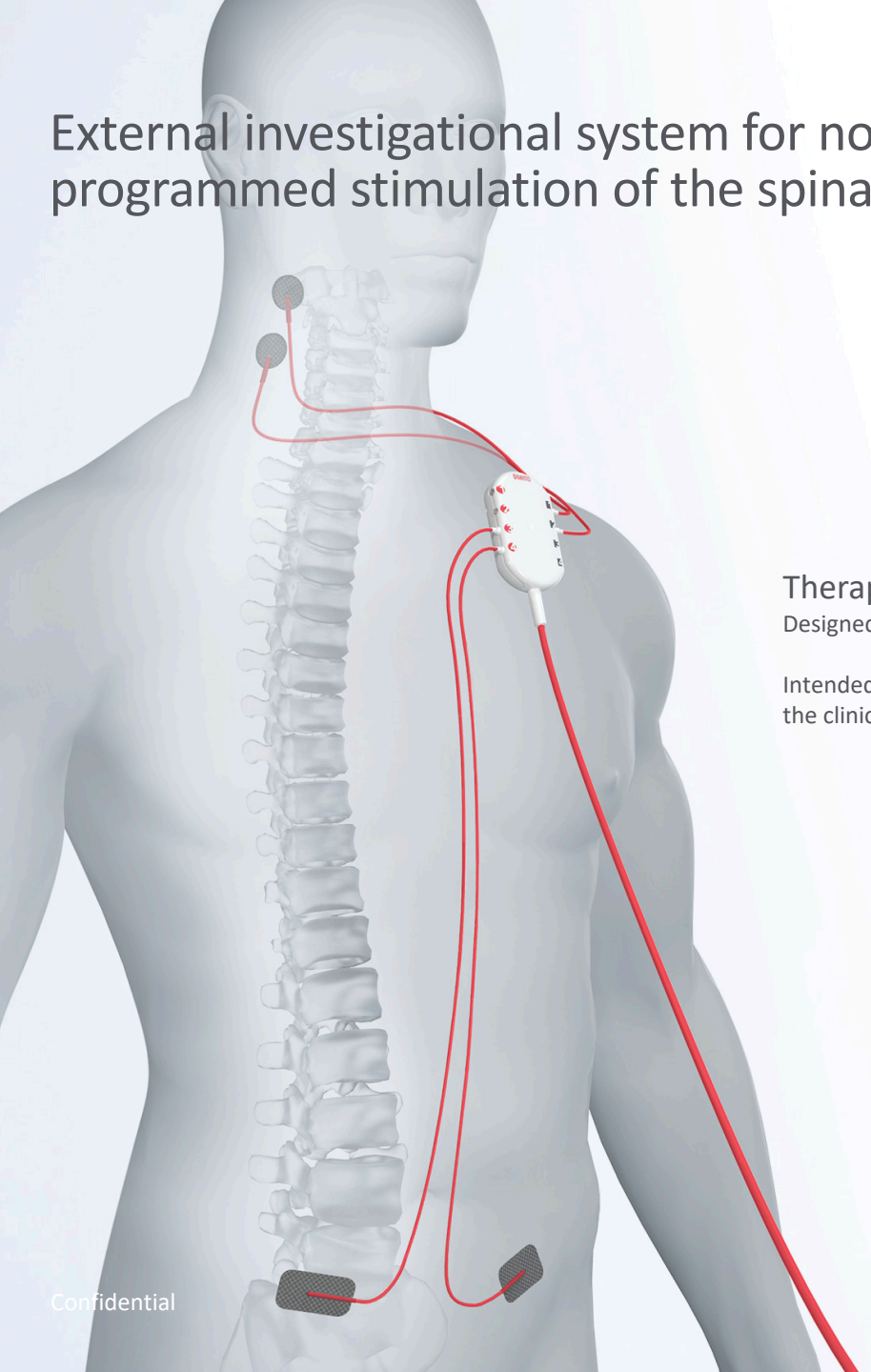
ARC IM™

Implantable Platform

IPG and leads for direct, programmed stimulation of the spinal cord

External Platform

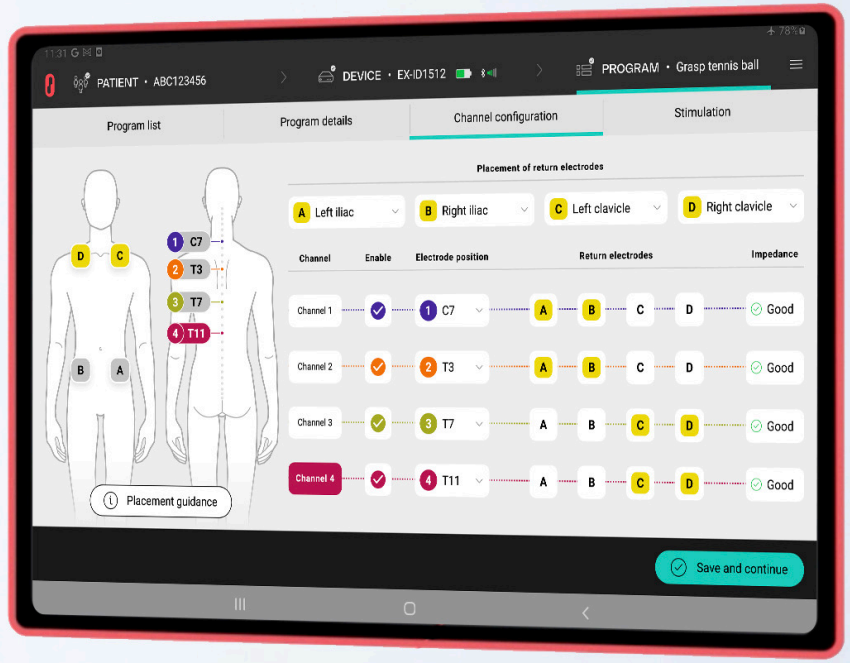
External investigational system for non-invasive, programmed stimulation of the spinal cord



Therapy

Designed to restore function in conjunction with rehabilitation

Intended to be used periodically during up to 60-minute sessions in the clinic or home



ARC^{EX} Programmer

ARC^{EX} Stimulator

Mechanism of Action

Proprietary waveform: Strength to deliver current to the spinal cord without causing pain or discomfort

ARC EX

First indication: Strength and function of the hands and arms

Implantable Platform

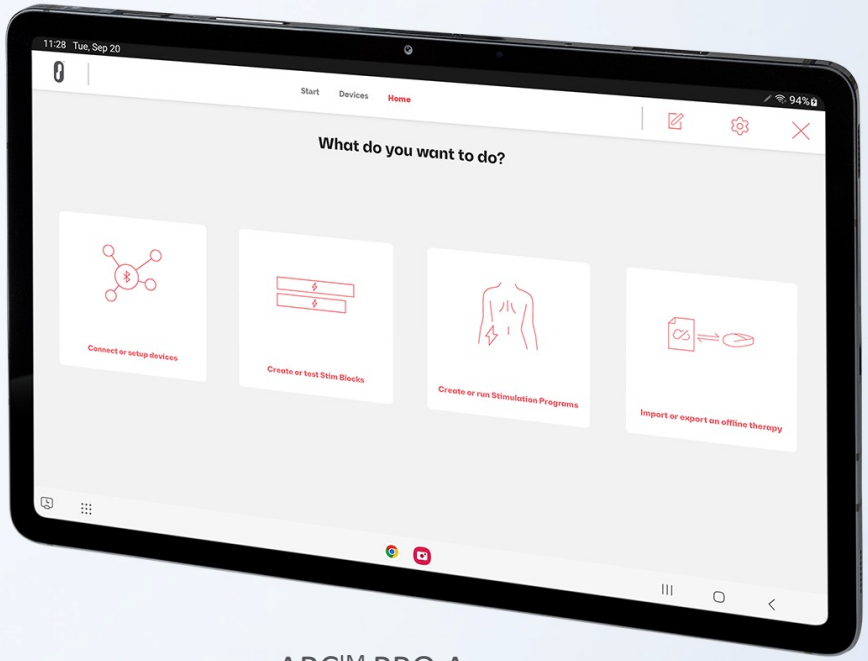
Investigational implanted pulse generator and leads for direct, programmed stimulation of the spinal cord

ARC^{IM} Lead Family

ARC^{IM} Neurostimulator (IPG)

ARC^{IM} Hub

myARC^{IM} App
via ARC^{IM} Controller



ARC^{IM} PRO App
via ARC^{IM} Programmer

Spinal Cord Injury and improved blood pressure regulation

Blood Pressure Indication

Improved hemodynamic control is important for the SCI population

Hemodynamic instability is highly prevalent, affecting almost 75% of people with SCI (nearly 500,000 people in the US & Europe)

The approach is also potentially applicable to those with Parkinson's disease

No rehabilitation is required

nature

DARPA

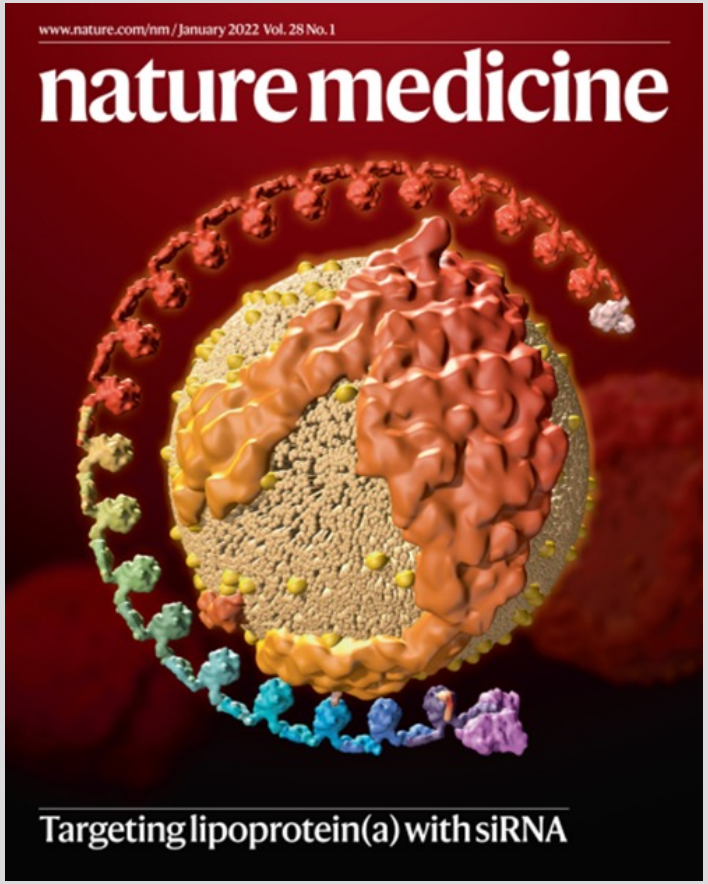
Paper detailing our approach was published January 2021

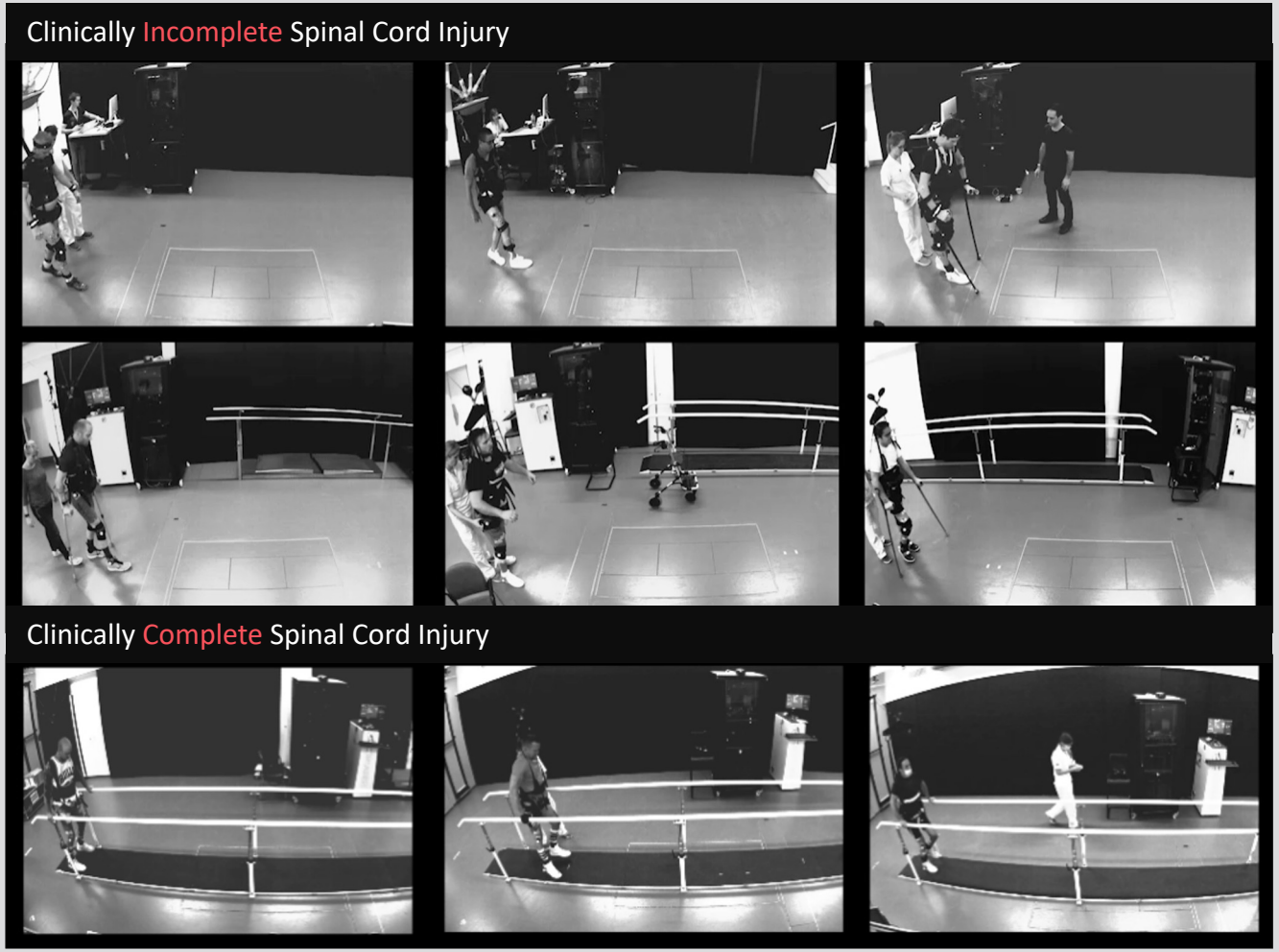
ONWARD and partners receiving up to $36M grant

Next indication: Standing and walking

Mobility - STIMO Trial

Ability to stand and walk restored in 9 participants with chronic injuries; even those with AIS-A severity





ClinicalTrials.gov Identifier: NCT02936453

Advocacy Organizations

Strong relationships with leading patient advocacy organizations to drive awareness and market access

Opportunities for engagement

- Drive awareness in the SCI community
- Reach patients and their families directly
- Shared media and government advocacy
- Support for clinical research
- Sources of non-dilutive funding

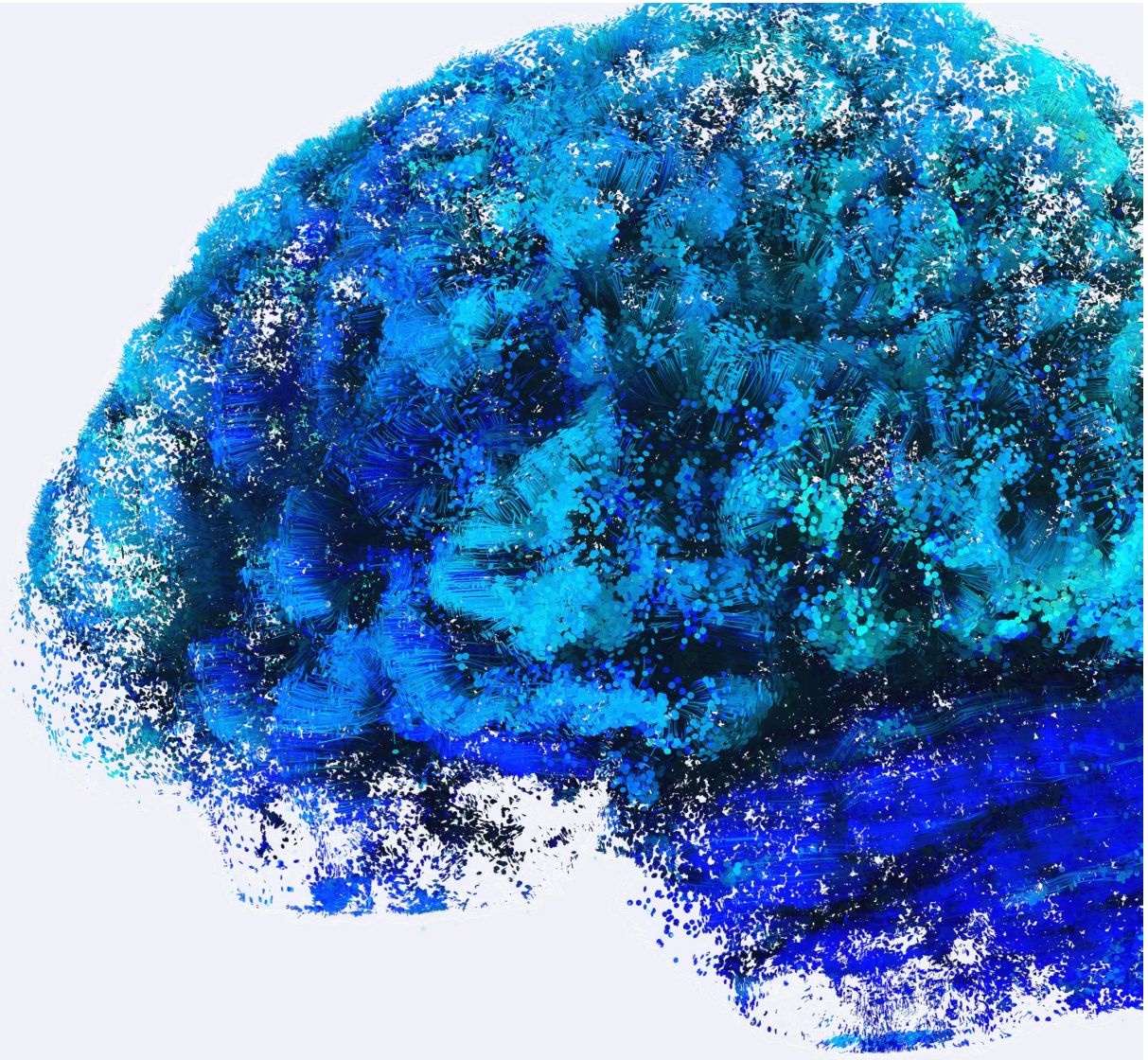
ONWARD & Brain Computer Interface

Targeted, programmed electrical stimulation of the spinal cord to restore movement, independence, and health in people with spinal cord injury

ONWARD™ EMPOWERING MOVEMENT™

INBRAIN
NEUROELECTRONICS

Decoding neural signals to restore patients' lives



US Department of Commerce

Feb 2022

WHO WE ARE

We are INBRAIN. Bringing deep, medtech and digital together, we use graphene to decode neural signals into breakthrough medical solutions.

