

Characterizing the neural populations of the cortical grasping network in tetraplegic humans

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Mackenzie J. Thurston

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The Caltech logo, featuring the word "Caltech" in a bold, orange, sans-serif font, centered within a light orange rectangular background.

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Mackenzie J. Thurston
ORCID: 0000-0001-7622-3305

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ABSTRACT

The cortical grasping network (CGN) is responsible for the ability to physically interact with the world around us using our hands. For patients with motor impairments due to neurodegenerative disease or traumatic injury, brain-machine interfaces (BMIs) offer a potential pathway towards restoration of dexterous hand control via recording neural activity throughout the CGN. However, grasping objects with robotic BMI devices has proved challenging, when utilizing neural signals from only motor cortex (MC, a subregion of the CGN). It is currently unclear how the presence of an object might compromise BMI performance; thus this work explores the interactive neural representation of grasp and objects throughout the CGN.

Three tetraplegic human participants performed grasp motor imagery during imagined object manipulation while we recorded neural activity from the supramarginal gyrus (SMG), anterior intraparietal cortex (AIP), motor cortex (MC), and primary somatosensory cortex (S1). All regions within the CGN represented whole hand configuration of imagined grasps during motor planning and imaged execution. Additionally, grasp-related neural activity in each region was modulated by context (motor planning vs. imagined execution and object present vs. not present). SMG and AIP represented object shape during motor planning. PPC encoded both grasp and object properties simultaneously from mostly unique subpopulations of neurons. This separability in higher cortical regions could be a critical for stable BMI grasp performance.

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NOMENCLATURE

AIP. Anterior Interparietal Cortex. A subregion within the Posterior Parietal Cortex.

BMI. Brain-Machine Interface. This is a device that records neural activity, typically related to cognitive functions, that can then be used to drive the action of an external device, such as a computer cursor or a robotic limb.

CGN. Cortical Grasping Network. This is a circuit in the human cortex that relays critical information related to grasping. The key regions involved are SMG, AIP, and M1.

Channel. This refers to one (1) microelectrode on the implanted array. May be used interchangeably with ‘Unit.’

c.i. 95% Confidence Interval.

dIPFC. Dorsolateral prefrontal cortex. A cortical region of the brain involved in higher level cognition, such as decision-making.

LDA. Linear Discriminant Analysis. This is a linear regression method used to classify the data.

MC. Motor Cortex. A cortex of the brain that processes information related to motor control and movement. Often referred to as M1 (primary motor cortex) in the literature.

Microelectrode array. This is the device chronically implanted in study participants. It is a 4x4mm grid containing 64-96 microelectrodes that are directly implanted into the cortex.

NHP. Non-Human Primates, such as macaques.

PMv. Ventral premotor cortex. A cortical region of the brain known for motor preparation and processing.

PPC. Posterior Parietal Cortex. A cortex of the brain known to integrate sensorimotor signals and communicate with many other brain regions.

S1. Primary Somatosensory Cortex. A cortex of the brain that processes information related to somatosensation.

S2. Participant in the study with implants in SMG and S1.

S3. Participant in the study with implants in SMG, AIP, PCG, S1, and PMv.

S4. Participant in the study with implants in SMG, AIP, PCG, S1, and dlPFC.

SCI. Spinal Cord Injury.

SMG. Supramarginal Gyrus. A subregion within the Posterior Parietal Cortex.

Tetraplegia. Loss of motor control and sensation (paralyzed) in all four limbs. Synonymous with quadriplegic.

Unit. A neuron. May be used interchangeably with ‘Channel.’

Chapter 1

INTRODUCTION

Imagine for a moment a favorite pastime. Turning the pages of a riveting book, plucking a carrot from the dirt, strumming a guitar. Intact hand function is critical in all these activities. Along with many recreational activities, the majority of activities of daily living (ADLs), commonly used as a clinical indicator of a person's ability to care for themselves independently, require the ability to interact with one's surroundings via grasp¹. For people with tetraplegia, these essential activities become incredibly difficult, if not entirely impossible. Every year, there are approximately 18,000 new cases of traumatic spinal cord injuries (SCI) in the US alone, with over half of the cases resulting in incomplete or complete tetraplegia². In a survey of people with SCI, when asked what would provide the largest improvement in quality of life, people with tetraplegia identified regaining hand and arm function as their top priority³. This is currently not possible.

In this dissertation, I will explore how we can get closer to this goal by utilizing brain-machine interfaces (BMIs). Specifically, I will focus on the brain regions throughout the cortical grasping network (CGN) and investigate their roles in the sensorimotor processing of grasp and object properties. By gaining a deeper understanding of higher-order brain areas such as the posterior parietal cortex (PPC) and a popular motor BMI target, the motor cortex (MC), we can offer important neuroscientific insights by investigating grasp encoding at the single-unit level but also learn how to better leverage each region for potential applications of intracortical BMIs.

In **Chapter 2**, I will explain in depth the neuroscience behind grasping, brain-machine interfaces (BMIs), and the hardware behind intracortical BMIs. I will dive into the regions of the cortical grasping network, their roles, and outline how they have the potential to be utilized for grasping BMIs. I will also provide background information on the current state of grasping BMIs.

In **Chapter 3**, I will detail how we collect and process our data using the chronic implantation of microelectrode arrays, the method we use to localize the arrays, and the pertinent information about each of our three participants, including how long they have been injured, level of injury, and implant locations.

Chapter 4 will demonstrate how grasp is encoded throughout the CGN and how this representation is altered by varying the context of grasp presentation. We ask participants to imagine performing various grasp types, with and without the presence of objects, and determine whether context influences grasp encoding. We discovered that while grasp remains decodable among all 3 contexts throughout the CGN, significant differences do occur. Specifically, our ability to decode grasp from all brain regions is lowest when the object is presented alone. Additionally, I will elaborate on the unique tuning of single-units we observe in each region.

Knowing that context influences grasp encoding, we move into **Chapter 5**, where we will demonstrate the effect of manipulating the object size on grasp encoding. Again, we ask participants to imagine performing various grasps, this time with the smallest and largest feasible hand apertures for each grasp type. This also allows us to investigate the encoding of object size throughout the CGN. Briefly, grasp encoding is unaffected by manipulation of object size and size and/or hand aperture is encoded in SMG and MC.

In **Chapter 6**, we explore the encoding of the object shape itself, independent of the grasp type. In the first two experiments, the same grasp type is always paired with the same object shape, resulting in four grasp-object sets. To determine object encoding in each brain region, we break up these previously paired sets and pair each grasp type with each object shape, thereby creating 16 total grasp-object sets. By investigating grasp decoding and object decoding separately, we can determine if grasp can still be decoded irrespective of what object it is paired with, and if the object shape itself can be decoded. We find that grasp decoding reaches similar levels in each brain region, and that the object shape is encoded in SMG and AIP. This finding makes SMG an attractive location for a grasping BMI.

Chapter 7 will conclude by discussing the major findings and implications within the fields of neuroscience and BMIs. Briefly, the role of the motor cortex (MC) is to process motor-related variables, such as grasp type and hand aperture, during both planning and imagined movement. The posterior parietal cortex (PPC) processes grasp and object properties. Specifically, the supramarginal gyrus (SMG) subregion encodes grasp type, object size, and object shape, while the anterior intraparietal cortex (AIP) subregion encodes grasp type and object shape, contrary to non-human primate literature. Imagined grasping results in robust decoding of grasp type in motor cortex and posterior parietal cortex and can be utilized in the context of a grasp BMI. This better understanding of how grasp and object properties are encoded throughout the CGN has the potential to enable BMIs to more effectively communicate with the brain during grasping movements, thereby improving the efficiency of such neuroprosthetic devices and offering hope of returning some autonomy back to people with tetraplegia.

Chapter 2

BACKGROUND

Grasp in the Brain

Grasping is one of the most fundamental motor behaviors performed by humans, yet it requires the coordinated activity of a distributed neural network that transforms visual information about an object into precise movements of the hand. Although grasping appears effortless, it depends on a series of complex sensorimotor computations, including object recognition, movement planning, hand preshaping, movement execution, and continuous sensory feedback⁴⁻⁶.

Neuroimaging studies, such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), have demonstrated that grasping is supported by a distributed network of cortical and subcortical regions rather than a single specialized area. Across studies in which participants performed grasping movements or interacted with objects, activation has been observed in the contralateral motor cortex (MC), premotor cortex, ventral supplementary motor area (SMA), cingulate cortex, superior parietal lobule (SPL), dorsal occipital cortex, prefrontal cortex (PFC), posterior parietal cortex (PPC) (including the anterior intraparietal cortex (AIP)), cerebellum, and pre- and post-central gyri, among other regions⁷⁻⁹. Collectively, these findings illustrate that successful grasping emerges from the coordinated activity of multiple interconnected brain regions that integrate visual, sensory, and motor signals to generate accurate grasp control. Within this distributed network, a subset of interconnected parietal and sensorimotor regions has emerged as particularly critical for grasping across non-human primates (NHPs) and humans. This circuit, commonly referred to as the cortical grasping network, has become the primary focus of contemporary systems neuroscience investigations into grasp.

The Cortical Grasping Network

The cortical grasping network (CGN) refers to a distributed set of interconnected cortical regions that collectively support the planning and execution of grasping movements. This network primarily consists of regions of the posterior parietal cortex (PPC), including supramarginal gyrus (SMG) and anterior intraparietal cortex (AIP), in addition to the ventral premotor cortex (PMv) and motor cortex (MC). The complementary computations performed across these regions enable flexible and accurate control of object-directed grasps.

Posterior parietal cortex serves as a critical hub for sensorimotor integration and movement planning^{10–13}. Lesions to PPC lead to apraxia and optic apraxia, an inability to plan movements and inaccuracies in reaching visual targets, respectively^{14,15}. Additionally, research has demonstrated the importance of PPC's involvement in transforming sensory information into coordinated motor plans^{16,17}. Within PPC, distinct subregions contribute specialized computations relevant to grasping and object manipulation.

The anterior intraparietal cortex has been extensively studied in both NHPs and humans. Along with encoding grasp and reach^{11,18,19}, it has been suggested that AIP plays a role in the visual processing of object sizes and shapes in non-human primates (NHPs)^{4,12,20}. AIP contains three major types of neurons: motor, visual, and visuo-motor²¹. It is generally accepted that the initial step of visuomotor transformation necessary to incorporate object properties for accurate hand shaping and grasping is driven by the visual neurons in AIP^{22,23}. Further supporting this functional role, reversible inactivation of AIP disrupts hand preshaping during grasping, resulting in mismatches between the object's intrinsic properties and the hand shape necessary to grasp it, despite preserved reaching ability²⁰.

The supramarginal gyrus, another key region within PPC, has been implicated in higher-order aspects of object-directed behavior. SMG, also referred to as Brodmann Area 40, is thought to be involved in tool use^{24–26}, grasping and manipulating objects^{27,28}, and reaching²⁹.

Lesions to SMG result in ideomotor apraxia, the inability to correctly imitate hand gestures and reduce skills associated with tool use^{30,31}.

Ventral premotor cortex serves as an intermediate node between parietal representation of objects and motor execution in motor cortex. Different subpopulations of neurons in PMv have been shown to encode goal-directed behavior, specific actions, and finger and hand configurations, essentially forming a repertoire of possible grasps³². PMv communicates with AIP to receive information about grasp-selective properties before sending this information to the motor cortex. Reversible disruption of this region using repetitive transcranial magnetic stimulation (rTMS) results in an inability to plan accurate hand configurations¹⁸.

The motor cortex is a primary motor area that encompasses grasp and reach regions and represents the final node in this network. MC is thought to be primarily involved in motor execution, sending out a descending motor command for the body to execute. Single neurons in the MC have demonstrated encoding of motor kinetics, such as direction and gain³³, as well as grasping movements during motor execution¹². One recent study in NHPs suggests object-specific information is also encoded in MC³⁴. Lesions or inactivation to MC result in force deficit, flaccidity, and severe impairment of individual finger movements^{6,35}.

Anatomical and functional connectivity between PPC, PMv, and MC suggest that these regions operate as a tightly coupled circuit with feedback rather than independent processing stages (**Fig. 3-1**). Perturbation studies and connectivity analyses have

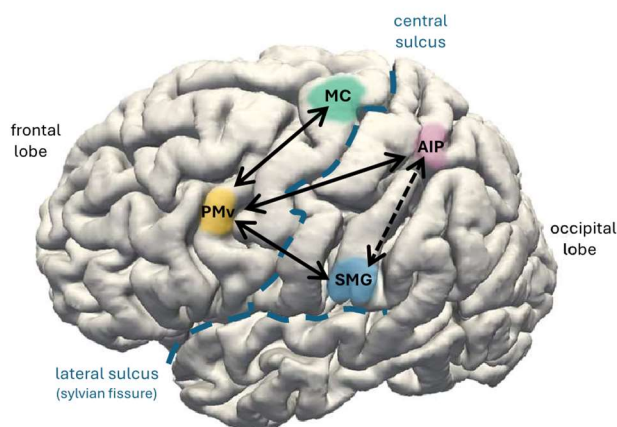


Figure 2-1. Proposed Human Cortical Grasping Network. Adapted from non-human primate studies of the cortical grasping network (Davare et al., 2011). Solid line = observed connections; dashed line = proposed connections as seen in Orban & Caruana (2014). AIP: anterior intraparietal cortex; SMG: supramarginal gyrus; PMv: ventral premotor cortex; MC: motor cortex.

demonstrated that effective grasping depends on the dynamic interaction of this network¹⁸. Despite all we know about these regions, how grasps and objects are encoded at the level of single neurons remains an outstanding question in systems neuroscience.

Actual vs. Imagined Grasping

To study grasp in the brain, we utilize a motor imagery grasp task using tetraplegic participants. Due to varying degrees of residual motor function, we chose imagery rather than attempted grasping. This produces less fatigue for the participants and ensures a more consistent comparison across participants as they are all imagining. This naturally raises the question: do imagined movements activate the cortical grasping network in the same way that actual or attempted movements do?

Several neuroimaging studies using fMRI have investigated the question of actual versus imagined movements in the brain. One study investigated the motor cortex of intact human participants while they performed actual and imagined finger-to-thumb movements. They found largely overlapping neural networks that were engaged during both actual and imagined finger movements³⁶. One key difference was motor imagery resulted in decreased signal intensity relative to actual movements. Another fMRI study went beyond motor cortex and investigated the broad neural networks associated with movement. Using a similar task paradigm, intact humans performed actual and imagined finger-thumb opposition movements. They found that both actual and imagined movements shared the vast majority of cortical networks, specifically the contralateral primary motor cortex (MC), dorsal premotor cortex (PMd), parietal regions, and supplementary motor area (SMA)³⁷. They also noted several key differences, such as select regions demonstrating activity exclusive to actual (portions of the primary MC and somatosensory cortex) and imagined movements (ipsilateral primary motor cortex and ipsilateral PMd), as well as a decrease in activity in the contralateral MC during imagined movement.

Similarly, an ECoG study in intact human participants performed actual and imagined hand movements while recording from a large swath of cortex, including premotor, motor, sensory, and parietal cortices. They found an overlapping spatial distribution of cortical activity between actual and imagined hand movements³⁸. Initially, cortical activity during motor imagery was 25% lower than actual; however, once participants learned to control a cursor with the imagined activity, the activity increased and even exceeded actual motor movement activity.

The same findings can be seen at the single neuron level. Within the human motor cortex of tetraplegic participants, observing, imagining, and attempting actions activates shared populations of movement-related neurons³⁹. However, these patterns of activation are not identical, as neural activity from the MC could be used to distinguish between the volitional states. Another intracortical study also of the human motor cortex used an actual and imagined wrist extension task in tetraplegic participant with residual wrist function. They found that the motor cortex maintains the same population dynamics during actual and imagined motor movement during wrist extension⁴⁰.

Taken together, these results demonstrate the overwhelming similarity in cortical activation that results from actual and imagined movements, specifically the hand. This similarity can be seen from the population down to the single neuron level. This suggests that imagined grasp is a reasonable way to investigate grasp processing in the cortical grasping network.

What are BMIs?

Brain-machine interfaces (BMIs) are devices that can record and utilize behaviorally relevant neural activity from the central or peripheral nervous system to control an external device. Often, BMIs are considered in the context of using neural activity related to a certain function (i.e., grasping) to control an external device (i.e., robotic limb) with the goal of restoring that function to an individual who can no longer perform the function on

their own. One important population that may benefit from BMI applications is individuals living with tetraplegia. Tetraplegia is characterized by impairment of motor and/or sensory function affecting all four limbs and the torso, with the extent of functional impairment varying depending on the level and severity of the neurological injury. Tetraplegia may result from spinal cord injury (SCI), stroke, or neurological disease. In the United States alone, more than 300,000 individuals are living with traumatic SCI, with approximately 18,000 new injuries occurring annually, and over half of these individuals experience tetraplegia^{41,42}. Tetraplegia can substantially affect many aspects of daily life, including mobility, self-care, communication, employment, and participation in social activities. Although experiences vary widely, many require long-term rehabilitation, assistive technologies, and caregiver support to accomplish activities of daily living. SCI is also associated with an increased risk of secondary medical complications and significant lifetime healthcare costs, with direct medical expenses often reach several million dollars over a patient's lifetime⁴³. These challenges underscore the importance of developing technologies that restore functional independence and improve quality of life for individuals living with paralysis.

Several types of BMIs exist, using different recording technologies to acquire neural activity. Each modality comes with a tradeoff between invasiveness, spatial and temporal resolution, signal stability, and the type of neural information that can be recovered.

Electroencephalography (EEG) is the least invasive BMI. It functions by recording electrical activity through electrodes placed directly on the scalp. This feature makes it widely accessible and has subsequently been utilized in a variety of ways, such as for communication⁴⁴, wheelchair control⁴⁵, and robotic arm control⁴⁶. However, the presence of the skull and surrounding tissue attenuates electrical signals, resulting in relatively poor spatial resolution and limited access to high-frequency neural activity associated with individual neural populations⁴⁷.

Electrocorticography (ECoG) is a semi-invasive approach in which non-penetrating electrode grids are placed directly on the cortical surface beneath the skull. This method substantially improves signal quality and spatial resolution compared to EEG. ECoG arrays record local fluctuations of field potentials from multiple neural sources, known as local field potentials (LFPs)⁴⁸. ECoG has been successfully used to decode movement intentions and speech making it an attractive compromise between invasiveness and decoding performance^{49,50}. However, neural activity arises from aggregates of large populations of neurons, rather than single, individual neurons, making complex movements challenging to decode.

Intracortical BMIs (iBMIs) use penetrating microelectrodes implanted directly on the cortical surface to record spiking activity of single neurons with high signal-to-noise ratio (SNR), high spatial resolution, and high temporal resolution⁵¹. While there are many forms of BMIs, these qualities make intracortical BMIs an ideal candidate for neuroprosthetics.

Microelectrode (Utah) Arrays

The gold standard for intracortical neural recording technologies are microelectrode arrays, which provide stable, chronic access to extracellular action potentials from populations of neurons in the cerebral cortex^{52,53}. By directly recording neuronal spiking activity, microelectrode arrays can be used to investigate neural populations at the single-channel level, leading to discoveries in basic neuroscience, as well as providing the foundation for high-performance neural decoders for clinical BMI applications.

The microelectrode (Utah) array was first developed in 1991 by Richard Normann at the University of Utah and was being used for chronic implantation in NHPs a few years later^{54,55}. In NHPs, investigators found that intended arm trajectories could be reconstructed directly from neural activity⁵⁵⁻⁵⁷, demonstrating that movement intentions could be decoded from cortical populations and laying the groundwork for translation to humans. In 2004, the first human participant with tetraplegia was implanted. This was the first

demonstration that motor cortical activity in humans could be used to control a computer cursor⁵⁸. Only 20 years later and the capabilities of the microelectrode array have dramatically expanded, with robotic arms reaching and grasping⁵⁹, decoding handwriting⁶⁰, and communicating via imagined movements⁶¹.

Modern microelectrode arrays are a 4 x 4 mm grid of 64-96 densely packed electrodes. The high electrode density enables high spatial resolution, one of the major benefits of this technique⁵¹. Along with high signal-to-noise ratio, we can sample the surrounding tissue via the electrode rapidly (30,000 samples/sec), providing excellent temporal resolution. Individual electrodes penetrate approximately 1-1.5 mm into the cortical surface⁵⁴. Another important advantage of the microelectrode array is their suitability for long-term implantation. Several studies have demonstrated stable neural recording over multiple years following implantation in both NHPs and humans^{53,62}. Among our own participant cohort, one subject (S2) has been implanted for over nine years and still demonstrates strong neural signal and recordings.

Within the laboratory, our participants are chronically implanted with 4-6 microelectrodes each. Our participants perform a motor imagery task, where they are shown which grasp to imagine by viewing a static image on a computer screen (**Fig. 2-2**). The participant is directly connected to neural signal processors via their percutaneous headstages. This

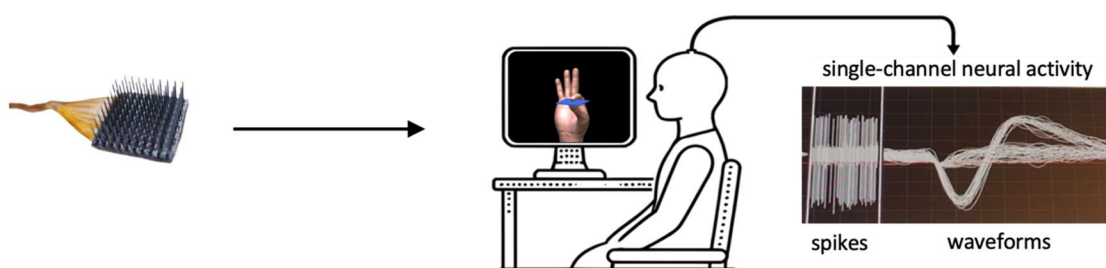


Figure 2-2. Microelectrode arrays in the lab setting. Our participants are chronically implanted with microelectrode arrays. In the lab, they perform a motor imagery task where they view a computer screen that cues them to which grasp they should imagine. While they perform this task, they are directly connected to neural signal processors via their headstages. This connection allows us to see the spike and waveform activity of single neurons in real-time.

connection allows us researchers to observe the spike and waveform activity of their single neurons in real time.

Surgical Implantation of Microelectrode Arrays

While intracortical microelectrode arrays boast many advantages among brain recording technologies, they are also the most invasive class of BMIs. Implantation requires an extensive neurosurgical procedure in which a craniotomy is performed to expose the dura, followed by opening the dura to provide access to the cortical surface. Individual microelectrode arrays are then carefully positioned over their intended cortical targets and inserted into the cortex using a pneumatic insertion device that rapidly drives the electrodes to their full depth while minimizing cortical deformation⁶³. In our participants, 4-6 arrays are implanted in each participant, with array locations selected based on preoperative functional magnetic resonant imaging localization (see **Chapter 3: Implant Localization**). Once implanted, percutaneous connectors (headstages) are secured to the skull to provide a stable interface between the implanted arrays and the external recording system. The bone flap is then replaced and secured, and the surgical site is closed. Depending on the number and location of implanted arrays, the procedure typically requires 6-10 hours.

The invasiveness of this procedure is one of the primary challenges in widespread clinical adoption of iBMIs. It is important to note that many potential participants, particularly individuals with spinal cord injury, have typically already undergone multiple surgical interventions related to their injury, making elective neurosurgery a substantial consideration. Our participants demonstrate unique bravery in undergoing these surgeries to advance our understanding of the brain and get closer to achieving the goal of restoring motor function. The exceptional spatial and temporal resolution afforded by microelectrode arrays make it exceptionally well suited for this purpose.

iBMIs for Grasp

The success of an iBMI depends on the cortical region from which neural signals are recorded. The choice of implantation site determines the neural activity and subsequently, the types of information that can be recovered. For restoration of upper-limb function, regions within the CGN are attractive targets, as they encode grasp-related information such as grasp intention, hand configuration, and movement execution. For individuals with SCI, the neural circuits responsible for planning and generating movement often remain intact despite interruption of the descending motor pathways. BMIs offer a unique opportunity to restore motor function to SCI individuals as they function by circumventing the injury in the spinal cord and harnessing information directly from neural activity in the healthy, functional cortex to control robotic limbs and restore hand movement.

