

Epidural micro-ECoG provides a robust interface to the cortex over 4 years in non-human primates

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ABSTRACT: Implantable brain-computer interfaces (BCIs) are on the verge of transitioning from the research and investigational phase to clinical readiness stage. Micro-electrocorticography (μ ECoG) is one possible choice of recording modality and shows promising long-term results in both epi- and subdural implantations with direct clinical translational impact. In this paper, we present longitudinal data from epidural implantation in non-human primates. The results show that neural patterns stay comparable over the course of multiple years, and that task- and condition-specific cortical signal dynamics can be distinguished. The findings satisfy two of the most important criteria for μ ECoG-based chronic BCIs: long-term stability of neural signal quality and the presence of potentially decodable information.

INTRODUCTION

Chronically implantable brain-computer interfaces (BCIs) are getting growing attention worldwide [1, 2, 3]. During the past 20+ years various technologies were used to electrically interface with the brain, showing a broad range of performance and longevity. The use of electrocorticography (ECoG) as a recording modality has become a viable option for long-term recordings from the cortical surface. Its use has markedly increased in a miniaturized form termed μ ECoG (usually considered electrode arrays with inter-contact spacing smaller than 10 mm), due to the better trade-off between invasiveness, spatial resolution and coverage, and without the need to penetrate the cortex. In addition, μ ECoG electrode arrays may be placed below or above the dura mater, i.e., either sub- or epidurally, the latter with the aim of further minimizing the surgical intervention. While both epi- and subdural μ ECoG electrode placement has advantages and disadvantages regarding signal quality, implantation risk, and long-term performance, the impact of electrode placement remains to be fully characterized [4]. Here, we report on neural signals obtained with silicone elastomer-based μ ECoG electrode arrays implanted epidurally in two non-human primates (NHPs) for up to 4 years, while experiments in one animal are ongoing. We report on the reliability and robustness of the recorded signals obtained while the animals performed a task and during non-engagement and drowsy periods,

thus demonstrating that the basic requirements for BCI applications are met: longitudinal signal stability and ability to capture neural cortical dynamics with high fidelity and measurable differences between conditions. These findings have direct implications for the use of μ ECoG electrode arrays in preclinical and clinical BCI research and applications.

MATERIALS AND METHODS

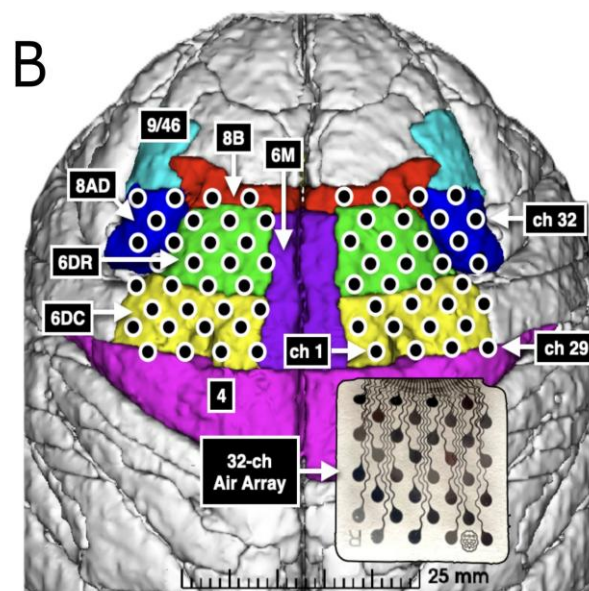
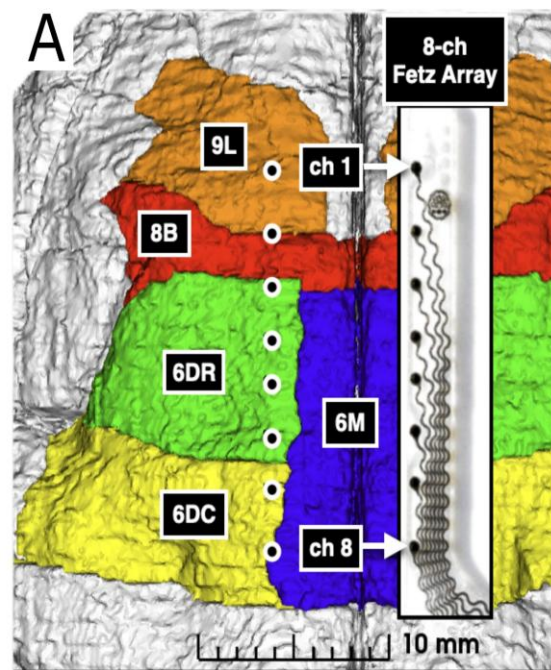
Design & Manufacturing of μ ECoG Grids: The employed μ ECoG grids (arrays) were fabricated in cleanrooms (CorTec GmbH, Freiburg, Germany) applying a method first described in detail in [5] and briefly explained in two modifications for the two designs used here in the following paragraphs.

