Neuroprosthetics: The Restoration of Brain Damage

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In the case of a severe accident that would cause spinal cord injury or the loss of a limb, the patient would consequently suffer paralysis or the need for an amputation. Thanks to decades worth of studies dedicated to a wide range of neurotechnologies, such patients will be able to regain their once lost abilities, as seen in Figure 1. Neuroprosthetics, which remain in development to this day, are devices that are crucial to helping survivors regain their ability to move on their own through electric stimulation to the paralyzed or prosthetic limbs. As nervous system disorders additionally affect the economy and larger-scale social situations, neuroprosthetics would benefit society in the long term (Borton).

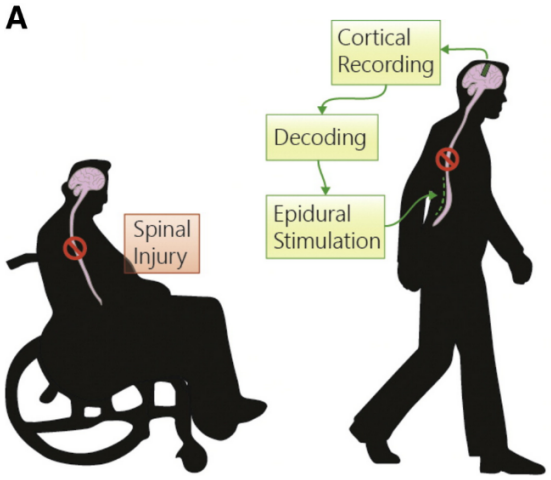

Figure 1: A simplified visual of how BMI could help a paralyzed SCI patient (Moxon).

The device is placed onto the motor cortex, sending electrical signals to the area of intended movement, as well as receiving neural signals from surrounding areas of the brain. Then, signals are sent to a computer, which translates and sends back the message. This is an extremely impactful device in neuroscience, as it can provide neurologically disabled or severely injured people the new opportunity to be physically independent.

The origin of neuroprosthetics began in 1949, when Hermann von Helmholtz had conducted an experiment in which he ran a nerve fibre current through a dissected frog's muscle

calf, leading to the muscle contracting, or “kicking.” The observation showed that actions are regulated by the electric activity that is highly interactive between the nervous system and muscles, and such currents that were used for this discovery are continued to be in use to this day to stimulate paralyzed areas of the body (Pernu). The journey of this device in clinical use started out with having patients complete simple tasks, such as reaching for and grabbing objects and aiming at targets with the damaged or prosthetic limb, and is currently going through trials of advancements in capturing touch senses. There is still a number of ethical issues, including occasional corrosion in the device, privacy interferences, and the neuroprosthetic’s trial failures to precisely translate the accepted message to the computer. Privacy debates revolve around who is responsible for certain aspects and potential flaws of the device and protection against third parties invading the information transfer between the brain’s signals and the device. Such obstacles and holes in our current knowledge to maximize the safety and functional accuracy of neuroprosthetics remain, despite it already being approved for clinical use. It is important to clarify what we can currently do with the neuroprosthetics that we have today, what still needs to be done, and what the main barriers exist to achieve this.