Over the past two decades, substantial progress has been made in an effort to restore motor function to this population. Participants have demonstrated the ability to reach, grasp, and transport objects using only their neural activity^{59,64}. Despite these impressive advancements, current grasp BMIs remain substantially slower and less precise, and require greater cognitive effort compared to natural hand movements^{59,64,65}. Additionally, interactions with physical objects pose an additional challenge. The presence of an object drastically alters neural activity in motor cortex, resulting in decreased decoding performance during object interaction⁶⁶.

These limitations highlight an important gap in our understanding of the neural representations of grasp. Many decoders focus primarily on intended movement variables, such as hand position, gripping force, or velocity, while comparatively little attention has been devoted to how the brain encodes the objects themselves. Because object properties, such as size and shape, strongly influence grasp selection, incorporating object information may serve as an important step in developing a more natural and adaptive grasp BMI. Therefore, a more complete understanding of how grasp and object properties are encoded in the CGN is essential.

Chapter 3

METHODOLOGY

Implant Localization

The targeted areas for implantation across participants were regions of the cortical grasping network (CGN): the left supramarginal gyrus (SMG), anterior intraparietal cortex (AIP), primary motor cortex (M1), primary somatosensory cortex (S1), and ventral premotor cortex (PMv).

Exact implant sites were determined using fMRI. For S3 and S4, several tasks were performed to identify implant locations, such as asking the participant to imagine moving each finger up and down, imagined grasping, and internal speech. For S2, implant locations were determined by an experimenter reaching into the MRI with a wooden pole and repeatedly pressing at one of three points of residual paresthetic sensation on the bicep, forearm, and thenar eminence of the subject. S2 was instructed to attend to any sensation felt and report the number of times the experimenter touched him on the cued location⁶⁷. This work will focus on the SMG, AIP, and M1 implants, as well as S1 when relevant.

Study Participants

This project was completed with three tetraplegic participants that were recruited for an IRB- and FDA-approved clinical trials of a brain-machine interface. All participants gave informed consent to participate. fMRIs of each participant with approximate implant locations are shown in **Fig. 3-1**.

Participant S2 suffered a spinal cord injury (SCI) at cervical level C5 2 years prior to enrollment. S2 has four arrays, one 96-channel multi-electrode array (Neuroport Array, Blackrock Microsystems, Salt Lake City, UT) in SMG and PMv and two 7 x 7 sputtered iridium oxide film (SIROF)-tipped microelectrode arrays with 48 channels each in S1.

Participant S3 suffered a SCI at cervical level C5-6 3 years prior to enrollment. S3 has six multi-electrode array implants total (81 electrode SIROF array, with 64 connected, Blackrock Microsystems, Salt Lake City, UT). He is implanted in SMG, AIP, MC, PMv, and has two arrays in S1.

Participant S4 suffered a SCI at cervical level C5, 51 years prior to enrollment. S4 has six multi-electrode array implants total (81 electrode SIROF array, with 64 connected, Blackrock Microsystems, Salt Lake City, UT). He is implanted in SMG, AIP, MC, dlPFC, and has two arrays in S1.

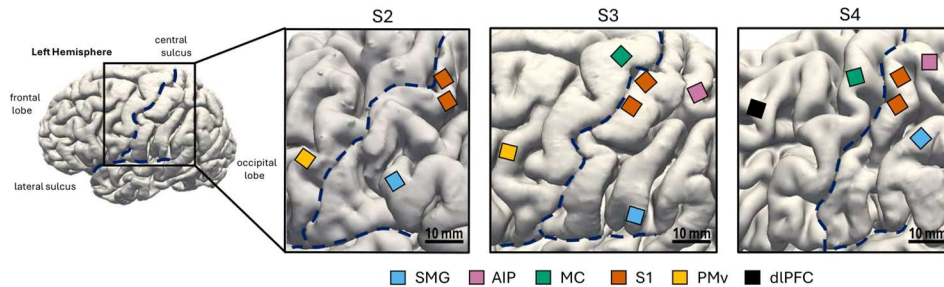


Figure 3-1. Implant locations of each participant. Anatomical scans of each participant and the locations of each array.

Data Collection

Single-unit neural data for this work was collected between 2023 and 2025. We recorded broadband electrical activity from the arrays using Neural Signal Processors developed by Blackrock Microsystems and Ripple Neuromed interchangeably from August 2023 to May 2025. Analog signals were amplified, bandpass filtered (0.3-7500 Hz), and digitized at

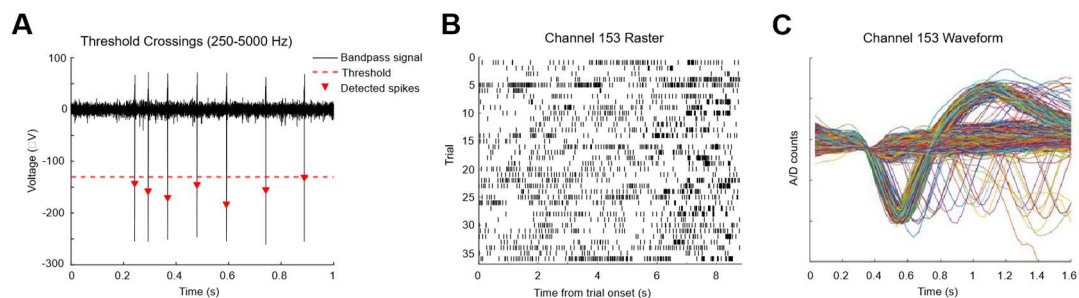


Figure 3-2. Data processing pipeline. A) Data undergoes a second bandpass filter (250-5000 Hz) to keep spike-relevant signal. A threshold is set at -4.5 the estimated root-mean-square voltage of the noise. Signal that passes the threshold are identified as action potentials (spikes). B) Raster plot of example channel's spiking activity across all trials in one block. C) Example channel's corresponding waveform.

30,000 samples/sec. Data were bandpass filtered again (250-5000 Hz) with a threshold at -4.5 the estimated root-mean-square voltage of the noise to identify action potentials (**Fig. 3-2**). Channels were included from a session in post-processing by achieving a minimum firing rate of 2 Hz. Channels that do not meet this threshold are excluded from analysis. The average percentage of excluded channels per session can be found in **Table. 3-1**. The rounded average number of recorded units per session can be found in **Table 3-2**. Multi-unit activity at each channel, in spikes/sec (Hz), are the data underlying this work.

Participant	Altered Context Task	Pixelated Task	Varied Sizes Task	Disassociation Task
S2	SMG: $68.3 \pm 3.6\%$ PMv: $89.1 \pm 3.2\%$ S1: $46 \pm 1.8\%$	SMG: $71.4 \pm 3.0\%$ PMv: $75.7 \pm 11.1\%$ S1: $40.7 \pm 7.8\%$	SMG: $49.6 \pm 7.2\%$ PMv: $75.7 \pm 6.1\%$ S1: $38.2 \pm 5.8\%$	SMG: $44.1 \pm 11.1\%$ PMv: $57.4 \pm 11.4\%$ S1: $32 \pm 9.4\%$
S3	SMG: $3.1 \pm 0.7\%$ PMv: $44.3 \pm 2.4\%$ S1: $60.8 \pm 8.3\%$ AIP: $31.8 \pm 3.0\%$ MC: $1.3 \pm 0.5\%$	SMG: $3.1 \pm 1.4\%$ PMv: $32.3 \pm 8.1\%$ S1: $45.6 \pm 5.1\%$ AIP: $23.4 \pm 2.8\%$ MC: $3.1 \pm 1.1\%$	SMG: $3.3 \pm 0.9\%$ PMv: $41 \pm 1.5\%$ S1: $29.5 \pm 4.8\%$ AIP: $28.1 \pm 2.2\%$ MC: $4.3 \pm 1.4\%$	SMG: $5.5 \pm 0.9\%$ PMv: $45.8 \pm 2.9\%$ S1: $23.8 \pm 4.4\%$ AIP: $25.5 \pm 1.3\%$ MC: $4.4 \pm 1.1\%$
S4	SMG: $4.5 \pm 1.1\%$ S1: $15.4 \pm 4.5\%$ AIP: $6.2 \pm 0.8\%$ MC: $4.7 \pm 1.0\%$ dlPFC: $61.2 \pm 2.1\%$	N/A	SMG: $33.7 \pm 4.0\%$ S1: $45 \pm 1.5\%$ AIP: $46.4 \pm 2.8\%$ MC: $18.8 \pm 1.4\%$ dlPFC: $72.3 \pm 1.4\%$	SMG: $31 \pm 5.2\%$ S1: $50.2 \pm 4.6\%$ AIP: $61.4 \pm 8.9\%$ MC: $19.6 \pm 1.7\%$ dlPFC: $71.4 \pm 1.5\%$

Table 3-1. Discarded Units per Session. Average percentage of units $\pm$ standard error of the mean discarded per session across all experiments, rounded to the nearest decimal point.

Participant	Altered Context Task	Pixelated Task	Varied Sizes Task	Disassociation Task
S2	SMG: 30 ± 3 PMv: 10 ± 3 S1: 52 ± 2	SMG: 27 ± 3 PMv: 23 ± 11 S1: 57 ± 8	SMG: 48 ± 7 PMv: 23 ± 6 S1: 59 ± 6	SMG: 54 ± 11 PMv: 41 ± 11 S1: 65 ± 9
S3	SMG: 62 ± 0 PMv: 36 ± 2 S1: 50 ± 11	SMG: 62 ± 1 PMv: 43 ± 5 S1: 70 ± 6	SMG: 62 ± 1 PMv: 38 ± 1 S1: 90 ± 6	SMG: 61 ± 1 PMv: 35 ± 2 S1: 98 ± 6

	AIP: 44 ± 2 MC: 63 ± 0	AIP: 49 ± 2 MC: 62 ± 1	AIP: 46 ± 1 MC: 61 ± 1	AIP: 48 ± 1 MC: 61 ± 1
S4	SMG: 61 ± 1 S1: 108 ± 6 AIP: 60 ± 1 MC: 61 ± 1 dlPFC: 25 ± 1	N/A	SMG: 42 ± 3 S1: 70 ± 2 AIP: 34 ± 2 MC: 52 ± 1 dlPFC: 18 ± 1	SMG: 44 ± 3 S1: 64 ± 6 AIP: 25 ± 6 MC: 51 ± 1 dlPFC: 18 ± 1

Table 3-2. Recorded Units per Session. Average number of units $\pm$ standard error of the mean recorded per session across all experiments, rounded to the nearest whole number.

Quantification and Statistical Analysis of Data

All analyses were performed using MATLAB R2023b.

Neural firing rates and single-unit identification

In this work, single-channel is used to refer to the activity recorded from a single microelectrode. Threshold crossings (see Data Collection) were binned into 50 ms time bins, divided by bin length, and smoothed using a Gaussian filter with a 50ms kernel width to estimate instantaneous firing rates for each channel during each trial. To identify single-unit responses, the average firing rate (Hz) per timebin of each channel was calculated as a function of each feature (grasp type, object shape, size) within sessions.

Linear regression analysis

Units that selectively fire (tuned) for the different variables were identified by linear regression in two ways: 1) step by step in 50 ms timebins to assess for tuning across the entire trial; 2) average firing rates across the Planning (2s) and Action (4s) phases to compare between both phases. The model returns a fit that estimates the firing rate of a unit based on the following variables:

$$FR_{\text{grasp/shape}} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4$$

and

$$FR_{\text{size}} = \beta_0 + \beta_1 X_1 + \beta_2 X_2$$

where FR represents the firing rate of that unit and β corresponds to the estimated regression coefficients. X represents an indicator variable that contains which data correspond to which feature (grasp type, object shape, size). The first 8 rows of X correspond to the average firing rate of the ITI phase. These rows contain only zeros and form the baseline variable, β_0 . The other rows of the indicator variable indicate the trial data, such that each row contained one numerical value that corresponds to a feature (grasp types 1-4, object shapes 1-4, sizes 1-2). For example, if the first trial contained the grasp type “Lateral,” there would be a 1 in row 1. This method was used to identify single-units tuned to each variable (grasp, size, shape) for each session. We could then determine which phases (Planning, Action, both), contexts (Hand, Hand+Object, Object, overlapping), or selectivity (selective (tuned to only one class within a variable) or mixed-selective (tuned to two or more classes)) these tuned units demonstrated.

Linear regression significance testing

To determine the significance of unit tuning to each feature, the linear regression analysis was repeated with shuffled labels, creating a null dataset. 95% confidence intervals were computed with this null dataset and compared to the actual data. Data higher than the 95th percentile of the null distribution was denoted with a * symbol.

Classification

A classifier was used to determine how well each feature could be differentiated within each phase, and throughout the entirety of the trial, using the neural firing rates recorded during each task. For each task, each session and each array were analyzed individually using linear discriminate analysis (LDA), assuming an identical diagonal covariance matrix for each set of variables. These assumptions, compared to a full diagonal covariance matrix, resulted in the best classification accuracies as determined by Wandelt et al. (2022). Classifiers were trained in two ways: 1) using z-scored average firing rate data from each phase (Cue: 2

seconds, Action: 4 seconds), and 2) using z-scored average firing rate data from each 50 ms timebin throughout the entire trial. The 10 highest principal components (PCs), or the PCs explaining >90% of the variance (whichever was higher), were selected via principal component analysis (PCA) and served as feature selection on the training set. When fewer than 10 PCs were available, all features were used. Decoding performance was estimated using leave-one-out cross validation, and a 95% confidence interval was computed using the standard error of the mean.

Cross-region classification

Cross-region classification was computed using an LDA classifier with leave one out partitioning. Again, we assumed an identical covariance matrix. We extracted training data trials and testing data from same trial indices to learn alignment for each region. The alignment was performed as described in Nakanishi et al. (2020). Briefly, to calculate the linear transformation matrix we must solve:

$$W = \operatorname{argmin}_W \|X_{\text{test}}W - X_{\text{train}}\|^2$$

This is the least-squares regression, and W can be estimated as:

$$W = (X_B^T X_B)^{-1} X_B^T X_A$$

where W is the linear transformation matrix, X_A is the training data from region A, X_B is the corresponding testing data from region B. We can then use W to align region B to region A by:

$$X_{\text{aligned}} = X_{B_test} * W$$

where X_{B_test} is unused testing data from region B and X_{aligned} is the data we will use to project into region A's PCA subspace. We perform PCA on training data to determine the PCs explaining >95% of the variance. After identifying the eigenvectors corresponding to the

PCs, we project training and testing data into new PCA space, train the LDA model on training data from region A and use the model to predict test data from region B.

Classification performance significance testing

To determine the significance of classification performance, we produced a null dataset by repeating classification with shuffled labels. 95% confidence intervals were computed for the null dataset and compared to the actual data. A t-test was used to compare the classification performances between actual and shuffled data. A false-detection rate correction was then applied and bins with $p > 0.05$ are determined. Bins were ultimately determined to be significant if there were ≥ 3 consecutive bins with $p > 0.05$ and denoted with a line above the bins. Onset of Planning and Execution latencies were determined using the same classification method, with a null dataset created by repeating classification with shuffled labels 1000 times. Onset of Planning activity was determined by the first timebin to achieve significant decoding above the 95% confidence interval of the null dataset. Onset of execution was determined by training an LDA classifier to identify Go vs. No-Go trials, ensuring equal number of trials. The first timebin to achieve significant decoding above the 95% confidence interval of the null dataset was determined for each session and served as the execution latency of each region.

Cross-phase and Cross-context classification and significance testing

To assess the shared neural activity between different task phases (cross-phase), we averaged neural activity across each phase and used the LDA classifier described above to train the classifier on one phase (ie., Planning) and to test it on all phases (ITI, Planning, Delay, Action). This was repeated for each session individually, and a 95% confidence interval of the mean was calculated across sessions. A paired two-tailed t-test along with FDR correction of the p-values was performed to determine significant differences in classification accuracies between phases. P-values ≤ 0.05 are denoted with a * symbol, ≤ 0.01 with **, and ≤ 0.001 with ***.

***. As we were predominantly interested in generalization between Planning and Action, those results are shown, along with ITI which serves as a control.

The same method was used to assess the shared neural activity across different contexts (cross-context), this time training the classifier on one context (ie., Hand only) and testing it on all contexts (Hand only, Hand+Object, Object only). Significance was determined and denoted as above.

Neuron Dropping Curves

Neuron dropping curves (NDCs) were computed using a neuron grid containing the first 5 units, the 7th, then increments of 3 units until reaching the unit minimum number of units for each region. The lowest number of units recorded in a single session was identified to ensure that all sessions were included in the analysis. The average firing rate for each channel was calculated and z-scored for each phase. For each step, we randomly selected unit(s) then partitioned with a K-fold of 8. We trained an LDA classifier with cross validation and averaged across folds. We repeated this 50 times for each neuron count, obtaining the expected decoding accuracy using k randomly sampled neurons. NDCs were calculated for each session and then averaged across sessions. Peak classification accuracies in each chapter were determined using the peak accuracies from the NDCs.

Chapter 4

GRASP ENCODING DURING ALTERED CONTEXTS THROUGHOUT THE CORTICAL GRASPING NETWORK OF TETRAPLEGIC HUMANS

Introduction

Most activities of daily living (ADLs), a commonly used clinical indicator of a person's ability to care for themselves independently, require the ability to grasp¹. For people with tetraplegia, these activities become incredibly difficult, if not entirely impossible. In a survey of people with Spinal Cord Injuries (SCI), when asked what would provide the largest improvement in quality of life, people with tetraplegia identified regaining hand and arm function as their top priority³.

Brain-Machine Interfaces (BMIs) offer a unique opportunity to restore motor function to SCI individuals. BMIs operate by circumventing the injury in the spinal cord and harnessing information directly from neural activity in healthy, functional cortex to control robotic limbs and restore hand movement⁵⁹. Intracortical BMIs use microelectrodes implanted directly into the cortex to record spiking activity at the level of single neurons with high signal-to-noise ratio (SNR) and high spatial and temporal resolution⁵¹. While BMIs can take many forms, these qualities make intracortical BMIs an ideal candidate for restoring motor control via neuroprosthetics.

The cortical grasping network (CGN), the brain regions responsible for the ability to grasp, are the top candidates for microelectrode implantation sites for a grasp BMI. The CGN includes regions of the posterior parietal cortex (PPC), such as the supramarginal gyrus (SMG) and anterior intraparietal cortex (AIP), and motor cortex (MC). Much of what we know about this network comes from non-human primate (NHP) research^{12,18,68,69}. MC is a primary motor area that encompasses grasp and reach regions^{70,71}. Yan et al. (2026) recently demonstrated that MC also contains object-specific information during grasping³⁴. PPC is

known to be an integration site for sensorimotor transformations and movement intentions¹⁰. Along with encoding grasp and reach¹¹, it has been suggested that AIP plays a role in the visual processing of object sizes and shapes¹².

While NHP research serves as an invaluable guide, NHP and human findings can vary and thus it is necessary to determine human cortical functionality. In humans, it is widely accepted that MC plays an essential role in executing motor commands^{72,73}. Roles for grasp and reach in AIP are also supported by findings in humans^{18,19}, though more investigation is needed to understand these processes at the single neuron level. SMG is a uniquely human region, with no homologous structure in NHPs, and is thought to be involved in tool use²⁴⁻²⁶, along with grasping and manipulating objects^{27,28}, and reaching²⁹. With PPC encompassing this wide range of functions, it offers unique potential for utilization in a grasp BMI.

MC has been a key region of investigation into its potential use in a motor BMI^{59,64,74,75}, although a functional grasp BMI has yet to be realized. Additionally, more information about how objects are represented in the cortex is vital for BMI development. Downey et al. (2017) developed a grasp BMI using neural activity from the motor cortex but found that the presence of an object in the visual field drastically decreased the performance of their BMI such that participants could no longer consistently grasp using a robotic limb⁶⁶. While computational methods could increase performance, accuracy was still significantly decreased relative to the initial decoding performance without the object present. A better understanding of how the presence of an object influences the regions of the CGN is vital to producing a BMI that can adapt to an ever-changing environment.

This work helps to close this gap in knowledge by investigating the CGN in human tetraplegic participants using a grasp motor imagery task. We asked participants to imagine performing a grasp, either with or without an object. They were cued with a static image depicting the grasp interacting with an object, the grasp alone, or the object alone. We investigated how object presence altered neural activity and how the encoding of grasp

changed across contexts. These findings have the potential to inform the development of a functional grasp BMI.

Methods

We implemented a motor imagery task that cued four different grasp types with static visual images originally taken from the “Human Grasping Database”⁷⁶ and modified using Unity. The grasps selected cover a range of different hand configurations and are labeled “Lateral,” “MediumWrap,” “PalmarPinch,” and “Sphere3Finger.” Each grasp type is shown with and without the presence of an object (**Fig. 4-1**).

Altered Context Task

Each trial consisted of four phases: ITI, Planning, Delay, and Action (**Fig. 4-2**). Trials were performed in blocks of three contexts: a hand alone (H), a hand grasping an object (HO), or an object alone (O). Each trial began with a 2-second intertrial interval (ITI), in which the screen was blank, and the participant was asked to clear their mind. Then participants were visually cued

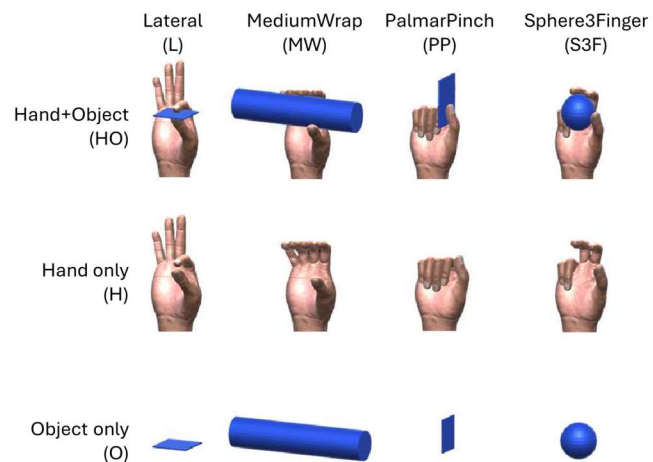


Figure 4-1. Grasps in Altered Contexts. Each of the individual, distinct grasp types used to assess the encoding of grasp. Grasps are shown in 3 contexts: Hand and object together (HO), hand alone (H), and object alone (O).

with a static image of one of four grasp types. There was a brief 0.5 second delay before the Action phase, where the participant saw either a green or red dot for 4 seconds. The green dot cued the participant to either imagine performing the grasp that was shown (H) or imagine performing the grasp and interacting with that object (HO and O). The red dot cued the participant to abort the motor plan and perform no imagined action. 40 trials were

recorded per block (8 repetitions of 4 grasps = Go trials, 2 repetitions of 4 grasps = No-Go trials), with 2 blocks per condition (HO, H, and O) every session.

Pixelated Task

A visual control task was created where we pixelated the images previously presented in the Go/No-Go Task (Fig. 4-2), such that the grasps and objects were unrecognizable to the participants. Half of the trials followed the exact

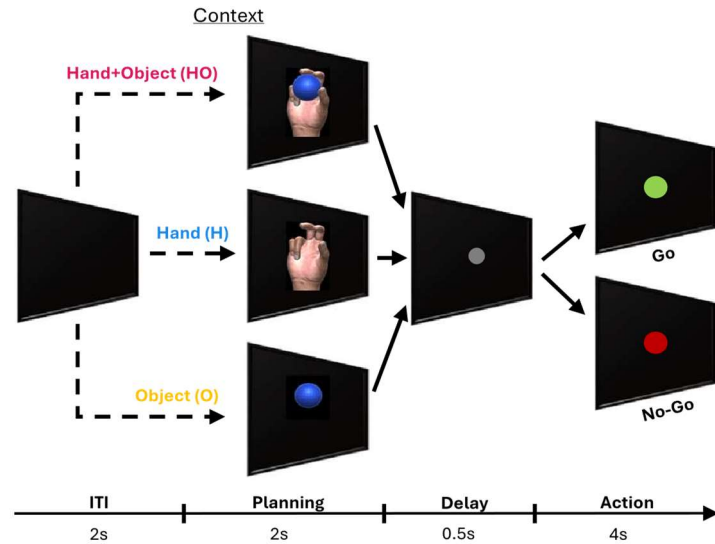


Figure 4-2. Altered Context Task Experimental Design. Example shown of Sphere3Finger in all 3 different contexts.

trial structure outlined above, and half of the trials consisted of pixelated versions of those same images. Images were presented in random order. Participants received instructions to perform the task as previously described if the image that appeared was “Regular.” If it was “Pixelated,” they were instructed to visually take in the image during the Planning phase and perform no imagined motor action during the Action phase (Fig. 4-3). Pixelated images share the same visual statistics as Regular images without being recognizable as a specific grasp type or object shape. 24 trials were recorded per block (3 repetitions x 4 grasps = Regular images, 3 repetitions x 4 pixelated grasps = Pixelated images), with 2 blocks per context every session.

