

Copyright
by
Justin Kilmarx
2023

**The Dissertation Committee for Justin Kilmarx Certifies that this is the approved
version of the following Dissertation:**

**Decoding Mental Representations for Neurofeedback in Motor and
Imagery Tasks**

Committee:

James Sulzer, Supervisor

Jarrold Lewis-Peacock, Co-Supervisor

José del R. Millán

Farshid Alambeigi

Dragan Djurdjanovic

**Decoding Mental Representations for Neurofeedback in Motor and
Imagery Tasks**

by

Justin Kilmarx

Dissertation

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Doctor of Philosophy

The University of Texas at Austin

August 2023

Dedication

This dissertation is dedicated to my family who have always supported and encouraged me throughout my life and my wife who is my motivation and inspiration.

Acknowledgements

I would like to first thank my advisors, James Sulzer and Jarrod Lewis-Peacock – for providing a tremendous environment and support system to pursue my passions. This work would not have been possible without their constant advice and constructive feedback. My undergraduate research team from The University of Tennessee, Xiaopeng Zhao, Reza Abiri, and Soheil Borhani – for taking me under their wing, introducing me to the Brain-Computer Interface field, and encouraging me to pursue a graduate degree. All of my colleagues and lab mates in engineering and psychology – for listening to my countless lab presentations, providing thoughtful feedback, participating in my research, and for their friendship throughout this journey. Ethan Oblak and Remington Mallett – whose initial work and ideas laid the foundation for my first project. José del R. Millán – whose insight and advice made this research possible. Ivan Tashev and the Microsoft BCI team – for providing the opportunity to rekindle my passion for BCI and providing the resources necessary to complete this research. My funding sources from the National Science Foundation (Grant No. DGE-1610403), Robert J. Kleberg, Jr. and Helen C. Kleberg Foundation Medical Research grant, and the National Eye Institute of the National Institutes of Health (Award No. R01EY028746). My parents, Robert and Tami Kilmarx, and the rest of my family – for always believing in me and encouraging me to be the best that I can be. Last but not least, my wife, Savannah Kilmarx – whose love and support keeps me sane and grounded.

Abstract

Decoding Mental Representations for Neurofeedback in Motor and Imagery Tasks

Justin Kilmarx, Ph.D.

The University of Texas at Austin, 2023

Supervisor: James Sulzer

Co-Supervisor: Jarrod Lewis-Peacock

The inability to execute coordinated movements can have a profound impact on an individual's ability to complete the activities of daily living. Often times, these impairments arise as a result of neurological injury such as a stroke. Conventional physical therapy of the affected limb is often ineffective, possibly because it treats the symptom rather than the cause of the problem: impaired motor control circuitry in the brain. A potential method to address this issue is to employ neuroimaging technology to guide neuroplastic changes in the brain to restore motor function. The first aim of this dissertation was to develop and validate the use of a neurofeedback training target derived from functionally aligned data of healthy individuals. Our results showed a significant improvement in classification accuracy of individual finger presses when group data was aligned based on function rather than anatomy. This indicates that our functionally aligned template could provide an effective target for neural reinforcement of finger individuation beyond traditional anatomically aligned templates.

For more severely impaired individuals, neuroimaging can also be used to develop assistive technologies by creating a connection between the brain and an external device, a technology known as a Brain-Computer Interface (BCI). In this work, we sought to address some of the current gaps in BCI usability by investigating the implementation of a visual imagery control paradigm. The second aim in this dissertation attempted to characterize the flexibility of visual imagery by mapping out the neural representational space of imagery for multiple image categories. While we were able to significantly identify when an individual was engaged in visual imagery compared to resting, our classifier was unable to accurately discern between the category-level neural activity. Our third aim expounded on this topic by investigating some of the key experimental components that contribute to successful performance. The results showed that visual imagery following a perception cue provided a stronger, more easily classifiable signal than visual imagery following an auditory cue. These results indicate that visual imagery is a challenging, yet possible BCI paradigm that could be useful in situations where other methods are ill suited.

Table of Contents

List of Figures	xii
CHAPTER 1.....	1
INTRODUCTION.....	1
Brain-Computer Interface	2
Brain Imaging Modalities	2
Rehabilitative BCIs.....	3
Analysis of fMRI Data.....	6
Neurofeedback for Stroke Recovery.....	7
Assistive BCIs.....	9
Common BCI Control Paradigms.....	10
Visual Imagery-Based BCIs	14
CHAPTER 2.....	17
CREATING A COMMON TEMPLATE FOR NEURAL REINFORCEMENT OF FINGER	
INDIVIDUATION	17
Abstract	17
Introduction.....	18
RESULTS	23
Hyperalignment provides improved between-subject classification	23
Physical and representational overlap between neighboring fingers.....	25
Hyperaligned common model generalizes to novel fingers.....	27
Hyperaligned common model generalizes to new individuals	29
Effect of subject order on common model generation.....	30
How much data should be collected for a new participant?	32

Discussion	33
Methods.....	36
Participants.....	36
Apparatus	37
Imaging parameters.....	37
Region of interest.....	38
Data collection	38
Within-subject decoding of individual finger presses	39
Between-subject decoding of individual finger presses using anatomical alignment	40
Between-subject decoding of individual finger presses using hyperalignment.....	40
Calculating mean deviation of uninstructed fingers	41
Representational similarity analysis	42
Removing fingers from hyperalignment parameter calculations.....	42
Aligning a new participant to a pre-established common model.....	42
Varying amount of training data	43
Statistical Analysis.....	43
CHAPTER 3.....	44
DETERMINING THE NEURAL REPRESENTATIONAL SIMILARITY OF MULTIPLE OBJECT CATEGORIES DURING VISUAL IMAGERY.....	44
Abstract	44
Introduction.....	45
Limitations of current BCI control paradigms.....	45
Investigating visual imagery as an alternative BCI control strategy	47

Limitations of previous visual imagery studies	48
Mapping the representational space of visual imagery categories	49
Methods.....	51
Participants.....	51
Inclusion criteria	51
Task Protocol	52
Experimental setup	54
Data preprocessing.....	54
Feature extraction and category-level classification.....	55
Item-level classification	56
Rest vs. Imagery classification	57
Evaluation of performance.....	57
Results.....	58
Visual Imagery Black Hole Algorithm.....	63
Discussion.....	65
CHAPTER 4.....	68
EVALUATING THE FEASIBILITY OF VISUAL IMAGERY FOR AN EEG-BASED BRAIN- COMPUTER INTERFACE.....	68
Abstract	68
Introduction.....	68
Limitations of current BCI control paradigms.....	70
Investigating visual imagery as an alternative BCI control strategy	72
Limitations of previous visual imagery studies	73
Identifying neural mechanisms contributing to BCI performance	74

Including additional biological signals can improve BCI performance	75
Methods.....	76
Participants.....	76
Task protocol	76
Stimuli.....	79
Data preprocessing.....	80
Visual perception classification	80
Visual Imagery Classification.....	80
Cross-task classification	81
Improving signal-to-noise with averaged data.....	81
Evaluation of performance.....	82
Pupillometry data analysis	82
Results	83
Discussion	90
CHAPTER 5.....	94
CONCLUSIONS AND FUTURE WORK.....	94
Conclusions.....	94
Future work.....	95
REFERENCES.....	98

List of Figures

- Figure 1.1: Overview of fMRI neurofeedback. A participant first performs a task during fMRI imaging to identify the unique patterns of brain activity associated with each action. This map between the brain activity and behavior is used as a training target for subsequent neurofeedback experiments. During neurofeedback, the participant is provided a visual representation of how well their brain activity during that trial matches the established training target in order to reinforce the desired behavior. 5
- Figure 1.2: Overview of hyperalignment. Hyperalignment uses the Procrustes transformation to align the neural data of multiple individuals according to neurological function. 8
- Figure 1.3: Overview of common BCI paradigms. Exogenous paradigms include the visual P300 stimulus, the steady state visual evoked potential, visual observation of images, auditory stimulation, or somatosensory (tactile) stimulation. Endogenous paradigms include motor imagery (sensorimotor rhythms and imagined body kinematics), visual imagery, speech imagery, or mental effort (mental object manipulation, math calculations, etc.). 11
- Figure 2.1: Overview of functional-based alignment. Neural patterns are rotated from subjects' native space into a common template space. This template can then serve as a surrogate neurofeedback training target for a new participant who is unable to create an autologous target due to neurological injury. 21

Figure 2.2: Experimental task protocol. Participants were cued to press one finger for 10 seconds while maintaining a constant force on the non-cued fingers. Feedback representing the number of correct presses was presented at the end of each trial. This process was repeated for 8 runs of 20 trials each. 22

Figure 2.3: Classification model comparison. Hyperalignment provides better between-subject classification accuracy (88.8%) than conventional anatomical alignment (46.0%). Within-subject classification (94.7%) is also included for comparison. Individual participants are presented beside the mean as circles with a black outline. Error bars indicate a 95% confidence interval. * $p < .05$, ** $p < .001$ 24

Figure 2.4: Representational overlap between neighboring digits contribute to increased misclassification of finger presses. (A) Confusion matrix of classifier predictions trained on hyperaligned data. (B) Mean deviation from baseline force of the uninstructed fingers (filled bars) compared to the mean press force of each instructed finger (hollow bars). Error bars indicate a 95% confidence interval. (C) Average representational dissimilarity matrix of neural patterns associated with finger presses. (D) Two-dimensional projection of the representation structure using multidimensional scaling. Dissimilarity is reflected by the distance in the 2 dimensions. The mean representation across participants in panel d is shown as an 'X'. Individual digits are represented by different colors and numbers (see key in center). Data is only shown from the 11 participants from Oblak et al.¹¹⁷ whose force data was collected. 26

Figure 2.5: Hyperaligned common template generalizes to novel fingers. Overall classification accuracy for all four fingers when all fingers are included in hyperalignment parameter calculations (88.8%), when one finger is removed during hyperalignment (80.6%), when two fingers are removed during hyperalignment (66.5%), and anatomical alignment with all fingers included (46.0%). Individual participants are presented beside the mean as circles with a black outline. Error bars indicate a 95% confidence interval. Dashed line indicates chance level (25%). ** $p < .001$ 28

Figure 2.6: Decoding effects of using all participants to create a template space versus hyperaligning a new participant to a pre-established template. Individual participants are presented beside the mean as circles with a black outline. Error bars indicate a 95% confidence interval.....30

Figure 2.7: Histogram of mean classification accuracy for hyperalignment of 2000 permutations of random subject order. Red vertical bars demarcate the 95% confidence interval. 31

Figure 2.8: Number of runs needed to hyperalign individuals and train an accurate classifier. The results indicate that at least two runs are necessary to accurately align a new participant to a pre-established common model. At least three runs are necessary for the between-subject classifier using all participants to create the common model and the within-subject classifier trained in a subject's native space. Shaded outline indicates 95% confidence interval. * $p < .05$, ** $p < .001$ 33

Figure 3.1: Experimental task protocol. (A) Set of 30 images from the six different object categories. (B) Each trial, individuals performed visual imagery of the cued images. One image and its word association from each category was familiarized before each run. Participants rated how difficult it was to imagine each image at the end of every run. 53

Figure 3.2 Category-level classification results. To assess the ability to classify between the visual imagery of various object categories, we implemented a long short-term memory (LSTM) neural network. The data from each trial was divided into three overlapping windows and fed into the LSTM network. This provided an overall classification accuracy of 19.72% (significance threshold = 25%). While the overall accuracy across the six categories was not significant, the classifier was able to identify human faces and natural objects more accurately. 59

Figure 3.3 Item-level classification results. A. Confusion matrix for 30-class item-level classification results (mean accuracy 6.67%, significance threshold 4.06% ($p < 0.01 \times 10^{-10}$) B. Multi-Dimensional Scaling plot of classification results shows strong bias to items that appeared within the same experimental run. 61

Figure 3.4 Imagery vs Rest classification results. Our results indicate that our classifier can accurately detect the performance of visual imagery compared with rest beyond the level of chance (75.4%, significance threshold 52.33%, $p < 0.01 \times 10^{-15}$). 62

Figure 3.5 Black hole algorithm implementation outlined by Lorella et al. ¹⁰⁶ The data is split into three groups: two for creating and training the CNN model using the black hole algorithm and one left-out group for validation of the model.....	63
Figure 3.6 Black hole algorithm results. A. Confusion matrix obtained using the best model configuration identified from the black hole algorithm on the internal testing set. B and C. Box plot for the classification scores within two representative subjects showing that the model is overfitting to the data used within the black hole search.....	65
Figure 4.1: Overview of a closed-loop BCI system. Participant performs visual imagery while neural data is recorded. That data is processed and classified to predict the user's intention. Feedback representing the predicted class is provided to allow self-modulation.....	70
Figure 4.2: Task protocol. (A) Observation cue block protocol. (B) Auditory cue block protocol.	78
Figure 4.3 Sample images used during experimental procedure. Participants selected one familiar image for each category of animals, famous faces, objects, or recognizable scenery and landmarks.	79
Figure 4.4. Classification of observation periods. A. Mean confusion matrix obtained from classification of neural data during visual observation of the four image categories. B. Heatmap of accuracy obtained during channel-wise classification of observation periods across all subjects.....	84

Figure 4.5. Classification of imagery periods following observation cue. A. Mean confusion matrix obtained from classification of neural data during visual imagery of the four image categories following the observation cue demonstrates significantly above chance classification accuracy of 30.05% (significance threshold: 29.58%, $p < 0.05$). B. Heatmap of accuracy obtained during channel-wise classification of imagery periods following the observation cue across all subjects. C. Heatmap of accuracy obtained during channel-wise classification of imagery periods following the observation cue for the subject with the highest accuracy. 85

Figure 4.6. Classification of imagery periods following auditory cue. Mean confusion matrix obtained from classification of neural data during visual imagery of the four image categories following the auditory cue provides an average classification accuracy of 26.45%. 86

Figure 4.7 Cross-task classification results. Classification accuracy of each condition when the data from A. observation (38.47%) and imagery periods following observation cue (27.30%) were concatenated together, B. observation (36.50%) and imagery periods following auditory cue (26.42%) were concatenated, and C. imagery periods following observation cue (27.90%) and auditory cue (25.70%) were concatenated. ...87

Figure 4.8 Mean pupil diameter for a representative subject. A. Mean pupil diameter during the observation cue blocks B. Mean pupil diameter during the auditory cue blocks. The gray shaded region from -1 to 0 indicates the baseline period used for baseline correction. The blue shaded region around the pupil diameter trace demarcates the 95% confidence interval....89

CHAPTER 1

INTRODUCTION

The inability to execute coordinated movements can have a profound impact on an individual's ability to complete the activities of daily living. Often times, these impairments arise as a result of neurological injury such as a stroke. Each year, approximately 15 million people worldwide suffer from a stroke making it the leading cause of serious long-term disability¹. Conventional physical therapy of the affected limb is often ineffective, possibly because it treats the symptom rather than the cause of the problem: impaired motor control circuitry in the brain²⁻⁴. Symptom-based therapy could lead to unintended maladaptive neuroplasticity in which the neural representations for a given movement are remapped in a suboptimal way^{5,6}. A potential method to address this issue is to employ neuroimaging technology to guide neuroplastic changes in the brain to restore motor function. For more severely impaired individuals, neuroimaging can also be used to develop assistive technologies by creating a connection between the brain and an external device. In this way, the interface can decode the user's intention and allow them to interact with the external world without making any overt movement. This work explores to lay the groundwork for these approaches by **(1)** developing a proper neural training target for the rehabilitation of finger individuation and validating its use in healthy individuals, **(2)** exploring the neural representation boundaries between object categories during visual imagery, and **(3)** investigating the experimental factors contributing to successful performance in a visual imagery Brain-Computer Interface.

BRAIN-COMPUTER INTERFACE

A brain-computer interface (BCI) is a technology that facilitates communication between the brain and an external device without input from peripheral nerves or muscles⁷⁻⁹. The BCI instead translates measured brain activity to a control signal that reflects the user's intended action¹⁰. Such a device could allow an individual with movement impairments¹¹ or even the general public^{12,13} a new way to interact with the world around them. BCIs can be classified as either rehabilitative or assistive depending on their application¹⁴. A rehabilitative BCI aims to improve or restore a desired behavior through direct manipulation or self-modulation of a target neural activity¹⁴. On the other hand, an assistive BCI aims to substitute lost functions by providing a direct connection between an external device and an intended action¹⁴.

BRAIN IMAGING MODALITIES

One of the first steps when designing a BCI system is to identify how best to acquire the neurological signal. These measurements can involve either invasive or noninvasive techniques. Electrocorticography (ECoG) is perhaps the most common invasive method that measures neural activity from sensors placed directly on the cortical surface⁸. Other invasive methods used in BCI applications include intracranial neuron recordings such as single-unit activity, multi-unit activity, and local field potentials⁸. The high spatial and temporal characteristics of these invasive methods have shown significant success in BCI applications; however, they have significant drawbacks due to the risks associated with surgical implantation and the degradation of recorded signals as the cortex reacts to the implanted electrodes¹⁰. For this reason, noninvasive approaches such as functional magnetic resonance imaging (fMRI), near-infrared spectroscopy (NIRS),

magnetoencephalography (MEG), and electroencephalography (EEG) have become more popular for use in human participants¹⁰.

EEG is the most common noninvasive method for BCI applications due to its direct measures of neural activity, low cost, and portability^{8,10}. This method measures the electrode activity in the brain during synaptic excitations of neuronal dendrites through electrodes placed on the surface of the scalp¹⁰. While EEG can provide a good temporal resolution of measured brain activity, the poor spatial resolution can limit its success in applications that requires more precise measurements such as with individual finger movements. In these applications, fMRI can provide a more comprehensive spatial coverage of the necessary brain regions.

fMRI provides an indirect approximation of brain activity through the measurement of the blood oxygenation level dependent (BOLD) signal¹⁵. This signal measures the contrast of hemoglobin versus deoxyhemoglobin in small areas of the brain known as voxels¹⁶. In fMRI measurement, these voxels are typically on the scale of 2-3 mm. Furthermore, this change in local oxygenation level is not an instantaneous process. The measured peak in the BOLD signal typically occurs at a 6 sec delay after the start of neural activation. This can cause difficulty in BCI applications involving real-time feedback as the participant will not receive information about their neural activity until several seconds after their behavior.

REHABILITATIVE BCIs

A rehabilitative BCI, also known as a neurofeedback-based BCI, aims to restore or improve a target behavior through manipulation or self-modulation of neural activity^{14,17}. Studies using noninvasive brain stimulation have demonstrated that restoration of healthy

brain activity in the ipsilesional hemisphere through direct manipulation can engender functional recovery in an impaired hand^{18–21}. This is supported by one hypothesis referred to as negotiated equilibrium²². This hypothesis posits that plasticity in the cortex and spinal cord exists in equilibrium where changes in the brain mediates changes in the spinal cord. When a movement occurs, the spinal cord feeds information to the brain regarding the performance which can alter the neural representations. After stroke, damage to the ascending sensory tracts has removed the input necessary to guide neuroplasticity²². Additionally, this damage might not sufficiently reward the activity in the corticospinal tract to induce and maintain beneficial plasticity²³. This might be a contributing factor to why strengthening the residual motor representations through brain stimulation can lead to functional recovery while traditional physical therapy of the affected limb falls short.

While transcranial stimulation has been shown to facilitate improvements in hand function, it is not suitable for all applications such as for the recovery of individual finger movements. The primary motor cortex contains populations of neurons whose activity correspond to individual finger presses with considerable overlap²⁴. Transcranial stimulation targeting the entire motor cortex would be unable to localize each individual finger. However, it is possible to target this granular activity through functional magnetic resonance imaging²⁵.

Neurofeedback has been proposed as a method to both monitor and target the affected circuitry in the brain²⁶. In this procedure, participants are presented with a visual, auditory, and/or haptic representation of their neural activity in real time for the purpose of self-modulation¹⁷ (**Figure 1.1**). Neurofeedback relies on the principles of operant

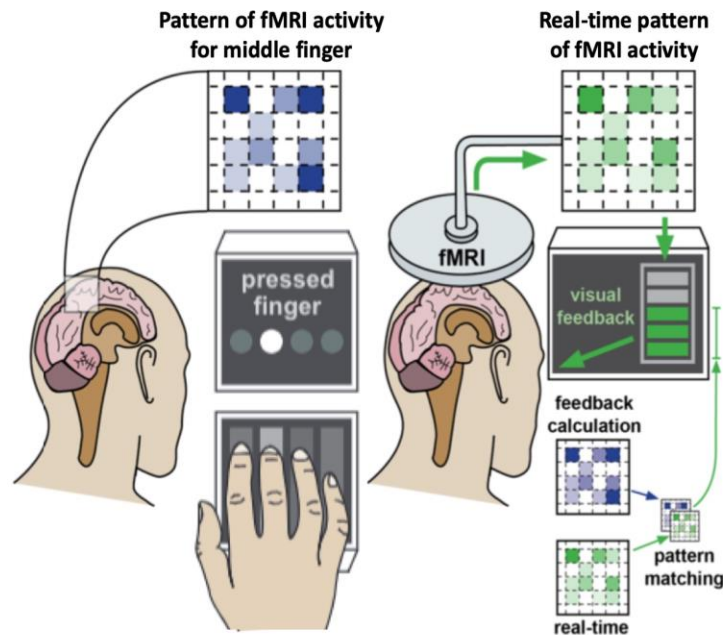


Figure 1.1: Overview of fMRI neurofeedback. A participant first performs a task during fMRI imaging to identify the unique patterns of brain activity associated with each action. This map between the brain activity and behavior is used as a training target for subsequent neurofeedback experiments. During neurofeedback, the participant is provided a visual representation of how well their brain activity during that trial matches the established training target in order to reinforce the desired behavior.

conditioning where the provided feedback serves as a reinforcement for a desired behavior²⁶. In a seminal work by Shibata et al.²⁷, fMRI neurofeedback was shown to influence neural activity in the visual cortex. Participants in this study learned to self-modulate an autologous target pattern of brain activity corresponding to a visual grating without stimulus presentation or explicit instruction. This ability to learn to self-modulate neural activity resulted in improved behavioral performance for the target. Neurofeedback has also been explored in therapeutic fields such as the treatment of schizophrenia^{28,29},

depression^{30,31}, Parkinson's disease³², attention disorders^{33,34}, chronic pain³⁵, and addiction^{36,37}. There have also been several studies investigating neurofeedback as a treatment for motor recovery after stroke³⁸⁻⁴⁰, although none of these have attempted to target fine-motor control of individual fingers.

