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Review article

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The state of clinical trials of implantable brain–computer interfaces

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Abstract

Implanted brain–computer interfaces (iBCIs) translate brain activity recorded intracranially into commands for virtual or physical machines to restore or rehabilitate motor, sensory or speech functions. Currently, no iBCIs have been approved by regulatory agencies for the medical device market despite being in clinical trials since 1998, with little information available about their progress and outcomes. To address this gap, we conducted a review of all identified clinical trials of iBCIs for communication, motor control or restoration of tactile perception conducted between 1998 and 2023. We summarize findings from 21 research groups worldwide and their 67 participants who received implants to understand the challenges and opportunities in the iBCI field. This analysis highlights the importance of improving participant diversity, creating a participant registry to inform future research, regulatory and payer approvals, investor funding and new applications, adopting governed data sharing and standards, and boosting collaborative research.

Sections

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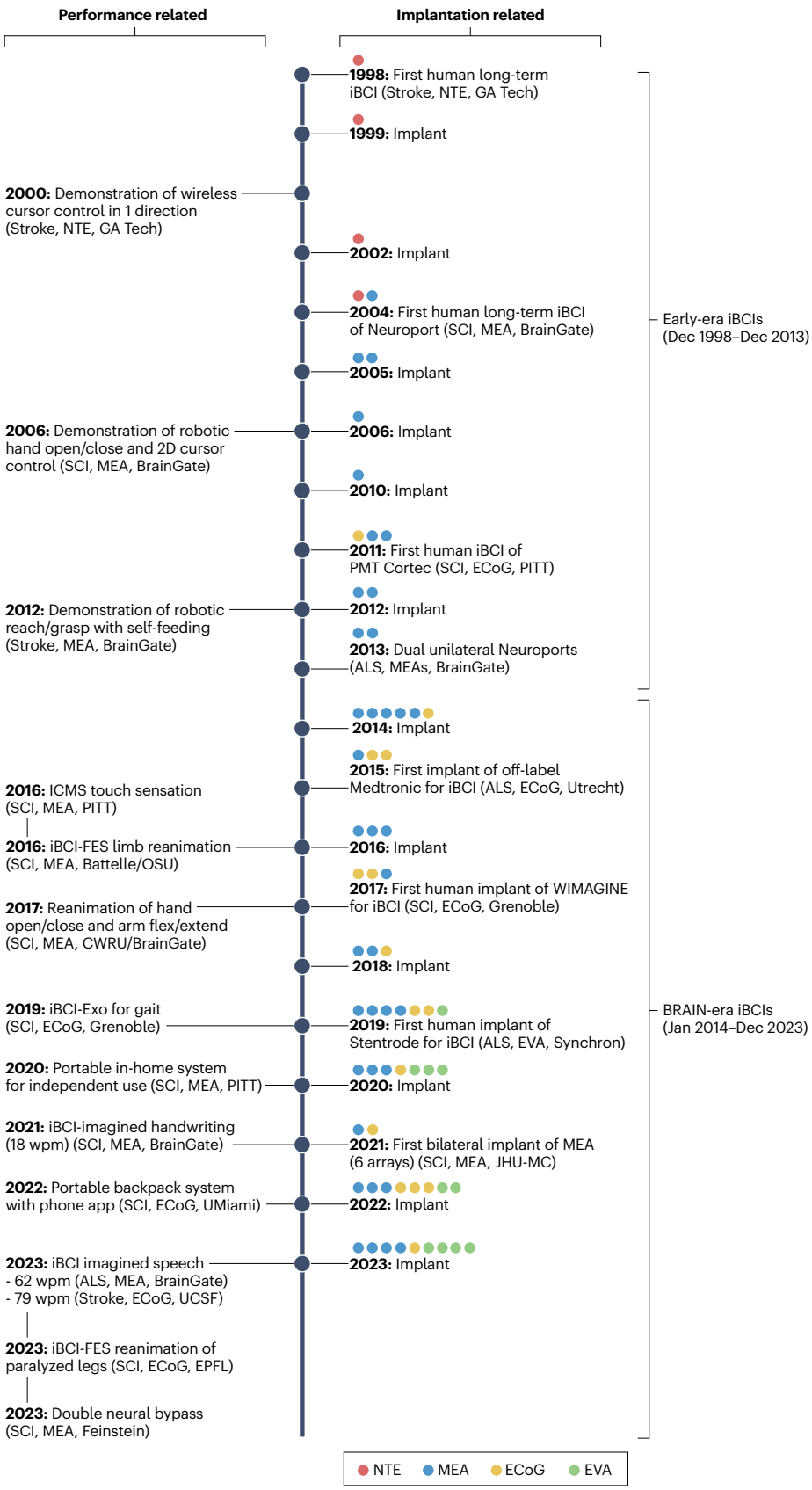


Fig. 1 | Timeline of chronic iBCIs. Progress in implanted brain–computer interfaces (iBCIs) has been separated into the early era and Brain Research Advancing Innovative Neurotechnologies (BRAIN) era. Implantation information is on the right side and is based on the date provided in publications or through personal communication with research groups, whereas the corresponding performance improvements are on the left with dates corresponding to the year of publication[46,99–227]. The small circles located on the right side indicate the number of implantations during that year with the colour indicating the type of electrodes implanted. See Table 1 and Supplementary Tables 1 and 2 for a list of resources used in identifying information in Fig. 1. ALS, amyotrophic lateral sclerosis; CWRU, Case Western Reserve University; ECoG, electrocorticography; EPFL, Swiss Federal Institute of Technology Lausanne; EVA, endovascular array; FES, functional electrical stimulation; GA Tech, Georgia Institute of Technology; ICMS, intracortical microstimulation; JHU-MC, Johns Hopkins University-Motor Control group; MEA, microelectrode array; NTE, neurotrophic electrode; OSU, Ohio State University; PITT, University of Pittsburgh; SCI, spinal cord injury; UCSF, University of California, San Francisco; UMiami, University of Miami; wpm, words per minute.

implantations in 2012 using the MEA Neuroport[31,32]. The ECoG trials have been completed, whereas five of the six participants implanted with a MEA remain active in clinical trials. The California Institute of Technology trial began shortly after, with their first participant receiving an implant in 2013 using the same array[33]. During this early phase, implantations in new participants were irregular (Figs. 1 and 2a), with a total of 16 participants working with 4 research groups from 1998 to 2023.

In 2014, two large publicly funded initiatives, the BRAIN Initiative and the HBP, boosted the number of research groups and participants, expanding the geographic footprint of iBCIs to the EU, Asia and Australia. Since 2014, iBCIs have been implanted regularly, with the number of research groups more than quadrupling (Fig. 2a). Due to the stark contrast in research activity before and after the BRAIN Initiative and HBP funding began, we divided iBCI research into an 'Early' (before 2014) and a 'BRAIN' era (2014–2023).

A total of 21 research groups were identified (Supplementary Table 1), with Johns Hopkins University having two separate groups, one working in motor control and the other in communication (Fig. 2a). The research groups are geographically distributed in Asia ($n = 2$), the EU ($n = 6$) and the USA ($n = 12$), with one group working in both Australia and the USA. Of the 21 groups, 13 were actively working at the end of 2023 with participants who received an implant. These groups have implanted a total of 67 participants geographically located in Asia ($n = 2$), Australia ($n = 4$), the EU ($n = 10$) and the USA ($n = 51$). All participants met the inclusion criteria due to one of three aetiological categories: injury ($n = 29$), including SCI ($n = 28$) and brachial plexus injury ($n = 1$); motor neuron degenerative diseases ($n = 20$), including ALS ($n = 18$), mitochondrial myopathy ($n = 1$) and spinocerebellar degeneration ($n = 1$); or stroke ($n = 11$), with 7 aetiologies unidentified. Of the 67 total participants, 31 (46%) are currently active with the following distribution: motor neuron disease ($n = 6$), SCI ($n = 17$), stroke ($n = 2$), and six unidentified. A total of 28 clinical trials were identified: 24 on ClinicalTrials.gov, 1 on the ISRCTN Registry, 1 on the German Federal Institute for Drugs and Medical Devices (BfArM), 1 on the Chinese Clinical Trial Registry and 2 without identified registrations. Of these trials, 2 were conducted in Asia (7%), 1 in Australia (4%), 7 in the EU (25%) and 18 in the USA (64%). There are 3 additional iBCI trials identified on ClinicalTrials.gov not included in Table 1 because they were withdrawn due to either location change ($n = 2/3$) or device unavailability ($n = 1/3$).

