The Epistemological Consequences of Artificial Intelligence, Precision Medicine, and Implantable Brain-Computer Interfaces

DOI: 10.52214/vib.v10i.12654

Ian Stevens*

ABSTRACT

I argue that this examination and appreciation for the shift to abductive reasoning should be extended to the intersection of neuroscience and novel brain-computer interfaces too. This paper highlights the implications of applying abductive reasoning to personalized implantable neurotechnologies. Then, it explores whether abductive reasoning is sufficient to justify insurance coverage for devices absent widespread clinical trials, which are better applied to one-size-fits-all treatments

Keywords: Artificial Intelligence, Precision Medicine, Implantable Brain-Computer Interfaces, Neurotechnologies, Ethics

INTRODUCTION

In contrast to the classic model of randomized-control trials, often with a large number of subjects enrolled, precision medicine attempts to optimize therapeutic outcomes by focusing on the individual.[1] A recent publication highlights the strengths and weakness of both traditional evidence-based medicine and precision medicine.[2] Plus, it outlines a tension in the shift from evidence-based medicine's *inductive* reasoning style (the collection of data to postulate general theories) to precision medicine's *abductive* reasoning style (the generation of an idea from the limited data available).[3] The paper's main example is the application of precision medicine for the treatment of cancer.[4] I argue that this examination and appreciation for the shift to abductive reasoning should be extended to the intersection of neuroscience and novel brain-computer interfaces too.

As the name suggests, brain-computer interfaces are a significant advancement in neurotechnology that directly connects someone's brain to external or implanted devices.[5] Among the various kinds of brain-computer interfaces, adaptive deep brain stimulation devices require numerous personalized adjustments to their settings during the implantation and computation stages in order to provide adequate relief to patients with treatment-resistant disorders. What makes these devices unique is how adaptive deep brain stimulation integrates a sensory component to initiate the stimulation. While not commonly at the level of

* Ian Stevens, MA Philosophy University of Tasmania in Australia, MS Bioethics Harvard Medical School Center for Bioethics

sophistication as self-supervising or generative large language models,[6] they currently allow for a semi-autonomous form of neuromodulation. This paper highlights the implications of applying abductive reasoning to personalized implantable neurotechnologies. Then, it explores whether abductive reasoning is sufficient to justify insurance coverage for devices absent widespread clinical trials, which are better applied to one-size-fits-all treatments.[7]

ANALYSIS

I. The State of Precision Medicine in Oncology and the Epistemological Shift

While a thorough overview of precision medicine for the treatment of cancer is beyond the scope of this article, its practice can be roughly summarized as identifying clinically significant characteristics a patient possesses (e.g., genetic traits) to land on a specialized treatment option that, theoretically, should benefit the patient the most.[8] However, in such a practice of stratification patients fall into smaller and smaller populations and the quality of evidence that can be applied to anyone outside these decreases in turn.[9] As *inductive* logic helps to articulate, the greater the number of patients that respond to a particular therapy the higher the probability of its efficacy. By straying from this logical framework, precision medicine opens the treatment of cancer to more uncertainty about the validity of these approaches to the resulting disease subcategories.[10] Thus, while contemporary medical practices explicitly describe some treatments as "personalized", they ought not be viewed as inherently better founded than other therapies.[11]

A relevant contemporary case of precision medicine out of Norway focuses on the care of a patient with cancer between the ventricles of the heart and esophagus, which had failed to respond to the standard regimen of therapies over four years.[12] In a last-ditch effort, the patient elected to pay out-of-pocket for an experimental immunotherapy (nivolumab) at a private hospital. He experienced marked improvements and a reduction in the size of the tumor. Understandably, the patient tried to pursue further rounds of nivolumab at a public hospital. However, the hospital initially declined to pay for it given the "lack of evidence from randomised clinical trials for this drug relating to this [patient's] condition."[13] In rebuttal to this claim, the patient countered that he was actually similar to a subpopulation of patients who responded in "open-label, single arm, phase 2 studies on another immune therapy drug" (pembrolizumab).[14] Given this interpretation of the prior studies *and* the patient's response, further rounds of nivolumab were approved. Had the patient not had improvements in the tumor's size following a round of nivolumab, then pembrolizumab's prior empirical evidence in isolation would have been insufficient, inductively speaking, to justify his continued use of nivolumab.[15]