ANALYSIS OF FMRI DATA

Conventional analyses of fMRI data focused on characterizing the relationship between a cognitive task and an activated brain region. In this approach, the average level of neural activity in different brain regions is quantified using what is known as a univariate analysis. While this approach can provide useful information about the underlying neurological functions associated with a given task in a particular region of the brain, it often removes the fine-grained patterns and signals from weaker voxels that can be beneficial in discriminating between the experimental conditions⁴¹. In contrast, multivariate approaches have been developed to analyze these spatially distributed patterns of brain activity to better glean information about an individual's cognitive state⁴². This approach, termed multivariate or multi-voxel pattern analysis (MVPA), can be used to better understand how information is represented and organized in a given brain region⁴³. MVPA works on a voxel-by-voxel level to identify patterns in the activity levels corresponding to different stimuli.

While MVPA can be used to identify differences in the neural patterns between experimental conditions, the representational structure of these responses between conditions can be operationalized by performing a representational similarity analysis⁴⁴. This approach allows the comparison of representational geometry regardless of modality by assessing the pairwise distances between categories rather than the responses

themselves⁴⁵. Kriegeskorte and colleagues pioneered this approach using fMRI in humans and single-cell recordings in non-human primates by demonstrating that object representations in the inferior temporal cortex form categorical clusters that are similar across species⁴⁵. Recent studies using magnetoencephalography (MEG)⁴⁶ and EEG⁴⁷ have also used the same image sets as Kriegeskorte⁴⁴ to further study the structure and temporal evolution of the representational space of these objects. Correlation in the brain activity between the stimuli or classifier evidence from multivariate pattern classifications can be used to reveal the category selectivity in response to the various experimental conditions.

NEUROFEEDBACK FOR STROKE RECOVERY

In a typical neurofeedback experiment, the neural target to be reenforced is derived anatomically or functionally from the participant⁴⁸. After stroke, however, altered neural representations possibly resulting from maladaptive neuroplasticity and an inability to individuate finger movements^{49,50} would make autologous neural training targets untenable. Therefore, it is necessary to develop a template of fMRI brain activity from healthy participants to serve as a surrogate training target.

Creating an fMRI template requires compounding data from multiple participants to generate a representative brain activation pattern for a given movement. Anatomical alignment based on brain landmarks is perhaps the most conventional method of between-subject analysis; however, this alignment procedure is often imperfect due to topographic variability between individuals⁵¹⁻⁵⁴ and produces lackluster classification

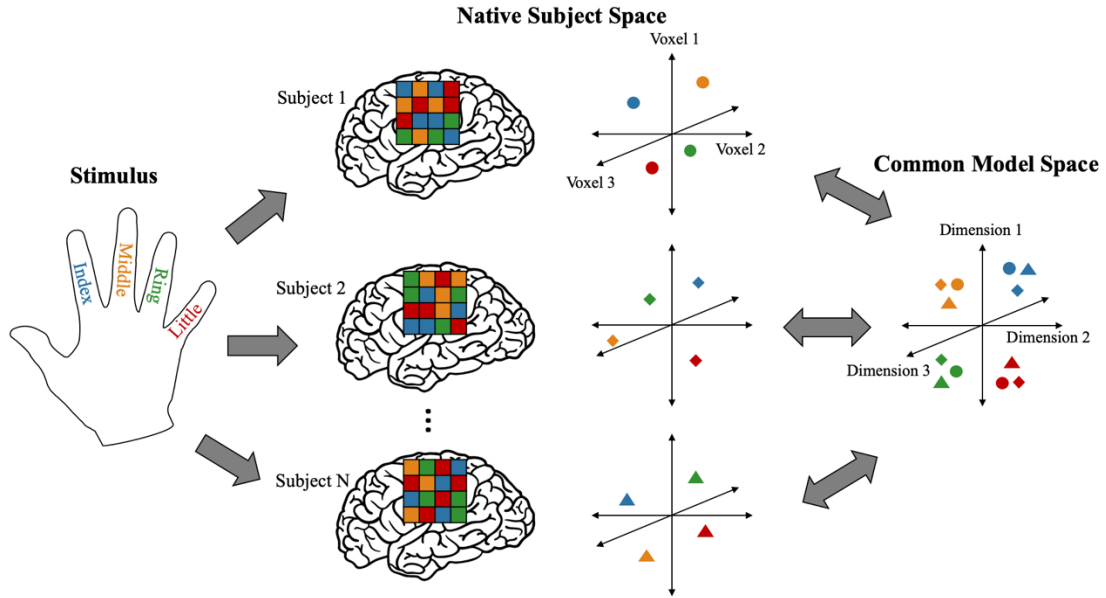


Figure 1.2: Overview of hyperalignment. Hyperalignment uses the Procrustes transformation to align the neural data of multiple individuals according to neurological function.

performance^{55–57} that is likely insufficient for neurofeedback training⁵⁸. More recently, a new technique known as *hyperalignment* has emerged as a method for improving across-subject fMRI analysis^{56,59,60}. Hyperalignment works by applying the Procrustean transformation⁶¹ to functionally align voxel activity across individuals into a common model space (**Figure 1.2**). By compounding data across multiple individuals, a hyperaligned model benefits from a greater pool of training data and can often outperform within-subject methods^{55,57,62}.

Hyperalignment transformation is carried out in three stages⁵⁶. In the first stage, data from two participants are brought into optimal alignment using the Procrustean transformation. Then, a third individual is brought into alignment with the mean response

from the first two participants. This process is continued for each remaining individual by iteratively aligning them to the mean responses of the previous participants. In the second stage, this iterative process is repeated to align each individual with the group mean response from the first stage. The third stage consists of calculating the transformation parameters necessary to bring each participant into alignment with the common model space generated in stage two.

The first aim of this dissertation was to investigate the use of functional alignment of brain data across healthy participants to create an idealized neural template to be used as a training target for new participants. To accomplish this, we employed multi-voxel pattern analyses in an offline study with healthy individuals to assess the prediction accuracy and robustness to missing data of pre-trained functional templates corresponding to individual finger presses. This analysis also addressed important questions for verifying the use of hyperalignment for motor cortical regions, the effect of subject order on hyperalignment, and the amount of data needed to create an accurate surrogate template.

ASSISTIVE BCIs

The goal of an assistive BCI is to substitute lost functions by providing a direct connection between an external device and an intended action¹⁴. This concept has gained traction in recent years as a potential way to provide patients with severe neuromuscular disorders a way to communicate and interact with the world around them^{11,63}. This can improve the individual's quality of life as well as reduce the cost of intensive care⁸. This technology has since grown to cover applications such as robotic control^{64–66}, communication^{67,68}, and even entertainment and gaming^{12,69–71}.

A BCI system consists of five primary stages to translate a measure brain activity into a control signal: signal acquisition, preprocessing and signal enhancement, feature extraction, classification, and the control interface⁸. In the first stage, the neural signal is captured through invasive or noninvasive means (see **Brain Imaging Modalities** above for more information). Next, the signal undergoes several preprocessing steps in order to remove artifacts and noise and prepare the signal for further processing. In the feature extraction phase, relevant temporal, spatial, or spectral features are identified in the signal to be used for prediction of the user's intent. This extraction of meaningful information is a challenging task as the brain signals are nonstationary and easily distorted by overlapping neural activity or artifacts such as from motion or other physiological properties. The classification stage uses these discriminant features to predict the intended action of the user. Finally, the control interface stage translates this prediction into a command signal for the connected device⁸.

COMMON BCI CONTROL PARADIGMS

When designing a BCI system, one major consideration is the means of interaction a participant will use to perform the task. These control paradigms can be divided into two methodologies: exogenous paradigms based on the brain's response to an external stimulus, and endogenous paradigms where participants learn to modulate their brain activity using mental imagery¹⁰ (**Figure 1.3**). One of the most popular exogenous paradigms in EEG relies on the visual P300 response^{10,67}. The P300 is an event-related potential (ERP) that occurs as a response to an infrequently presented stimulus¹⁰. This potential is identified as a positive peak in the ERP amplitude with a latency between 250 to 500 ms after an event onset⁷². This ERP is predominantly seen

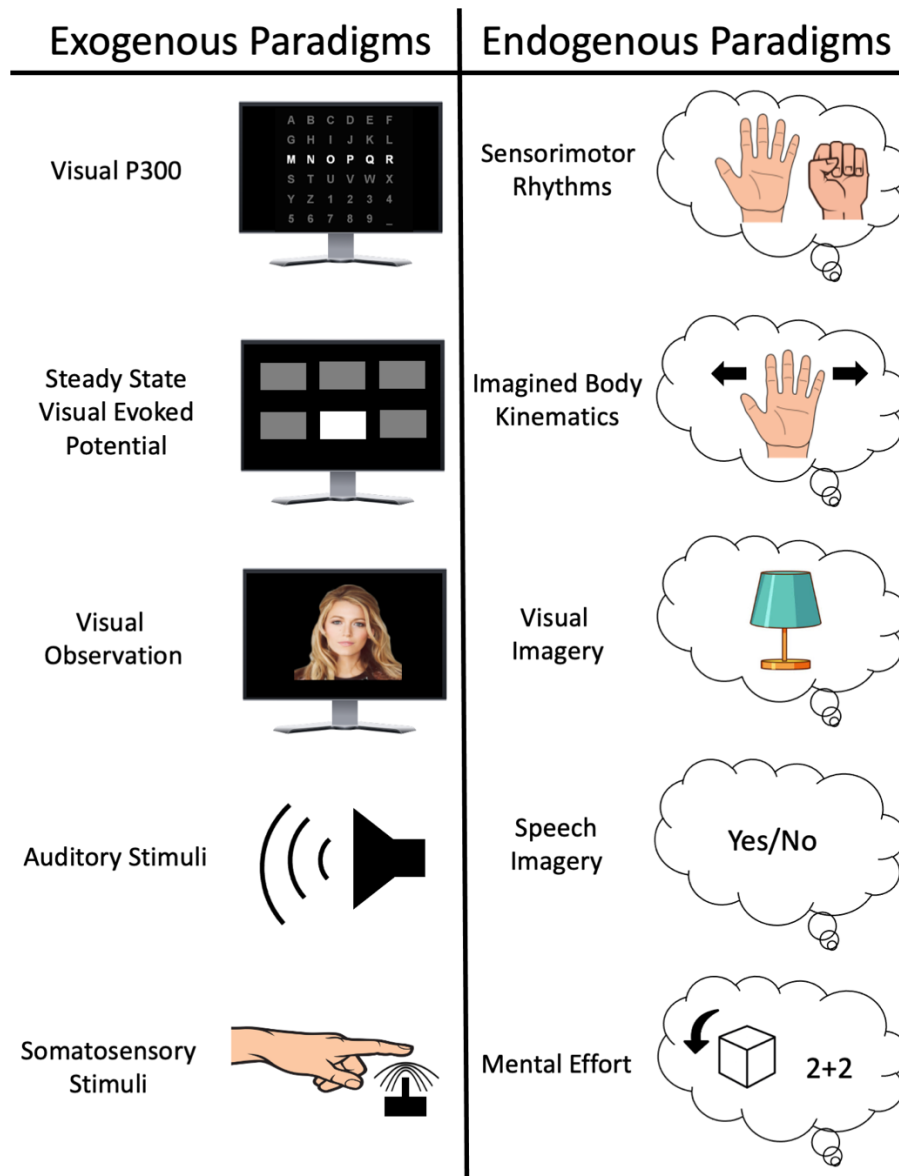


Figure 1.3: Overview of common BCI paradigms. Exogenous paradigms include the visual P300 stimulus, the steady state visual evoked potential, visual observation of images, auditory stimulation, or somatosensory (tactile) stimulation. Endogenous paradigms include motor imagery (sensorimotor rhythms and imagined body kinematics), visual imagery, speech imagery, or mental effort (mental object manipulation, math calculations, etc.).

over the midline electrodes and increases in amplitude from frontal to parietal locations⁷³. One widely used BCI application is the P300 speller which allows a user to type words or phrases by maintaining their gaze on a grid of letters whose rows and columns light up at different intervals⁷⁴. In this procedure, the BCI system matches the timing of the ERP response with the changing intensity levels of one of the letters to identify which letter the user is attending to. Most participants can learn to use this paradigm with high accuracy and minimal training¹⁰. However, this procedure is slow and requires a high level of sustained attention and visual focus which can cause fatigue⁷⁵ and would not be suitable for individuals with visual impairments⁷⁶. A related paradigm, known as the steady state visual evoked potential (SSVEP), presents the user with an array of targets flickering at various frequencies¹⁰. When a participant focuses their gaze on one of the targets, the constant flickering frequency on their retina imparts a similar frequency pattern in their EEG measured over the visual cortex⁷⁷. Participants can learn this with little to no training, and the stimuli can be presented at many different frequencies resulting in high number of possible command inputs for a BCI¹⁰. However this method can be uncomfortable and lead to fatigue, particularly when using a low flickering frequency, and it is not well suited for participants with visual impairments or photosensitivity⁷⁸. Lesser studied exogenous paradigms include the use of auditory stimuli^{10,79,80}, visual observation of images^{81,82}, and somatosensory (tactile) stimuli^{10,80}. While exogenous paradigms can provide a BCI user with high accuracy after minimal training, there is often large variability in performance across individuals^{83,84}. Furthermore, the control strategy may not be the most intuitive, and it can take focus away from the desired application. For example, the user would have to remember which flickering target corresponds to the intended action instead of attending to the action directly.

To overcome these challenges, endogenous paradigms with mental imagery can be used instead. Motor imagery of the movements of large body parts (e.g., right vs. left hand) is the most popular imagery-based paradigm¹⁰. This strategy, known as sensorimotor rhythms (SMR), causes event-related desynchronization or synchronization in the mu (8-12 Hz) and beta (18-26 Hz) bands of brain activity when participants imagine movement or relax, respectively^{10,85}. These signals are most prominent over the electrode locations directly above the primary sensorimotor cortex⁸⁶. Limitations for this approach include lengthy training times (weeks to months)¹⁰, large inter- and intra-subject performance variations⁸⁷, and a non-intuitive control scheme for certain applications such as prosthetic movement⁸⁸. Additionally, SMR is limited in the variety of classes available for BCI control⁸⁹. An alternative motor imagery approach, named imagined body kinematics (IBK), seeks to expand the motor imagery strategy to include information about position, velocity, or acceleration of the desired motion¹⁰. Participants using this paradigm are instructed to imagine moving a single body part in a multi-dimensional space^{65,90}. The kinematic information of this movement is extracted from the low-frequency components (less than 1 Hz) of the EEG data⁹¹. While this approach can provide a more intuitive control strategy with less training required than SMR⁹¹, usability is often unreliable as a result of nonstationarities and noise in the EEG signals, motivation, fatigue, and the participant's subjective ability to visualize the intended action⁹⁰. Lesser studied endogenous paradigms include visual imagery^{81,89,92} (conceptual reconstruction of a perceptual experience), speech imagery^{89,93-95} (Imagery of speech production), and mental effort⁹⁶ (mental object rotation, math calculations, etc.).

There is also the challenge of “BCI Illiteracy” in which a substantial percentage of participants (approximately 15 to 30%) remain unable to achieve proper control of a BCI

even after adequate training⁹⁷. Even for the participants who can attain some control, performance often falls short of the desired threshold rate for effective control^{98,99}. These difficulties have been observed across all BCI paradigms regardless of the neural signal used¹⁰⁰. Some studies have even seen that participants who are deemed “BCI illiterate” using one paradigm can learn to reach proficiency using another¹⁰¹. For these individuals, the availability of a different mental imagery paradigm may be beneficial to achieve proper BCI control.

VISUAL IMAGERY-BASED BCIs

Visual imagery, or the mental simulation of visual information from memory¹⁰², could be a useful BCI control strategy that has not yet been sufficiently tested⁸¹. The human brain is predominantly visual: 90% of the information transmitted by the brain is visual¹⁰³, and it can process images 60,000 times faster than text^{81,104}. Visual imagery may also be a more intuitive control strategy than any of the paradigms listed above⁸⁹. For example, if a person would like to use a BCI system to control a light in their house, the user could directly imagine the lamp they would like to turn on instead of gazing at a flickering target or remembering which imagined movement for a limb corresponds to that light. Furthermore, visual imagery can provide a near infinite number of visual image categories whereas motor imagery is often limited to only four or five possible options⁸⁹.

Several studies have shown that various categories of images (e.g., faces, animals, and inanimate objects) can be reliably distinguished using EEG when participants are observing an image^{81,82,105}. However, very few studies have attempted to measure visual imagery using EEG, and those that do have shown mixed success^{81,89,92}. . Bobrov et al.⁹² provides the first investigation into the use of visual imagery as a BCI control paradigm.

In this study, they were able to reliably distinguish between visual imagery of faces, visual imagery of houses, and resting state with an average of 56% classification accuracy (chance 33%) during an online BCI control task. Lee et al.⁸⁹ was able to demonstrate a high average classification accuracy of around 40% (chance 7.69%; 22 participants) during an offline analysis of a single session of 13 visual imagery categories. This included words used for patient communication with concrete properties (e.g., ambulance, clock, or toilet) or abstract properties (e.g., hello, stop, or yes). In Kosmyna et al.⁸¹, researchers performed offline classification between two classes of flower vs. hammer during visual observation and imagery. They were unable to achieve above chance accuracy between the two classes during visual imagery (average classification accuracy 52%, chance 50%), but they were able to distinguish a difference between the trials when participants performed visual imagery vs rest (77% average classification accuracy; chance 50%) and between visual observation vs imagery (71% classification accuracy; chance 50%).

Identifying the cause of why some of the previous visual imagery studies were successful while others failed is difficult. Each study used different image categories, different signal processing techniques, different spectral and spatial features, and different machine learning methods. One possible explanation might be due to similarity in neurological activity elicited in response to the presented stimuli. In the study by Kosmyna et al.⁸¹, the classifier was unable to distinguish between visual imagery of two object categories of flower versus hammer. However, Bobrov et al.⁹² saw greater success in discriminating between categories of face and scene images. This might be because the imagined faces and houses are more distinct neurally allowing for easier classifier discrimination. **Therefore, the second aim of this dissertation was to map the neural representational space in EEG of various image categories using visual imagery.** The

goal of this aim was to provide insight into which categories can produce distinct neural activity patterns identifiable by EEG for use in a visual imagery BCI. However, our results revealed some major limitations in the experimental design that may be contributing to poor classification results in our study and others¹⁰⁶.

Another limitation in the aforementioned studies is that the two larger experiments by Kosmyna et al.⁸¹ and Lee et al.⁸⁹ displayed the target category each trial immediately before the imagery period. This could be considered more of a test of holding the object categories in working memory rather than spontaneous visual imagery. It is also unclear if the data from other conditions, such as visual perception of the target image, can be used to classify visual imagery. Recent studies have also provided evidence that the inclusion of additional biological signals can improve performance in a BCI application¹⁰. For example, changes in the diameter of the pupil can occur in response to psychophysical and psychological stimuli¹⁰⁷. For these reasons, **the third aim of this project will be to evaluate the feasibility of visual imagery as a BCI control strategy by investigating these key experimental factors that may contribute to successful performance.**

CHAPTER 2

CREATING A COMMON TEMPLATE FOR NEURAL REINFORCEMENT OF FINGER INDIVIDUATION¹

Abstract

The inability to individuate finger movements is a common impairment following stroke. Conventional physical therapy ignores underlying neural changes with recovery, leaving it unclear why sensorimotor function often remains impaired. Functional MRI neurofeedback can monitor neural activity and reinforce it towards a healthy template to restore function. However, identifying an individualized training template may not be possible depending on the severity of impairment. In this study, we investigated the use of functional alignment of brain data across healthy participants to create an idealized neural template to be used as a training target for new participants. We employed multi-voxel pattern analyses to assess the prediction accuracy and robustness to missing data of pre-trained functional templates corresponding to individual finger presses. We found a significant improvement in classification accuracy ($p < 0.001$) of individual finger presses when group data was aligned based on function (88%) rather than anatomy (46%). Importantly, we found no significant drop in performance when aligning a new participant to a pre-established template as compared to including this new participant in the creation

¹ This chapter, in full, was published in an article entitled “Towards a common template for neural reinforcement of finger individuation” published in Scientific Reports 2021. The dissertation author was the primary author of the manuscript along with coauthors Ethan Oblak, James Sulzer, and Jarrod Lewis-Peacock. The author was responsible for analysis and visualization of this research.

of a new template. These results indicate that functionally aligned templates could provide an effective surrogate training target for patients following neurological injury.

Introduction

Deficiencies in the strength and control of individual fingers are commonly seen post-stroke^{108,109}. These impairments of fine motor control manifest as an inability to move a single finger while keeping the other fingers stationary, impairing an individual's ability to complete activities of daily living^{49,50}. Conventional physical therapy of the affected limb often provides limited success at restoring fine-motor function²⁻⁴. It is difficult to determine why sensorimotor function remains impaired following stroke without a detailed understanding of how the brain recovers after injury. Even with this information, we currently lack the proper tools to intervene at the neural level. Evidence suggests that restoration of healthy brain patterns in the ipsilesional hemisphere, especially in those with milder injuries, is most closely associated with recovery and thus could be used as a model for neural interventions^{19,21,110,111}. In contrast to using a neural target, conventional therapy that targets behavior ignores underlying neural changes. This could result in unintended maladaptive neuroplasticity arising from activation of ipsilateral motor projections or competitive interactions which may limit functional gains^{5,6}. In order to advance physical therapy to the level of the injury, particularly in an application as granular as the fingers, brain imaging technology is required to guide neuroplasticity.