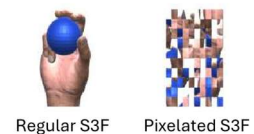


Figure 4-3. Regular vs. pixelated images used in Pixelated Task. Example of Sphere3Finger shown.

Subject	Altered Context Task	Pixelated Control Task
S2	7	9
S3	6	6
S4	7	0

Table 4-1. Breakdown of sessions performed of Altered Context and Pixelated Tasks with each participant.

Results

We found differential neural representations across the human cortical grasping network (CGN) for motor planning/execution during imagined grasping of objects. Across 3 human participants (**Fig. 3-2**), 13 chronically implanted micro-wire arrays spanned supramarginal gyrus (SMG), post-central gyrus (S1), anterior intraparietal area (AIP), and the hand region of the motor cortex (MC). Both single neuron and population-level dynamics revealed roles for grasping in posterior parietal, motor, and sensory cortices (**Fig. 4-4**).

To dissociate object properties from motor variables during planning and execution, we utilized a cued, delayed motor task (**Fig. 4-2**), instructing participants to imagine grasping objects. Sets of unique objects (ball, block, rod, card) and unique hand shapes (precision and power grasps) were selected from the “human grasping database”⁷⁶. With this paradigm, we manipulated the context of each object and motor action, asking subjects to perform grasps with/without objects (**Fig. 4-1**). We hypothesized motor and sensory regions would encode fundamental variables of motor control (grasp type, hand aperture). Across the CGN, we found that grasp is strongly encoded in motor cortex and PPC.

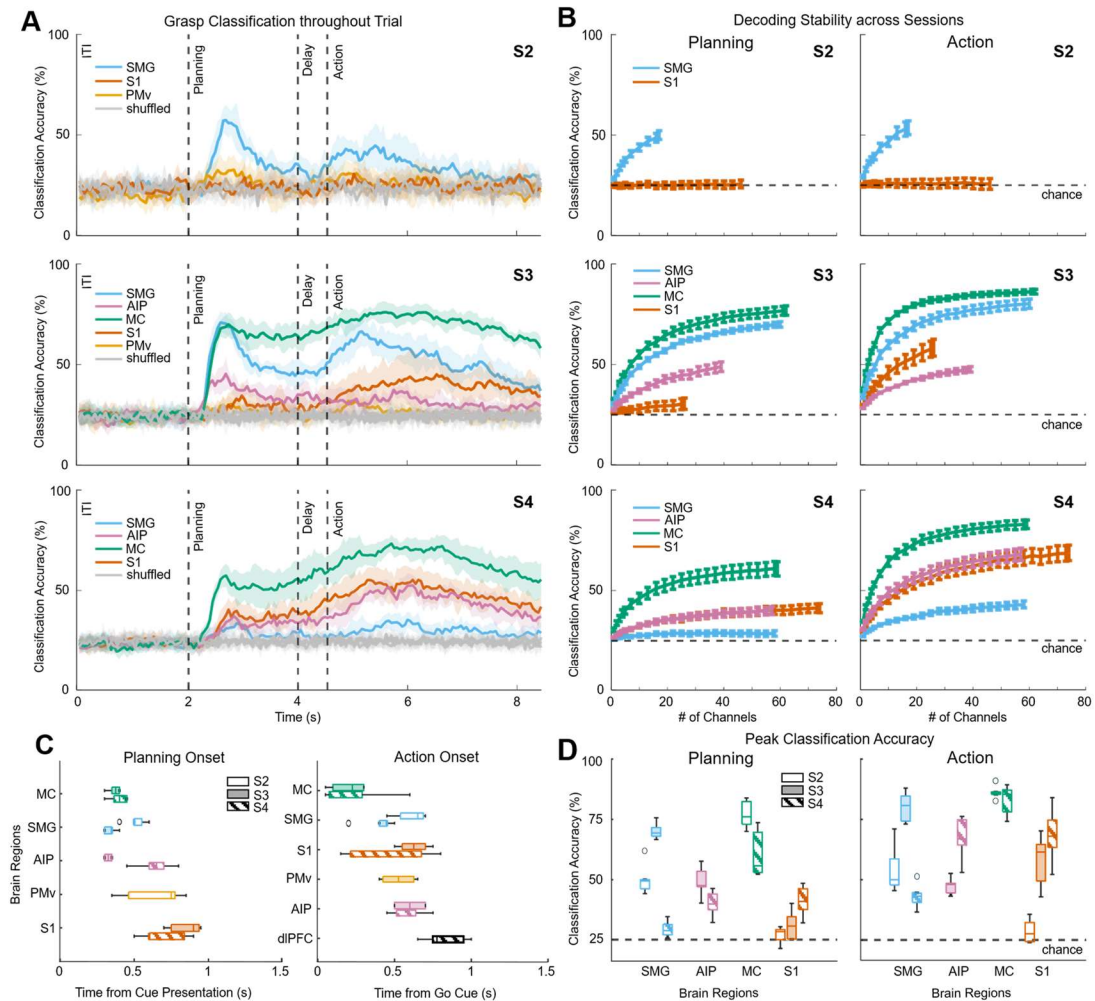


Figure 4-4. Network-wide investigation into grasp encoding. A) Session-averaged classification of grasp using an LDA classifier applied to each brain region within the cortical grasping network for 3 participants. B) Neuron Dropping Curves calculated using linear regression for each participant during Planning (column 1; S2: SMG: 50%, S1: 26%; S3: SMG: 70%, MC: 77%, AIP: 49%, S1: 30%; S4: SMG: 29%, MC: 61%, AIP: 40%, S1: 41%) and Action (column 2; S2: SMG: 54%, S1: 26%; S3: SMG: 80%, MC: 86%, AIP: 48%, S1: 58%; S4: SMG: 43%, MC: 83%, AIP: 68%, S1: 69%) phases. C) Planning latency (left) for each region determined by the onset of significant grasp decoding above chance during cue presentation. Planning latencies averaged across participants: MC: 383ms, SMG: 425ms, AIP: 483ms, PMv: 640ms, S1: 764ms. Execution latency (right) of each region determined by the onset of significant trial type (Go vs. No-Go trials) decoding above chance. Execution latencies averaged across participants: MC: 211ms, SMG: 511ms, S1: 520ms, PMv: 525ms, AIP: 589ms, dIPFC: 817ms. Regions are organized from shortest average latency (top) to longest average latency (bottom). See Methods for protocol details. D) Peak grasp classification accuracy of each brain region calculated from the Neuron Dropping Curves during Planning (left) and Action (right) phases.

Grasp type is decodable from all regions of the cortical grasping network

In all three participants, grasp type was broadly represented across the CGN, with MC consistently demonstrating the strongest encoding, followed closely by SMG, then AIP (**Fig. 4-4A,B**). Grasp classification was consistent and stable across sessions. Individual grasp

types were equally well classified in each area across sessions (**Fig. 4-5A**). Additionally, representational stability was maintained, demonstrated by stable peak classification accuracies during both Planning and Action phases and a similar number of recorded units within and across participants (**Fig. 4-5B**).

Neurons in the supramarginal gyrus (SMG) in two of the three participants (S2, S3) showed robust encoding of grasp type during motor planning (mean latency: 425 ms, accuracy: 60%) and imagined execution (mean latency: 511 ms, accuracy: 67%) (**Fig. 4-4C,D**), indicating sustained representation of motor engagement. Participant S4's SMG implant showed little neural representation of grasp; notably, its implant location was also anatomically distinct from S2 and S3 (**Fig. 3-2**). Positioned far more medially, on the lateral bank of the intraparietal sulcus, our data suggests implantation occurred in a different sub-region of SMG (see Discussion).

Recordings from the medial gyrus of the anterior intraparietal cortex (AIP) also demonstrated encoding of grasp type at the population level during motor planning (mean latency: 541 ms, accuracy: 45%) and imagined execution (mean latency: 589 ms, accuracy: 58%) (**Fig. 4-4C,D**).

Populations of neurons in motor cortex (MC) robustly represented motor variables throughout both the planning (mean latency: 383 ms, accuracy: 69%) and imagined execution (mean latency: 211 ms, accuracy: 85%) phases of the task (**Fig. 4-4A,B,C**). Across both participants (S3, S4), decoded grasp type was significantly higher than any other individual area (**Fig. 4-4B**), even during the planning phase. On average, MC was also the first region activated during both phases (**Fig. 4-4C**). While robust representation during motor planning was surprising, recent work from our group and others have suggested precentral gyrus may contain a mixture of planning and execution, rather than the “primary motor cortex” which is postulated to be in the central sulcus of human cortex^{77,78}.

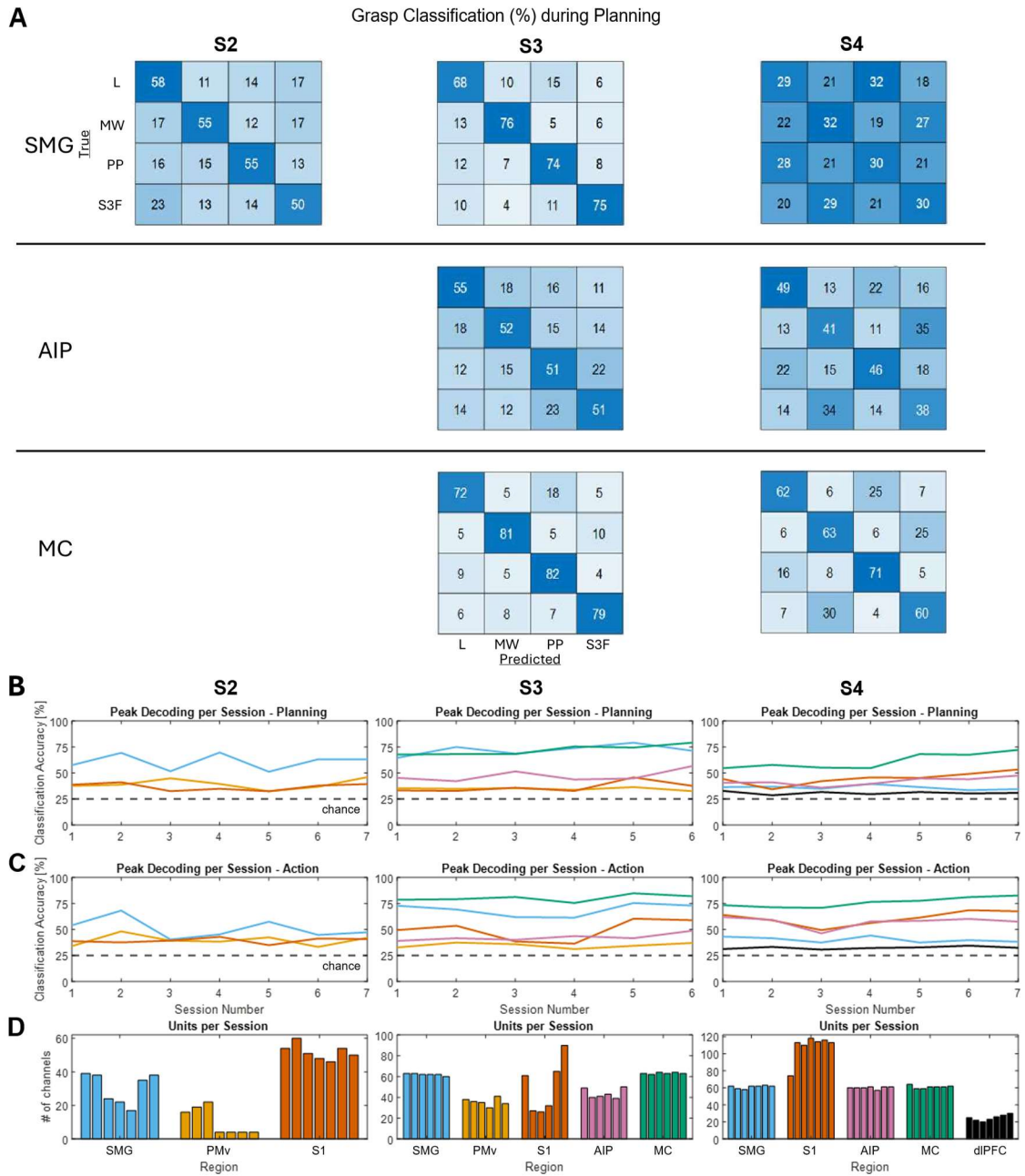


Figure 4-5. Representational stability across sessions. A) Classification accuracy (%) of each grasp type averaged across sessions per region. B/C) Peak grasp decoding performance for each region during each session determined by the highest classification accuracy in a single timebin during Planning (B) and Action (C) phases. Each line is a region, colors correspond to D. D) Number of channels across sessions is relatively stable and consistent within and between participants. Channels are channels that exhibited multi-unit activity during the task as determined by pre-processing threshold crossings (see Methods).

Sensation, and by extension, the somatosensory cortex (S1), is imperative to accurate grasping and manipulation of objects^{79,80} and has been shown to encode object characteristics

and grasp-related information in NHPs⁸¹. Our lab has also found S1 encodes reach direction during imagined reach⁸². Therefore, we investigated the role of S1 (if any) during imagined grasp. Across participants, somatosensory cortical neurons represented grasp type during imagined execution (**Fig. 4-4D**), but only when the array was implanted within the receptive field of the hand. Participant S2's array is located in the receptive field of the arm and only achieved a chance-level accuracy of 26% (**Fig. 4-4A,B: S2**), compared to participants S3 and S4 who are implanted within the receptive field of the hand and achieved an average accuracy of 64% (**Fig. 4-4A,B: S3, S4**). The time course of representation roughly mirrors AIP, suggesting efference copies (or projections) from posterior parietal and/or precentral gyrus may be driving this activity. This finding supports the previous finding from our lab of S1's encoding of imagined movement in the absence of sensory information⁸².

Grasp is encoded at the single-channel level throughout the CGN

Populations of neurons in SMG significantly encode grasp throughout motor planning and imagined motor execution (**Fig. 4-6A**; Wandelt et al. (2022)). Complete information about grasp type appeared early during planning (peak: 681 ms, accuracy: 67%) and execution (peak: 851 ms, accuracy: 60%), reaching peak decoding accuracy before any other region (**Fig. S4-1**). However, information about grasp type extends beyond population-level activity. Encoding of grasp was evident at the single-channel level, as many single units responded selectively and uniformly to grasp types during both motor planning and execution (**Fig. 4-6B,C**).

Throughout motor planning and execution, populations of neurons in AIP significantly encode grasp (**Fig. 4-6D**). Even though this area is predominantly thought of as a planning region, for one participant (S4), grasp encoding was much stronger during execution and was markedly similar to the primary sensorimotor areas (see Discussion). One possible explanation for this discrepancy is strongly maintained connections within the CGN due to increased intact sensation relative to our other participant, and therefore a stronger similarity in AIP performance to MC and S1. Encoding of grasp was also seen at the single-channel

level, with units selectively and uniformly tuned to grasp during motor planning and execution (**Fig. 4-6E,F**).

Populations of neurons in MC significantly encode grasp throughout the trial, with robust classification and tuning during planning and execution (**Fig. 4-6G**). MC had the strongest grasp classification of all CGN regions both at the timebin level and when averaged across entire phases (**Fig. 4-4A,B**, green line). Many single units in MC selectively encoded grasp and these units were uniformly distributed across grasp types (**Fig. 4-6H,I**).

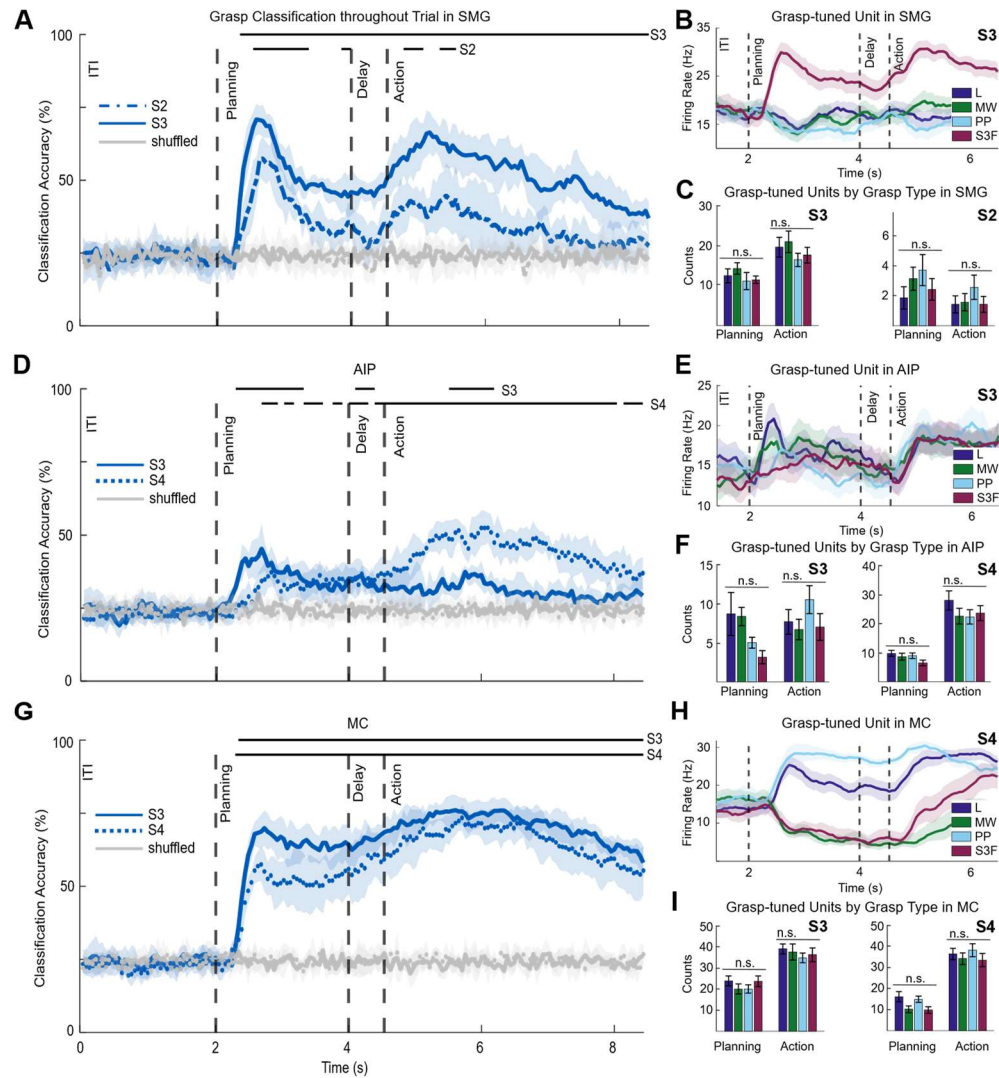


Figure 4-6. Grasp encoding at the single-channel level throughout the cortical grasping network. A) Session-averaged classification of grasp using an LDA classifier trained on SMG neural activity is significantly above chance during motor planning and imagined motor execution across both participants. Classification performed at each 50ms timebin, accuracies averaged across sessions with 95% standard error of the mean (SEM) confidence intervals (CIs). B) An example unit from SMG tuned to one specific grasp type (S3F) during motor planning and imagined motor execution. C) Number of units tuned to specific grasp types averaged across sessions for each participant. No significant difference in number of units tuned to each grasp type. Data from Hand+Object (HO) context, see **Supplementary Fig. S4-6** for all contexts. D) Session-averaged classification of grasp using an LDA classifier trained on AIP neural activity is significantly above chance during motor planning and imagined motor execution across both participants. E) An example unit from AIP demonstrates varied firing rates depending on the grasp type during motor planning, with a uniform response across all grasp types during imagined motor execution. F) Number of units in AIP tuned to specific grasp types averaged across sessions. No significant difference in grasp types. G) Session-averaged classification of grasp using an LDA classifier trained on MC neural activity is significantly above chance during motor planning and imagined motor execution across both participants. H) An example unit from MC demonstrates selective tuning to three grasp types during motor planning, and unique tuning to each grasp type during imagined motor execution. I) Number of units in MC tuned to specific grasp types averaged across sessions. No significant difference in grasp types.

Planning and imagined motor execution are two distinct cognitive processes

Although grasp types could be continuously decoded from each region during planning through execution, cross-phase decoding revealed distinct neural processes across these phases. In this analysis, a decoder was trained to distinguish grasp activity from one task phase, such as Planning, and tested on activity from ITI, Planning, and Action. In SMG, grasp encoding strongly generalized from planning to execution, but incompletely from execution to planning, suggesting imagined execution recruits additional or distinct neural processes beyond those engaged during planning (**Fig. 4-7A**). These findings are largely consistent across contexts and participants (**Fig. S4-2**). Due to the computational requirements of this analysis (cross-validation partitioning within each context) and necessary limiting of trials per session for participant comfort, the analysis could not be successfully implemented for participant S2. This finding may be explained by the large number of tuned units shared between phases (S3: 34%, S2: 53%), as well as the large proportion of units that were only tuned to grasp when the participant was imagining grasping (S3: 34%, S2: 23%) (**Fig. 4-7B**).

AIP exhibited strong phase-dependent grasp encoding during motor planning versus motor execution, with weak generalization between the phases (**Fig. 4-7C**). This finding is consistent across contexts and participants (**Fig. S4-2**). This may represent a more active integrating process during planning before taking on a more passive role in receiving feedback/input from the sensorimotor loop during execution. Across participants, 33-41% of units were shared between both phases and 33-55% were uniquely tuned during Action, further suggesting unique processes during motor planning and imagined execution (**Fig. 4-7D**).

Even in MC, while motor planning and imagined execution largely generalized during cross-decoding, they represent partly distinct neural processes, as evidenced by significantly higher grasp classification of the training phase than the testing phase during Planning (S3) and Action (S3, S4) (**Fig. 4-7E**). This finding is largely consistent across contexts and

participants (**Fig. S4-2**). This result is consistent with the composition of grasp-tuned units during Planning and Action phases. Most units were either tuned during both phases or only tuned during imagined execution, with only 3-4% uniquely tuned during motor planning (**Fig. 4-7F**).

Cognitive processes influence unit selectivity in each region

Single-channel tuning to grasp occurred in both Planning and Action phases in all CGN regions. These units could be selective (tuned to only one grasp type) or mixed-selective (tuned to two or more grasp types). A predominant pattern emerged in all CGN regions where while the participant was planning which grasp to imagine, the proportion of selective to mixed-selective units was roughly equivalent or slightly favored selectivity (**Fig. 4-7G**). However, when the participant imagined performing the grasp, there was a higher proportion of mixed-selective units. This finding is largely consistent across participants and cue contexts (**Fig. S4-3**). This pattern may reflect that during motor planning, receiving visual feedback of the exact grasp type the participant intends to perform could lead to activating a more selective population, whereas without any feedback, the populations are more broadly activated and thus mixed-selective. SMG was an outlier in that the population was roughly equivalent or favored selectivity during both phases.