FOUNDED IN
2020

SPIN-OFF FROM
GRAPHENE FLASGHIP

GRAPHENE FLAGSHIP

EU €1B

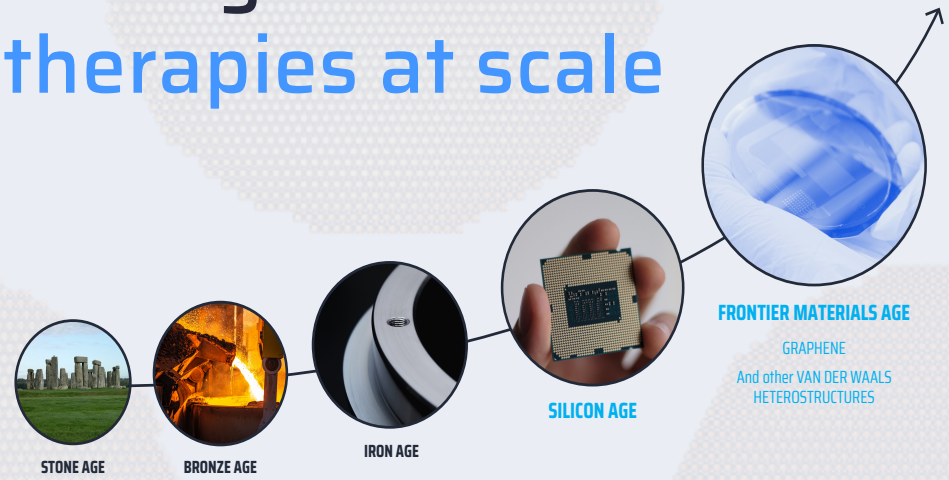
PEOPLE AT INBRAIN
50
>35% Women

MERCK COLLABORATION IN BIOELECTRONICS (INNERVIA)

MERCK

CONTEXT

Graphene represents a material breakthrough in driving neuroelectronic therapies at scale



GRAPHENE

- Nobel Prize Winner Material
- Thinnest Material Known to Man at One Atom Thick
- 200x Stronger Than Steel
- Flexible, Stretchable & Highly Impermeable
- Biocompatible
- Excellent conductor

"What is important about graphene is the new physics it has delivered"

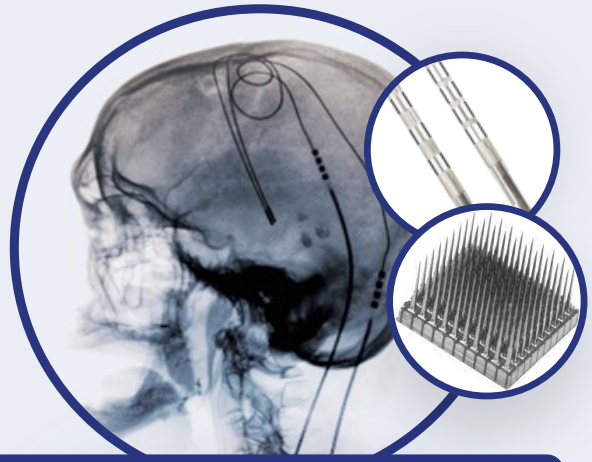
Geim, Nobel Prize 2010

PROBLEM

Current neuro & bioelectronic therapies are lagging behind

INVASIVE TECHNOLOGY

Current therapies are highly invasive driving 50% patient rejection



POOR OUTCOME REPRODUCIBILITY

Interfaces are made of metals with low count and resolution which impacts precision & patient to patient reproducibility[1]

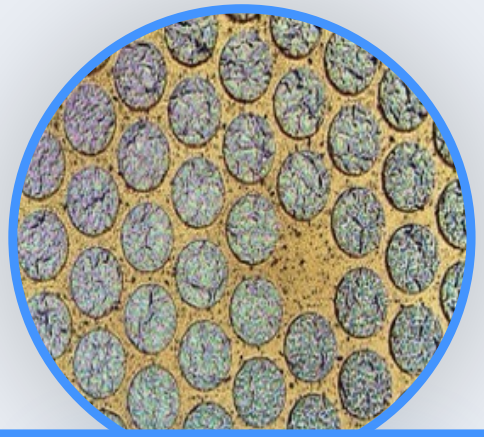
NOT PERSONALIZED

They don't consider patient or environment data and don't adjust to patient needs

1. Rolstone 2016

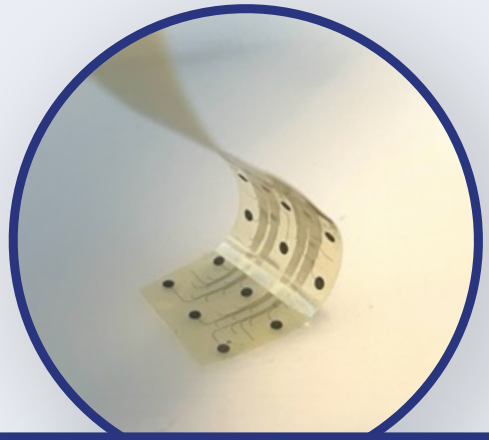
SOLUTION

Graphene enables safe and intelligent neuroelectronic therapies at scale



MINIMALLY INVASIVE

« Cell Like » size at an atom thick enabling miniaturization and modern electronics coupling



BETTER OUTCOMES

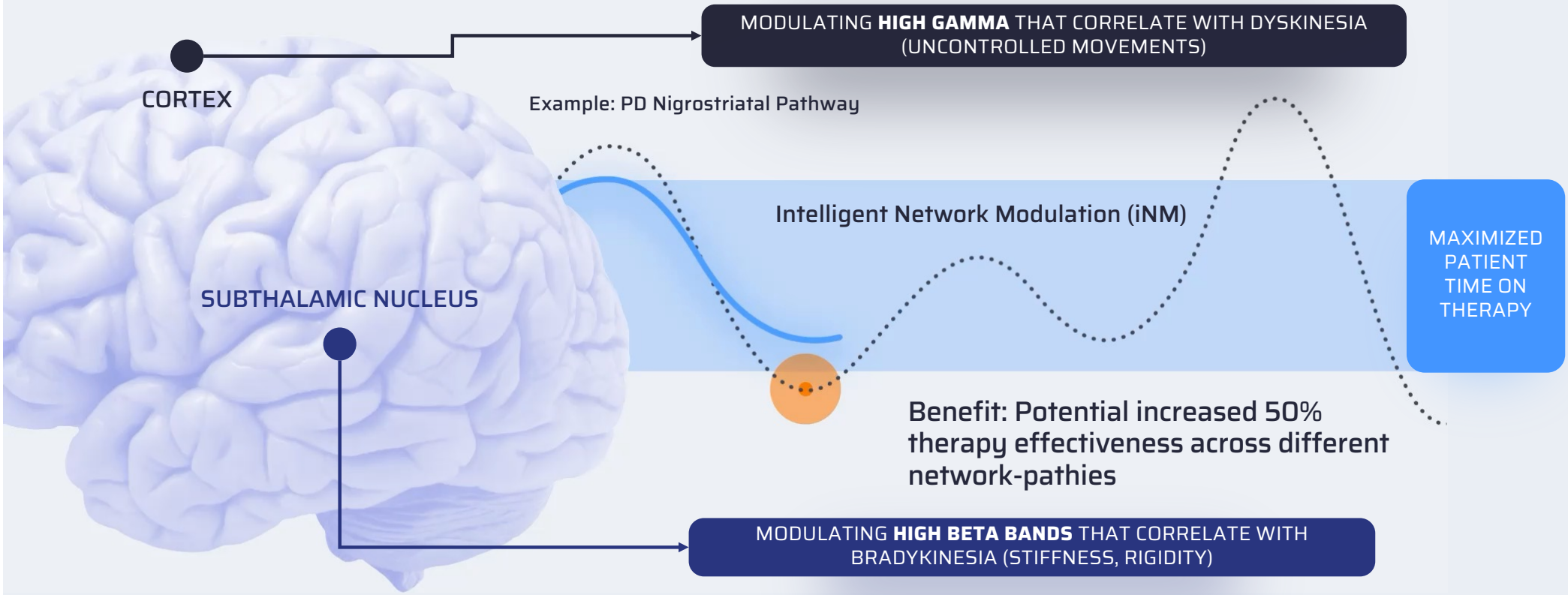
Bi-directional, flexible, ultra high density & high resolution for biomarkers detection and therapy personalization (closed loop)

PERSONALIZED

An intelligent implant that combines brain biomarker detection with patient lifestyle sensors data to deliver outcomes that matter to patients

SOLUTION

Our mission is to decode and modulate neural networks to maximize patient time on therapy

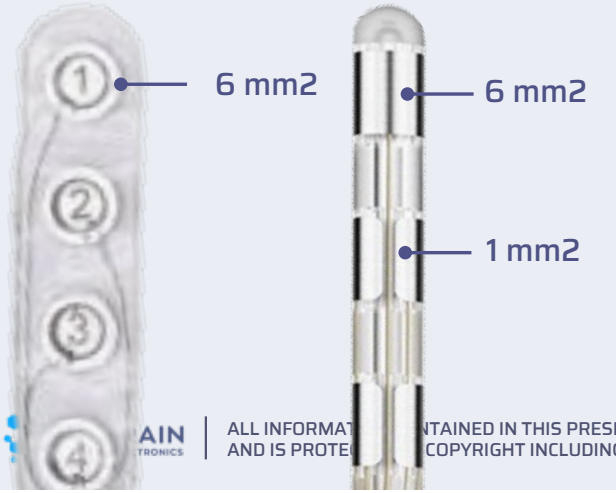


TECHNOLOGY

These are the graphene dots that power our intelligent neuroelectronic system

METAL TRADITIONAL

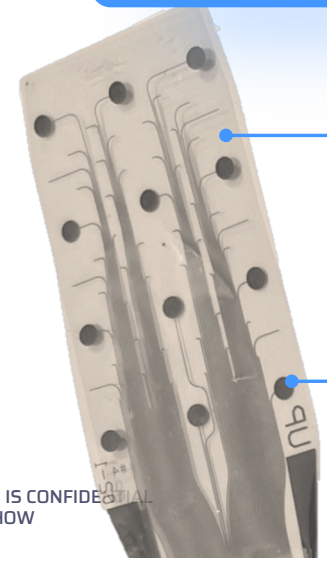
Metal & silicone technology with sub-optimal resolution



GRAPHENE & BI-DIRECTIONAL

Graphene flexible and ultra-high resolution cortical & sub-cortical interfaces for recording and stimulation

CORTICAL INTERFACE



Recording (reading) dots

Stimulation (writing) dots

SUB-CORTICAL INTERFACE

10.000x

SMALLER THAN SOTA

0.07 mm2
0.0005 mm2

TECHNOLOGY

EGNITE™ stands for Engineered Graphene for Neural Interfaces.

It is our patented Graphene innovation providing neurotechnological scalability

1. INBRAIN, Viana et al., Graphene-based thin film microelectrode technology for in vivo high-resolution neural recording and stimulation 2020 (in review at Nature Nanotechnology); Zhao et al., 2020, Nature Communications, Full activation pattern mapping by simultaneous deep brain stimulation and fMRI with graphene fiber electrodes

HIGHER PATIENT ADOPTION

50% to 90%

reduced power requirements (consumption & battery space)

Thanks to 200x higher charge injection limit and ~10x lower impedance, enabling more efficient therapy and increased battery lifetime

BETTER OUTCOMES

10x

more sensitive neural signal readouts[1]

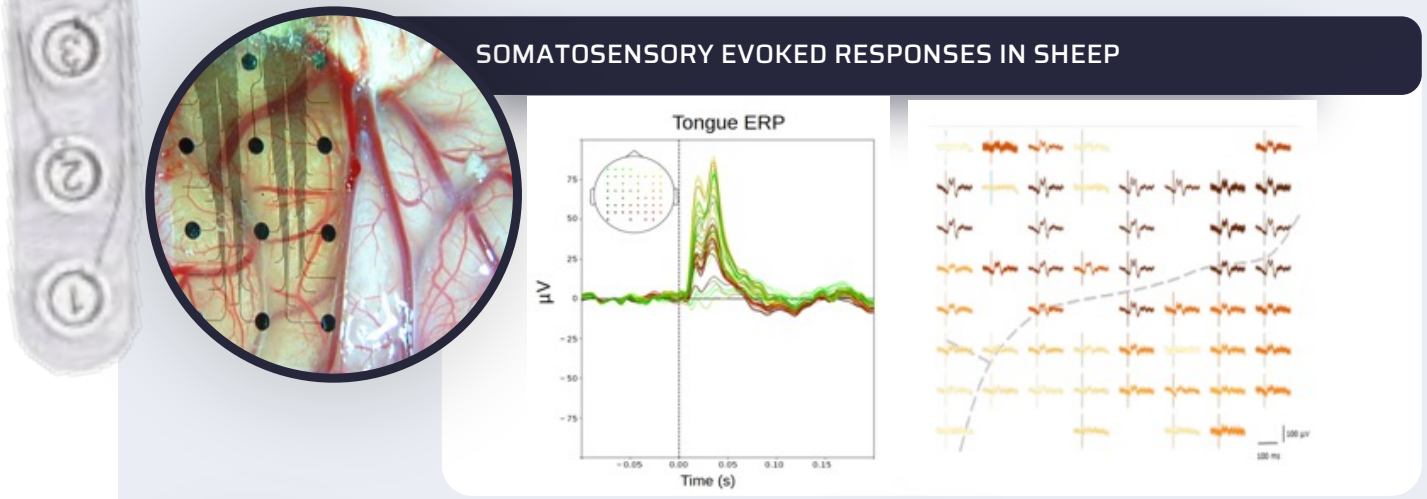
Enabling improvement of neuroelectronic therapies via more sensitive neural signal recording and modulation

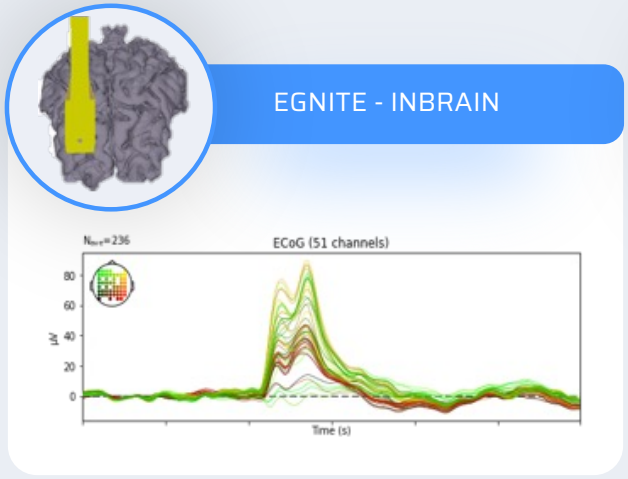
TECHNOLOGY

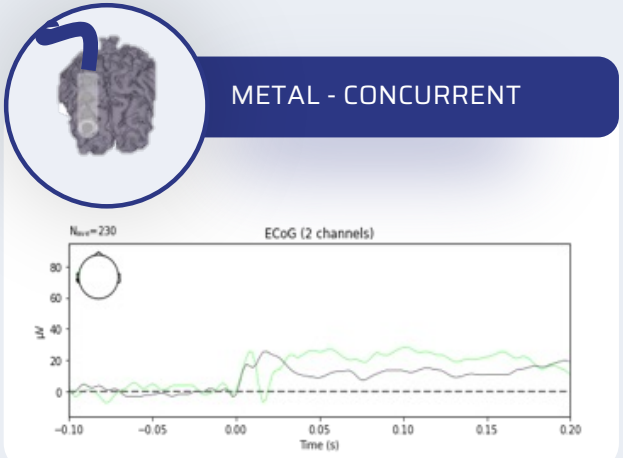
Cortical Module

We outperformed SOTA* both in small and large animal studies

At similar sizes, EGNITE provides 10X higher signal resolution than metals (Pt)







INBRAIN Data on file, Unpublished
* STANDARD OF THE ART

TECHNOLOGY

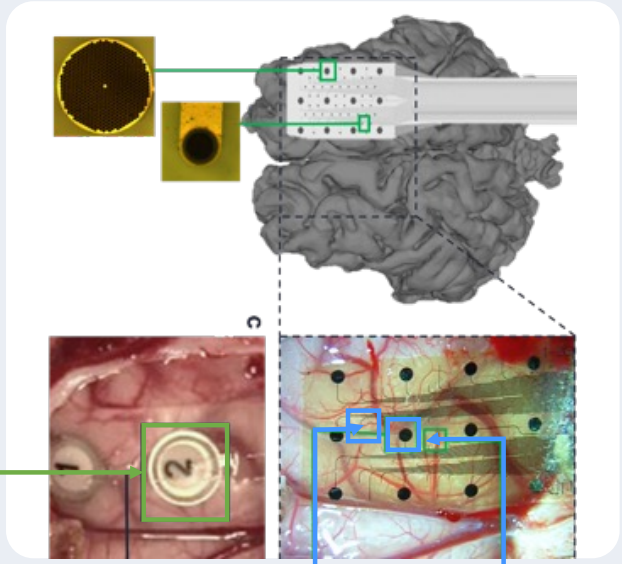
Cortical Module

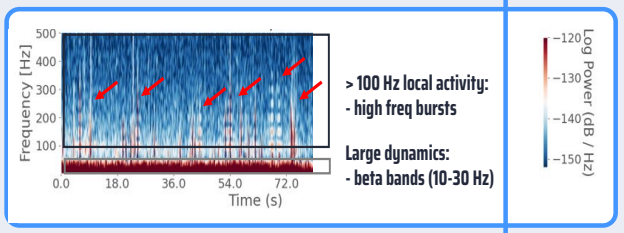
Graphene decodes what others can't

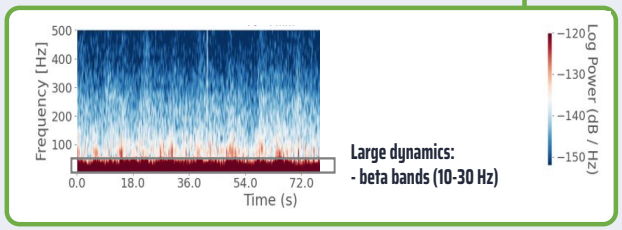
Graphene 1mm dots showed much higher sensitivity to 50-150 Hz signals as compared to Pt

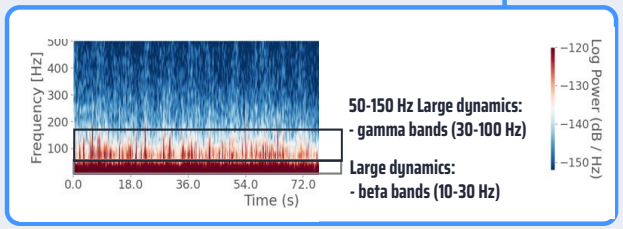
Additionally graphene 25 µm dots showed the ability to sense low frequency signals as well as to detect higher frequency (>200 Hz) bursts.

High frequency might become an extremely relevant biomarker for STN interface lead localization and high precision in closed loop therapeutics.









INBRAIN Data on file, Unpublished

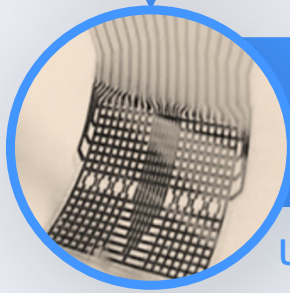
TECHNOLOGY

Cortical Module

Graphene decodes what others can't

FROM ACUTE HIGH-RESOLUTION DECODING IN BRAIN MAPPING

60 active sensors



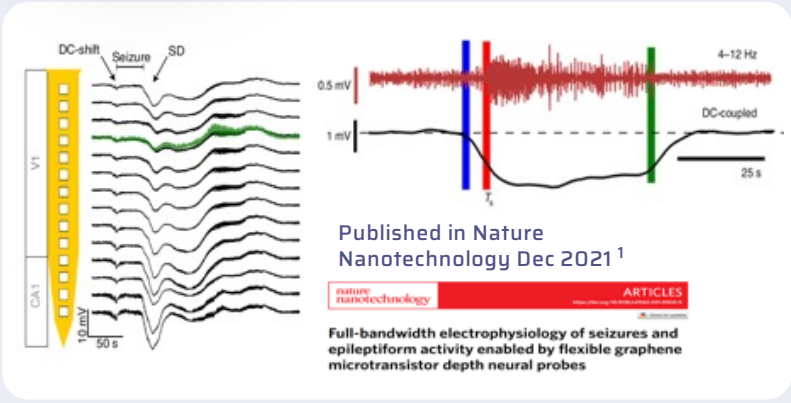
TO CHRONIC ULTRA-HIGH RESOLUTION DECODING IN PD, EPILEPSY AND STROKE (APHASIA, SPEECH SYNTHESIS)

Up to 1024 sensors per interface

Infra-slow activity (ISA) as a new health biomarker (<0.1Hz): Graphene enables monitoring of ISA in an epileptic model.

Records simultaneously:

- DC-shifts
- Infra-slow oscillations (<0.1 Hz)
- Local field potentials (0.1-80 Hz)
- higher frequencies (80-600 Hz)

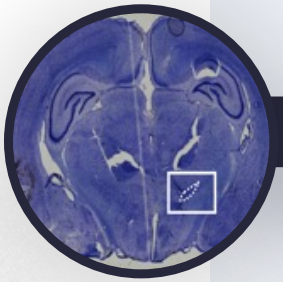


SOURCE: 1. Bonaccini Calia, A., Masvidal-Codina, E., Smith, T.M. et al. Full-bandwidth electrophysiology of seizures and epileptiform activity enabled by flexible graphene microtransistor depth neural probes. Nat. Nanotechnol. Dec 2021

TECHNOLOGY

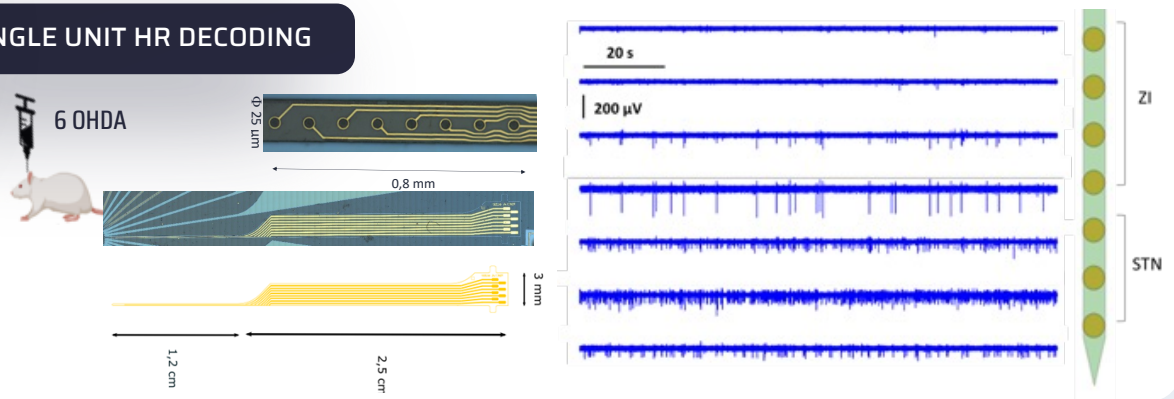
Sub-cortical module

We decoded and modulated PD biomarkers in high resolution, restoring neuro health by automated decoding and closed loop therapeutics



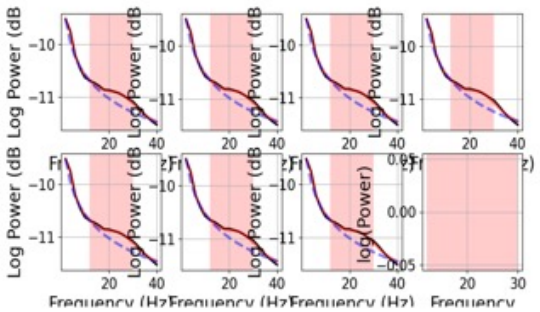
SINGLE UNIT HR DECODING

High Resolution Subthalamic Nucleus (STN) recording with 25um graphene dots

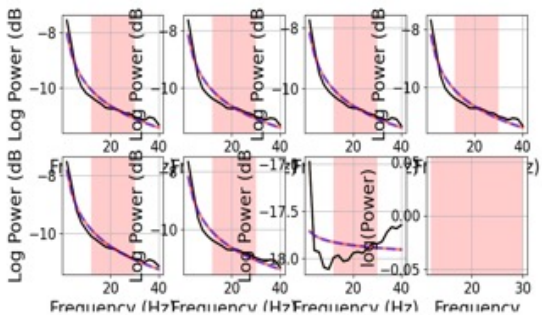


Subcortical STN modulation with 25um graphene dots (130Hz, 100µs, 75µA). Beta band suppression corrects rigidity and bradykinesia in PD

Beta Recording Pre-Stim



Beta Stimulation- Modulation



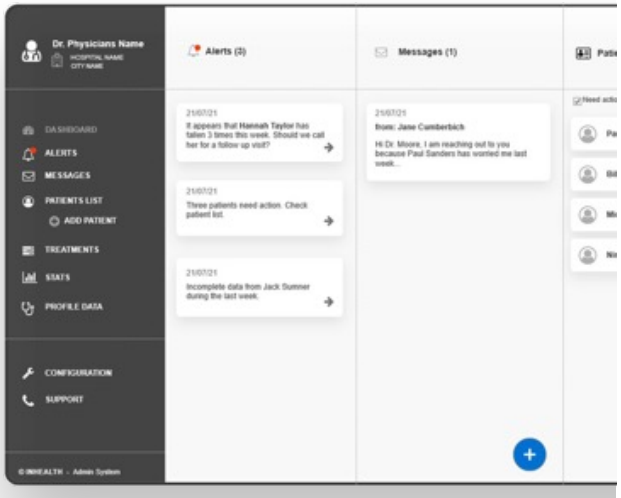
INBRAIN Data on file, unpublished

SYSTEM PLATFORM - DATA HUB

INBRAIN's intelligent data Hub decodes signals into medical solutions using machine & deep learning

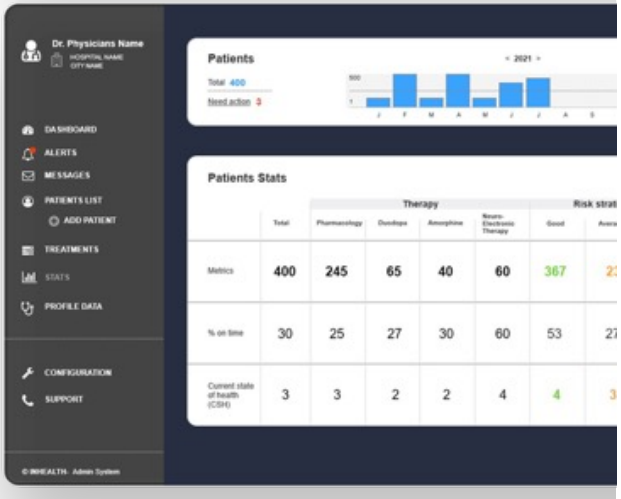
A Clinical Data Hub

- Realtime remote care;
- Patient empowerment;
- Higher value care.