Functional magnetic resonance imaging (fMRI) neurofeedback has been proposed as a method to both monitor and target the affected circuitry in the brain²⁶. In this procedure, participants are presented with a visual, auditory, and/or haptic representation

of their neural activity in real time for the purpose of self-modulation¹⁷. Neurofeedback relies on the principles of operant conditioning where the provided feedback serves as a reinforcement for a desired behavior²⁶. In a seminal work by Shibata et al.²⁷, fMRI neurofeedback was shown to influence neural activity in the visual cortex. Participants in this study learned to self-modulate an autologous target pattern of brain activity corresponding to a visual grating without stimulus presentation or explicit instruction. This ability to learn to self-modulate neural activity resulted in improved behavioral performance for the target. Neurofeedback has also been explored in therapeutic fields such as the treatment of schizophrenia^{28,29}, depression^{30,31}, Parkinson's disease³², attention disorders^{33,34}, chronic pain³⁵, and addiction^{36,37}. There have also been several studies investigating neurofeedback as a treatment for motor recovery after stroke³⁸⁻⁴⁰, although none of these have attempted to target fine-motor control of individual fingers.

Previous research has shown that individuated finger movement elicits distinct patterns of brain activity that are measurable by multi-voxel pattern analysis (MVPA) of fMRI data from the sensorimotor cortex^{112,113}. Strengthening these unique activity patterns has also been linked to improved motor control, such as improved reaction time and movement accuracy, in healthy individuals¹¹⁴⁻¹¹⁶. In a recent study from our group, finger preference during a motor task was altered after healthy participants were trained to endogenously shift their finger representations during fMRI neurofeedback training¹¹⁷. In a typical neurofeedback experiment, the neural target would be derived anatomically or functionally from the participant⁴⁸. After stroke, however, altered neural representations possibly resulting from maladaptive neuroplasticity and an inability to individuate finger movements^{49,50} would make autologous neural training targets untenable. Therefore, it is

necessary to develop a template of fMRI brain activity from healthy participants to serve as a surrogate training target.

Creating an fMRI template requires compounding data from multiple participants to generate a representative brain activation pattern for a given movement as outlined in **Figure 2.1**. Anatomical alignment based on brain landmarks is perhaps the most conventional method of between-subject analysis; however, this alignment procedure is often imperfect due to topographic variability between individuals^{51–54} and produces lackluster classification performance^{55–57} that is likely insufficient for neurofeedback training⁵⁸. More recently, a new technique known as *hyperlalignment* has emerged as a method for improving across-subject fMRI analysis^{56,59,60}. Hyperalignment works by applying the Procrustean transformation⁶¹ to functionally align voxel activity across individuals into a common model space. By compounding data across multiple individuals, a hyperaligned model benefits from a greater pool of training data and can often outperform within-subject methods^{55,57,62}.

One other advantage of hyperalignment is its ability to generalize to new data⁶². Recently, Taschereau-Dumouchel et al.⁵⁷ used hyperalignment to infer the neural representation for feared animals (e.g., a snake) in a given participant with a snake phobia based only on data from other participants. This allowed the researchers to obtain an accurate neural target of the feared animal without actually submitting the participant to the fearful stimulus. A similar strategy could be used for stroke patients who are unable to produce representations for a given finger due to neurological injury. For instance, if a patient is unable to produce an individuated movement in one finger, it may be possible to remove the impaired finger from the hyperalignment calculations and infer its representations from the data of healthy participants.

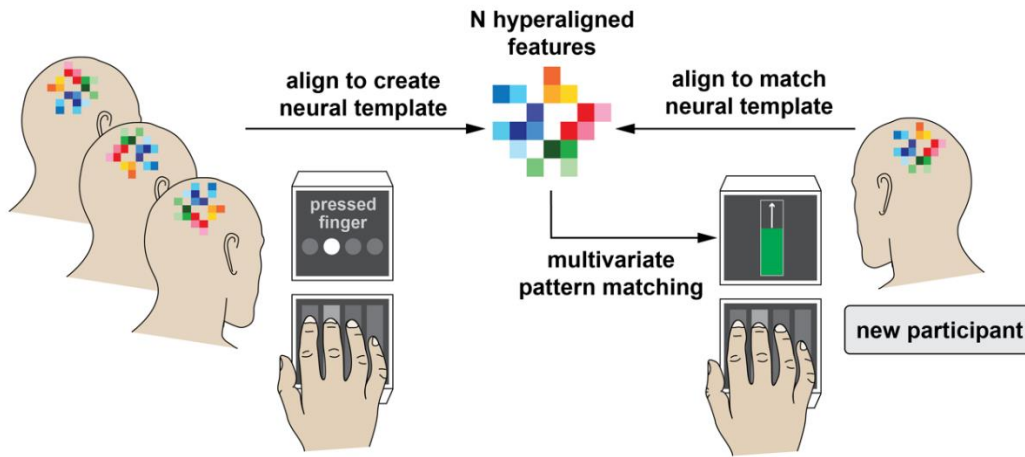


Figure 2.1: Overview of functional-based alignment. Neural patterns are rotated from subjects’ native space into a common template space. This template can then serve as a surrogate neurofeedback training target for a new participant who is unable to create an autologous target due to neurological injury.

In this study, we sought to investigate the use of hyperalignment to create a neural template of individual finger presses from healthy individuals. Such a template could be used in an fMRI neurofeedback intervention for patients with fine motor deficiencies and who are unable to provide a personalized training target. We conducted an offline analysis to validate this method on previously gathered data from $N=17$ healthy participants in a single session to identify unique fMRI activity patterns in sensorimotor cortex for each of the four fingers (index, middle, ring, and little) of the right hand^{58,117}. During this session, participants were asked to press one cued finger while maintaining a constant force with the non-cued fingers (**Figure 2.2**). The fMRI data was used to train three separate pattern classifiers to discriminate between the four fingers: a within-subject classifier trained in a participant’s native space, a between-subject classifier trained on

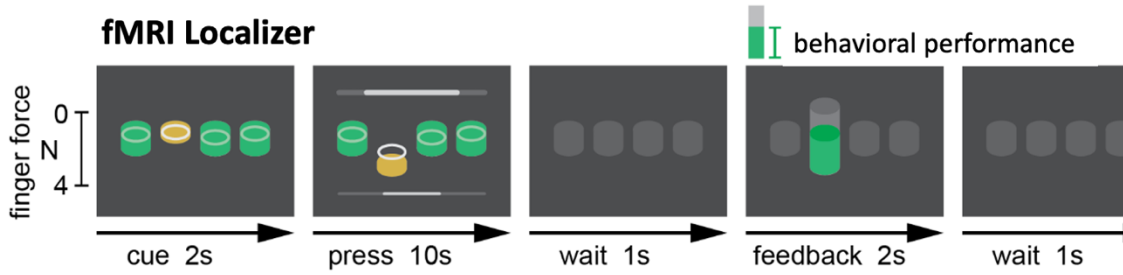


Figure 2.2: Experimental task protocol. Participants were cued to press one finger for 10 seconds while maintaining a constant force on the non-cued fingers. Feedback representing the number of correct presses was presented at the end of each trial. This process was repeated for 8 runs of 20 trials each.

anatomically aligned data in MNI152 (Montreal Neurological Institute) standard-space, and a between-subject classifier trained on hyperaligned data from other participants. Because our data was collected from healthy individuals with high individuation abilities, the results of the within-subject classifier serve as a theoretical maximum. The between-subject classifier trained on anatomically aligned data serves as the main point of reference for which we evaluate the performance of hyperalignment.

We hypothesized that hyperalignment would provide better classification results than the traditional anatomical alignment. We also tested the model’s ability to generalize to finger representations that have been removed during alignment. Finally, we addressed several important methodological questions about the implementation of hyperalignment: the effect of subject order on hyperalignment, the effect of aligning a new individual to a pre-established common model (compared to creating a new common model informed by all participants), and how much data is required to accurately align a new participant to a common model space. These results will address whether creating a common neural

template from healthy individuals can facilitate fMRI neurofeedback rehabilitation for patients with neurological impairment.

RESULTS

HYPERALIGNMENT PROVIDES IMPROVED BETWEEN-SUBJECT CLASSIFICATION

We first sought to compare the prediction accuracies between the three classifiers trained on hyperaligned, anatomically aligned, and within-subject data. The results are presented below in **Figure 2.3**. A one-way ANOVA revealed a statistically significant difference between groups ($F(2,27.1) = 57.8, p < .001$). The between-subject classification model trained on hyperaligned data performed significantly better than the classifier trained on anatomically aligned data (88.8% and 46.0%, respectively; Games-Howell post-hoc test, $p < .001$). The within-subject model trained on the participants' own data yielded 94.7% classification accuracy. As an additional test, a within-subject analysis on the participants' own data after anatomical alignment into MNI space provided 94.0% classification accuracy. This verified that warping participants' data into MNI space did not significantly affect classification accuracy ($t(16) = .871, p = .396$).

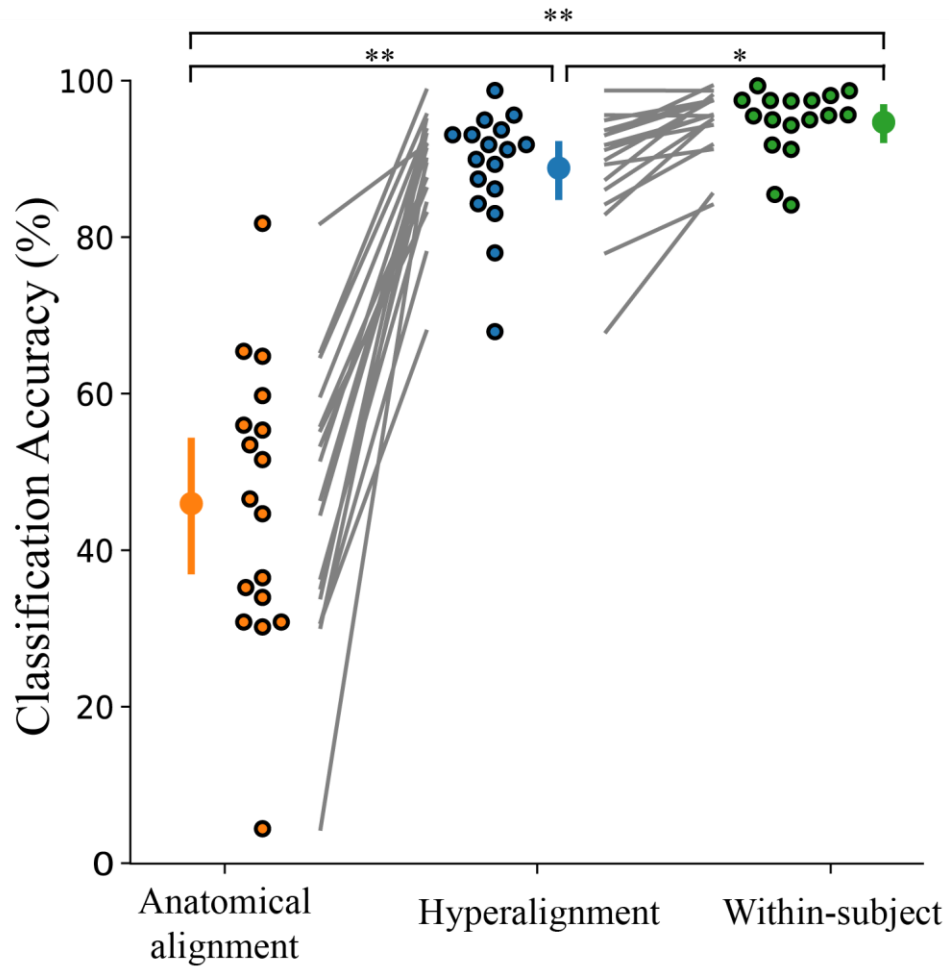


Figure 2.3: Classification model comparison. Hyperalignment provides better between-subject classification accuracy (88.8%) than conventional anatomical alignment (46.0%). Within-subject classification (94.7%) is also included for comparison. Individual participants are presented beside the mean as circles with a black outline. Error bars indicate a 95% confidence interval. * $p < .05$, ** $p < .001$.

PHYSICAL AND REPRESENTATIONAL OVERLAP BETWEEN NEIGHBORING FINGERS

A deeper look into the predictions of the classifier trained on hyperaligned data in **Figure 2.4a** indicates increased misclassification between the ring and neighboring fingers compared to the other finger pairs. To better understand how this classifier was influenced by the uninstructed fingers, we analyzed the degree of physical overlap, measured by mean deviation from baseline force¹¹⁸, and representational overlap, measured by representational similarity between neural patterns¹¹⁹. Only information from the 11 participants from Oblak et al.¹¹⁷ whose responses were collected with the force keyboard were included in these analyses.

The force data presented in **Figure 2.4b** shows the mean deviation from baseline force of the uninstructed fingers compared to the mean press force of the instructed finger. The mean deviation of each uninstructed finger was inappreciable at a target press of around 2.5 N, which would be expected at such a low level of target force¹¹⁸. However, the results of the representational similarity analysis revealed greater representational overlap in neighboring digits, particularly between the ring and little finger pair (**Figure 2.4c and d**). Therefore, these overlapping representations are responsible for the increased classifier confusion between neighboring digits.

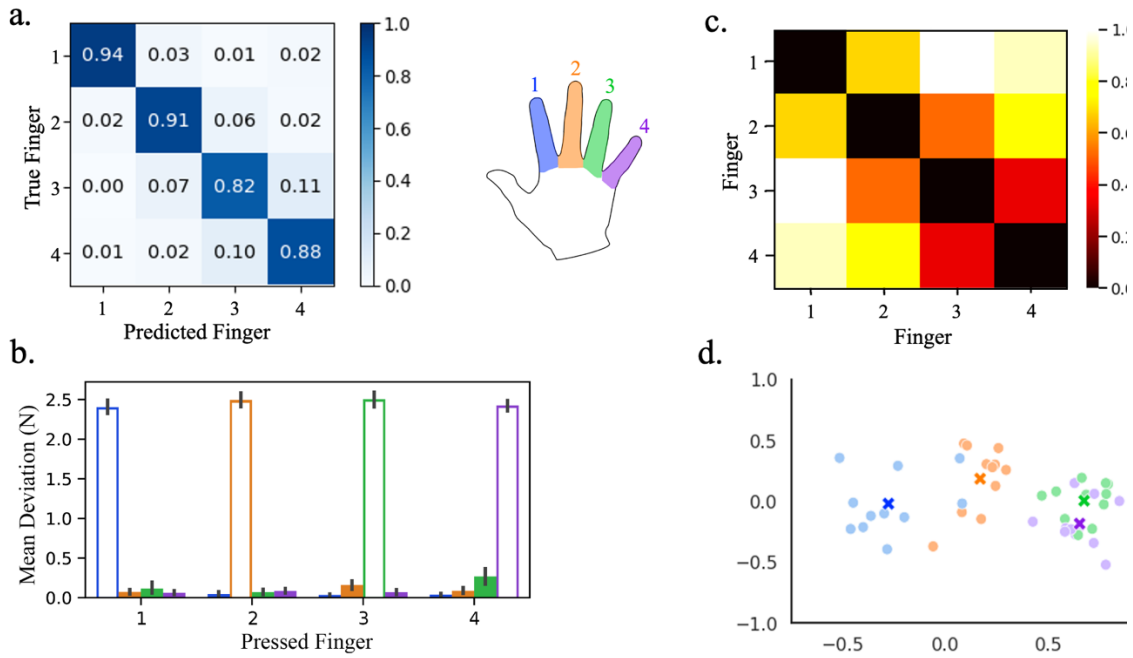


Figure 2.4: Representational overlap between neighboring digits contribute to increased misclassification of finger presses. (A) Confusion matrix of classifier predictions trained on hyperaligned data. **(B)** Mean deviation from baseline force of the uninstructed fingers (filled bars) compared to the mean press force of each instructed finger (hollow bars). Error bars indicate a 95% confidence interval. **(C)** Average representational dissimilarity matrix of neural patterns associated with finger presses. **(D)** Two-dimensional projection of the representation structure using multidimensional scaling. Dissimilarity is reflected by the distance in the 2 dimensions. The mean representation across participants in panel d is shown as an ‘X’. Individual digits are represented by different colors and numbers (see key in center). Data is only shown from the 11 participants from Oblak et al.¹¹⁷ whose force data was collected.

HYPERALIGNED COMMON MODEL GENERALIZES TO NOVEL FINGERS

To validate the common model's ability to generalize to new data, we removed the fMRI data from select fingers prior to feature selection and hyperalignment parameter calculations in all participants. Hyperalignment was performed on the remaining fingers to create the common model space and obtain a transformation matrix for each individual. These transformation matrices were then applied to the dataset containing fMRI data from all fingers. This provided a versatile source of inference of the removed finger representations for the test subject.

The hyperaligned model yielded an overall classification accuracy of 80.6% when one finger was removed during hyperalignment. Furthermore, the hyperaligned model was able to infer the representations of the removed finger from the surrogate participants and achieve above-chance classification (mean 69.3%, chance level 25%) for the removed finger (one-way ANOVA, $F(1,75.2) = 384$, $p < .001$). When two fingers were removed during hyperalignment, the classifier still provided above-chance classification of all fingers (mean 66.5%, $F(1,113) = 1035$, $p < .001$) and for the two removed fingers (mean 56.9%, $F(1,204) = 428$, $p < .001$). When three fingers were removed during hyperalignment, the overall classification accuracy dropped to 35.6%. While still significantly above chance ($F(1,82.8) = 55.9$, $p < .001$), this would likely not provide an accurate template.

Figure 2.5 shows the overall classification accuracies when one and two fingers were dropped during hyperalignment along with the prediction accuracy when all fingers were included in the hyperalignment procedure and during anatomical alignment for comparison. There was a statistically significant difference between groups ($F(3,194) = 92.0$, $p < .001$). While the model suffered a decrease in classification accuracy when one

or two fingers were removed compared when all fingers were included during common model generation, it still performed better than baseline anatomical alignment with all fingers included (Games-Howell post-hoc analysis, $p < .001$).

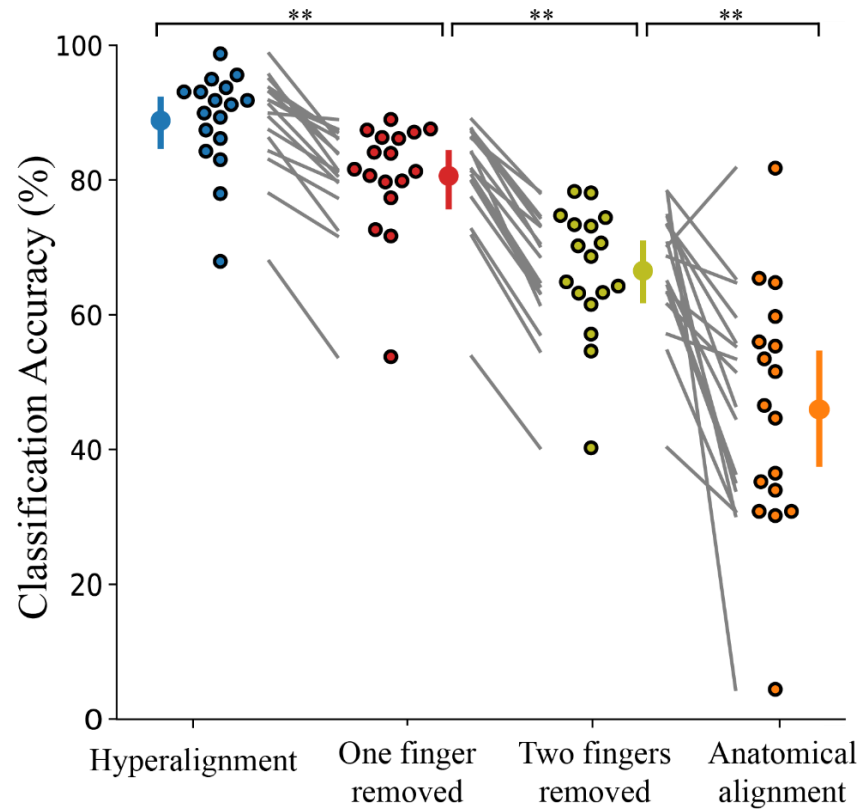


Figure 2.5: Hyperaligned common template generalizes to novel fingers. Overall classification accuracy for all four fingers when all fingers are included in hyperalignment parameter calculations (88.8%), when one finger is removed during hyperalignment (80.6%), when two fingers are removed during hyperalignment (66.5%), and anatomical alignment with all fingers included (46.0%). Individual participants are presented beside the mean as circles with a black outline. Error bars indicate a 95% confidence interval. Dashed line indicates chance level (25%). ** $p < .001$.

HYPERALIGNED COMMON MODEL GENERALIZES TO NEW INDIVIDUALS

To further validate the effectiveness of a surrogate training target, we evaluated the classification accuracy when a new individual was brought into alignment with a pre-established common model space. This would be the most likely scenario in a neurofeedback paradigm where a template is used as a training target for a new participant. Previous studies have indicated that classification accuracy decreased when mapping a new participant onto a previously created common model⁵⁵. However, we saw no significant difference between including a new participant in the creation of a new common model vs. aligning a new participant to a pre-established common model (**Figure 2.6**; $t(16) = .433$, $p = .67$). This difference of findings may be attributed to a lower degree of inter-subject variability in our experiment compared to other studies. Further deliberation is included in the Discussion.

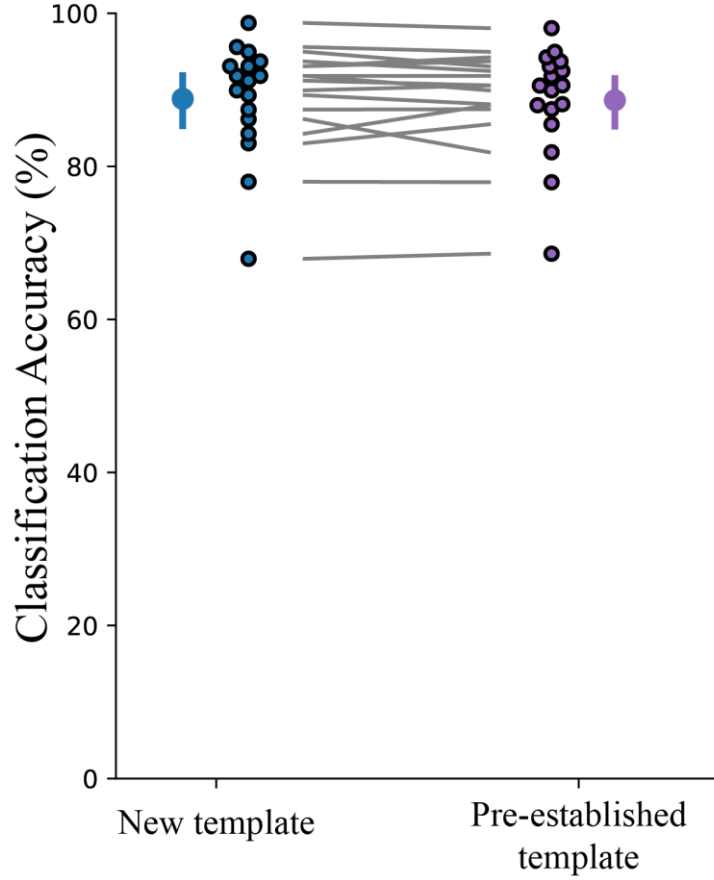


Figure 2.6: Decoding effects of using all participants to create a template space versus hyperaligning a new participant to a pre-established template. Individual participants are presented beside the mean as circles with a black outline. Error bars indicate a 95% confidence interval.

