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Exploring Cognition with Brain–Machine Interfaces

Richard A. Andersen,^{1,2} Tyson Aflalo,¹ Luke Bashford,¹
David Bjånes,¹ and Spencer Kellis^{1,2,3}

¹Division of Biology and Biological Engineering and Tianqiao & Chrissy Chen Brain–Machine Interface Center, California Institute of Technology, Pasadena, California 91125, USA; email: andersen@vis.caltech.edu

²USC Neurorestoration Center, Keck School of Medicine of USC, Los Angeles, California 90033, USA

³Department of Neurological Surgery, Keck School of Medicine of USC, Los Angeles, California 90033, USA

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Abstract

Traditional brain–machine interfaces decode cortical motor commands to control external devices. These commands are the product of higher-level cognitive processes, occurring across a network of brain areas, that integrate sensory information, plan upcoming motor actions, and monitor ongoing movements. We review cognitive signals recently discovered in the human posterior parietal cortex during neuroprosthetic clinical trials. These signals are consistent with small regions of cortex having a diverse role in cognitive aspects of movement control and body monitoring, including sensorimotor integration, planning, trajectory representation, somatosensation, action semantics, learning, and decision making. These variables are encoded within the same population of cells using structured representations that bind related sensory and motor variables, an architecture termed partially mixed selectivity. Diverse cognitive signals provide complementary information to traditional motor commands to enable more natural and intuitive control of external devices.

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Contents

INTRODUCTION	132
BRAIN–MACHINE INTERFACES: FROM NONHUMAN PRIMATES TO HUMANS	134
A BRIEF HISTORY OF FUNCTIONAL LOCALIZATION IN CORTEX	136
Localization Views of Cortex	136
Network View	136
Distributed Representations	137
Randomly Mixed Selectivity	137
HUMAN POSTERIOR PARIETAL CORTEX	137
IMAGERY	138
Motor Imagery	138
Imagined Grasp	138
Partially Mixed Selectivity	139
SEMANTICS	140
IMAGINED MOVEMENT: ACTIVATION OF THE SOMATOSENSORY CORTEX	142
Differences Between S1 and Posterior Parietal Cortex During Motor Imagery	142
SOMATOSENSATION	143
Cortical Electrical Stimulation	143
Somatosensory Activation of Posterior Parietal Cortex with Natural Stimuli	144
Imagined Somatosensations	145
LEARNING	147
DECISION MAKING	148
Expected Value	148
Memory Decisions	148
CONCLUSION	149
The Importance of Mixed Selectivity	149
Hybrid Brain–Machine Interface Systems	150
Mood Regulation	150
Awareness of Intent	151
Final Thoughts	151

Brain–machine interface (BMI):

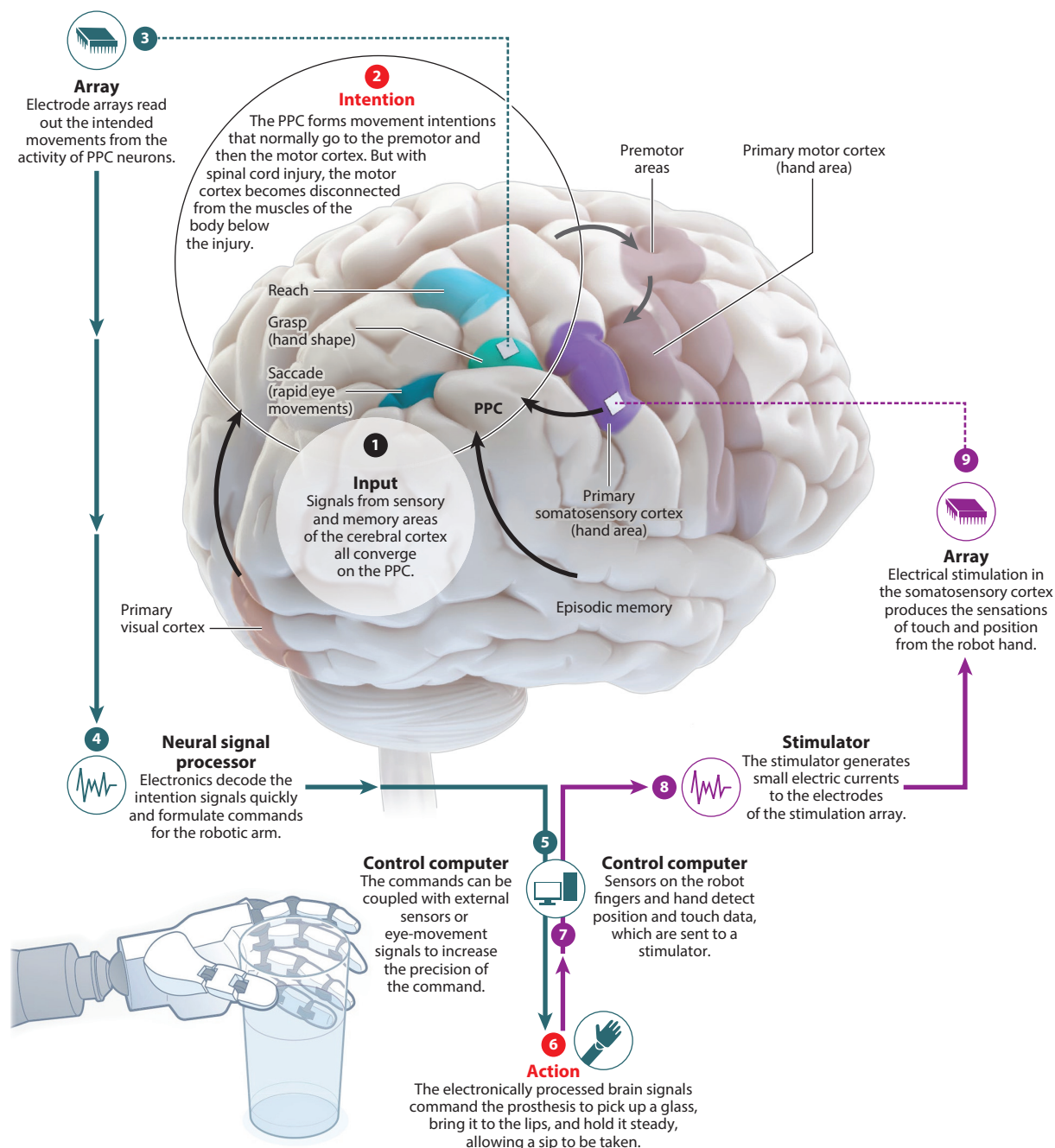
a device to record from and stimulate the brain, with algorithms to interpret intent from the neural signals and/or control the stimulation parameters; also referred to as a brain–computer interface

INTRODUCTION

Brain–machine interfaces (BMIs) have shown promise in interfacing with human cortex of paralyzed patients to decode the intent to make simple movements to control external devices, including computer cursors and robots. Generally, recordings are made from primary motor cortex (M1), and the decoded neural signals control the velocity of the effector. However, other brain areas, and to some extent even motor cortex, encode higher-level cognitive signals related to movement of the body (Andersen et al. 2010). These signals can be used to complement the simple movement commands from M1, enabling more sophisticated and advanced BMIs (**Figure 1**). The BMI paradigm also allows for the discovery of cognitive representations and functions in cortex that are of scientific interest. As the field evolves, a more mechanistic knowledge of cognition will provide the scientific framework for more sophisticated prosthetics.

In this review, we use the term BMIs; these devices are also termed brain–computer interfaces. The research in this field of neurotechnology has expanded greatly in the past 10 years, and it would be difficult to adequately cover all aspects of the field. As mentioned above, we focus on efforts to address paralysis, using population recordings of single neurons from the cerebral cortex.

Intent: the plan to make a particular action (e.g., an intended reach)



(Caption appears on following page)

Figure 1 (Figure appears on preceding page)

Schematic of a cognitive BMI. Translating decoded intentions of BMI users to enable them to interact with real-world objects and update the state of their environment through new sensory information requires an intricate device with many complex parts. Decoding high-level cognitive goals of a user (①), by processing (④) recorded electrical signals (③) of neural activity in PPC (②), a BMI sends control commands (⑤) to an assistive device (⑥). Instrumented with sensors, the device relays physical measurements (such as pressure, temperature, proprioception) back to the BMI (⑦). These signals are translated into a stimulation pattern (⑧) designed to evoke naturalistic somatosensations through activation of neurons in PPC (⑨). Figure adapted from Andersen (2019). Abbreviations: BMI, brain-machine interface; PPC, posterior parietal cortex.

Primary motor cortex (M1): this cortical area provides one of the main outputs of movement commands to the spinal cord and subcortical motor structures with emphasis on the desired trajectories of body parts

Effector: a part of the body responsible for a particular action

Posterior parietal cortex (PPC): an association cortical area situated between sensory and motor cortical areas; responsible for sensorimotor transformations between the sensory and motor areas and functionally involved in movement planning, attention, and spatial awareness

Sensorimotor transformation: the stage in sensorimotor cortical pathways at which sensory signals begin the transformation to motor commands

Starting in the early 2000s, the first attempts at motor control BMIs in nonhuman primates (NHPs) and humans used mostly implants in M1 (Ajiboye et al. 2017; Bouton et al. 2016; Carmena et al. 2003; Collinger et al. 2013; Friedenberg et al. 2017; Gilja et al. 2015; Hochberg et al. 2006, 2012; Pandarinath et al. 2017; Santhanam et al. 2006; Serruya et al. 2002; Taylor et al. 2002; Wessberg et al. 2000; Wodlinger et al. 2014). This choice makes good sense because M1 is the primary source of cortical motor control signals to subcortical motor areas and the spinal cord. We have extensively studied the posterior parietal cortex (PPC) in our laboratory (Aflalo et al. 2015, Musallam et al. 2004). We reasoned that this higher cortical area, which is involved in more cognitive aspects of motor control such as sensorimotor transformations, would have overlapping and complementary functions that would be advantageous for the operation of BMIs. As seen in this review, the population neural activity in small patches of human PPC encodes many variables, providing a rich repertoire of information for BMI applications (Aflalo et al. 2015, Zhang et al. 2017). This high dimensionality is made possible by single neurons coding multiple variables, allowing a plethora of thoughts to be read out from small areas of the PPC.