A Research Data Hub

- Algorithm prototyping;
- Therapy discovery;
- Therapy optimization



PEOPLE

Driving breakthroughs again and again

TEAM

Our experienced team counts with hundreds of years cumulated neurotech and frontier material expertise

BUSINESS & MANAGEMENT

Carolina Aguilar
CEO & Co-Founder
Former **Medtronic** DBS Global Business Director

Joan Adan
Finance & Operations Head
Former Qiagen

Jose A Garrido
Chief Scientific Officer & Founder
ICREA Professor
Catalan Institute of Nanotechnology
Spain ICN2

Simone Noussitou De Rham
People & Culture Head
Executive Coach and Leadership Developer
Ex Nestle Finance

ENGINEERING

Jurriaan Bakker
CTO INBRAIN
Former Director Product Dev. **ONWARD**
Former Principal Scientist at **Sapiens & Medtronic**

Bert Bakker
Implantable Neurotech Expert
Former CTO **ONWARD**
Former system Architect at Sapiens & Phillips

Antòn Guimerà
Co-Founder
CSIC, Spain

TECHNOLOGY ADVISORS

Michel Decré
Technology Advisor & Board Member
Former **Philips, Former CTO Sapiens Modulation** (Acquired by Medtronic)

Peter Knapen
Microfabrication Expert
Ex Philips

Eric Klasen
Regulatory & Quality Consultant
Former VP Regulatory & Quality
Medtronic

TEAM

We are supported by the leading scientific and clinical experts in our field

CLINICAL BOARD

Ludvic Zrinzo MD, PhD
Professor of Functional Neurosurgery, Clinical and Movement Neurosciences, UCL Queen Square Institute of Neurology, London, UK

Fiorella Contarino, MD, PhD
Assistant Professor in Neurology, Leiden University Medical Centre (LUMC), NL, and Neurologist coordinating the Deep Brain Stimulation program at the Haga Teaching Hospital, The Hague, NL.

Jordi Rumià, MD
Head of Functional and Stereotactic Neurosurgery at SJD Barcelona Children's Hospital and Hospital Clínic de Barcelona, Spain

Patricia Limousin, MD, PhD
Professor in Clinical Neurology and Honorary Consultant Neurologist, UCL Institute of Neurology and the National Hospital for Neurology & Neurosurgery, London, UK

Alfonso Fasano, MD, PhD
Associate Professor, Department of Medicine, Division of Neurology at University of Toronto, Toronto Western Hospital, Canada

Francesc Valldeoriola, MD, PhD
Associate Professor of neurology at the University of Barcelona, Consultant and Investigation Coordinator at the Institute Clinic of Neurosciences in the Hospital Clinic in Barcelona, Spain

Alex Green, MD
Spalding Associate Professor, Nuffield Department of Clinical Neurosciences. John Radcliffe Hospital, Oxford, UK

Volker Coenen, MD
Professor of Stereotactic and Functional Neurosurgery, Head of Division of Stereotactic Neurosurgery, Medical Center, University of Freiburg, Germany

Helen Bronte-Stewart
Director of the Human Motor Control and Neuromodulation Lab Stanford University, US

VISION BOARD

Kostya Novoselov
2010 Graphene Nobel Prize winner

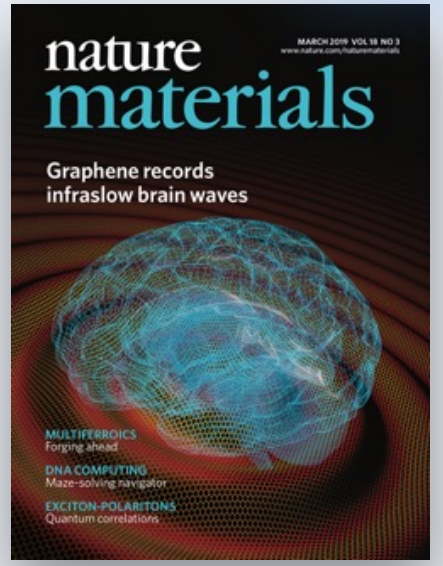
David Eagleman
Neuroscientist Professor at Stanford,
Neuroscientist Author

Jenniffer Chandler
Professor, University of Ottawa Faculty of Law - Brain, Mind and Law; Neuroethics;

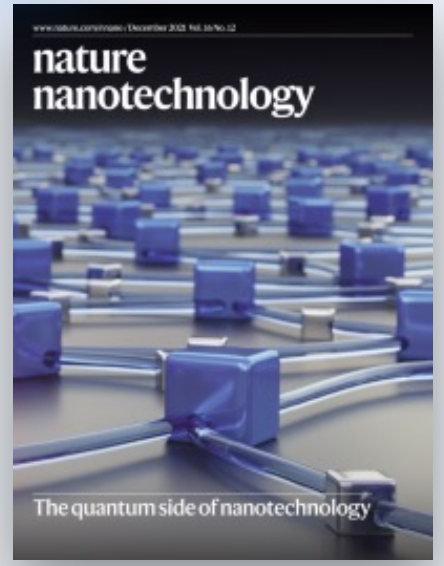
CREDIBILITY & VISIBILITY

Publications

RESEARCH PAPERS



Masvidal et al., Nat. Mater. 2019



Garrido et al., Nat. Neurot. 2021

MEDIA

sifted / FT

Bloomberg

"INBRAIN and Merck KgaA collaborate to develop the next generation of bioelectronic"

MedTech STRATEGIST

"INBRAIN, Neuralink, Kernel, Synchron, Blackrock, BrainQ make together a banner year for Neurotech"

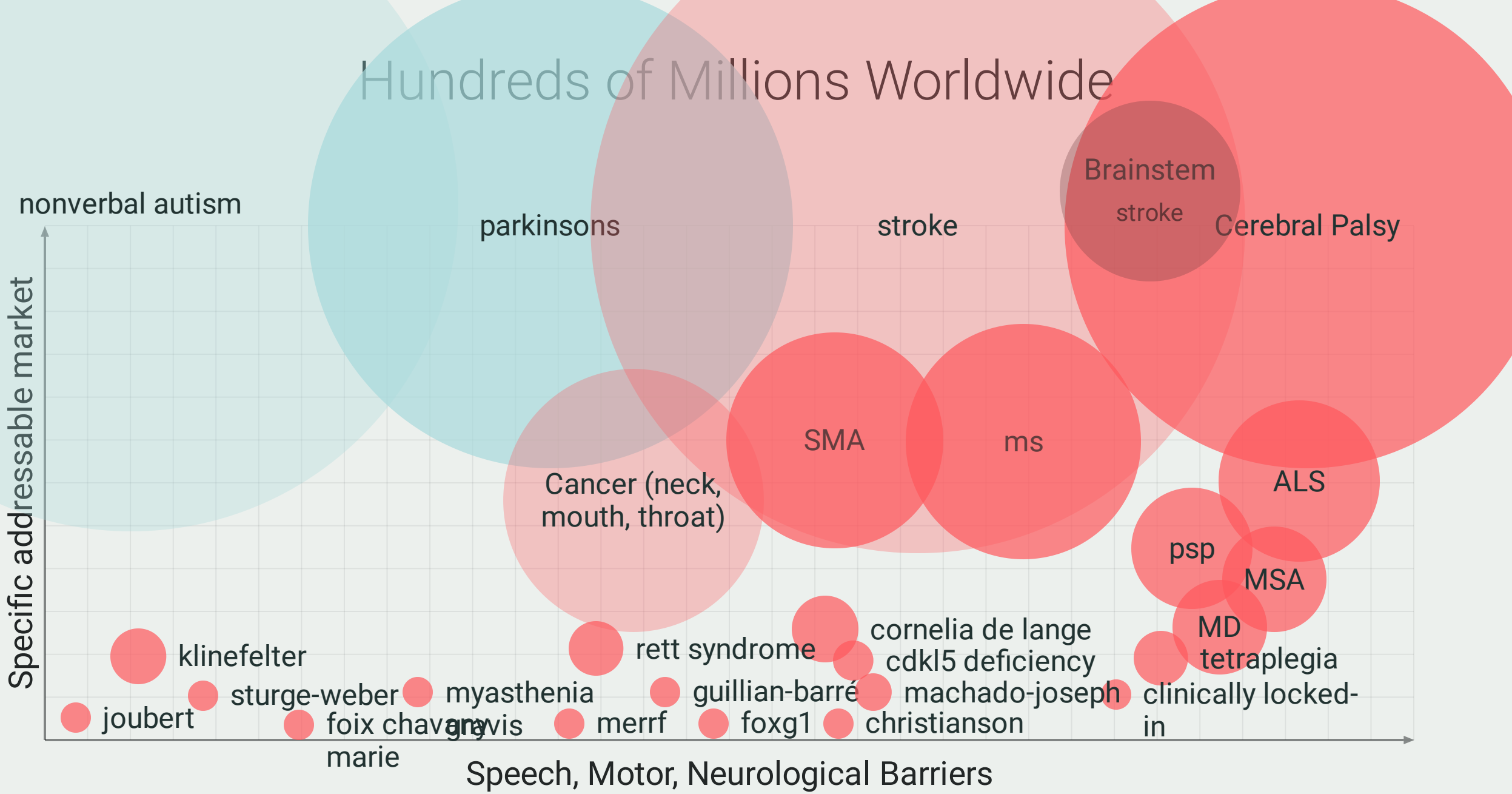
Cognixion

Cognixion ONE Assisted Reality Platform

Brain Computer Interface + Augmented Reality

Chris Ullrich, CTO, chris@cognixion.com

Hundreds of Millions Worldwide



The Problem

ALS/MND affects more than 25,000 Americans per year and more than 500,000 worldwide.

ALS is a progressive condition that leads to zero physical motor control with continuous cognition.

There are no HCI (Human Computer Interface) solutions that address the **entire** disease progression and patient journey.

ALS is our initial target but we expect to be able to apply our product to the hundreds of Millions of people with Motor, Speech & Language Disabilities worldwide.

ALS - Progressive Decline of Motor Control *requires* Progressive Sensory Controls in ***one system for end-to-end decline of motor function***

Poor Muscle; Slurred Speech

Need: Speech clarity; Personalized Communication System; Agency
Cognixion's New Standard: Adaptive Language System with Rapid Headpose Gesture Inputs

Limited Distal Movement; Speechless

Need: Voice synthesis; Increased communication speed; Independence
Cognixion's New Standard: Eye-tracking driven heads-up with robust natural language system that adapts to the users vocabulary

Clinically Locked-In

Need: Voice synthesis; Basic needs communication; Urgent Messaging
Cognixion's New Standard: Transition from Eye-Tracking to entirely BCI driven language system

Hand & Verbal Control > | *Head & Neck Control >* | *Eye-Pupil Control >* | *Brain Computer Interface (BCI)*

Non-Invasive | + Implanted

Cognixion's Natural Language Generation Platform addresses the needs of 1.6M disabled American adults, and 509 Million living with motor and speech disabilities globally

Solving for ALS first enables us to expand the platform for other conditions as well as Mass Market Accessibility & Personalization of AR

Similar Needs as Early ALS

Cerebral Palsy
Multiple Sclerosis
Stroke
Aphasia

>500k Adults (USA only)

Similar Needs as Middle ALS

Cerebral Palsy
Huntington's
Tetraplegia
Cancer (Neck, Mouth, Throat)

>500k Adults (USA only)

Similar Needs as Late ALS

Brainstem Stroke
Parkinson's
Traumatic Injuries
Locked-In Syndrome

>10,000 Adults (USA only)

100% of the world population encounters situational communication impairments at some point

>1 Billion Adults

Hands-Free, Voice-Free Human Machine Interaction While In Motion (vehicle, bicycle, sports)

>100 Million Adults

Requiring Discrete Silent Human to Human or Human to Machine Communication (military, space, diving)

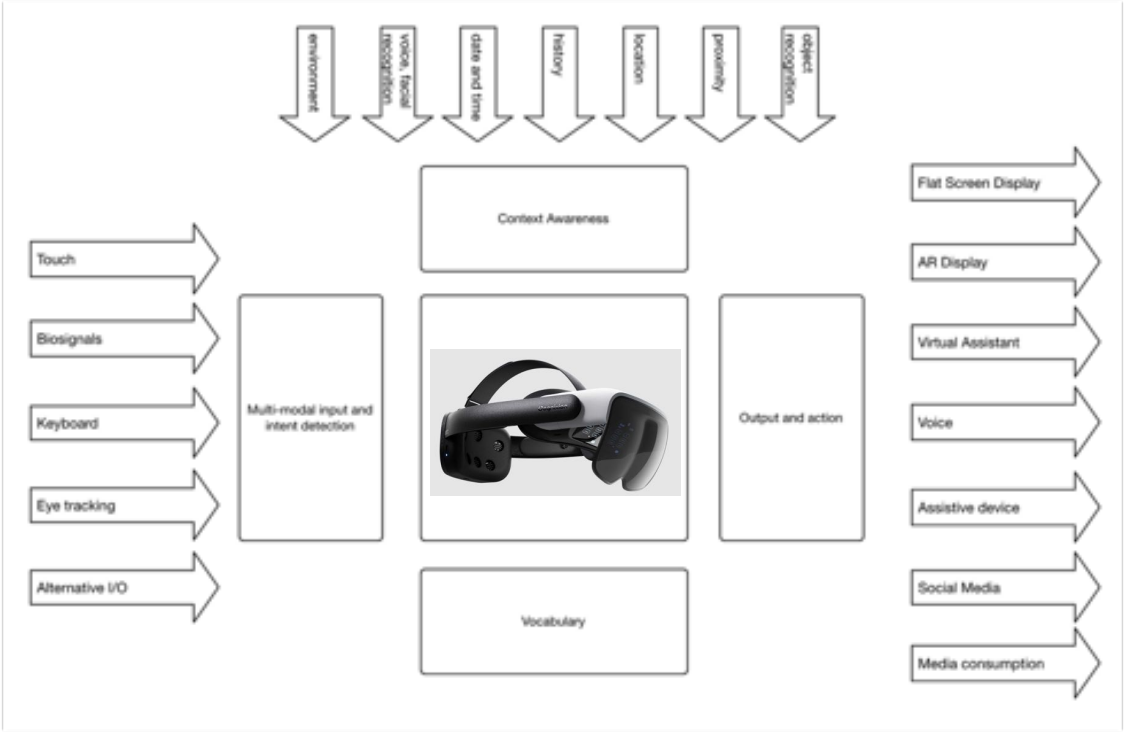
>100 Million Adults

Require HMI without Any Body Motion (Covert or Tasks When Hands Are Occupied)

OUR PLATFORM

Context aware system that can be deeply personalized to the person, which learns and adapts to their unique physiological and cognitive state and enhances their abilities in various situations.

Patent: US11237635B2



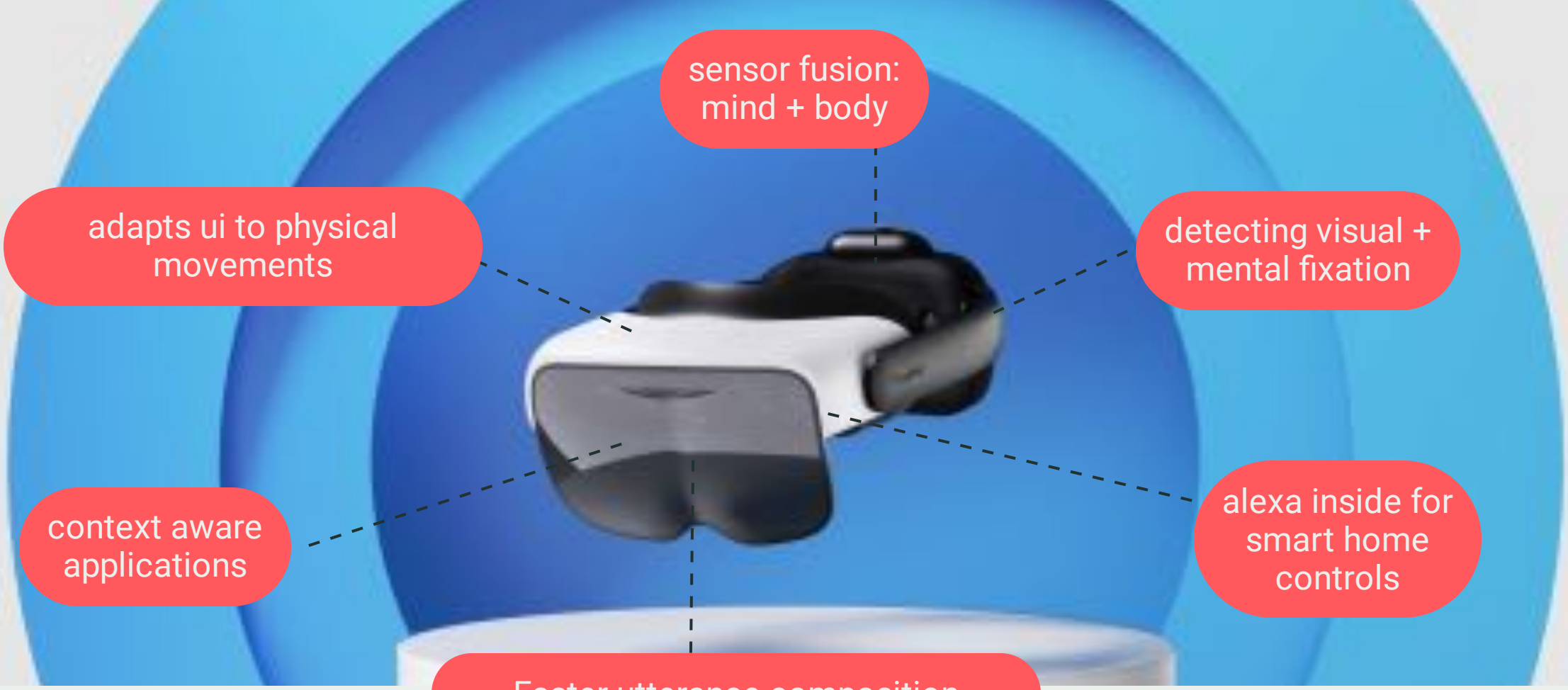
Cognixion

Cognixion ONE BCI Principle of Operation

1. Visual Stimuli

2. User attention

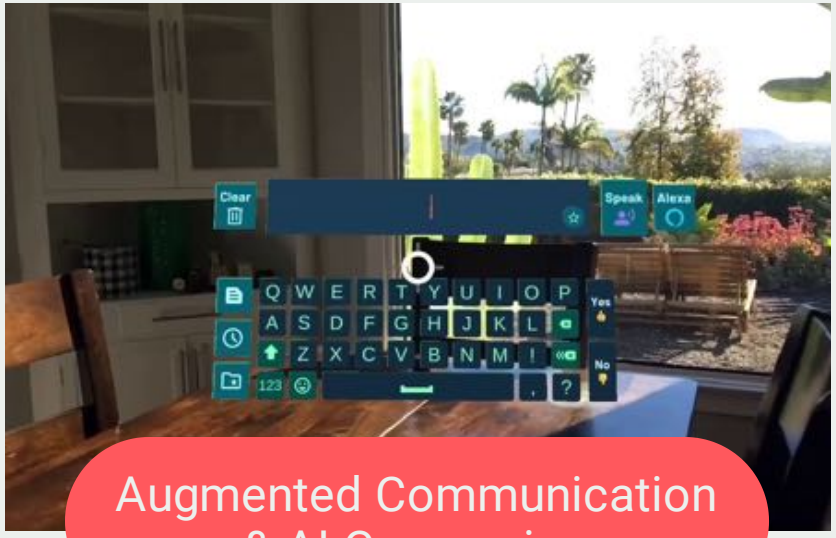
3. Brain sensing



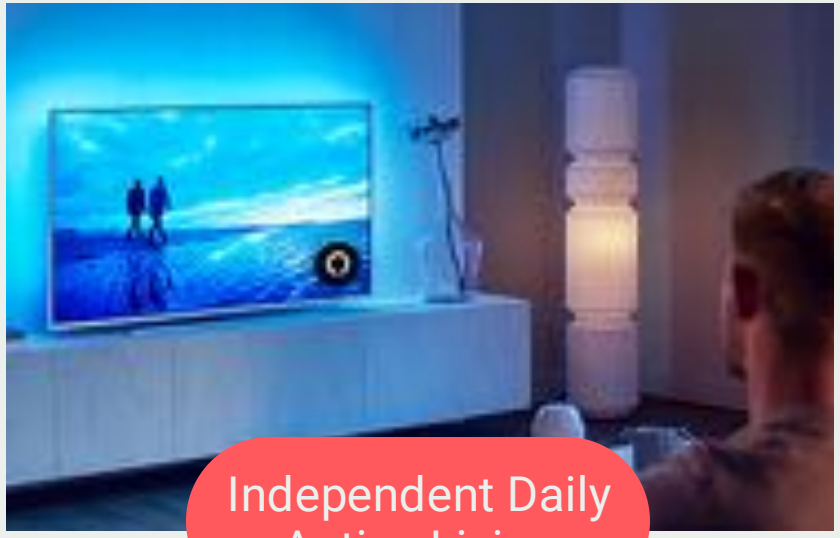
Cognixion ONE

Fully integrated BCI+AR system for Assisted Reality

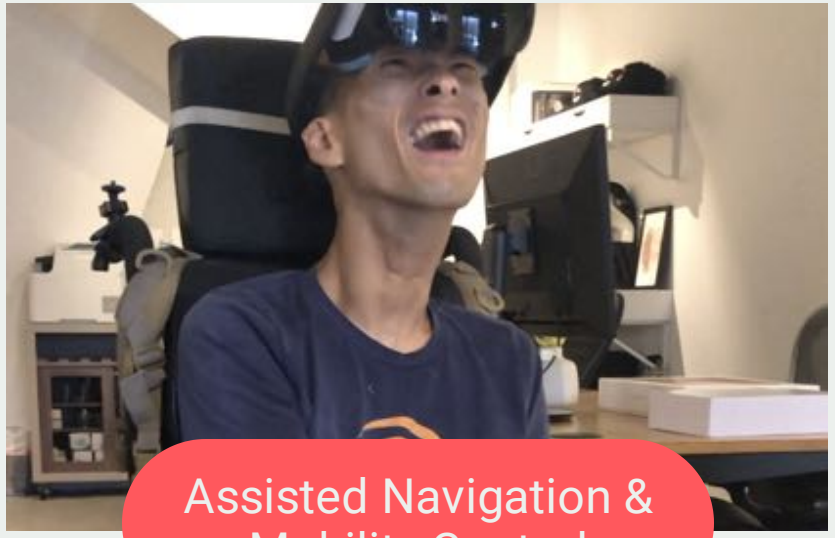
Wearable speech generation | Smart Home Controls | AI Companion/Assistant built-in