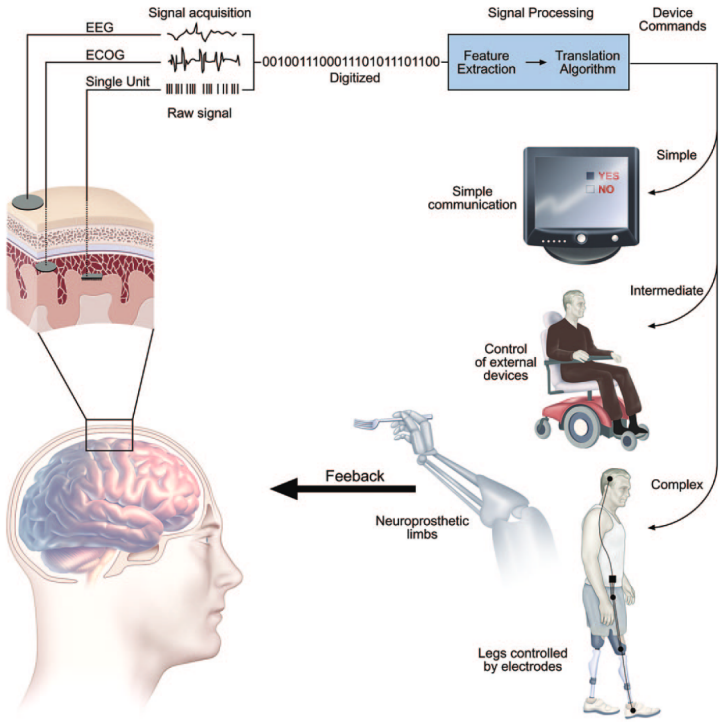

Figure 2: The range of abilities that BCI systems may have, from mentally controlling computer screen features to controlling an artificial limb for daily function (Leuthardt).

Brain-Computer Interfaces (BCIs)

Brain-computer interface (BCI), which can be used interchangeably with "brain-machine interface" (BMI), is a general term for any device that coordinates external stimuli with the user's intentions that are detected by signals passing through an electrophysiologically damaged area in the brain (Leuthardt). The original BCIs linked the brain with an artificial (prosthetic) limb, which remains the standard today, with its current range of possible functions presented in Figure 2. Researchers refer to the connection between prosthetic and brain signals as a "reciprocal link" because their signals go through a continuous feedback loop (a back and forth sequence). Brain signals go through an array of decoding in the BCI implanted in the cortex, which detects the intended motion from these signals, thus resulting in the user's purposeful flow

of motions. Conversely, the robotic limb sends microstimulation pulses that travel to the brain (Lebedev). Patients that BCIs could be most crucial for include stroke survivors, amputees, those with spinal cord injuries, and others suffering from neurophysiological disabilities (Leuthardt). BCIs can also function beyond robotic arms— they can also allow the user to control computer cursors, avatar bodies, drones, and wheelchairs (Lebedev).

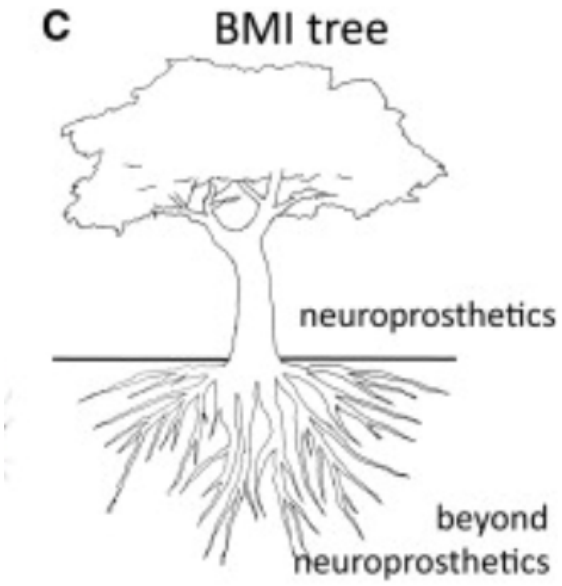

Figure 3: The BMI tree visually represents that there are various subtypes of BMI devices (Moxon).

Neuroprosthetics. Neuroprosthetics are a category of BCI (see Figure 3), in which its main distinction from the broad term is that during experiments, neuroprosthetics are based on maximizing performance among the subjects, while BMI experiments focus more on studying the interaction itself with the subject's own neurophysiological activity to perform the intended

action (Moxon). Neuroprosthetics can help treat amputees and patients that are suffering from severe spinal cord injury (SCI), strokes, or traumatic brain injury, which may all result in paralysis (Battro). Paralysis is due to an interruption in the brain's neural signals, resulting in that brain area's respective limb not receiving that message, thus it being unable to move. A failure occurring in any one processing loop in the brain could damage cognitive and motor abilities temporarily or permanently. For example, Parkinson's Disease (PD) is a result of dopamine transmission failure in the basal ganglia, disturbing the brain's output circuits that regulate motor function and leading to tremor and inadequate cognitive function (Borton). Another instance is multiple sclerosis (MS), in which demyelination (loss of myelin around the axon) leaves the neuron unprotected, which disturbs currents going through axons, therefore deteriorating the ability for body motion control (Borton). The neuroprosthetic would then substitute the functions in that "gap" between damaged signal transfers (see Figure 4). There are different types of neuroprosthetics, including functional electrical stimulation (FES), peripheral nerve stimulation, and spinal cord stimulation (SCS).