Electrodes

As of December 2023, clinical trials of iBCI for CSMC have only used four types of electrodes produced by six manufacturers (Table 2). The earliest one used at the Georgia Institute of Technology in four participants (6%) was the neurotrophic electrode (NTE) by Neural Signals (Duluth, GA, USA)[3]. These electrodes consist of a glass cone with the electrodes attached and neurites grown into the tip[34]. They are difficult to implant, require up to 3 months between implantation and participation in experiments to allow for recovery from surgery and, despite measuring neuronal activity, they offer only one or two channels per electrode as spatial resolution. However, they can collect signals even 13 years after implantation[29].

The Neuroport is a version of the Utah array approved for 30-day human use by the FDA; therefore, an investigational device exemption is needed for longer implantations. These MEAs are manufactured by Blackrock Neurotech (Salt Lake City, UT, USA; formerly Cyberkinetics) with the first human implant by BrainGate in 2004 (ref. 30). It consists of a 10 × 10 array of electrodes (other electrode options are available) implanted into the upper layers of the cortex using a pneumatic inserter. The MEA offers the highest spatial resolution among electrodes used in iBCI, with 96 electrodes, each spaced 400 µm apart, enabling measurement at the neuronal level, and has been used by 13 research groups in 38 (57%) participants, including in Asia ($n = 2$), the EU ($n = 3$) and the USA ($n = 33$). Participants implanted with the Neuroport could begin experiments less than a month after implantation; however, signal longevity across participants is variable, with some participants experiencing signal quality degradation within the first year of implantation and the electrode becoming unusable within 3 years, whereas others can continue for 4 years or longer[35,36]. As of December 2023, the longest active participation using MEA electrodes is 8.5 years, that is, the 'P2' enrolled participant at the University of Pittsburgh. Currently, 33.3% of active participants with MEAs received their implant in 2019 or before, with the earliest in 2015. Biological, material and mechanical failures causing signal degradation are being investigated[10,36,37].

The ECoG electrode array is an established diagnostic device that has been used in refractory epilepsy resection since the 1960s, is FDA approved for 30-day implantation and manufactured in different electrode configurations by multiple companies[38]. ECoG is an array of electrodes embedded in a silicone sheet that is placed either epidurally or subdurally. They have a spatial resolution with typical interelectrode spacing of 10 mm and measure local field potential rather than neuronal firing. However, because they lay on top of the cortex, they trigger a weaker foreign body response, which would degrade signal detection compared with MEAs[39,40]. At the University of Pittsburgh, ECoG arrays were first implanted for iBCI for CSMC applications using Cortac by PMT Corp (Chanhassen, MN, USA) for 1-month clinical trials in 2011, 2014 and 2015 (refs. 31,41). At the University Medical Center Utrecht, the Medtronic (Minneapolis, MN, USA) Resume II spinal cord stimulator was used off-label, which in 2015 was configured as an ECoG device with an amplifier and transmitter marketed for deep brain stimulation (Activa PC+S)[42]. The first human implantation of WIMAGINE by Clinetac (Grenoble, France) occurred in 2017 (ref. 5). The three brands of ECoG have been implanted in 15 (22%) participants, with Cortac in 7, off-label Medtronic in 4 and WIMAGINE in 4. There are currently 8 active participants using ECoG, 50% of whom were implanted in 2019 or before.

As of December 2023, the most recent electrode to enter clinical trials is the EVA Stentrode by Synchron (Brooklyn, NY, USA), with implantation based on the well-established cardiac stent endovascular implantation model[43]. Unlike other electrodes, the EVA does not require breeching of the cranium for implantation as it is inserted via the jugular vein and is deployed in the sagittal sinus, where venous wall tissue grows to encapsulate the electrode[44]. There is no identified explantation protocol as it is intended to be a permanent implant. No information on signal quality for durations of over 4 years is currently available as the clinical trials began in 2019 (ref. 16).

Typically, electrodes from only one manufacturer are used in participants of a research group (Table 1), with the exception of the University of Pittsburgh, at which three ECoG trials were conducted that lasted 1 month each during their early phases, before switching to long-term Neuroport MEAs for the trials[45]. At Johns Hopkins University, two research groups from different departments worked under separate investigational device exemptions and ClinicalTrials.gov ID numbers (Table 1). The Crone Lab participant received the Cortac ECoG to assess speech and communication, whereas the Human Brain

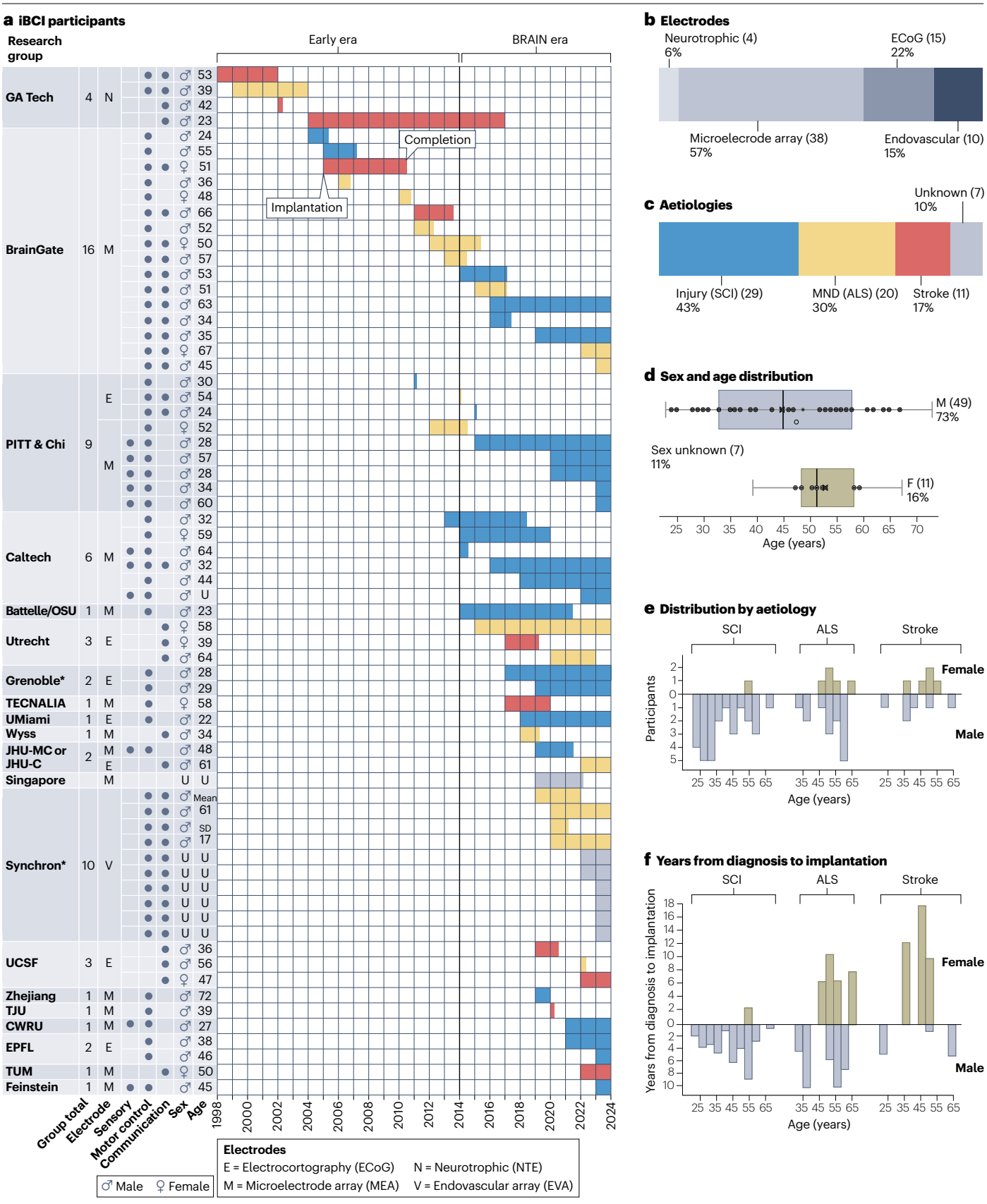

a iBCI participants
Research group
Early era
BRAIN era
Completion
Implantation
GA Tech 4 N
BrainGate 16 M
PITT & Chi 9 E M
Caltech 6 M
Battelle/OSU 1 M
Utrecht 3 E
Grenoble* 2 E
TECNALIA 1 M
UMiami 1 E
Wyss 1 M
JHU-MC or JHU-C 2 M E
Singapore M
Synchron* 10 V
UCSF 3 E
Zhejiang 1 M
TJU 1 M
CWRU 1 M
EPFL 2 E
TUM 1 M
Feinstein 1 M
Mean
SD
Group total
Electrode
Sensory
Motor control
Communication
Sex
Age
1998 2000 2002 2004 2006 2008 2010 2012 2014 2016 2018 2020 2022 2024
♂ Male ♀ Female
Electrodes
E = Electrocortography (ECoG) N = Neurotrophic (NTE)
M = Microelectrode array (MEA) V = Endovascular array (EVA)
b Electrodes
Neurotrophic (4) 6%
ECoG (15) 22%
Microelecrode array (38) 57%
Endovascular (10) 15%
c Aetiologies
Unknown (7) 10%
Injury (SCI) (29) 43%
MND (ALS) (20) 30%
Stroke (11) 17%
d Sex and age distribution
M (49) 73%
Sex unknown (7) 11%
F (11) 16%
25 30 35 40 45 50 55 60 65 70
Age (years)
e Distribution by aetiology
SCI
ALS
Stroke
Female
Male
Participants
25 35 45 55 65
Age (years)
f Years from diagnosis to implantation
SCI
ALS
Stroke
Female
Male
Years from diagnosis to implantation
Age (years)