The history of research on the functional organization of the cerebral cortex has shifted between a highly localized view and a more distributed view. A localized view means that anatomically constrained areas of cortex are responsible for a particular cortical process (e.g., grasp with the hands), whereas a distributed view means that a large part or all of cortex is involved in a process. The finding of many cognitive representations within a very small region of PPC shifts our understanding of the functional organization of association cortex toward a more distributed view. However, as we shall see in this review, the representations in PPC are not random but rather have a statistical structure. We refer to this structure as partially mixed selectivity (Zhang et al. 2017). Also, we shall see that primary areas are still more primary, having more restricted influences of cognition on their response properties (Jafari et al. 2020). The findings fit an emerging view that circuits account for behaviors and that areas of cortex are nodes in one or more circuits. Thus, the recordings from one area of cortex reflect the operation of that area and its network contributions to other nodes of the circuit.

BRAIN-MACHINE INTERFACES: FROM NONHUMAN PRIMATES TO HUMANS

Initial BMI experiments were performed in NHPs (Musallam et al. 2004, Santhanam et al. 2006, Serruya et al. 2002, Taylor et al. 2002). Arrays of microelectrodes were implanted in M1, PPC, and dorsal premotor cortex. The animals were trained to perform simple movement tasks in which they controlled the movement of a cursor on a computer screen with hand movements or reaches. Computer algorithms were trained to use the neural population activity to decode the movements. Finally, control of the cursor was switched from the actual behaviors to the decoded neural signals. The NHPs would learn that they did not have to move their limbs or hands to perform the task and could do it mentally. In M1, the primary control signal was the intended velocity of the effector. In PPC, the signals read out by the decoders were more abstract and indicated the spatial goal of

the movement (Musallam et al. 2004). However, there is also a trajectory signal in PPC that can be used for trajectory decoding. The dynamics of this PPC trajectory signal slightly lags those of the motor cortex trajectory signal and these dynamics are consistent with a state estimate of the current motion of the effector (Mulliken et al. 2008). A state estimate is an element of internal models that captures the current estimate of the state of the body as computed from motor command and sensory feedback signals. Such an internal estimate is thought to occupy higher-order motor areas such as the PPC. Thus, these NHP experiments, particularly those in PPC, were consistent with a cognitive neural prosthetic, one that uses the more abstract intended goals and internal representations of the state of the body.

The next landmark step was to move from animal models of BMIs to human clinical trials (Affalo et al. 2015; Bartels et al. 2008; Collinger et al. 2013; Hochberg et al. 2006, 2012) (**Figure 1**). The participants were paralyzed, most commonly from high-level spinal cord injuries that produced tetraplegia (paralysis of all four limbs), or partially paralyzed, from advanced stages of amyotrophic lateral sclerosis. Human clinical trials were an important step from a translational perspective. For the tetraplegic subjects, many had spinal cord injuries for years before entering into the clinical studies. Particularly for motor cortex, it was not clear whether disuse for such long periods would affect the response properties of the neurons. Thankfully, the motor cortex was found sufficiently intact for prosthetic control (Hochberg et al. 2006).

The ability to use neural signals to control devices represented a major advance for paralyzed individuals. However, patients suffering from paralysis often have significant sensory deficits in addition to motor paralysis. The loss of somatic sensation can pose immediate and significant health challenges, debilitating neuropathy and pain, and difficulty with essential bodily functions such as bladder and bowel control. In addition to functional outcomes and improvement in quality of life, the restoration of sensation could also improve control of assistive devices such as dexterous robotic hands (Bensmaia & Miller 2014, Weber et al. 2012). One approach toward solving this problem has been to introduce artificial sensation through microstimulation of the somatosensory cortex (**Figure 1**). The development of cognitive sensory BMIs has been recently accelerated due to verbal reports of the descriptive quality of evoked sensations from human participants.

For cognitive motor BMIs, the move to humans has opened a new frontier of possibilities (Affalo et al. 2015). Previously, it was difficult to know how NHPs were performing the BMI control tasks. In contrast, humans have language and can report their mental strategies for BMI control. Further, human participants can be instructed and require little training to perform various tasks. Thus, an expanse of cognitive variables can be tested in humans with minimal training. With NHPs, probing cognition requires months of training for each task. Such extensive training has limited the breadth of view of what an area of cortex does. A prime example is the lateral intraparietal area (LIP) of the PPC. This area is part of the eye movement cortical circuit, which receives sensory input such as dense visual projections from extrastriate cortex. It projects to eye movement areas, including the frontal eye fields and superior colliculus. The clear role of LIP in visuomotor integration and eye movements has made it a popular target for studying higher cognitive processes that inform eye movement behaviors. After months of training, single functional roles are assigned to this area depending on the nature of the task—attention, planning, categorization, object recognition, and decision making (Bisley & Goldberg 2003, Freedman & Assad 2006, Gnadt & Andersen 1988, Platt & Glimcher 1999, Shadlen & Newsome 1996, Snyder et al. 1997). As discussed in the section titled Partially Mixed Selectivity, LIP likely has a role in all these functions.

As mentioned above, an advantage of human studies is that little training is required, minimizing possible learning effects on the existing functional organization. Similar to human studies, experiments in NHPs are designed to understand the role a cortical region plays in aspects of

Population neural activity: the activity of populations of neurons in which functions are enabled not by single neurons but by the combined activity of many neurons

Partially mixed selectivity: describes neurons that respond to more than one variable, but there is a statistical structure in the neural population that may afford more efficient processing and learning

Internal model: the neural representation of the relation of the body with respect to the environment

Cognitive neural prosthetic: prosthetic that uses signals from premotor and association cortical areas that are more cognitive in nature and, for instance, indicate the goal or intent of an action

Tetraplegia: paralysis of all four limbs; can result from spinal cord lesions at high levels in the spinal cord

Coordinate transformation:

response to stimuli requires the transformation of where the stimulus is on the sensory epithelium into the proper activations of the muscles to achieve a goal

perception, cognition, or movement. The assumption is that the experiment reveals the underlying function of the region. However, the extensive training that precedes recordings in NHPs raises the question of how much learning plays a role in sculpting the neural circuits being investigated. The hypothesized function of a brain area guides the selection of the task to test the hypothesis. Although these hypotheses and tasks are usually selected on the basis of prior knowledge of an area, how much is the task responsible for creating the neural representations that are the hypothesized properties of the neural circuit?

The functions of cortex are diverse, accounting for nearly all aspects of our subjective experience of the world. How are these diverse functions organized in cortex? Furthermore, what might this say about choosing cortical locations for BMI applications? These important questions are addressed in the next section.

A BRIEF HISTORY OF FUNCTIONAL LOCALIZATION IN CORTEX

Localization Views of Cortex

Paul Broca's (1861) famous patient Tan, who had a profound language expression deficit after an injury to the frontal lobe, provided the first concrete example of localization of function within the cerebral cortex (although at the time he misattributed the underlying cause to the striatum). Broadly speaking, the localization view posits that the vast complex of human behavior can be segregated into specific functions, with each function localized to a specific region of cortex. Broca's result was consistent with Joseph Gall's (1798) extreme view of localization, phrenology, in which every patch of cortex had a distinct function. For instance, there were patches of cortex specialized for self-esteem, benevolence, combativeness, and imitation. At the other end of the spectrum, Karl Lashley (1929) proposed an equipotential theory of cortex in which cortex was undifferentiated for function and all cognitive capacities degraded monotonically with the size of cortical damage. This view was likely influenced by the selection of species (Lashley studied rodents, whose behaviors are mediated primarily by subcortical areas). In motor control, increased encephalization of function with the evolution of fine motor control makes the choice of animal model critical. Whereas human motor function can be devastated by strokes to motor cortex, rodents appear much less affected for movement execution, with only a reduction in the ability to learn new tasks (Kawai et al. 2015).

Network View

With the advent of electrophysiology and refined neuroanatomy, it became evident that simplistic notions of localization were untenable. Instead, cortical function emerges from the networked interactions of many brain areas, and each area is a node in the network. Functional magnetic resonance imaging (fMRI) further highlighted this view, showing activation of multiple areas with simple tasks. A central question now is, What distinguishes each node in a network and how might a network of nodes work together to produce complex behaviors? Researchers have proposed several organizational schemes within the motor system, including nodes for controlling different segments of the body (Andersen & Buneo 2002), different classes of behaviors (Graziano & Aflalo 2007, Kaas & Stepniowska 2016), and different computation stages ranging from perception to movement. For example, consider that control of movement involves many elements, such as the selection of goals based on current needs, coordinate transformations of the location of goals in eye coordinates into body coordinates, planning out the appropriate sequence of actions to achieve the goal, and the transformation of intended actions into specific sequences of muscle

activity. How are these computations encoded in populations of neurons and distributed across the cerebral cortex? This question can be approached from many directions of investigation in animals, including activation and inactivation of nodes. Human BMIs provide a unique window into this question by allowing for the recording of populations of neurons from several cortical areas combined with the communication of subjective experience.