EFFECT OF SUBJECT ORDER ON COMMON MODEL GENERATION

It has also been suggested that the order in which participants enter the hyperalignment process affects the overall model's performance⁵⁵. To assess the effects of subject order, we repeated our hyperalignment classification analysis over 2000

permutations of random subject orders. **Figure 2.7** presents the distribution of mean between-subject classification accuracies as a histogram with a mean classification accuracy of 88.95% (95% confidence interval, 88.61-89.31%). These results indicate a very minimal effect of subject order on overall model performance.

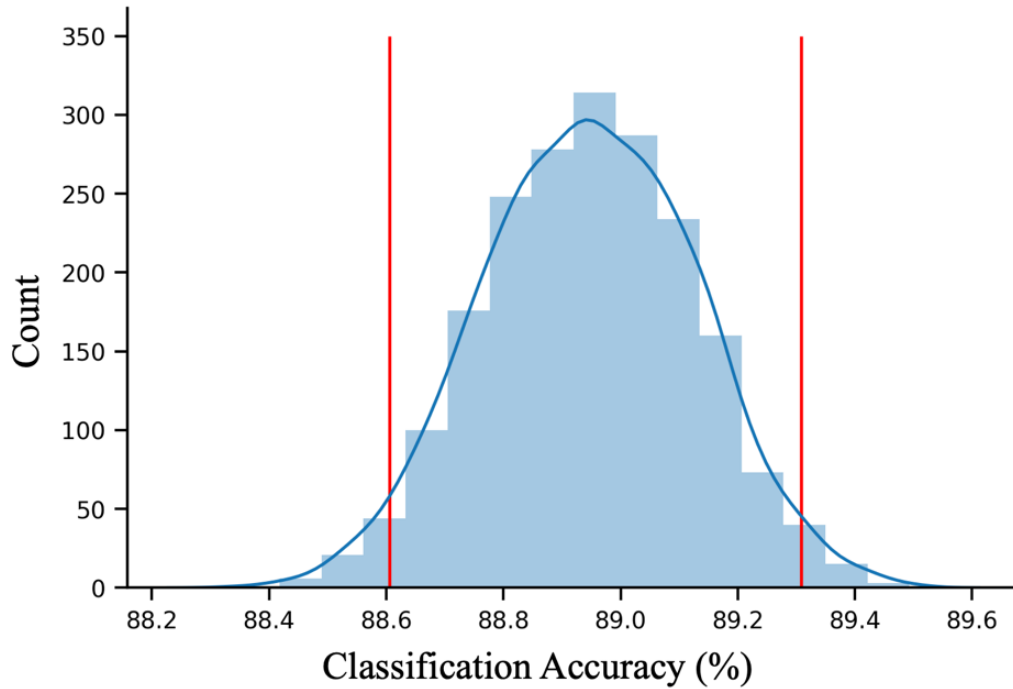


Figure 2.7: Histogram of mean classification accuracy for hyperalignment of 2000 permutations of random subject order. Red vertical bars demarcate the 95% confidence interval.

HOW MUCH DATA SHOULD BE COLLECTED FOR A NEW PARTICIPANT?

The final question we addressed was how much data needs to be collected from a new participant to accurately hyperalign them to a pre-established common model. **Figure 2.8** shows the classifier's performance as the number of runs included in hyperalignment calculations and classifier training was increased. A between-subject classifier using all participants to create a common model and a within-subject classifier trained on the same amount of data is also included for comparison. The results of a one-way repeated-measures ANOVA showed that there was a significant main effect of the number of runs included on prediction accuracy for the classifier where a new subject was aligned to a pre-established common model ($F(1.88,16) = 59.3, p < .001$), the classifier using all participants to create a common model ($F(2.10,16) = 50.6, p < .001$), and the classifier trained in a participant's native space ($F(1.46,16) = 51.3, p < .001$). Tukey post hoc tests revealed that the inclusion of additional data significantly improved classification accuracy up to three runs for the classifier using all participants to create a common model and the classifier trained in a participant's native space. The inclusion of additional data significantly improved classification accuracy only up to two runs for the classifier where a new subject was aligned to a pre-established common model.

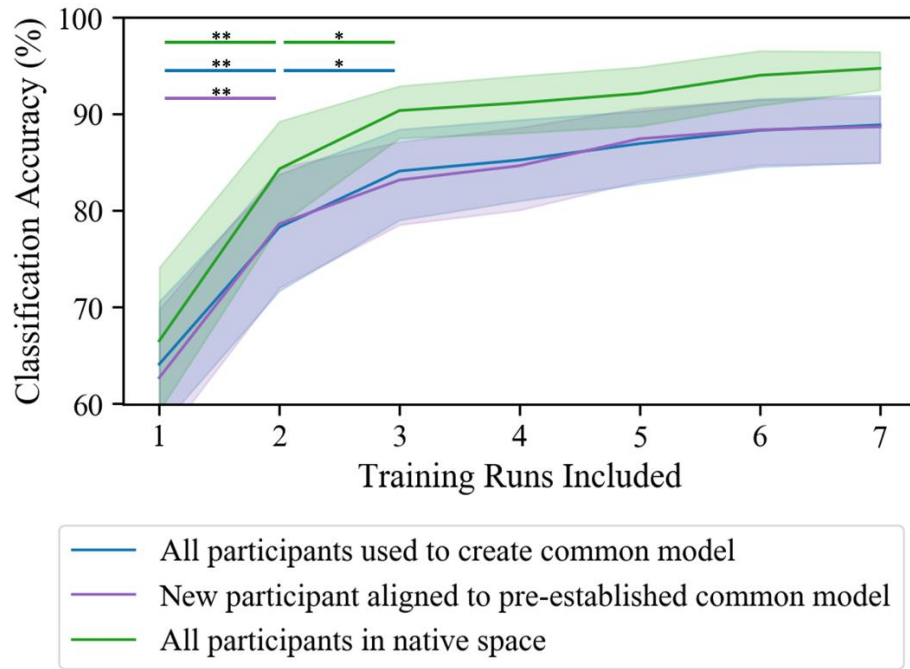


Figure 2.8: Number of runs needed to hyperalign individuals and train an accurate classifier. The results indicate that at least two runs are necessary to accurately align a new participant to a pre-established common model. At least three runs are necessary for the between-subject classifier using all participants to create the common model and the within-subject classifier trained in a subject’s native space. Shaded outline indicates 95% confidence interval. * $p < .05$, ** $p < .001$.

Discussion

The results of this study demonstrate the validity of using hyperalignment to construct a neural template of brain activity to be used as a surrogate training target in a neurofeedback experiment. Hyperalignment of the primary motor and somatosensory cortices across individuals provides a 42.8% improvement in classification accuracy of

individual finger presses compared to anatomical alignment. While other studies have reported improved classification accuracy after hyperalignment compared to within-subject analysis^{55,57,62}, participants in this study were able to elicit highly individuated finger movements which led to high within-subject classification. Due to this ceiling effect, our hyperaligned model was not able to outperform a within-subject model. However, we have shown that greater representational overlap between fingers contributes to increased classifier confusion. In patients with neurological injury, impairments in fine-motor control are accompanied by greater representational overlap which could substantially reduce a classifier's prediction ability. This may make identifying an appropriate autologous neurofeedback training target impossible. For this reason, we recommend functional alignment to a healthy neural template. This would provide a larger pool of data to boost classification performance and provide a more precise training target.

We have also shown that hyperalignment is able to generalize to missing data consistent with the findings of Taschereau-Dumouchel et al.⁵⁷. This would be advantageous for participants who have significant motor impairments and cannot produce distinct neural representations for each finger. The impaired finger could be removed during construction of the common model, and the data from the other fingers could be used to infer the representation of the removed digit. While there was a significant decrease in the predication accuracy of the removed finger itself, this functionally aligned classifier still outperformed a classifier trained on anatomically aligned data. Furthermore, the study conducted by Taschereau-Dumouchel et al.⁵⁷ removed only one out of 40 different categories whereas our study has shown significant prediction abilities even after half of the data has been removed (two out of four categories).

In a recent study conducted by Al-Wasity et al.⁵⁵, a similar approach of using a hyperaligned common model to predict imagined arm movements was significantly affected by the order in which participants were entered into the hyperalignment parameter calculations. We conducted an equivalent test with our data and found no significant impact on performance. This discrepancy might be attributed to increased variability between individuals in imagined vs. physical motor tasks as well as a difference in sample size between our study (N=17) and Al-Wasity's⁵⁵ (N=10). If participants have higher variability, the hyperalignment process may place unequal weight on the first individuals who set the initial reference point for alignment as well as the final participants whose data contributes more to the overall common model. If participants have higher inter-subject variability, the common model may be more influenced by subject order if an outlier enters alignment earlier or later in the hyperalignment process. Participants in our study demonstrated highly differentiable activity patterns (94.7% classification) for each of their executed finger movements. Perhaps in situations where the brain patterns are less well classified (e.g., in Al-Wasity's⁵⁵ study showing 48.3% classification of imagined movements), hyperalignment may be more sensitive to subject order and would benefit from larger pools of data.

Al-Wasity et al.⁵⁵ also saw that aligning a new participant to a pre-established common model suffered a 12.5% drop in classification accuracy compared to using all individuals to inform the common model space. We conducted a similar analysis and saw no significant drop in prediction accuracy between these two approaches. Once again, this difference in findings could be due to less variability in activity patterns during motor execution versus imagery. Furthermore, our pre-established common model was informed by data from 16 other participants while Al-Wasity's had only nine. Further research is

warranted on hyperalignment between participants performing motor tasks vs. mental imagery to identify the precise cause of these discrepancies. Finally, we investigated how much data is needed to properly create a common model space or to align a new participant to a pre-established common model. Our results indicated that only two (of eight) runs of data (40 trials) are necessary to obtain an accurate alignment to a pre-established template.

One limitation of our functionally aligned neural templates of finger presses is that they would only be effective in participants with mild to moderate impairment. If unique activity patterns are not identifiable in at least two of the fingers, an accurate template would likely not be generated. Additionally, all analyses in this study were performed on data from healthy young adults. It remains untested if hyperalignment provides similar results between different age groups or impairment levels. Future work will need to explore similar approaches in older adults and individuals with mild fine motor impairments.

In conclusion, we introduce here a common model of individual finger presses that can be used as a surrogate training target during fMRI neurofeedback for participants with motor impairments. This neural template was derived from information from healthy young adults with high individuation abilities. Using such a model can benefit new participants by compensating for impaired digits, providing a larger pool of data to boost classification accuracy, and providing a clearer goal of neural activity to work towards.

Methods

PARTICIPANTS

Data from N=17 participants recruited for previous studies^{58,117} was used in this experiment (6 female, all right-handed, average age 25.5 years, SD = 4.2). All participants

provided informed consent before participating in this study. The Institutional Review Board at the University of Texas at Austin provided ethical approval. All methods were performed in accordance with the relevant guidelines and regulations of the University of Texas at Austin Institutional Review Board.

APPARATUS

A custom-built, MRI compatible keyboard was developed to collect the finger presses of the right index, middle, ring, and little fingers. The keyboard was equipped with four piano-like keys, each incorporating a sensor (Honeywell FSS015) to record the isometric force of each press at 120Hz. Inside the scanner, the keyboard was secured to a wooden board which was placed in the participant's lap. Participants received visual instructions and feedback via a back-projection screen presented using Python and Pygame.

IMAGING PARAMETERS

Participants were scanned in a Siemens Skyra 3T scanner with a 32-channel head coil. The following EPI sequence was used for all individuals: TR=2s; 36 slices; in-plane resolution 2.3x2.3mm; 100x100 matrix size; 2.15mm slice thickness; 0.15mm slice gap; 2x multiband factor. A manual adjustment was performed after auto-alignment to the AC-PC plane to ensure adequate coverage of the sensorimotor cortex. A high-resolution anatomical scan (MEMPRAGE, 1mm isotropic voxels) was also acquired to identify the primary sensorimotor cortex using Freesurfer.

REGION OF INTEREST

The regions of interest (ROIs) were defined as the primary motor (M1) and primary somatosensory (S1) cortices (Brodmann areas 4A, 4P, 3A, and 3B) and were identified in each participant using Freesurfer. These areas were selected as individuation of finger movements receives contributions from the corticospinal tract (CST) whose origins lie primarily in the M1 region^{120–122}. This area produces low levels of force to control skilled movements¹²³. Finger strength on the other hand receives input through the reticulospinal tract (RST) which has more distributed origins¹²⁴. Furthermore, there is ample evidence of the connection between the M1 and S1 regions during motor tasks^{125–128}. For the representational similarity analysis, the region of interest was further restricted to the hand knob area of the primary somatosensory cortex as described in Oblak et al.¹¹⁷.

DATA COLLECTION

Each participant underwent one task familiarization session outside the MRI and one localizer session inside the MRI scanner to identify unique representations in the sensorimotor cortex corresponding to each of the four fingers (index, middle, ring, and little). During the familiarization session, participants were allowed to practice the individual finger pressing task presented in **Figure 2.2** for 15 minutes. Each trial of the task consisted of 2 seconds to cue the target finger, 10 seconds of individual finger pressing, 1 second of rest, 2 seconds of feedback, and 1 second of rest before the next trial. The localizer session consisted of 8 runs of 20 trials each, lasting about 1 hour.

Participants were instructed to hit the yellow targets with the cued finger while maintaining a constant force with the other fingers. One point was awarded for each target hit in this manner. No points were awarded if the non-cued fingers were outside the constant force cylinder, the participant did not remain within the target cylinder for 200ms,

or if the cued finger force exceeded the target force during a press. These measures ensured the participant was only pressing the target finger with an appropriate amount of force and speed. During each trial, a score bar was presented at the top of the screen along with a timer bar at the bottom. The score bar decreased in size as targets were hit up to a score of 15. After 15 points were acquired, the bar turned green and expanded in size.

After 10 seconds of finger pressing, a feedback thermometer was presented indicating the number of targets hit during the trial. The thermometer cylinder was colored green if 15 or more targets were hit or gray if less than 15 targets were hit. The initial maximum height of the feedback thermometer was equivalent to 15 points. This height was adjusted for each finger as participants increased their maximum score. The numerical score for the trial was also presented below the feedback thermometer. At the end of each run, the total score for all trials were displayed on the screen. For further details on experimental design or stimulus presentation, refer to Oblak et al.^{58,117}.

WITHIN-SUBJECT DECODING OF INDIVIDUAL FINGER PRESSES

The fMRI data from the localizer session was used to train a classification model for individual finger presses. Standard preprocessing (rigid body motion correction, z-scoring, and detrending) was performed. The preprocessed fMRI data from last 6 seconds of the pressing period was averaged to account for the hemodynamic delay resulting in a total of 160 time-averaged trials, 40 per finger. An ANOVA-based feature selection was also implemented to identify the top 100 voxels with highest variability. A support vector machine (SVM; scikit-learn) classifier was trained using a leave-one-run-out cross-validation.

BETWEEN-SUBJECT DECODING OF INDIVIDUAL FINGER PRESSES USING ANATOMICAL ALIGNMENT

Individual participants' functional data was transformed to the MNI152 (Montreal Neurological Institute) standard-space using FSL. Linear registration of each participant's functional data to structural data was carried out using FSL's FLIRT function. Nonlinear registration of structural data to the MNI template was implemented with FSL's FNIRT function. Finally, all functional data was transformed to MNI space using applywarp. A new mask for sensorimotor ROI was also generated in the MNI space to be used by all participants. Data preprocessing was carried out in a similar manner as the within-subject analysis; however, a sensitivity analysis on the number of features used during classification revealed that including all voxels from the new sensorimotor mask yielded the best results. An SVM classifier was then trained using a leave-one-subject-out cross-validation approach.

BETWEEN-SUBJECT DECODING OF INDIVIDUAL FINGER PRESSES USING HYPERALIGNMENT

Hyperalignment transformation was carried out in three stages⁵⁶. In the first stage, data from two participants were brought into optimal alignment using the Procrustean transformation. Then, a third individual was brought into alignment with the mean response from the first two participants. This process was continued for each remaining individual by iteratively aligning them to the mean responses of the previous participants. In the second stage, this iterative process was repeated to align each individual with the group mean response from the first stage. The third stage consisted of calculating the transformation parameters necessary to bring each participant into alignment with the common model space generated in stage two.

Data preprocessing and feature selection was carried out prior to hyperalignment as described previously. The common model space was generated from all participants using the seven runs left out during cross-validation. The SVM classifier was then trained on these seven runs from all but one left out subject (leave-one-subject-out) and tested on the one run not used for feature selection or hyperalignment calculation for the left-out subject (leave-one-run-out). This was to ensure that the model was only trained on data from other participants and that there was no peeking between data in the training and testing set.

CALCULATING MEAN DEVIATION OF UNINSTRUCTED FINGERS

The enslavement of the uninstructed fingers was calculated by finding the mean deviation of force from baseline in accordance with Xu et al.¹¹⁸. For each press (p) in a single trial ($t = 10s$), the mean deviation of force from each uninstructed finger ($F_{p,j}$) from that finger's baseline force (BF_j) was calculated. This was averaged over all trials (T) for each target finger:

$$menDevP = \frac{1}{T} \sum_{t=1}^T \sqrt{\sum_{j=passive} (F_{p,j} - BF_j)^2} \quad (1)$$

where j signifies the j th uninstructed finger.

During each press of the target finger, participants were instructed to keep the uninstructed fingers within a force range of 0.2-1.5 N. The baseline force for each uninstructed finger during the pressing of any given target finger was obtained by taking the mean force of the uninstructed finger when the target finger press was released (force < 1.5 N). The enslaved deviation force was then obtained for the uninstructed finger by

averaging the mean force of that finger when the target finger was pressed (force > 2 N) subtracted by that finger’s baseline force.

REPRESENTATIONAL SIMILARITY ANALYSIS

Representational similarity of the individual finger activity patterns was obtained by calculating the Pearson’s correlation (r) between the averaged fMRI data of each finger¹¹⁹. The dissimilarity was then found by subtracting r from unity. The dissimilarity matrices were calculated for each participant and averaged to provide the mean dissimilarity presented in **Figure 2.4a**. Multidimensional scaling was also applied to project the representational structure into a two-dimensional plot.

REMOVING FINGERS FROM HYPERALIGNMENT PARAMETER CALCULATIONS

Data from one, two, or three fingers was removed from the dataset before feature selection and creation of the common model. Feature selection and hyperalignment calculations were conducted on the remaining fingers and applied to the dataset including all fingers. The SVM classifier was then trained and tested on this dataset in a leave-one-subject-out cross-validation. This process of data removal was repeated for each finger combination. The purpose of this process was to completely prevent information from the removed fingers from being used to inform the common model. This enforced the model to use only the data from the remaining fingers and other participants to infer the representations of the removed digits.

ALIGNING A NEW PARTICIPANT TO A PRE-ESTABLISHED COMMON MODEL

To create this common model space, we performed feature selection and hyperalignment as described above on all runs from $N-1$ participants. Then, the left-out

individual was brought into alignment with this template using a leave-one-run-out cross-validation for feature selection and hyperalignment parameter calculations. An SVM classifier was trained on the data from the 16 participants used to create the template and tested on the left-out individual following each cross-validation fold.

VARYING AMOUNT OF TRAINING DATA

To assess how much data is required to accurately hyperalign individuals and train a classifier, we reconducted our classification analyses using varying amounts of training data. We conducted a leave-one-run-out cross-validated analysis to hyperalign and train each classifier as described above starting with only two runs of data for each participant. One additional run was added after each calculation up to eight total included runs.

STATISTICAL ANALYSIS

A one-way analysis of variance (ANOVA) was run to compare classification accuracies between the hyperaligned, anatomically aligned, and within-subject models. A similar ANOVA test was also run to compare classification accuracies between groups when select fingers were removed during hyperalignment. A Welch F-test was performed due to the violation of the homogeneity of variance assumption in both cases. A Games-Howell post hoc test was conducted to elucidate the differences between groups. A two-sided paired t-test was used to compare difference in prediction accuracy between groups using all participants to create the common model space and aligning a new individual to a pre-established common model space. A one-way repeated ANOVA with Greenhouse-Geisser correction was used to identify improvements in classification accuracy as training data is increased. Tukey post hoc tests were utilized to identify how many runs were needed accurately align individuals and train a classifier.

CHAPTER 3

DETERMINING THE NEURAL REPRESENTATIONAL SIMILARITY OF MULTIPLE OBJECT CATEGORIES DURING VISUAL IMAGERY

Abstract

It is currently unclear to what degree EEG data can discriminate between visual imagery of different object categories. Prior research in this area, as well as our own preliminary studies¹²⁹, have demonstrated the ability to successfully discriminate between imagery of faces and scenes⁹² but not between imagery of flowers and hammers⁸¹. This may be due to a higher representational similarity¹¹⁹ between the brain activity patterns for the flower and hammer stimuli. We hypothesized that certain categories of mental imagery (e.g., manmade and natural objects) may produce too similar patterns of brain activity to be identified in EEG making them unusable for BCI applications. To test this hypothesis, N=18 participants underwent two EEG sessions involving mental imagery of human faces, human bodies, animal faces, animal bodies, fruits and vegetables, and manmade objects. Multivariate pattern analysis of the EEG signals were used to quantify the representational similarities of all imagined images⁴⁷. Unfortunately, we were unable to obtain significantly above chance classification accuracy (19.72%, chance level 16.67%) between the six image categories used in this experiment. While the 30-class item level classification did achieve significantly above chance performance (6.75%, chance 3.33%, $p < 0.01 \times 10^{-10}$), it also revealed a significant temporal bias in predictions to items that appeared within the same run. For this reason, it remains unclear if the representational boundaries during visual imagery are strong enough to support BCI.