(1) *Fetz Array:* A 130 μ m layer of liquid MED1000 (Nusil, Carpinteria, USA) silicone diluted 1:1 with n-Heptane was deposited to a mechanical carrier by spin-coating. After onset of curing, a perforated 15 μ m Parylene-C foil (SCS, La Haux-de-Fonds, Switzerland) was laminated on top. Another 130 μ m layer of diluted silicone was deposited by spin-coating, embedding the parylene foil. A 25 μ m of Pt90Ir10 foil (Goodfellow, Cambridge, UK) was laminated to the stack and a laser (picosecond pulse width, UV wavelength) was used to cut the perimeter of electrode contacts, integrated meandering tracks and weld pads. Excess PtIr foil was manually removed. A final silicone layer (130 μ m) was deposited. This silicone layer was removed from the electrode contact sites and the weld pads using the laser. Subsequently, the outer contour of the grid was cut with the laser. The Fetz Array (Fig. 1A) is a strip-like μ ECoG grid of 2.5 mm width and 28 mm length. It has 8 electrode contacts of 0.3 mm diameter and is about 0.4 mm thin.

(2) *4x8 Square 45° Grid:* This grid was produced similar to the Fetz Array, but instead of a parylene layer another PtIr metal layer was integrated that allows higher contact density. The 0.4 mm thin grid covers an area of 24.5 mm x 20 mm and has 32 electrode contacts of 1 mm diameter Fig. 1B).

(3) *Interconnection/Wiring:* The two electrode array types were lifted from the mechanical carrier and 75 μ m diameter Pt90Ir10 wires with 7 μ m polyesterimide insulation (Alleima, Sandviken, Sweden) were spot-

We implanted two male *Macaca mulatta* (13 and 15kg) non-human primates (NHP). In NHP1 (Fig. 2A), a Fetz Array was implanted epidurally adjacent to the midline, over the left prefrontal (areas 8B, 9L) and premotor (areas 6DC, 6DR). In NHP2 (Fig. 2B), two of the 32 contact arrays (4x8 Square 45° Grid) were placed bilaterally and epidurally over prefrontal (areas 8B, 8AD, 9/46) and premotor (areas 6DC, 6DR, 6M) cortices. We used a well-developed imaging and biophysical modeling pipeline to accurately implant the electrodes; surgical details can be found in prior studies [6, 7]. Pre- and post-implant MR/CT imaging enabled modeling (3D Slicer) of the animal’s skull and brain, which were co-registered with whole-brain 3D morphological models of NHP brain structures [8], as shown in Fig. 2. Although not directly relevant to the interpretation of the results in this work, it should be noted that the animals were implanted with custom neuromodulation platforms that rigidly held multiple segmented deep brain stimulation (DBS) leads (Heraeus Medevio, Minneapolis, USA), each scaled for the NHP, within rostral and caudal aspects of the central lateral (CL) thalamus. These animals are part of ongoing preclinical studies linked to our longstanding clinical efforts to treat chronic cognitive dysfunction in moderate-to-severe traumatic brain injury (TBI) [9].