Distributed Representations

One way to understand a node is to understand its contribution to a cortical function. In early experiments from our laboratory, we examined how extrapersonal space is represented in the cortex of NHPs. The PPC plays a pivotal role in the awareness of extrapersonal space, as demonstrated from lesions in humans and NHPs (Holmes 1918, Mishkin & Ungerleider 1982, Rudolph Bálint 1909). We reasoned that visual space would be coded by receptive fields of PPC neurons that are independent of the retinal location of a stimulus. Instead, in single neurons recorded in NHP, we found that eye position signals were combined with retinal stimulus position signals and that there is generally no invariant representation of space at the single-neuron level (Andersen et al. 1985). The eye position's effect on the visual receptive fields approximates a multiplication of a monotonic eye position signal by the visual receptive field, and we referred to this type of interaction as a gain field. At the time, three-layer neural networks and back-propagation learning (the precursors of modern artificial intelligence and machine learning) were just developed (Rumelhart et al. 1986). We showed that a neural network trained to represent space extracted from retinal stimulus and eye position formed the same distributed representation in which invariant spatial location could only be read out from the neural population (Zipser & Andersen 1988). Eye position gain fields are not restricted to PPC and have been found in several cortical areas (for a review, see Salinas & Thier 2000).

Randomly Mixed Selectivity

Another way to understand the contributions of nodes within a network is to find how different regions encode information. Neurons in the prefrontal cortex of NHPs (Rigotti et al. 2013) and in PPC of rats (Raposo et al. 2014) encode random nonlinear mixtures of task variables. This randomly mixed selectivity is proposed to have the computational advantage of representing many states in small populations of neurons that can be easily decoded with linear decoders (Fusi et al. 2016). Further, it has been proposed that areas that process information with highly specialized neurons would have lower dimensions than those that exhibit mixed selectivity. Direct comparisons of association cortical areas with primary sensory and motor areas may determine whether association areas use a more mixed selectivity strategy when compared to primary areas.

HUMAN POSTERIOR PARIETAL CORTEX

As outlined above, recordings from association cortical areas in NHPs produced the remarkable finding of high-dimensional encoding of variables distributed across the population of neurons. With recordings from association cortex of tetraplegic humans, primarily from the PPC, it is now becoming clear that a similar encoding strategy of mixing variables is found in humans. These representations are not mixed randomly but rather have defined structures, a partially mixed selectivity. In the following sections we review, in humans, the types and structures of variables found in an exemplary association area, the PPC, and a primary sensory area, the primary somatosensory cortex (S1).

Randomly mixed selectivity: enables the encoding of many functions within a small set of neurons

Primary somatosensory cortex (S1): the first cortical region to receive somatosensory signals from the body; these signals convey tactile (touch) and proprioceptive (body position) sensations

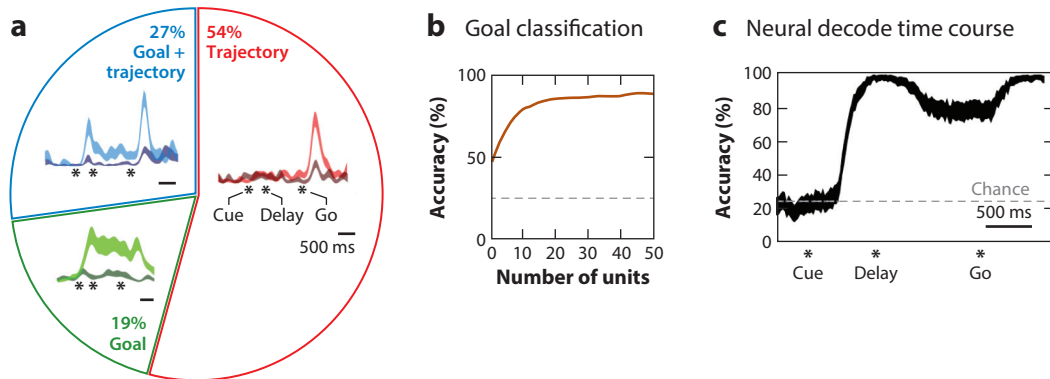


Figure 2

Cognitive coding of motor intent in human PPC. (a) PPC neurons encode both movement goals and trajectories with a heterogeneous mix of neurons. The pie chart indicates the proportion of different response types in the population of PPC neurons. Insets show the activity (mean $\pm$ SEM) of three representative example neurons. Each neuron shows the response through time to the target evoking maximal activity (*light blue*) and in response to the opposite target (*dark blue*). (b) A small population of cells enable accurate decoding of the intended target. (c) The time course of the neural decode computed from offline data demonstrates accurate encoding of the intended target within 190 ms of target presentation (300-ms sliding window, 95% confidence interval). Figure adapted from Aflalo et al. (2015). Abbreviations: PPC, posterior parietal cortex; SEM, standard error of measurement.

IMAGERY

Motor Imagery

Imagery is thought to be introspective activations of cortical circuits that overlap with the normal function of those circuits. For instance, imagined movements would activate populations of neurons that are involved in movement planning and execution. In NHPs, the PPC is active during reach planning and execution, whereas M1 is active primarily during just the execution phase (Crammond & Kalaska 2000, Snyder et al. 1997).

Recordings from M1 in human tetraplegic participants have shown activation for imagined (Hochberg et al. 2006) and attempted (Collinger et al. 2013, Hochberg et al. 2012) movements. These activations were related primarily to the desired velocity of the movement. Recordings from human PPC show activation during both the planning and the execution of an imagined movement (Aflalo et al. 2015) (**Figure 2**). The planning activity is related to the goal of the movement. Advantages of the goal decoding include the following: Very few neurons are required to specify goals; decoding goals is very fast (~ 200 ms); and representations are bilateral, with some neurons coding the contralateral limb to the recording hemisphere and others the ipsilateral limb. Encoding of the goal generalized across direct or symbolic cueing. Control experiments indicated that the persistent activity in delay tasks was indeed coding the intention of the participant. An earlier study of BMI in NHPs showed similar intended goal coding and was proposed to be an instantiation of a cognitive BMI that decodes as well as executes motor goals (Musallam et al. 2004).

Anterior intraparietal area (AIP): an area in the posterior parietal cortex that has specificity for grasping

Imagined Grasp

Initial human implants in PPC targeted sites in the left PPC that were active for grasps and reaches through the use of fMRI. The grasp area was at the junction of the intraparietal and postcentral sulci and may be a homolog of the anterior intraparietal area (AIP) in NHPs (Connolly et al. 2003). The reach-selective area was in the superior parietal lobule and may correspond to Brodmann's area 5d (area 5d) in NHPs (Cavina-Pratesi et al. 2010). Because it is difficult to make homologies

between NHPs and humans in association cortex, we have also referred to the presumed AIP site by a more neutral anatomical descriptor, the postcentral-intraparietal area. A second grasp-selective site was chosen in one subject located in the supramarginal gyrus.

AIP in NHPs is a part of a grasp circuit, with AIP coding the visual structure of graspable objects, ventral premotor cortex coding the intermediate sensory and motor components, and M1 coding the motor components (Gerbella et al. 2017, Schaffelhofer & Scherberger 2016). Specific grasp shapes can be decoded from M1 in NHPs (Vargas-Irwin et al. 2010) and humans (Rastogi et al. 2021, Wodlinger et al. 2014). M1 decoding with BMIs supports simple grasps with robotic hands (Hochberg et al. 2006, Wodlinger et al. 2014). From a cognitive BMI perspective, single neurons in AIP are selective for object shapes that can specify an entire grasp (Murata et al. 2000).

In human AIP, the imagined shape of the hand, independent of an object to be grasped, can be decoded (Klaes et al. 2015). Visual cues as well as the imagination of the appropriate hand shape to grasp the object-activated AIP. By contrast, auditory cues did not activate AIP, but the hand shape instructed by the auditory cue produced the same imagination-evoked activations, enabling decoding of the imagined grasp. Although area 5d did show a response to the visual cue, its neurons were not selective for the imagined hand shape. This result is consistent with NHP recordings and human imaging studies of a separation of grasp and reach processing within PPC.

Partially Mixed Selectivity

The findings of bilateral imagined movement (Affalo et al. 2015) and grasp activity (Klaes et al. 2015) in human AIP begged the question of what other cognitive variables are represented in this cortical area. In NHP studies using recordings and inactivations around the intraparietal sulcus (IPS), a consistent preference for effectors was found, with greater representation of eye movements in LIP, reach movements in the parietal reach region, and grasps in AIP (Andersen & Buneo 2002). Early fMRI studies of humans presented more mixed results, with some studies reporting segregation by effectors (Astafiev et al. 2003, Connolly et al. 2003, Culham et al. 2003, Gallivan et al. 2011, Prado et al. 2005) and others reporting an intermixing of effectors (Beurze et al. 2009, Heed et al. 2011, Hinkley et al. 2007). Effector representation for reach and grasp was bimanual (Gallivan et al. 2013), consistent with recordings from human AIP (Affalo et al. 2015).

A study was designed to examine the degree of representation of three variables: attempted or imagined movement, ipsilateral or contralateral body side, and the effectors of shoulder and hand (Zhang et al. 2017) (**Figure 3**). The eight possible combinations of these variables were used as cues to instruct the participant's movements. The cues were presented as text instructions and were followed by a delay and then a go cue to produce the response. For example, one trial type was the text "imagine right hand," which instructed the participant to imagine (visualize the movement in their mind) squeezing their right hand. Surprisingly, all these variables were found in the AIP population and were mixed, with single neurons often responding to more than one variable. However, the mixing was not random and had structure. If one side of the body was represented it was more likely that the other side was as well; the same was true for the cognitive strategies of attempted or imagined movement. However, for effectors the mixing of single neurons was random. As an example, a neuron representing a hand movement was as likely as not to also represent a shoulder movement. Although only different effectors showed a strong separation, all combinations of the three variables within a task could be decoded.

This mixing was referred to as partially mixed selectivity due to the statistical structure. Possible advantages to the correlations in this structure are to enable the transfer of learning between the same effectors on each side of the body (Amemiya et al. 2010) and to improve motor execution using motor imagery (Dickstein & Deutsch 2007). The segregation in effectors could potentially reduce interference for computations involved in moving different parts of the body.