Introduction

The concept of using brain signals recorded via electroencephalography (EEG) to control external devices has gained traction in recent years as a potential way to provide patients with severe neuromuscular disorders a way to communicate and interact with the world around them^{11,63}. This technology, termed brain-computer interface (BCI), has since grown to cover applications such as robotic control^{64–66}, communication^{67,68}, and even entertainment and gaming^{12,69–71}. Various control strategies exist for BCI interaction, but each come with their own limitations that prevent BCIs from obtaining widespread use outside the lab¹⁰. The imagined movements of large body parts is perhaps the most common control paradigm for EEG BCI applications; however, it often suffers from lengthy training times¹⁰ with inconsistent and unstable performance⁸⁷, and a restricted range of options for imagined movements⁸⁹. Most attempts to address the limitations of this paradigm focus on advancing EEG signal processing and classification techniques⁹⁸; however, an often overlooked solution is investigating other imagery-based control strategies^{130,131}. For this reason, our primary objective in this aim is to investigate the efficacy of using visual imagery for EEG BCI control. Visual imagery has a potentially infinite number of available classes which can provide a more ecological connection between the mental imagery and intended action. Our first goal in this experiment was to map the neural representational space in EEG of various image categories using visual imagery to identify the categories of imagery available for BCI use.

LIMITATIONS OF CURRENT BCI CONTROL PARADIGMS

When designing a BCI system, one major consideration is the means of interaction a participant will use to perform the task. These control paradigms can be divided into two

methodologies: exogenous paradigms based on the brain's response to an external stimulus, and endogenous paradigms where participants learn to modulate their brain activity using mental imagery¹⁰. The most popular exogenous paradigms in EEG rely on measuring the brain's response to visual stimuli such as a flickering target^{10,67,74,77}. Most participants can learn to use these paradigms with high accuracy and minimal training¹⁰. However, these procedures can be time intensive and require a high level of sustained attention and visual focus which can cause fatigue⁷⁵ and would not be suitable for individuals with visual impairments or photosensitivity^{76,78}. Furthermore, there is often large variability in performance across individuals^{83,84}, perhaps because the control strategy is not intuitive, and this confusion can take focus away from the desired application. For example, the user would have to remember which flickering target corresponds to the intended action instead of attending to the action directly.

To overcome these challenges, endogenous control paradigms with mental imagery can be used instead. Motor imagery of the movements of large body parts (e.g., right vs. left hand) is the most popular imagery-based paradigm¹⁰. Limitations for this approach include lengthy training times (weeks to months)¹⁰, large inter- and intra-subject performance variations⁸⁷, non-intuitive control schemes for certain applications⁸⁸, and a limited variety of classes available for BCI control⁸⁹. Furthermore, factors such as noise in the EEG signals, motivation, fatigue, and difficulty visualizing the intended action can greatly impact a user's ability to gain control of the BCI⁹⁰. This leads to a challenge referred to as "BCI Illiteracy" in which a substantial percentage of participants (approximately 15-30%) remain unable to achieve proper control of a BCI even after a standard training period⁹⁷. Even for the participants who can attain some control, performance often falls short of the desired threshold rate for effective control (often set at 60% or 70%

accuracy)^{87,98,99}. These difficulties have been observed across all BCI paradigms regardless of the neural signal used¹⁰⁰. Some studies have even seen that participants who are deemed “BCI illiterate” using one paradigm can learn to reach proficiency using another¹⁰¹. For these individuals, the availability of a different mental imagery paradigm may be beneficial to achieve proper BCI control.

INVESTIGATING VISUAL IMAGERY AS AN ALTERNATIVE BCI CONTROL STRATEGY

Visual imagery, or the mental simulation of visual information from memory¹⁰², could be a useful BCI control strategy that has not yet been sufficiently tested⁸¹. The human brain is predominantly visual: 90% of the information transmitted by the brain is visual¹⁰³, and it can process images 60,000 times faster than text^{81,104}. Visual imagery may also be a more intuitive control strategy than any of the paradigms listed above⁸⁹. For example, if a person would like to use a BCI system to control a light in their house, the user could directly imagine the lamp they would like to turn on instead of gazing at a flickering target or remembering which imagined movement for a limb corresponds to that light. Furthermore, visual imagery can provide a near infinite number of visual image categories whereas motor imagery is often limited to only four or five possible options⁸⁹.

Several studies have shown that various categories of images (e.g., faces, animals, and inanimate objects) can be reliably distinguished using EEG when participants are observing an image^{81,82,105}. However, very few studies have attempted to measure visual imagery using EEG, and those that do have shown mixed success^{81,89,92}. Bobrov et al.⁹² provides the first investigation into the use of visual imagery as a BCI control paradigm. In this study, they were able to reliably distinguish between visual imagery of faces, visual imagery of houses, and resting state with an average of 56% classification accuracy (chance

33%) during an online BCI control task. Lee et al.⁸⁹ was able to demonstrate a high average classification accuracy of around 40% (chance 7.69%; 22 participants) during an offline analysis of a single session of 13 visual imagery categories. This included words used for patient communication with concrete properties (e.g., ambulance, clock, or toilet) or abstract properties (e.g., hello, stop, or yes). In Kosmyna et al.⁸¹, researchers performed offline classification between two classes of flower vs. hammer during visual observation and imagery. They were unable to achieve above chance accuracy between the two classes during visual imagery (average classification accuracy 52%, chance 50%), but they were able to distinguish a difference between the trials when participants performed visual imagery vs rest (77% average classification accuracy; chance 50%) and between visual observation vs imagery (71% classification accuracy; chance 50%).

LIMITATIONS OF PREVIOUS VISUAL IMAGERY STUDIES

One shortcoming in the aforementioned studies is that the two larger experiments by Kosmyna et al.⁸¹ and Lee et al.⁸⁹ displayed the target category each trial immediately before the imagery period. This could be considered more of a test of holding the object categories in working memory rather than spontaneous visual imagery. Additionally, these two studies only performed an offline analysis on a single session of data for each participant. While this could give a good baseline about a person's ability to perform visual imagery, it does not give a full picture of the efficacy of using visual imagery as a BCI control strategy. Imagery-based BCIs often require participants to undergo multiple training sessions in which they learn to modulate the specific frequencies of brain activity associated with the desired action¹⁰. This allows both the user and the BCI system to adapt for better performance. In this way, the user can learn to modulate suitable patterns of brain

activity while the BCI system can adapt to better identify the differences in these patterns¹³². The experiment by Bobrov et al.⁹² accounted for this by including 4 sessions of online BCI interaction. However, this study was limited by the number of recruited subjects (N=7), amount of data collected (four sessions each approximately 5 min long), and the quality of data collected (first three sessions used the 16 channel Emotiv Systems Inc. Epoc headset).

Identifying the cause of why some of the previous visual imagery studies were successful while others failed is difficult. Each study used different image categories, different signal processing techniques, different spectral and spatial features of the data, and different machine learning methods. One possible explanation might be that Kosmyna et al.⁸¹ was not able to distinguish between visual imagery of the two object categories because the brain activity associated with flowers and hammers are too representationally similar. On the other hand, Bobrov et al.⁹² might have been more successful because imagined faces and houses are more distinct neurally. Therefore, the goal of this study was to map the neural representational space in EEG of various image categories using visual imagery. We hypothesized that visual imagery of certain categories of images, such as between natural and manmade objects, will produce more similar patterns of brain activity than other categories, such as human faces which may be more unique. This experiment will provide insight into which categories can produce distinct neural activity patterns identifiable by EEG for use in a visual imagery BCI.

MAPPING THE REPRESENTATIONAL SPACE OF VISUAL IMAGERY CATEGORIES

The representational structure of the categorical responses to various image categories can be operationalized by performing a representational similarity analysis⁴⁴.

This approach allows the comparison of representational geometry regardless of modality by assessing the pairwise distances between categories rather than the responses themselves⁴⁵. Kriegeskorte and colleagues pioneered this approach using fMRI in humans and single-cell recordings in non-human primates by demonstrating that object representations in the inferior temporal cortex form categorical clusters that are similar across species⁴⁵. The comparisons between response patterns for each stimulus can be summarized using a “representational similarity matrix”. Each cell of the matrix compares the correlation in the brain activity between two stimuli. Recent studies using magnetoencephalography (MEG)⁴⁶ and EEG⁴⁷ have also used the same image sets as Kriegeskorte⁴⁴ to further study the structure and temporal evolution of the representational space of these objects. This image set is comprised of six categories of images including human faces, human bodies, animal faces, animal bodies, natural objects, and manmade objects. The representational similarity matrices for these studies were constructed by using multivariate pattern classification to reveal category selectivity in response to the presentation of the visual stimuli^{46,47}. In this way, similarity in the brain activity patterns between classes is reflected by increased classifier confusion. For this experiment, we will use an approach similar to Kaneshiro et al.⁴⁷ to quantify the representational similarity between image categories using confusion matrices generated from multi-class classifications. This will allow us to perform a direct comparison of the representational structure measured by EEG during observation and visual imagery.

Methods

PARTICIPANTS

A total of N=20 healthy adults between the ages of 18-40 years old were recruited from the Austin community for participation in this study. However, the data from two participants was removed from the analyses (one subject did not complete both sessions, and one other encountered issues with the EEG equipment during the experiment). This left a final total of N=18 participants (10 female, average age 24 years, SD=5.97). A statistical power analysis using G*Power¹³³ for *a priori* calculations was performed for sample size estimation. This analysis was based on a similar study that conducted an RSA of EEG data during visual observation of the same image set in N=10 participants⁴⁷. The effect in this study of $d=14.62$ was considered to be extremely large using Cohen's criteria. To be conservative and to account for the greater difficulty in classifying visual imagery compared to observation, we assumed a large effect size of 0.8, $\alpha < 0.05$ and $\beta > 0.80$ which produced an estimated sample size of N=15. Thus, our obtained sample size of N=18 should be more than adequate.

INCLUSION CRITERIA

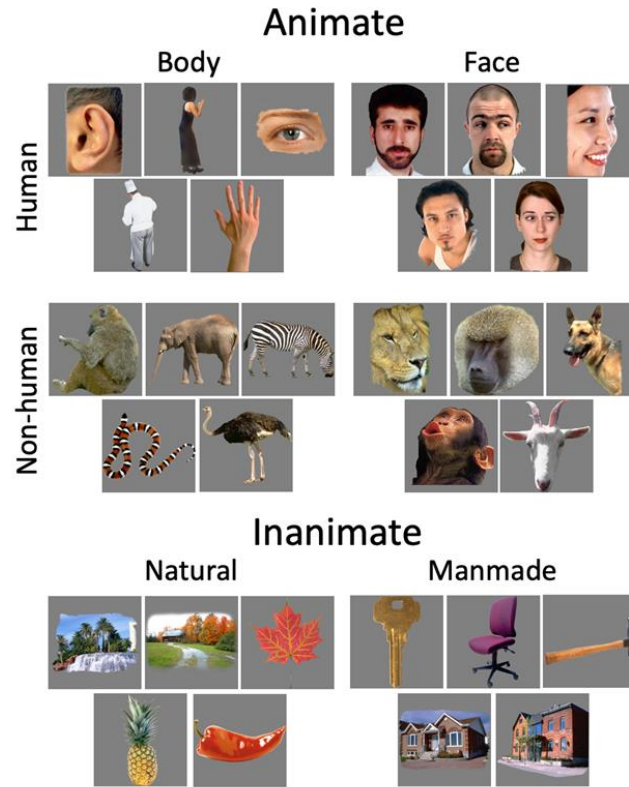
The experiment conducted in this study involved participants performing visual imagery of a cued stimulus presented on a computer monitor. Participants' neural activity was measured by EEG throughout the experiment. As such, all participants were required to meet the following inclusion criteria: ability to provide informed consent, not be currently using any medication for psychiatric reasons, not be currently using any sedatives, no history of major psychotic disorders (including schizophrenia and bipolar disorder), no history of epilepsy or photosensitivity, no substance dependence, and good

vision or minimal correction with contacts or eyeglasses. Participants were also asked to remove hair braids or any other tight hair styles and have clean hair (no oils, hair spray, or any other hair product) before participating in EEG recordings. This study also incorporated eye tracking, for which case individuals were excluded from participation in this study if they have glasses with more than one power (such as bifocals, trifocals, or progressive lenses), eye surgery (such as corneal, cataract, or intraocular implants), or eye movement or alignment abnormalities (such as amblyopia, strabismus, or nystagmus).

TASK PROTOCOL

Participants in this study underwent two sessions of data collection spaced between one and seven days apart. In each session, participants were asked to perform visual imagery of six object categories: human faces, human bodies, animal faces, animal bodies, natural objects, and manmade objects. These image categories were obtained from the same image set as the previous fMRI⁴⁵, MEG⁴⁶, and EEG⁴⁷ studies to allow a direct comparison of visual observation and imagery. The full image set consists of 92 pictures in categories of human faces, human bodies, animal faces, animal bodies, natural objects, and manmade objects. However, due to the additional time necessary for imagery, only five images per category were used for a total of 30 images (**Figure 3.1 A**). The stimuli were presented using PsychoPy software in 5 runs of 120 trials. Before each run, the participants were shown six images, one from each category, with a descriptive word beneath them (**Figure 3.1 B**). Then, during each trial, the participant was shown only the word cue for 1.5 sec, a blank screen for 2.5 sec, and a fixation cross for 1 sec. Participants were instructed to maintain visual focus on the center of the screen during each trial. When the screen was blank, the participants were instructed to produce a vivid mental image of

A.



B.

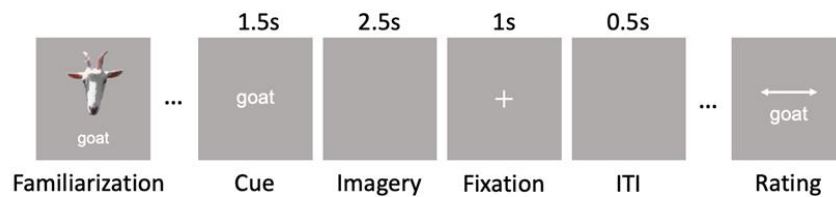


Figure 3.1: Experimental task protocol. (A) Set of 30 images from the six different object categories. **(B)** Each trial, individuals performed visual imagery of the cued images. One image and its word association from each category was familiarized before each run. Participants rated how difficult it was to imagine each image at the end of every run.

the previously learned stimulus associated with the word cue. A brief, 0.5 sec inter-trial interval (ITI) consisting of a blank screen was included between each trial. A 10 sec break was provided every 30 trials with a longer, self-paced break between each run to limit fatigue. At the end of each run, the participants rated how difficult it was to visualize each of the six target images for that run by using the mouse cursor to select a spot on a continuous line labeled from “not challenging at all” to “very challenging”.

EXPERIMENTAL SETUP

The EEG experiments were performed in a private, sound-dampened room to prevent distractions. Participants were seated comfortably in a fixed chair in front of a computer monitor. EEG data was recording using an ActiCap 32-channel active electrode system with a LiveAmp amplifier (Brain Products GmbH, Gilching, Germany). Five additional electrodes were connected to measure the electrooculogram (EOG) to be used for the removal of eye movement artifacts. Electrodes were placed above and below the right eye, and another two on the left and right infraorbital rim, respectively. These electrodes for the EEG and EOG data were all connected to the LiveAmp amplifier and recorded with a sampling rate of 500 Hz. A Tobii Pro Nano was also used to track eye movements and pupil diameter throughout the experiment with a sampling rate of 60 Hz. Visual instructions were presented to the participant using PsychoPy. Synchronization between the recording devices and stimulus presentation was mediated through the use of Lab Streaming Layer and recorded using the Lab Recorder software.

DATA PREPROCESSING

All data processing was carried out using the MNE Python package. Data from channels labeled as “bad” were removed and interpolated from the surrounding electrodes.

Then, the signal was re-referenced to the common average to remove any background noise that is common across all channels. Eye movement and blink artifacts were removed from the signal using an independent component analysis (ICA)¹³⁴. Artifact removal via ICA was carried out using the following procedure: implementing a high-pass filter at 1 Hz to remove signal drift, implementing notch filters at 60 Hz and its harmonics to remove powerline interference, annotating the task and break periods, running the ICA using MNE's ICA algorithm with 32 components, manually selecting components that contained artifacts, removing these components, and applying the solution to the unfiltered data. Finally, the data was bandpass filtered between 0.3 – 125 Hz with a notch filter at 60 Hz and 120 Hz to prepare the signal for feature extraction.

FEATURE EXTRACTION AND CATEGORY-LEVEL CLASSIFICATION

For this experiment, we used an approach similar to Kaneshiro et al.⁴⁷ to quantify the representational similarity between image categories using confusion matrices generated from multi-class classifications. Various frequency domain features (1-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), low gamma (30-60 Hz), and high gamma (60-100 Hz) were tested. This included using different combinations of the full spectrum, mean, variance, minimum, maximum, skewness, kurtosis, and entropy values for the various power bands. We also tested the use of Common Spatial Patterns⁸⁹ (CSP) features with various components.

We tested the multivariate analysis of the category-level classification with various classifiers including support vector machine, logistic regression, linear and quadratic discriminant analysis, multilayer perceptron, long short-term memory neural networks, and 1D and 2D convolutional neural networks. For the analysis presented in **Figure 3.2**, a long

short-term memory (LSTM) neural network using the TensorFlow Python library was implemented. This network consisted of a single LSTM layer with 128 nodes, a fully connected Dense layer with 64 nodes, a 20% dropout layer, and a Dense output layer with 6 nodes. The network was trained with the Adam optimizer with a learning rate of 0.0005 and a batch size of 12. Early stopping with a patience of 10 epochs was implemented using sparse categorical crossentropy to monitor the validation loss during training.

A sliding window was implemented to segment the data from the 2.5 sec imagery period into 1.25 sec periods with a 50% overlap. This yielded a total of 3 windows per trials. This allowed the LSTM network to gain additional information through the temporal relationship between the windows. The mean power from 15 logarithmically spaced frequencies between 5-100 Hz were extracted from these periods and all 32 channels using Morlet Wavelets. Data was portioned for classification using an 80/10/10 split (80% training, 10% validation, and 10% testing).

ITEM-LEVEL CLASSIFICATION

Due to the limited amount of training data (20 trials per image), we were unable to evaluate the use of the neural network classifiers for item-level classification. The results presented in **Figure 3.3** were obtained using a Logistic Regression (LR) classifier with a newton-cg solver implemented using the sci-kit learn Python library. A sliding window was implemented to segment the data from the 2.5 sec imagery period into 1.25 sec periods with a 50% overlap. The LR classifier was trained using the mean power in the alpha, beta, low gamma, and high gamma bands obtained using the Fast Fourier Transform. The LR classifier was evaluated using a leave-one-run-out (5-fold) cross-validation approach.

REST VS. IMAGERY CLASSIFICATION

Since there was no explicit resting period in the experimental protocol, the last 1.25 sec period in each trial was used as a resting condition. This period includes the fixation and inter-trial period after imagery and before the next trial starts. To balance the amount of data for imagery vs rest, only the middle 1.25 sec window of the imagery period was used to represent the neural activity during visual imagery. An LR classifier using a leave-one-run-out (5-fold) cross-validation was used to predict between the two conditions.

EVALUATION OF PERFORMANCE

The classifier's performance will be evaluated based on the number of trials where the EEG classification output matches the target category for that trial beyond the level of chance. However, small sample sizes can lead to false positives, and Combrisson and Jerbi¹³⁵ have suggested to address this issue by adjusting the chance level as a function of sample size (n) and number of classes (c) using a binomial cumulative distribution. Using this method, the probability of a classification model to predict the correct label at least z times by chance is given by the equation:

$$P(z) = \sum_{i=z}^n \binom{n}{i} \times \left(\frac{1}{c}\right)^i \times \left(\frac{c-1}{c}\right)^{n-i}$$

In this study, the statistically significant threshold level was calculated using the MATLAB (Mathworks Inc., MA, USA) function $St(\alpha) = \text{binoinv}(1 - \alpha, n, 1/c) \times 100/n$, where α is the significance level given by $\alpha = z/n$. For example, the LSTM model used in the category-level classification was evaluated using only 60 observations across six classes which provide a significance threshold of 25% at $p=0.05$. Thus, the model must

obtain at least 25% accuracy to be considered successful beyond the level of chance. For the item level classification, the cross-validated model included 1800 observations (600 trials x 3 windows per trial) across 30 classes providing a significance threshold of 4.06% at $p < 0.05$. The rest vs. imagery classifier contained 1200 observations and 2 classes providing a significance threshold of 52.33% at $p < 0.05$.

Results

Our first test was to determine the category-level classification ability between the six classes used in this experiment. Both sessions of data from $N=18$ participants were preprocessed to remove noise and common muscle artifacts (see **Methods** for more details on signal preprocessing). We tested various combinations of frequency domain power in the delta (1-4 Hz), theta (4-8 Hz), alpha (8-13 Hz), beta (13-30 Hz), and gamma (30-100 Hz) bands computed using Fast Fourier Transform and Morlet wavelets as features for classification. We also tested the use of various numbers of Common Spatial Patterns (CSP) features which Lee et al.⁸⁹ found to provide high classification accuracy in a visual imagery task. Multiple classifiers were tested including support vector machine, logistic regression, linear and quadratic discriminant analysis, multilayer perceptron, long short-term memory neural networks, and 1D and 2D convolutional neural networks. In all scenarios, no results significantly exceeded chance level. As an example, the results for the long short-term memory (LSTM) neural network are shown in **Figure 3.2**. For this analysis, a sliding window was implemented to segment the data from the 2.5 sec imagery period into 1.25 sec periods with a 50% overlap. This yielded a total of 3 windows per trials. The mean power from 15 logarithmically spaced frequencies between 5-100 Hz were

extracted from these periods and all 32 channels using Morlet Wavelets. Data was portioned for classification using an 80/10/10 split (80% training, 10% validation, and 10% testing). A long short-term memory (LSTM) neural network was then used on this data to predict between the six imagery categories which yielded a mean classification accuracy of 19.72%.