Behavioral Task, Recording Setup & Data Analysis: The animals were trained to perform various visuomotor reaction time tasks for liquid rewards, as done in prior studies [6, 7]. Briefly, each trial of the vigilance task was

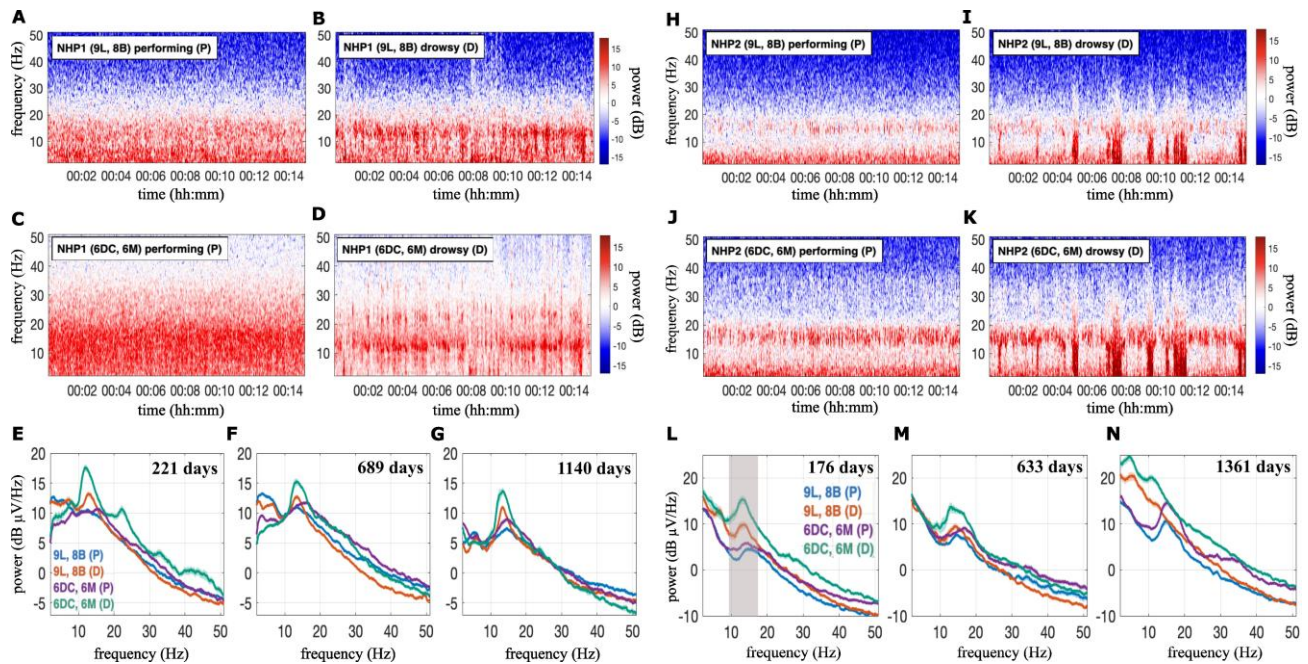


Figure 3: (A-D) Spectrograms of the epidural μ ECoG signal recorded over more frontal (9L/8B, contact 2 in Fig.2A) and more parietal/pre-motor areas (6DC/6M, contact 8 in Fig.2A) in NHP1, while the animal performed the vigilance task (performing (P), subpanels A, C) and while the animal exhibiting periods of drowsiness, eye closures, and disengagement from the task (drowsy (D), subpanels B, D), 221 days following implantation. (E-G) Average power spectral profile for the data shown in A-D at 221, 689 and 1140 days after implantation. (H-K) The same as in A-D but for NHP2, with electrode contacts at the transition of adjacent areas (9L/8B and 6DC/6M, respectively). (L-N) The same as in E-G, but for NHP2 and for 176, 633 and 1361 days after implantation. For results shown in E-N, note the largely consistent spectral profile patterns for each condition (P and D) across the implantation period, however, with varying levels, especially on day 1361 for NHP2 in which the animal exhibited drowsiness in while performing the task.