Augmented Communication & AI Companion



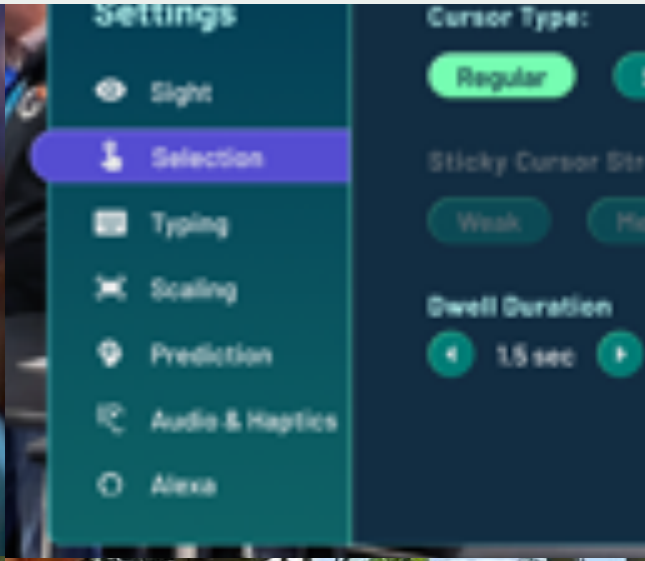
Independent Daily Active Living



Assisted Navigation & Mobility Control

Creating the ultra-accessible world we all want to live in.

Adaptive and Personalized Experiences



Clinical Efficacy

ALS Patient Validation

- First in-home BCI technology validated with Clinically Locked-In ALS Patient without Eye Control & Caregiver training

"Your device could make a huge difference for people with ALS"
- Spouse of ALS patient

Executed IRB approved longitudinal field study in Sept-Oct. 2022

- 9 subjects across a variety of conditions including ALS, CP, Stroke, TBI

The Assisted Reality Platform For Healthcare Market

The Wearable Computer for the Neural Interface Industry

Interface

- **Wireless Switch & Handheld Controllers**
- Head Pointing
- Pupil Tracking
- Brain Sensing
- + API and UX specifically designed for Implantable BCI wireless integrations
- **...and more potential**
- Wireless data from implantable devices

Applications

- **Speech Generation**
- AI Assistant Inside
- Smart Home Control
- Media Control
- Robot Control
- Mobility Control
- **... and more potential**
- Remote Diagnostics
- Remote Monitoring
- Telehealth Services
- AI Companionship
- Sensor Fusion
- ...and more!

Connectivity

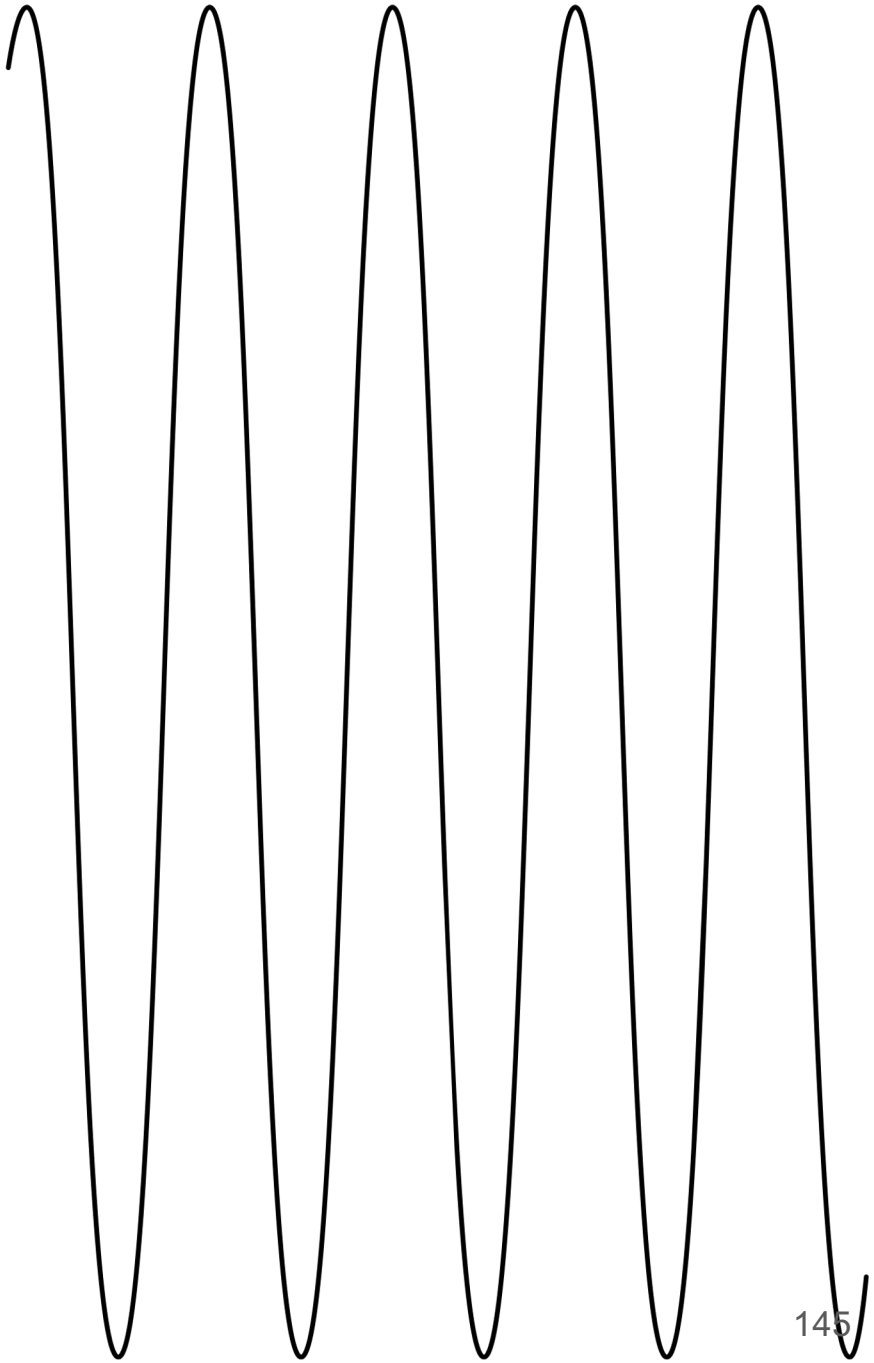
- **5G - mobile**
- Wifi - home & away
- Bluetooth - Sensor Fusion
- BLE 5 - accessories
- **...and more potential**
- Local Data Processing
- Edge Data Processing
- Cloud Data Processing

Cognixion

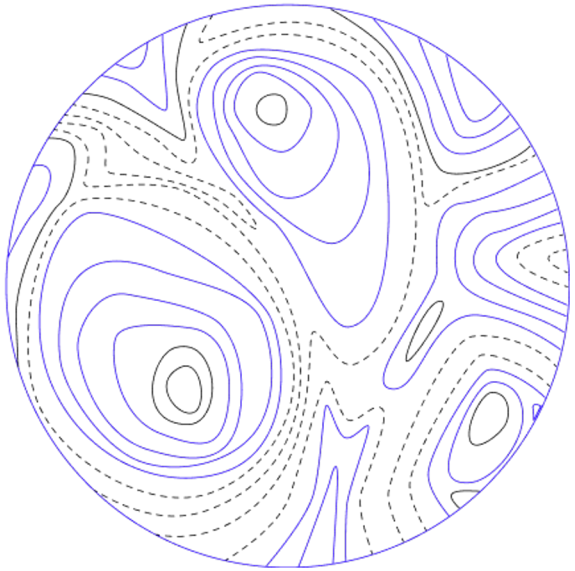
The mind. Unlocked.

DR. RAMSES ALCAIDE, CEO + CO-FOUNDER

NEURABLE

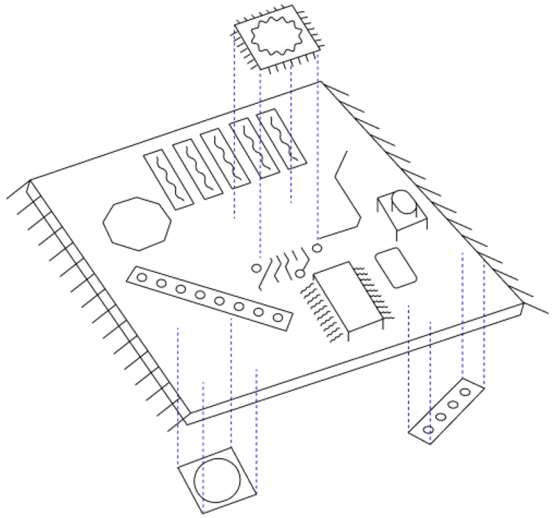


The Mind. Unlocked.



Cognitive Biomarkers And Tracking

DATA SIZE: Medium ~4000



Brain-computer interface control
and silent communication

DATA SIZE: Large ~40M


EmTech

The Problem: Current systems are bulky or have poor performance

LABORATORY GRADE

High Quality Signal

Large Device

Requires An Expert

Not For Everyday Use

CONSUMER GRADE

Low Quality Signal

Mobile

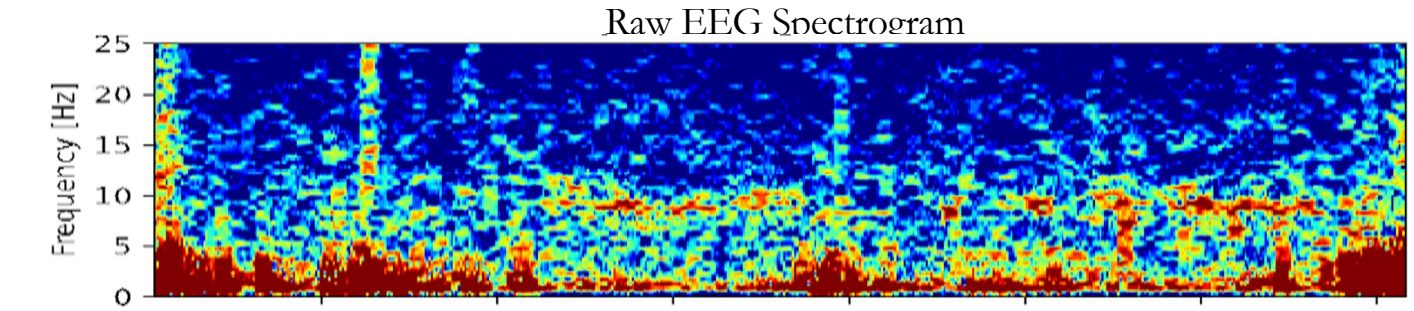
Not For Continuous Use

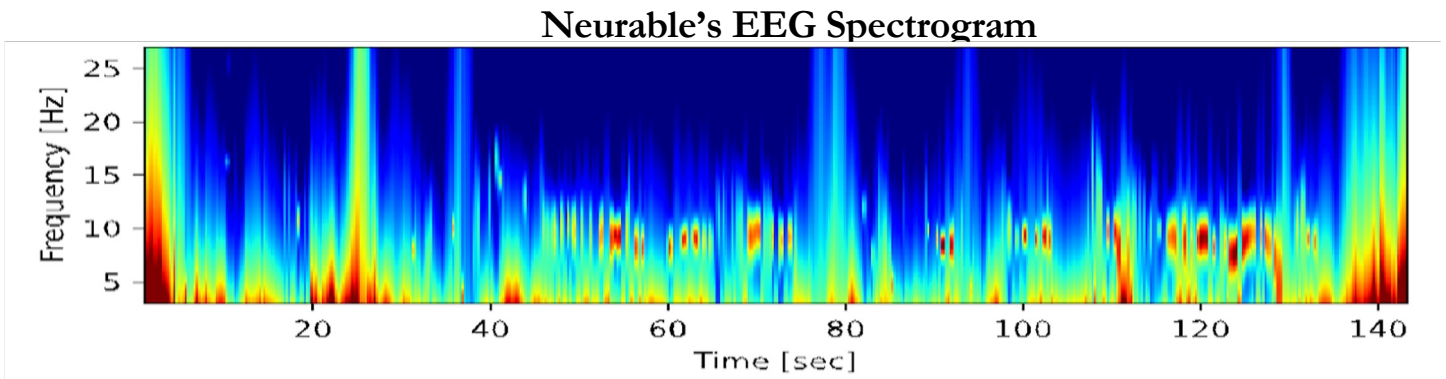
Solution: We need a high performance, everyday BCI that is used at scale

Solution: Neurable's Brain OS

- Neurable's IP enables the highest signal to noise ratio in EEG, and has been covered in Nature, Journal of Neural Engineering (1,2) and Taylor Francis' Journal on Brain Computer Interfaces (BCI)
- Over 30 patents covering signal processing, software, sensor fusion and hardware
- Neurable's Brain OS Platform has been refined from data of over 4K participants over seven years

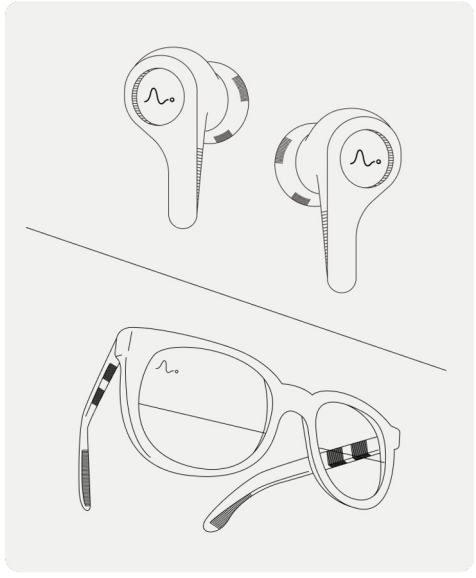
This differentiation allows Neurable to implement technology into **everyday devices** while still maintaining a **high level of signal to noise**





Our signal processing improvements (**Brain OS)** over the last 10 years have enabled us to build high-performance consumer-grade BCIs

2011	2015	2018	2021	2023+
University of Michigan Signal Processing Breakthrough	Reduced electrodes from 128 to 22 (2015-Early 2021)		Reduced requirements of electrode positions from over head to ear (2020-2021)	Launch headphones and License technology (2022+)



33 PATENTS, 100S OF GIGS OF DATA AND 100X FASTER

Leadership Team

Dr. Ramses Alcaide
CEO, CO-FOUNDER,
UNIVERSITY OF MICHIGAN

Jamie Alders
VP OF PRODUCT,
BOSE

Adam Molnar
CO-FOUNDER, HEAD OF PARTNERSHIPS,
FORBES 30 UNDER 30

Engineering & Science

Dr. Mavi Ruiz-Blondet
RESEARCH ENGINEER,
BINGHAMTON UNIVERSITY,
PROXIMITYHCI

Dr. David Stanley
COMPUTATIONAL NEUROSCIENTIST,
BOSTON UNIVERSITY

Dr. David Eagleman
NEUROSCIENTIST, AUTHOR,
TECHNOLOGIST, ENTREPRENEUR

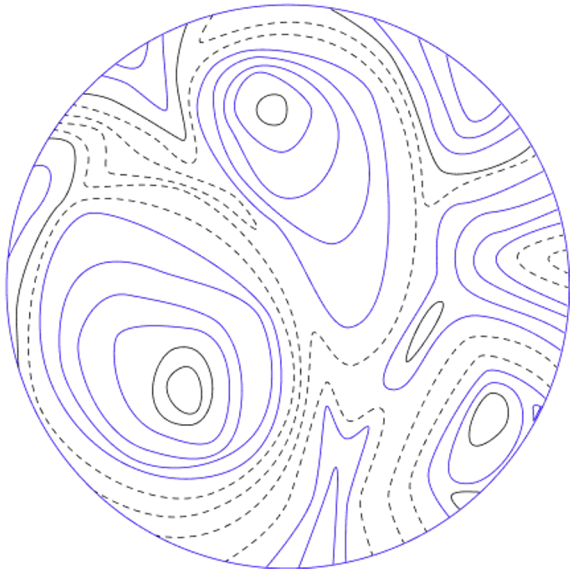
Tom Rand
Product Advisor
WHOOP

Dr. Ali Yousefi
LEAD SCIENTIST,
HARVARD MEDICAL SCHOOL,
KERNEL

Dr. John Donoghue
PROFESSOR OF NEUROSCIENCE AND ENGINEERING AT BROWN UNIVERSITY

UNIVERSITY OF MICHIGAN · Forbes 30 UNDER 30 · BOSE · SHURE · PROXIMITYHCI · Forbes NEXT 1000 · HARVARD UNIVERSITY · HARVARD MEDICAL SCHOOL · kernel · LOCKHEED MARTIN · BOSTON UNIVERSITY

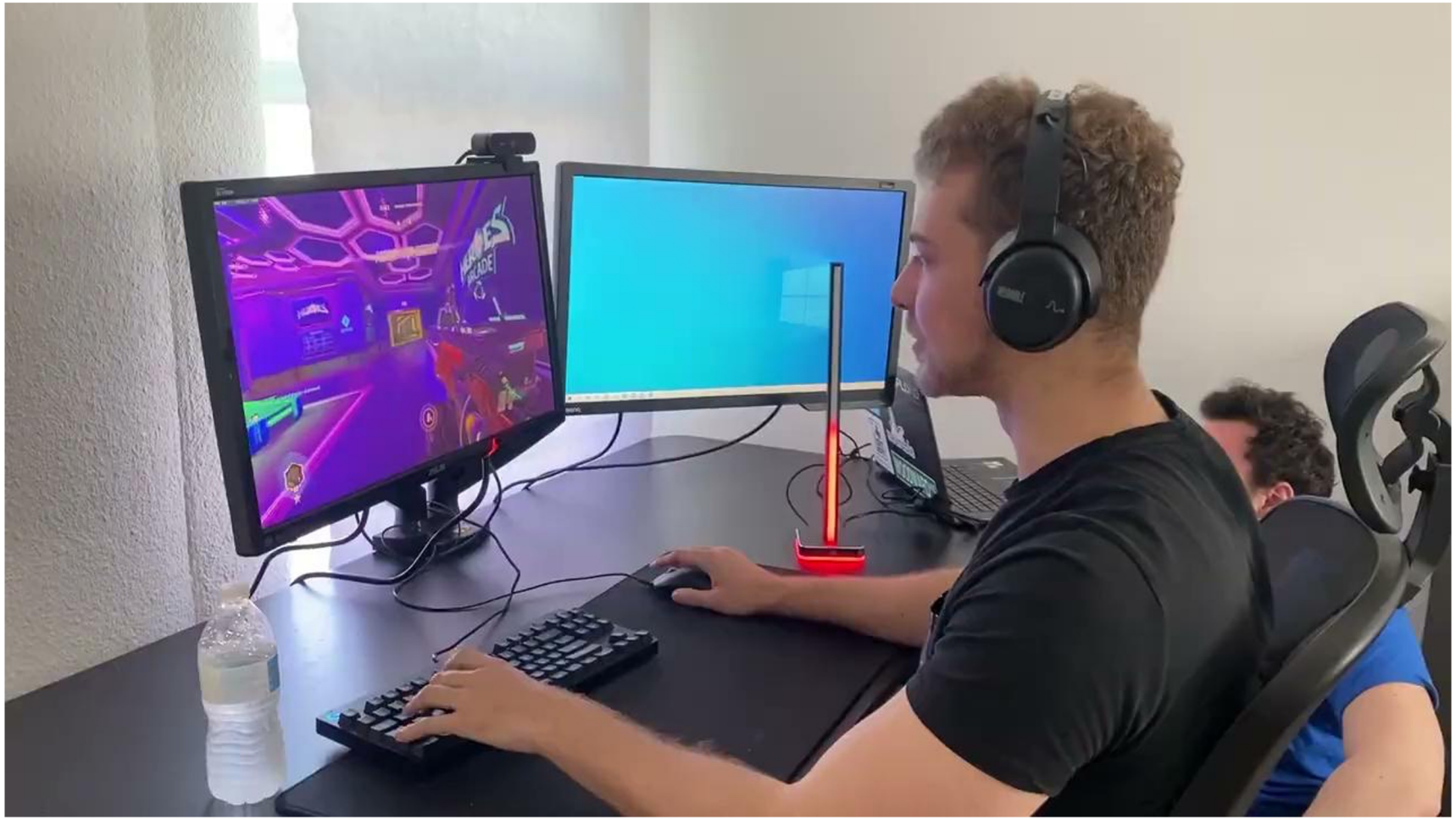
The Mind. Unlocked.