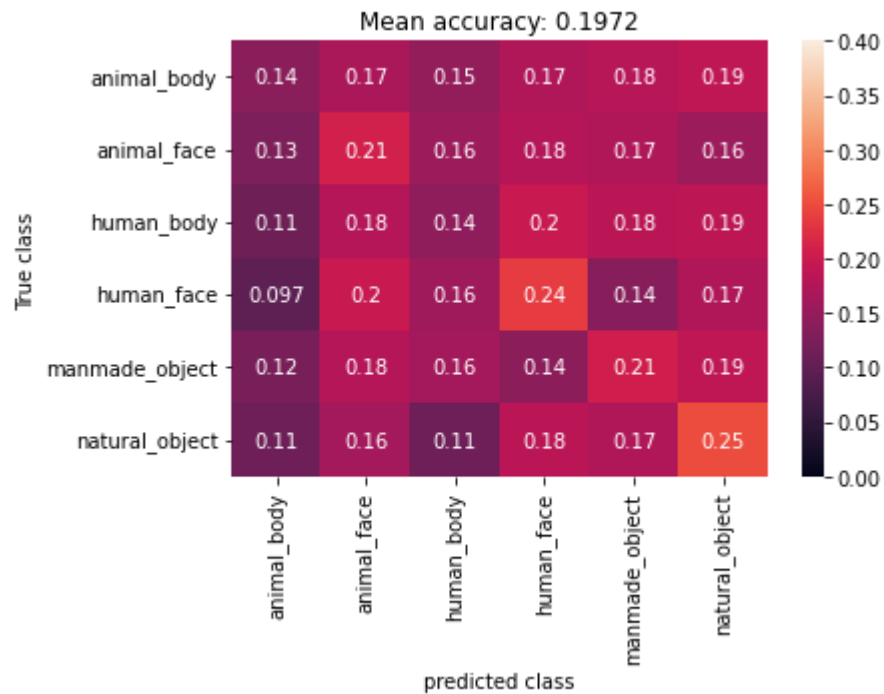
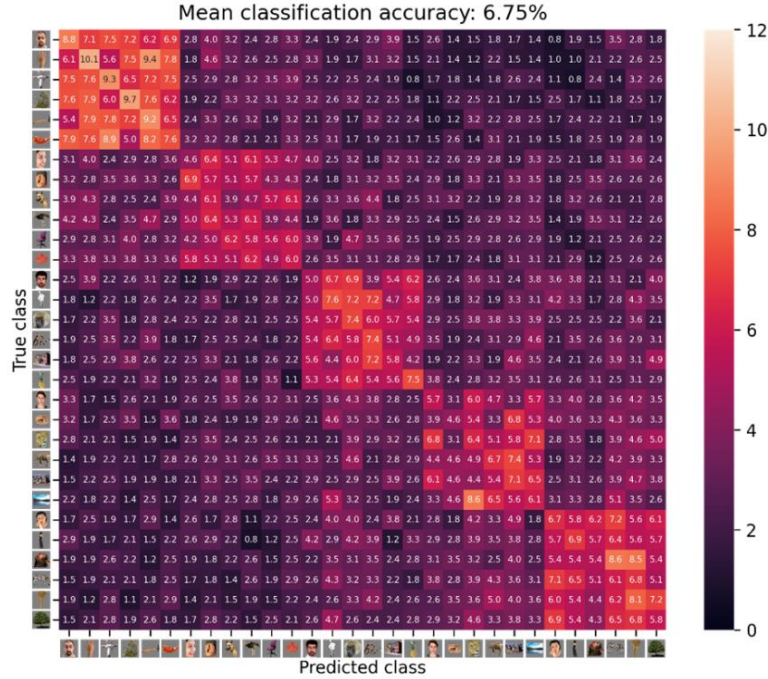


Figure 3.2 Category-level classification results. To assess the ability to classify between the visual imagery of various object categories, we implemented a long short-term memory (LSTM) neural network. The data from each trial was divided into three overlapping windows and fed into the LSTM network. This provided an overall classification accuracy of 19.72% (significance threshold = 25%). While the overall accuracy across the six categories was not significant, the classifier was able to identify human faces and natural objects more accurately.

We next tested the ability to predict between the mental imagery of the 30 individual pictures used during this experiment. Since the number of observations for each image was much lower in this analysis, a logistic regression (LR) classifier was used instead of the previously used LSTM network. The LR classifier was trained using the mean power in the alpha, beta, low gamma, and high gamma bands using a leave-one-run-out cross-validation approach. This yielded a mean classification accuracy of 6.75% across all subjects (**Figure 3.3**). While this value was significantly above the significance threshold of 4.06% ($p < 0.01 \times 10^{-10}$), the confusion matrix revealed a strong bias towards images that appeared during the same run of the experiment. We attempted to address this run bias using various methods such as performing a manual baseline correction for each trial. To accomplish this, we subtracted the mean signal value from the 0.5 sec ITI period preceding each of the trials using the MNE Python library's baseline correction function. This yielded nearly equivalent results (6.60% classification accuracy) along with the same temporal bias. We also tried averaging trials to improve the signal-to-noise following the procedure outlined in Xie et al.¹³⁶ This involved Splitting the image trials into five groups each (4 trials per group), averaging the data, and performing a leave-one-group-out cross-validation with a linear SVM. This process was repeated for 25 iterations of random group assignment and the final classification result was taken as the average accuracy from each iteration. This process also yielded equivalent results (6.64% classification accuracy) with the same temporal bias. Finally, we attempted to classify between the six images within each run individually using the LR classifier with a 5-fold cross-validation approach. This did not provide significantly greater than chance results (17.9% classification accuracy) likely because of the limited amount of data within each run.

A.



B.

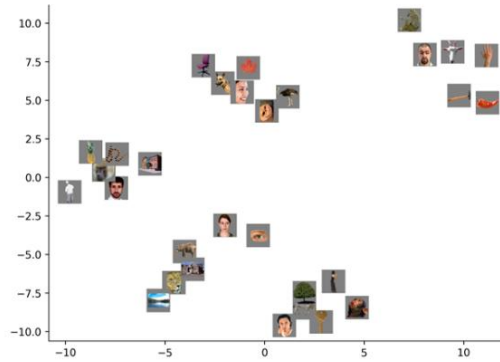


Figure 3.3 Item-level classification results. **A.** Confusion matrix for 30-class item-level classification results (mean accuracy 6.67%, significance threshold 4.06% ($p < 0.01 \times 10^{-10}$)) **B.** Multi-Dimensional Scaling plot of classification results shows strong bias to items that appeared within the same experimental run.

Our final experiment was to perform a simple binary level classification between the imagery periods and the resting periods between each run. To accomplish this, we used the last 1.25 sec interval of each trial consisting of the fixation and ITI periods as the resting condition. The middle 1.25 sec window of the imagery period represented the neural activity during visual imagery. We trained an LR classifier with a 5-fold cross-validation approach to predict between these two periods with a 75.4% accuracy which is significantly above the significance threshold of 52.33% ($p < 0.01 \times 10^{-15}$) (**Figure 3.4**).

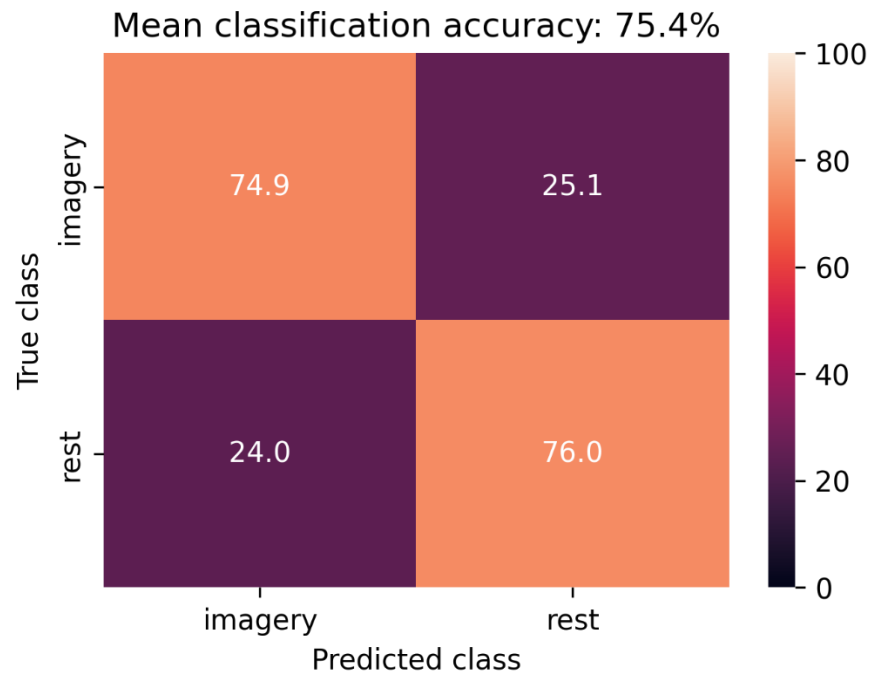


Figure 3.4 Imagery vs Rest classification results. Our results indicate that our classifier can accurately detect the performance of visual imagery compared with rest beyond the level of chance (75.4%, significance threshold 52.33%, $p < 0.01 \times 10^{-15}$).

VISUAL IMAGERY BLACK HOLE ALGORITHM

During the analysis of this project, a journal article by Lorella et al. was published which presented the results of a 12-class visual imagery study in EEG with a classification accuracy of near 29% accuracy (chance 8.3%)¹⁰⁶. This study introduced the use of a *black hole algorithm* as a heuristic approach to tune the hyperparameters for a CNN classifier individually for each subject to obtain an optimal configuration. In the black hole algorithm, a number of stars (representing possible solutions to the given problem) are set in motion around a singular black hole (the star with the best solution). As the algorithm is iterated, an equation of motion is used to update the position of the stars around the black

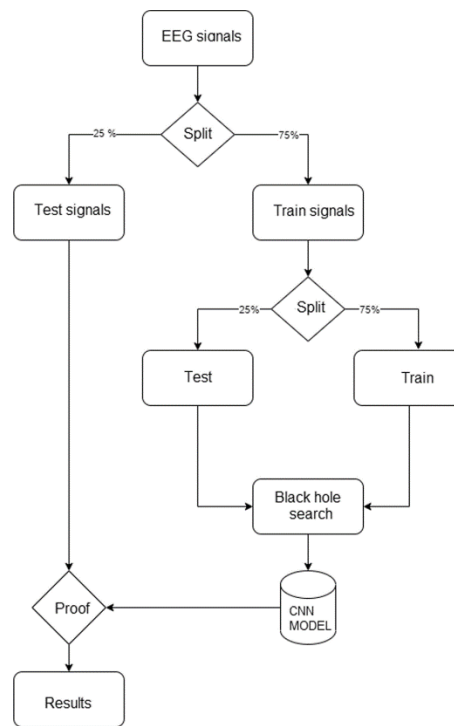


Figure 3.5 Black hole algorithm implementation outlined by Lorella et al.¹⁰⁶ The data is split into three groups: two for creating and training the CNN model using the black hole algorithm and one left-out group for validation of the model.

hole. If a star obtains a better solution, it becomes the new black hole. If it does not, the parameters are slightly changed, and the star is moved closer to the black hole. If the star continues to provide lower scores, it will fall into the black hole and be replaced by a new star. This prevents the algorithm from reaching a local minimum and allowing the full search space to be explored.

The steps Lorella et al.¹⁰⁶ used to evaluate their black hole algorithm is presented in **Figure 3.5**. In this configuration, the data is divided into three groups, where two of these groups are used to create and train the CNN model and the third group is used for validation. Following a similar approach, we were unable to obtain an above chance result on the left-out testing data. It appears that within the black hole search, the model is overfitting to the internal testing data (**Figure 3.6 A**) After many iterations of various network configurations, the black hole algorithm could find one that fits the training data very well. However, this model was not able to generalize to the left-out validation set. To demonstrate this, instead of using a single left-out validation set, we performed a leave-one-block-out (5-fold) cross-validation using the optimal CNN network configuration identified from the black hole algorithm within each subject. **Figure 3.6 B** and **C** show the distribution of scores obtained from two representative subjects for this analysis. For each subject, it can be seen that the testing set used to evaluate the performance of the model within the black hole search yields a high accuracy, but the cross-validation indicates that's the same model is not able to generalize to the other testing cases. After presenting these findings to the authors of the initial paper implementing the black hole algorithm for visual imagery, they identified an error in their code which led to a higher estimation of the classifier's prediction ability. Fixing this error led them to obtain near chance level classification on the validation set as we have found.

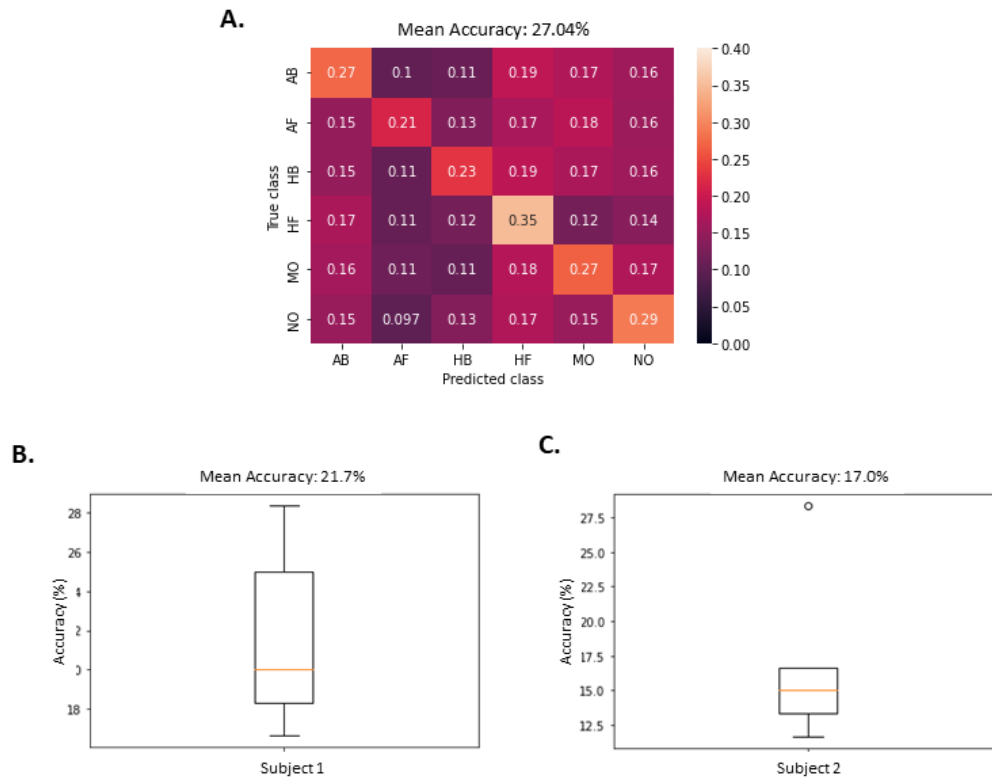


Figure 3.6 Black hole algorithm results. **A.** Confusion matrix obtained using the best model configuration identified from the black hole algorithm on the internal testing set. **B** and **C.** Box plot for the classification scores within two representative subjects showing that the model is overfitting to the data used within the black hole search.

Discussion

We were unable to confirm our initial hypothesis that multivariate classification of EEG can accurately discriminate between various imagery categories. The initial work by Kaneshiro et al.⁴⁷ using visual perception provided promising results for the ability to decode category-level responses to images using EEG. We believed that similar patterns

would be found during visual imagery based on the sensory recruitment hypothesis¹³⁷ which posits that the neural representations activated during perception can also be activated during short-term retention. While we did see some trends like higher classification accuracy in human faces, we were unable to achieve an above chance result for the overall classification. It appears that the activity produced during visual imagery is either too small, too variable, or too widespread to be accurately identified in EEG. We were able to get a significant result when predicting whether the subject was performing visual imagery or just resting between trials. This finding is consistent with Kosmyna et al.⁸¹ and indicates that visual imagery can be identified using EEG, but the activity may be too representationally similar to discriminate between. Visual perception is primarily defined by activity in the visual sensory regions of the occipital cortex. Since visual imagery does not have the same sensory component, its activity has greater definition in the more frontal and parietal regions associated with memory or emotion¹³⁸. For this reason, the neural responses to the various images may not behave the same for both perception and imagery and therefore it may not be possible to combine them into groups.

The item-level classification in this experiment did show some promising results. However, the confusion matrix presented in **Figure 3.3** did reveal a significant bias in the classifier to items that appeared within the same run. Our attempts to address this bias by performing baseline correction and the averaging data to improve signal-to-noise did not obviate the issue. Treating the runs individually also did not provide a significant result likely due to the limited amount of data available for training the classifier. It is likely that the classification model was being influenced by another factor such as the participant's fatigue throughout the experiment rather than just visual imagery activity alone. Future work is needed to evaluate if item-level predictions of visual imagery is possible with EEG.

Future experiments should also be careful to balance the presentations of images equally throughout the experiment to account for the effects like fatigue level that can change over the course of the session.

Finally, our investigation into the implementation of the black hole algorithm revealed an error in the results presented in Lorella et al.¹⁰⁶ It appears that the model is overfitting the data within the black hole search and unable to generalize to a left-out validation set. The authors of this paper have been made aware of this issue and have found the error in their code which led to a higher estimation of the classification accuracy obtained with their data.

CHAPTER 4

EVALUATING THE FEASIBILITY OF VISUAL IMAGERY FOR AN EEG-BASED BRAIN-COMPUTER INTERFACE

Abstract

Despite promising initial work in visual imagery BCIs^{89,92,139}, the mechanisms underlying successful performance remain unclear. For example, one of the major limitations in previous visual imagery studies is that the target image was displayed directly before the imagery period. This could be considered more a short-term retention of the image in working memory rather than performing spontaneous mental imagery from long-term memory. Results from this study show that visual imagery following a perception cue of the target image provides a stronger, more easily classifiable signal (30.05% classification accuracy) than visual imagery following an auditory cue (26.45% classification accuracy). We have also shown that visual imagery and perception share commonalities in the most predictive electrodes and spectral features. However, visual imagery received greater influence from frontal EEG electrodes whereas perception was mostly confined to occipital electrodes. This work provides the first direct comparison of short-term and long-term visual imagery tasks and provides greater insight into the feasibility of using visual imagery as a BCI control strategy.

Introduction

The concept of using brain signals recorded via electroencephalography (EEG) to control external devices has gained traction in recent years as a potential way to provide

patients with severe neuromuscular disorders a way to communicate and interact with the world around them^{11,63}. This technology, termed brain-computer interface (BCI), has since grown to cover applications such as robotic control^{64–66}, communication^{67,68}, and even entertainment and gaming^{12,69–71} (**Figure 4.1**). Various control strategies exist for BCI interaction, but each come with their own limitations that prevent BCIs from obtaining widespread use outside the lab¹⁰. The imagined movements of large body parts is perhaps the most common control paradigm for EEG BCI applications; however, it often suffers from lengthy training times¹⁰ with inconsistent and unstable performance⁸⁷, and a restricted range of options for imagined movements⁸⁹. Most attempts to address the limitations of this paradigm focus on advancing EEG signal processing and classification techniques⁹⁸; however, an often overlooked solution is investigating other imagery-based control strategies^{130,131}. The objective of this aim is to investigate the efficacy of using visual imagery for EEG BCI control. Visual imagery has a potentially infinite number of available classes which can provide a more ecological connection between the mental imagery and intended action.

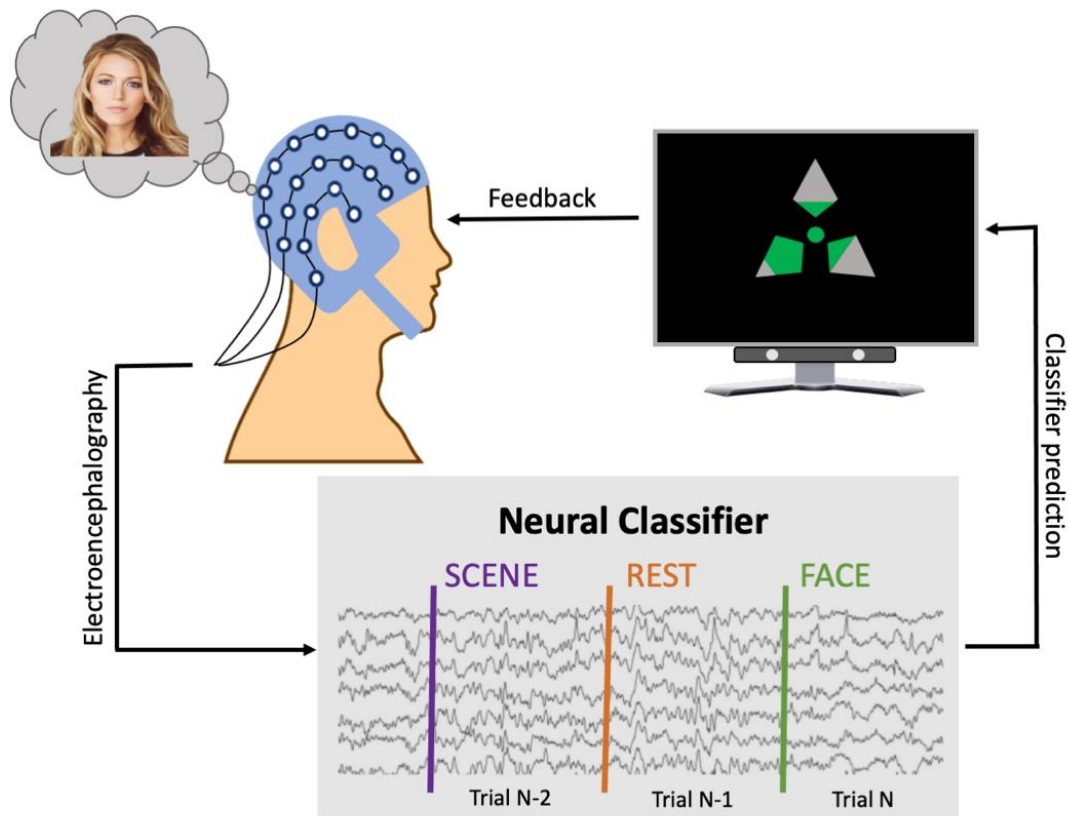


Figure 4.1: Overview of a closed-loop BCI system. Participant performs visual imagery while neural data is recorded. That data is processed and classified to predict the user's intention. Feedback representing the predicted class is provided to allow self-modulation.