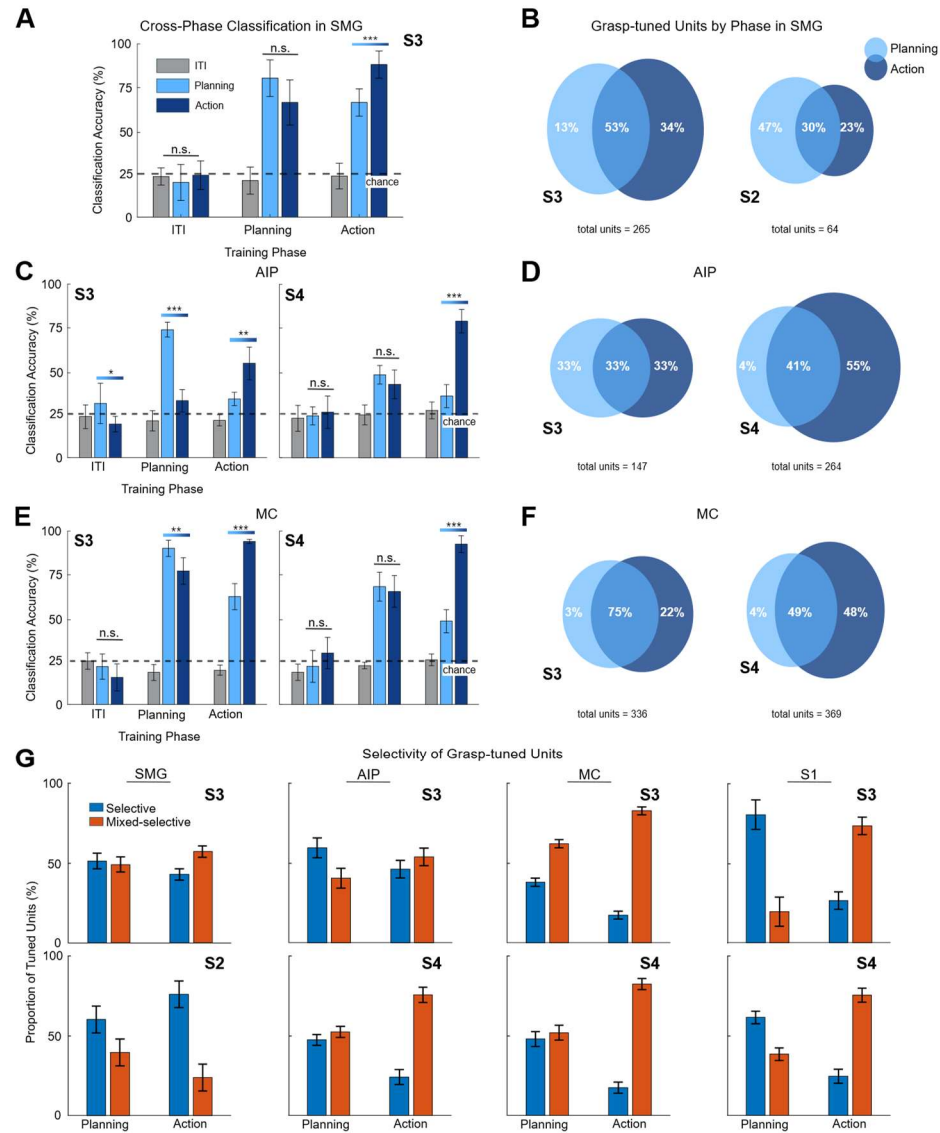


Figure 4-7. Phase properties of grasp-tuned units in the CGN. A) Evaluating shared information across each phase (Intertrial interval (ITI), Planning, Action) in SMG. Cross-decoding generalized between Planning and Action phases, with complete generalization from Planning to Action and incomplete generalization from Action to Planning. Example shown for Hand+Object and is consistent across contexts (see **Supplementary Fig. S4-2**). B) Proportion of grasp-tuned units during Planning (light blue) and Action (dark blue) for two participants (S3, S2). There is substantial overlap between phases and the recruitment of many grasp-tuned units during Action only. HO results shown as example and results are largely consistent across contexts (see **Supplementary Fig. S4-7**). C) Evaluating shared information across each phase in AIP. Cross-phase classification showed incomplete generalization between Planning and Action phases. D) Proportion of grasp-tuned units in AIP during Planning and Action for two participants (S3, S4). E) Evaluating shared information across each phase in MC. Planning and Action phases incompletely generalize to each other and demonstrate phase-dependent neuronal modulation. F) Proportion of grasp-tuned in MC during Planning and Action for two participants (S3, S4). G) Selective vs. Mixed-selective grasp-tuned units during Planning and Action for each region. Example shown for Hand+Object; see **Supplementary Fig. S4-3** for selectively during each context.

Grasp encoding is context-dependent

In previous work, grasp encoding in SMG was demonstrated using images depicting a hand interacting with an object²⁷. We hypothesized altering this context and separating the image into its individual components might result in contextually specific encoding. It is possible that each context might engage distinct neural control strategies, with the Hand only (H) context eliciting position-based encoding of individual digit configurations and endpoint placement, whereas the Hand+Object (HO) context might recruit isometric force production mechanisms associated with grasp stabilization or object squeezing. However, it is also likely that these strategies would not be engaged due to the task involving imagined rather than attempted hand movements. Cross-context decoding revealed that grasp encoding was modulated by the context in which a grasp was presented, while still retaining shared grasp-related structure across contexts. As in the cross-phase decoding, in this analysis, a decoder was trained to distinguish grasp activity from one context, such as Hand, and tested on activity from Hand, Hand+Object, and Object. Participant S2's data could not be used for this analysis due to the same constraints discussed in cross-phase decoding. Contexts involving a hand generally produced similarly high classification accuracies during motor planning and execution (**Fig. 4-8A**). Cross-context decoding further showed that grasp representation was partially context-specific; while cross decoding accuracies generally remained above chance, decoding accuracies significantly varied between contexts. Context-specificity was particularly evident during planning but remained present in the Hand and Hand+Object contexts during execution as well. A higher proportion of units were tuned to grasp in SMG during planning when both the hand and object were presented compared to the hand or object presented alone (**Fig. 4-8B**). From these tuned units, distinct populations were recruited within each context, with overlap among intuitive contexts (such as contexts showing a hand) (**Fig. 4-8C**). These context-specific units may be driving the increase in classification accuracy for contexts involving the hand.

Grasp encoding was also modulated by context in AIP. During both planning and execution, decoding generalized only partially between grasps cued by a grasp with the hand and object

together and grasps cued by the hand or object alone, and vice versa (**Fig. 4-8D**). Although a similar proportion of units were tuned to grasp across the three contexts during execution (**Fig. 4-8E**), the cross-context decoding suggests that these units did not encode grasps in a fully context-invariant manner (**Fig. 4-8D**). However, we observed a large, unique population of grasp-tuned units when the hand and object are presented together, and a large amount of overlap among all contexts during execution, although this was more pronounced in participant S4 (**Fig. 4-8F**). Together, this suggests there is additional information in units recruited by the hand and object interaction that aids in grasp classification, potentially representing a critical integration role in AIP.

When we examined the subpopulations of neurons tuned to grasp in each context in MC, the story became more complex. Despite stable single neuron representation across planning and execution (**Fig. 4-8I**), the population encoding was dominated by hand representation (93-94% Hand peak vs. 73-82% Object peak, **Fig. 4-8G**). Hand and Hand+Object contexts demonstrated high generalization across each other, suggesting a shared grasp representation that weakens in the Object only context (**Fig. 4-8G**). While the proportion of neurons encoding grasp during the Object context may be similar to other contexts, a reduced total number of neurons may partially explain this result (**Fig. 4-8H**).

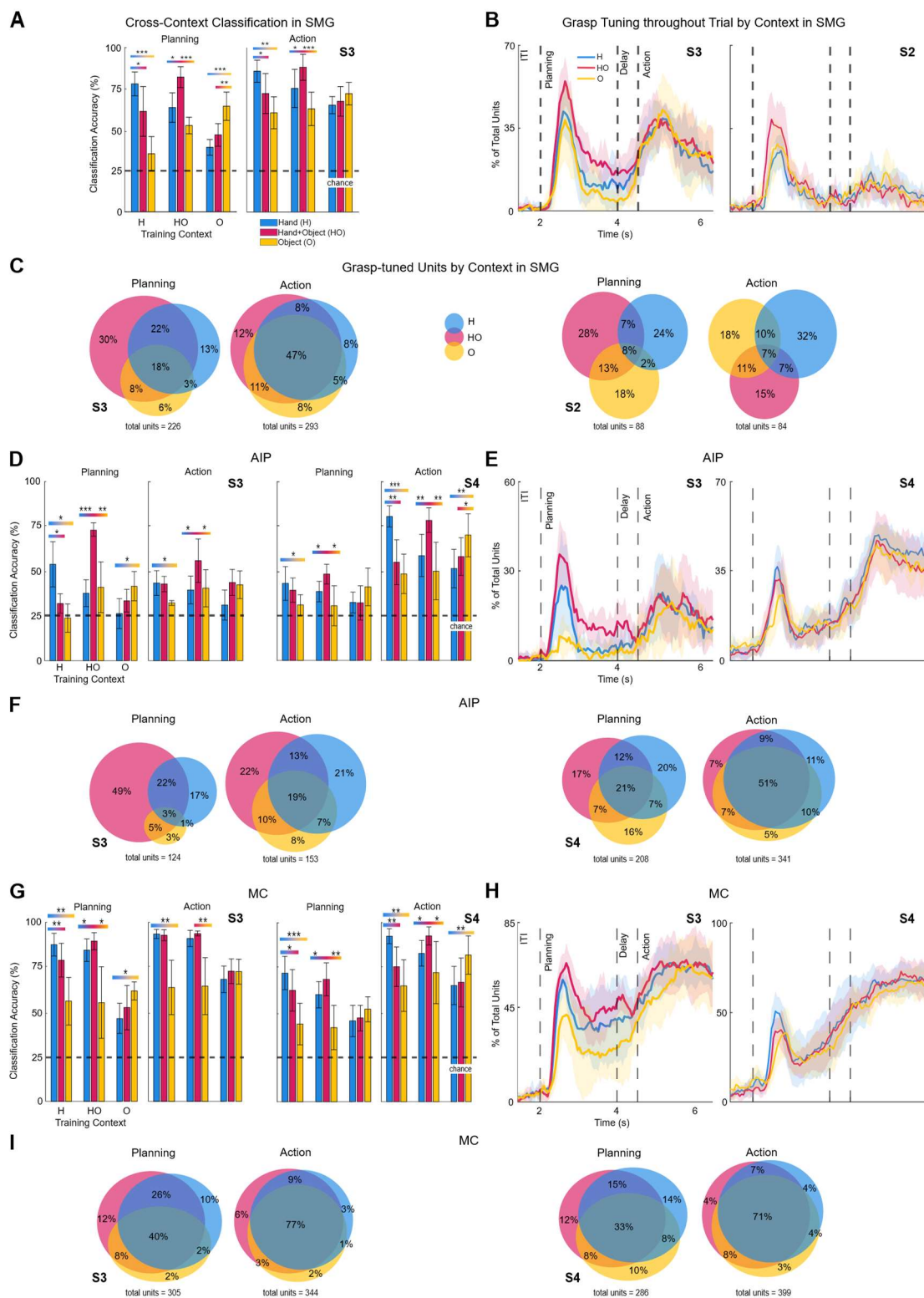


Figure 4-8. Encoding of grasp in the cortical grasping network is modulated by context. A) Evaluating shared information across each context in SMG through cross-decoding analysis. More complete generalization during Action than during Planning, but predominantly incomplete generalization among contexts during both phases. B) Percentage of units tuned to grasp across time within each context in SMG. Both participants demonstrate increased tuning when the hand and the object are shown simultaneously. C) Evaluating the grasp-tuned units in SMG in each context and how these units overlap among contexts. Hand+Object (HO) recruits the most units. D) Evaluating shared information across each context in AIP. During Planning, context generalization was weaker than during Action. When generalization did occur, it was predominantly incomplete. E) Percentage of units tuned to grasp across time within each context. Both participants demonstrate decreased tuning during Planning when the object is shown alone. Proportions during Action are similar across contexts. F) Evaluating the grasp-tuned units in AIP in each context and how these units overlap among contexts. Hand+Object (HO) recruits the most units. Overlap among all three contexts increases during Action. G) Evaluating shared information across each context in MC. During Planning and Action, contexts involving the hand (H & HO) reach higher classification levels than the object alone (O), with complete generalization during Action, compared to incomplete generalization to the object alone (O). H) Percentage of units in MC tuned to grasp across time within each context. Both participants demonstrate similar proportions of tuning, with contexts involving a hand recruiting more units. I) Evaluating the grasp-tuned units in MC in each context and how these units overlap among contexts. Most units demonstrate extensive overlap, meaning they are tuned to grasp during all three contexts.

Results are due to grasp and object encoding, not visual stimuli

One may reasonably consider that the neural tuning differences we see among the three contexts (hand only, object only, hand+object) are the result of differing visual statistics. It follows that the object contains the least amount of visual information and the object presented with the hand contains the most; therefore, the increased tuning we see to the hand and object presented together compared to the decreased tuning when the object is presented alone could be explained purely by a decrease in visual information. To test this hypothesis, we performed the Pixelated Task by interspersing trials where participants are cued normally (“Regular”) or cued with pixelated images of each grasp/object (“Pixelated”) (**Fig. 4-3**; see Methods for details). A very small number of units were tuned to pure visual stimuli during the motor planning, but this amount was not significantly different among contexts and did not significantly contribute to the total number of tuned units that were recruited by Regular images (**Fig. 4-9A**). This suggests any differences among contexts are a result of differences in how the hand, object, and their interaction affect motor planning rather than differences in visual statistics presented.

Participants are performing motor imagery task

Participants correctly performed the imagined motor execution during the Action phase of the task. Results from No-Go trials demonstrated equivalent percentage of tuned units

throughout the trial until the Action phase, where there was a sharp drop off of tuned units to baseline (ITI) levels quickly after the presentation of the No-Go cue (**Fig. 4-9B**). This indicates the participants were imagining executing the grasp only during Go trials, and that the tuned units we observed during the Go trials were directly related to performing the imagined motor execution.

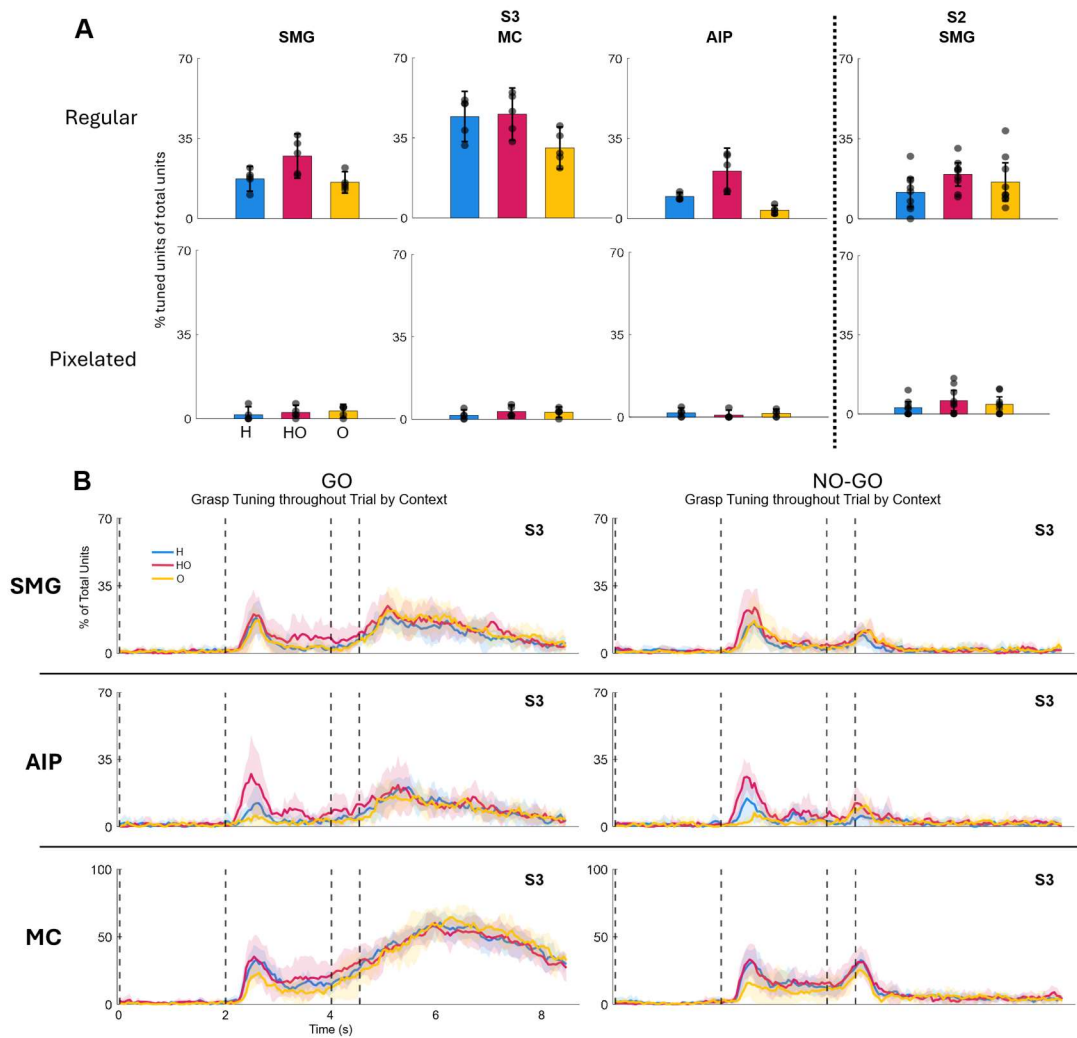


Figure 4-9. Control experiments demonstrate that participants are performing the task appropriately and the results are due to motor planning, not visual stimuli. A) Tuning to pixelated images during the Planning phase show that very few units within each region are tuned to purely visual stimuli. B) No-Go trials result in similar tuning level until the Action phase, where tuned units precipitously drop off. Data shown here are from participant S3, but the result is the same among all participants.

Discussion

Throughout the human cortical grasping network (CGN), grasp is robustly represented both at the single neuron and population level, during motor planning and imagined execution. Across three (right-handed) human participants, chronically implanted in the contra-lateral hemisphere (**Fig. 3-2**), grasp type is significantly represented in each region of the cortical grasping network (**Fig. 4-4A**), including supramarginal gyrus (SMG), anterior intraparietal cortex (AIP), and hand-knob region of the motor cortex (MC). Somatosensory cortex (S1) also encodes grasp during execution, within the receptive field of the digits (**Fig. 4-4D**).

Our results suggest different processes occur during motor planning and imagined grasping (**Fig. 4-7**), with grasp representation increasing during imagined motor execution for most regions (**Fig. 4-6**). Activity related to planning begins in PPC and MC (ns, $p = 0.5$ (S3), $p = 0.625$ (S4))⁸³; but during execution, MC activates before all other regions, evidence of a far-reaching network-wide motor feedback signal, to which even pre-frontal cortex (PFC) has access (**Fig. 4-4C**). The hand-knob region of motor cortex strongly encodes grasp planning information, supporting evidence observed previously in our lab and adding further evidence that MC may be a hybrid pre-motor/primary motor area^{77,78}.

Context matters

Developing a robust neuroprosthetic assistive device for performing dexterous manipulations of objects and activities of daily living (ADLs) will require demonstrations of flexible, context-independent control in real-world naturalistic environments. An important component in achieving these goals is the development of accurate BMI algorithms, which quickly translate recorded cortical signals of the participant's motor intention into action⁸⁴. Previous work has shown many context-dependent effects on control signals from MC, including object interaction^{65,66,85}, immersive environment⁸⁶, cognitive load⁸⁷, arm posture⁸⁸, task goals⁸⁹, reward⁷⁴, speech⁹⁰, and sensory feedback^{91,92}. To achieve stable performance,

either all these effects must be accounted for or cortical signals independent of context must be identified.

In our work, we have observed regions during a variety of contexts (planning vs. execution) and object interaction (a hand and object together vs. its individual components), with both independent (SMG and AIP) and dependent (MC) effects on the neural representation of grasp. Understanding how context influences our ability to classify grasp can help us determine how best to train and utilize decoders for a grasp BMI. Our results demonstrate that the neural processes occurring during motor planning and execution are partly distinct in each brain region (**Fig. 4-7**). Specifically, these results suggest that it may be possible to design BMI decoder that selectively engage during execution, thereby reducing the likelihood of premature grasp execution. This is important in BMIs because it affords the BMI user agency over when to perform the movement. Additionally, as demonstrated with other motor modalities (i.e., reaching³⁹), our participants can perform highly accurate grasp with purely imagined activity. As shown with motor control of speech, imagined actions may be even easier to perform and produce less fatigue for the user than attempted actions⁶¹.

Across all regions and participants, we observed lower grasp classification accuracies when the object was presented alone (O only) compared to contexts where the hand was presented (H or H+O) (**Fig. 4-8**). Despite the same verbal task instructions, different visual cues shown during the planning phase (hand alone, hand+object, and object alone) were significant enough to impact representation during active motor imagery. There are a few possible explanations. First, different networks may be recruited when a hand is explicitly shown^{93,94}. In our data, different contexts may recruit different subpopulations in each region (**Fig. 4-8C,F,I**). Second, while participants were instructed to perform the same action, it is possible that individual differences in motor imagery strategies across contexts could have a large effect on decoder performance⁹⁵, though this is less likely given the consistency in results across participants. Third, lack of an explicit hand position (Object only) during planning could lead to increased variance in the imagined grasp and worsen BCI performance.

AIP populations are selectively activated by context

Our data suggests variable and context-dependent encoding of grasp in AIP across two participants. In one participant, we observed highly selective tuning for object and hand interaction (**Fig. 4-8E**, S3). During motor planning, we saw the highest percentage of tuned units when the hand and the object are interacting, the lowest percentage when the object was presented alone, with the hand being presented alone falling between them. This result is unlikely to be explained solely due to increased complexity of visual stimuli (**Fig. 4-9B**), and our data may be further evidence of compositional encoding within AIP⁹⁶. With approximately 20% of the neurons in planning/action shared among the contexts (**Fig. 4-8F**), each participant had significant populations of uniquely tuned neurons to each context. These three contexts may also selectively activate known sub-populations of AIP neurons, preferential to encoding visual information (corresponding to the object alone), motor information (hand alone), or a combination known as visual-motor (hand and object together)²¹.

Planning activity present in MC

While we expected to see substantial activity in MC during imagined grasping^{36,37,39,40,86}, we also observed decodable grasp activity in MC during motor planning^{77,83,97,98} (**Fig. 4-6G**). There are a few possible explanations. The first is our implanted regions of MC (hand knob) may record from pre-motor neurons⁷⁷ or descending tracts to subcortical regions⁹⁹, in addition to primary motor neurons. Secondly, MC may receive information from SMG and AIP related to the grasp during the earliest stages of motor planning. Reciprocal connectivity between MC and PPC may explain why information about an object can be incorporated into a grasping action in roughly 100-150 ms¹⁸. In our analysis, latencies between the areas were approximately 50-100 ms during planning; however, differences were not significant within participant (**Fig. 4-4C**). Thirdly, others in our lab have demonstrated that if MC is not actively engaged in a motor task, it may encode information from other connected regions (including PPC). This has also been previously observed in primary motor cortex during

bimanual movement¹⁰⁰. When only the ipsilateral hand is engaged, the contralateral motor cortex encodes the movement. When both hands are engaged, the contralateral cortex suppresses activity from the ipsilateral side. Additionally, complex movements such as grasp demonstrate correlated contralateral/ipsilateral representations compared to more independent representations for reach¹⁰¹.

Subject differences

Across three SMG implants, participant S4's did not significantly encode grasp, size, or shape, in sharp contrast to our other two participants (**Fig. 4-4A, Fig. 4-5A, S4**), while maintaining similar numbers of total recorded neurons (**Fig. 4-5B, S4**). SMG is hypothesized to contain different specialized sub-divisions related to language, phonetic processing, tool use, visual and sensory integration among others^{102,103}. We do find motor task modulating neurons, but little unique selectivity in individual grasps (**Fig. S4-4A**), suggesting this implant is in a different sub-region of SMG, than the other two participants. Additionally, S4's SMG implant did not record any neurons selective for object size or object shape (**Fig. S4-4B**). A difference in anatomical location of S4's SMG implant relative to S3's and S2's, may also support our hypothesis of a different SMG sub-region (**Fig. 3-2**).