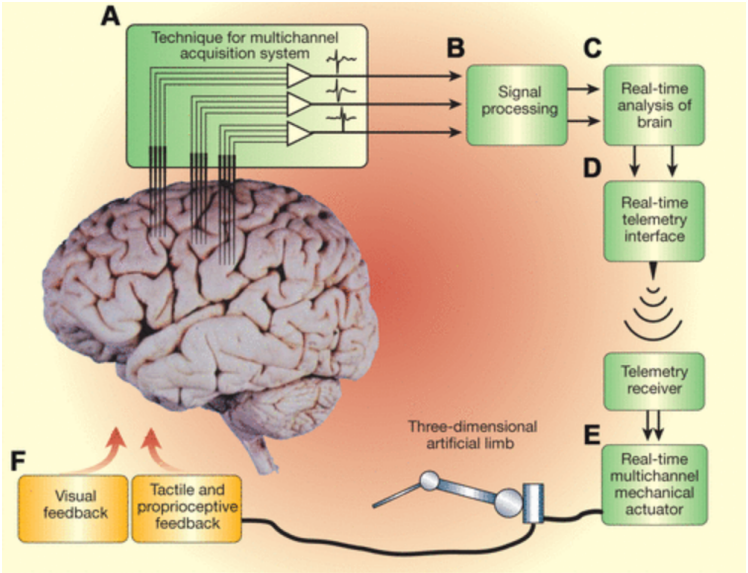

Figure 4: Overall step-by-step cortical BCI function using a prosthetic limb (Lebedev).

Neuroprosthetics and Brain Function. In a prosthetic limb, the electrodes that are connected to a computer through a signal are placed in the motor cortex, which altogether coordinate with the intended movement of the prosthetic. The motor cortex of the brain is in charge of movement execution, sending signals through the spinal cortex and into the muscle to perform a certain action, while the posterior parietal cortex (PPC) is in charge of movement planning, focusing on the intention itself. Brain networks are densely interconnected and efficiently merge external input with “internal circuits" (previous knowledge) to generate an output, but unfortunately, exactly how this happens is vaguely known to researchers. Neural connections may be individually interrupted when an SCI occurs, but the motor cortex as an entirety can still function, so neuroprosthetics are key in reconnecting that interrupted piece. Neuroprosthetics help maintain the flow of neural activity in the “broken” spot because the brain signals caught there by the neuroprosthetics are decoded by the computer and transferred to the robotic prosthetic or the individual’s own (paralyzed) limb. To understand the brain would lead to building more productive neurotechnology. In functional electrical stimulation (FES), the most advanced stimulators consist of multiple pathways to trigger specific pre-programmed sequences, each corresponding to its respective muscle group (Mayr, Krenn, & Dimitrijevic). In one study, FES was used to try and help a 53 year old paralyzed male regain his movement that was lost from tetraplegia (severe high-cervical SCI). Two intracortical microelectrode arrays were implanted in the hand-controlling area of his motor cortex, allowing him to perform small, volitional movements, with more electrodes being added onto various arm-controlling areas throughout the trials. After 311 days had passed since the implant, his task in using FES was to cortically command arm movements to aim at a target, resulting in an 80-100% accuracy, and was eventually able to use his paralyzed arm to grab a cup of coffee and drink from it (11 out of

the 12 attempts) and eat by himself (Ajiboye). Despite there being just enough findings on the general functions of the brain to create neuroprosthetics that present this adequate efficiency, the lack of thorough knowledge on brain processes interferes with the device accurately imitating the biology of neuron behavior (Battro). With the absence of nature's true processes, the technology consequently remains limited, and flaws and errors are bound to occur, such as inconsistently capturing precise signals. The software portion of the problem is the computer translating the incorrect message back to the neuroprosthetic, while the hardware obstacle is that the neuroprosthetics that can most accurately capture messages are too bulky and require too much energy. This ultimately results with the system slowing down too soon (Battro). Correcting the circuit's malfunctions with today's available information means committing to sending foregin electrical impulses through the organism with just an ambiguous sense of how the currents work with the brain's computations. Still, neuroprosthetics work quite efficiently overall, as seen in Figure 5, but these barriers must be solved in order to replicate the complex biological functions.