LIMITATIONS OF CURRENT BCI CONTROL PARADIGMS

When designing a BCI system, one major consideration is the means of interaction a participant will use to perform the task. These control paradigms can be divided into two methodologies: exogenous paradigms based on the brain's response to an external stimulus, and endogenous paradigms where participants learn to modulate their brain activity using mental imagery¹⁰. The most popular exogenous paradigms in EEG rely on

measuring the brain's response to visual stimuli such as a flickering target^{10,67,74,77}. Most participants can learn to use these paradigms with high accuracy and minimal training¹⁰. However, these procedures can be time intensive and require a high level of sustained attention and visual focus which can cause fatigue⁷⁵ and would not be suitable for individuals with visual impairments or photosensitivity^{76,78}. Furthermore, there is often large variability in performance across individuals^{83,84}, perhaps because the control strategy is not intuitive, and this confusion can take focus away from the desired application. For example, the user would have to remember which flickering target corresponds to the intended action instead of attending to the action directly.

To overcome these challenges, endogenous control paradigms with mental imagery can be used instead. Motor imagery of the movements of large body parts (e.g., right vs. left hand) is the most popular imagery-based paradigm¹⁰. Limitations for this approach include lengthy training times (weeks to months)¹⁰, large inter- and intra-subject performance variations⁸⁷, non-intuitive control schemes for certain applications⁸⁸, and a limited variety of classes available for BCI control⁸⁹. Furthermore, factors such as noise in the EEG signals, motivation, fatigue, and difficulty visualizing the intended action can greatly impact a user's ability to gain control of the BCI⁹⁰. This leads to a challenge referred to as "BCI Illiteracy" in which a substantial percentage of participants (approximately 15-30%) remain unable to achieve proper control of a BCI even after a standard training period⁹⁷. Even for the participants who can attain some control, performance often falls short of the desired threshold rate for effective control (often set at 60% or 70% accuracy)^{87,98,99}. These difficulties have been observed across all BCI paradigms regardless of the neural signal used¹⁰⁰. Some studies have even seen that participants who are deemed "BCI illiterate" using one paradigm can learn to reach proficiency using another¹⁰¹. For

these individuals, the availability of a different mental imagery paradigm may be beneficial to achieve proper BCI control.

INVESTIGATING VISUAL IMAGERY AS AN ALTERNATIVE BCI CONTROL STRATEGY

Visual imagery, or the mental simulation of visual information from memory¹⁰², could be a useful BCI control strategy that has not yet been sufficiently tested⁸¹. The human brain is predominantly visual: 90% of the information transmitted by the brain is visual¹⁰³, and it can process images 60,000 times faster than text^{81,104}. Visual imagery may also be a more intuitive control strategy than any of the paradigms listed above⁸⁹. For example, if a person would like to use a BCI system to control a light in their house, the user could directly imagine the lamp they would like to turn on instead of gazing at a flickering target or remembering which imagined movement for a limb corresponds to that light. Furthermore, visual imagery can provide a near infinite number of visual image categories whereas motor imagery is often limited to only four or five possible options⁸⁹.

Several studies have shown that various categories of images (e.g., faces, animals, and inanimate objects) can be reliably distinguished using EEG when participants are observing an image^{81,82,105}. However, very few studies have attempted to measure visual imagery using EEG, and those that do have shown mixed success^{81,89,92}. Bobrov et al.⁹² provides the first investigation into the use of visual imagery as a BCI control paradigm. In this study, they were able to reliably distinguish between visual imagery of faces, visual imagery of houses, and resting state with an average of 56% classification accuracy (chance 33%). However, this study was limited by the number of recruited subjects (N=7), amount of data collected (four sessions each approximately 5 min long), and the quality of data collected (first three sessions used the 16 channel Emotiv Systems Inc. Epoc headset). Lee

et al.⁸⁹ was able to demonstrate a high average classification accuracy of around 40% (chance 7.69%; 22 participants) during an offline analysis of a single session of 13 visual imagery categories. This included words used for patient communication with concrete properties (e.g., ambulance, clock, or toilet) or abstract properties (e.g., hello, stop, or yes). In Kosmyna et al.⁸¹, researchers performed offline classification between two classes of flower vs. hammer during visual observation and imagery. They were unable to achieve above chance accuracy between the two classes during visual imagery (average classification accuracy 52%, chance 50%), but they were able to distinguish a difference between the trials when participants performed visual imagery vs rest (77% average classification accuracy; chance 50%) and between visual observation vs imagery (71% classification accuracy; chance 50%).

LIMITATIONS OF PREVIOUS VISUAL IMAGERY STUDIES

One shortcoming in the aforementioned studies is that the two larger experiments by Kosmyna et al.⁸¹ and Lee et al.⁸⁹ displayed the target category each trial immediately before the imagery period. This could be considered more of a test of holding the object categories in working memory rather than spontaneous visual imagery. In the previous study (**Chapter 3**), we attempted to address this limitation by providing subjects with a word cue for the intended target each trial instead of the actual visual stimulus. The classification accuracy was unable to exceed chance level, so it remains an open question if spontaneous visual imagery can be decoded from EEG. To answer this question, this current study provides participants with both visual and auditory cues of the intended mental imagery in separate experimental blocks.

Furthermore, the addition of the actual image during the cue period will allow us to more directly compare the neural signals elicited during observation and imagery. A study by Xie et al.¹³⁶ followed a similar procedure while looking for similarities between the mental activity during visual observation and imagery and found a correlation in the alpha band (8-13 Hz) between the two conditions. This is supported by the sensory recruitment hypothesis¹³⁷ which posits that the neural representations activated during perception can also be activated during short-term retention. However, the study by Lee et al.⁸⁹ found that activity in the higher gamma band (30-100 Hz) contained the most informative activity for visual imagery. This study will seek to add to this ongoing investigation for the most informative features for visual imagery decoding and the similarities between the neural activity during perception and imagery.

IDENTIFYING NEURAL MECHANISMS CONTRIBUTING TO BCI PERFORMANCE

It is poorly understood why certain individuals are unable to control a BCI after a standard training protocol⁸⁷. Previous literature from motor imagery has suggested many factors could play a role in performance variability including the user's basic demographics^{140,141} (e.g., lifestyle, gender, or age), psychological traits^{99,142,143} (motivation, confidence, or frustration), physiological traits^{144–147} (e.g., recruitment of motor imagery related brain networks), and anatomical structure¹⁴⁸ (e.g., structural integrity and myelination quality). Previous work from our group has indicated that difficulty learning to modulate desired brain activity in an fMRI neurofeedback task could be due to greater similarity in the brain activity patterns for each category¹⁴⁹ or overly rigid activity patterns (i.e., insufficient variability) for each category¹¹⁷. For this reason, we followed a similar approach as Kaneshiro et al.⁴⁷ (outlined previously in **Chapter 3**) to

quantify the representational similarity⁴⁴ between image categories using confusion matrices generated from multi-class classifications. We also administered a Vividness of Visual Imagery Questionnaire¹⁵⁰ (VVIQ) before the start of the experiment along with questionnaires of perceived psychological traits such as motivation, alertness, and frustration after each session. Participants' attention and engagement throughout the experiment were monitored using eye tracking and pupillometry. Together, this information was collected to allow a more thorough exploration into the conditions contributing to successful decoding of visual imagery.

INCLUDING ADDITIONAL BIOLOGICAL SIGNALS CAN IMPROVE BCI PERFORMANCE

Recent studies have also provided evidence that the inclusion of additional biological signals can improve performance in a BCI application¹⁰. For example, changes in the diameter of the pupil can occur in response to psychophysical and psychological stimuli¹⁰⁷. A study by Rozado et al.¹⁵¹ used pupillary response to improve users' performance in a motor imagery BCI. In this study, they found that motor imagery can lead to increases in pupil diameter compared to a resting condition, and this can be used as a switch for the BCI to identify when the user is attempting to perform an action. Eye tracking and measuring the electrooculogram (EOG) can also be used to improve BCI performance by providing more operational instructions, improving accuracy, and reducing signal detection time beyond that of EEG alone^{134,152}. These measurements can also be useful at identifying and correcting artifacts in the EEG data as a result of eye movements or blinks¹³⁴. For these reasons, we included measurements of EOG, gaze tracking, and pupillometry during our experiments to investigate if these additional biological signals can be used to improve visual imagery BCI performance.

Methods

PARTICIPANTS

A total of N=30 healthy younger adults between the ages of 18 and 40 years old were recruited from the Austin area for participation in this study. However, only N=26 subjects (18 female, average age 22 years, SD=4.17 years CI) were included in the analysis due to issues encountered during data collection. A statistical power analysis using G*Power¹³³ for a priori calculations was performed for sample size estimation. The analysis was based on the studies of Lee et al.⁸⁹ (N=22) and Bobrov et al.⁹² (N=7) who performed a classification analysis of EEG data during visual imagery. Both studies reported an extremely large effect size above $d=1$. To be conservative during our estimation, we assumed an effect size of 1, $\alpha < 0.05$ and $\beta > 0.80$ which projects a sample size of N=10. Thus, our collected sample size of N=26 should be more than adequate. The same inclusion criteria from **Chapter 3** were followed for this experiment (see **Chapter 3 Methods**).

TASK PROTOCOL

This study involved a single session of data collection. During the experiment, the participants were asked to perform mental visual imagery of four different categories of human faces, animals, objects, and scene images. Before the experiment, participants selected a single image from each of these categories to use during the session (see below **Stimuli** for more information about the images used during this experiment). The task included 5 blocks of visual imagery following either a visual observation or auditory cue (**Figure 4.2 A** and **B**, respectively). During the observation cue blocks, the target image for each category was displayed with a small fixation cross at the center of the screen for 2.5

sec and the participant was instructed to passively view it while attempting to keep their gaze on the center cross. The image was then removed from the screen for 3 sec. and the participant was instructed to picture the image that they just saw in vivid detail while keeping their eyes open and fixated on the center cross. The auditory cues followed a similar procedure, except that a verbal cue of “face”, “scene”, “animal”, or “object” was played over a speaker and the participant was instructed to recall the associated image and picture it as vividly as possible in their mind.

After each imagery period in both conditions, an image was flashed on the screen for 200 ms. The displayed images were randomly presented with a 70% chance of being the target image and a 30% chance of being a non-target image. The participant was then instructed to quickly respond with a left or right button press if the presented image was the target category or a non-target category for that trial, respectively. If the response was correct, the fixation cross turned green. If the response was incorrect, the fixation cross would turn red. If the participant responded too slowly or did not provide a response for the trial, the fixation cross turned yellow. The primary purpose of this memory test was to keep participants actively engaged throughout the experiment and prevent mind wandering. This data could be used to remove trials where the participants may have missed the cue for that trial. Furthermore, this procedure was designed to mimic a typical BCI scenario where feedback of the predicted target is displayed at the end of each trial. This allows us to investigate for the presence of Error Related Potentials (ErrPs) when a non-target image was presented. The identification of ErrPs can be beneficial during an actual BCI by allowing the BCI to correct misclassified data, or allowing online adaptation of the classifier through continued use¹⁰.

The full experiment included 5 blocks of the observation cues and 5 blocks of the auditory cues. Each of the observation cue blocks consisted of 40 trials and lasted approximately 6 minutes. The auditory cue blocks had a shorter cue duration, so 48 trials were included for each block and also lasted approximately 6 minutes. After each block, the participants were required to take a minimum of 1 min break before continuing on with the experiment, but they were allowed to take additional time if needed. A 10 sec resting period preceded each block in which the participants were asked to fixate their gaze on the center cross and keep their mind blank. The entire session lasted approximately 1 hr and 15 min.

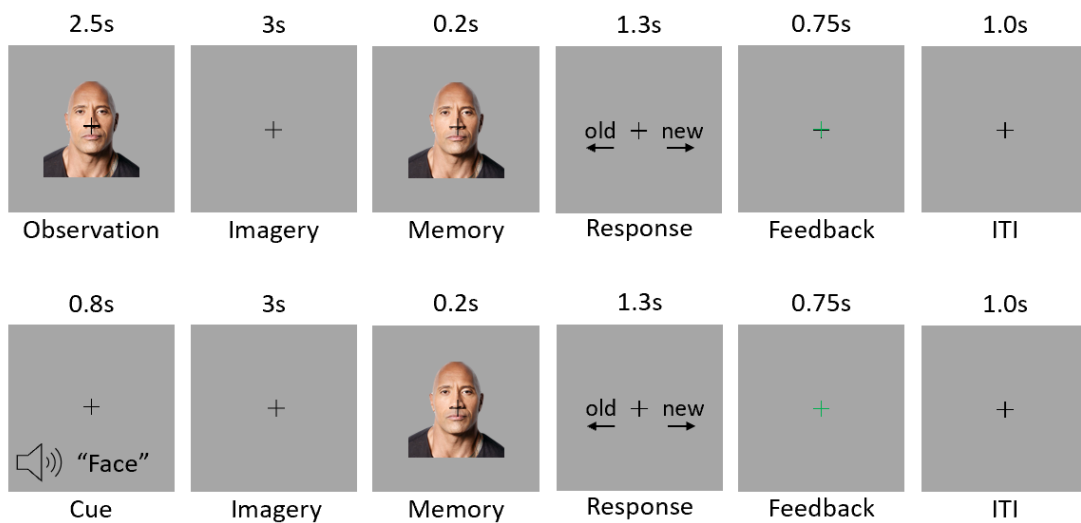


Figure 4.2: Task protocol. (A) Observation cue block protocol. **(B)** Auditory cue block protocol.

STIMULI

Images for this experiment were obtained from an in-lab dataset of famous faces, animals, objects, and scenes (**Figure 4.3**). The faces included images of famous male and female actors/actresses, artists, athletes, and politicians. The animal images included full body images of land (dog, cat, monkey, etc.) and nonland animals (fish, birds, etc.). The object images included manmade objects (chairs, tools, food, etc.). The scene images included recognizable manmade structures (Empire State building, the Eiffel Tower, the University of Texas Tower, etc.) or natural landscapes (beaches, mountains, rivers, etc.). Participants were instructed to select one image per category to use throughout the experiment that they were familiar with and could easily remember. All images were presented at a similar size (viewing angle $\approx 3^\circ$) with a neutral gray background.

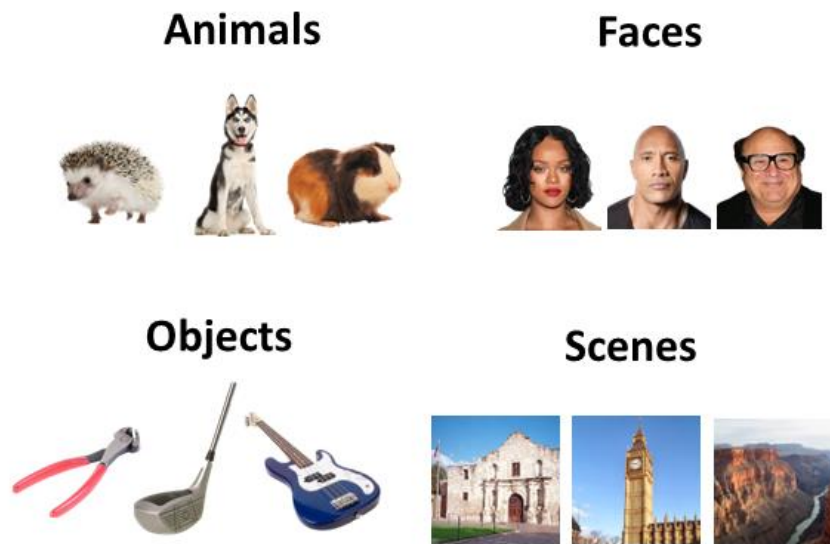


Figure 4.3 Sample images used during experimental procedure. Participants selected one familiar image for each category of animals, famous faces, objects, or recognizable scenery and landmarks.

DATA PREPROCESSING

Data preprocessing included interpolation of bad channels, rereferencing to common average, removing eye and muscle artifacts using ICA, bandpass filtering, and z-scoring the data using the MNE python package as outlined previously in **Chapter 3**.

VISUAL PERCEPTION CLASSIFICATION

Before feature selection, the data was bandpass filtered between 1-30 Hz to remove low frequency signal drift and high frequency noise. Previous literature on decoding visual observation from EEG suggests that alpha band activity from the occipital region of the brain carries the most informative information. For this reason, we employed Morlet Wavelets in the 1-15 Hz range equally spaced every 2 Hz to extract the frequency components of the time-series data over the 8 posterior EEG channels (O1, O2, Oz, P3, P4, P7, P8, and Pz). The mean power in each frequency bin was used as features for classification. The features were then normalized using the MinMaxScaler from the scikit-learn Python package to scale the features between 0-1. A Linear Discriminant Analysis (LDA) classifier with a shrinkage term of 0.1 was used to predict between the visual perception of the four image categories. The classifier was cross-validated using a leave-one-block-out (5-fold) cross-validation approach.

VISUAL IMAGERY CLASSIFICATION

For both visual imagery conditions, the data was first band-passed between 1-40 Hz. Due to the inherently low signal-to-noise ratio involved with visual imagery, an additional preprocessing stage of removing trials with signal amplitude exceeding 100 mV was implemented. This stage effectively removes trials where the participant may have been moving during the trials. This stage removed less than 5% of trials for each subject.

Mean Morlet Wavelets in the 1-15 Hz and 1-30 Hz bands equally spaced every 2 Hz were used to extract the frequency components in the observation cue and auditory cue blocks, respectively. This approach provided improved classification accuracy compared to using features obtained using the Fast Fourier Transform (FFT) in the same range. In addition to the 8 EEG channels used during the visual perception classification, some frontal channels were found to carry information relevant to imagery classification. In grid search analysis of the best channels for visual imagery led us to include channels O1, O2, Oz, P3, P4, P7, P8, Pz, TP10, F7, F8, and FC6. A Logistic Regression (LR) classifier with a newton-cg solver was implemented using a leave-one-block-out (5-fold) cross-validation approach.

CROSS-TASK CLASSIFICATION

Due to the similarities between the experimental conditions, we were interested in seeing if the inclusion of data from another condition can improve the classification accuracy. For example, can the inclusion of the perception periods improve the classification of the visual imagery periods? To test this approach, we concatenated the data from two conditions and performed a leave-one-block-out (10-fold) cross validation. For this analysis, we used the mean power in the 1-15 Hz band obtained by Morlet Wavelets over the 8 posterior channels used during the perception classification.

IMPROVING SIGNAL-TO-NOISE WITH AVERAGED DATA

Previous literature has suggested that averaging the EEG data across multiple trials of the same condition can improve classification accuracy by boosting the signal-to-noise¹³⁶. To accomplish this, we first aggregated the data randomly from each trial into 10 groups for each condition (6 trials per group). The preprocessed data of each group was then averaged, and features were extracted according to the methods outlined above. We

also tested averaging the trials after the feature extraction phase. A Logistic Regression classifier was then used to classify the group's label in a 10-fold cross-validation scheme. This process was iterated for 100 iterations of random group assignment. The final result was obtained as the mean classification accuracy achieved across all iterations.

EVALUATION OF PERFORMANCE

The classifier's performance is evaluated based on the number of trials where the EEG classification output matches the target category for that trial beyond the level of chance (25%). We used the methods from Combrisson and Jerbi¹³⁵ to adjusting the chance level as a function of sample size, number of classes, and the desired confidence interval using a binomial cumulative distribution (see **Chapter 3 Methods** for greater detail on how this calculation was performed). For this study, each session included a total sample size of 240 observations for the observation period and visual imagery period following the observation cue. There were 288 observations for the visual imagery period following the auditory cue. The experiment consisted of four classes which provided a significance threshold of 29.58% at $p = 0.05$ for the observation and visual imagery periods following the observation cue. The imagery periods following the auditory cue have significance threshold of 29.17%. In other words, the classification model must achieve a classification accuracy above this threshold to be considered statistically significant.

PUPILLOMETRY DATA ANALYSIS

Eye tracking data was captured throughout the experiment using a Tobii Pro Nano device. This data consisted of the x and y gaze positions along with the pupil diameters for each eye recorded at a sampling rate of 60 Hz. The pupillometry data was preprocessed using the methods outlined in Winn et al.¹⁵³ and Mathot and Vilotijevic¹⁵⁴. First, the data

was segmented into trials starting from the onset of the cue to one second after the start of the memory test. Then, eye blink artifacts were corrected by identifying segments with nan values, removing 5 datapoints from the beginning and end of the *nan* segments, and interpolating the values from the surrounding data points. Trials where over 30% of the data was nan values were labeled as bad and were removed from the analysis. The data was then filtered with a second order Butterworth bandpass filter between 1 and 10 Hz to remove low frequency drift and high frequency noise and standardized using z-score. The trials were then baseline corrected by subtracting out the mean pupil dilating from the 1 sec long inter-trial period before the onset of each trial.

Results

Our first test was to observe the classification accuracy between the four imagery categories during the observation period. To accomplish this, we employed an LDA classifier trained on the mean Morlet wavelets in the 1-15 Hz range equally spaced every 2 Hz from the eight posterior EEG channels. This yielded a mean classification accuracy of 42.11% across all 26 subjects (**Figure 4.4 A**). This was significantly higher than the significance threshold of 29.58% ($p < 0.01 \times 10^{-7}$). As a comparison, spectral features obtained from FFT over the same frequency bins provided a mean classification accuracy of 32.11%. To localize the most predictive channels for the prediction of the observation trials, we also performed a searchlight analysis where only the data of a single EEG channel was used to perform the classification (**Figure 4.4 B**). As expected, this analysis revealed that the posterior electrodes directly over the primary visual cortex obtained the highest classification accuracy.