With S4's AIP array, we obtained much higher grasp classification accuracies during imagined motor execution compared to motor planning (**Fig. 4-6D**, dotted line). This was surprising, as we consider AIP to be a higher order region involved in movement planning. Interestingly, between AIP and S1, when controlling for equal neural population size, decoding performance was identical (**Fig. 4-4B**), suggesting this subregion of PPC may be receiving efferent copies from MC, like S1, resulting in similar results among the three regions. Additionally, this region demonstrates the same results as primary sensorimotor regions during cross-phase and cross-context decoding (**Fig. S4-5**).

Conclusion

In this study, we elucidated the grasp-related roles of key regions within the human cortical grasping network using single-unit firing rates from populations in SMG, AIP, and MC during motor imagery. All three regions encode grasp from the single channel to the population level in behaviorally relevant ways. MC comes online first and achieves the highest classification accuracies, followed by SMG, then AIP. While units largely demonstrate equivalent tuning across contexts, altering the context of a grasp during planning is sufficient to decrease classification accuracy during imagined motor execution. Additionally, motor planning and imagined motor execution are two distinct processes, an important finding and desirable feature for BMIs.

Chapter 5

MANIPULATION OF OBJECT SIZE; ITS EFFECT ON GRASP ENCODING AND ITS ENCODING THROUGHOUT THE CORTICAL GRASPING NETWORK

Introduction

One picks up a ball and does not need to conceptualize the exact location of each finger before the ball is in one's hand. One simply picks it up. Deceptively simple, grasping is one of the most sophisticated motor behaviors humans perform. Successful grasping requires not only accurate motor commands, but also the integration of visual and sensory information related to the object.

Before a movement even begins, the visual system estimates object properties such as size, shape, weight, texture, orientation, all of which contribute to selecting an appropriate grasp strategy⁵. The object features are transformed into motor commands through interactions among the regions of the cortical grasping network (CGN), allowing the hand to be pre-shaped in anticipation of contact^{4,16}.

Several studies have demonstrated that grasp kinematics are highly dependent on object properties. An object's orientation determines wrist orientation and finger placement. The purpose of the object determines finger selection and placement (e.g., picking up a mug to drink from it (grab handle with some or all fingers) vs. moving a mug from one place to another (grab body with all fingers)). One study identified that variations in surface texture and weight of an object influence magnitude and timing of grip force adjustments⁷⁹. These rapid, and often subconscious, motor adaptations demonstrate that grasping is not solely determined by intended action, but rather by continuous sensorimotor integration of object properties. Consequently, neural activity of grasp must account not only from the desired movement, but also the physical characteristics of the object to be manipulated.

Neurophysiological studies have shown that neurons throughout the CGN encode object properties. In the anterior intraparietal sulcus (AIP), neurons demonstrate tuning to object geometry and grasp/object interactions, playing a substantial role in the transformation of visual information into motor plans^{21,104}. The supramarginal gyrus (SMG) is associated with tool use²⁵, which requires the integration of object and movement intention in order to successfully use the tool. Additionally, a recent EEG study in humans found that object's intrinsic properties (size and shape) are encoded in the parietal region¹⁰⁵. Both SMG and AIP (subregions of PPC) are thought to send information about the object/tool to the premotor/motor cortex^{18,25}, suggesting that object property information is highly distributed throughout the CGN, yet the extent to which individual object properties are explicitly represented in humans remains incompletely understood.

When it comes to grasping, size is a major determinant of hand configuration. As object size increases, grip aperture must scale accordingly to ensure stable contact with the object being manipulated¹⁷. Humans are able to precisely scale grasp depending on object size even before contact occurs⁵. Additionally, a case report of a patient with lesions to the occipitoparietal and occipital regions demonstrated that grasping objects and perceiving objects are two distinct processes¹⁰⁶. These findings suggest that information about object size is incorporated into movement planning, rather than being corrected only through sensory feedback.

While grasp-selective neurons have been identified throughout the CGN (**Chapter 4**) and behavioral studies have established that object size strongly influences grasp kinematics, considerably less is known regarding the neural representation of object size at the single-neuron level in humans. In particular, it remains unclear whether neurons encode object size independently of grasp, whether grasp and size are represented simultaneously within the same neuronal populations, and how these representations evolve throughout movement planning and execution. Furthermore, it is unknown how these representations differ across regions of the cortical grasping network. Behaviorally, we have witnessed that object size

changes the intended grasp, but we still do not know how, where, and when object size is encoded in the cortex.

In this work, we altered object property of size to investigate if and how manipulating object size alters neural activity related to grasp and whether these regions encode the size of the object. This information is vital to understanding how the brain integrates sensorimotor information about an object's size with motor plans. We hypothesized that neurons in PPC would encode object size, and MC would not. We observed size/aperture encoding in SMG and MC, predominantly during planning and imagined execution, respectively. Encoding grasp and object size could provide complementary information that could enable more natural and adaptable grasp for BMIs.

Methods

Varied Sizes Task

To investigate how manipulating the size of an object affected grasp encoding, and whether the object property of size itself was encoded in the CGN, a variation of the task of the Altered Context Task (**Fig. 4-2**) was designed. The overall trial structure was maintained (**Fig. 5-1**), but we altered each hand to create the smallest and largest feasible grasps for each grasp type, corresponding to Small and Large objects, respectively (**Fig. 5-2**). During the Action phase, participants are still asked to perform imagined motor imagery, paying particular attention

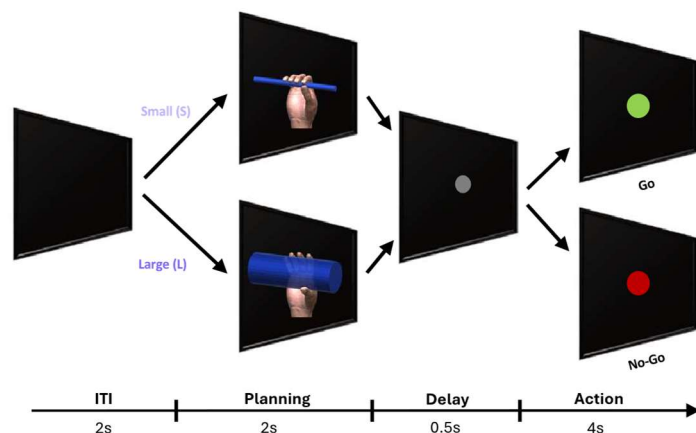


Figure 5-1. Varied Sizes Task Experimental Design. Example shown of MediumWrap.

to adjusting the size of the grasp accordingly. During blocks where only the object was presented (Object only), small blue dashes were added to indicate which fingers were to be used and where they were to be placed. 28 trials were recorded per block (2 repetitions of 4 grasps x 2 sizes = Go trials, 1 repetition of 4 grasps x 2 sizes = No-Go trials), two blocks per condition every session.

Subject	Varied Sizes Task
S2	8
S3	8
S4	7

Table 5-1. Breakdown of sessions performed of Varied Sizes Task with each participant.

Results

We found differential neural representations across the human cortical grasping network (CGN) for object size during imagined grasping. Both single neuron and population-level dynamics revealed roles for object processing in posterior parietal and motor cortices.

To investigate the encoding of object size and how this property influenced the motor variable of grasp during planning and execution, we utilized a cued, delayed motor task (**Fig. 5-1**), instructing participants to imagine grasping objects of varying sizes (**Fig. 5-2**). We hypothesized motor and sensory regions would continue to encode fundamental variables of motor control (grasp type) and would also encode hand aperture (how open/closed the hand is) remaining

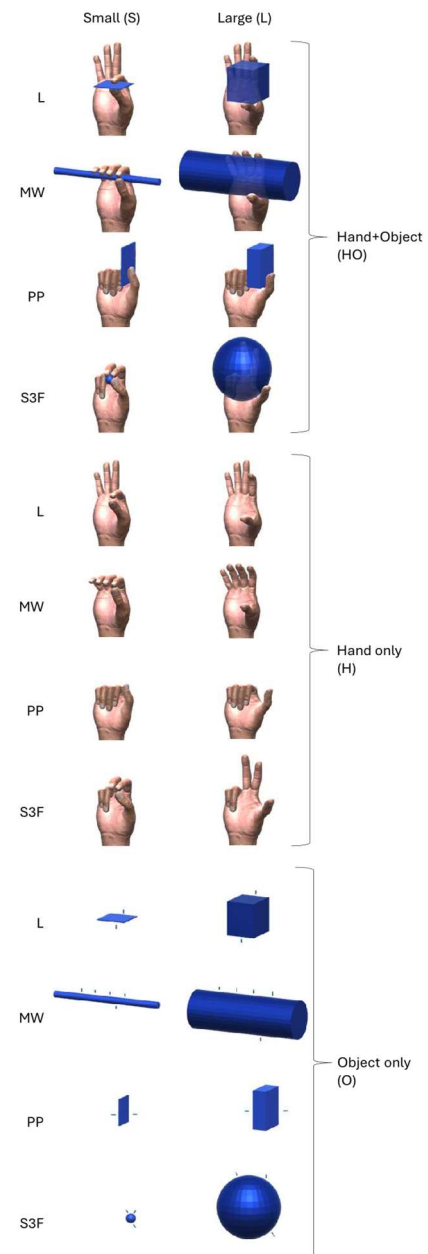


Figure 5-2. All grasp/size/context combinations. Blue dashes added to the Object only context to indicate to participants which fingers to use and where they should image grasping the object.

invariant to object manipulation, while posterior regions would preferentially encode the object property of size.

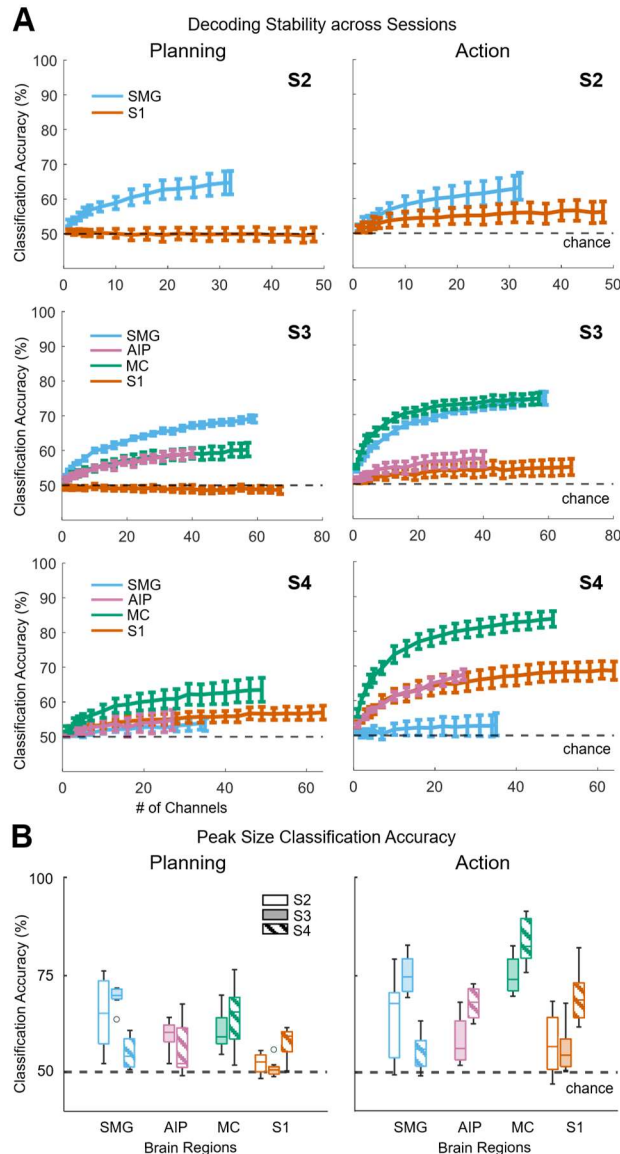


Figure 5-3. Size classification across the CGN. A) Neuron Dropping Curves calculated using linear regression for each participant during Planning (column 1; S2: SMG: 65%, S1: 50%; S3: SMG: 69%, MC: 60%, AIP: 59%, S1: 49%; S4: SMG: 53%, MC: 63%, AIP: 55%, S1: 57%) and Action (column 2; S2: SMG: 64%, S1: 57%; S3: SMG: 75%, MC: 75%, AIP: 57%, S1: 55%; S4: SMG: 53%, MC: 84%, AIP: 67%, S1: 69%) phases. B) Peak size classification accuracy of each brain region calculated from the Neuron Dropping Curves during Planning (left) and Action (right) phases.

Across the CGN, we found that only specific regions of the CGN selectively encode object size during specific phases (**Fig. 5-3**). Object size was immediately available in SMG during motor planning and continued to be decodable during imagined execution, when MC also robustly encoded hand aperture (**Fig. 5-3**). Contrary to what we expected from NHP literature, AIP did not appear to encode object size (**Fig. 5-5F**).

Object size is decodable from selective CGN regions at specific times

Independent of grasp type, object size was represented robustly in SMG and MC across all three participants (**Fig. S5-1A**). Neurons in the supramarginal gyrus (SMG) in two of three participants (S2, S3) showed significant decoding of object size during motor planning (mean accuracy: 67%) and imagined motor execution (mean accuracy: 70%)

(**Fig. 5-3**). SMG demonstrated the highest classification accuracy during planning, with rates comparable to MC during execution.

Neurons in the MC also significantly encoded size, though we believe what is really being encoded is hand aperture (see Discussion). We will thus be referring to size as aperture when discussing motor cortex for the remainder of this chapter. Aperture encoding appeared weakly during planning (mean accuracy: 62%) before strongly coming online during imagined execution (mean accuracy: 80%) (**Fig. 5-3**).

Surprisingly, we observed weak and variable classification accuracy of size in AIP during both planning (mean accuracy: 57%) and execution (mean accuracy: 62%) (**Fig. 5-3**). Based on NHP literature, we hypothesized robust size encoding in AIP, particularly during planning (Scherberger et al., 2016). Unfortunately, due to typical degradation, fewer neurons were recorded from S4's AIP array during this task (**Table 3-1 & Table 3-2**, S4 AIP). We lost the ability to classify grasp from this array, demonstrating loss or significant reduction in task modulation at the implant location of this array. Due to this, S4's AIP data was excluded from the rest of the results in this chapter.

Grasp decoding is size-independent in CGN

To investigate whether manipulation of object size affected our ability to decode grasp, we performed classification of grasp type across all trials, independent from object size. In SMG, AIP, and MC, we found grasp remained decodable independent of object size (**Fig. 5-4**). The

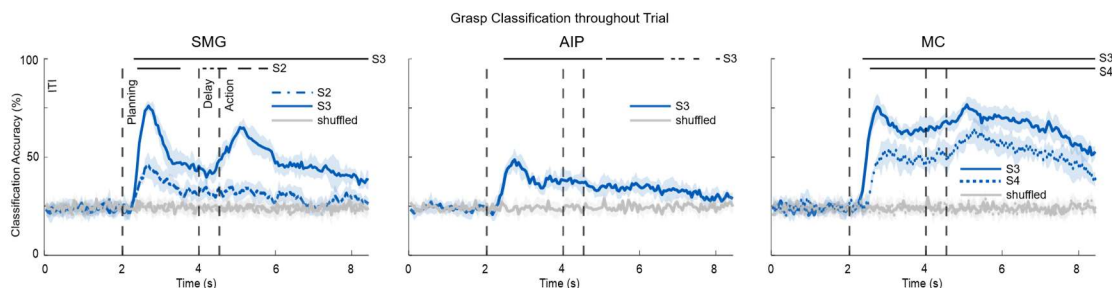


Figure 5-4. Grasp encoding is size-independent in CGN. Session-averaged classification of grasp using an LDA classifier is significantly above chance during motor planning and imagined motor execution across all participants. Grasp can still be accurately classified when manipulating object size, as the accuracies and timing structure are nearly identical to the Altered Context Task.

overall decoding architecture for each participant in each region was maintained and markedly similar to the grasp decoding observed in the Altered Context Task (Fig. 4-6).

Size is encoded at the single-channel level in SMG and MC

Due to SMG's role in tool use and grasping, we hypothesized that object size would be encoded in this region. We found that size was encoded from the population to the single-

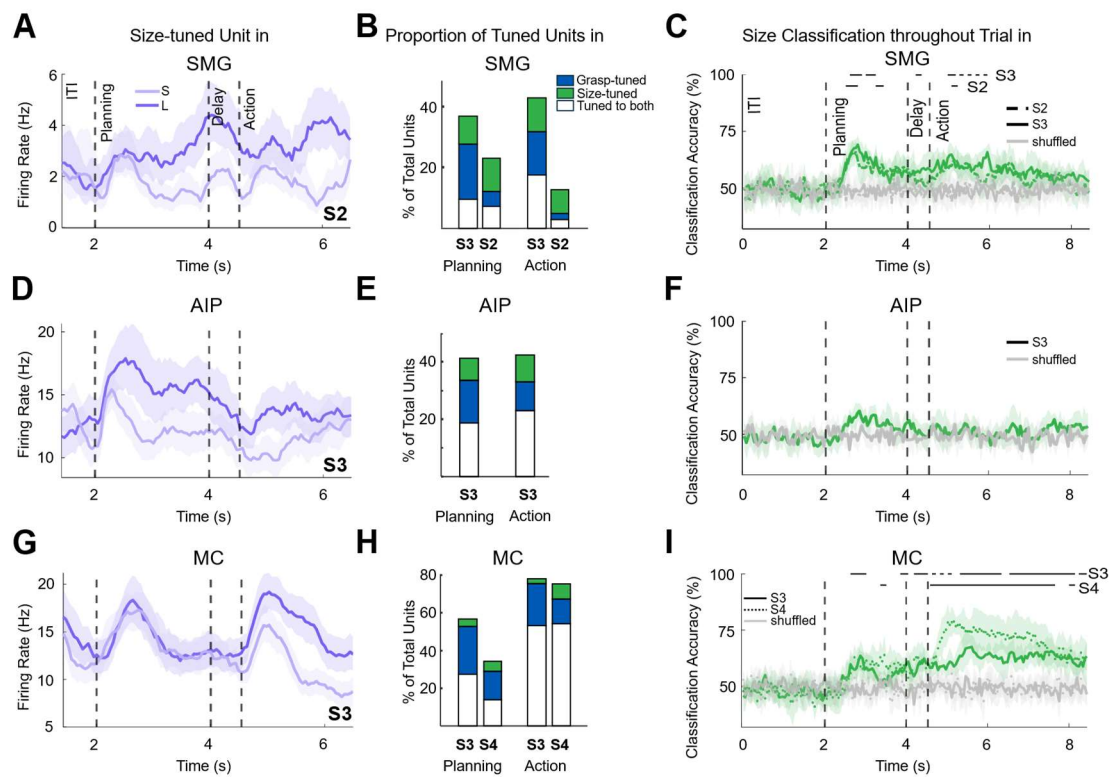


Figure 5-5. Size encoding throughout CGN from the population to the single-channel level. A) A size-tuned example unit in SMG is shown where the unit's firing rate is higher for an object that is Large and roughly baseline level response for Small throughout the trial. B) Proportion of single units in SMG tuned to grasp (blue), size (green), or both (white) for each participant during Planning (left) and Action (right) phases. A similar proportion of units are tuned to size during Planning and Action. Roughly half of the units are uniquely tuned to object size. C) Size is significantly classified during Planning and Action in both participants at the timebin-level in SMG. D) A size-tuned example unit in AIP is shown where the unit's firing rate is higher for an object that is Large and lower for Small, but both invoke similar response patterns (increasing and decreasing at similar times). E) Proportion of single units in AIP tuned to grasp, size, or both. A similar proportion of units are tuned to size during Planning and Action. Largely overlaps with grasp-tuned units. F) Size is not significantly classified at any point in the trial at the timebin-level in AIP. G) An example unit in MC demonstrates an equivalent response to both apertures early in motor planning but diverge during imagined motor execution with the Large aperture resulting in an increased firing rate relative to the Small. H) Proportion of single units in MC tuned to grasp, hand aperture, or both. A very small proportion of units are uniquely tuned to aperture compared to grasp, with a substantial increase from Planning to Action. Size-tuned units almost entirely overlap with grasp-tuned units. I) Aperture is significantly classified weakly during Planning and consistently during Action in both participants at the timebin-level in MC.

channel level in SMG (**Fig. 5-5**). Independent from grasp, single units tuned to size (Small vs. Large) were identified (**Fig. 5-5A**). Distinct populations of size-specific units arose, suggesting the encoding of object size at the single-channel level (**Fig. 5-5B**). We observed a similar proportion of single units tuned to size during Planning and Action. Roughly half of the units were uniquely tuned to object size (units that demonstrated tuning to size only, not grasp). At the population level, object size was significantly decoded during planning and persisted into motor execution (**Fig. 5-5C**).

As noted, we hypothesized that AIP would demonstrate strong encoding of object size, particularly during planning. We found single units tuned to object size (**Fig. 5-5D**). This subpopulation of single units tuned to size was roughly equivalent during planning and execution and was comparable to the proportion of grasp-tuned units (**Fig. 5-5E**). However, the proportion of uniquely size-tuned units was quite small, with most units also tuned to grasp. Despite these single-channel findings, there was no significant decoding of size at any point in the trial (**Fig. 5-5F**).

As expected, individual neurons in MC responded selectively to hand aperture, predominantly during motor execution (**Fig. 5-5G,H**). A smaller proportion of single units were tuned to aperture compared to grasp, with a substantial increase from Planning to Action. Additionally, size-tuned units overlapped almost entirely with grasp-tuned units. At the population level, aperture was significantly decoded as early as the planning period, but much more strongly and consistently during execution (**Fig. 5-5I**).

Size encoding is influenced by grasp type

We found that size/aperture was encoded independent of grasp type in SMG and MC. However, there were specific grasp types that resulted in higher classification accuracies within each region. Interestingly, SMG had a “preference” for some grasp types over others, such that for MediumWrap and Sphere3Finger grasps, we observed higher classification accuracies during both motor planning and imagined motor execution compared to Lateral

and PalmarPinch grasps (**Fig. 5-6A**). However, our ability to classify size was not limited to these two grasps, as the Lateral grasp did reach significance during imagined motor execution.

Similarly, we also observed grasp-dependent aperture decoding from neural activity in the MC. In both participants, the highest classification accuracies of aperture resulted when the grasp type was Lateral or Sphere3Finger (**Fig. 5-**

6B). This was consistent during motor planning and imagined motor execution. The other two grasps (MediumWrap and PalmarPinch) also reached significance during imagined motor execution, but their accuracies remained lower than the preferred grasp types.

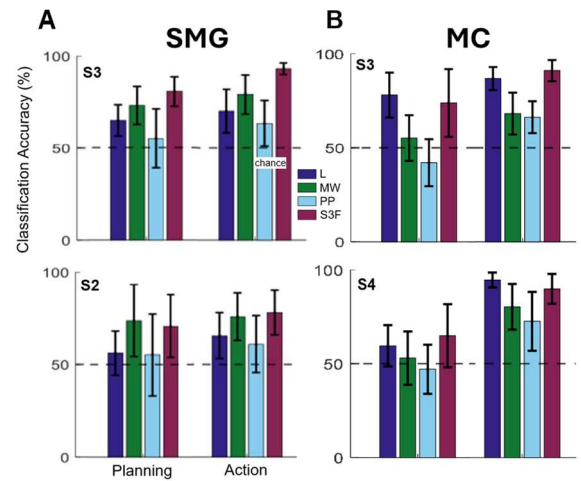


Figure 5-6. Classification of size/aperture by grasp type in SMG (A) and MC (B) during Planning and Action demonstrate higher classification accuracies of size within specific grasp types.