initiated by the animal first touching and then holding its hand over an infrared (IR) switch (Crist Instruments Company Inc., Hagerstown, MD, USA). The switch, attached to the front of the animal's behavioral chair, was linked to custom behavioral task programs designed in MonkeyLogic [10]. This setup controlled the visual appearance of a central gray-scale Gabor-patch (3 deg of visual angle) embedded in a $1/f$ noise pattern on an LCD screen placed 100 cm in front of the animal. The animal had to maintain fixation on the Gabor within an invisible constraint window as the spatial phase of the Gabor changed (every 300 ms) for a variable number of phase transitions (lasting 1–5 s) before changing orientation (from 0 deg to 11.25 – 90 deg). The change in orientation was the 'GO' cue for the animal to remove its hand from the IR switch, within 1 s, to receive a liquid reward. Experimental sessions typically lasted until the animal was satiated (typically within 1 to 3 h). Broadband neuronal activity was recorded with an RZ2-4 data acquisition system (TDT – Tucker Davis Technologies Inc., Alachua, FL, USA) at a sampling rate of 1-25 kHz while running TDT's Synapse software. A customized vibration sensor (801S) was attached to the behavioral chair to detect large body movements, which did at times lead to motion artifacts that were recorded in the neuronal signals (see Fig. 3B, D, I, K). Behavioral performance data and body movements were simultaneously recorded along with neural signals. The Chronux toolbox [11] was

used to generate multi-taper estimates of the power spectral density (PSD) of the μ ECoG signals. Time-frequency spectra were created to detect qualitative and quantitative differences between task-related and engaged/fatigued conditions as shown in Fig. 3. Plots showing average PSD profiles for engaged task-related and non-engaged/fatigued conditions were created for three time points (NHP1: 221, 689 and 1140 days post implantation; NHP2: 176, 633 and 1361 days) as shown in Fig. 3.

RESULTS

Electrophysiology results: Viable signals were recorded in both animals up to 4 years post-implantation and we obtained large-scale cortical μ ECoG activity (Fig. 3 and Fig. 4) during the experimental sessions. The animals typically performed well at the start of each session (Fig. 3A, C, H, J) and then performance degraded as time on task increased, due to satiety and boredom (Fig. 3B, D, I, K), at which time the animals exhibited signs of fatigue and drowsiness, which included extended eye blinks and that proceeded full eye closures. As shown in Fig. 3 for data snippets lasting ca. 15 minutes, oscillatory power within the alpha band (ca. 9-16 Hz) was significantly increased during non-engaged/drowsy conditions, as compared to when the animals were engaged and performing the task correctly.