Figure 5: A successful attempt of a man with paralyzed hands, wrists, and elbows using FES to grab an ice cream cone, eat it, and put it back down all by himself (Rupp).

Sensory Neuroprosthetics. Improving the neuroprosthetic user's accuracy and efficiency with the prosthetic limb does not stop at simply being able to perform intended actions—touch sensory also plays an important role for this result. Sensory features in robotic limbs through brain-controlled neuroprosthetics bring more to the patient than just allowing them to physically feel again: they improve prosthetic limb use precision and allows for more calculated movements, thus making it even easier for the patient to proceed with their daily life. Cathy Hutchinson, a stroke survivor patient using neuroprosthetics, was able to perform typical, daily actions, such as lifting a bottle with a straw to drink from it, "regaining" her abilities all the way

down to wiggling “her” fingers. Similarly to another patient, Igor Spetic, who lost his arm in an accident, she was still not able to feel the object. Spetic reported being unable to properly handle objects, such as bruising fruit by grabbing it too tight. In such situations, sensory feedback would allow the patient to make more precise intended movements. Prosthetic limbs depend on neurofeedback loops of efferent nerve signals (from brain to muscle) and afferent sensory feedback (from receptor to brain) for a more thorough function restoration in the conscious use of a BMI device (Moxon & Kwok). Sensory organs send electrical messages to our brain representing information directly from the environment, also known as input. Our neural network in the central nervous system (CNS) greatly modifies the original input, such as light, sound, and mechanical forces, computing it into new representation patterns that we understand once it is interpreted and processed in the brain. These filtered patterns are spread through the brain’s many networks, keeping a continuous flow of movement computations. Voluntary movement occurs when the brain organizes sensory signals and previously known information in a certain way that plans an upcoming action, releasing electrical patterns that result in that coordinated muscle movement (Battro). It is still very unclear to researchers what specific processes occur during natural brain computation involving senses beyond just the back and forth travels of signals. There is enough uncovered information to compute neural hardware for both hearing and vision, but this level of knowledge is insufficient to allow for the creation of neuroprosthetics with sensory features dedicated to movement (Battro). Additionally, there remains a continuous debate on determining whether neural codes are fundamentally based on the *rate* of individual neurons firing or *when* exactly neurons fire, also referred to as temporal coding (Moxon). There is still hope though: the information gained from research is growing rapidly. Sensory device features are currently divided into functions of the brain, muscles, peripheral nerves, and body

kinematics. Lately, researchers have been focusing their studies on coordination between position and velocity of muscle activity, peripheral nerve signals, and dorsal root ganglion (DRG). These enter a closed-loop system of motor commands and sensory feedback, an aspect of sensory devices previously mentioned (Borton). According to Mayr, Krenn, and Dimitrijevic, it has already been found that externally controlled sensory neurons initiate the sensory areas of paralyzed muscles, which allows for supplementary touch-sensory input that makes up for the impaired corticospinal excitatory pathways.

In prosthetics, targeted reinnervation is a method used to redirect touch senses coming from the very surface of the hands to the chest. Intraneural peripheral electrodes have been found to subtly reactivate peripheral nerve sensors, which is additionally used in decoding electrical activity of forearm muscles providing grip information. Bidirectional peripheral interfaces additionally provide an opportunity in prosthetic limbs to translate incoming information into clear sensory feedback in real time (Borton). Lost somatosensory perception is retained through sensory substitution, which has been found to greatly advance BMI performance, and can be accomplished through direct intracortical microstimulation that enhances directly obtained senses immediately. The main obstacles, though, are inaccurate perceptions of those senses, largely due to unpredictable neural activation reactions, the difficulty of reporting sensations through animal-based studies, and the ambiguity of senses (Borton).