Classification of size/aperture is affected by context

In SMG and M1, similar proportions of units tuned to size were recruited whether the object was present or not across all 3 participants (**Fig. S5-2**). However, context-specific differences appeared when we observed our ability to classify size within contexts. In SMG, size classification accuracy increased during planning when a hand was present (H & HO) across both participants (**Fig. 5-7A**). This effect did not persist, however, and we were able to classify size across all three contexts with

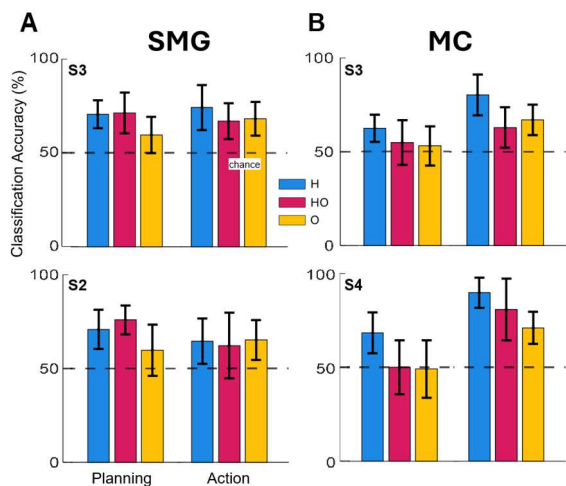


Figure 5-7. Classification of size/aperture by context in SMG (A) and MC (B) during Planning and Action phases. Results demonstrate size classification is influenced by context.

roughly equivalent accuracies during execution.

MC demonstrated more context-dependence in that classification was highest when only a hand was shown (H) (**Fig. 5-7B**). Size could only be significantly classified during planning if the hand was presented alone; if the hand was presented with the object (HO) or the object was presented alone (O), we observed chance level classification. This was true during both planning and execution and across both participants. While size could be classified significantly during motor execution across all contexts, the preference for the hand alone is notable.

Discussion

Grasp representations are preserved despite manipulation of object size

Manipulating object properties raises the possibility that neural representations of grasp may be altered, potentially reducing the ability to decode intended grasp when object characteristics vary. However, our results demonstrate that grasp could be decoded reliably from each cortical region despite changes in object size, with classification accuracies comparable to those obtained in the original task (**Fig. 5-4**). These findings indicate that grasp representations are largely invariant to change in object size and suggest the underlying neural subspace encoding grasp is preserved across variations in size. This stability of grasp decoding suggests that information related to both grasp and size coexist in the CGN without substantially degrading the representation of grasp itself. This observation is consistent with neuronal populations encoding multiple task-relevant variables simultaneously^{67,107}.

Grasp type and context can influence object size decoding in SMG and MC

Our data exhibit partial mixed selectivity within SMG at the population level, encoding grasp type and object size, suggesting a crucial role in processing motor plans and object characteristics. SMG has a “preference” for some grasp types over others. For MediumWrap and Sphere3Finger grasps¹⁰⁸, we could decode size with higher accuracy during both motor

planning and imagined motor execution compared to Lateral and PalmarPinch grasps (**Fig. 5-6A**). If SMG encodes positional information of the intended end effectors, the required increased dimensionality of the control signal with increased number of effectors (i.e. the virtual finger hypothesis¹⁰⁹, may increase the separability of the population activity. These preferences differed across other areas (**Fig. 5-6B**); thus, this finding is unlikely due to increased task demands or complexity of the particular grasp conditions.

Human AIP may be distinct from NHP AIP

Our results demonstrate that neurons in the medial gyrus of the anterior intraparietal cortex (human AIP) do not encode object size, compared to the AIP NHP homologue, shown to predominantly encode object properties (i.e. size¹²).

Size was not significantly decodable during motor planning in AIP (**Fig. 5-5F**). This is surprising, given historical evidence for involvement in planning or higher-order processing^{11,18,19}. NHP studies have demonstrated homologue AIP plays a strong role in object processing^{12,17,21,68}. Since SMG has been shown to encode object size, is canonically known for its role in tool use^{25,27}, and has no known homologous region in NHPs, it is possible that human cortex has multiple cortical regions dedicated to object representation and manipulation. Support for this hypothesis includes enhanced human hand dexterity driven by complex object/tool use^{110,111}, structural reorganization of association cortices throughout evolution¹¹², human-specific multi-region lateralized networks that allow fronto-parietal connectivity¹¹³, connectivity driving neural dynamics¹¹⁴, and the postulated connectivity between AIP and SMG²⁵.

MC encodes hand aperture rather than object size

MC significantly encodes hand aperture during motor imagery. While it is possible that MC encodes an object property such as size, we believe hand aperture is encoded rather than object size. Firstly, we could predominantly decode this variable during imagined motor execution rather than motor planning (**Fig. 5-5I**), with significant size decoding during motor

planning occurring only when the hand alone was shown (**Fig. 5-7B**). This suggests involvement in motor commands rather than object processing, which we would expect to see during motor planning, as with SMG. Secondly, the “preferred” grasp types with the highest size classification accuracies were the ones with the largest delta for hand aperture (**Fig. 5-6B**). Anecdotally, participant S4 reported “feeling the stretch” in their hand when imagining performing these grasps, and size or hand aperture was decodable from S1 during movement (**Fig 5-3A**, S4). Thirdly, the literature overwhelmingly supports MC’s involvement in processing motor variables^{12,68,70,71} like hand aperture, rather than object properties, like object size, although this was found in one recent NHP study³⁴. Further, Schaffelhoef & Scherberger (2016) found that NHP MC (M1) only encodes motor information (not object size or shape) and this only occurs during motor execution¹².

Object properties drive grasp selection

One limitation of this study is that object weight is almost always inextricably linked when manipulating object size, such that something that is smaller is typically assumed weigh less than a similar but larger object. Intrinsic properties like weight influence grasp selection and our motor plan, presumably even when imagined⁴. We attempted to maintain and depict objects with the same intrinsic properties across all objects (blue, similar textures, location, orientation), but it is possible that our participants attributed other properties to individual objects either consciously or subconsciously. Even with this potential change in perception, it is unlikely that this is driving our results, as we see similar size encoding across multiple participants (**Fig. 5-5C,I**; SMG during planning, MC during execution). Additionally, weight is unlikely to be the driving factor, as most of our Large objects are also transparent (suggesting a small weight, more similar to the weight of the Small objects (**Fig. 5-2**)). If weight was encoded rather than size, we would expect the best classification in the grasp/object pairing that is not transparent (PP) and poor classification among the others (S3F); we see the opposite (**Fig. 5-6**), further supporting that what we are seeing is encoding of size.

Additionally, in this grasping task, object size was inextricably linked with hand aperture. While we have additional evidence to support size encoding in SMG (such as independent subpopulations of single neurons tuned to size, **Fig. 5-5B**), we cannot definitively say that what SMG was encoding was not hand aperture. Similarly, it is possible that we do not see object size encoding in AIP for this very reason. Additional studies are needed to further distinguish between hand aperture and object size. Even if what we have found is hand aperture encoding in SMG and MC, this is still valuable as it was previously unknown that this grasp kinematic was encoded in these regions and could be identified at the single-channel level.

Subject differences

Due to typical degradation of S4's AIP array, fewer neurons were recorded between the Altered Context Task and the Varied Sizes Task (**Fig. 4-4B** compared to **Fig. 5-3A**, S4; **Tables 3-1 & 3-2**). This is meaningful as it resulted in loss of ability to classify grasp, which was strongly encoded during the Altered Context Task (**Fig. 4-6D**, S4). Due to this loss/severe decrease in task modulation, we decided to remove S4's AIP data from the results in this chapter, as we felt the loss of units compromised our ability to draw strong conclusions about size encoding in this region.

Conclusion

In this study, we elucidated the roles related to object size processing of key regions within the human cortical grasping network using single-unit firing rates from populations in SMG, AIP, and MC during motor imagery. SMG and MC significantly encode object size/hand aperture from the single channel to the population level in behaviorally relevant ways. Surprisingly, AIP did not demonstrate encoding of object size. This is in contrast with NHP literature and suggests that human AIP is distinct from NHP AIP. SMG demonstrated the highest size classification accuracy during motor planning, while MC demonstrated the highest during imagined motor execution. We believe that SMG encodes object size, while

MC encodes hand aperture. Importantly, all regions retained their grasp encoding despite the manipulation of object size.

Chapter 6

OBJECT SHAPE IS ENCODED IN THE POSTERIOR PARIETAL CORTEX

Introduction

The act of grasping inherently requires the presence of an object, something to grasp. In order to successfully grasp an object, the nervous system must identify the properties of the object and incorporate that information into the motor plan. This process, known as visuomotor transformation, relies on visual features of an object such as size, shape, orientation, and location that influence hand shape prior to contact with an object¹⁷. Seamless integration of perception and action allows the nervous system to continuously map object properties onto the intended movements required for interaction.

The posterior parietal cortex, and the anterior intraparietal cortex specifically, has been established as playing an important role in visuomotor transformation^{17,19,21}. Both AIP and SMG receive visual information related to object features and send this information to premotor and motor cortices^{4,25,115}. Additionally, neurophysiological studies in NHPs have demonstrated that AIP neurons respond selectively to object characteristics such as size, shape, and orientation, while simultaneously exhibiting activity related to grasp planning^{12,21,104}. PPC appears to be located in a privileged position between visual perception and motor execution, playing a vital role in integration.

Conversely, the motor cortex (MC) is traditionally known for representing the execution of the movement itself. Several electrophysiological studies have identified M1 neurons that encode grasp type¹², direction¹¹⁶, force¹¹⁷, velocity and position¹¹⁸. While MC and PPC are both involved in grasping, their roles are quite distinct. PPC is thought to largely integrate visual and motor information, whereas MC is primarily responsible for the descending motor command to execute the movement.

Despite decades of research seeking to understand grasp in the CGN, an important question remains unanswered in humans: do neurons encode the object itself or only the movement used to interact with it? This question is a difficult one to answer, as object shape and grasp selection are naturally linked. Different objects typically require different grasps, making it difficult to determine if changes in neural activity are due to the object or the motor action. Similarly, we can present an object by itself visually, but if that object is linked to a specific grasp, it is not possible to disentangle the cause of the neural response.

Shape is extremely behaviorally relevant as it relates to grasping, as it is a driving factor in determining grasp selection. Specifically, object shape directly constrains finger configuration, hand/wrist orientation, and contact locations necessary for successful manipulation. Shape therefore provides substantial information related to grasp. If PPC serves as the location for visuomotor integration, we would expect to see neurons in this region related to object shape, in addition to grasp-related neurons. Conversely, if object shape is only an affordance¹¹⁹ and therefore the neural activity is primarily related to motor intention, object shape should not be encoded once the grasp is specified.

While studies in NHPs have identified neurons tuned to object properties within AIP and the CGN^{12,21}, evidence for independent object representations in the human CGN remains limited. Functional imaging studies have demonstrated activation of human PPC to object properties (shape, size) and grasp affordances (tool use) at the population level^{105,120,121}. Yet, we still do not know how individual neurons in the CGN represent object shape.

To address this question, we developed a motor imagery task in which participants imagined grasping multiple objects using several distinct grasp types. By allowing object shape and grasp to vary independently, this design enabled neural representations of each variable to be examined while controlling for the other. We hypothesized that regions of PPC would encode both object shape and grasp, while MC would only encode grasp-related information. We found that object shape is robustly encoded in SMG and AIP, while MC does not encode shape. Identifying independent representations of object shape advances our understanding

of how visual information is transformed into action but also provides insight into the types of information available for future BMI use.

Methods

Disassociation Task

To investigate object shape encoding separate from grasp type encoding, another variation of the task was created to disassociate the grasp-object pairs (**Fig. 4-1**).

In this task, we maintain the same trial structure and participants receive the same instructions as the Altered Context Task; however, during Planning, a static image of one grasp type interacting with one object is the stimulus every time (**Fig. 6-1A**). This stimulus varies, as each grasp type is paired with each object shape, such that each unique object is grasped by all 4 grasp types (**Fig. 6-1B**). Dimensions of each shape were altered slightly to ensure feasible

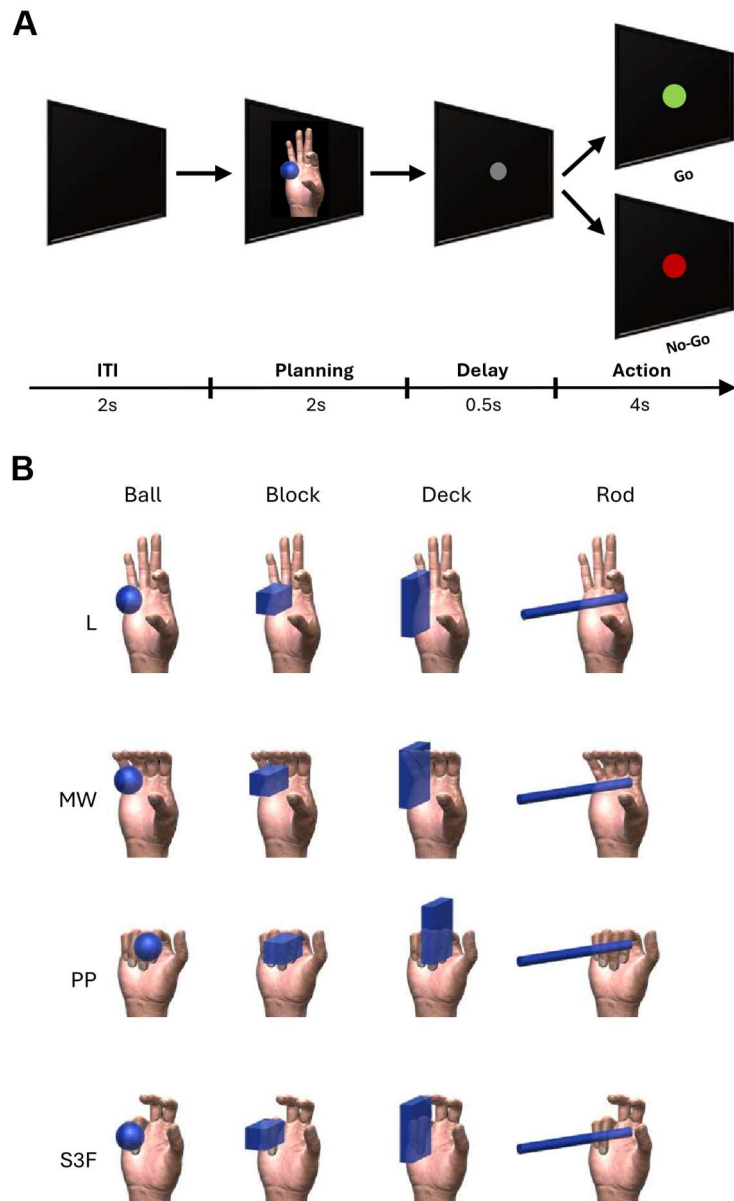


Figure 6-1. Disassociation Task Experimental Design. A) Trial structure. Example shown of Lateral grasp paired with Ball. B) Static images for Disassociation Task depicting each grasp paired with each object (object dimensions were altered to enable feasible grasping by each grasp type).

grasping by each grasp type. This task variation had no hand only or object only contexts, as the grasp and object pairs are now decoupled and thus a hand and object must always be used to cue which grasp/object combination to perform. 40 trials were recorded per block (2 repetitions of 4 grasps x 4 objects = Go trials, 2 repetitions x 4 grasps = No-Go trials), with three blocks recorded every session, along with one block of each original context (HO, H, and O) from the Altered Context Task for direct comparison.

Subject	Disassociation Task
S2	8
S3	6
S4	7

Table 6-1. Breakdown of sessions performed of Disassociation Task with each participant.

Results

We found differential neural representations across the human cortical grasping network (CGN) for object shape during imagined grasping. Both single neuron and population-level dynamics revealed roles for object processing in the posterior parietal cortex.

To investigate the encoding of object shape and how this property influenced the motor variable of grasp during planning and execution, we utilized a cued, delayed motor task (**Fig. 6-1A**), instructing participants to imagine using four different grasps to grab four distinct objects (**Fig. 6-1B**). We hypothesized manipulating the shape of the object may alter our ability to decode grasp type from the motor cortex (based on findings from Downey et al., (2017)). We also hypothesized that the posterior parietal cortex would encode object shape, while the motor cortex would not.

Across the CGN, we found that PPC selectively encodes object shape predominantly during motor planning (**Fig. 6-2**). Object shape is immediately available in SMG and AIP during motor planning, with some weak classification persisting during imagined motor execution

(Fig. 6-4C,F). As expected, MC does not significantly encode object shape at any point during the trial (Fig. 6-4I).

Shape is decodable from PPC during motor planning

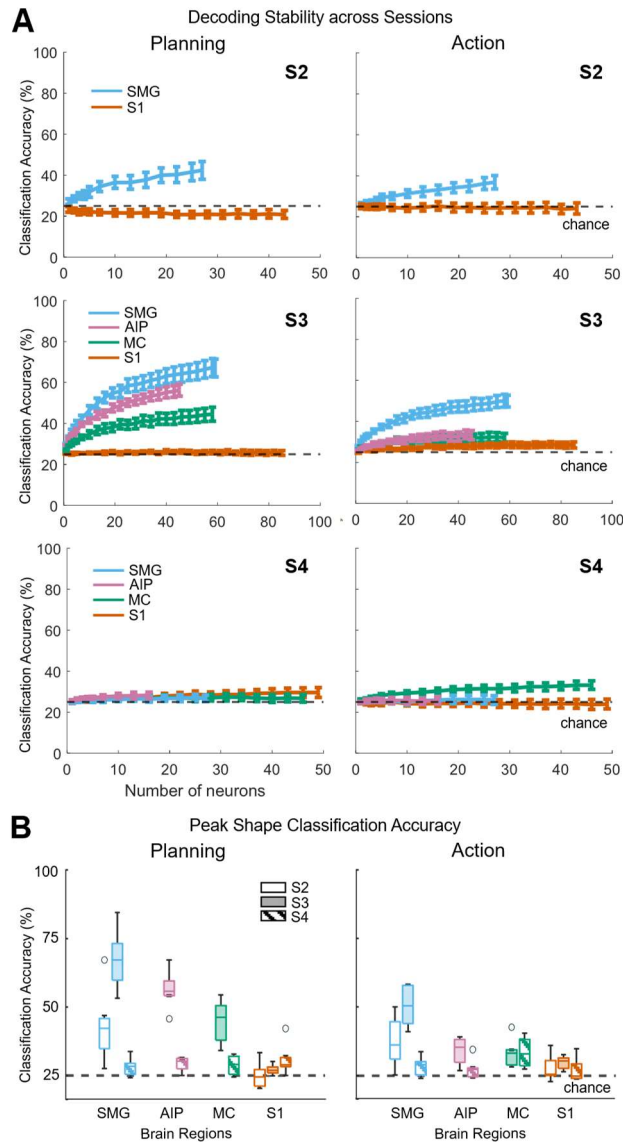


Figure 6-2. Shape classification across the CGN. A) Neuron Dropping Curves calculated using linear regression for each participant during Planning (column 1; S2: SMG: 42%, S1: 23%; S3: SMG: 67%, MC: 45%, AIP: 56%, S1: 26%; S4: SMG: 27%, MC: 27%, AIP: 28%, S1: 30%) and Action (column 2; S2: SMG: 37%, S1: 25%; S3: SMG: 50%, MC: 32%, AIP: 34%, S1: 29%; S4: SMG: 26%, MC: 33%, AIP: 26%, S1: 25%) phases. B) Peak shape classification accuracies of each brain region calculated across sessions from the Neuron Dropping Curves.

Independent of grasp type, object shape was represented robustly in PPC, namely SMG and AIP. Neurons in the supramarginal gyrus (SMG) in two of three participants (S2, S3) showed significant decoding of object shape during motor planning (mean accuracy: 55%) and imagined motor execution (mean accuracy: 44%) (Fig. 6-2). SMG demonstrated the highest classification accuracy of shape during both planning and execution.

Neurons in AIP also significantly encode object shape. Shape encoding was strong in AIP during planning (mean accuracy: 56%) and weakly persisted during imagined execution (mean accuracy: 34%), just below SMG's classification performance (Fig. 6-2). Unfortunately, S4's AIP array continued to have fewer task modulated neurons and the data from that array was therefore excluded from

the rest of the results in this chapter (Tables 3-1 & 3-2).

As expected, we predominantly observed near chance level classification of object shape in MC. Modest classification accuracy of shape in MC did arise in one participant during planning (mean accuracy: 36%; S3 peak = 45%), although this did not hold up in later analyses (Fig. 6-4I). Classification returned to near chance level during execution (mean accuracy: 33%) (Fig. 6-2).

Grasp decoding is shape-independent in CGN

To investigate whether manipulation of object shape affected our ability to decode grasp, we performed classification of grasp type across all trials, independent from object shape. In SMG, AIP, and MC, we found grasp remained decodable independent of object size (Fig. 6-3). The overall decoding architecture for each participant in SMG and MC was maintained and markedly similar to the grasp decoding seen in the Altered Context Task (Fig. 4-6). In AIP, the decoding architecture as well as accuracies remained similar to the original grasp decoding during planning; however, classification accuracies dropped to predominantly chance levels during execution. Along with decreased classification accuracies during execution, we also observed a decrease in neurons tuned to grasp during execution (Fig. 6-4E) compared to grasp-tuned neurons observed during the Varied Sizes Task (Fig. 5-5F). This could be due to a preferential role in AIP to process object properties (Scherberger et

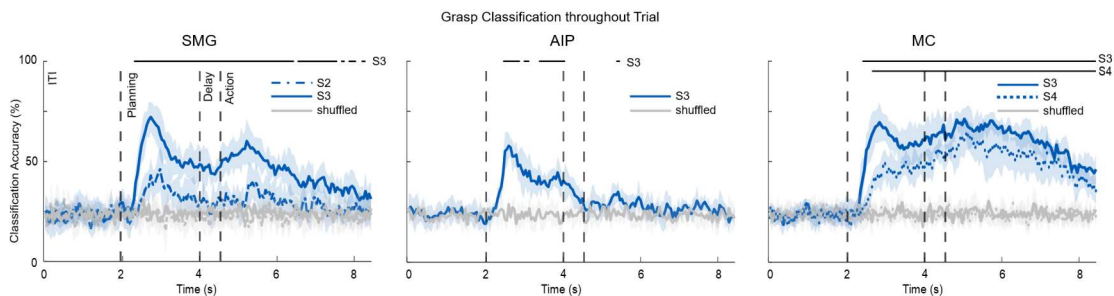


Figure 6-3. Grasp encoding is shape-independent in CGN. Session-averaged classification of grasp using an LDA classifier is significantly above chance during motor planning and imagined motor execution across all participants. Grasp can still be accurately classified when manipulating object shape, as the accuracies and timing structure are nearly identical to the Altered Context Task.

al., 2016), prioritizing encoding of object shape and subsequently pulling focus away from encoding grasp type.

Shape is encoded at the single-channel level in PPC

Due to SMG's role in tool use and grasping and our previous results indicating object size encoding, we hypothesized that object shape would also be encoded in this region. We found that shape was encoded from the population to the single-channel level in SMG (**Fig. 6-4**).