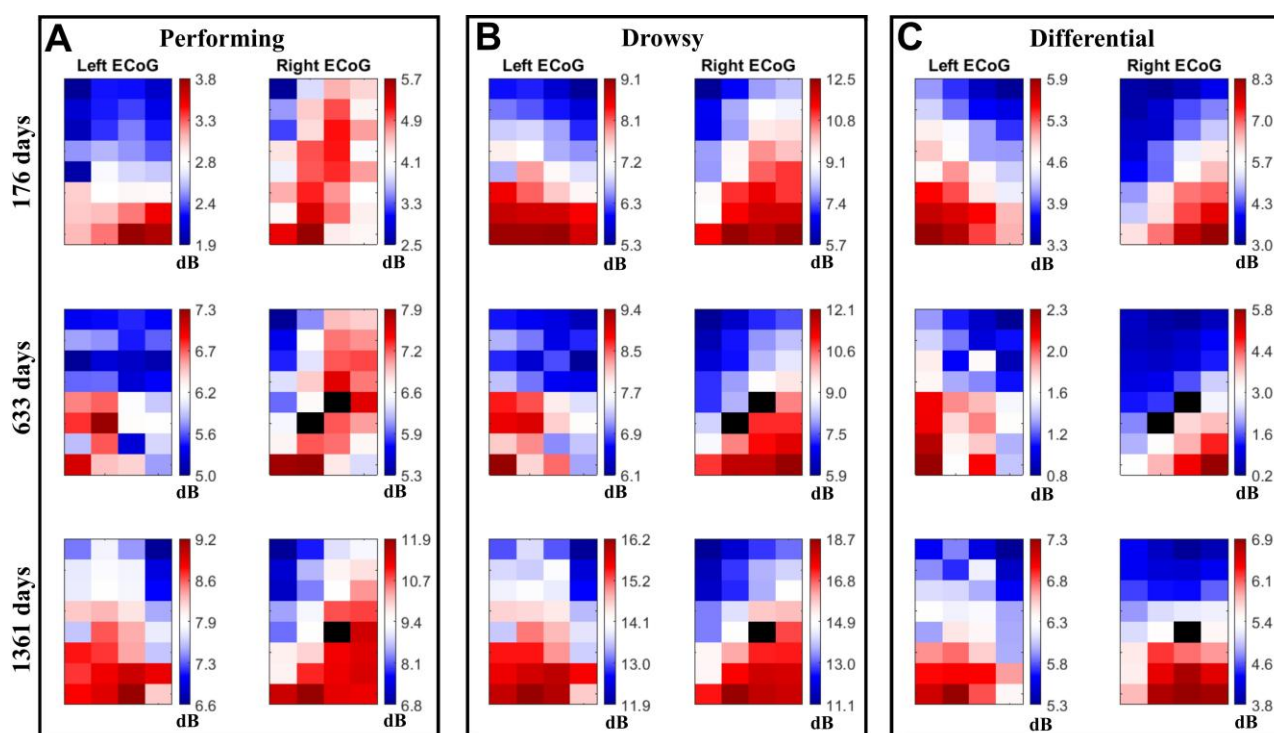


Figure 4: Spatial distribution of alpha band (9-16 Hz) spectral power changes shown for the 3 investigated time points in NHP2 (176, 633 and 1361 days after implantation) for left and right hemisphere ECoG electrode arrays and for (A) performing condition, (B) drowsy condition and (C) the differential of performing and drowsy condition. Note the varying levels of band power/activity across the left and right arrays, yet largely consistent spectral profiles and differentials across the investigated time points. Alpha band spectral power was estimated from between 9-16 Hz depicted by the gray-shaded area in Fig. 2L. Black rectangles depict dysfunctional electrode contacts. The orientation of heatmaps corresponds to the orientation of electrode arrays on the cortex of NHP2 as shown in Fig. 2B.

PSD profiles for NHP1 (Fig.3E, F, G) show slightly varying magnitude with a tendency of decreasing signal power across the three time points, however, with clear differences between the two investigated conditions (alert/performing versus drowsy) preserved.

Results for NHP2 (Fig.3L, M, N) show similar variability over time. Here, clear differences between the two conditions are seen for the first two time points (176 and 633 days), but the difference is less pronounced for the third time point (1361 days). Overall, the signal quality and spectral content under the two conditions were stable across the investigated time periods. The data shown in Fig.3 were obtained from electrode contacts placed over frontal (9L/8B) and pre-motor areas (6DC, 6M) and are representative of the recording and signal quality across both electrode arrays. Animal NHP1 tended to move more in the behavioral chair. These movements were captured by the motion sensor and also produced broadband electrical disturbances as seen in the spectrogram in Fig.3I, K (starting around 00:05). These periods were excluded from the analysis.

To investigate signal stability and preservation of spatial distribution of alpha band activity across the implantation period and across the two μ ECoG arrays for NHP2, activity was plotted as heatmaps for the performing and drowsy conditions as well as the differential of the two conditions (Fig.4). Despite varying activity levels for the three investigated time points (176, 633 and 1361 days

after implantation) a largely preserved spatial pattern for the performing (Fig.4A) and drowsy condition (Fig.4B), and most importantly a clear and robust preservation of spatial pattern for the differential (Fig.4C) can be identified for both left and right ECoG electrode arrays. These results further demonstrate μ ECoG signal stability on individual electrode contacts and across the footprint of the whole μ ECoG electrode arrays.