Fig. 2 | Systemic knowledge integration graph of iBCI participants, aetiology, electrode arrays and research groups. a, Summary of all known implanted brain–computer interface (iBCI) participants ($n = 67$), organized first by research group ($n = 21$) and then by implantation date. Each row provides information for a participant with the coloured section indicating the year of implantation, months of participation (length of coloured bar) and the participant's aetiology (colour of the bar). Participant age at implantation, sex and the types of experiments (communication, motor control or sensory) based on published works, presentations or communication with the corresponding research group are shown on the left of the participation bar. Synchron has reported the mean age of their first four participants is 61 years, with a standard deviation of 17 years[16]. Additionally, Synchron media has indicated that their systems are being developed for both communication and motor control, therefore both are included. Each research group uses a single type of electrode, indicated in the 'Electrode' column, except for the University of Pittsburgh (PITT; using 1-month electrocorticography (ECoG) electrode array in three participants from 2011 to 2015 and long-term microelectrode array (MEA) implantation starting in 2014) and Johns Hopkins University (JHU), which has two separate research groups in different departments using different electrodes (designated as JHU-MC (motor control group) and JHU-C (communication group)). The total number of participants identified for each research group is shown in the second column, with the name of the research group in the first. All research groups were contacted to verify the correctness of the information, with an asterisk (*) denoting groups with no response. **b**, Distribution of electrode types used in the 67 participants. **c**, Frequency of aetiologies among the 67 participants. **d**, Sex and age demographics of participants. **e**, Sex and age demographics, if known, of participants by aetiology. **f**, The number of years between diagnosis and implantation, if known, by age, sex and aetiology. The authors acknowledge the potential for other participants that may not have been identified in this exhaustive search, noting that 25% of participants were identified through press releases and personal communication with research groups (see Table 1 and Supplementary Tables 1–3 for a list of resources used in identifying information contained in this figure). Moreover, participants who received implants after December 2023, including the participant in the 2024 clinical study conducted by Neuralink along with other studies receiving less media coverage, which happened after the end date of data collection for this Review, are not included. Furthermore, the authors acknowledge the exclusion of two identified individuals implanted with a BCI who died from disease (in 1996) and whose participation in the study ended owing to device failure (in 2017); and the exclusion of two additional research groups who received authorization to conduct iBCI clinical trials but with no discoverable participants as of 31 December 2023: Ottawa Hospital (Ottawa, Ontario, Canada) and Neuralink (Freemont, CA, USA). ALS, amyotrophic lateral sclerosis; BRAIN, Brain Research Advancing Innovative Neurotechnologies; Caltech, California Institute of Technology; Chi, University of Chicago; CWRU, Case Western Reserve University; EPFL, Swiss Federal Institute of Technology Lausanne; GA Tech, Georgia Institute of Technology; MND, motor neuron disease; OSU, Ohio State University; SCI, spinal cord injury; TJU, Thomas Jefferson University; TUM, Technical University of Munich; U, unknown; UCSF, University of California, San Francisco; UMiami, University of Miami; Utrecht, The University Medical Center Utrecht.

Physiology and Stimulation Laboratory participant received Neuroport MEA to assess motor control (Supplementary Fig. 2b).

The functional longevity of the implanted electrodes is critical to the commercial success of iBCIs for CSMC. Despite limited information being available on electrode signal quality as a function of implantation duration, there is a lack of information across iBCI participants. Participation duration is not a viable proxy for determining signal longevity because information on explantations is sparse[15,46]. News articles and recorded interviews were thus used to deduce the drop-out reasons for a minority of participants, including a lack of desire to continue, end of funding, principal investigator relocation, as well as device-related complications such as adverse events necessitating removal or leading to equipment failure[47]. However, data on participation duration could be used to evaluate trends in the duration of device usage (Fig. 3). The average number of months of enrolment across all participants is 35.5 with a median of 24 ± 31 (Fig. 2a). Disaggregation of average participation months by era, electrode and trial participation status reveals that, in the Early era, the average length of trial participation is 36.8 months. Removing the outlier of 156 months decreases the length of participation to 27.1 months. In the BRAIN era, participants who are no longer enrolled averaged 27.9 months whereas those still enrolled as of December 2023 averaged 40.2 months, a 32.7% increase over the Early era without the outlier.

Emerging electrodes. In addition to those used in clinical trials, there are at least 14 additional electrodes for the detection of brain signals that are currently moving toward in-human long-term trials (Table 3). Despite not yet being marketed for use in iBCIs for CSMC, these electrodes could provide alternative electrode solutions to iBCI systems. For example, Neuropixels by IMEC (Leuven, Belgium) and Layer 7 by Precision Neuroscience (New York, NY, USA) have both completed biocompatibility testing, and Connexus by Paradromics (Austin, TX, USA) has received funding to begin human trials[48].

Technical considerations

Electrodes receive a considerable amount of attention owing to their prominent role in iBCIs; however, they are a single component in a complex system. Each component, along with the system, faces challenges such as thermal management, mechanical endurance, failure mode and effects, cleanability, protection from electric hazards, and lifecycle management[49–51]. Detailed reports on adverse events and duration of electrode implantation for the NeuroPort iBCI as well as demographic and clinical data for 14 clinical trial participants have been reported by an iBCI group[15]; for example, the summaries for Stentrode[16] and NTE[52] are less comprehensive at the time of publication, possibly owing to the needs of protecting participant privacy, intellectual property or recent entry into clinical trials. Information on the duration of electrode implantation or trial participation, reason for explantation or end of participation, adverse events, signal quality, and duration, which could be very useful to researchers, is rarely provided in the iBCI literature. Early-era publications included implantation dates, but recent articles regularly omit this information likely due to the need to protect the participant's privacy and comply with federal guidelines (that is, the Health Insurance Portability and Accountability Act). Individual groups have analysed the long-term performance of Neuroport electrodes but there is no identified assessment of electrode performance across groups (13 research groups for Neuroport), with only one article comparing multiple electrode types in evaluating artefact suppression from electrostimulation across electroencephalography, ECoG and MEAs[53]. Still, detailed information on performance, signal quality, electrode longevity and their ability to provide a minimal viable signal is missing. Analysing data aggregates could inform on what might change the longevity of the electrode signal, the role of stimulation on electrode outcomes, and the minimum spatial and temporal resolutions required for decoding, calibration and control of iBCI systems, among others.

Table 1 | Research groups

Research group, lead principal investigator	Participants with implants	Country	First implant	Last active participant	Electrode	iBCI type	Clinical trial ID
Battelle/Ohio State University, A. Rezai	1	USA	2014	2021	Neuroport	Sensorimotor control	NCT01997125
Singapore National Neuroscience Institute, (unknown)	1	Singapore	2019	2021	Neuroport	NA	NCT03811301
BrainGate (Brown University), L. Hochberg	16	USA	2004	Current	Neuroport	Communication and motor control	NCT00912041, NCT03482310, NCT05470478
Caltech, R. A. Andersen	6	USA	2013	Current	Neuroport	Communication and sensorimotor control	NCT01849822, NCT01958086, NCT01964261
CWRU, A. B. Ajiboye	1	USA	2021	Current	Neuroport	Motor control	NCT03898804
EPFL, G. Courtine	2	Switzerland	2021	Current	WIMAGINE	Motor control	NCT04632290, NCT05665998
GA Tech[52], P. R. Kennedy	4	USA	1996	2017	Neurotrophic	Communication and motor control	NA
University Hospital, Grenoble, S. Chabardes	2	France	2017	Current	WIMAGINE	Motor control	NCT02550522
JHU-C, N. E. Crone	1	USA	2018	Current	PMT Cortac	Communication	NCT03567213
JHU-MC, P. A. Celnik	1	USA	2019	2021	Neuroport	Motor control	NCT03161067
Northwell Health Feinstein Institute, C. Bouton	1	USA	2023	Current	Neuroport	Sensorimotor control	NCT03680872
University of Pittsburgh, J. Collinger	9	USA	2011	Current	Neuroport/PMT Cortac	Communication and sensorimotor control	NCT01393444
Synchron, T. Oxley	10	USA, Australia	2019	Current	Stentrode	Communication and motor control	NCT03834857, NCT05035823
TECNALIA[95], A. Ramos-Murguialday	1	Spain	2017	2020	Neuroport	Motor control	ISRCTN 10150672
Thomas Jefferson University, M. Serruya	1	USA	2020	2020	Neuroport	Motor control	NCT03913286
TUM (S. Jacob, personal communication), S. Jacob	1	Germany	2022	Current	Neuroport	Communication	NA
UCSF, E. Chang	3	USA	2019	Current	PMT Cortac	Communication	NCT03698149
UMC Utrecht, N. Ramsey	3	Netherlands	2015	Current	Medtronic	Communication	NCT02224469
University of Miami, J. Jagid	1	USA	2018	Current	Medtronic	Motor control	NCT02564419
Wyss Institute[96], J. Zimmerman	1	Switzerland	2018	2019	Neuroport	Communication	BfArM 5640-S-036/18
Zhejiang University[97], H. Jiang	1	China	2019	2020	Neuroport	Motor control	ChiCTR 2100050705