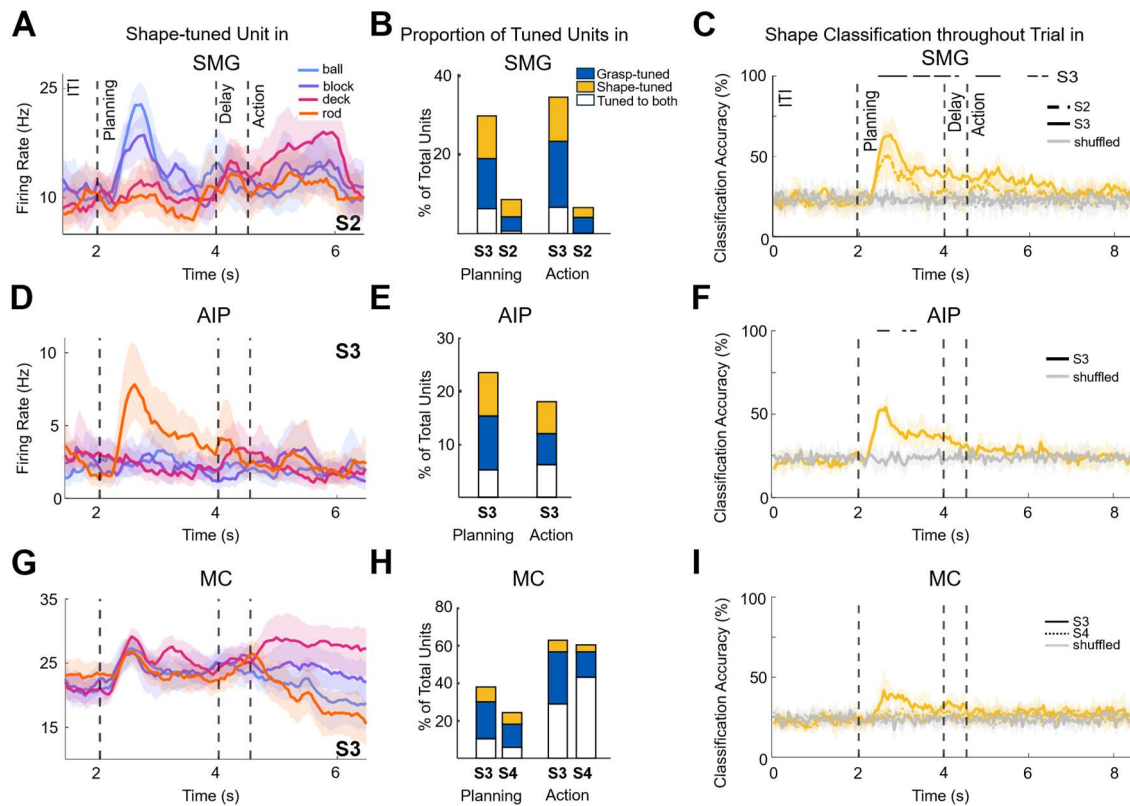


Figure 6-4. Shape encoding throughout CGN from the population to the single-channel level. A) An example unit in SMG is shown that is tuned to ball and block, responding only during motor planning. B) Proportion of single units in SMG tuned to grasp (blue), shape (yellow), or both (white). There is a unique shape population comparable to grasp-tuned units with little overlap. C) Shape is significantly classified during Planning and Action in one participant and trending during Planning in the other participant at the timebin-level in SMG. D) A shape-tuned example unit in AIP is shown that is tuned to rod, responding only during motor planning. E) Proportion of single units in AIP tuned to grasp, shape, or both. The shape-tuned population is comparable to grasp-tuned population with a mix of overlapping and uniquely shape-tuned units. F) Shape is significantly classified during Planning at the timebin-level in AIP. G) A shape-tuned example unit in MC demonstrates varied firing rates depending on the object shape during imagined motor execution, with a near uniform response across all grasp types during motor planning. H) Proportion of single units in MC tuned to grasp, shape, or both. A smaller proportion of units are uniquely tuned to aperture compared to grasp, with a modest increase from Planning to Action. Most of the shape-tuned units overlap with grasp-tuned units. I) Shape is not significantly classified during Planning or Action in either participant at the timebin-level in MC.

Independent from grasp, single channels tuned to shape were identified (**Fig. 6-4A**). Distinct populations of shape-specific units arose, suggesting the encoding of object shape at the single-channel level (**Fig. 6-4B**). We observed a similar proportion of single units tuned to shape during Planning and Action. There were comparable proportions of grasp- and shape-tuned units, and these subpopulations largely did not overlap (i.e., the units that were tuned to shape were unique and distinct from the units that are tuned to grasp). At the population level, object shape was significantly decoded during planning and persisted into motor execution (**Fig. 6-4C**).

We hypothesized that AIP would demonstrate strong encoding of object shape, particularly during planning. Many neurons in AIP demonstrated tuning to object shape predominantly during motor planning (**Fig. 6-4D**), with a mix of overlapping and uniquely shape-tuned units and proportions that rival grasp-tuned units (**Fig. 6-4E**). Populations of neurons significantly decoded object shape during planning, at accuracies comparable to grasp, demonstrating that AIP strongly encodes object shape (**Fig. 6-4F**).

As expected, shape was not encoded in MC. Interestingly, while we observed the occasional single neuron modulated by object shape (**Fig. 6-4G**), these rare units were predominantly also tuned to grasp (**Fig. 6-4H**). There was also a modest increase in shape-tuned units from Planning to Action. In conjunction with no significant decoding of object shape, our data suggests MC does not encode object properties (**Fig. 6-4I**).

Selectivity is associated with shape classification performance

To investigate what might be driving the ability to classify object shape from PPC regions, we looked at the tuning properties of shape-tuned neurons in each region. We found that unit selectivity and overlapping between phases may affect object classification. Specifically, SMG demonstrated mostly selective tuning during Planning (in both participants) and Action (one participant: S3) (**Fig. 6-5A**) and we could decode object shape throughout both phases

(Fig. 6-4C). Additionally, approximately 28% of units tuned to shape were recruited in both planning and execution (Fig. 6-5B).

Conversely, while AIP demonstrated tuning during both phases, shape-tuned neurons in AIP were only selective during planning, before switching to predominantly mixed-selective during execution (Fig. 6-5C). These units were also phase-specific, meaning the units recruited during planning were distinct from the units tuned during execution, with only 4% of units tuned during both phases (Fig. 6-5D). This could help explain why despite many units demonstrating tuning to shape in AIP during execution, we were only able to significantly classify shape during motor planning (Fig. 6-4F).

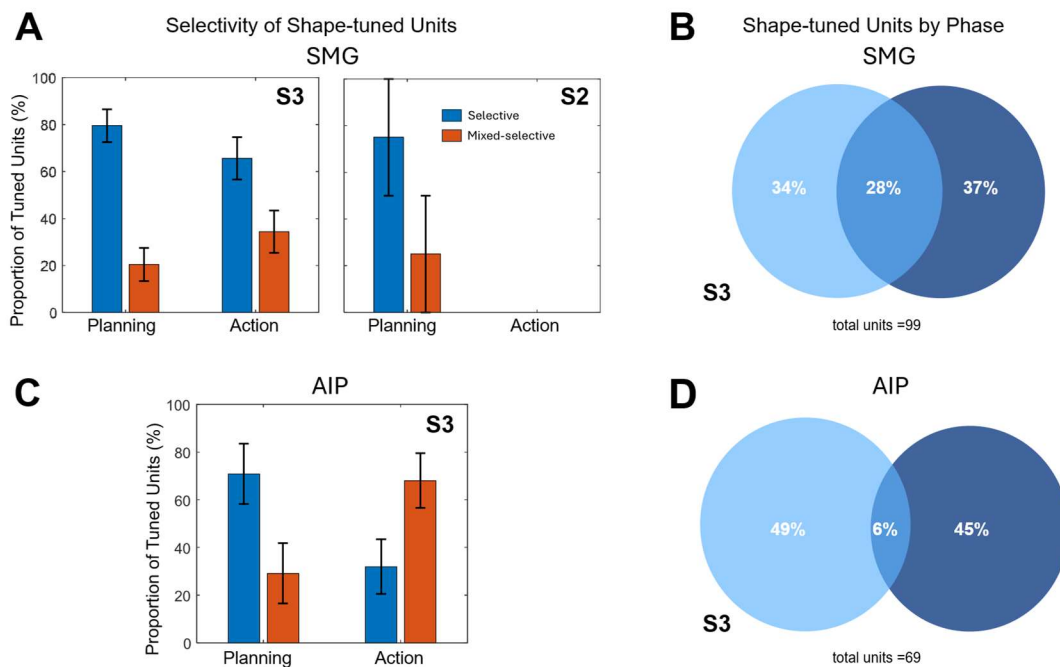


Figure 6-5. Tuning properties of shape-tuned neurons in PPC. Selective vs. Mixed-selective shape-tuned units during Planning and Action in SMG (A) and AIP (C). Shape-tuned units during each phase in SMG (B) and AIP (D).

Discussion

Grasp representations are preserved across changes in object shape

Due to object shape being a primary determinant of grasp selection, varying object shape has the potential to alter neural representations of grasp and reduce the ability to decode intended grasp across different objects. However, our results demonstrate that grasp could be decoded reliably from each cortical region despite changes in object shape, with classification accuracies comparable to those obtained in the original task (**Fig. 6-3**). These findings indicate that grasp representations are largely invariant to change in object shape and suggest the underlying neural subspace encoding grasp is preserved across variations in object geometry. The robustness of grasp decoding across different object shapes further suggests that SMG, AIP, and MC maintain a stable representation of grasp while simultaneously incorporating information about the object. In PPC, we observed that rather than replacing or disrupting grasp-related activity, information about object shape coexists with grasp-related signals (**Fig. 6-4C,F**). This capacity for mixed-selectivity in PPC is consistent with neuronal populations in this region encoding multiple task-relevant variables simultaneously^{67,107}.

PPC's role in visuomotor transformation

Our findings demonstrate that, in addition to encoding intended grasp, posterior parietal cortex encodes object shape, with robust classification observed in both SMG and AIP (**Fig. 6-4C,F**). Notably, object shape encoding was strongest during motor planning, prior to imagined execution, suggesting that these representations contribute to the formation of an appropriate motor plan. This temporal profile is consistent with the proposed role of PPC as an intermediary between visual perception and motor execution, integrating information about object properties and motor intentions to generate a grasp plan⁴. This finding is consistent with NHP literature demonstrating that AIP neurons are selective for object features, such as shape²¹, during motor planning¹². Likewise, functional imaging studies in humans have implicated PPC in processing intrinsic object properties¹⁰⁵ and successful tool use¹²¹. Our results extend this literature by demonstrating that object shape can be decoded from single neurons in human PCC (**Fig. 6-4A,D**), providing direct electrophysiological evidence that object-related information is represented within PPC during grasp planning.

Activity in MC is modulated by object properties, like shape

While we see MC modulated by object properties during both motor planning and imagined motor execution, these properties were not modulating MC in such a way that they were encoded in this region. Rather, it seems these properties affected the firing rates resulting in tuning (**Fig. 6-4H**), but not in a way that is unique, and therefore classifiable, for each object shape (**Fig. 6-4I**). This is similar to the finding in Downey et al. (2017) which showed the presence of an object altering MC (M1) firing rates⁶⁶. Our findings support other studies done in NHPs demonstrating that MC does not encode object properties such as shape¹², although a recent study showed that object shape information was present in M1 throughout grasping³⁴.

Tuning properties in PPC regions may contribute to accurate object shape identification

We found that in PPC, single channels were tuned to shape (**Fig. 6-4A,B,D,E**) and shape could be significantly classified during motor planning (**Fig. 6-4C,F**), suggesting robust encoding of object shape. Interestingly, the tuning architecture differed between PPC regions and across phases. During motor planning, both SMG and AIP were dominated by channels that exhibited high selectivity for individual object shapes, suggesting that shape was represented with considerable specificity before movement onset (**Fig. 6-5A,C**). This specificity could aid in discriminating between potential target objects.

While both regions exhibited selective tuning during planning, their selectivity diverged during motor execution. SMG largely preserved its shape-selective organization and maintained significant shape classification during execution, with an overlap in units tuned during planning and execution, suggesting a relatively stable representation of object shape across the movement (**Fig. 6-5A,B**). In contrast, AIP transitioned toward greater mixed-selectivity, with individual channels responding to multiple object shapes and little overlap in tuning between planning and execution, and overall classification performance declined (**Fig. 6-5C,D**). This shift may mark a change in AIP's role, from visuomotor transformation

and shape integration during planning to receiving feedback about the motor execution to update the plan as necessary during execution¹⁸.

PPC as potential location for grasping BMI

The ability to decode object information is incredibly useful, as evidenced by the presence of objects severely affecting the ability to operate grasp BMIs⁶⁶. The fact that we can independently decode grasp type and object shape, paired with fast latencies and high classification accuracies, make PPC a desirable implant location for grasp BMIs.

Object properties drive grasp selection

One limitation of this study is that different object shapes carry intrinsic properties, and intrinsic properties influence grasp selection, presumably even when imagined⁴. We did our best to maintain and convey the same properties across all shapes by keeping the same appearance (blue, equally transparent which may convey similar weights, similar size, similar location in space/relative to the hand), but we do not know how our participants interpreted these shapes, either consciously or subconsciously. Texture varies slightly, as the ball is rounded and therefore has a more textured appearance than the other shapes that appear smooth. Despite these subtle potential changes, we believe that object shape is being encoded in PPC, as shape is the most salient object property conveyed. This is supported by our ability to significantly classify each object shape (**Fig. S5-1B**). This is not to say that additional object features are not being encoded in PPC; there likely are. Additional research needs to be done to further investigate the encoding of object properties.

Conclusion

In this study, we elucidated the roles related to object shape processing of key regions within the human cortical grasping network using single-unit firing rates from populations in SMG, AIP, and MC during motor imagery. Both regions of PPC (SMG and AIP) strongly encode object shape from the single channel to the population level in behaviorally relevant ways.

Both demonstrate similar classification accuracies during planning, with decoding in SMG persisting into motor execution. As expected, we did not observe object encoding in MC; however, tuning to shape suggests that object properties do modulate the firing rates in MC, which could affect real-time decoders. Importantly, all regions retained their grasp encoding despite the manipulation of object shape.

Chapter 7

CONCLUSION

The overarching goal of this dissertation was to investigate how the human cortical grasping network represents intended grasp and object characteristics at the single-channel level. While previous work has largely focused on movement encoding in the motor cortex, considerably less was known regarding the distribution of grasp- and object-related properties throughout the CGN and how context can affect these representations, particularly in humans. By systematically manipulating context, object size, and object shape while recording intracortical activity from supramarginal gyrus (SMG), anterior intraparietal cortex (AIP), and the precentral gyrus near the hand knob (MC), this work provides new insights into how grasp intentions and object information are distributed across the CGN and how these representations may be leverages for future brain-machine interfaces.

Functional specialization within the cortical grasping network

Taken together, the findings presented in this dissertation support a model in which the cortical grasping network contains both distributed and region-specific representations of grasp and object properties.

Within the posterior parietal cortex, SMG exhibited the richest representation of task-relevant variables. In addition to robust grasp encoding, SMG encoded both object size and shape, demonstrating partial mixed selectivity at the population level. Importantly, the encoding of each variable occurred during motor planning and persisted into motor execution, suggesting that SMG maintains grasp and object information throughout the grasping process. This stable representation is consistent with the proposed role of SMG as a key site in tool use, where sensory information about the object/tool is combined with motor intentions to support accurate object-directed actions.

AIP likewise encoded grasp and object properties, although its functional role appeared more specialized. Whereas non-human primate studies have emphasized AIP's role in processing object features, our findings suggest that human AIP selectively encodes specific object characteristics, with robust encoding of object shape but no significant encoding of object size. This finding is contrary to what we find in NHP literature, with single neurons encoding object properties related to size. Our results suggest that while human AIP and NHP AIP may share certain similarities, they are in fact distinct regions and there are key differences between them that need to be investigated. Furthermore, encoding of grasp and object shape were predominantly strongest during motor planning. This supports much of the literature surrounding AIP and its role in the transformation of visual object information into an appropriate motor plan prior to the onset of movement.

In contrast, neural populations in MC demonstrated encoding largely restricted to motor-related variables. Grasp and hand aperture were robustly encoded, whereas object properties such as shape were not. This pattern is consistent with decades of electrophysiological work demonstrating that MC primarily represents variables related to movement rather than visual characteristics of objects. Our findings also suggest that while MC does not encode object properties, the neural activity in MC can be affected by their presence. Together, these findings reinforce the hierarchical organization of the CGN, in which PPC integrates object information with intended actions while MC executes the selected motor command.

Collectively, these results contribute to a growing understanding of distributed sensorimotor representations within the human cortical grasping network. Rather than functioning as isolated nodes, regions of the CGN appear to encode complementary aspects of object-directed behavior. Grasp representations are broadly distributed throughout the network, whereas object properties are concentrated within the posterior parietal cortex, supporting its role as a critical integration site for visuomotor transformation.

Implications for the intracortical brain-machine interface

Beyond advancing our understanding of basic human neuroscience of sensorimotor processing, these findings have important implications for the future design of intracortical brain-machine interfaces.

One of the most encouraging observations was that grasp encoding remained remarkably stable despite manipulation of object properties. Grasp could be decoded reliably across changes in both object size and shape, suggesting that these object characteristics do not substantially disrupt the neural representation of intended grasp. This stability suggests that future neural decoders may simultaneously extract information about both the intended grasp and the object itself without sacrificing decoding performance. Such robustness is essential for practical prosthetic systems, which must be able to adapt and interact with objects of varying geometries and dimensions. Whether this stability persists during online, closed-loop control remains an important avenue for future study.

This work also highlights the utility of motor imagery as a control signal for BMIs. Functional imaging studies have demonstrated that motor imagery utilizes the same brain regions as real or attempted movements, although the resulting activation of such regions is typically less^{36–40}. It was unclear whether this motor imagery activation would be sufficient to determine intended grasp throughout the CGN. Distinct representations were observed during motor planning and imagined motor execution, demonstrating that execution-related activity is distinct from planning-related activity. Because this neural activity is distinct, planning activity cannot be mistaken for execution activity and therefore the intended action would not be initiated until the user was ready to execute the action. This has practical implications for individuals with spinal cord injury (SCI), for whom motor imagery could provide a sustainable and intuitive method of controlling assistive devices while maintaining full autonomous control over movement timing.

An exciting implication of this work is the potential role of PPC as a source of object information for a grasp BMI. Unlike MC, which primarily encodes grasp-related variables, PPC encodes grasp intention, as well as the object characteristics of size and shape.

Importantly, object-related information emerged during motor planning, before imagined motor execution. Such signals could enable future decoders not only to determine how a user intends to grasp, but also what object they intend to interact with. Because object size and shape are significant determinants of grasp selection, incorporating these signals may improve grasp decoding and allow prosthetic devices to “pre-shape” the hand prior to contact, similar to the anticipatory hand shaping that occurs in intact individuals before grasping an object. Leveraging these higher-order object representations may serve as an important step toward more natural and adaptive neuroprosthetic control.

Future directions

While this dissertation aimed to advance our understanding of grasp and object processing throughout the cortical grasping network, it also raised several questions that warrant further investigation.

First, although grasp could be robustly decoded across cortical regions, the precise nature of these representations remains unclear. It is currently unknown whether neural populations encode grasp as an integrated motor action or individual effectors, such as specific finger positions or joint configurations. Future experiments comparing whole-hand grasps with isolated finger movements may help distinguish between these possibilities and further elucidate the neural basis of grasp representations in the CGN.

Second, the role of the primary somatosensory cortex (S1) within the CGN remains an important unanswered question. Successful grasping critically depends on somatosensory feedback, yet much is still unknown about how S1 interacts with the broader CGN during motor planning and execution. Grasp could be decoded during motor execution from neural populations located within the receptive field of the hand in S1. This suggests S1’s involvement in the grasping network and its potential contribution to grasp-related neural signals. Future studies should therefore investigate how perturbing S1 activity influences grasp encoding in PPC and MC. Experiments utilizing intracortical microstimulation (ICMS)

during motor imagery tasks could determine whether altering S1 activity disrupts grasp encoding and where in the network this occurs.

Understanding these interactions is critical for the development of bidirectional BMIs. Restoring motor control alone is unlikely to produce truly dexterous object manipulation. In order to successfully grasp an object, the subject must also receive sensory feedback regarding the object they are interacting with. If grasp encoding remains stable during ICMS in S1, BMIs may be capable of combining neural decoding of intended grasp with sensory feedback about the object. Such bidirectional devices have the potential to restore more natural and effective grasp/object manipulation for individuals with SCI.

Third, the findings presented in this work should be extended beyond offline analyses into online, closed-loop neural control. This research demonstrates that grasp, object size, and object shape are encoded within the CGN; however, participants did not receive visual or sensory feedback related to their decoded neural activity. In natural grasping, motor commands are continuously updated based on sensory feedback, and it remains unknown how these online corrections influence the neural encoding of grasp- and object-related properties in PPC and MC. Future work should therefore examine how neural activity evolves during closed-loop control, whether object-related encoding remains stable during online decoding, and how visual and somatosensory feedback alter population dynamics.

Addressing these questions will be essential for translating the conceptual framework established here into clinically viable BMIs.

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APPENDIX A: SUPPLEMENTARY FIGURES

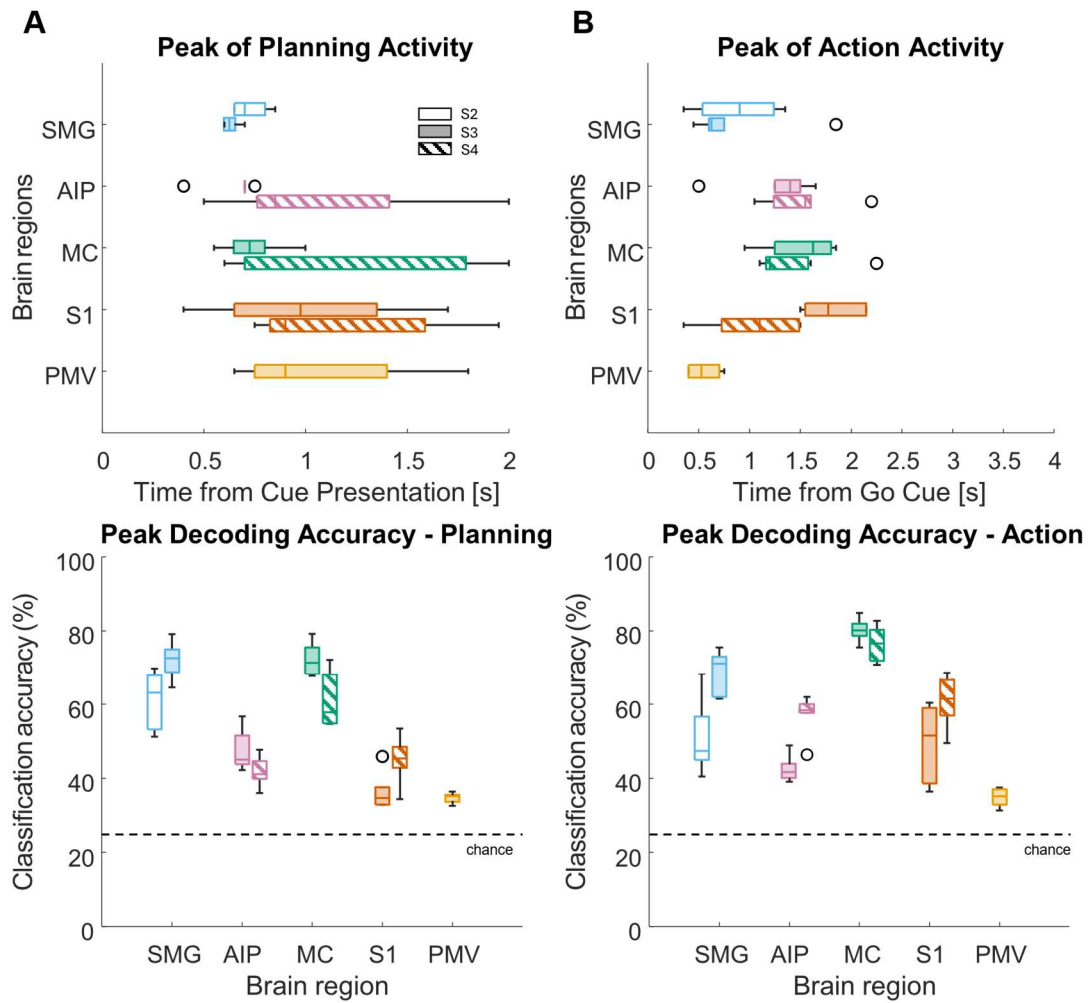


Figure S4-1. Peak classification accuracies during Planning and Action. A) During Planning: SMG peaks at 681 ms (S2,S3) with 67% average, AIP peaks at 854.1667 ms (S3,S4) with 45% average, M1 peaks at 945.8333 ms (S3,S4) with 67% average, S1 peaks at 1094 ms (S3,S4) with 41% average, PMv peaks at 1066.7 ms (S3) with 35% average. B) During Action: SMG peaks at 851 ms (S2,S3) with 60% average, AIP peaks at 1402 ms (S3,S4) with 50% average, M1 peaks at 1473 ms (S3,S4) with 78% average, S1 peaks at 1437 ms (S3,S4) with 55% average, PMv peaks at 550 ms (S3) with 35% average.