Technical results: Post-op reconstruction of the μ ECoG electrode array contacts confirmed that they were positioned in the epidural space. In NHP1, all 8 electrode contacts were functional and provided a good electrical coupling to the brain until the animal was euthanized according to the study protocol, and the array was removed. Studies with NHP2 are ongoing and high-quality neural signals are still being obtained from the implanted μ ECoG arrays, now more than 4 years post-implantation. Notably, in NHP2, only one out of 64 implanted electrode contacts has stopped working (high impedance) after ca. 14 months of implantation, with another one being temporarily defective at time point 633 days after implantation. We anticipate a technical failure in the one contact which will be further investigated after study finalization, which is possibly related to an experimental rejuvenation protocol applied to the individual contacts, as described by O'Sullivan and colleagues [12].

DISCUSSION

For many applications, μ ECoG grids provide an alternative to penetrating intracortical electrode arrays, for which multiple failure modes have been identified; a loss of channels (capability of sensing unit activity) over time is consistently reported in the literature [13] along with local neuronal reconfiguration, which includes neuronal death, glial scar formation, and persistent local inflammation. The signal quality and longevity of the brain interface provided by the μ ECoG electrode arrays observed in this study is consistent with findings of other groups using ECoG, e.g., that of Yang and colleagues [14] who also used electrodes produced with the same materials and methods. Although Yang et al. report data from almost 2 years in a subdural setting from two NHPs, our study demonstrates more than double the longevity for similar electrode arrays, here implanted epidurally. Davis and colleagues [15] reported on 5 years of stable use of subdural silicone-elastomer ECoG strips in a spinal cord injured patient and another study reported that cortical modulations could be observed more than 18 months post-implantation with subdural ECoG arrays in one NHP [16]. Vansteensel and colleagues [17] were able to collect successfully data from an ALS patient over the course of 7 years using the same implant technology as Davis et al. [15]; however, signal quality declined towards the end of the study which was associated with brain atrophy, “although alternative explanations are plausible” as suggested by [17]. Recently, longitudinal data from a chronic epidural electrode-based BCI system were reported [18]. The data from two patients implanted for 32 and 14 months, respectively, showed high stability over time regarding various metrics like RMS, SNR and spectral distribution [18]. Other studies investigated the impact of the dura mater on the signal amplitude and concluded that the attenuation of signals is stronger for smaller ECoG electrodes [19], similar to the electrode arrays used in this study.

These and other studies were recently incorporated into a comprehensive review by Branco and colleagues [4], which investigated the differences between epi- and subdural recordings in humans and non-human primates (NHPs). The authors reveal considerable variability in the results from the various studies, and concluded that 1) epidural recording signals attenuated more compared to subdural signals; 2) they are both subject to issues of complications and decodability of signals over time [4]. Similar to the meta-findings by Branco et al., the results in this paper show a longitudinally stable and preserved alpha band spatial pattern on the one hand and a varying signal amplitude level with a tendency of decreasing signal strength on the other. In addition, the human dura is thicker compared to that of NHPs which has to be taken into account when interpreting the results regarding signal strength in general and longitudinal signal behavior in the light of human BCI applications. However, while the decodability of the signals collected in this study were not assessed, our findings suggest that the information content in the neural signals captured

during the two behavioral conditions are different enough to be decodable. This is supported by data from one of the animals in this study where a linear classifier was used to detect the drowsy state from the μ ECoG signals and to then trigger central thalamic DBS that restored performance [20]. Of note, the studies in NHP2 are ongoing, and the complication rate is nearly zero, but standard histology has yet to be conducted to examine any potential tissue changes linked to surgical- or implantation-related complications. Furthermore the results shown in this study comprise only three days within the almost 4-year period. Although data shown across the whole μ ECoG arrays shows very well preserved spatial patterns over the investigated time points, a more comprehensive analysis will be necessary to fully characterize the longitudinal behavior of μ ECoG signals in this dataset. In summary, the longitudinal results presented in this work add to the available data in the epidural implantation realm and demonstrate the viability of implantation of μ ECoG electrode arrays above the dura as an alternative to subdural implantation for chronic μ ECoG-based brain-computer interfacing devices and applications.