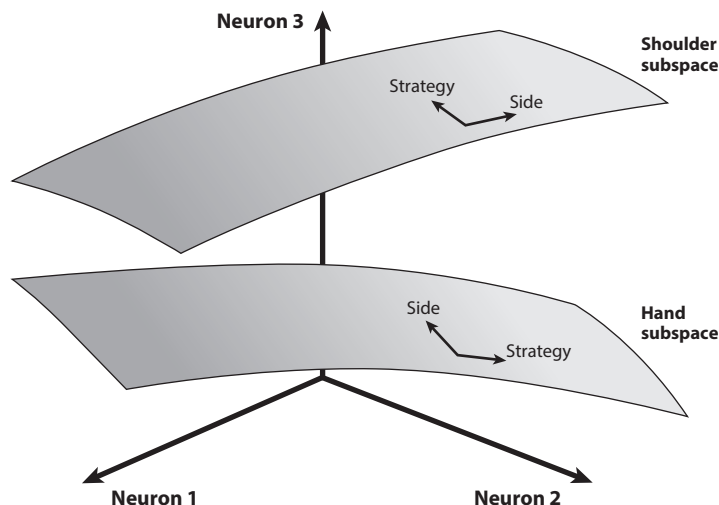


Figure 3

Schematic illustration of partially mixed selectivity. PPC codes multiple movement variables in a structured manner. The body movements (hand or shoulder) are encoded in distinct subspaces (*gray planes*). The other movement variables (body side, left versus right; and movement strategy, imagined versus attempted movements) are encoded in shared subspaces, organized within their respective body movements. Movement planes are shown for three neurons for illustrative purposes but are embedded within the full space of the recorded population. Figure adapted from Scherberger (2017). Abbreviation: PPC, posterior parietal cortex.

An important question is whether the partially mixed structure is maintained across contexts. A strong and especially important test from the BMI perspective is whether the structure for open-loop training remains during closed-loop brain control. It was found that the representation of different movement conditions is largely maintained between the two conditions (Zhang et al. 2020).

SEMANTICS

Language is a core aspect of human cognition. However, because language is a uniquely human capability, many aspects of how language is represented by neural populations have gone unanswered. Functional imaging studies suggest that the meaning of language, the basic semantic or conceptual underpinnings of our understanding of the world, is distributed across the human cortex (Binder & Desai 2011, Huth et al. 2016, Lambon Ralph et al. 2017, Martin 2016, Meyer & Damasio 2009, Pulvermuller 2013). Specific semantic classes of words, such as action verbs or colors, typically activate corresponding higher-order motor control or perceptual regions of cortex. For example, ventral occipitotemporal cortex is activated both when perceiving color and during semantic retrieval of color information (Murphey et al. 2008). Likewise, action verbs activate regions important for the sensory processing of movements, the action observation network (Aziz-Zadeh et al. 2006, Raposo et al. 2009, Tettamanti et al. 2005, Wurm & Caramazza 2019). The action observation network is composed of the PPC and the lateral occipital temporal cortex (Lingnau & Downing 2015) and frontal motor planning circuits (Andersen & Cui 2009, Graziano 2006, Rizzolatti & Luppino 2001).

We recently recorded from single neurons in human PPC while participants read action verbs and watched movies of the corresponding actions from varied viewpoints (Affalo et al. 2020) (Figure 4a). We found that neurons are selective for different observed actions, similar to what

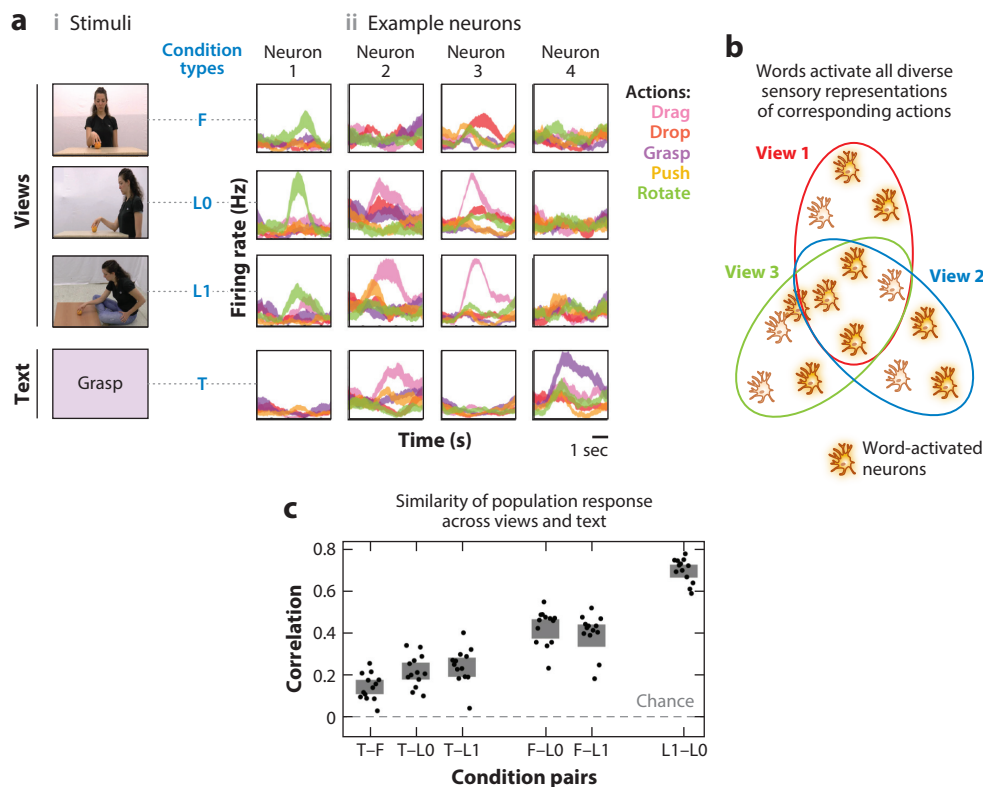


Figure 4

Single neurons in PPC are selective for observed actions and action verbs in a shared neural substrate. (a) Example stimuli and neurons illustrating diverse selectivity patterns across views of the same actions and action verbs. Each column in subpanel ii illustrates the responses of the same unit to the four condition types (F, frontal view; L0, lateral view 1; L1, lateral view 2; T, text). The images in subpanel i are static images from the movies presented as stimuli to the participant. (b) Schematic illustration of results showing that text activates a statistical sampling of neurons with the same action preferences. Each oval contains the population of neurons that is selective for a particular viewpoint; overlap between ovals indicates neurons that have the same neural responses across views. The possible patterns of overlap are simplified for schematic purposes. Yellow neurons indicate that text generates the same neural response as the observed action, whereas gray neurons do not. Yellow neurons are an unbiased sample, suggesting that text links with all diverse neural representations of the corresponding action. (c) Across-condition correlations between neural population responses (x-axis labels indicate the condition pairs). Each dot indicates the result of a single session. Rectangles indicate 95% bootstrapped CI over sessions. The dashed horizontal line shows chance correlation values. Figure adapted from Aflalo et al. (2020). Abbreviations: CI, confidence intervals; PPC, posterior parietal cortex.

has been reported for NHPs (Caggiano et al. 2011, Lanzilotto et al. 2019). Further, neural coding for different views of the same action could be characterized by a statistical distribution of similar and distinct coding across views (compare example neurons 1 and 3 in **Figure 4a**). Text responses activated this entire distribution without preference, thus associating with a statistical sampling of the diverse sensory representations related to the corresponding action concept (**Figure 4b**). This finding argues against other possibilities, for example, that humans connect the representation of a word to an abstracted, invariant, and therefore universal visual representation or to a particular canonical example (Pulvermuller 2013).

Microelectrode

array: typically small device that has on the order of ~100 microelectrodes that penetrate the cortex

At the population level, there is a structure similar to the partially mixed selectivity for movements (Zhang et al. 2017) in which views of similar actions are correlated, and there is less correlation between views of different actions (**Figure 4c**). A series of control experiments and analyses supported the interpretation that the neural response to action verbs could be attributed to semantic processing and not to implicit imagery, short-term learned associations, or covert speech. Taken together, the results suggest that words automatically activate the consolidated visuomotor experience of the reader, with the interesting implication that word meaning is truly unique to each individual.

IMAGINED MOVEMENT: ACTIVATION OF THE SOMATOSENSORY CORTEX

As highlighted above, clinical human studies have begun implanting sensory regions of cortex with microelectrode arrays to allow artificial sensations to be written into the brain. These same electrode arrays also enable recording single-neuron activity and thus provide the opportunity to better understand and compare the activity of single neurons in sensory cortex with high-level regions such as PPC. Although S1 is considered a primary sensory area responsible for processing somatosensation, it is also closely connected to the motor system. S1 has direct connections with M1 and spinal cord and is important for the perception of body posture and the registration of the sensory consequences of movement. In NHPs, S1 neurons are active during movements of the body (London & Miller 2013, Nelson 1987, Soso & Fetz 1980), and electrical stimulation of S1 in both humans and NHPs can produce movements (London & Miller 2013, Nelson 1987, Penfield & Boldrey 1937, Soso & Fetz 1980). However, the close association of S1 with the motor system makes it difficult to further delineate its role in sensation, anticipated sensation, or motor processing. Recordings from human S1 from clinical trial participants with tetraplegia provide an opportunity to dissociate the sensory and movement components in S1. Participants do not have sensory feedback from limbs; thus, activity arising internally as a consequence of movement (imagined or attempted) can be studied in isolation, in the absence of sensation.

Differences Between S1 and Posterior Parietal Cortex During Motor Imagery

In a variant of a task used in NHPs (Pesaran et al. 2006), a tetraplegic subject was asked to perform an imagined delayed reaching task while neural activity in Brodmann's area 1, a subregion of S1, was recorded. The task manipulated the point of fixation, the initial imagined position of the limb, and the location of the imagined reach target at various points during a trial (Jafari et al. 2020). As healthy NHPs position their hands at different initial locations and reach toward target locations, PPC exhibits responses to the cue, delay, and reach and codes for the position of the eyes and the hand. Likewise, in humans, PPC codes the cue, plan, and imagined execution of a reach (Affalo et al. 2015).