Deep-Brain Stimulation and Utah Array Comparison. According to Bullard, deep-brain stimulation (DBS) is a neuroprosthetic type that is considered to be the “most widespread intracranial clinical system” and has been approved by the U.S. Food and Drug Administration (FDA) to be chronically implanted intracranially. It has been used throughout decades to treat

both motor and neuropsychiatric disorders, such as epilepsy, Parkinson's Disease (PD), depression, obsessive-compulsive disorder (OCD), and Alzheimer's, with the overall purpose of manipulating functional activity level (Battro & Bullard). DBS is made up of a multicontact lead (which goes through a burr hole and into a target structure inside the head), an internal pulse generator, and an extension cable (Bullard). In the instance of PD, DBS functions through stimulating a targeted spot in the basal ganglia, which is in charge of planning and performing movements and basic cognitive functions, at approximately 100 times per second. It has been implemented in over 150,000 people, but symptoms in Parkinson's disease have only declined, rather than eliminated. Bullard claims that silicon-based Utah arrays, however, are the "most widespread intracranial human *experimental* system" (Bullard). These neuroprosthetics are not approved for long-term clinical use all on their own: the FDA has only approved the Utah array for 30 day implantation, with a longer duration only permitted with a supporting investigational device. Bullard conducted trials to determine and compare the safety of DBS and silicon-based Utah arrays. The most common defects observed in DBS use included 4.57% infection rates, hemorrhage (excessive blood loss) (2.86%), 2.56-2.58% experiencing lead fracture and migration, and 2.22% causing skin erosion. There were far less adverse elements in the Utah array, in which the longest time range that a subject used a Utah array was reported to be 1975 days— about 5.4 years. Although not prevalent in this individual trial, the Utah array remains leaving the user at the risk of infection, in which the surrounding tissue responds through glial scarring, inflammation, and neuronal death. Consequently, clinically implanted neuroprosthetic systems using the Utah array are required to be accompanied by systems that record and respond to the stimuli themselves, as mentioned. The risks have not been officially confirmed, though,

since there were minimal studies done on the effects that chronic intracortical electrodes placed in the motor cortex have on motor function (Bullard).

Privacy and Accountability Concerns

Uncertainty regarding neuroprosthetics stretches beyond explanations behind the brain's physical interaction with the device. As it goes with our most recent and advanced technology that we use on a daily basis, privacy happens to be a major controversial issue. The information processed in the brain that passes through neuroprosthetics is absorbed in tiny amounts through an input-output manner, but since neurotechnology is developing at a rapid rate, future BMIs will be able to record brain activity through higher spatial resolution. The question in accountability, though, is to what extent would the user and manufacturer be held responsible when the device is in use, and for what? Since the neuroprosthetic is directly linked to the brain, it is difficult to come to a clear conclusion in this debate. For obligation purposes, it is important to confirm the division of what aspects of the device both the user and the manufacturer are held responsible for. User responsibility includes voluntarily rejecting the "veto" implanted into the device's system (which should be accurately programmed by the manufacturer) and being directly informed and aware of the device's limited abilities (such as holding a baby when the device was knowingly not made for such a circumstance). The manufacturers, on the other hand, should be held accountable for the overall safety of the product and should minimize risks, as well as being transparent with the patient about its limits, specific abilities, risks, and anything else that is crucial for the user to be aware of. Regarding security and privacy, an obstacle in protecting both is that an electronically amplified biological signal to another device could easily be obtained by a third party, which can then be manipulated and potentially distributed, also referred to as

“brainjacking”. It can become a disastrous situation, in which the third party may use it violently through blackmail or physically controlling the person. Transmitting information through any wireless system, such as Wi-Fi, is not necessarily privacy-safe. This happens to be a major problem with most BMIs, as their purpose is to pass information directly from the brain through wireless systems (Clausen). There are still plenty of questions left unanswered, such as where would this information go, who would have access, and how could manufacturers confirm that (or if) the information is safely stored? To this day, there has not yet been found a concrete answer to protecting security and privacy. However, applications from various related fields, like digital communication, may contribute to working towards finding that answer (Clausen). To ensure the most privacy-safe experience for BMI device users, strict standards for information protection must be established, but regardless of the extent of protection, BMI users must be informed on the kinds of data captured and stored by the device.