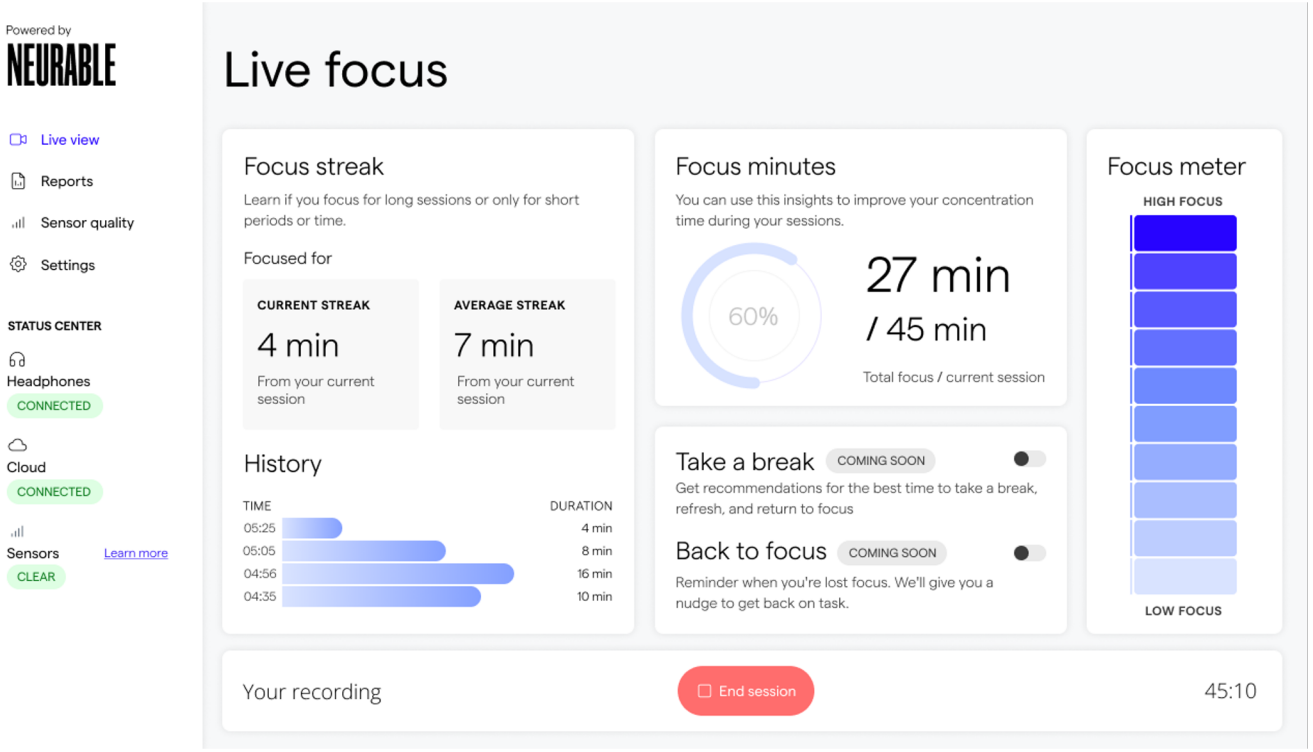
Cognitive Biomarkers And Wellness

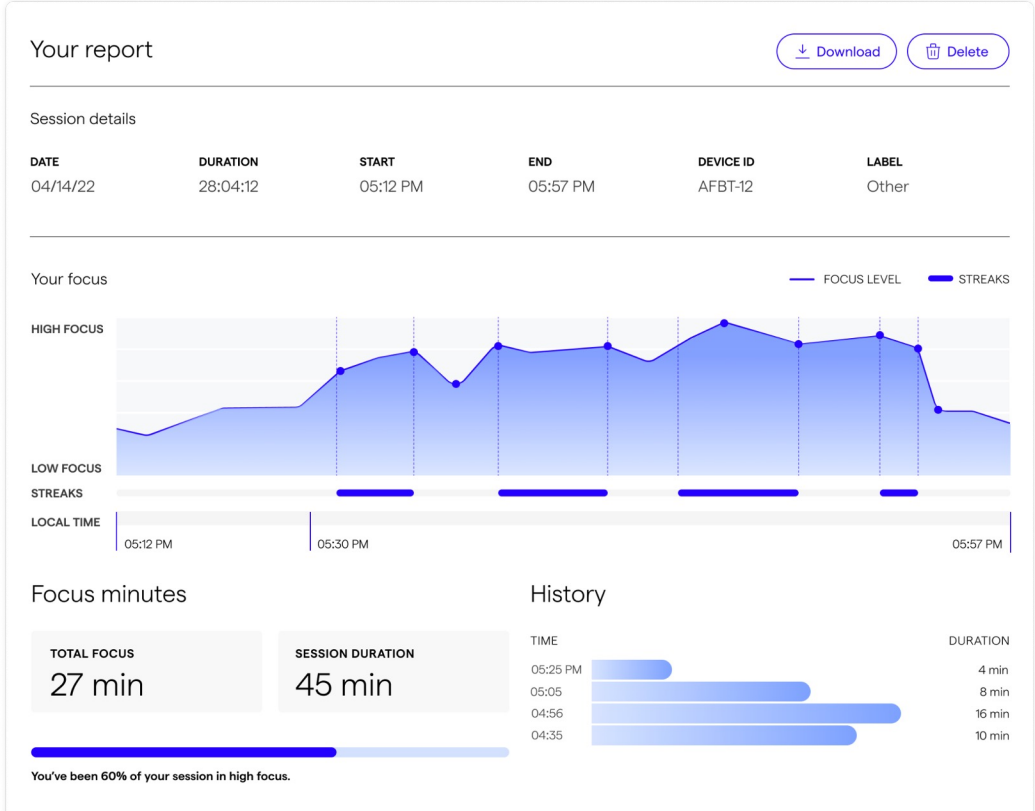
DATA SIZE: Small ~4000
Difficulty: Low

Focus Bar demo or use video

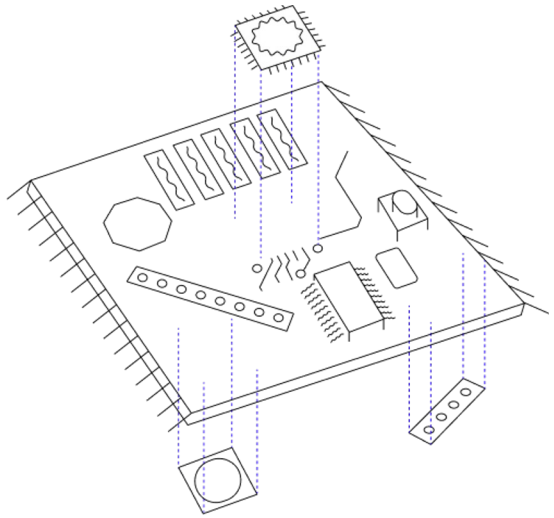


Neurable App





The Mind. Unlocked.



Brain-computer interface control
and silent communication

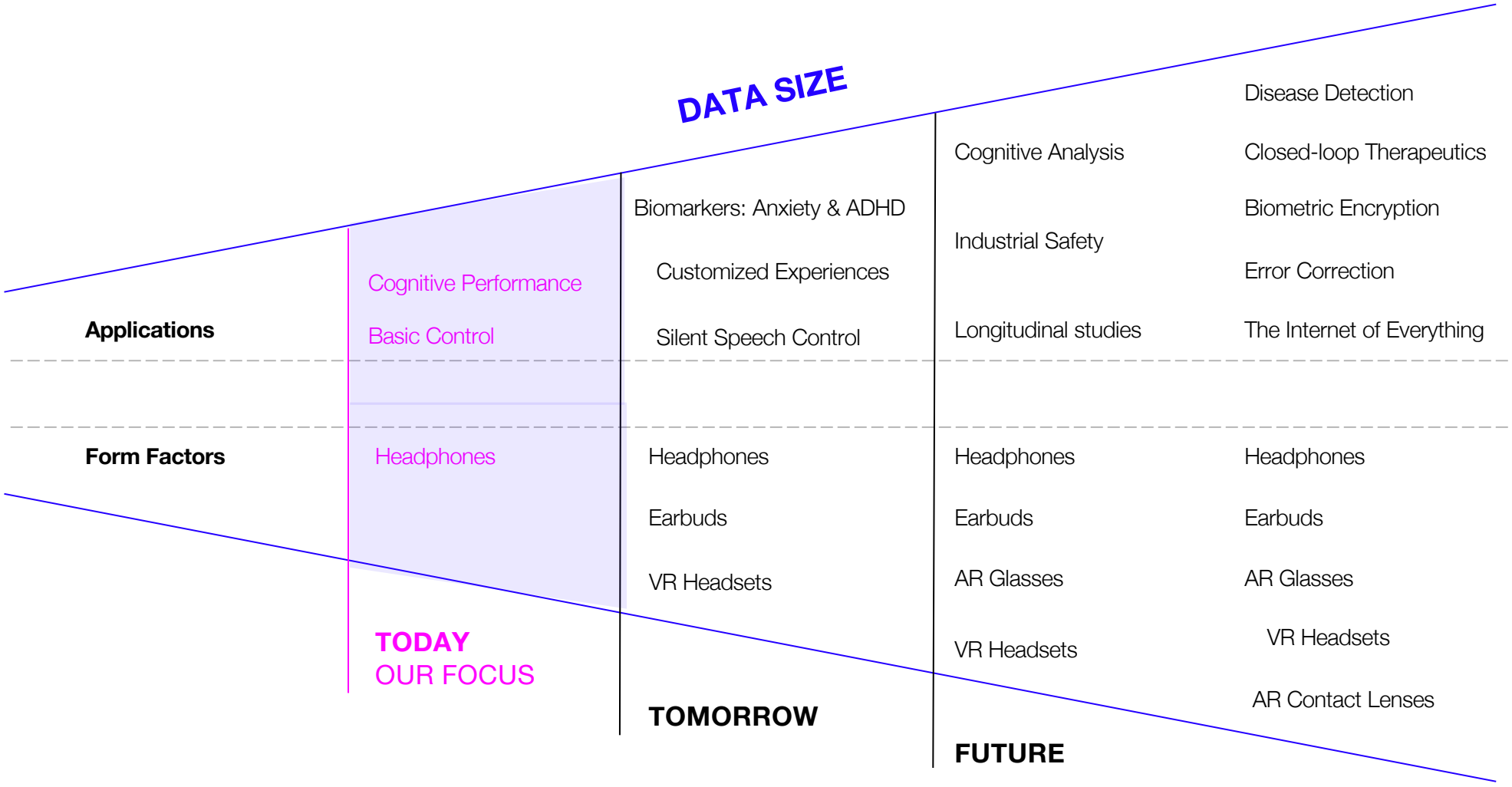
DATA SIZE: Large ~40M
Difficulty: High


EmTech


Songs Of
Leonard Cohen

With greater data our Brain OS platform will enable more for developers and OEMs

Neurable's Brain OS Platform



Neurable’s Brain OS Enables The Most Advanced & Scalable Neurotech Devices

- Air Force & Army Grants and an Air Force sponsor
- Completed Air Force Tech Validation in 2022
- Over 10 existing agreements with leading companies
- First product will launch in 2023 with OEM contracts for 2024 & 2025
- Independent Mayo Clinic study showed 20 decrease in stress and 70% increase in end of day happiness using our technology
- 8 Published papers including in nature

Ruggedized Brain-Computer Interface for Cognitive Vitals

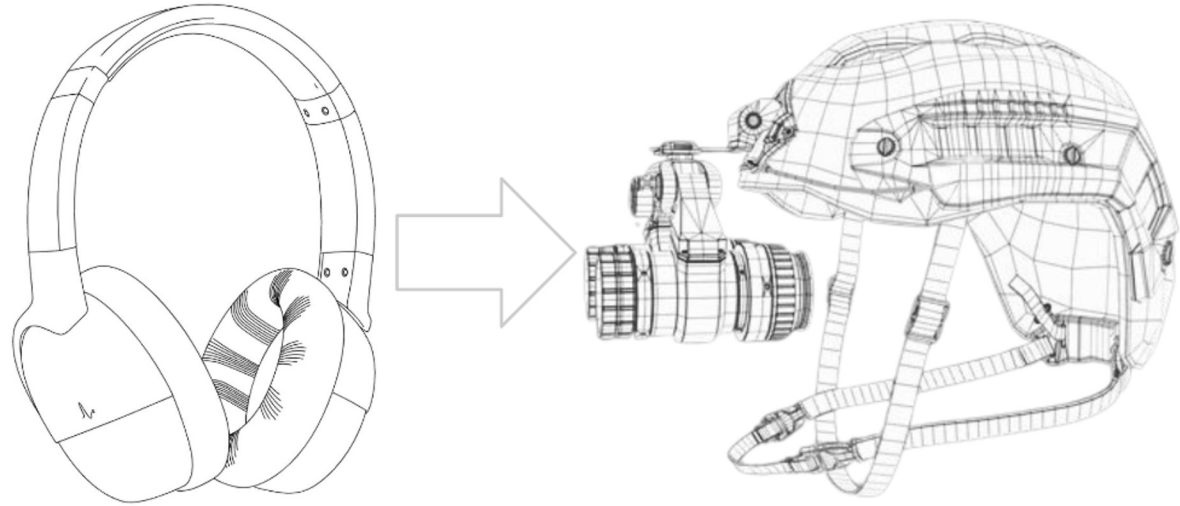
NEURABLE The mind. Unlocked.

22.4D Phase 1 Contract#: FA864923P0207

OVERVIEW.

Neurable's core technology is a **highly accurate and non-invasive EEG signal processing solution** powered by an AI engine that collects, cleans, and interprets EEG data alongside other biological signals to deliver actionable insights via API to commercial and defense end-user applications.

Fatigue, for example, is an insidious threat to aviation safety. In the last two decades, it has been identified as the probable cause of **21–23% of major aviation accidents.**

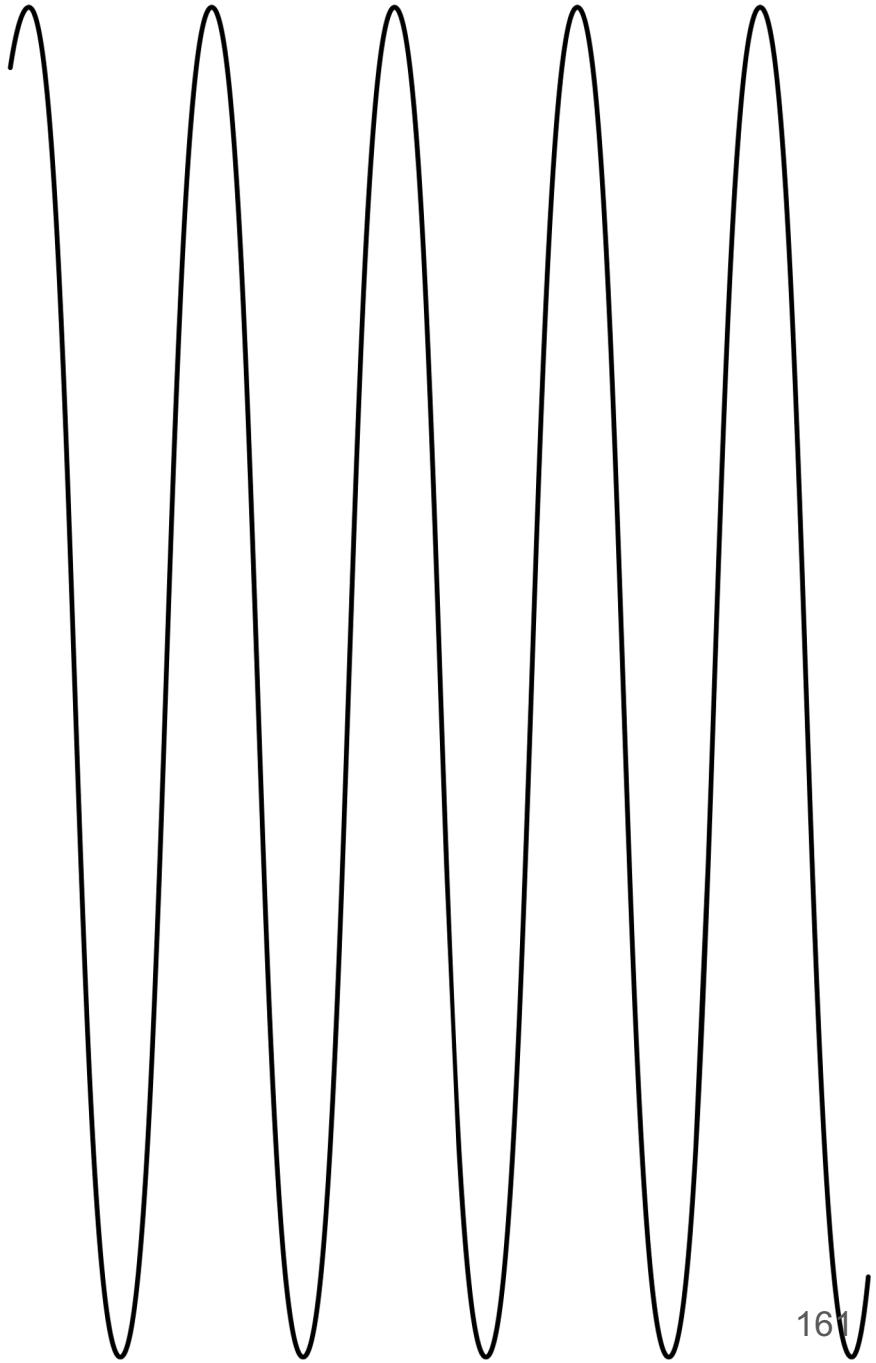


Neurable's non-invasive EEG hardware + software solution is being adapted for the warfighter to monitor cognition, tracking fatigue, and improving human performance when it matters most.

The mind.
Unlocked.