The table only includes the institute and name of the principal investigator or investigational device exemption holder who corresponded with the authors. Please consult references for complete team information. BfArM, German Federal Institute for Drugs and Medical Devices; Caltech, California Institute of Technology; CWRU, Case Western Reserve University; EPFL, Swiss Federal Institute of Technology Lausanne; GA Tech, Georgia Institute of Technology; iBCI, implanted brain–computer interface; JHU-C, Johns Hopkins University-Communication group; JHU-MC, Johns Hopkins University-Motor Control group; NA, not available; TUM, Technical University of Munich; UCSF, University of California San Francisco; UMC Utrecht, The University Medical Center Utrecht.

Sociotechnological aspects of iBCIs

Standardization

The lack of standardization in the BCI field has long been recognized, with working groups, such as those formed by the Institute of Electrical and Electronics Engineers Brain (IEEE brain) Standard Association Industry Connections Working Groups, attempting to address this deficiency[54,55]. In this regard, it is imperative to create and adopt standards for performance assessment and benchmarking for data representation, storage and sharing, user needs, sensor technology, and end effectors[54]. Moreover, defining a unified terminology and a standardized functional model are essential to establishing a baseline understanding across the field[56].

Data storage. As neuroscience increasingly leverages the power of computation and artificial intelligence, addressing data-sharing concerns becomes more important. Numerous standards have been proposed as a standardized annotated storage format for neural data sets but none has been adopted[55,57,58], likely due to BCI systems typically integrating multiple elements or components at different levels of maturity and fidelity, considerable variability of standards across

Key points

- A total of 21 research groups focusing on implanted brain–computer interfaces (iBCIs) were identified worldwide and have conducted 28 clinical trials with 67 participants (31 currently active) with an iBCI using 4 types of electrode arrays, generating 165 peer-reviewed publications over 25 years.
- The timeframe from implantation to the first publication averages 3 years.
- Women are considerably underrepresented, even when accounting for differences in disease-based and injury-based prevalence.
- The longevity of chronic iBCIs in humans is increasing, with a mean participation longevity of 40.2 months for patients currently active in trials. However, the consistency and performance of these systems varies across individuals.
- Ethical considerations need to be addressed, including an equitable population representation in clinical trials, data ownership and guidelines for ending usage in palliative care, among others.
- Improvements in the governance of data sharing, metrics, standards and collaborative science are critical for accelerating the translation and commercialization of iBCIs.
- Medical specialist shortages, geographic access disparity and public perception of the technology will strongly influence the adoption of iBCIs.

Introduction

Public and private investments, accelerated by the 2014 launch of the Brain Research Advancing Innovative Neurotechnologies (BRAIN) Initiative in the USA and the Human Brain Project (HBP) in the European Union (EU), have led to groundbreaking neurorestorative and neurorehabilitation demonstrations in implantable brain–computer interfaces (iBCIs). There are patients for whom cognitive and motor control centres of the brain remain largely intact but the ability to produce the volitional motor execution required for speech or body movement or to perceive sensory feedback is disrupted due to spinal cord injury (SCI), motor neuron degenerative diseases such as amyotrophic lateral sclerosis (ALS), or brainstem stroke[1]. iBCIs use different types of electrode arrays implanted intracranially to detect analogue cortical electrical activity, which is then converted into digital signals that infer and realize user intent by decoding those signals into commands to control external physical or virtual devices (Box 1). Example devices include speech synthesizers[2], computer cursors[3], spellers, assistive robotic end effectors[4,5] and functional electrical stimulation devices[6,7], along with systems that provide tactile feedback via intracortical microstimulation[8]. Recent developments have focused on the design and material composition of the implanted electrodes[9,10] as well as on improving decoding speed and accuracy[11]. The latter has mainly been driven by advances in signal processing and the application of new machine learning and deep learning algorithms, including large language models used in speech iBCIs[12,13]. These improvements have enabled more precise, reliable and versatile connections between the brain and external devices[14]. Nevertheless, the efficacy of chronically implanted electrodes for iBCIs in humans as a lifetime viable solution remains unproven[15,16]. Despite this limitation, device manufacturers have begun conducting clinical trials; for example, Synchron began trials in 2019 using the permanently implanted endovascular array (EVA) Stentrode, which is inserted using minimally invasive endovascular catheterization and is the only electrode that does not require a craniotomy[17]. In 2024, Neuralink began long-term human testing of their microelectrode array (MEA), which is implanted using a custom robot. Corporate involvement in iBCI clinical trials to assist patients with communication and sensorimotor control (CSMC) impairments has propelled the field to the forefront of scientific inquiry and public media.

Nonetheless, there is currently no consolidated repository of global iBCI information to identify research groups, clinical trials, participant demographics or electrodes used. This limits the ability to analyse past and present progress in clinical trials to inform and guide future research, translation and implementation of iBCIs. To fill this gap, we conducted a comprehensive knowledge integration review of all discoverable iBCIs for CSMS available from 1998 to 2023 (Supplementary Fig. 1). The data presented was obtained from different sources, including a PubMed search for publications reporting interaction with participants with an iBCI, information on implantation, experimental results, explantations, histology or participant summaries. This Review focuses on long-term iBCIs; therefore, short-term studies on speech, tactile feedback and motor control in humans using diagnostic electrocorticography (ECoG) for diseases such as epilepsy were not included[18–20]. In addition, the ClinicalTrials.gov data base, research group website publication lists, and Google Scholar and ORCID profiles of principal investigators were consulted to identify eventual missing publications from the PubMed search (Supplementary Fig. 1). From the identified publications (Supplementary Table 1), the research groups, clinical trials, participant demographics and electrodes used were catalogued, and the source of information for each participant was identified (Supplementary Table 2). The BrainGate research group is the only group that has published a summary of their longitudinal clinical trials, cataloguing participant demographics and adverse events along with other details[15]. Using only peer-reviewed publications is not entirely accurate because of delays between implantation and publication (2–3 years) (Supplementary Fig. 2a). Thus, institutional and corporate press releases were searched for additional information on research groups, participants or progress not available in the literature, with data collection ending in December 2023 (ref. 21). All information was cross-checked with the corresponding group (19/21 of them replied, ~90%) to ensure data accuracy and eventual updates on the status of participants (continuing or completed), the number of months participated and any other information they were willing to share. This Review could be used as a roadmap to help identify the barriers, challenges and opportunities for advancing iBCI systems.

