Brain Machine Interfaces using Operant Conditioning of Neural Activity

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Individuals with sensorimotor deficits resulting from disease, cardiovascular injury or traumatic injury are often unable to effectively interact with the world around them. This dramatically reduces their quality of life as they are unable to perform their activities of daily living (ADLs).[1,2] Brain machine interfaces (BMIs) and brain computer interfaces (BCIs) are an emerging set of technologies that aim to provide these individuals with a novel way of interacting with their environment. BMIs and BCIs (hereafter referred to collectively as BMIs) function by converting neural activity from the brain into various forms of output commands that can be used to control external devices (such as robotic arms, computer cursors, wheelchairs, etc.) or neuroprostheses.[3,4]

The source of the neural activity determines its spatial and temporal specificity. Non-invasive imaging techniques such as near infrared spectroscopy (NIRS) decode neural activity by observing changes in metabolic activity but provide low spatial and temporal resolution.[5,6] Non-invasive electromagnetic recording techniques such as electroencephalography (EEG) and magnetoencephalography (MEG) provide greater temporal resolution. As a result, these techniques can record temporally precise population activity and whole-brain oscillatory rhythms that have significant motor and behavioural correlates. For instance, novel work by Marquez-Chin and colleagues has shown that EEG signals can be used to predict specific hand movements with high accuracy, by observing desynchronization of neuronal oscillations above the sensorimotor cortices of the human brain.[7] The limitation of EEG and MEG recording techniques is that they provide poor spatial resolution and have a lower signal to noise ratio, making it impossible to accurately localize the source of specific neuronal activity.[8] Since the brain is known to function with high spatial specificity (i.e. specific foci of the brain are known to be responsible for specific behavioural and motor correlates), it becomes necessary to record activity at the spatial resolution of the brain using invasive techniques such as intracranial electroencephalography (iEEG). iEEG provides access to local field potentials and activities of single neurons, which can then be used to decipher more specific intents from neuronal activity.

Traditional invasive BMI systems function by correlating a specific pattern of neural activity to an overt behavioural or motor intent. A mathematical model is then developed based on this correlation, to convert the neural activity into a desired control signal, which can in turn be used to control an actuator (any kind of electrical device, for example a computer cursor, a robotic arm, or a neuroprosthesis). However, the underlying assumption made in this approach is that a specific pattern of neural activity is responsible for a specific motor or behavioural intent, and the goal of the mathematical model is to decipher and decode this neural activity in order to extract that specific intent. Through training, participants learn to volitionally drive and adapt these existing neuronal circuits in order to obtain effective control over the actuator. For the past two decades, BMI research has mainly focused on recording from ever larger populations of neurons and improving the mathematical algorithms used to decode this activity into useful commands. And while there is ample evidence of volitional modulation of cortical neuron activity in human and animal models, BMI systems have limited performance for reasons that are not well understood. For example, a study found that the prediction accuracy of movement parameters increased with the number of neurons included in the decoding algorithm; however, accuracy plateaued below 100%. Extrapolating these prediction accuracy curves shows an asymptotic trend for an infinite number of neurons, even when recording from motor-related areas.[9]

While the prevailing view in BMI research is to assume that the motor cortex encodes static movement parameters,[9-11] which can be extracted and decoded with high density neural interfaces and improved mathematical algorithms, an alternative approach has been proposed based on research from the early 1970's involving operant conditioning of neural activity. A series of studies by Fetz and colleagues provided some of the first evidence for the volitional modulation of single neuron activity using biofeedback.[12,13] In these experiments, the activity of a single cortical neuron was explicitly reinforced every time the firing rate surpassed a threshold, in this case by giving a food reward to a monkey. After a few minutes, the activity of the neuron changed drastically from baseline levels. Interestingly, the monkeys would quickly learn to modulate newly isolated neurons, even when two contiguous neurons (recorded from by the same electrode) would be trained to perform opposing tasks (upregulation vs. downregulation). If the selected cortical neuron happened to be the primary motor cortex, upregulation of the activity of this neuron was typically accompanied with a physical movement (corresponding to the somatotopic location of the neuron) in the early experiments. As the animal practiced and became more proficient at modulating the activity of this neuron, the physical movements disappeared. This meant that the animal learned to dissociate the activity of a neuron from an explicit motor task that it was previously involved in, and associated it with a completely new motor representation, i.e. using the neuron to control a non-physiological actuator. This dissociation has been documented in multiple BMI experiments,[4,9,14] which shows the flexibility of the motor system in solving complex problems (e.g. controlling a real and an artificial limb with the same neuronal population).