DR. RAMSES ALCAIDE, CEO + CO-FOUNDER (reaa@neurable.com)

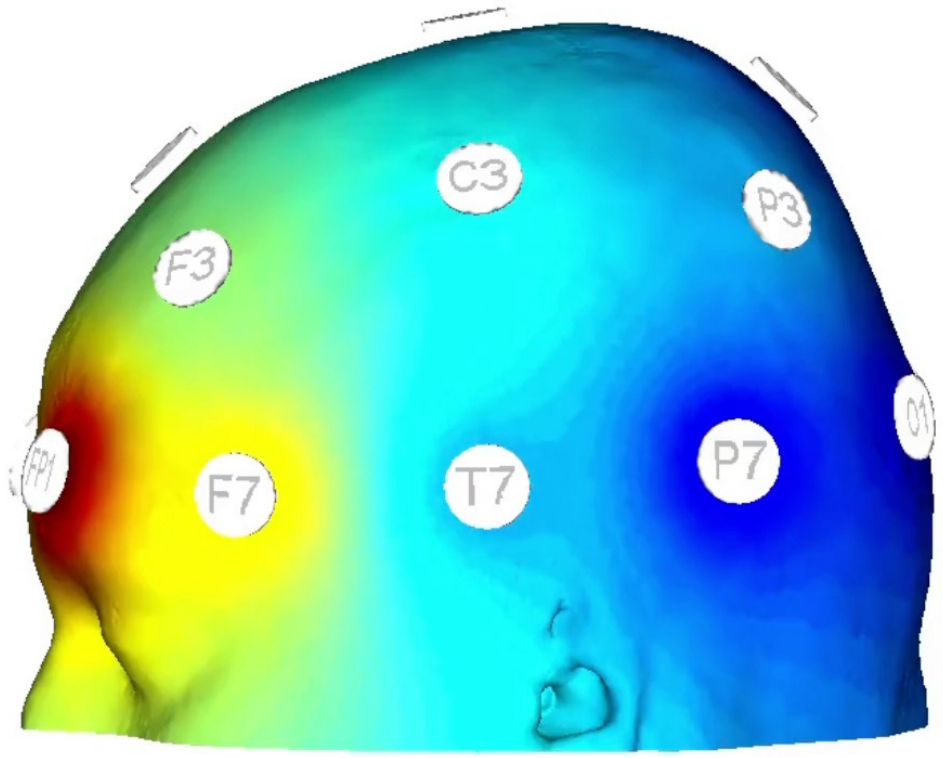
NEURABLE



Neuroelectrics® personalized brain therapy

Ana Maiques
Co-founder & CEO
ana.maiques@neuroelectrics.com

20200803-CONFIDENTIAL


C3
P3
F3
FP1
F7
T7
P7
O1

The Starstim System: Noninvasive read/write platform

At-home TES-EEG with real-time remote supervision

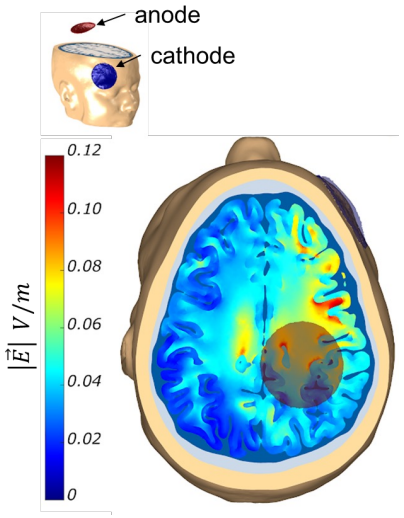
- Simple, easy-to-use design optimized for home use
- Real-time remote access control and monitoring
- Variety of waver forms for different applications
- Simultaneous EEG recordings
- Up to 32 independently-controlled stimulation electrodes
- Platform covered by 7 issued U.S. and European patents
- Manufactured in-house at Barcelona facility

Our Therapeutic Approach: Transcranial Electrical Stimulation (TES)

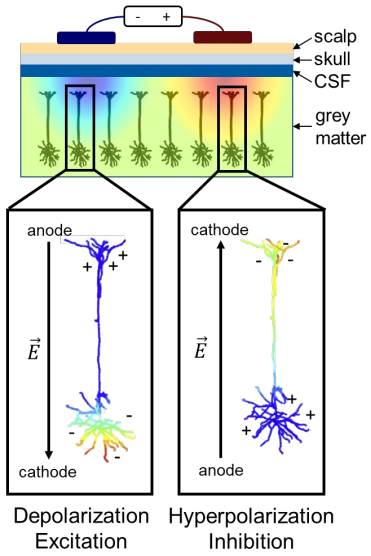
Non-invasive procedure in which a **low-intensity electrical** current is applied to the scalp via multiple electrodes

- Depending on electrode placement, technique can stimulate/suppress neuronal activity in highly specific regions of the brain to correct hypoactivity/hyperactivity
- Studied in >100 clinical trials involving >2,000 patients in a wide variety of CNS and other indications with well established safety profile

Magnitude of Stimulation



Mechanism of Action



Introduction of current generates electric field in the brain

Electric field couples with neurons, altering their membrane potential

Modulating neuronal firing patterns → heightening/reducing excitability

Leading to synaptic remodeling → "rewiring" the brain

Portable technology ideal for home use

Key Advantage of TES: Safety

Similar mechanism of action to electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS), but with much lower electrical fields involved

- Unlike fields generated in ECT and TMS, TES fields are sub-threshold – raise/lower probability
- of neuronal firing but do not “force” firing

Lower TES electric fields allow for more/longer dosing sessions without raising safety/tolerability concerns

Dosing Comparison – Typical Session

Metric (Units)	TES	TMS	ECT
Peak electric field in cortex, E (V/m)	0.2	150	400
Summed time per session, T (s)	1800	~1	0.2
Summed exposure per session, E*T (V*s/m)	360	150	80

Safety meta-analysis by Antal et al (2017) found **no reports of serious adverse events** in over 18,000 patient administrations of TES

Integrated EEG Monitoring Functionality Enables More Complete TES Solution

Safe, non-invasive technique for recording various types of electrical activity within the brain

- Used to diagnose/monitor a wide variety of CNS conditions (e.g., epilepsy, stroke, sleep disorders)

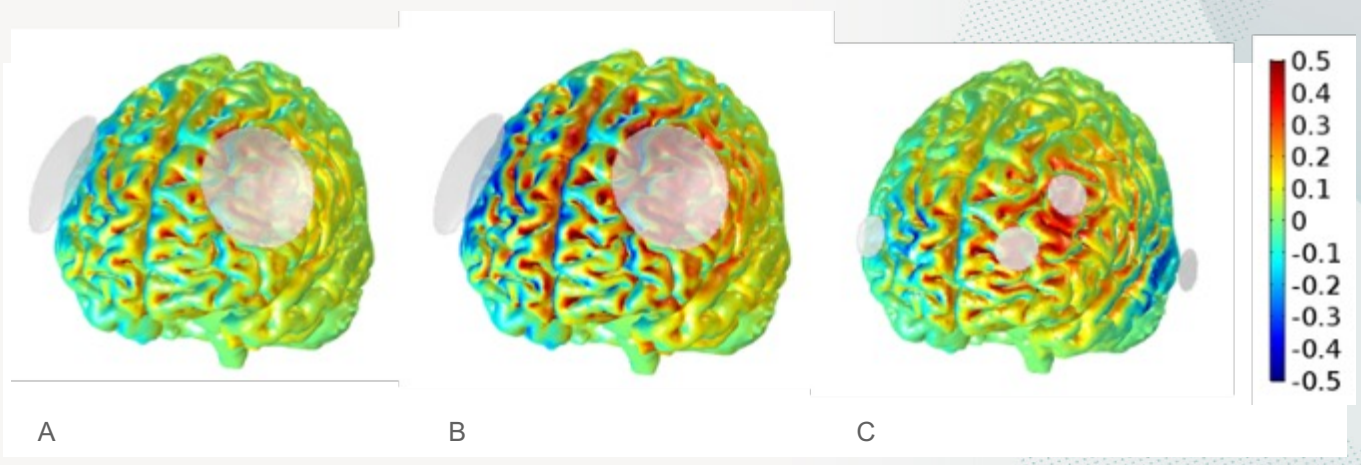
Currently under investigation as a **potential biomarker** in multiple CNS indications

- Diagnostic applications in Parkinson's Disease, Alzheimer's Disease, and ADHD (Ruffini 2019, Rodrigues-Brazete 2016, Motolaisir 2010, Dubreuil-Vall 2020)
- Baseline EEG can predict response to antidepressant medications (Wu 2020)
- Treatment-emergent EEG signatures can predict response to TMS therapy (Isserles 2018)

Necessary element of any **"closed loop" solution** in which TES treatment dynamically and automatically adapts to real-time electrophysiological data

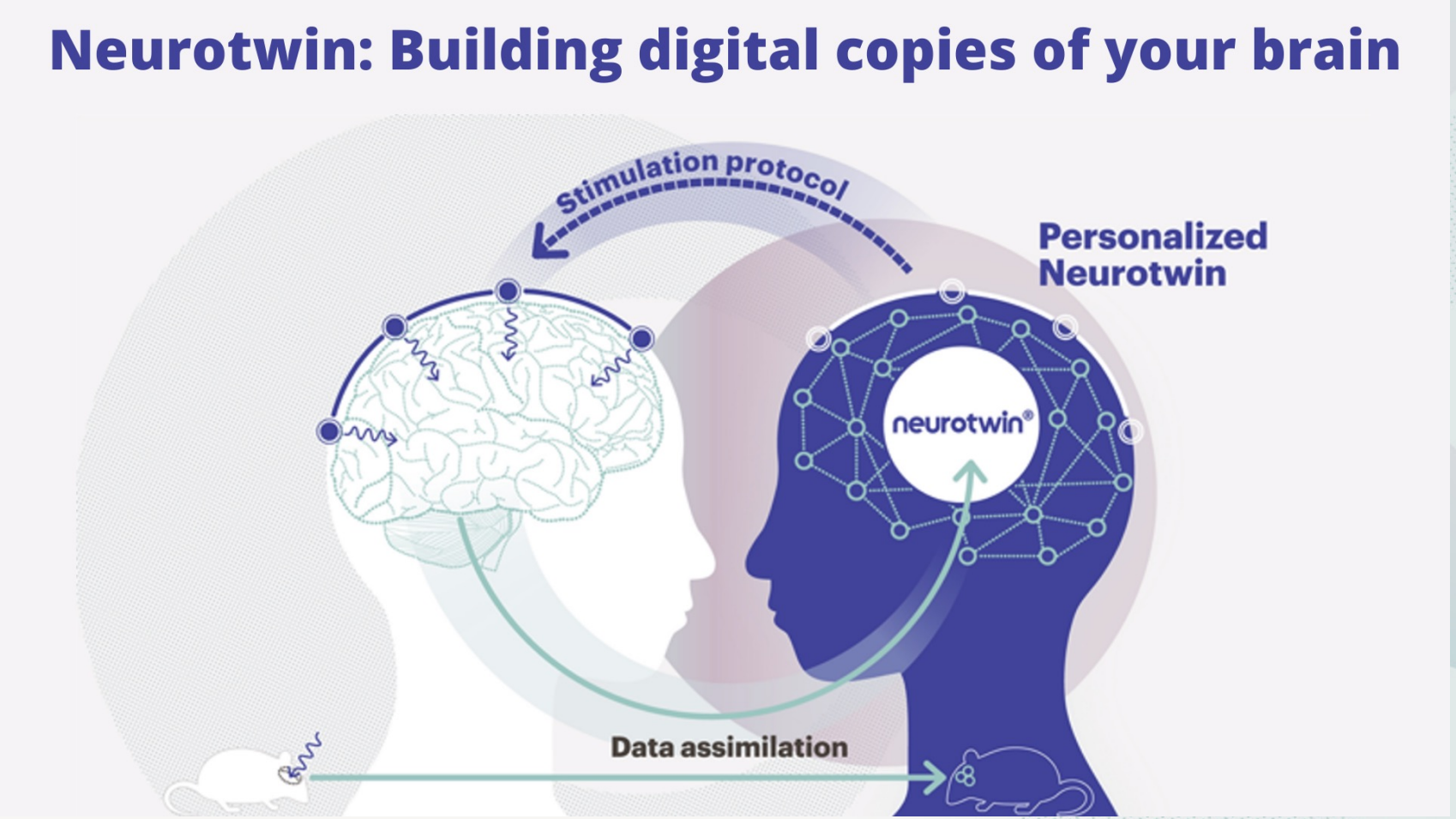
Key Competitive Advantage: Precision

- Traditional bi-polar (two-electrode) approach: “active” anode/(cathode) placed directly over single localized area targeted for neural excitation/(inhibition); return electrode placed over “inactive” area
  - Relatively large electrodes: surface area typically 25-35cm^2
- Starstim multichannel approach: up to 32 bi-directional electrodes (π cm^2 surface area), each with independently-controlled currents
  - Current focal epilepsy and at-home MDD trials utilize 8-channel/39-position version of Starstim device for ease-of-use
- Multichannel montages enable more precise solutions for small, multiple and extended cortical targets
  - Minimal off-target E-fields and multiple electrodes allow higher total current → higher on-target E-fields, lower off-target E-fields

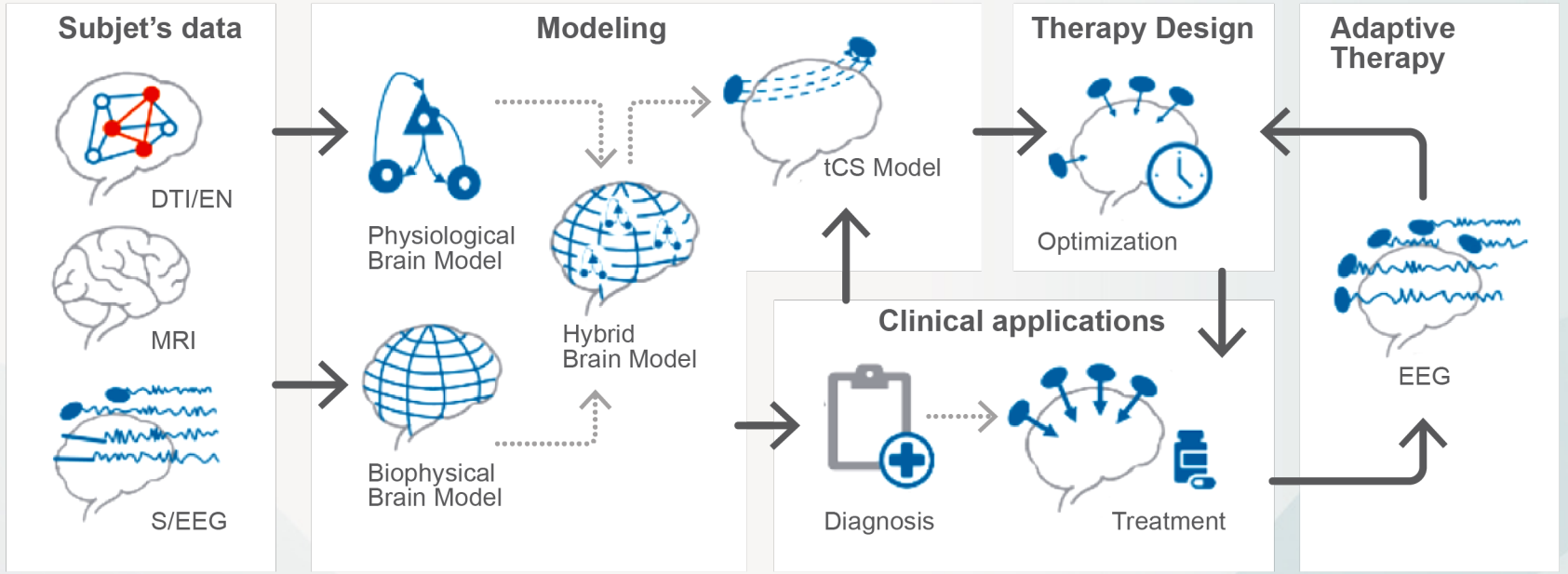


Estimated normal E-field distribution for typical F3/F4 experimental MDD montage with standard 2.0 mA/electrode current limit (image A); normal E-field distribution for F3/F4 montage with electrode current limit raised to 3.1 mA (image B) to match total current of Neuroelectrics multichannel MDD montage; normal E-field distribution for 4-electrode montage used in Neuroelectrics MDD pilot study (image C). Translucent disks represent electrodes.

The Future: Neurotwin



Neurotwin: Truly Personalized Medicine



Workflow for the creation of hybrid models model-driven tES optimization. DTI and anatomical MRI data are combined to create a finite element biophysical model (FEM), which is then personalized using EEG, SEEG, EN and other data to reflect both biophysical and physiologic characteristics – from excitation/inhibition balance to plastic potential (long-term effects physiological model). The personalized hybrid brain model can be used to generate EEG and to simulate the effects of brain stimulation. As a result, personalized diagnosis and treatment can be applied, such as optimized stimulation protocols. Since tES protocols are typically multisession, EEG data collected over time (e.g., at the patient's home using telemedical solutions) can be used to refine models and adapt the stimulation protocols (target map, dosing).


MRI

Epilepsy

neuroelectrics®

Boston Children's Hospital
Until every child is well™

Co-Principal Investigator
Dr. Alexander Rotenberg

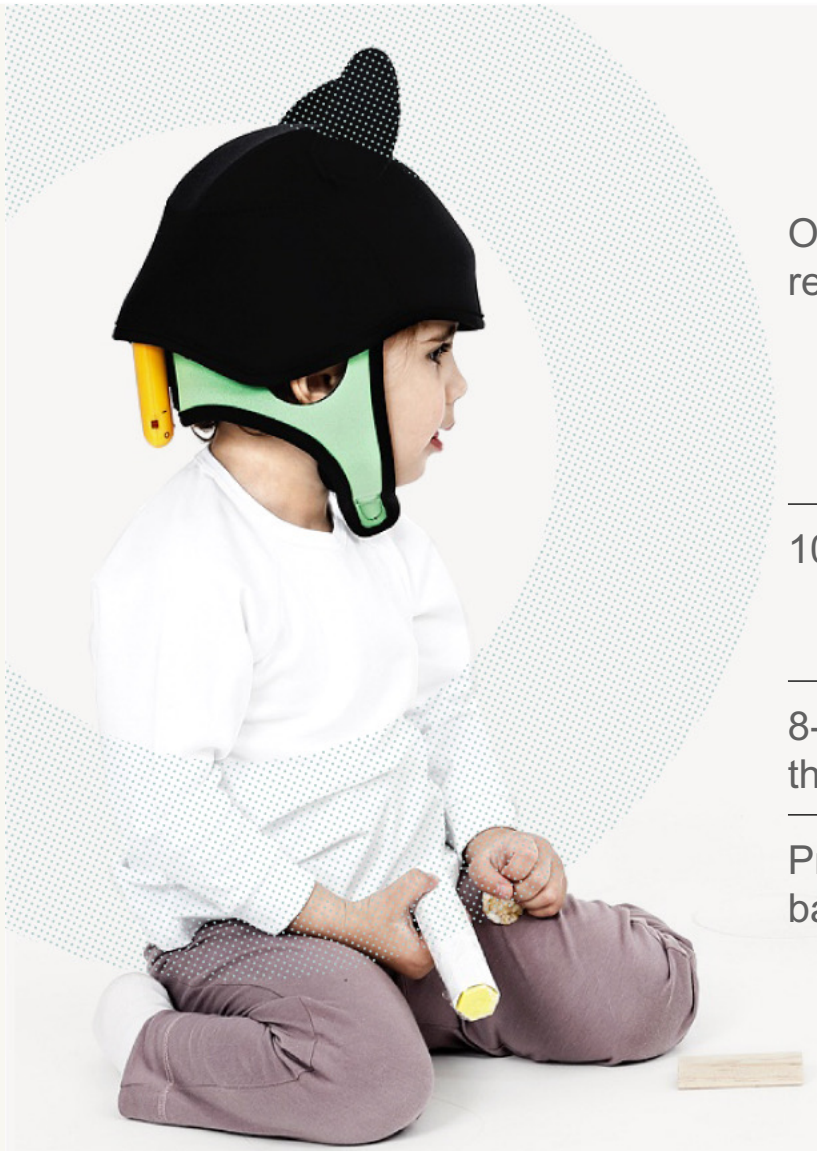
HARVARD MEDICAL SCHOOL

Beth Israel Deaconess Medical Center

MASSACHUSETTS LIFE SCIENCES CENTER

FDA **Breakthrough Designation**

Epilepsy Pilot Study Design



Open-label study in pediatric and adult subjects with medically-refractory, focal epilepsy (N=20)

- Two sites: Boston Children's Hospital and the National Institute of Neurology and Neurosurgery (Mexico City)
- Co-PIs: Alexander Rotenberg, M.D., Ph.D. (BCH, HMS) and Mouhsin Shafi, M.D., Ph.D. (BIDMC, HMS)

---

10 20-minute in-clinic TES sessions over 2 weeks

- TES treatment montages personalized to patient baseline EEG and MRI to ensure focality

---

8-week mandatory follow-up period; many patients followed through week 12

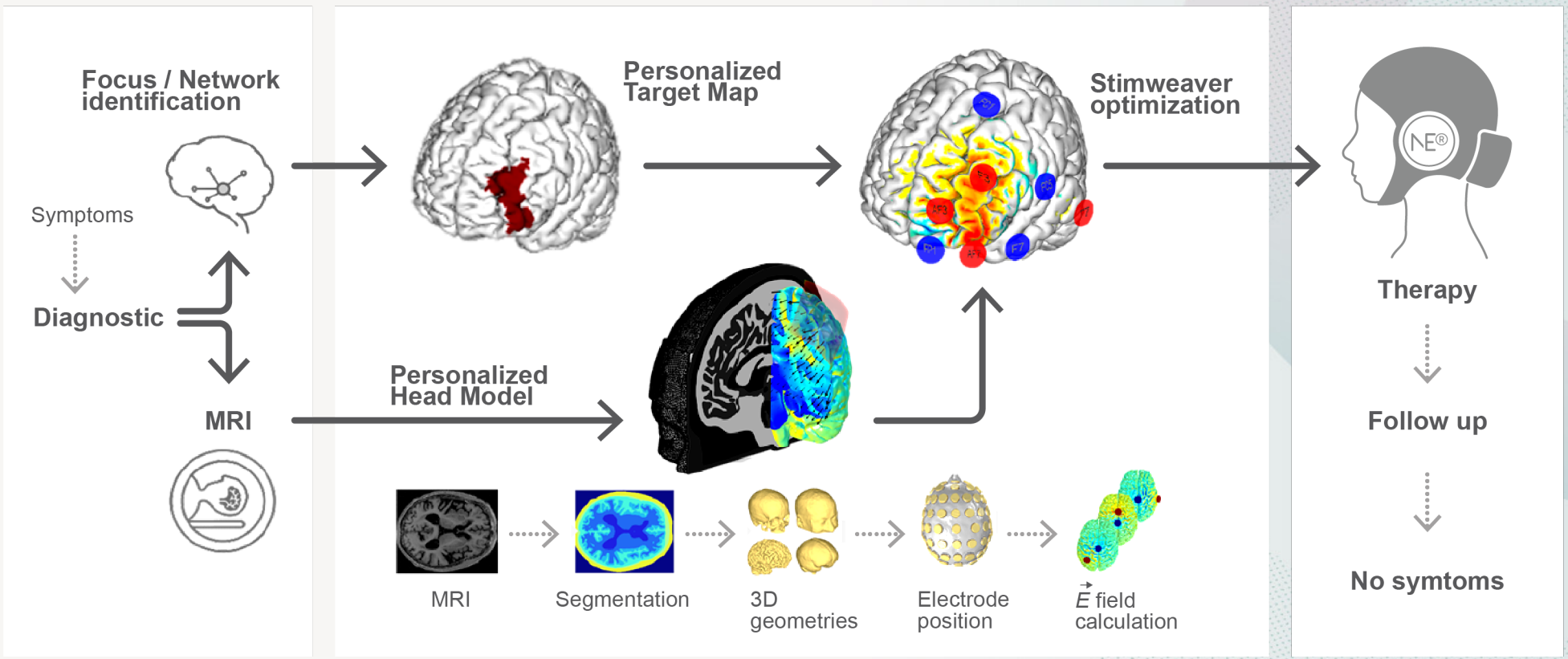
Primary endpoint: seizure frequency reduction from 8-week baseline to 8-week follow-up

Starstim Treatment Paradigm

Step 1: Diagnosis
Electrophysiological focus of disorder identified by doctor using MRI, EEG, etc.