The case demonstrates a shift in reasoning from the traditional *induction* to *abduction*. The phenomenon of 'cancer improvement' is considered causally linked to nivolumab and its underlying physiological mechanisms.[16] However, "the weakness of abductions is that there may always be some other better, unknown explanation for an effect. The patient may for example belong to a special subgroup that spontaneously improves, or the change may be a placebo effect. This does not mean, however, that abductive inferences cannot be strong or reasonable, in the sense that they can make a conclusion *probable*."[17] To demonstrate the limitations of relying on the abductive standard in isolation, commentators have pointed out that side effects in precision medicine are hard to rule out as being related to the initial intervention itself unless trends from a group of patients are taken into consideration.[18]

As artificial intelligence (AI) assists the development of precision medicine for oncology, this uncertainty ought to be taken into consideration. The implementation of AI has been crucial to the development of precision medicine by providing a way to combine large patient datasets or a single patient with a large

number of unique variables with machine learning to recommend matches based on statistics and probability of success upon which practitioners can base medical recommendations.[19] The AI is usually not establishing a causal relationship[20] – it is predicting. So, as AI bleeds into medical devices, like brain-computer interfaces, the same cautions about using abductive reasoning alone should be carried over.

II. Responsive Neurostimulation, AI, and Personalized Medicine

Like precision medicine in cancer treatment, computer-brain interface technology similarly focuses on the individual patient through personalized settings. In order to properly expose the intersection of AI, precision medicine, abductive reasoning, and implantable neurotechnologies, the descriptions of adaptive deep brain stimulation systems need to deepen.[21] As a broad summary of adaptive deep brain stimulation, to provide a patient with the therapeutic stimulation, a neural signal, typically referred to as a local field potential,[22] must first be detected and then interpreted by the device. The main adaptive deep brain stimulation device with premarket approval, the NeuroPace Responsive Neurostimulation system, is used to treat epilepsy by detecting and storing "programmer-defined phenomena."[23] Providers can optimize the detection settings of the device to align with the patient's unique electrographic seizures as well as personalize the reacting stimulation's parameters.[24] The provider adjusts the technology based on trial and error. One day machine learning algorithms will be able to regularly aid this process in myriad ways, such as by identifying the specific stimulation settings a patient may respond to ahead of time based on their electrophysiological signatures.[25] Either way, with AI or programmers, adaptive neurostimulation technologies are individualized and therefore operate in line with precision medicine rather than standard treatments based on large clinical trials.

Contemporary neurostimulation devices are not usually sophisticated enough to be prominent in AI discussions where the topics of neural networks, deep learning, generative models, and self-attention dominate the conversation. However, implantable high-density electrocorticography arrays (a much more sensitive version than adaptive deep brain stimulation systems use) have been used in combination with neural networks to help patients with neurologic deficits from a prior stroke "speak" through a virtual avatar.[26] In some experimental situations, algorithms are optimizing stimulation parameters with increasing levels of independence.[27] An example of neurostimulation that is analogous to the use of nivolumab in Norway surrounds a patient in the United States who was experiencing both treatment-resistant OCD and temporal lobe epilepsy.[28] Given the refractory nature of her epilepsy, implantation of an adaptive deep brain stimulation system was indicated. As a form of experimental therapy, her treatment-resistant OCD was also indicated for the off-label use of an adaptive deep brain stimulation set-up. Another deep brain stimulation lead, other than the one implanted for epilepsy, was placed in the patient's right nucleus accumbens and ventral pallidum region given the correlation these nuclei had with OCD symptoms in prior research. Following this, the patient underwent "1) ambulatory, patient-initiated magnet-swipe storage of data during moments of obsessive thoughts; (2) lab-based, naturalistic provocation of OCD-related distress (naturalistic provocation task); and (3) lab-based, VR [virtual reality] provocation of OCD-related distress (VR provocation task)."[29] Such signals were used to identify when to deliver the therapeutic stimulation in order to counter the OCD symptoms. Thankfully, following the procedure and calibration the patient exhibited marked improvements in their OCD symptoms and recently shared her results publicly.[30]