Do all cortical areas that process sensorimotor transformations represent the same variables? For instance, it has been reported that small patches of premotor cortex represent the whole body (Willett et al. 2020) and are not dissimilar from PPC (Zhang et al. 2017). Or are there differences between the cortical areas, with a hierarchical structure between primary and association cortical areas?

Although S1 did not respond to the visual cues or encode the movement plan (**Figure 5**), it did respond while the participant was actively imagining movement. This response considered the imagined initial position of the hand and produced an imagined movement vector in hand coordinates (see figure 4 in Jafari et al. 2020). Thus S1 cortex is markedly different from PPC in the same task. Whereas PPC codes the cue, plan, and movement, S1 codes only the movement.

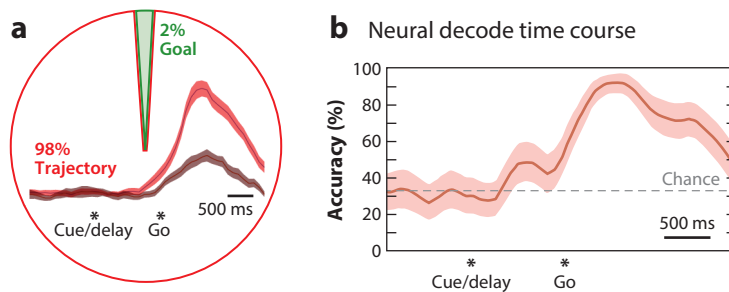


Figure 5

Primary sensory cortex activation during imagined movements. (a) S1 neurons responsive primarily during active motor imagery but not during the cue or delay phase of the task. The pie chart indicates the proportion of different response types in the population of S1 neurons. The response through time of a representative neuron is shown for the preferred (light red) and nonpreferred (dark red) movements (mean $\pm$ SEM). Compare with **Figure 2a,b**. (b) Cross-validated classification accuracy as a function of time summarizing the time course of information encoding in human S1. Preferential activation during imagined movement can be contrasted with responses in PPC (see **Figure 2c**). Abbreviations: PPC, posterior parietal cortex; SEM, standard error of measurement.

The finding that the initial imagined hand position was present only at the imagined movement phase of the task strongly suggests that the computation of the movement vector in hand coordinates is made in a different cortical area and projected onto S1. This signal is consistent with an efference copy of motor command signals to S1 (London & Miller 2013) and may be used to update internal models for predicting the sensory consequences of movement. Another possibility, given direct descending projections from S1 to the spinal cord (Rathelot & Strick 2006), is that S1 may play a direct role in helping control the motor periphery, presumably complementary to descending projections from frontal motor areas (Omrani et al. 2017). The finding that S1 does not code the visual targets, the imagined initial hand position, or the planned movement indicates that at the very least it codes a set of variables different from those found in PPC.

SOMATOSENSATION

The above sections discuss primarily higher cognitive variables representing action; in the following subsections, we discuss higher cognitive variables representing somatosensation. Providing sensory feedback is hypothesized to greatly improve the BMI experience, both by increasing the accuracy of control and by helping improve the user's sense of agency. Individuals who suffer spinal cord injury are unable to move or feel sensation below the level of the injury. Whereas sensation above the injury is preserved and can be explored by interactions between the participants, the experimenter, and the environment, sensations below the injury must be elicited by alternative methods. For example, intracortical microstimulation to S1 can elicit naturalistic percepts (Armenta Salas et al. 2018, Fifer et al. 2020, Flesher et al. 2016), and performing somatosensory imagery—the vivid recall of previously experienced sensations—can elicit neurophysiological responses specific to the sensations being imagined (Bashford et al. 2021, Chivukula et al. 2021).

Cortical Electrical Stimulation

Somatosensation plays a substantial role in motor performance, as evidenced by significant deficits in intact motor control when either tactile or proprioceptive sensations are lost due to deafferentation (Ghez et al. 1995, Gordon et al. 1995, Rothwell et al. 1982). This opportunity to disassociate sensation and motor control in individuals suffering spinal cord injuries or neurodegenerative

Intracortical microstimulation (ICMS):

an electrical stimulation delivered through microelectrodes positioned within the cortex

Neuroprosthetic:

device designed to assist patients with neurological deficits, including a brain-machine interface and an assistive device such as a robotic limb or computer for communication

diseases offers a valuable window of study into the coordination and individual roles of M1 and S1 within the sensorimotor control loop. Furthermore, the importance of sensory feedback in intact motor control underlies the hypothesis that dexterity in BMI applications might also be significantly improved with sensory feedback, especially with the manipulation of objects in sensorized robotic hands. Evidence of somatotopic organization within S1 existing years after injury, amputation, or cortical inactivity (Kikkert et al. 2021, Makin & Bensmaia 2017) adds credence to the possibility of restoring naturalistic sensations. Actual somatosensations could be evoked by stimulating these networks to recreate missing sensory feedback in the sensorimotor control loop.

One method to provide this stimulation is by delivering electric current through electrocorticography (ECoG) contacts (Hiremath et al. 2017, Lee et al. 2018). These electrodes are arranged in a grid and laid onto the surface of cortex underneath the dura and are referred to as subdural arrays. Even with small contacts (2-mm-diameter exposed contact), a considerable amount of current, in the milliamperage range, is required to activate somatosensory cortex. An advantage of these grids is that they can cover a larger area of cortex and thus allow artificial sensations to be delivered to entire regions of the body (Hiremath et al. 2017). Stimulation through ECoG contacts yields reproducible somatotopic maps that can be used for conveying sensory information about contact and shape of an object (**Figure 6a–c**). A disadvantage is that the current delivered through each contact activates substantial volumes of cortex, reducing the spatial and temporal specificity of the delivered stimulation. Thus, the artificial sensations are not specific and are generally described by participants as tingling or electric.

In contrast to electrical stimulation through ECoG contacts, intracortical microstimulation (ICMS) uses microelectrode arrays that penetrate the cortex. An advantage of ICMS is that sensations can be evoked with very low currents in the range of tens of microamperes (Bjånes & Moritz 2019). These low currents stimulate many fewer neurons than do currents delivered through ECoG contacts and, in principle, should provide more natural sensations through more local stimulation. In NHPs, this stimulation can produce behaviors consistent with natural sensations (Romo et al. 1998), and the elicited percepts can be utilized in BMI applications (Dadarlat & Sabes 2016, Klaes et al. 2015, O'Doherty et al. 2011). Only recently has ICMS been applied to human participants in BMI studies (Armenta Salas et al. 2018, Fifer et al. 2020, Flesher et al. 2016). These studies show somatotopically localized fields similar to those observed from stimulation through ECoG contacts (**Figure 6d–f**), but the sensations are reported as more natural (**Figure 7a**). The sensations at an electrode could often be modulated by changing various stimulation parameters. Furthermore, the addition of sensory feedback by ICMS to human S1 improves the time to grasp objects with a robotic limb controlled by motor cortex activity in a human, compared with the previous standard of visual feedback only (Flesher et al. 2021).

Somatosensory Activation of Posterior Parietal Cortex with Natural Stimuli

To date, most studies of single-neuron responses to sensory stimuli in human PPC have explored its visual response properties (Aflalo et al. 2015, Klaes et al. 2015, Rutishauser et al. 2018). However, single-neuron recordings from NHPs have demonstrated a high degree of convergence of somatosensory and visual signals in PPC (Avillac et al. 2007, Graziano 1999, Graziano & Gross 1993, Seelke et al. 2011). The somatosensory receptive fields, though spatially restricted, are large and bilateral. Human fMRI studies suggest a similar integration of vision and somatosensation in PPC, but fMRI cannot resolve the structure of the receptive fields due to limitations in spatial resolution (Sereno & Huang 2014). Recent single-neuron recordings from a tetraplegic participant in a neuroprosthetic clinical trial found touch receptive fields on the sensate parts of the body (Chivukula et al. 2021) (**Figure 8a**). The receptive fields were bilateral and spatially restricted but large and included all the sensate parts of the body above the spinal cord injury.