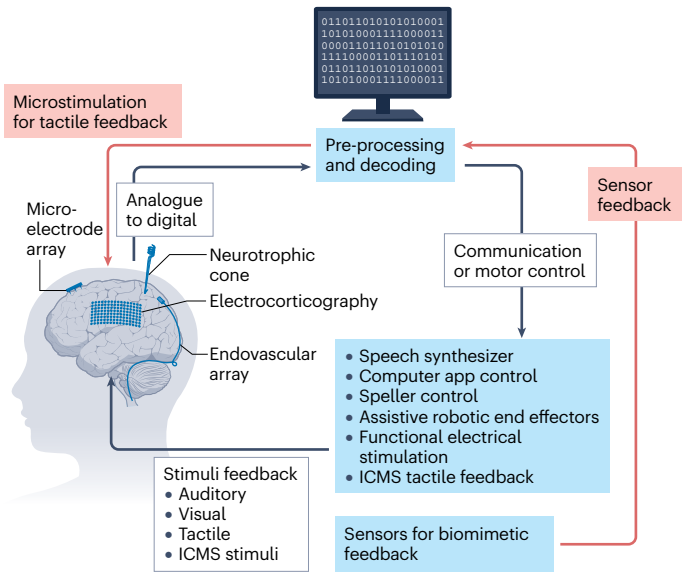
The state of iBCIs

Progress in clinical trials

The recent progress in iBCIs is the result of over 150 years of published research to understand how the brain controls the body. In 1874, Roberts Bartholow reported the effects of human brain electrical stimulation on body motor functions. He used stimulation electrodes inserted into a section of exposed brain caused by bone cancer[22]. Almost a century later, in 1964, W. Grey Walter tested the hypothesis that recorded segments from electrodes implanted in patients' motor cortex were related to intentional actions by testing the ability to use

Box 1 | Mechanisms of iBCIs

Implanted brain–computer interfaces (iBCIs) for communication or sensorimotor control are composed of four main components: electrodes to detect brain signals, a computer to receive and process the signal and create usable output capabilities, a prosthetic application or device fed by the brain signals, and a feedback loop. Electrodes are implanted under the cranium and are positioned over or in regions of the brain that provide signals to assist or restore the desired functions (communication or motor control). For certain motor control applications, additional electrodes are placed in the sensory cortex to stimulate the brain as feedback, that is, an input iBCI. The brain signals received undergo an analogue-to-digital conversion and are then fed into the computer for signal pre-processing for other algorithms (such as feature extraction and decoding), depending on the application. This driver signal is then sent to the prosthetic application or device to stimulate speech, movement or feeling of touch. Patients then hear or see the resulting speech or movement and can change their thoughts or intentions to modulate the outcome.



Box Fig. 1 | Overview of iBCI systems. The electrode collects the signal, an analogue-to-digital converter sends the digital signal to a computer for pre-processing and decoding to either drive a computer application or send a signal to control an external device such as a prosthetic arm. The feedback from the application or device enables participants to tune the device functionality. For participants who receive tactile feedback, sensors are included in the prosthesis, which provides biomimetic feedback for the implanted electrodes to deliver intracortical microstimulation (ICMS) to simulate the sense of touch.

neural activity to control a mechanical device[23]. To do so, he asked patients to press a button to progress a carousel projector; however, the button was a placebo that was not connected to the projector, and the carousel was being advanced by the patient's neural activity[24]. Shortly after, in 1968, the Laboratory for Neural Control was founded in the National Institutes of Health's National Institute of Neurological Disorders and Blindness to leverage information from the nervous system to control external devices[25]. Already in 1969, foundational research on the neural origins of volitional motor control using non-human primates had begun[26]. In parallel, in 1965, a digital system architecture for online conversion of analogue brain signals into digital inputs for computers was being developed, culminating in the 1973 publication of an expanded design coining the term 'brain–computer interface'[27,28].

To our knowledge, the first long-term iBCI electrodes were implanted in 1998 at the Georgia Institute of Technology (Fig. 1); the participant, who had locked-in-syndrome subsequent to brainstem stroke 2 years prior to implantation, became the first person with long-term implants who was able to control a computer cursor using brain signals. The cursor moved from left to right across the screen by combining the neural activity with electromyography and other signals to control a speller for communication[3]. Three additional participants were implanted by the same group, the last in 2004 with the longest duration between implantation and final data collection[3,29] (13 years; Fig. 2a). In 2004, the BrainGate group implanted their first participant; a patient with SCI and tetraplegia who was able to use intended hand motion to drive a computer cursor in two dimensions, simulating daily activities such as opening emails and operating a television, as well as using the intent to control a multi-joint robotic arm and opening and closing a prosthetic hand[30]. Since then, BrainGate has continuously conducted clinical trials with between one and four participants with an implant at any time and has the largest number of total participants (16 participants; Fig. 2a). These initial studies indicated viability and were followed by trials at the University of Pittsburgh starting with 1-month implantations in 2011 of ECoG electrodes and extended

Table 2 | Established electrodes

Company	Type	Name	Year of entry of implanted brain–computer interface	Channels	Size	Depth	Stimulation	FDA status
Blackrock	MEA	Neuroport	2004	96	4 mm x 4 mm	1 or 1.5 mm	Yes	510(k) (K042384)
Medtronic	ECoG	Resume II	2015	4	60 cm	1.3 mm	Yes	510(k) (K040568)
Neural Signals	NTE		1998	31	2 mm x 5 mm	1.5 mm	No	NA
Clinatec	ECoG	WIMAGINE	2017	64	50 mm x 50 mm	6 mm	No	NA
PMT Corp	ECoG	Cortac	2014	Multi	Multi	0.5 mm	No	510(k) (K964224)
Synchron	EVA	Stentrode	2019	16	8 cm (est.)	8 mm	Yes	IDE

ECoG, electrocorticography; EVA, endovascular array; IDE, investigational device exemption; MEA, microelectrode array; NA, not available; NTE, neurotrophic electrode.

components[54] and, potentially, a lack of coordination across organizations involved in developing standards. Without data standards and addressing these issues, extracting shareable and usable information from data sets across research projects and groups remains difficult.

Experimental performance assessment and benchmarking. Standardizing the assessment and benchmarking of experimental performance enables comparison of results. Historically, tests such as the centre-out task (Fig. 4, top) are routinely used to track performance over time to allow comparison with the literature and to familiarize the participant with iBCI systems. However, these tasks typically do not relate to daily living activities and may therefore be of questionable value to the participant. Moreover, comprehensive across-session results from these standardized tests are rarely reported in the literature as they do not include new findings. A total of 128 specialized tasks were identified from 90% of the included publications; some are specific to one publication, whereas others use similar tasks to analyse neural activity, technical developments, or compare algorithm performance and report their results using a range of metrics specific to the primary objective of the study. Removing all the tasks performed only once and the qualitative ones yield a set of 10 tasks (Fig. 4).

Notably, the experiment most frequently reported is the centre-out cursor control task performed by 14 participants with an iBCI, reported in 55 publications of which only 19 reported quantitative results. The motor control tasks of centre-out, target, reach and grasp, and evoked arm movement achieved median performances in success or accuracy metrics of above 85%. Spellers performed with a median of 15 correct clicks per minute whereas neural decoding of speech reports a median of 38 words per minute. Remarkably, improvements in speech decoding have recently been reported (64 and 79 words per minute, respectively)[12,13]; however, these values should be interpreted with caution because little information was provided on the participant's level of experience with the task beyond classifying them as an experienced iBCI user. Participants typically spend two to four sessions a week either in the lab or in a research environment set up at home, with sessions lasting 3–4 h each. Assuming a participant is active 40 weeks a year with three sessions a week of 4 h each session, they will have spent 480 h a year. It is unreasonable to expect the entirety of these sessions to be reflected in the literature. Notably, the ratio of publications to active participants is often less than one (Supplementary Fig. 2c), which is likely due to a growing number of participants, lag from implantation to publication, focus on new findings, and technical, medical or logistic complications. Standardizing performance and benchmarking would enable cross-comparisons also accounting for previous experience, duration and levels of task complexity[54,56].

Device development and components. The exclusion of patients and their caregivers in all aspects of device development has been suggested as a reason for market failure[59]. Clinical researchers from the

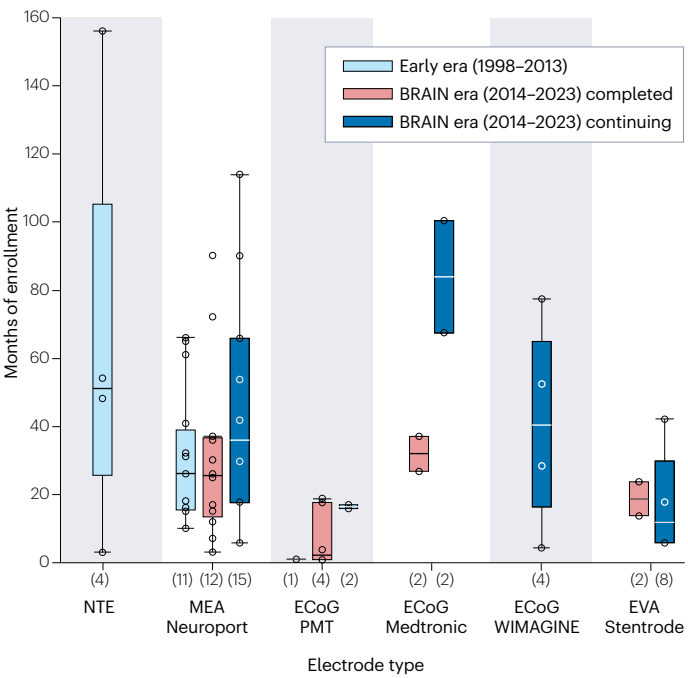


Fig. 3 | Duration of participation per electrode type. Light blue indicates months of participation in the Early era of the neurotrophic electrode (NTE), microelectrode array (MEA) and PMT electrocorticography (ECoG) electrode array. Pink indicates participants in the Brain Research Advancing Innovative Neurotechnologies (BRAIN) era who have completed participation. Dark blue shows the duration of participants currently (as of December 2023) enrolled in clinical trials. The numbers in brackets indicate the number of participants for each cohort per electrode type. See Table 1, Supplementary Tables 1 and 2, and Supplementary Fig. 1 for a list of resources used in identifying information contained in Fig. 2. EVA, endovascular array.