In recent years, Moritz and colleagues utilized a similar approach of operantly conditioning neural activity to train monkeys to control a simple grasping neuroprosthesis.[15] They implanted functional electrical stimulation (FES) electrodes in a transiently paralyzed monkey's hand flexor and extensor muscles, which generated torque when stimulated. Impressively, the monkeys gained control of the stimulation to acquire torque targets only within minutes using single cortical neurons, making virtually no errors during peak performance, with nearly a four-fold increment from initial performance.

Although both of these approaches rely on establishing a relationship between a specific pattern of neural activity and a behavioural intent, the primary difference is that instead of decoding an existing correlation between neural activity and an observable behavior, the operant conditioning approach allows the brain to utilize its existing plasticity mechanisms to learn a new motor (or abstract) skill. By doing so, the operant conditioning approach empowers the brain to be the primary learning entity, instead of having a complex algorithm learn to decipher existing neural activity.

So, if the brain has an enormous amount of processing power for solving complex motor problems and performing intricate tasks with ease, what is stopping us from developing high performing BMI systems? It is a well-known fact that sensory and proprioceptive feedback is essential for learning and executing new motor skills.[16-20] Hence, a potential roadblock to further developing these operant conditioning-based BMIs may be the inability to provide rich sensory feedback. On this end, there have been efforts to provide feedback by electrically stimulating afferent sensory pathways, or directly stimulating the brain using intracortical microstimulation (ICMS) to provide rich sensory feedback.[16,21-24] Although early results are promising, this still remains an area of active research. Another potential limiting factor for existing operant conditioning BMI studies may be that different cortical neurons have different efficacies with which they can be volitionally controlled. For instance, in our lab, we have found evidence of specific neuron types that are easier to volitionally control and would facilitate BMI implementation,[25] even for actuators with multiple degrees of freedom.

BMIs are typically developed and operated under a neuroprosthetic definition, in which neural activity is used to control an extrinsic or prosthetic device. However, the implications of these operant conditioning-based BMIs extend far beyond this neuroprosthetic definition. As Moxon and Foffani recently pointed out, operant conditioning-based BMIs enforce a truly causal relationship between a specific neural activity (such as the firing rate of a single neuron or the power of a cortical oscillation), and an observable behaviour (such as the movement of a cursor or a robotic arm).[26] Since operant-conditioning-based BMIs require participants to learn a new procedural skill, this causality can be used to study the underlying plasticity mechanisms that are essential for acquiring new skills. For instance, inspiring work by Koralek and colleagues has shown that plasticity in the cortico-striatal networks is essential for operantly conditioning the activity of neurons in the motor cortex, which also happens to be the network responsible for acquiring new motor skills.[19,20]

Operant conditioning-based BMIs also provide us with an alternative perspective on an individual's ability to regulate their own neuronal activity, down to a single neuron. Large bodies of work have been dedicated to using biofeedback, or neurofeedback, when the feedback constitutes some form of neural activity, to help train individuals to regulate their own neural activity, from a single neuron all the way up to large-scale cortical oscillations.[27] Many neurological conditions present with alterations in specific types of neuronal activity. For instance, individuals with epilepsy often present cortical hyperexcitability (and a corresponding loss of inhibitory activity), which can lead to recurrent epileptic seizures that can be truly debilitating. A potential treatment for these individuals who do not respond well to medications is to provide neurofeedback training in which their neural activity is operantly conditioned to upregulate inhibitory oscillations in the brain, such as the sensorimotor rhythm (SMR) and slow cortical potentials (SCP).[28] There is evidence that such neurofeedback therapy can potentially reduce seizure frequency and improve one's control over their own seizure activity.[28-30] Similar neurofeedback training approaches have been studied extensively in the treatment of ADHD[31-33] and have also been investigated for auditory dysfunction,[34,35] insomnia,[36] autism spectrum disorder,[32] schizophrenia,[37] and Parkinson's Disease.[37]

Thus, BMIs, and specifically those that utilize operant conditioning of neural activity have the potential to not only provide individuals with sensorimotor deficits new and more effective ways of interacting with the environment around them, but also serve as new scientific tools that unlock new possibilities for basic brain research. These novel BMIs also have the potential to modulate neural activity to obtain volitional control over certain neurological disease states, potentially improving clinical outcomes and overall quality of life.

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