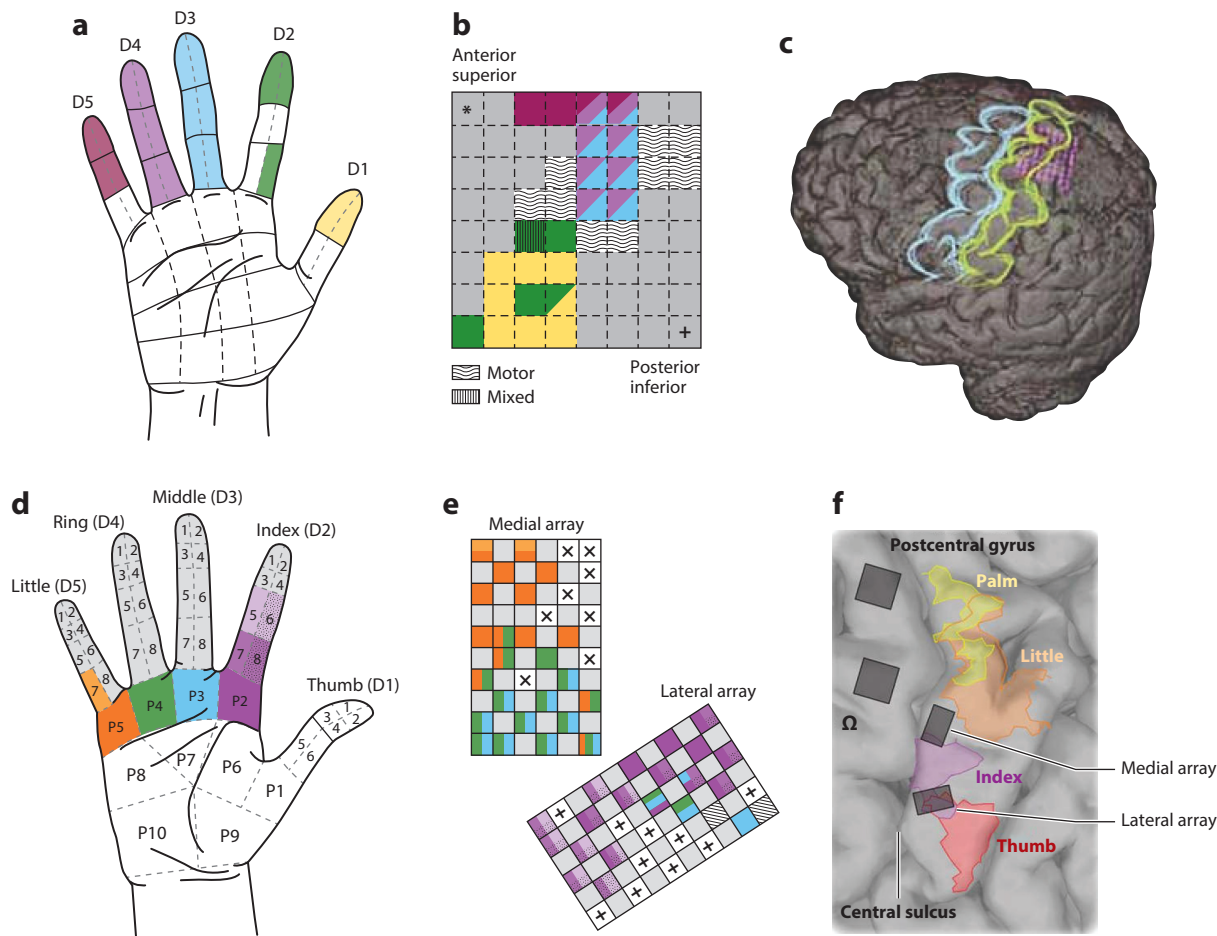


Figure 6

Hand receptive fields from stimulation through (a–c) a subdural ECoG grid and (d–f) two microelectrode arrays (Utah Arrays) implanted in different patients over primary sensory cortex. (a) This participant reported a variety of sensations and commonly used descriptions such as pulsing, electricity, and a feeling of movement. (b) Locations of these percepts are overlaid with color-coded receptive fields from all tested electrodes on the grid. Some electrode pairs induced sensations in single digits, and others had receptive fields that spanned across multiple neighboring digits. Multiple colors on those electrodes indicate sensations occurred on multiple digits. Wavy and stripped patterns illustrate electrodes that elicited motor-only and mixed (motor-sensory) responses, respectively. (c) Reconstructed images of the grid placement of where primary motor cortex (blue) and primary somatosensory cortex (yellow) are in relation to the ECoG minigrid. Panels a–c adapted from Lee et al. (2018). (d) This participant reported a mix of naturalistic and unnatural sensations in response to ICMS such as touch, pressure, vibration, warmth, and electrical. (e) Colored boxes indicate the cumulative projected fields for each electrode and correspond to the colors and patterns in panel d. Multiple colors and patterns in a single box indicate an electrode with a projected field that spanned more than a single area. (f) MEG mapping was used to identify regions in the somatosensory cortex that were responsive to imagined and actual somatosensory input. Panels d–f adapted from Flesher et al. (2016). Abbreviations: ECoG, electrocorticography; ICMS, intracortical microstimulation; MEG, magnetoencephalography.

Imagined Somatosensations

The above studies indicate that somatosensation in humans can be evoked from ICMS of S1 and that regions within PPC have a robust somatosensory as well as motor representation in the neural population. An interesting question is how imagined somatosensation, in terms of both the

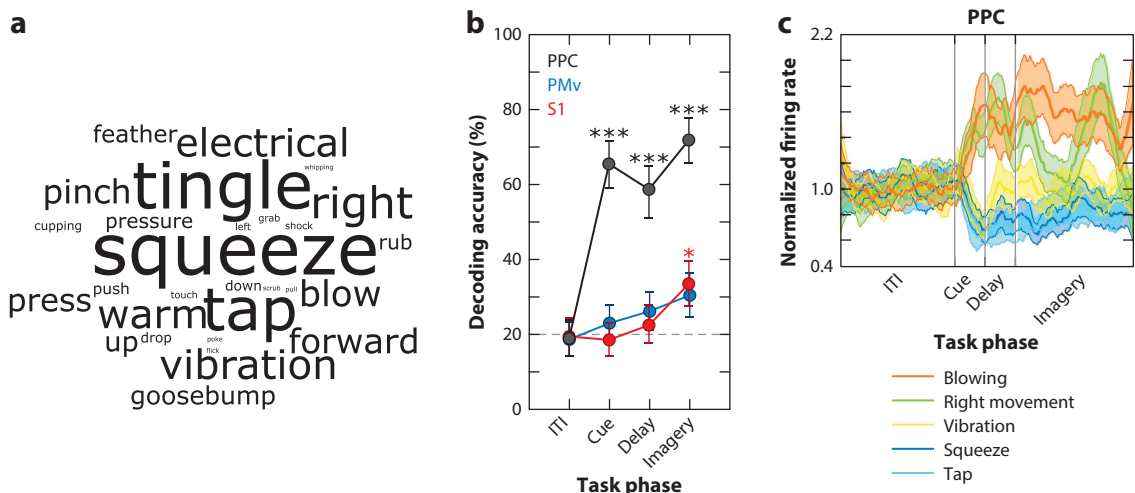


Figure 7

Stimulation evoked and imagined somatosensation. (a) ICMS in human S1 elicited a range of naturalistic sensations in two participants. The word cloud shows responses from participants in two human trials of ICMS (Armenta Salas et al. 2018, Flesher et al. 2016). The descriptions of the sensory experiences span both cutaneous (e.g., mechanical, temperature, or electrical) and proprioceptive (e.g., movement) sensations. (b) Given that ICMS of human S1 evokes naturalistic sensations, it follows that the cortical network in which the electrodes stimulate must also encode those sensations. This was investigated with somatosensory imagery, the vivid recall of the somatosensory experience (Bashford et al. 2021). Participants were asked to recall the five most elicited sensations during ICMS (Armenta Salas et al. 2018): blowing, right movement, vibration, squeeze, and tap. These sensations could be classified significantly above chance in sensorimotor cortical areas using the multiunit firing activity recorded from the same array from which ICMS was delivered. PMv and S1 encoded sensations primarily during the act of somatosensory imagery. By contrast, SMG encoded sensations from the moment of cue presentation through the end of the somatosensory imagery, demonstrating cognitive processing in PPC. Panel b adapted from Bashford et al. (2021). (c) Multiunit activity recorded at a single channel shows how multiple sensations are represented in neuronal firing patterns in PPC. Panel c adapted from Bashford et al. (2021). Abbreviations: ICMS, intracortical microstimulation; ITI, intertrial interval; PMv, ventral premotor; PPC, posterior parietal cortex; S1, primary somatosensory cortex; SMG, supramarginal gyrus.

descriptive quality of sensation (e.g., cutaneous, proprioceptive) and the spatial location on the body, might be represented in the single-neuron activity in PPC.

fMRI studies have shown that motor imagery activates the somatosensory system (Hodge et al. 1996, Porro et al. 1996), and primary and secondary somatosensory cortical areas are activated by tactile imagery. Bashford et al. (2021) asked the participant in a previous study (Armenta Salas et al. 2018) to imagine the five most commonly evoked percepts from ICMS. In this participant, microelectrode arrays were implanted in S1, in a grasp region in the supramarginal gyrus (SMG) of the PPC, and in ventral premotor cortex. The different imagined sensations could be classified in all three areas with spike and local field potential recordings (see **Figure 7b,c** for spikes). The task involved the written word of the sensation to be imagined (e.g., squeeze) followed by a delay and then a cue to imagine the sensation. Although all three areas showed classification during the imagery period, SMG further showed classification during the cue and delay periods. The result from SMG indicates that it plays an additional, cognitive role in the task. The network organization of PPC representing sensorimotor properties could further be investigated with ICMS, just as has been performed in S1. Stimulation in human PPC with a surface electrode (Desmurget et al. 2009, 2018; Fox et al. 2020; Sacheli et al. 2018; Young et al. 2020) elicits the strong desire or intention to move but does not produce overt movements.

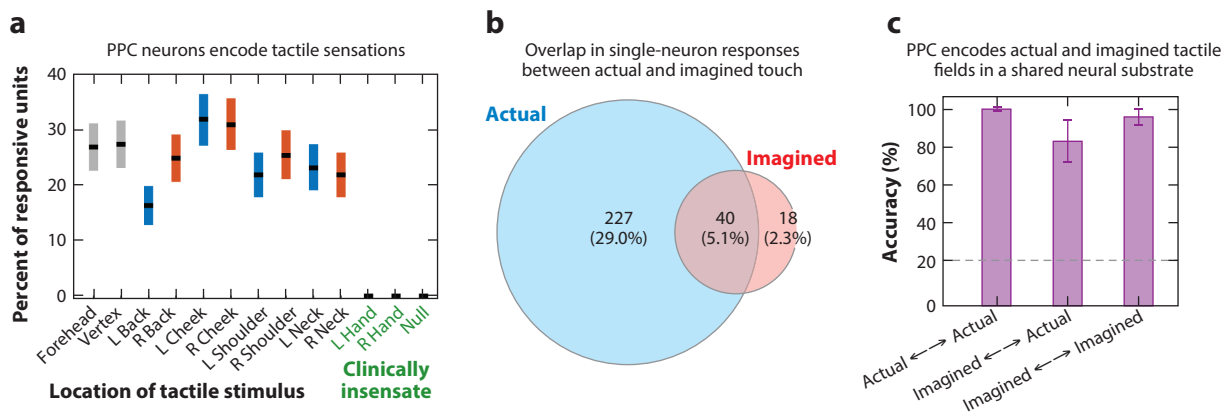


Figure 8

PPC encodes actual and imagined tactile sensations in a shared neural substrate. (a) Percent of neurons in PPC that were responsive to tactile sensations at the indicated body location ($p < 0.05$, FDR corrected, mean $\pm$ 95% CI). Body locations in green were clinically insensate below the level of spinal injury. (b) Imagined tactile sensations at specific body locations activated the same population of cells responsive to actual tactile stimulation. (c) A within- and across-classification analysis revealed that the pattern of population activity that defined different body locations for actual movements was similar to the pattern for imagined movements (see high across-classification accuracy between imagined and actual sensations). Figure adapted from Chivukula et al. (2021). Abbreviations: CI, confidence interval; FDR, false discovery rate; PPC, posterior parietal cortex.