Table 3 | Emerging electrodes

Manufacturer	Type	Channels	Name	Regulatory approval
Axoft (Cambridge, MA, USA)	ECoG	1,024	NA	FDA Breakthrough (Oct 2022)
CorTec (Freiburg, Germany)	ECoG	32	AirRay	FDA 510(k) (Mar 2019)
Gbrain (Incheon, South Korea)	MEA	32 or 128 (ref. 98)	Phin Array	NA
IMEC (Leuven, Belgium)	CMOS	384	Neuropixels	NA
INBRAIN (Barcelona, Spain)	ECoG	1024	NA	FDA Breakthrough (Sep 2023)
Neuralink (Freemont, CA, USA)	MEA	3072	N1	FDA Breakthrough (Jul 2020)
NeuraMatrix (Beijing, China)	NA	NA	NA	NA
Neuropace (Mountain View, CA, USA)	ECoG	4	The RNS System	FDA PMA (Nov 2013)
Neurosoft (Geneva, Switzerland)	ECoG	4-64	NA	NA
NeuroXess (Shanghai, China)	ECoG	multiple	SilkTrode & SurfTrode	NA
Paradromics (Austin, TX, USA)	MEA	421	Connexus	FDA Breakthrough (May 2023)
Precision Neuro (New York, NY, USA)	ECoG	1024	Layer 7	FDA Breakthrough (Oct 2023)
StairMed (Shanghai, China)	MEA	1024	Ultra-Flexible Micro-Nano Electrodes	NA
Wise (Milan, Italy)	ECoG	4	WISE Cortical Strip	CE (May 2021) FDA 510(k) (Nov 2022)

Table 3 lists electrodes potentially entering the implanted brain–computer interface market as of December 2023. Neuralink has been included because their clinical trials began after December 2023, the date when data collection for this Review was terminated. Two electrocorticography (ECoG) electrodes with similar names could cause confusion: PMT Corp, a medical device company in the USA, which manufactures an ECoG with the brand name of Cortac; and a German medical device company, CorTec, which manufactures an ECoG with the brand name of AirRay. CMOS, complementary metal-oxide semiconductor; MEA, microelectrode array; NA, not available.

North American Neuromodulation Society working group (Institute on Neuromodulation) are now working to standardize the connectors for neuromodulation devices based on their experiences with patients; for example, by adapting the standards model for device connectors and other components currently used by the cardiac pacemaker and defibrillator industry, which was adopted in the 1990s[60].

Data sharing

Across all 67 participants, a total of 2,380 months of data were collected (Fig. 2a). BrainGate, involving 16 participants across two decades, has accrued the most data collection months (504), 21% of the total. They only use the Neuroport MEAs, which limits comparison across electrodes. Rehab Neural Engineering Labs (Pittsburgh) is the only research centre to have used both Cortec ECoG and Neuroport MEA. Their ECoG sessions were limited to 1 month and were completed in 2015, which again limits cross-comparison of electrodes, signal processing algorithms and participant experience[45]. Although project collaborators share data, concerns for patient privacy and data misuse limit external exchanges. Only 39% of iBCI publications (reporting on participant data) include a data-sharing statement, of which only a third provide a direct link to the data. Data sharing has been implemented in scientific publishing since 2014 (ref. 61); however, a data-sharing statement may not enforce the actual sharing of data, which would be required to advance the technology[62]. Moreover, data sharing must be balanced against privacy considerations because the sparse number of participants and the media publicity they typically receive often make them personally identifiable. Repositories such as the Data Archive for the BRAIN Initiative, which hosts data generated from research funded by the BRAIN Initiative, provide a portal for downloading or requesting access to shared data sets.

Clinical and quality-of-life outcomes

iBCIs are designed to assist people with substantial impairments, often including strong comorbidities[63,64]. However, only few reports have included clinical outcome information such as whether movement restoration through functional electrical stimulation and sensory restoration is associated with decreases in muscle atrophy, bone loss, or circulatory dysfunction or whether improved communication enables a participant with advanced neuromotor degenerative disease to convey discomfort, which might indicate developing infection or decubitus ulceration. Despite not being the primary objective of the research, such information would be invaluable for medical providers, regulatory agencies and participants to assess the risks and benefits of iBCIs[63,64]. Beyond the disease processes, few publications offer assessments of the psychological effects of using iBCI or quantitative measurements of changes in the quality of life of participants or their ability to perform activities of daily living[30,44,65,66]. Some groups have included psychological support and regular assessment as part of their clinical trials[45], and those that have reported such outcomes have indicated overall improvements in emotional health and quality of life. For example, a 71-year-old patient with tetraplegia experienced improved cognition after implantation and participation in clinical trials[67].

Usability

Operating iBCIs requires specialized teams of research scientists and engineers to calibrate the equipment for data collection. Typically, medical providers and end-users favour equipment that fits seamlessly into their workflow and is easy to operate, which are critical requirements for successful clinical translation. A substantial portion of end-users need caregivers as primary assistants for any set-up or debugging; therefore, designing an accessible and user-friendly system might be able to accommodate the high turnover rate of hired caregivers in the USA, estimated at 77.1% in 2022, and improve adoption of iBCIs, even in home settings[14,45,68].

Ethical implications

Implanting electrodes to read brain signals undeniably raises ethical questions. Current iBCI systems are limited to few patients with paralysis, tetraplegia or dysarthria who live near research facilities. Speculation on future applications (including non-clinical ones) after broad commercialization raises concerns of free consent and maintenance of privacy, agency and identity[69,70]. Moreover, iBCIs

might influence pre-existing social biases, such as limited access in low-resource settings, lower representation of women participants (see section 'Diversity, equity, inclusiveness and access') or increasing prejudices against patients by highlighting the social stigma of disability[71]. Identifying and addressing these biases, along with ensuring iBCI ethical practices are aligned with medical objectives, including those for responsible palliative care, can minimize possible negative effects of iBCI adoption[71–73].

Participants are subject to substantial risks in the name of advancing knowledge on assistive devices yet receive only minimal compensation and uncertainty of personal benefit despite spending 6–16 h per week performing research-related tasks for data collection and analysis, which benefit academics and corporations. As one of the guiding principles of the Belmont Report, which guides the conduct of human-subject testing, is 'do no harm', the question is then raised as to what long-term obligation do researchers, industry and funding agencies have to participants who wish to keep the implanted device[74]. Those who keep the device implanted need to decide whether it should remain functional, which in turn raises questions on clinical and financial responsibilities on device maintenance, concerns that have yet to be resolved[75].

Similar concerns are raised for patients whose devices are no longer manufactured or maintained[76,77]. Requiring manufacturers to incorporate long-term care responsibilities into their business plan or implement healthcare-as-a-service models for sustained revenue has been suggested, albeit with no resolution so far[74]. Other concerns, such as data rights, can even become business concerns; in 2021, Chile passed legislation to protect the rights of its citizens to data collected through neurotechnologies[78]. In 2023, a Chilean senator imported and collected data from an EMOTIV (San Francisco, CA, USA) device, after which they requested data removal from EMOTIV's servers. Upon EMOTIV not honouring the request, they filed and won a lawsuit against the company for violating Chilean laws on the collection and usage of neural data[70,79].