CONCLUSION

Consistent with the experience collected in scientific literature about implanted ECoG grids, the study here used μ ECoG grids with 1.0 mm and 0.3 mm electrode contact diameter provide a robust electrical coupling to the cortex of two NHPs using epidural recordings. This permitted neural signal sensing with high fidelity to detect condition-specific brain oscillation changes especially in the alpha band over the observation time of ca. 4 years. The results complement the existing scientific literature reporting on chronic epidural electrode array implantation and its suitability for long-term μ ECoG-based implantable BCI devices.

ACKNOWLEDGEMENTS

This work was supported by National Institute of Neurological Disorders and Stroke grant NIH-NIHDS NS111019 and the Daedalus Fund for Innovation at Weill Cornell Medicine.

REFERENCES

- [1] Kawala-Sterniuk A, Browarska N, Al-Bakri A, Zygarlicki J, et al. “Summary of over Fifty Years with Brain-Computer Interfaces—A Review,” *Brain Sciences*, vol. 11, no. 1, Jan. 2021, doi: 10.3390/brainsci11010043.
- [2] Maiseli B, Abdalla AT, Massawe LV, Mbise M, Mkocha K, Nassor NA, et al. “Brain-computer interface: trend, challenges, and threats,” *Brain Inf.*, vol. 10, no. 1, p. 20, Aug. 2023, doi: 10.1186/s40708-023-00199-3.
- [3] Patrick-Krueger KM, Burkhart I, Contreras-Vidal JL. “The state of clinical trials of implantable brain-