In both cases, there is a similar level of abductive justification for the efficacy of the delivered therapy. In the case study in which the patient was treated with adaptive deep brain stimulation, they at least had their neural activity tested in various settings to determine the optimum parameters for treatment to avoid them being based on guesswork. Additionally, the adaptive deep brain stimulation lead was already placed before the calibration trials were conducted, meaning that the patient had already taken on the bulk of the

procedural risk before the efficacy could be determined. Such an efficacy test could have been replicated in the first patient's cancer treatment, had it been biopsied and tested against the remaining immunotherapies *in vitro*. Yet, in the case of cancer with few options, one previous dose of a drug that appeared to work on the patient may justify further doses. However, as the Norwegian case presents, corroboration with known responses to a similar drug (from a clinical trial) could be helpful to validate the treatment strategy. (It should be noted that both patients were resigned to these last resort options regardless of the efficacy of treatment.)

There are some elements of inductive logic seen with adaptive deep brain stimulation research in general. For example, abductively the focus could be that patient X's stimulation parameters are different from patient Y's and patient Z's. In contrast, when grouped as subjects who obtained personalized stimulation, patients X, Y, and Z demonstrate an inductive aspect to this approach's safety and/or efficacy. The OCD case holds plenty of abductive characteristics in line with precision medicine's approach to treating cancer and as more individuals try the method, there will be additional data. With the gradual integration of AI into brain-computer interfaces in the name of efficacy, this reliance on abduction will continue, if not grow, over time. Moving forward, if a responsive deep brain stimulation treatment is novel and individualized (like the dose of nivolumab) and there is some other suggestion of efficacy (like clinical similarities to other patients in the literature), then it may justify insurance coverage for the investigative intervention, absent other unrelated reasons to deny it.

III. Ethical Implications and Next Steps

While AI's use in oncology and neurology is not yet as prominent as its use in other fields (e.g., radiology), it appears to be on the horizon for both.[31] AI can be found in both the functioning of the neurotechnologies as well as the implementation of precision medicine. The increasing use of AI may serve to further individualize both oncologic and neurological therapies. Given these implications and the handful of publications cited in this article, it is important to have a nuanced evaluation of how these treatments, which heavily rely on abductive justification, ought to be managed.

The just use an abductive approach may be difficult as AI infused precision medicine is further pursued. At baseline, such technology relies on a level of advanced technology literacy among the general public and could exclude populations who lack access to basic technological infrastructure or know-how from participation.[32] Even among nations with adequate infrastructure, as more patients seek out implantable neurotechnologies, which require robust healthcare resources, the market will favor patient populations that can afford this complex care.[33]

If patients already have the means to pay for an initial dose/use of a precision medicine product out of pocket, should insurance providers be required to cover subsequent treatments?[34] That is, if a first dose of a cancer drug or a deep brain stimulator over its initial battery life is successful, patients may feel justified in having the costs of further treatments covered. The Norwegian patient's experience implies there is a precedent for the idea that some public insurance companies ought to cover successful cancer therapies, however, insurance companies may not all see themselves as obligated to cover neurotechnologies that rely on personalized settings or that are based on precision/abductive research more than on clinical trials.