Reimbursement and market viability

Clinical translation of medical devices is an arduous process of establishing intellectual property, managing regulatory pathways, obtaining

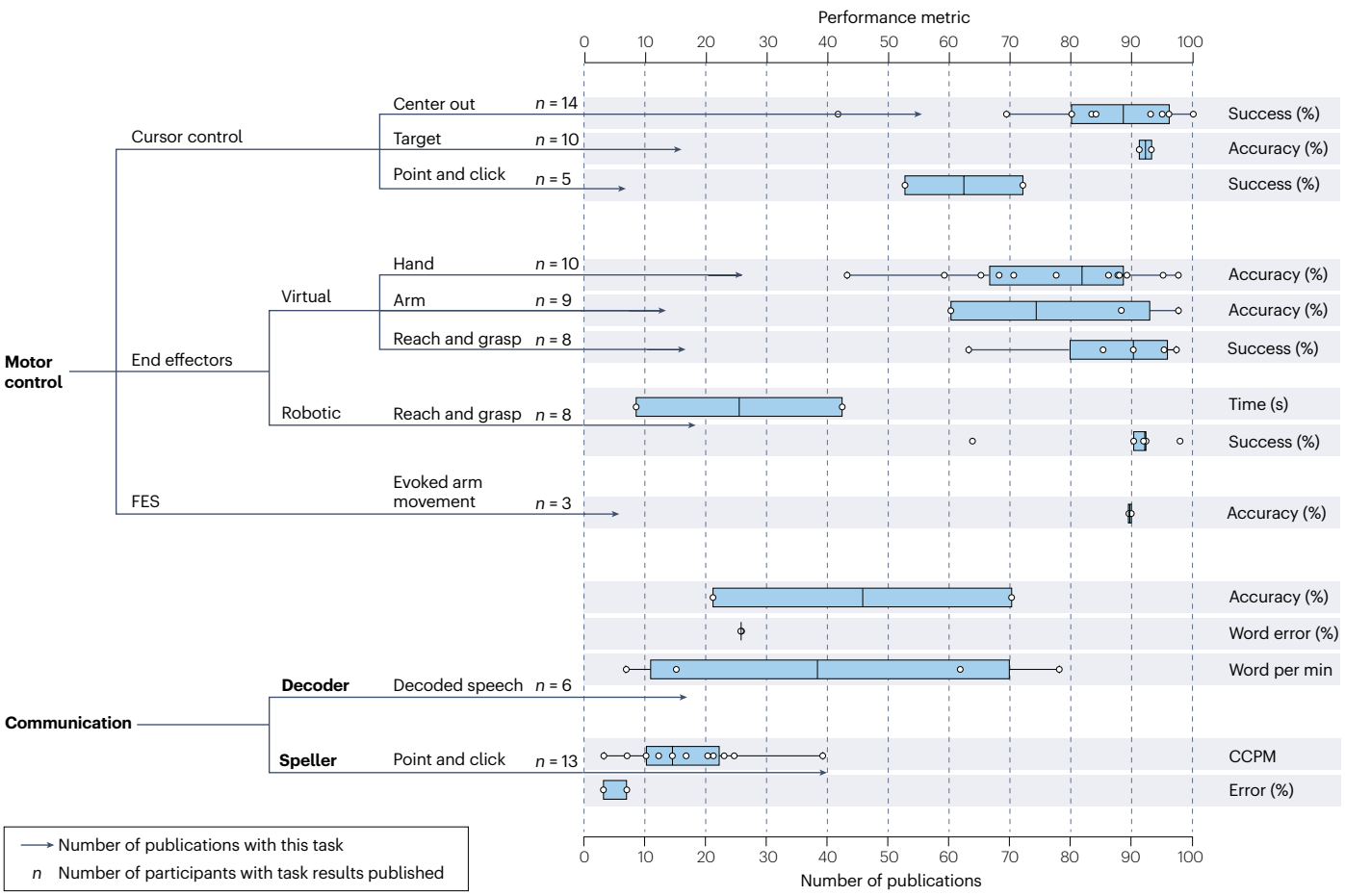


Fig. 4 | Summary of published data on implanted brain–computer interfaces. Tasks that recur in multiple publications with a numeric metric assessing task performance. Published task-performance results are compiled in the horizontal box charts on the right of the tree. The performance (top scale), the number of total publications (bottom scale) reporting each task and the number of participants (*n*) next to the task are also illustrated. The extension of the tree indicates the number of publications reporting on the performance of each task. Participants may repeat the task in multiple publications or one publication may have multiple participants. The metric measured is on the far right, with the bar chart assessing all included values, identified as detailed in Supplementary Table 4. CCPM, correct characters per minute; FES, functional electrical stimulation.

Table 4 | Female participants

Aetiology	Percentage of female sex in given aetiology	Total iBCI participants	Female iBCI participants	Binomial probability
Amyotrophic lateral sclerosis or other motor neurodegenerative diseases	46%	20	5	0.0461
Spinal cord injury or other injury	22%	29	1	0.0085
Stroke	56%	11	5	0.341

Null hypothesis of low female representation happening by chance under fair representation was evaluated using a one-tailed binomial probability test. iBCI, implanted brain–computer interface.

reimbursement, funding and exit strategies, among others[80,81]. The FDA recognized this gap (also known as the 'valley of death') and introduced the Total Product Life Cycle Advisory Program pilot in 2023 to engage early in the translation process by bringing together regulatory, reimbursement, industry and key stakeholder representatives.

Over the past 20 years, many neural implants have been awarded regulatory and third-party payer approval but were unable to remain solvent[82]. For example, SecondSight, which received US Centre for Medicare and Medicaid Services reimbursement at US $150,000 per individual, could not cover infrastructure costs. In parallel to SecondSight's entry into the consumer market, an alternative treatment entered the market for their primary target population[82]. Thus, they filed for insolvency and ended operations in 2021 (ref. 76). These types of devices require substantial time and money investment for product development, approval processes and market entry, including long-term costs (equipment maintenance and data management such as monitoring changes in user abilities, predictive diagnostics or future research) for which little information is available. For example, Neuralink publicly estimated an implantation cost of US $40,000 per patient prior to their first human clinical trial. Because iBCIs might also be connected to mobile apps or sophisticated robotic prostheses, longitudinal costs may further increase. Moreover, if the data is considered part of the patient's medical record, it may be subject to retention laws, which vary by location and type of facility, with most states in the USA requiring 5–10 years retention post treatment for adults. Associated costs will depend on the quantity and accessibility of the saved data; for emerging electrode arrays with over 1,024 sensors that can record at 5 Mbps, full-resolution collection for 24 h without compression results in over 400 Gb per day, which would add hundreds of dollars a month to the costs of Health Insurance Portability and Accountability Act-compliant data management in the USA (A. Condon, personal communication).

Clinical and patient acceptance

Before adoption, physicians and medical care providers ask for devices that integrate into their workflow, demonstrate benefit over standard-of-care and have a reasonable cost-to-risk ratio. For neurotechnologies, an additional barrier is the assumption that these devices are a last effort after all pharmacological and non-invasive treatments have been exhausted, despite indications that earlier use might yield better outcomes (for instance, using deep brain stimulation in treating Parkinson disease)[83].

Patient acceptance is a separate challenge; a Pew Research survey conducted in 2022 reported that the general population still does not trust this technology, with only 13% responding that 'computer chip implants in the brain' are a good idea for society and 83% desiring an increase in testing standards to ensure safety and effectiveness[84]. Such results could be attributed to the people surveyed not benefiting directly from iBCIs (that is, not being or having someone close with tetraplegia, dysarthria or locked-in-syndrome). Understanding these concerns is essential to ensuring clinical adoption and market success; a similar example was the Deaf community's response to cochlear implants in 1984, which was spurned as a cultural insult, resulting in only 5–10% of qualified adults receiving an implant as of 2017 (refs. 85,86).

Outlook

This comprehensive Review on the state of human iBCI clinical trials worldwide highlights aspects in the field that need further attention.

Diversity, equity, inclusiveness and access

iBCI participants in clinical trials to date are not equitably represented, with only 11 participants reported as female across aetiologies (Table 4). Such a small number could represent chance (statistically speaking), at least for patients who had a stroke. Moreover, there are age distribution imbalances between men and women; although the implantation age for men ranges from 22 to 72 years with a mean of 44.6 years, the ages of women range from 39 to 67 years with a mean of 52.6 years (Fig. 2d). In the age range 22–45, there are 26 men and only 1 woman, which follows historic trends of women in peak reproductive years being excluded from clinical trials[87].

The FDA guidance document Implanted Brain-Computer Interface (BCI) Devices for Patients with Paralysis or Amputation – Non-clinical Testing and Clinical Considerations, recommends the exclusion of those who are "Pregnant or of child-bearing potential and not using contraception." However, since 2018, the FDA has been developing a guidance document discussing aspects of including pregnant women in clinical trials. Nonetheless, women may be more likely to decline participation potentially owing to risk aversion in healthcare decisions (especially those with risk of physical harm)[88,89]. A similar disparity is reflected in the level of partner abandonment after a serious illness (such as cancer), with women being left partnerless six times more often than men (20.8% versus 2.9%) and with partnerless women having reduced participation in clinical trials (65.2% versus 92.2%)[90]. These factors, combined with the level of commitment required to participate in clinical trials (often three or four sessions a week for the duration of the study), indicate that the under-representation of female participants could be due to a lack of support.

Including end-users in product development

Recruiting end-users to participate in product development improves awareness of the challenges they face when designing equipment[91] (Box 2). For example, electrode manufacturers are working to improve clinical acceptance of iBCIs prior to market entry by participating in conferences, reaching out to patients with SCI, ALS, and stroke and their families, art exhibits by iBCI participants,

podcasts, and other social events involving support networks such as the BCI Pioneers Coalition[47,92]. These efforts aim to present iBCI as a viable medical solution to healthcare providers and potential future adopters.