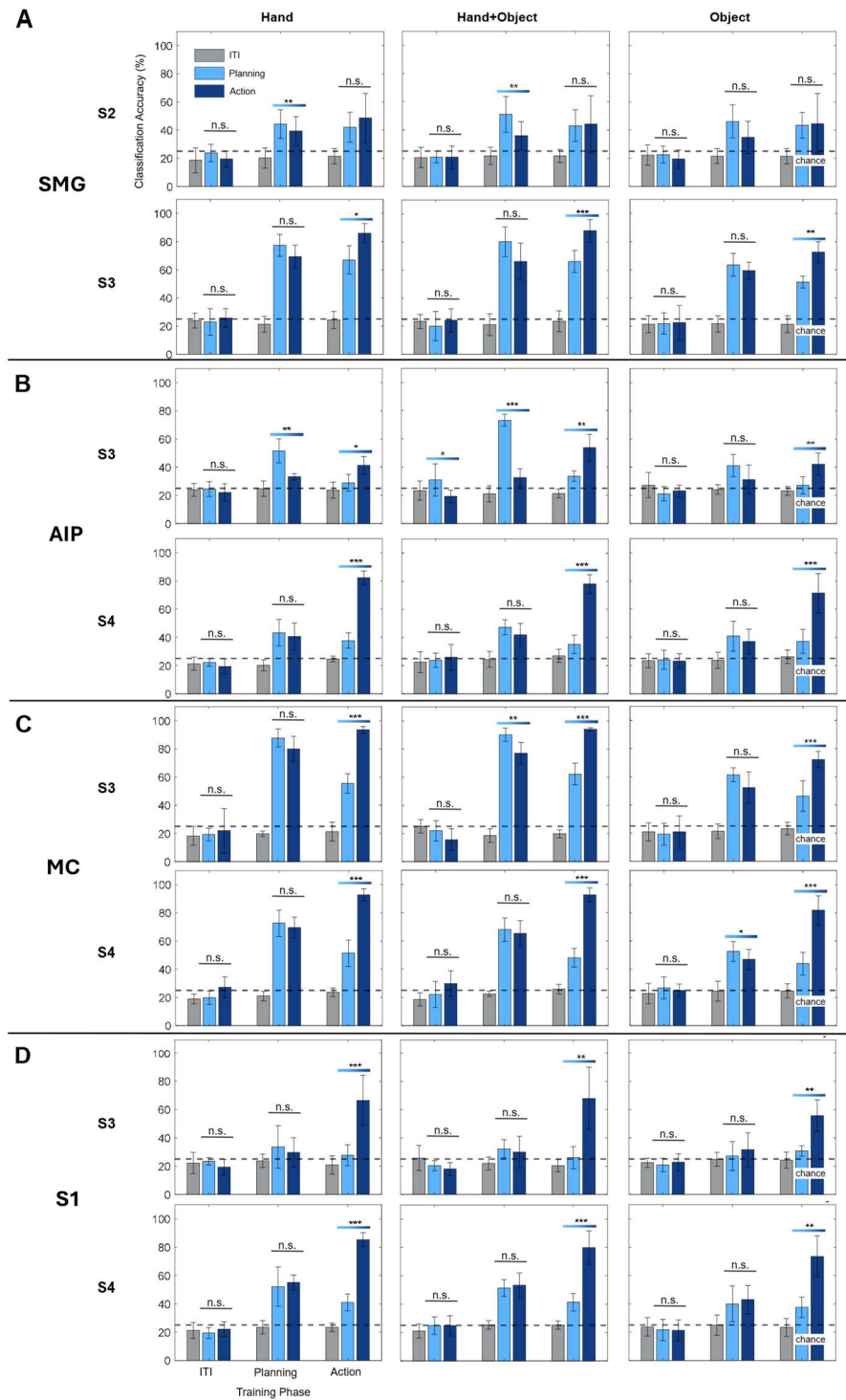


Figure S4-2. Cross-phase classification by context. Cross-phase classification separated by each context (Hand only (col. 1), Hand+Object (col. 2), and Object only (col. 3)) in SMG (A), AIP (B), MC (C), and S1 (D). Planning does generalize to Action, but Action does not generalize to Planning. P-values ≤ 0.05 are denoted with a * symbol, ≤ 0.01 with **, and ≤ 0.001 with ***.

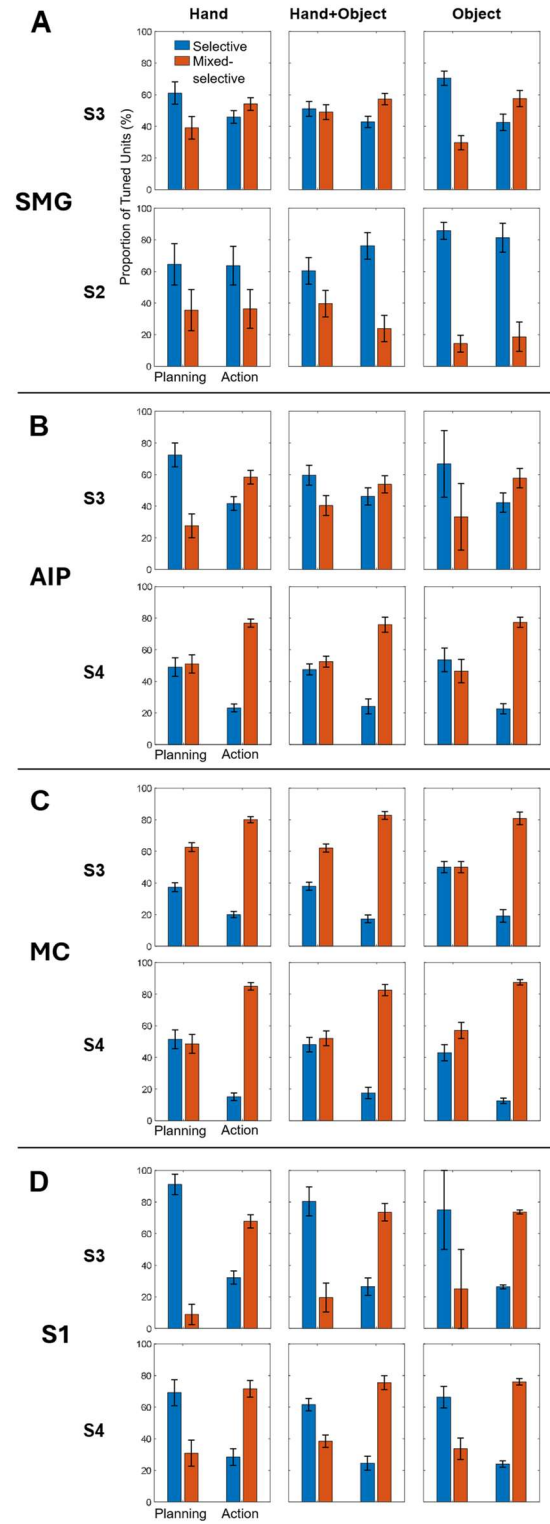


Figure S4-3. Selectivity of Grasp-tuned Units by Context. Proportions of selective vs. mixed-selective grasp-tuned units during Planning and Action in SMG (A), AIP (B), MC (C), and S1 (D) during each context: Hand only (col. 1), Hand+Object (col. 2), and Object only (col. 3).

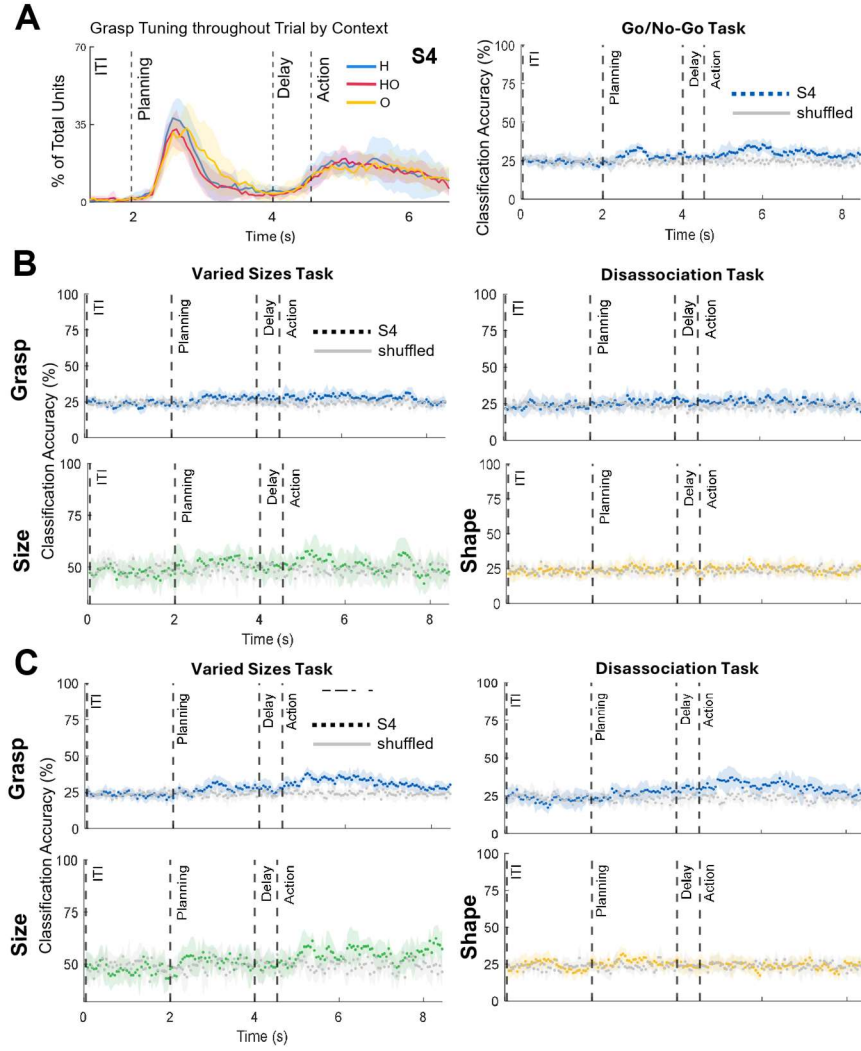


Figure S4-4. S4's tuning and classification results in SMG and AIP. A) S4's SMG array demonstrates tuning to grasp in each context (right), but no significant grasp classification (left). B) Classification of grasp (top), size (bottom right), and shape (bottom left) from S4's SMG array are all chance level. These results are consistent for every task. C) Classification of grasp (top), size (bottom right), and shape (bottom left) from S4's AIP array are nearly all chance level. Some residual grasp decoding appears in the Varied Sizes task, but this is drastically decreased from the Go/No-Go task accuracies and is completely non-significant during the Disassociation task.

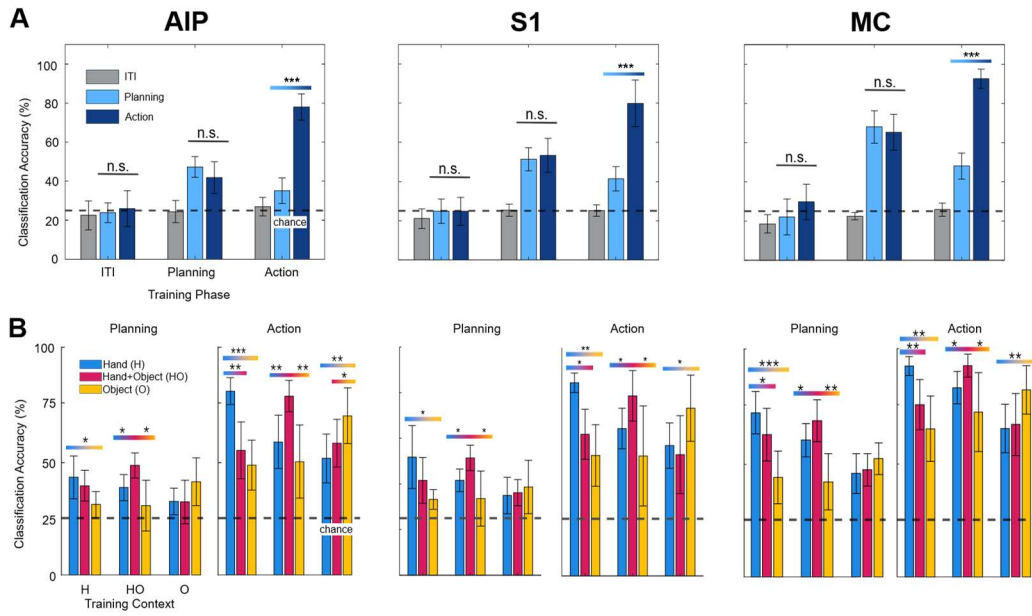


Figure S4-5. S4's AIP has similar response to primary sensorimotor areas. A) Cross-phase classification reveals a similar pattern of complete generalization from Planning to Action, but incomplete generalization from Action to Planning in AIP (left), S1 (middle), and MC (right). Example of HO shown. B) Cross-context classification reveals markedly similar classification patterns during Planning and Action, with each context reaching similar classification accuracies. During Planning, training on HO consistently leads to incomplete generalization. During Action, we observe predominantly incomplete generalization of each context.

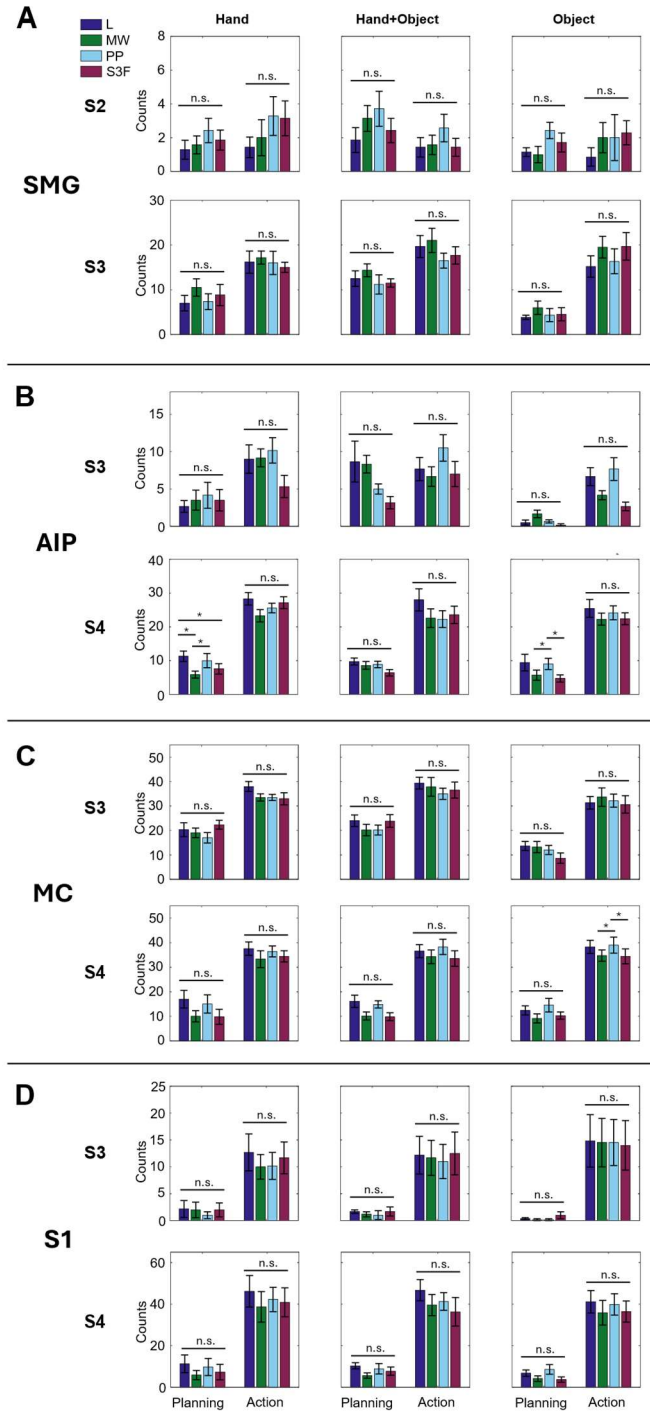


Figure S4-6. Units tuned to each grasp type by context.

Number of units tuned to specific grasp types averaged across sessions for each participant in SMG (A), AIP (B), MC (C), and S1 (D). P-values ≤ 0.05 are denoted with a * symbol, ≤ 0.01 with **, and ≤ 0.001 with ***.

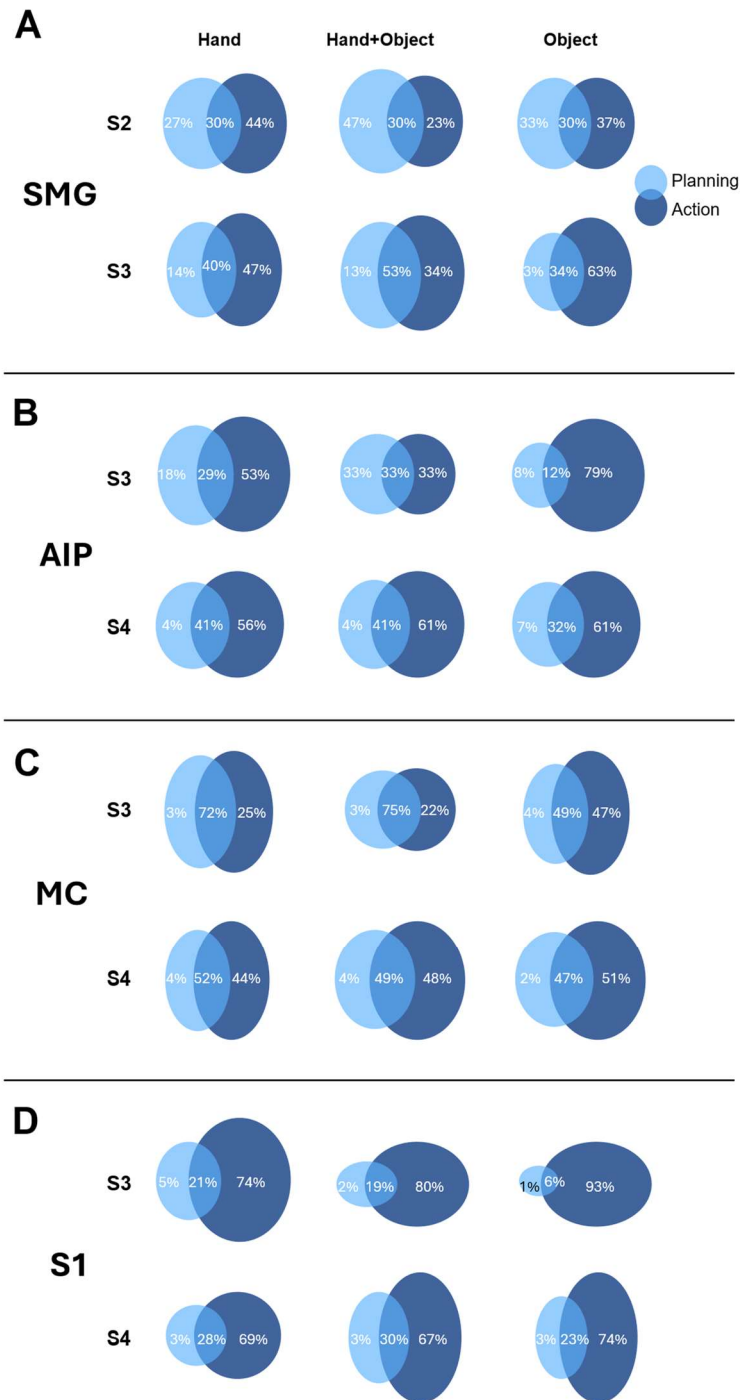


Figure S4-7. Grasp-tuned units during each phase for each context. Proportion of grasp-tuned units during Planning (light blue) and Action (dark blue) for each participant in SMG (A), AIP (B), MC (C), and S1 (D).

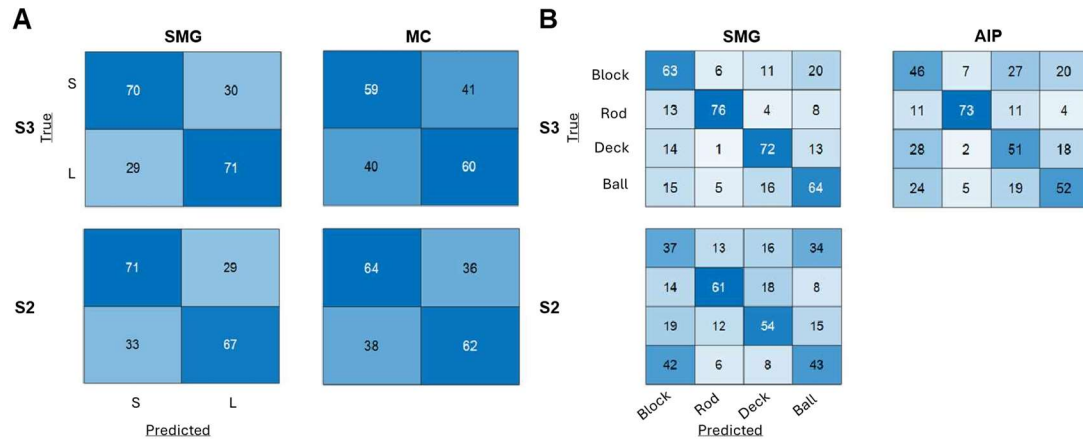


Figure S5-1. Decoding of individual sizes and shapes during Planning. A) Both sizes are classified equally well during Planning in SMG and MC. B) While all shapes are classified above chance (25%), specific shapes are classified with higher accuracy than others. SMG demonstrates a minor preference for the rod and deck, whereas AIP demonstrates the highest accuracy for classifying the rod.

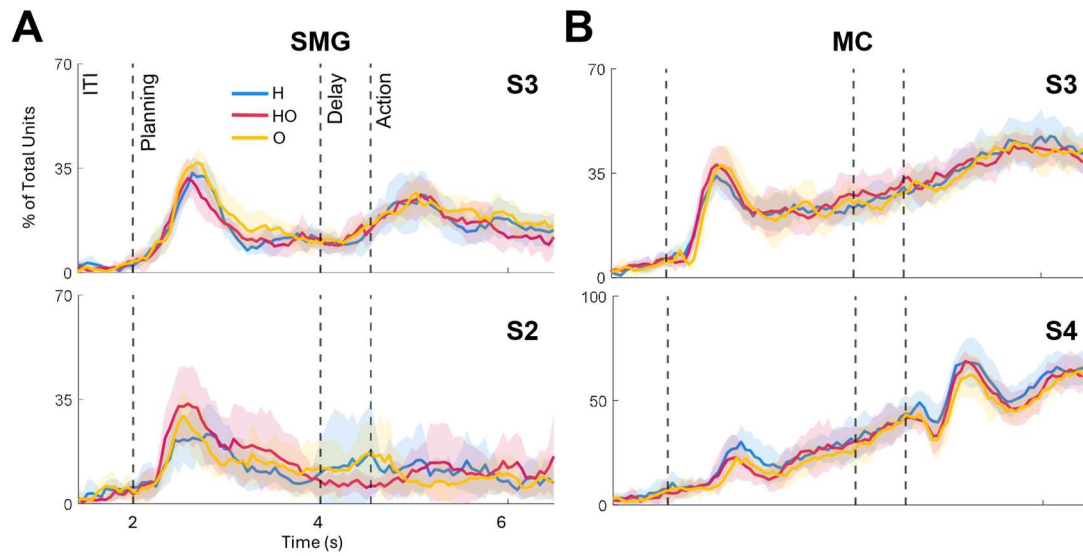


Figure S5-2. Size-tuned units by context. Similar proportions of units are tuned to size within each context during both Planning and Action phases in SMG (A) and MC (B).