CONCLUSION

The fact that the cases outlined above rely on abductive style of reasoning implies that there may not be as strong a justification for coverage by insurance, as they are both experimental and individualized, when

compared to the more traditional large clinical trials in which groups have the same or a standardized protocol (settings/doses). If a study is examining the efficacy of a treatment with a large cohort of patients or with different experimental groups/phases, insurance companies may conclude that the resulting symptom improvements are more likely to be coming from the devices themselves. A preference for inductive justification may take priority when ruling in favor of funding someone's continued use of an implantable neurostimulator. There are further nuances to this discussion surrounding the classifications of these interventions as research versus clinical care that warrant future exploration, since such a distinction is more of a scale[35] than binary and could have significant impacts on the "right-to-try" approach to experimental therapies in the United States.[36] Namely, given the inherent limitations of conducting large cohort trials for deep brain stimulation interventions on patients with neuropsychiatric disorders, surgically innovative frameworks that blend abductive and inductive methodologies, like with sham stimulation phases, have traditionally been used.[37] Similarly, for adaptive brain-computer interface systems, if there are no large clinical trials and instead only publications that demonstrate that something similar worked for someone else, then, in addition to the evidence that the first treatment/dose worked for the patient in question, the balance of reasoning would be valid and arguably justify insurance coverage. As precision approaches to neurotechnology become more common, frameworks for evaluating efficacy will be crucial both for insurance coverage and for clinical decision making.

ACKNOWLEDGEMENT

This article was originally written as an assignment for Dr. Francis Shen's "Bioethics & AI" course at Harvard's Center for Bioethics. I would like to thank Dr. Shen for his comments as well as my colleagues in the Lázaro-Muñoz Lab for their feedback.

[1] Jonathan Kimmelman and Ian Tannock, "The Paradox of Precision Medicine," *Nature Reviews. Clinical Oncology* 15, no. 6 (June 2018): 341–42, https://doi.org/10.1038/s41571-018-0016-0.

[2] Henrik Vogt and Bjørn Hofmann, "How Precision Medicine Changes Medical Epistemology: A Formative Case from Norway," *Journal of Evaluation in Clinical Practice* 28, no. 6 (December 2022): 1205–12, https://doi.org/10.1111/jep.13649.

[3] David Barrett and Ahtisham Younas, "Induction, Deduction and Abduction," *Evidence-Based Nursing* 27, no. 1 (January 1, 2024): 6–7, https://doi.org/10.1136/ebnurs-2023-103873.

[4] Vogt and Hofmann, "How Precision Medicine Changes Medical Epistemology," 1208.

[5] Wireko Andrew Awuah et al., "Bridging Minds and Machines: The Recent Advances of Brain-Computer Interfaces in Neurological and Neurosurgical Applications," *World Neurosurgery*, May 22, 2024, S1878-8750(24)00867-2, https://doi.org/10.1016/j.wneu.2024.05.104.

[6] Mark Riedl, "A Very Gentle Introduction to Large Language Models without the Hype," *Medium* (blog), May 25, 2023, https://mark-riedl.medium.com/a-very-gentle-introduction-to-large-language-models-without-the-hype-5f67941fa59e.

[7] David E. Burdette and Barbara E. Swartz, "Chapter 4 - Responsive Neurostimulation," in *Neurostimulation for Epilepsy*, ed. Vikram R. Rao (Academic Press, 2023), 97–132, https://doi.org/10.1016/B978-0-323-91702-5.00002-5.

[8] Kimmelman and Tannock, 2018.

[9] Kimmelman and Tannock, 2018.

[10] Simon Lohse, "Mapping Uncertainty in Precision Medicine: A Systematic Scoping Review," *Journal of Evaluation in Clinical Practice* 29, no. 3 (April 2023): 554–64, https://doi.org/10.1111/jep.13789.

[11] Kimmelman and Tannock, "The Paradox of Precision Medicine."

[12] Vogt and Hofmann, 1206.

[13] Vogt and Hofmann, 1206.

[14] Vogt and Hofmann, 1206.

[15] Vogt and Hofmann, 1207.

[16] Vogt and Hofmann, 1207.

[17] Vogt and Hofmann, 1207.

[18] Vogt and Hofmann, 1210.

[19] Mehar Sahu et al., "Chapter Three - Artificial Intelligence and Machine Learning in Precision Medicine: A Paradigm Shift in Big Data Analysis," in *Progress in Molecular Biology and Translational Science*, ed. David B. Teplow, vol. 190, 1 vols., Precision Medicine (Academic Press, 2022), 57–100, https://doi.org/10.1016/bs.pmbts.2022.03.002.