Participant's registry

The number of participants in iBCI clinical trials for CSMS is rapidly growing; of the total number of people who have received an implant to participate in iBCI clinical trials (from 1998 up to December 2023), 25% received their implant in 2022 or 2023 (Fig. 2a). As peer-reviewed publications in the field often appear 1–5 years after implantation (Supplementary Fig. 2a), 42% of the active participants would remain unaccounted for if their data is not stored and reported accurately. Missing or incomplete reporting hinders the advancement of the field. Additionally, this lack of information is not evenly distributed among electrodes; excluding participants not reported in peer-reviewed publications removes 21% of Neuroports (8 from the total of 38), 50% of WIMAGINE (2 of 4) and 14% of Cortac (1 of 7) iBCIs, which highlights the statistical weight of such omissions.

With the current pace of iBCI progress, it is essential to provide an updated and realistic state of the field to prevent misinformation. Thus, it is critical to create and maintain a repository of iBCI participant information, including the demographic, longevity and electrode, alongside any additional information deemed necessary for benchmarking.

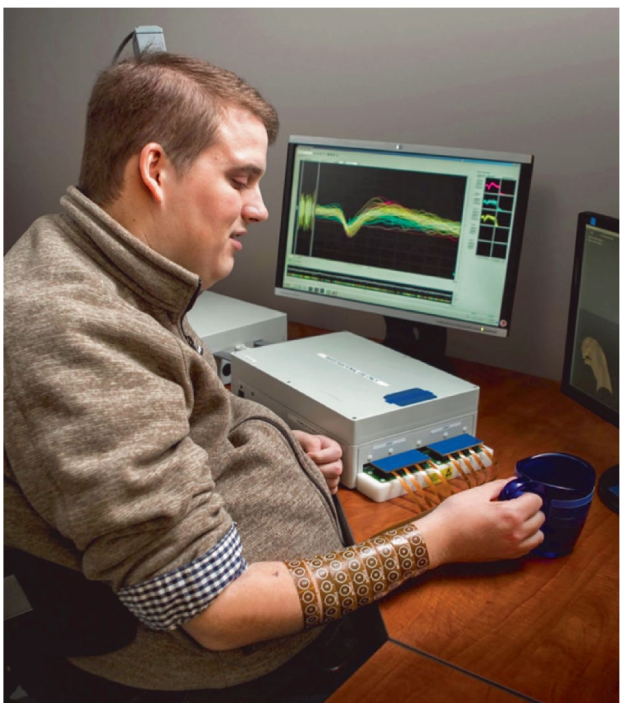
Box 2 | A patient's perspective on enrolling in an iBCI clinical trial

Following a traumatic spinal cord injury at the age of 19, I was eager for anything to improve my autonomy. After completing traditional therapy (which included inpatient physical and occupational therapy geared towards strengthening muscles that I have volitional control over and using assistive tools and devices to overcome outstanding deficits), the primary hindrance to my independence was my lack of hand movement. Owing to the proximity of my residence to Battelle and Ohio State University, I was one of very few who had access to a brain–computer interface (BCI) clinical trial focused on movement restoration. My healthcare team was aware of my interest in researching the prospects for someone in my condition. When the clinical trials for implanted BCI (iBCI) began recruiting, I fit all the criteria; therefore, my healthcare team asked if I wanted to meet with the research team. Once I learned the possibilities, I was all in.

The trial was designed to last 18 months with the goal of restoring hand and arm movements in patients with tetraplegia by using an iBCI to control surface muscle stimulation. With this device, I became the first person in the world with paralysis to reanimate a limb. Given the success, we received internal funding to continue the study at various intervals for a total of 7.5 years. However, after fund depletion, I had to face the difficult decision of either keeping the device hoping for future funding or explanting it. Would I want to have multiple surgeries to implant and explant a device each time funding was available, and would that even be sustainable? Ultimately, I was glad to have participated in such a groundbreaking trial for so long, which created new possibilities and hope for many. This experience transformed my life, and I am now dedicated to ensuring that this technology can get into the hands of others.

As BCI devices continue to mature, the field needs to remain steadfast in the core rationale for development: improving the lives of individuals with disabilities. There are still many safety concerns related to neural technology that need to be addressed, including the ownership and ability to access the neural data produced, which device is best suited for an individual, and how this technology will fit into daily life. In the near term, concerns about the reliability of the technology remain. Minimizing the adjustments to adapt the system for each individual's needs or updating the decoding algorithms can be the difference between fast adoption by patients or just being seen as a parlour trick. iBCIs should ideally be portable and fully implanted, and ensuring users are involved in each design step is vital for proper development.

Importantly, the balance between releasing and refining technology as well as the patient perspective should be considered by device manufacturers and governing bodies to ensure and guide access to potentially life-saving iBCI technology.



Box Fig. 2 | Ian Burkhart is the co-founder of the BCI Pioneers Coalition. He was implanted with the microelectrode array Neuroport in 2014 following a traumatic spinal cord injury from a swimming accident in 2010. Here, you can see him connected to the iBCI, which is being used to control the external functional electrical stimulator on his forearm to restore hand function to grasp the mug. The monitor in the background shows an expanded view of one channel of the Neuroport that can detect multiple discrete neuron firings.

Such repositories may also include performance metrics (signal quality, longevity of each implanted array and information on individual electrodes on the array), experimental design and standardized task-performance metrics (the latter can be included after publication). These repositories would enable longitudinal tracking of participants, electrode and performance data, which could be used by developers, regulators, third-party players and end-users.

Workforce development

The mounting shortage of medical specialists has long been acknowledged, with the Association of American Medical Colleges reporting a shortage of 'other specialities', which includes neurology, of between 10,300 and 35,600 in the USA in 2021 (refs. 93,94). Once iBCIs reach the market, this deficit (including for other health professionals such as neurologists, speech pathologists, occupational therapists and physical therapists, which are needed to support patients after implantation) will limit market penetration. Synchron's electrode is implanted using established endovascular stent placement, which could shorten the duration of the intervention. Similarly, Neuralink's robot implantation, developed to minimize tissue damage, could also simplify neurosurgeon efforts. However, neither of these addresses the need for additional physical or occupational therapists nor the requirement for the technical workforce for software development and the designing, prescribing, maintaining, repairing and securing of iBCIs. The current transition period is an opportunity for therapists, physicians, engineers and clinical technologists to be trained in the field.

Data sharing

To accelerate iBCI progress, sharing of de-identified data must increase, combined with the development and adoption of a standardized annotated data storage architecture and Common Data Elements, which standardizes data collection to facilitate data sharing and benchmarking. Such data standardization will enable multiple researchers to develop signal processing and artificial intelligence algorithms to improve the capabilities of iBCIs (including leveraging citizen science efforts). Ideally, this data could include both published and unpublished results for a more complete analysis.

Translation and commercialization

Most of the recent developments in iBCIs for CSMC have been demonstrated in single participants using systems developed by academic and non-profit research laboratories conducting clinical trials with electrodes produced by private manufacturers. An exception is Synchron, which conducted clinical trials under corporate operations using a proprietary electrode and iBCI system. Given the current pace of progress, industry representatives have projected that iBCIs will enter the medical device market as early as 2026, further urging the need to address clinical and translational gaps as well as patient acceptance.

Conclusions

Industry–university partnerships are needed to improve the technology and accelerate its translation, adoption and acceptance. Concerted efforts, such as the Industry–University Cooperative Research Center for Building Reliable Advances and Innovations in Neurotechnologies (IUCRC BRAIN), are a first step in harnessing such partnerships, which have resulted in the current knowledge integration review. Furthermore, in March 2024, the Implanted BCI Collaborative Community was created to bring together all stakeholders in the field through a platform that develops and uses harmonized approaches to drive continuous innovation and equitable access to iBCIs. For people with tetraplegia, locked-in-syndrome or dysarthria caused by SCI, ALS or stroke, their families, and their healthcare providers, iBCIs could be life-changing. Addressing these challenges, gaps and opportunities will help bring this technology into the real world.

Citation diversity statement

We acknowledge that papers authored by scholars from historically excluded groups are systematically under-cited. Here, we have made every attempt to reference relevant papers in a manner that is equitable in terms of racial, ethnic, gender and geographical representation.

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Author contributions

K.M.P.-K. participated in conceptualization, methodology, software, formal analysis, investigation, data curation, writing of original draft, review and editing, visualization, supervision and project administration. I.B. participated in investigation, data curation, writing, review and editing. J.L.C.-V. participated in conceptualization, methodology, formal analysis, writing, review and editing, visualization, supervision, funding acquisition and project administration.

Competing interests

I.B. is a consultant to Blackrock Neurotech and the FDA and co-founder of the BCI Pioneers Coalition. K.M.P.-K. and J.L.C.-V. declare no competing interests.

Additional information

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