Step 2: Personalization
Neuroelectrics builds individual brain/head model and calculates optimal protocol montage.

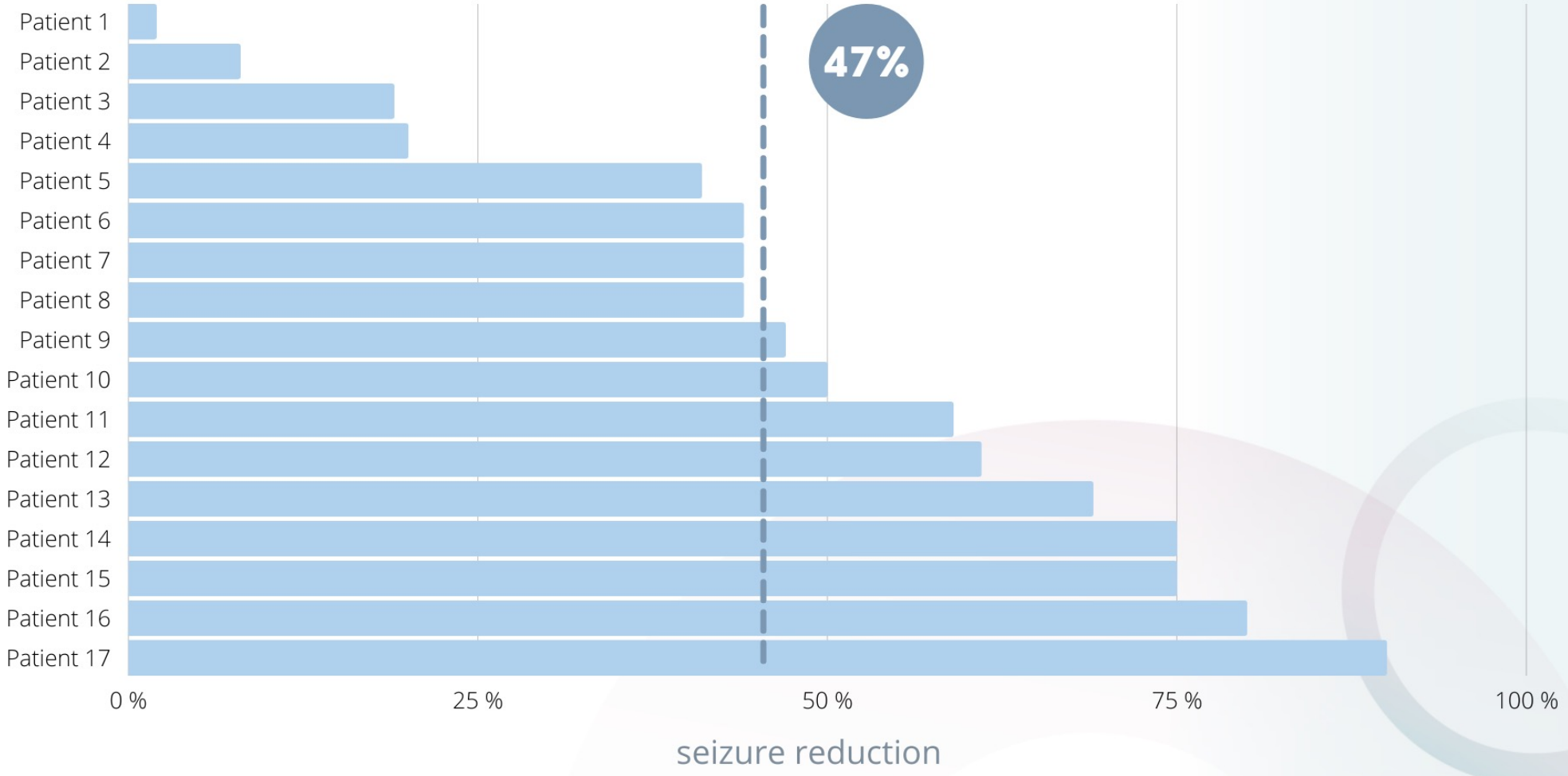
Step 3: Treatment
Personalized protocol montage downloaded into hardware; treatment begins.



Starstim Treatment Paradigm

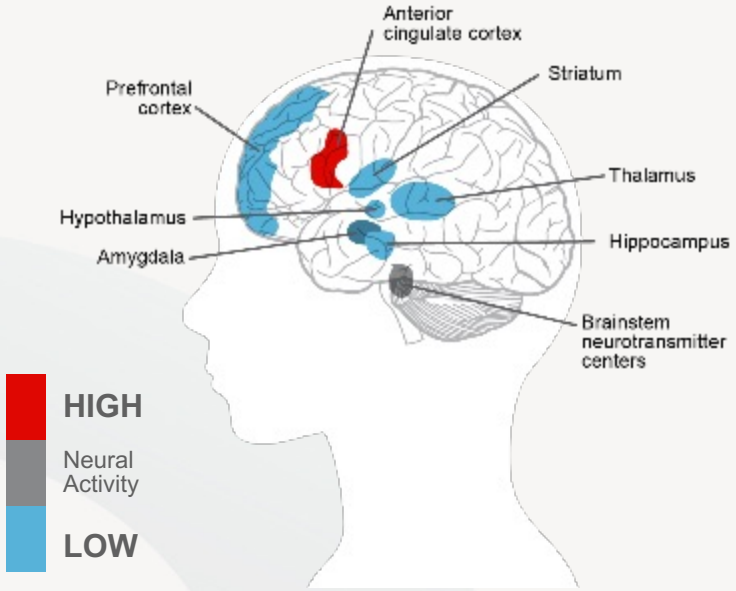
REDUCING SEIZURES BY 47%

FDA Breakthrough Device Designation



Follow-On Indication: Depression FDA IDE study

Major Depressive Disorder (MDD)



In MDD, some areas of the brain are Hypoactive and others are Hyperactive

Target indication: refractory MDD

- 1.9M U.S. refractory patients; >28M globally
- Therapeutic alternatives include TMS, VNS, ECT

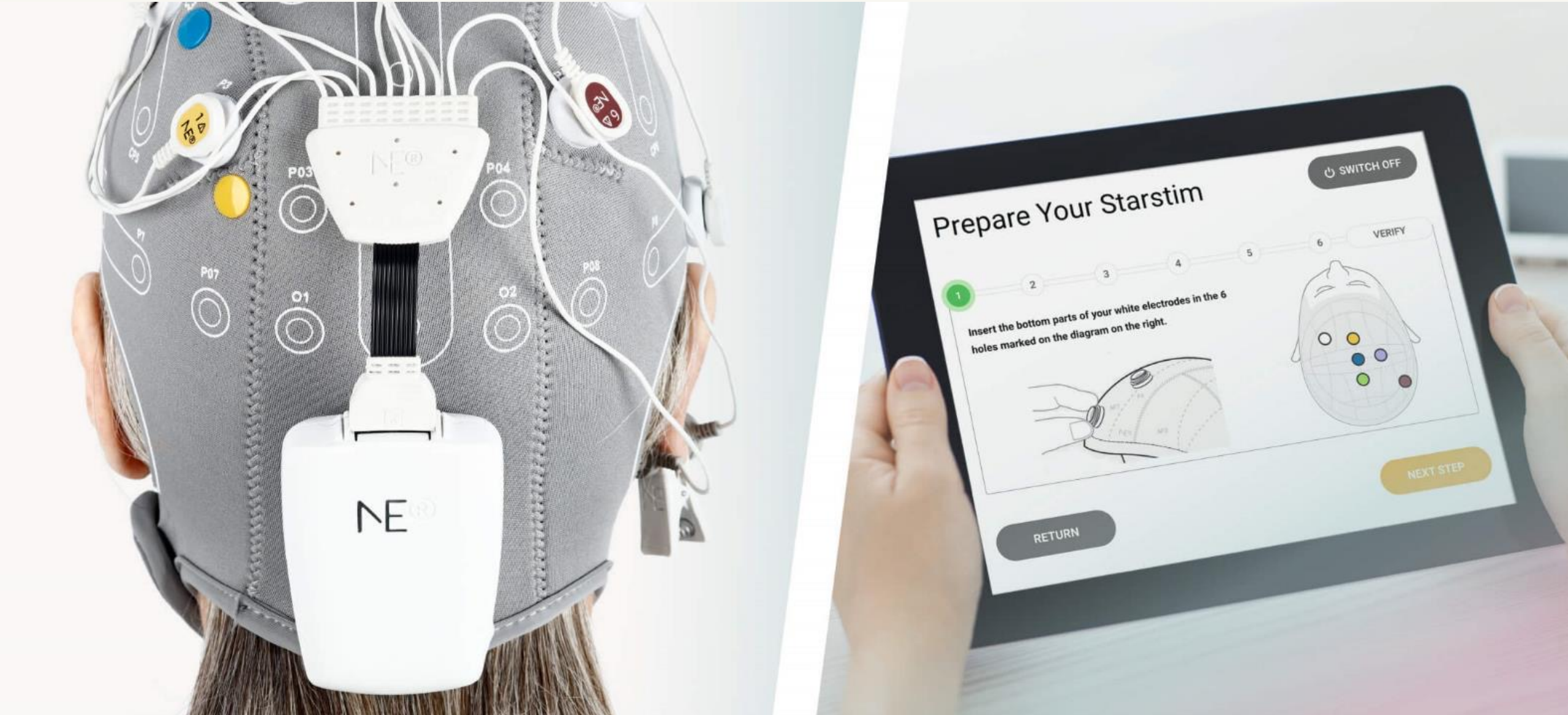
Mechanistic rationale

- MDD characterized by reduced left vs right neuronal activity in dorsolateral prefrontal cortex (DLPFC)
- Application of neuromodulatory electric field on left DLPFC stimulates neuronal activity in this region, restoring electrophysiological function
- Plasticity from repeated application believed to lead to healthy rewiring of fronto-limbic network

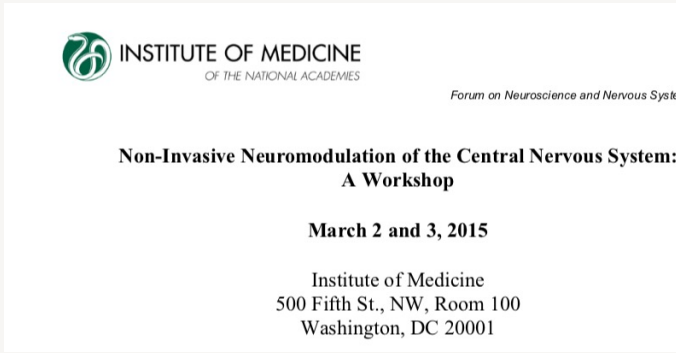
Protocol

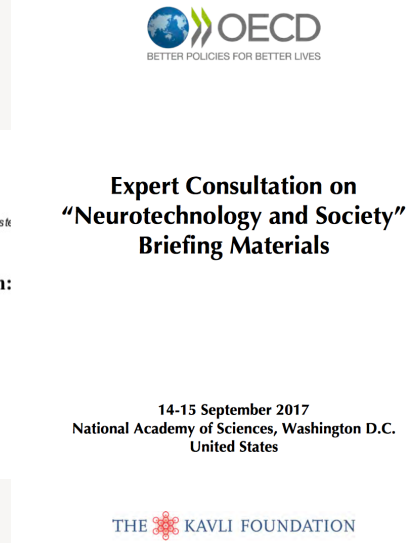
- 30 patient, open-label, 12-week safety/feasibility study in refractory MDD
- 37 at-home TES sessions administered by patient with help from caregiver
- 30-min sessions; 2.0mA total injected current limit across all electrodes
- Primary efficacy endpoint: change in MADRS score
- Secondary endpoints: QIDS-SR, QLES-Q-SF, CogState

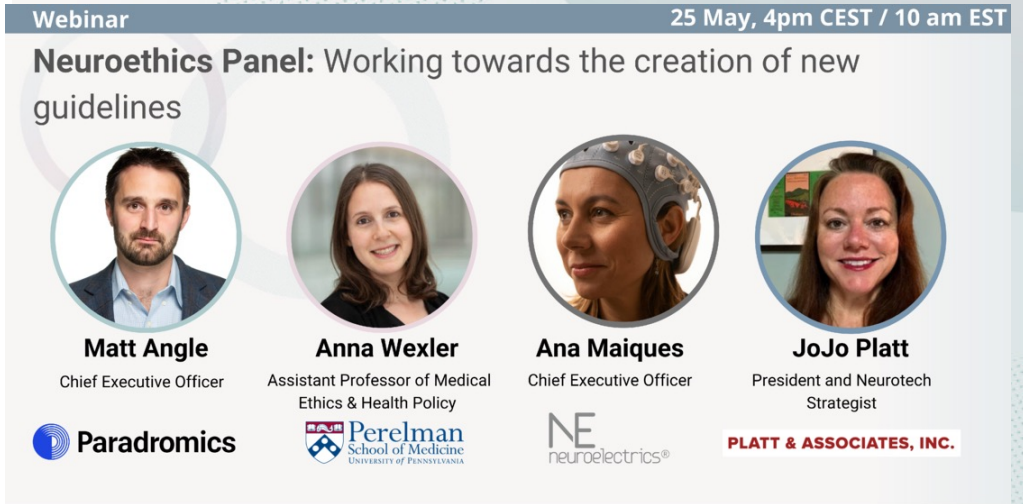
Home use


P03
P04
P07
O1
O2
P08
Prepare Your Starstim
SWITCH OFF
VERIFY
1
2
3
4
5
6
Insert the bottom parts of your white electrodes in the 6 holes marked on the diagram on the right.
NEXT STEP
RETURN

My Neuroethics Journey





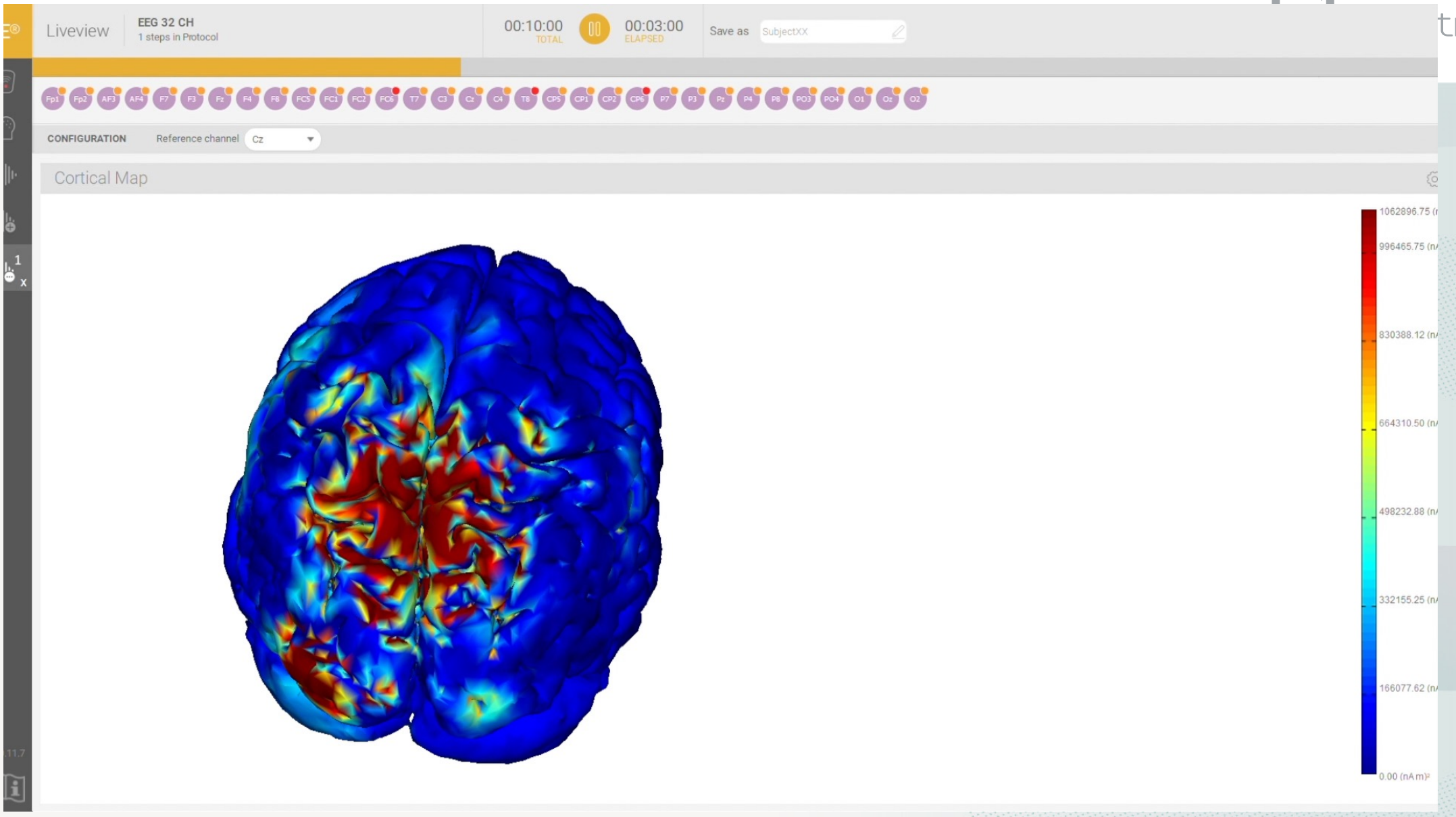


Some discussion issues

- On the ethical side would be good to have a set of guidelines like for IBI taking issues like responsibility, data privacy, identity and equity.
- The FDA has been amazing, but some questions remain on the regulation of personalization pieces like Neurotwin. Brain therapy at home still has some open issues.
- In general the complexity, cost and time to market of non invasive technologies for patient population is still a big burden for most innovators/entrepreneurs and patients are waiting.
- There are 15k users in reddit doing self stimulation and a potential increase of consumer devices in similar technologies to increase memory, learning or others.

Our Team

neuroelectrics®


Liveview
EEG 32 CH
1 steps in Protocol
00:10:00
TOTAL
00:03:00
ELAPSED
Save as
SubjectXX
Fp1 Fp2 AF3 AF4 F7 F3 Fz F4 F8 FC5 FC1 FC2 FC6 T7 C3 Cz C4 T8 CP5 CP1 CP2 CP6 P7 P3 Pz P4 P8 PO3 PO4 O1 Oz O2
CONFIGURATION
Reference channel
Cz
Cortical Map
1062896.75
996465.75
830388.12
664310.50
498232.88
332155.25
166077.62
0.00 (nA m)²

Thanks for helping us

Ana Maiques
Co-Founder and CEO
ana.maiques@neuroelectrics.com

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Rune Labs

Brian Pepin

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Q&A

BCI Commercialization Part II

Brain Computer Interface Export Controls Conference

February 16-17, 2023

FDA

U.S. FOOD & DRUG ADMINISTRATION

Regulation of Brain Computer Interface (BCI) Devic

David McMullen, MD

Office Director

OHT5: Office of Neurological and Physical Medicine Devices
Office of Product Evaluation and Quality (OPEQ)
Center for Devices and Radiological Health (CDRH)
Food and Drug Administration (FDA)

No Financial Disclosures

FDA U.S. FOOD & DRUG ADMINISTRATION

FDA


Center for Food Safety & Applied Nutrition


Center for Drug Evaluation & Research


Center for Biologics Evaluation & Research

Center for Tobacco Products


Center for Devices & Radiological Health


Center for Veterinary Medicine


National Center for Toxicological Research

Office of Health Technology 5: Office of Neurological and Physical Medicine Devices

David McMullen, MD, Office Director

John Marler, MD, Deputy Office Director

CAPT Nina Mezu-Nwaba, PharmD, MPH, MSc, Deputy Office Director

Christopher Loftus, MD, Chief Medical Officer

Sergio de del Castillo, Associate Director for Policy

Division 5A: Division of Neurosurgical, Neurointerventional, & Neurodiagnostic Devices

Xiaolin Zheng, PhD, Division Director

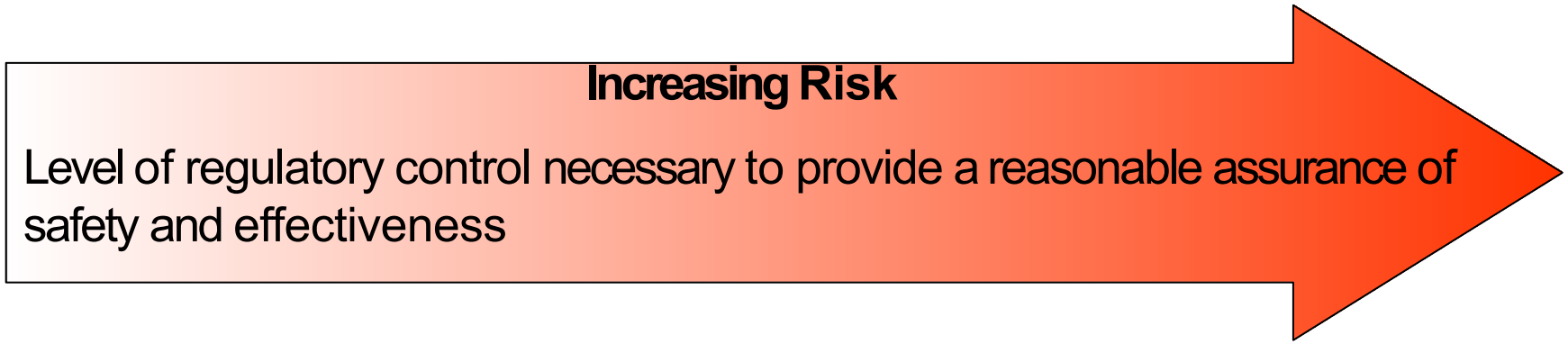
Neurosurgical Team Adam Pierce, PhD	Neurointerventional Team Naira Muradyan, PhD	Neurodiagnostic Team Jay Gupta, MS,
Cranial Materials Other Neurosealants Materials Neuro-Ablative Devices Surgical Instruments Stereotactic Systems	Embolization Coils Flow Diverters Guidewires & Catheters Neurothrombectomy devices CSF Shunts and Drainage Catheters	EEG+ Non EEG devices Neurocognitive Devices Mobile Medical Applications for Neurodiagnostic uses