[20] Stefan Feuerriegel et al., "Causal Machine Learning for Predicting Treatment Outcomes," *Nature Medicine* 30, no. 4 (April 2024): 958–68, https://doi.org/10.1038/s41591-024-02902-1.

[21] Sunderland Baker et al., "Ethical Considerations in Closed Loop Deep Brain Stimulation," *Deep Brain Stimulation* 3 (October 1, 2023): 8–15, https://doi.org/10.1016/j.jdbs.2023.11.001.

[22] David Haslacher et al., "AI for Brain-Computer Interfaces," 2024, 7, https://doi.org/10.1016/bs.dnb.2024.02.003.

[23] Burdette and Swartz, "Chapter 4 - Responsive Neurostimulation," 103–4; "Premarket Approval (PMA)," https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P100026.

[24] Burdette and Swartz, "Chapter 4 - Responsive Neurostimulation," 104.

[25] Burdette and Swartz, 126.

[26] Sean L. Metzger et al., "A High-Performance Neuroprosthesis for Speech Decoding and Avatar Control," *Nature* 620, no. 7976 (August 2023): 1037–46, https://doi.org/10.1038/s41586-023-06443-4.

[27] Hao Fang and Yuxiao Yang, "Predictive Neuromodulation of Cingulo-Frontal Neural Dynamics in Major Depressive Disorder Using a Brain-Computer Interface System: A Simulation Study," *Frontiers in Computational Neuroscience* 17 (March 6, 2023), https://doi.org/10.3389/fncom.2023.1119685; Mahsa Malekmohammadi et al., "Kinematic Adaptive Deep Brain Stimulation for Resting Tremor in Parkinson's Disease," *Movement Disorders* 31, no. 3 (2016): 426–28, https://doi.org/10.1002/mds.26482.

[28] Young-Hoon Nho et al., "Responsive Deep Brain Stimulation Guided by Ventral Striatal Electrophysiology of Obsession Durably Ameliorates Compulsion," *Neuron* 0, no. 0 (October 20, 2023), https://doi.org/10.1016/j.neuron.2023.09.034.

[29] Nho et al.

[30] Nho et al.; Erik Robinson, "Brain Implant at OHSU Successfully Controls Both Seizures and OCD," OHSU News, accessed March 3, 2024, https://news.ohsu.edu/2023/10/25/brain-implant-at-ohsu-successfully-controls-both-seizures-and-ocd.

[31] Awuah et al., "Bridging Minds and Machines"; Haslacher et al., "AI for Brain-Computer Interfaces."

[32] Awuah et al., "Bridging Minds and Machines."

[33] Sara Green, Barbara Prainsack, and Maya Sabatello, "The Roots of (in)Equity in Precision Medicine: Gaps in the Discourse," *Personalized Medicine* 21, no. 1 (January 2024): 5–9, https://doi.org/10.2217/pme-2023-0097.

[34] Green, Prainsack, and Sabatello, 7.

[35] Robyn Bluhm and Kirstin Borgerson, "An Epistemic Argument for Research-Practice Integration in Medicine," *The Journal of Medicine and Philosophy: A Forum for Bioethics and Philosophy of Medicine* 43, no. 4 (July 9, 2018): 469–84, https://doi.org/10.1093/jmp/jhy009.

[36] Vijay Mahant, "'Right-to-Try' Experimental Drugs: An Overview," *Journal of Translational Medicine* 18 (June 23, 2020): 253, https://doi.org/10.1186/s12967-020-02427-4.

[37] Michael S. Okun et al., "Deep Brain Stimulation in the Internal Capsule and Nucleus Accumbens Region: Responses Observed during Active and Sham Programming," *Journal of Neurology, Neurosurgery & Psychiatry* 78, no. 3 (March 1, 2007): 310–14, https://doi.org/10.1136/jnnp.2006.095315.