- computer interfaces,” *Nat Rev Bioeng*, vol. 3, no. 1, pp. 50–67, Jan. 2025, doi: 10.1038/s44222-024-00239-5.
- [4] Branco MP, Geukes SH, Aarnoutse EJ, Ramsey NF, Vansteensel MJ. “Nine decades of electrocorticography: A comparison between epidural and subdural recordings,” *European Journal of Neuroscience*, vol. 57, no. 8, pp. 1260–1288, 2023, doi: 10.1111/ejn.15941.
 - [5] Schuettler M, Stiess S, King BV, Suaning GJ. “Fabrication of implantable microelectrode arrays by laser cutting of silicone rubber and platinum foil*,” *J. Neural Eng.*, vol. 2, no. 1, p. S121, Feb. 2005, doi: 10.1088/1741-2560/2/1/013.
 - [6] Baker JL, Ryou JW, Wei XF, Butson CR, Schiff ND, Purpura KP. “Robust modulation of arousal regulation, performance, and frontostriatal activity through central thalamic deep brain stimulation in healthy nonhuman primates,” *Journal of Neurophysiology*, vol. 116, no. 5, pp. 2383–2404, Nov. 2016, doi: 10.1152/jn.01129.2015.
 - [7] Janson AP, Baker JL, Sani I, Purpura KP, Schiff ND, Butson CR. “Selective activation of central thalamic fiber pathway facilitates behavioral performance in healthy non-human primates,” *Sci Rep*, vol. 11, no. 1, p. 23054, Nov. 2021, doi: 10.1038/s41598-021-02270-7.
 - [8] Calabrese E, Badea A, Coe CL, Lubach GR, Shi Y, Styner MA, et al. “A diffusion tensor MRI atlas of the postmortem rhesus macaque brain,” *NeuroImage*, vol. 117, pp. 408–416, Aug. 2015, doi: 10.1016/j.neuroimage.2015.05.072.
 - [9] Schiff ND, Giacino JT, Butson CR, Choi EY, Baker JL, et al. “Thalamic deep brain stimulation in traumatic brain injury: a phase 1, randomized feasibility study,” *Nat Med*, vol. 29, no. 12, pp. 3162–3174, Dec. 2023, doi: 10.1038/s41591-023-02638-4.
 - [10] Hwang J, Mitz AR, Murray EA. “NIMH MonkeyLogic: Behavioral control and data acquisition in MATLAB,” *Journal of Neuroscience Methods*, vol. 323, pp. 13–21, Jul. 2019, doi: 10.1016/j.jneumeth.2019.05.002.
 - [11] Bokil H, Andrews P, Kulkarni JE, Mehta S, and Mitra PP. “Chronux: A platform for analyzing neural signals,” *Journal of Neuroscience Methods*, vol. 192, no. 1, pp. 146–151, Sep. 2010, doi: 10.1016/j.jneumeth.2010.06.020.
 - [12] O’Sullivan K, Orazem M, Otto KJ, Butson CR, Baker JL. “Electrical rejuvenation of chronically implanted macroelectrodes in nonhuman primates,” *J Neural Eng*, vol. 21, no. 3, p. 10.1088/1741-2552/ad5703, Jun. 2024, doi: 10.1088/1741-2552/ad5703.
 - [13] Bjånes DA, Kellis S, Nickl R, Baker B, Aflalo T, Bashford L, et al. “Quantifying physical degradation alongside recording and stimulation performance of 980 intracortical microelectrodes chronically implanted in three humans for 956–2130 days,” *Acta Biomaterialia*, vol. 198, pp. 188–206, May 2025, doi: 10.1016/j.actbio.2025.02.030.
 - [14] Yang H, Fukuma R, Namima T, Okuda K, Nishi A, Iwata T, et al. “Longitudinal multitask wireless electrocorticography data from two fully implanted nonhuman primates,” *Sci Data*, vol. 13, no. 1, p. 63, Dec. 2025, doi: 10.1038/s41597-025-06359-w.
 - [15] Davis KC, Wyse-Sookoo KR, Raza F, Meschede-Krasa B, Prins NW, Fisher L, et al. “5-year follow-up of a fully implanted brain–computer interface in a spinal cord injury patient,” *J. Neural Eng.*, vol. 22, no. 2, p. 026050, Apr. 2025, doi: 10.1088/1741-2552/adc48c.
 - [16] Degenhart AD, Eles J, Dum R, Mischel JL, Smalianchuk I, Endler B, et al. “Histological evaluation of a chronically-implanted electrocorticographic electrode grid in a non-human primate,” *J. Neural Eng.*, vol. 13, no. 4, p. 046019, Jun. 2016, doi: 10.1088/1741-2560/13/4/046019.
 - [17] Vansteensel MJ, Leinders S, Branco MP, Crone NE, Denison T, Freudenburg ZV, et al. “Longevity of a Brain–Computer Interface for Amyotrophic Lateral Sclerosis,” *New England Journal of Medicine*, vol. 391, no. 7, pp. 619–626, Aug. 2024, doi: 10.1056/NEJMoa2314598.
 - [18] Larzabal C, Bonnet S, Costecalde T, Auboiroux V, Charvet G, Chabardes S, et al. “Long-term stability of the chronic epidural wireless recorder WIMAGINE in tetraplegic patients,” *J. Neural Eng.*, vol. 18, no. 5, p. 056026, Sep. 2021, doi: 10.1088/1741-2552/ac2003.
 - [19] Bundy DT, Zellmer E, Gaona CM, Sharma M, Szrama N, Hacker C, et al. “Characterization of the Effects of the Human Dura on Macro- and Micro-Electrocorticographic Recordings,” *J Neural Eng*, vol. 11, no. 1, p. 016006, Feb. 2014, doi: 10.1088/1741-2560/11/1/016006.
 - [20] Baker JL, Toth R, Deli A, Zamora M, Fleming JE, Benjaber M, et al. “Regulation of Arousal and Performance of a Healthy Non-Human Primate Using Closed-Loop Central Thalamic Deep Brain Stimulation,” in *2023 11th International IEEE/EMBS Conference on Neural Engineering (NER)*, Apr. 2023, pp. 1–6. doi: 10.1109/NER52421.2023.10123754.