An especially powerful aspect of single-neuron recordings is the ability to precisely measure whether the same population of neurons responds in similar ways across different contexts. Chivukula et al. (2021) measured neural responses both to actual tactile stimuli applied to different locations on the body and during a tactile imagery task using corresponding locations on the body. Although the imagery task engaged a smaller proportion of the population, there was a tendency for the same neurons to be activated in both conditions (**Figure 8b**). At the population level, the pattern of activity that defined how specific body locations were encoded was similar across imagined and actual conditions, indicating a shared neural substrate (**Figure 8c**). Such a shared substrate may provide a mechanism that links cognition to our perceptual experience of the world. Intriguingly, actual tactile stimulation below the level of the participant's injury did not evoke neural responses whereas tactile imagery did, consistent with the idea that the brain maintains an internal representation of tactile sensations that can be engaged through electrical stimulation.

LEARNING

Improvements observed in BMIs over the years can be broadly categorized as control over increasing degrees of freedom (Wodlinger et al. 2014), improvements in movement accuracy at increased speeds (Pandarinath et al. 2017), and control over increasing types of behaviors that are represented in BMIs such as movement goals (Aflalo et al. 2015) and speech (Wilson et al. 2020). BMIs require brain signals to represent each feature being decoded; thus, to facilitate these improvements, multiple features need to be represented at once. These signals either may be learned by the brain or may be intrinsic to the brain area from which the neural signal is recorded. Thus, it is important to consider what areas of cortex to target to achieve desired variables for BMIs.

One approach to derive multiple variables from cortical activity is for the brain to learn to control the neural signal, for example, a single-unit firing rate, for each desired variable. Early research showed that NHPs can learn within minutes to control the activity of individual neurons

Locked-in: a state of advanced paralysis (e.g., in late-stage amyotrophic lateral sclerosis) in which the person remains conscious but unable to move, feel, or communicate

in motor cortex (Fetz 1969, Fetz & Baker 1973). Following the type of conditioning implicit in BMI control paradigms, some M1 NHP neurons change their tuning properties over a longer period, which has been attributed to skill learning (Oby et al. 2019, Zhou et al. 2019). We have seen quick learning by individual neurons in human PPC similar to that observed by Fetz (1969), but the subject reported that he controlled the activity by imagining movements (Affalo et al. 2015). However, there is likely a limit to the number of variables that can be encoded in this way, and it is important to consider that learning may be more limited to the typical function of a cortical area. Quantitative studies in which large rotations must be learned do not show changes in the intrinsic activity patterns in NHP M1 (Golub et al. 2018), NHP PPC (Hwang et al. 2013), or human PPC (Sakellaridi et al. 2019); in the last case the subject verbally reported a cognitive reaiming strategy.

Twelve years after sensory deafferentation of the upper limb of NHPs, it was found through the use of microelectrode mapping experiments (Pons et al. 1991) that the cortical maps of the body in S1 were substantially reorganized. However, M1 remains functional in humans years after spinal cord injury (Hochberg et al. 2006), and stimulation of S1 produces topographically organized sensations to the deafferented regions of cortex (Armenta Salas et al. 2018, Flesher et al. 2016, Makin & Bensmaia 2017). These results suggest that a good deal of the structure remains after spinal cord lesions.

The benefit therefore of a cognitive BMI that records from higher-order brain areas such as PPC is that it can provide many different and useful variables for BMI control without having to first learn those variables individually. The neurons can encode goals of movements as well as trajectories, effector-specific responses for both sides of the body and seemingly for all parts of the body, activity related to the intended goal of the movement and not just its desired trajectories, and the somatosensory responses that accompany the actions (Affalo et al. 2015, Bashford et al. 2021, Zhang et al. 2017).

DECISION MAKING

Expected Value

In NHPs, the PPC has been implicated in action-based decisions (Platt & Glimcher 1999). This type of decision making is studied often by varying the amount, probability, or type of expected reward. In brain control trials in NHPs in which these variables were varied, the preferred and nonpreferred value of goals along with the intended goal location could be read out with high accuracy (Musallam et al. 2004) (**Figure 9**). This finding was proposed as a prime example of a cognitive neural prosthetic, which could decode goals as well as their expected value. Further, the decoding of value would provide a readout of the motivation and perhaps mood of the patient, which would be especially valuable for locked-in patients (i.e., individuals without any forms of overt movement including speech and eye movements).

Memory Decisions

Evidence from fMRI and evoked potentials has implicated the PPC in encoding of memories, distinguishing between novel and familiar stimuli and the confidence of those decisions (reviewed in Rutishauser et al. 2018). Lesions to PPC produce memory deficits for spatial locations (Bisiach & Luzzatti 1978, Guariglia et al. 2005, Mishkin & Ungerleider 1982). These findings suggest a role for PPC in memory and spatial recognition.

Recent recordings from AIP in BMI clinical trials found two classes of neurons. Memory-selective neurons prefer either novel or familiar visual stimuli, and the response scales with

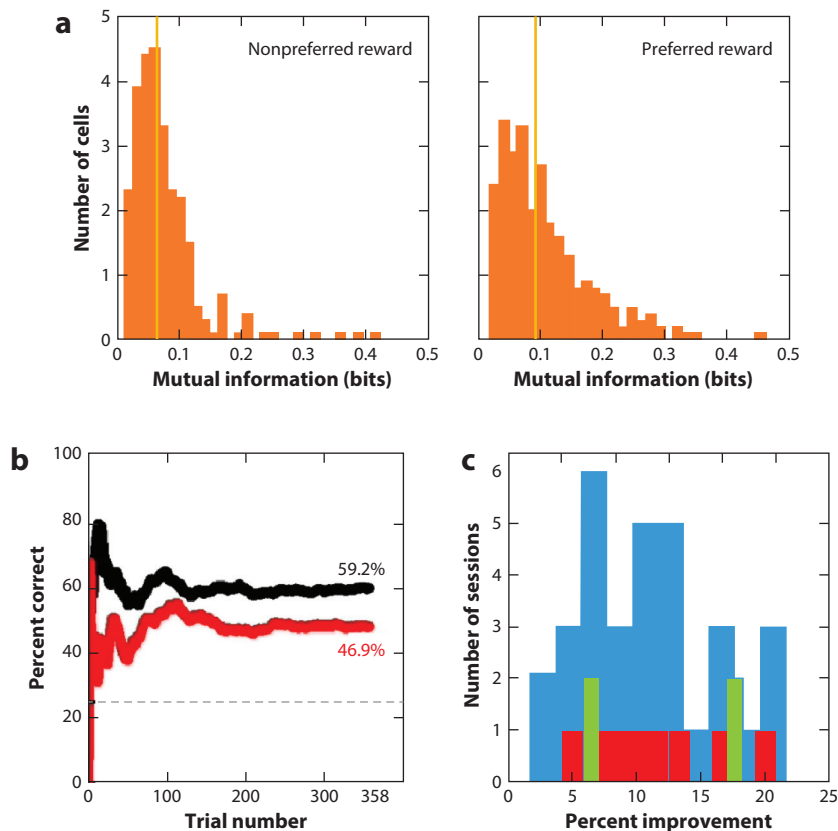


Figure 9

(a) Mutual information for neurons decoding the intention to reach when anticipating nonpreferred (*left*) and preferred (*right*) rewards. The yellow line through the histograms indicates the median of the distributions (0.067 nonpreferred, 0.091 preferred). (b) Decode performance from one session in which two independent decoders were run online for preferred (*black*) and nonpreferred (*red*) intermixed rewards. (c) Improvement in decode between preferred and nonpreferred rewards. Blue bars refer to variable magnitude (high volume, 0.12 mL; low volume, 0.05 mL); red bars, variable type (juice versus water, volume = 0.12 mL); green bars, variable probability (high probability = 80%, low probability = 40%). Total number of sessions is 44 (32 reward magnitude, 4 reward probability, and 8 reward type). Figure adapted from Musallam et al. (2004).

confidence. Confidence-selective neurons signaled confidence regardless of familiarity. Error trial analysis indicated that the signals represented the choice of the subjects, unlike hippocampal cells that encode the ground truth (Rutishauser et al. 2018).

CONCLUSION

The Importance of Mixed Selectivity

The number of variables encoded by PPC is truly remarkable. The same population of neurons encodes motor strategy (imagined or attempted), movement of much of the body, visual and somatosensory signals, imagined touch, action observation, semantics, and memory decisions. This view is different from what has been reported for PPC in NHPs, in which effector specificity is segregated by areas and inactivations of those areas affect the behavior of specific effectors

(Andersen & Buneo 2002; Christopoulos et al. 2015, 2018; Yttri et al. 2014). One possibility, mentioned above, is that NHPs cannot be practically trained to perform enough tasks and that they are highly overtrained for the tasks they do perform. However, this does not explain the observation that AIP encodes movements of the hand and shoulder in the same anatomical region but in distinct ways within a mixed population of cells.

Another possibility is that the areas around the IPS of NHPs are earlier in the sensorimotor pathway compared with areas around human IPS. Alternatively, the larger number of variables encoded in human intraparietal regions may reflect species-level differences, expressing a richer encoding of the sensorimotor variables that enable human behavior.