Safety Concerns. Signal attenuation is the gradual loss of strength in neuroprosthetics, and is a current key issue in chronic neuroprosthetic applications. In an experiment using scanning electron microscopy (SEM) on animals, this weakening has been found to cause sensor failure and recorded signals to eventually fade. SEM is used to detect any changes occurring in chronically implanted neuroprosthetics, and in this case, it found corroded platinum electrode tips, physically altered silicon, and the parylene insulation near the threshold of collapsing. Meninges, which protects the CNS, has been hypothesized to cause the array to shift from its place in the cortex, causing signal loss. However, an experiment with 5 Rhesus Macaques was conducted, with eight intracortical microelectrode arrays (MEAs) implanted in each: four males and one female. MEAs are frequently used in sensory devices to record single-unit activities, but

must accurately operate for at least ten years to be approved for medical use; signal recordings through MEAs have been observed to fade over time in various animal studies. In this Rhesus Macaque study, from the seven of eight arrays being collected for data analysis, there was no serious spatial orientation shift among the electrodes, excluding some tissue density variation. Though, gliosis has disrupted the cortical structure, which occurs within months of implementation but does not truly affect recordings until a few years of use. The gliosis may have been insulating the electrode from surrounding neurons, disallowing diffusion (Barrese). Other devices like DBS can additionally lead to side effects that may damage cognition, suggested to be due to its larger size, the lack of precision in placement, or even an unsuitable stimulation pattern (Battro). Research on overcoming these obstacles continues, but standards for how neuroprosthetics should be built and interact with the surrounding brain tissue have already been set. The design should precisely correspond with the specific function that requires restoration, along with the correct size (this is vital for the body to accept the foreign device, and in this case, a scar will form around it), shape, biocompatibility, material, and implementation procedure, overall being minimally invasive (Cutrone).

Conclusion

So far, it has been clearly established that neuroprosthetics mainly function through electrical activity, which was a method used since 1949 when the cooperation between brain function and electrical activity was first discovered. We have been progressively advancing features and the accuracy of neuroprosthetics and BMIs, considering that there are various types and we are striving towards being able to substitute the full experience of physical feeling and motions through such devices in those that have lost such abilities. Through the study comparing DBS

and Utah-arrays, it was emphasized how different neuroprosthetic types have advantages and disadvantages over others, as well as showing us what we have accomplished so far and what work still needs to be done. The most significant areas of neuroprosthetics that need advancements are signal attenuation, precise neuroprosthetic sizes, and biocompatibility, as well as protecting the patient's privacy and deciding on the division among who is responsible for what in the device's use. There is still no significant progress towards a solution among any of these bigger issues, but the continuing studies and debates allow this fascinating and crucially beneficial device to reach its optimal level of function and to minimize any potential risks. Our progress in sensory features mainly comes from targeted reinnervation and the immense focus on bidirectional methods; continuous feedback loops have been shown to be an extremely important aspect of maximizing neuroprosthetic performance. Despite the lack of concrete answers, we have still come quite far in advancements, in which more types of neuroprosthetics are being certified for clinical use, and the ones that are already in such use have greatly improved the patients' lives. Studies on safety measures should consist of: identifying what the specific issue is, what is causing it, and how to reduce or prevent the negative effects. Studies do not have to only be in the field of neuroscience— as discussed, both philosophy and digital communication can be of great help in contributing to future discoveries. Neuroprosthetics have the power to entirely change people's lives, from being unable to even lift a finger to gaining a completely new world of independence, in which patients can now eat and drink by themselves without requiring any help. With this, we have accomplished something spectacular, and the journey of neuroprosthetics continues towards enhancing its already remarkable performances.

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