Division 5B: Division of Neuromodulation and Physical Medicine Devices

Vivek Pinto, PhD, Division Director

Neurostimulation-Neurology Team CDR Jitendra Virani, MS	Neuromodulation – Psychiatry Team Pamela Scott, MS	Physical Medicine – Acute Injury Team Heather Dean, PhD	Physical Medicine – Neurodegenerative Team Amber Ballard, PhD
Deep Brain Stimulation and non-invasive devices for Alzheimer's Disease Epilepsy Headache Movement Disorders	Deep Brain Stimulation Vagal Nerve Stimulation Computerized Behavioral Therapy Digital Therapeutics for Major Depression PTSD Anxiety Insomnia	Assistive Devices **Brain Computer Interface Devices** Medical Exoskeletons Prosthetic Devices Orthoses Wheelchairs Walkers	Pain Therapy Devices Spinal Cord Stimulation Diathermy Devices Transcutaneous electrical stimulation Powered muscle stimulation Traction devices

A Risk Based Approach for Medical Devices since 1976

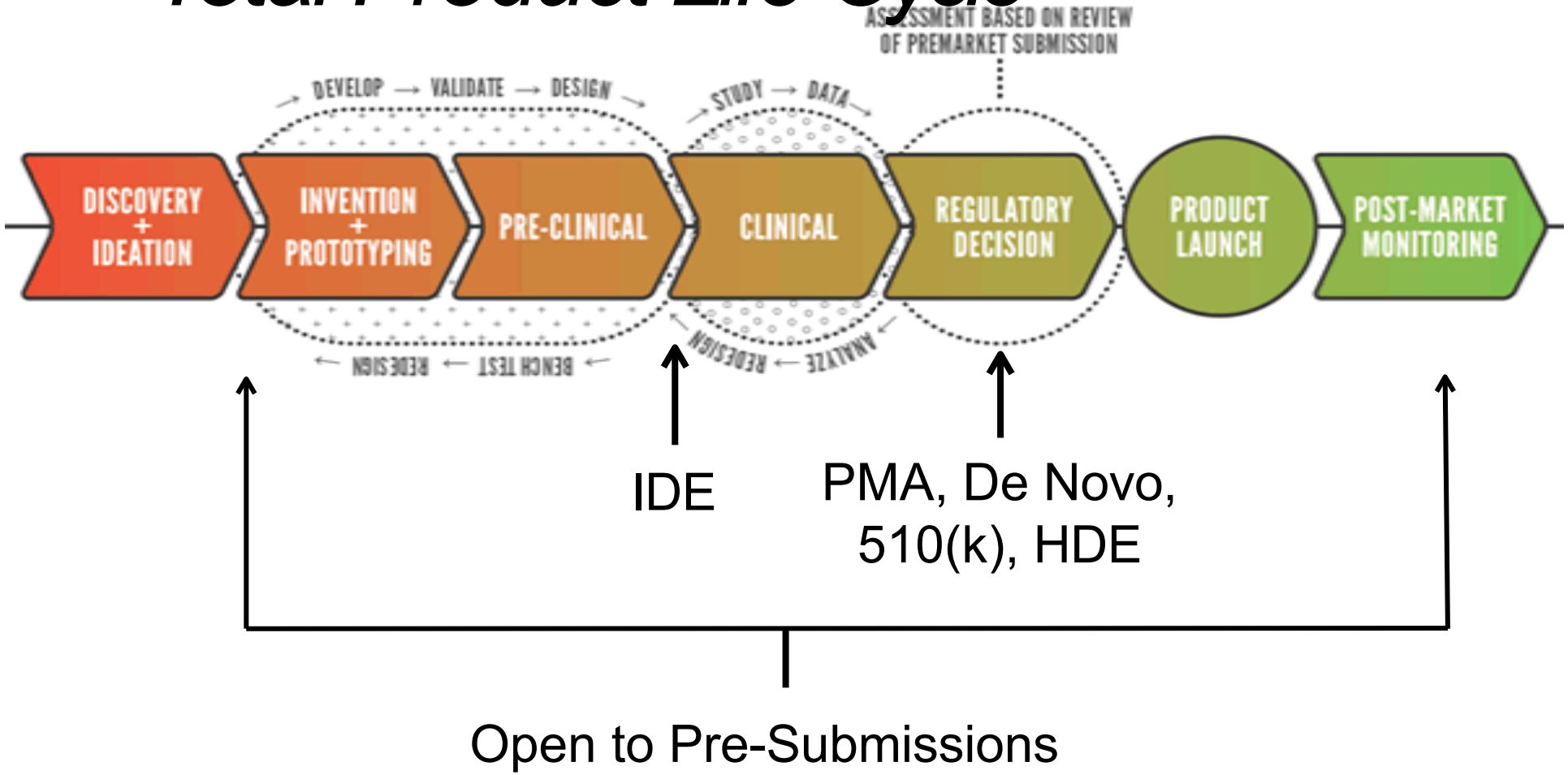


Class I
Low Risk
- Generally exempt from premarket review
- In some cases require 510(k) / De Novo

Class II
Moderate/Controlled Risk
- Requires 510(k) to demonstrate substantial equivalence
- OR De Novo if no classification exists

Class III
High Risk
- Requires PMA (Premarket approval)

Total Product Life Cycle



BCI Clinical Trials

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Recruiting	COMMAND Early Feasibility Study: **Implantable** BCI to Control a Digital Device for People With Paralysis	• Neurologic Disorder • Paralysis • Paralysis; Stroke • (and 9 more...)	• Device: Motor Neuroprosthesis (MNP)	• Mount Sinai Health System New York, New York, **United States** • University of Pittsburgh Medical Center Pittsburgh, Pennsylvania, **United States**
2	☐	Completed Has Results	ECoG Direct **Brain Interface** for Individuals With Upper Limb Paralysis	• Tetraplegia • Spinal Cord Injury • Brachial Plexus Injury • (and 3 more...)	• Device: Implantation of ECoG sensors on the **brain** surface	• University of Pittsburgh Pittsburgh, Pennsylvania, **United States**
3	☐	Completed	Microelectrode **Brain**-Machine **Interface** for Individuals With Tetraplegia	• Tetraplegia • Spinal Cord Injury	• Device: Implantation of NeuroPort Arrays in the motor cortex	• University of Pittsburgh Pittsburgh, Pennsylvania, **United States**
4	☐	Recruiting	Acute Modulation of Stereotyped High-Frequency Oscillations	• Epilepsy	• Device: **Brain** Interchange System	• Baylor College of Medicine Houston, Texas, **United States** • University of Houston Houston, Texas, **United States**
5	☐	Recruiting	Cortical Recording and Stimulating Array **Brain**-Machine **Interface**	• Tetraplegia • Spinal Cord Injury • Brainstem Stroke • (and 2 more...)	• Device: Implantation of CRS Arrays	• University of Pittsburgh Pittsburgh, Pennsylvania, **United States**
6	☐	Recruiting	Investigation on the Cortical Communication (CortiCom) System	• Tetraplegia • Locked-in Syndrome • Brainstem Stroke • Amyotrophic Lateral Sclerosis	• Device: Surgical implantation of CortiCom system	• Johns Hopkins Medicine Baltimore, Maryland, **United States**
7	☐	Recruiting	Optimization of Human Cortical Stimulation	• Epilepsy • **Brain** Injury	• Procedure: Low-level cortical stimulation	• Harborview Medical Center Seattle, Washington, **United States**
8	☐	Recruiting	Visuomotor Prosthetic for Paralysis	• Quadriplegia	• Device: Neural Communication System	• University of California Los Angeles Los Angeles, California, **United States** • California Institute of Technology Pasadena, California, **United States** • Casa Colina Centers for Rehabilitation Pomona, California, **United States**
9	☐	Completed Has Results	Providing **Brain** Control of Extracorporeal Devices to Patients With Quadriplegia	• Tetraplegia	• Device: Neural Prosthetic System	• Rancho Los Amigos National Rehabilitation Center Downey, California, **United States** • University of Southern California

From clinicaltrials.gov

Neuro/BCI specific Resources

- Webinar on Implanted BCI Devices for Patients with Paralysis or Amputation - Non-clinical Testing and Clinical Considerations Final Guidance
  - https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/webinar-implanted-bci-devices-patients-paralysis-or-amputation-non-clinical-testing-and-clinical

- Implanted Brain-Computer Interface (BCI) Devices for Patients with Paralysis or Amputation - Non-clinical Testing and Clinical Considerations
  - https://www.fda.gov/media/120362/download

- Overview on Neurological Devices
  - http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/NeurologicalDevices/default.htm

- FDA Perspectives on the Regulation of Neuromodulation Devices
  - https://onlinelibrary.wiley.com/doi/abs/10.1111/ner.13085

- FDA Regulation of Neurological and Physical Medicine Devices: Access to Safe and Effective Neurotechnologies for All Americans
  - https://www.cell.com/neuron/pdf/S0896-6273(16)30786-3.pdf

What Is a Collaborative Community?

Collaborative communities are continuing forums where public and private sector members proactively work together to:

- Achieve common objectives and outcomes
- Solve shared challenges
- Leverage collective opportunities in an environment of trust, respect, empathy and openness.

Please visit CDRH website (https://www.fda.gov/about-fda/cdrh-strategic-priorities-and-updates/collaborative-communities-addressing-health-care-challenges-together) for a Collaborative Communities Toolkit.

CONTACT INFORMATION

- David McMullen, MD David.McMullen@fda.hhs.gov
- Director, Office of Neurological and Physical Medicine Devices, Office of Product Evaluation and Quality

- Heather Dean, PhD Heather.Dean@fda.hhs.gov
- Assistant Director, Physical Medicine – Acute Injury Devices Team, Division Neuromodulation and Physical Medicine Devices

- Julia Slocomb, PhD Julia.Slocomb@fda.hhs.gov
- Lead Reviewer, Physical Medicine – Acute Injury Devices Team, Division of

Patients are at the Heart of What We Do

CDRH Vision

Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Global Collaboration

The University of Texas at Austin
WHAT STARTS HERE CHANGES THE WORLD

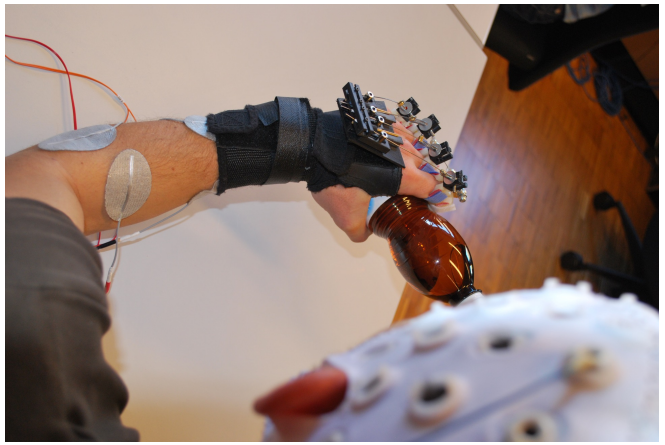
Brain-Computer Interfaces: A Collaborative, International Enterprise

José del R. Millán

Dept of Electrical and Computer Engineering

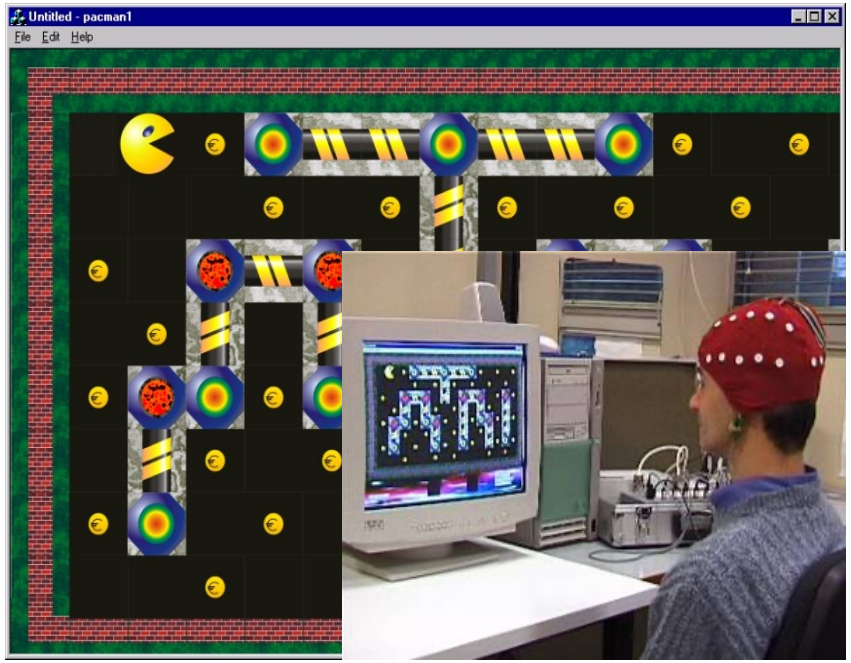
Dept of Neurology

University of Texas at Austin

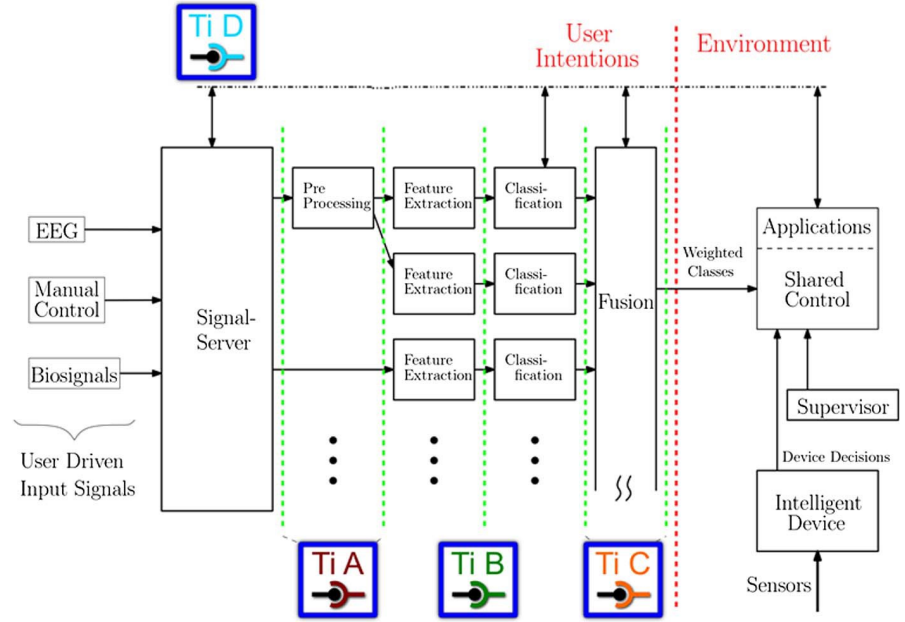


BCI: EU Perspective and Years

- Multinational cooperative projects, including industry partners
- Multidisciplinary
- PI of several projects: 1st BCI, largest BCI (13 partners)



Joint Research Centre of the EU, Italy



Swiss Federal Institute of Technology, Lausanne

International BCI Society

> 500 members

> 40 countries

Board member since inception in 2015, current Past-President

8th Int. BCI Meeting, June 7-9, 2021 (virtual):

395 delegates, 271 labs, 41 countries

Cybathlon: Mutual Learning

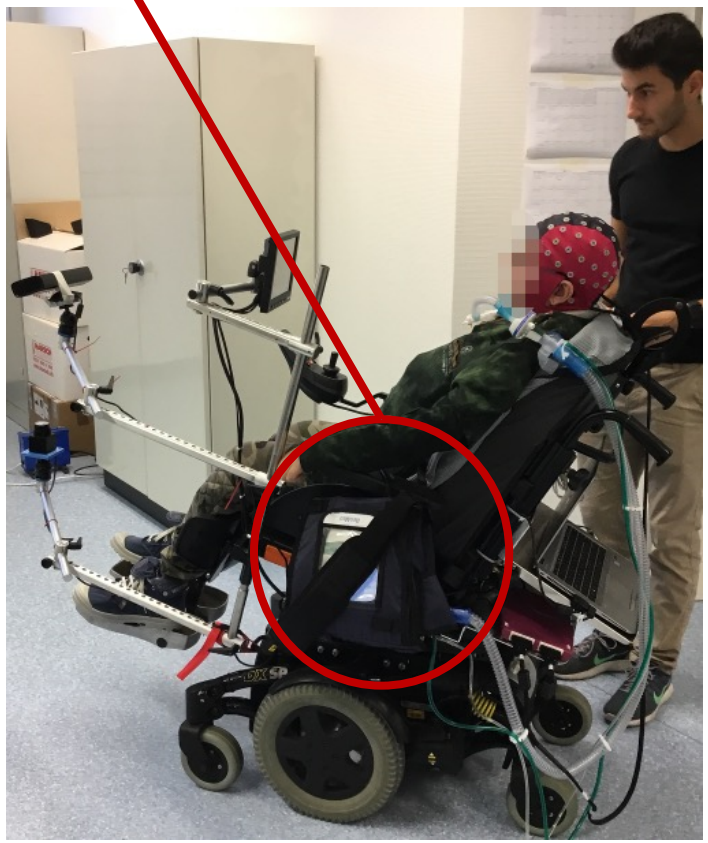
- first competition for disabled individuals in control of bionic assistive technologies
- 2 tetraplegic pilots
- 7/3 months of training
- Gold medal, race time record

(Perdikis et al., IEEE Spectrum 2017; PLoS Biol 2018)

Brain-Controlled Wheelchair: Clinical Evaluation

Patient P1

- Age: 25
- Pathology: Complete tetraplegia sub C3
- *Assisted ventilation*



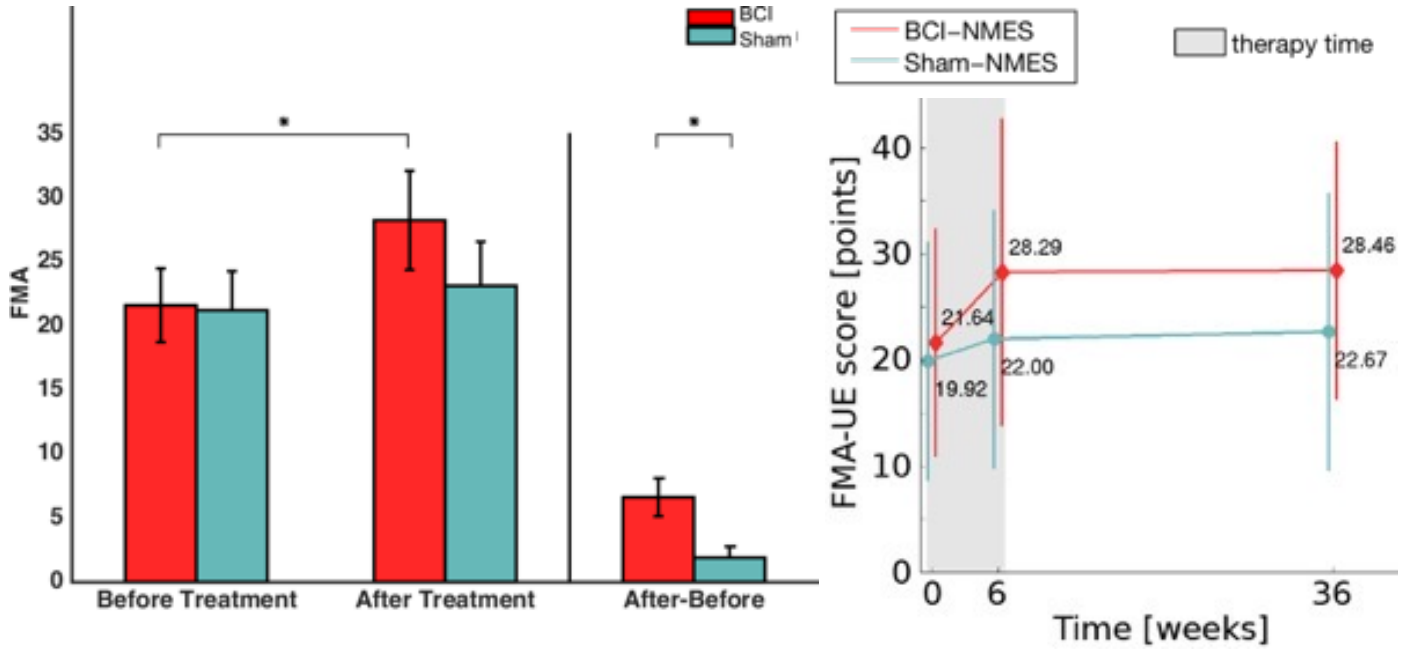
Universitätsklinikum
Bergmannsheil
Bochum, Germany

(Tonin et al., iScience 2022)

Motor Rehabilitation: Stroke

- BCI + Neuromuscular electrical stimulation (NMES)

  Promoting brain plasticity by closing the loop between motor intention and proprioceptive feedback



(Biasiucci et al., Nature Comm 2018)

BCI: Participants

> 1,300 subjects

> 200 subjects with severe motor disabilities

increase this figure

expand to cognitive disabilities

accelerate translation

strong, multidisciplinary ecosystem
academia, industry, healthcare

open collaborations foster innovation

BCI field & Society: young, dynamic, friendly!

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Q&A

David McMullen, Julia Slocomb
Heather Dean, and José del R. Millán

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Summary of Day 1

Amanda Pustilnik
University of Maryland Law

Brain Computer Interface Export Controls Conference

February 16-17, 2023

Thank you

Reconvene at 9:00 a.m.