Context may also be responsible. In NHP prefrontal cortex, the selectivity of neurons changed with the task (Rigotti et al. 2013). In the case of human PPC, the partially mixed selectivity maintained its structure such that selectivity preferences were largely stable from offline to online brain control. This stability suggests that the encoded variables are robust generalizable features of representation. However, PPC is embedded in a network of cortical and subcortical areas. Context switching within these circuits could explain the diversity of variables, as those listed above were generally collected in different contexts. Likewise, the lesion deficits, which seem more circumscribed, are usually tested within a specific context and may not generalize for all tasks.

Future directions of cognitive BMIs include speech, hybrid BMI systems, mood regulation, and awareness of intent. Especially for subjects who are rendered mute by neurological diseases or trauma, a speech prosthetic that could directly convey speech would be tremendously beneficial (Brumberg et al. 2010). Moreover, such a prosthetic would undoubtedly operate at much faster rates than keyboard-based prosthetics. Several laboratories are working toward making high-performance communication prosthetics (Anumanchipalli et al. 2019, Bocquet et al. 2016, Herff et al. 2019, Willett et al. 2021). For example, decoding attempted handwriting from a paralyzed individual produced faster rates of communication than did point-and-click typing (Willett et al. 2021).

Hybrid Brain–Machine Interface Systems

Technological advancements in machine learning and computer vision for industrial robots and autonomous robotic interaction in human environments provide a substantial opportunity for BMI users (Allison et al. 2011, Katyal et al. 2014). Rather than decode low-level trajectories and individual muscle forces for grasping or other dexterous coordinated actions, a hybrid BMI could focus on decoding high-level cognitive goals (e.g., “reach for the blue cup” or “walk forward”) from cortical areas such as PPC (Musallam et al. 2004). This hybrid system could give the user a range of possible actions in a given environment, empowering the embedded intelligent system with control over the low-level steps needed to accomplish each decoded goal (Hayati & Venkataraman 1989, Sheridan 1992, Wolpaw 2007). As uninjured humans rarely consider their own individual muscle movements during common motor activities such as walking or grasping, hybrid BMIs could similarly free users of the high cognitive load typically needed for complex, high-dimensional control with current BMI devices (McMullen et al. 2014) to improve their speed and accuracy (Royer & He 2009).

Mood Regulation

Common psychological conditions such as depression, anxiety, and compulsive behaviors (Malone et al. 2009), along with disruptive motor disorders (e.g., Parkinson’s disease, essential tremor), are thought to be by-products of dysregulation between multiple cortical processing areas

(Beuter et al. 2014, Herron et al. 2015). As cognitive BMIs grow in their complexity and technological ability to record and stimulate widely across many target locations in the brain, identifying and disrupting irregular patterns of neural activity or strengthening weakened connections between damaged cortical areas may be successful treatments for these disorders (Shanechi 2019).

Awareness of Intent

Although still controversial, psychological studies suggest that under certain experimental designs subjects are aware of their intent only several hundred milliseconds after beginning to plan movements (Fried et al. 2011, Libet et al. 1983). We sometimes find this to be the case in prosthetic control, in which subjects feel that they have begun to move the prosthetic effector even before they intended to. These new findings suggest that implicit intent must be taken into account for the user to feel more embodied with their, at times, nascent plans.

Final Thoughts

Cognitive BMIs may offer many advantages as a scientific platform both for deepening our understanding of complex, interconnected cortical networks and for developing prosthetic devices, treatments, and therapies for those suffering crippling diseases or injury. By recording higher-order cortical signals from such areas as PPC, researchers can decode a rich set of behavioral and internal features to augment control signals for human BMIs and to discover the inner workings of the brain.

Future scientific research will further explore what can be decoded from the brain for cognitive neural prosthetics. Given the prior research reviewed above, the most likely approach for maximum performance will be to record from areas of the brain that naturally encode the desired control signals. For instance, recording from speech areas of cortex may allow communication interfaces that operate at the speed of speech. Recordings from prefrontal areas can potentially provide executive control signals that can enhance the range of planning, context, and decision signals to benefit the design of advanced decoders.

As indicated in this review, many cognitive control signals can already be used for prosthetic control of assistive devices such as computers and robotics. Demonstrations of control have been impressive. However, these successes have been restricted thus far to clinical trial/laboratory settings. The field of neural prosthetics is a relative newcomer in the area of neurotechnology. Whereas cochlear implants for deafness and deep brain stimulation implants for Parkinson's disease are now widely used as clinical devices, neural prosthetics require technical refinements and advances before they become a routine therapy. Among these challenges are to improve micro-electrode arrays so they can access deeper parts of the cortex and be flexible to movement of the tissue for better recording stability. These arrays need to be designed with materials that extend the lifetime of the implant, which with current technology is generally five years. Other refinements include miniaturizing the electronics and making implants wireless. Although these technological advances are achievable in the near term, they require a substantial investment of resources to produce a routinely used clinical device.

A desirable advance would be to reduce the invasiveness of the implants. In the short term, this may be achieved by refining surgical techniques. However, the current implants require brain surgery involving opening the scalp, skull, and dura and penetrating brain tissue with the electrodes. Less-invasive technologies, such as ultrasound recording, potentially require less invasive surgeries by replacing a small bit of the skull with an ultrasound-transparent material without opening the dura or penetrating brain tissue (Norman et al. 2021). The temporal resolution of

ultrasound recording is not as precise as single electrical recordings, as it is limited by the hemodynamic response, but has excellent spatial resolution and shows promise as an example of future, less invasive BMIs. Refinement of this technique, and other minimally invasive technologies that may be on the horizon, would make neural prosthetics more appealing to larger populations of patients.

DISCLOSURE STATEMENT

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Contents

Recollecting What We Once Knew: My Life in Psycholinguistics <i>Lila R. Gleitman and Claire Gleitman</i>	1
Memory and Reward-Based Learning: A Value-Directed Remembering Perspective <i>Barbara J. Knowlton and Alan D. Castel</i>	25
Normative Principles for Decision-Making in Natural Environments <i>Christopher Summerfield and Paula Parpart</i>	53
Speech Computations of the Human Superior Temporal Gyrus <i>Irina Bhaya-Grossman and Edward F. Chang</i>	79
Cognitive, Systems, and Computational Neurosciences of the Self in Motion <i>Jean-Paul Noel and Dora E. Angelaki</i>	103
Exploring Cognition with Brain–Machine Interfaces <i>Richard A. Andersen, Tyson Aflalo, Luke Bashford, David Bjånes, and Spencer Kellis</i>	131
Brain Mechanisms Underlying the Subjective Experience of Remembering <i>Jon S. Simons, Maureen Ritchey, and Charles Fernyhough</i>	159
Neurophysiology of Remembering <i>György Buzsáki, Sam McKenzie, and Lila Davachi</i>	187
The Basis of Navigation Across Species <i>Cody A. Freas and Ken Cheng</i>	217
Computational Psychiatry Needs Time and Context <i>Peter F. Hitchcock, Eiko I. Fried, and Michael J. Frank</i>	243
Persistence and Disengagement in Personal Goal Pursuit <i>Veronika Brandstätter and Katharina Bernecker</i>	271
Social Motivation at Work: The Organizational Psychology of Effort for, Against, and with Others <i>Adam M. Grant and Marissa S. Shandell</i>	301

Attitudes, Habits, and Behavior Change <i>Bas Verplanken and Sheina Orbell</i>	327
Childhood Antisocial Behavior: A Neurodevelopmental Problem <i>Stephanie H.M. van Goozen, Kate Langley, and Christopher W. Hobson</i>	353
Human Cooperation and the Crises of Climate Change, COVID-19, and Misinformation <i>Paul A.M. Van Lange and David G. Rand</i>	379
Diversity Training Goals, Limitations, and Promise: A Review of the Multidisciplinary Literature <i>Patricia G. Devine and Tory L. Ash</i>	403
Psychology and Indigenous People <i>Roberto González, Héctor Carvacho, and Gloria Jiménez-Moya</i>	431
Psychology Within and Without the State <i>H. Clark Barrett</i>	461
Personality Psychology <i>Brent W. Roberts and Hee J. Yoon</i>	489
Personal Values Across Cultures <i>Lilach Sagiv and Shalom H. Schwartz</i>	517
Educational Psychology Is Evolving to Accommodate Technology, Multiple Disciplines, and Twenty-First-Century Skills <i>Arthur C. Graesser, John P. Sabatini, and Haiying Li</i>	547
Cultivating Resilience During the COVID-19 Pandemic: A Socioecological Perspective <i>Ning Zhang, Shujuan Yang, and Peng Jia</i>	575
What Are the Health Consequences of Upward Mobility? <i>Edith Chen, Gene H. Brody, and Gregory E. Miller</i>	599
The Social Effects of Emotions <i>Gerben A. van Kleef and Stéphane Côté</i>	629
Catching Up on Multilevel Modeling <i>Lesia Hoffman and Ryan W. Walters</i>	659
Optimizing Research Output: How Can Psychological Research Methods Be Improved? <i>Jeff Miller and Rolf Ulrich</i>	691
Replicability, Robustness, and Reproducibility in Psychological Science <i>Brian A. Nosek, Tom E. Hardwicke, Hannah Moshontz, Aurélien Allard, Katherine S. Corker, Anna Dreber, Fiona Fidler, Joe Hilgard, Melissa Kline Strubl, Michèle B. Nuijten, Julia M. Robrer, Felipe Romero, Anne M. Scheel, Laura D. Scherer, Felix D. Schönbrodt, and Simine Vazire</i>	719

Quantum Cognition	
<i>Emmanuel M. Pothos and Jerome R. Busemeyer</i>	749

Indexes

Cumulative Index of Contributing Authors, Volumes 63–73	779
Cumulative Index of Article Titles, Volumes 63–73	784

Errata

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