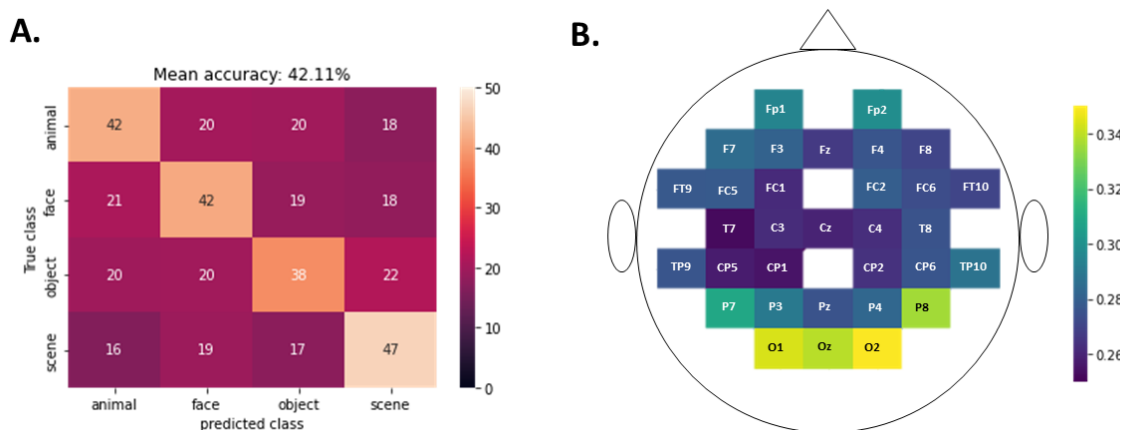


Figure 4.4. Classification of observation periods. **A.** Mean confusion matrix obtained from classification of neural data during visual observation of the four image categories. **B.** Heatmap of accuracy obtained during channel-wise classification of observation periods across all subjects.

We next attempted to classify between the four visual imagery classes following the observation cue. Similar preprocessing and feature extraction methods as the classification of the observation periods were used (see **Methods** for a detailed explanation of the exact features used). However, we found that a Logistic Regression classifier produced better results than the previously used LDA classifier. The LR classifier yielded a mean classification accuracy of 30.05% across all subjects which was significantly higher than the significance threshold of 29.58% ($p < 0.05$) (**Figure 4.5 A**). Unfortunately, the searchlight analysis for the most predictive channels did not reveal a conclusive result across all subjects with all channels averaging out to around chance level accuracy. However, on the subject level, it appears that some of the more frontal channels carried informative information for visual imagery. **Figure 4.5 B** presents the average channel-wise heatmap across all subjects, which shows the trend that some of the frontal electrodes

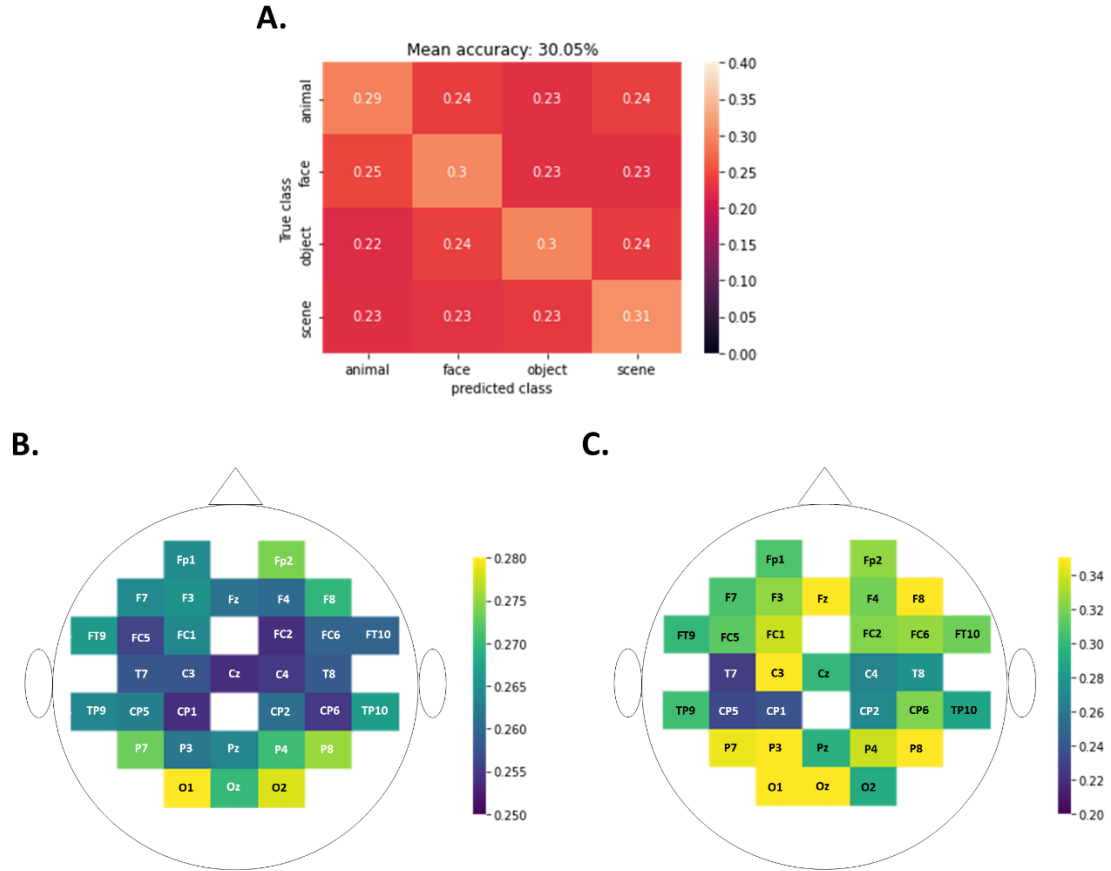


Figure 4.5. Classification of imagery periods following observation cue. **A.** Mean confusion matrix obtained from classification of neural data during visual imagery of the four image categories following the observation cue demonstrates significantly above chance classification accuracy of 30.05% (significance threshold: 29.58%, $p < 0.05$). **B.** Heatmap of accuracy obtained during channel-wise classification of imagery periods following the observation cue across all subjects. **C.** Heatmap of accuracy obtained during channel-wise classification of imagery periods following the observation cue for the subject with the highest accuracy.

carried relevant information in addition to the posterior channels seen during the observation periods. Also included in **Figure 4.5 C** is the channel-wise heatmap of the best subject to highlight the relevant channels for visual imagery.

Finally, we tested the classification accuracy of the four visual imagery classes following the auditory cue. This yielded a mean classification accuracy of 26.45% across all subjects which did not pass the significance threshold of 29.58% (**Figure 4.6**). Likewise, no significant channels were revealed during the channel-wise searchlight analysis.

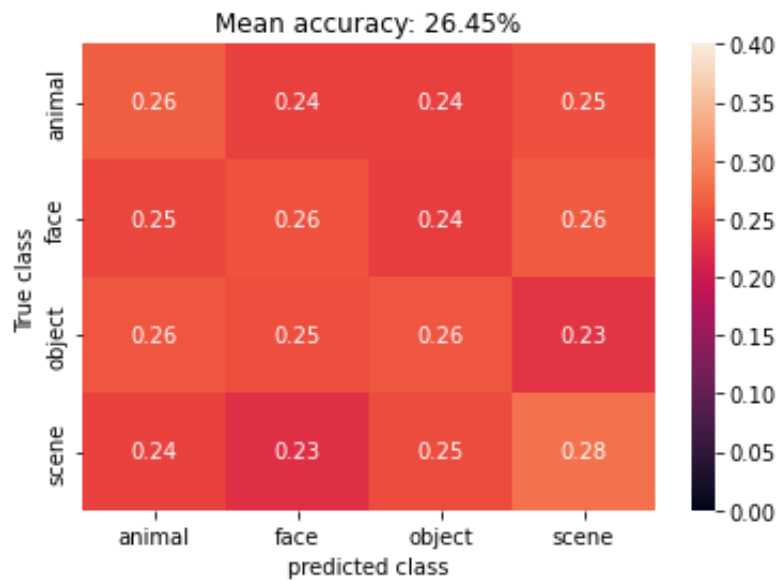


Figure 4.6. Classification of imagery periods following auditory cue. Mean confusion matrix obtained from classification of neural data during visual imagery of the four image categories following the auditory cue provides an average classification accuracy of 26.45%.

To improve the classification accuracy of the imagery periods, we were interested to see if the addition of data from the other conditions would improve the prediction ability. For example, would the addition of data from the observation periods improve the classifier for the imagery periods? To accomplish this, the data from two conditions were concatenated together and a leave-one-run-out (10-fold) cross validation was performed.

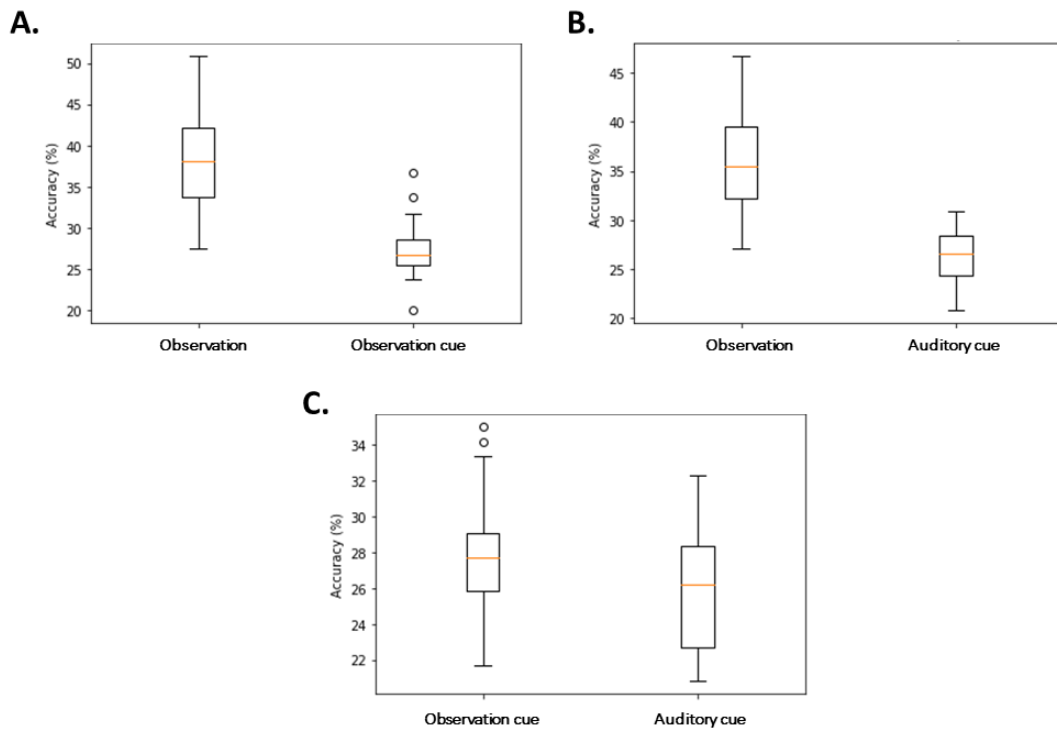
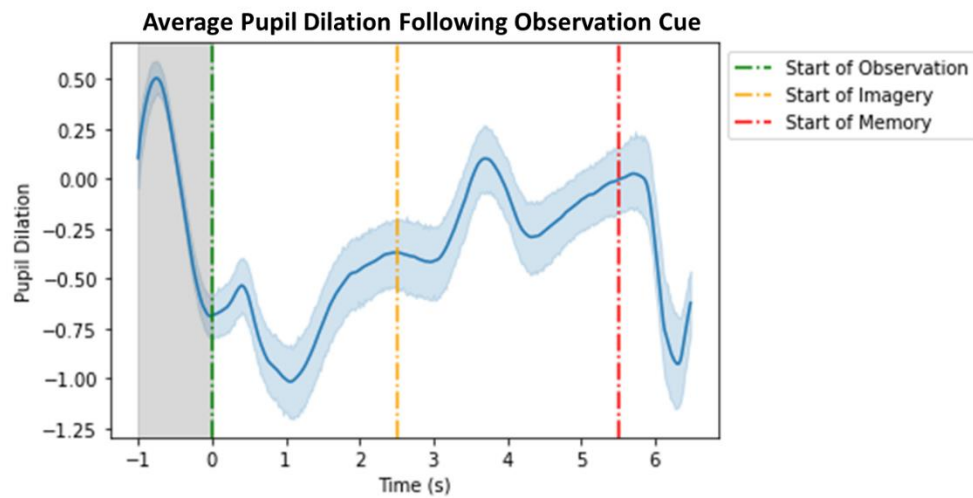


Figure 4.7 Cross-task classification results. Classification accuracy of each condition when the data from **A.** observation (38.47%) and imagery periods following observation cue (27.30%) were concatenated together, **B.** observation (36.50%) and imagery periods following auditory cue (26.42%) were concatenated, and **C.** imagery periods following observation cue (27.90%) and auditory cue (25.70%) were concatenated.

The classification results from this procedure were then separated into the two conditions for easier comparison and are presented in **Figure 4.7**. **Figure 4.7 A** displays a boxplot of the classification accuracies for the observation periods (left) and the imagery periods following the observation cue (right) when the data from both periods were concatenated. The results for the observation periods (left) and imagery periods following the auditory cue (right) are shown in **Figure 4.7 B**, and **Figure 4.7 C** shows the results when the two imagery periods were combined. In all cases, the addition of the data from another condition lessened the ability to classify the target image below the accuracy obtained when only the data from one condition was used.

We also analyzed the pupillometry data to see if this could be used to identify when a participant was engaged in the visual imagery task. **Figure 4.8 A** and **B** presents the mean pupil dilation across all trials for a single, representative subject during the observation cue blocks and the auditory cue blocks, respectively. During the observation cue blocks, pupil dilation decreases with the onset of the stimulus presentation. When the images are removed and the participant was instructed to perform visual imagery, the pupils start to dilate back up to baseline. The pupils contract again after the image is flashed during the memory periods. During the auditory cue blocks, there are no substantial changes in pupil dilation following the auditory cue. These trends are similar for most of the participants in this experiment.

A.



B.

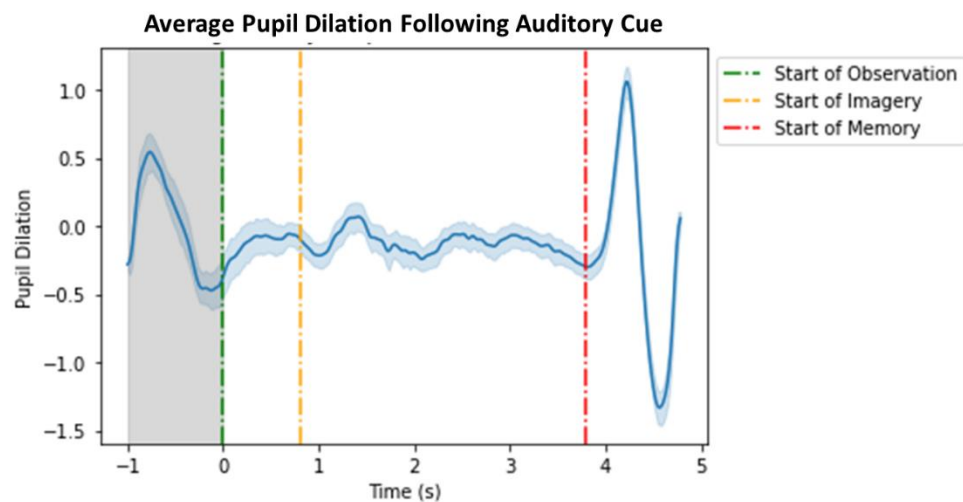


Figure 4.8 Mean pupil diameter for a representative subject. A. Mean pupil diameter during the observation cue blocks **B.** Mean pupil diameter during the auditory cue blocks. The gray shaded region from -1 to 0 indicates the baseline period used for baseline correction. The blue shaded region around the pupil diameter trace demarcates the 95% confidence interval.

Discussion

This study demonstrates that decoding visual imagery from EEG is a challenging, yet possible task. From the early work of Bobrov et al.⁹², Kosmyna et al.⁸¹, Lee et al.^{89,139}, and Xie et al.¹³⁶, one of the major points of contention between the experimental procedures was the presentation of the target image during the task directly before the imagery period. It could be argued that this is not a true test of spontaneous visual imagery but rather holding the object in working memory. Our study presents the first direct comparison between the ability to decode visual imagery following observation of the target image and following an auditory cue for the target image. Our classifier was able to achieve greater accuracy in predicting between the four image categories following the observation cue compared to the imagery periods following the auditory cue. Compared with actual visual observation of the images, visual imagery produces a more nuanced pattern of activity that is difficult to untangle using EEG.

In an early study by Ganis et al.¹³⁸, researchers examined the differences in brain areas activated during visual perception and imagery. This study used fMRI to analyze the shared neural processes when participants visualized or observed drawings of various object categories. The results of this study showed considerable overlap in activity between the two conditions in many of the brain areas; however, this overlap was neither uniform nor complete. Frontal regions, including the inferior frontal gyrus, middle frontal gyrus, superior frontal gyrus, medial frontal gyrus, insular cortex, precentral gyrus, and anterior cingulate gyrus, provided a nearly complete overlap in activity. These frontal regions are involved in various types of cognitive control processes such as the retrieval of episodic information, performing the visual inspection, and the generation of visual images¹⁵⁵. Parietal regions, including the precuneus, left angular gyrus, supramarginal gyrus, inferior

parietal lobule, superior parietal lobule, and the postcentral gyrus, also exhibited a complete overlap in activity. These regions are thought to contribute to the cognitive control networks along with the frontal cortices¹⁵⁶. They are also involved in attention¹⁵⁷, spatial working memory¹⁵⁸, and visuospatial processing^{159–161}. On the other hand, the activations in the occipital cortex were stronger and more diffuse during perception than during imagery, including the middle occipital gyrus, left superior occipital gyrus, lingual gyrus, and calcarine cortex. This exemplifies that the occipital regions are more strongly driven by sensory information rather than the information stored in memory. These regions are responsible for facilitating object detection and identification that are not necessarily required for the visualization of mental images¹³⁸.

Similar results were shown in this current study. The channel-wise searchlight results showed a large overlap in the areas that were most informative for prediction during visual observation and imagery. The observation task was mostly driven by the occipital electrodes which were receiving the sensory information, but some of the frontal electrodes also seemed to carry relevant information. The imagery task showed much lower classification accuracies in the occipital channels and a greater influence of the frontal electrodes.

We also saw that spectral power below 15 Hz, and specifically alpha band power (8-13 Hz), provided the most informative feature for classification during the observation periods and the imagery periods following the auditory cue. While this is consistent with the results found by Xie et al.¹³⁶, our previous findings from **Chapter 3** along with the results from Lee et al.⁸⁹ and Kosmyna et al.⁸¹ indicates that higher gamma activity (30-100) Hz carries information relevant for visual imagery. Additionally, even though we found similar features and channels between the conditions, we were unable to utilize the data

from the other conditions to improve the classification accuracy. It is possible that even though there is a significant overlap between the activity associated with the different experimental conditions, there is still too much variance or too little training data for the classifier to make use of the additional information. For example, the observation trials were mainly driven by activity in the occipital cortex related to the sensory perception of the presented image while the imagery trials received more contributions from the frontal areas associated with memory. Additionally, the two imagery conditions may be confounded by a difference in the memory conditions used. The imagery periods following the observation cue are more of a short-term working memory task while the imagery periods following the auditory cue are more of a long-term memory retrieval task.

In a study by Ishai et al.¹⁶², researchers have shown a differential effect in the visual responses generated during visual imagery generated from short-term memory and long-term memory. They found that visual perception and imagery of famous faces activated similar areas in the inferior occipital gyri, lateral fusiform gyri, superior temporal sulcus, and the amygdala. Additionally, imagery activated areas in the bilateral calcarine, hippocampus, precuneus, intraparietal sulcus, and inferior frontal gyrus. In all of these regions, the activity was greater during short-term memory when the subjects were asked to memorize specific pictures of celebrities. During the long-term task where they were asked to imagine the famous person without the presentation of an image, the activations were lower. However, focusing on specific features of the imagined faces such as the eyes, lips or nose was shown to increase activation in the right intraparietal sulcus and right inferior frontal gyrus regardless of the memory type. These results suggest that the type of cue and the instructions given to the participants can play a large role in the neural processes used and the activity evoked during mental visual imagery.

In the current experiment, pulling the image from long-term memory following the auditory cue rather than retaining a more concrete image from short-term working memory could result in greater variability in the mental activity that is much more difficult to decode. Furthermore, the participants in this study were not given an explicit strategy for visualizing each of the pictures. They were only told to recreate the image as it was shown in their mind and visualize the details as clearly as possible. However, in the post-experiment survey responses, multiple subjects reported strategies of repeating the objects' name in their mind or thinking about the colors of the images which may not be an optimal strategy. Future work may benefit from providing more detailed instructions for how to visualize the target category or providing feedback on the classifier's prediction in real-time to allow the participants to adapt their strategy throughout the experiment.

Previous literature has also suggested that mental imagery can lead to increases in pupil dilation¹⁰⁷, but the results from our pupillometry data revealed that pupil diameter did not substantially change during the auditory cue blocks. In the observation cue blocks, we did see a decrease in the diameter when the stimulus was presented and an increase in diameter when the stimulus was removed as expected. However, it is difficult to say if the dilation was due to the mental activity of imagery or if the diameter was just returning to baseline. One of the limitations of this study is that the trial periods were rather short which may not be optimal for the analysis of pupillometry data^{153,154}. Also, the inter-trial period of 1 sec may not be an appropriate time to allow the pupil diameter to return to baseline. The large variability during this period may be due to eye blinks or movements which could interfere with the ability to interpret the data from the remainder of the trial. Future work in this could benefit from longer imagery periods and longer resting periods between trials to make a definitive conclusion.

CHAPTER 5

CONCLUSIONS AND FUTURE WORK

CONCLUSIONS

The work from this dissertation presents novel brain-centered methods for the rehabilitation or, in more severe cases, augmentation of impaired function following neurological injury. The first aim of this work provides a systematic investigation into the use of functional-based hyperalignment of multiple subjects' fMRI data to create a surrogate training target for neurofeedback. Our results showed that functional-based hyperalignment can significantly outperform conventional anatomical alignment of fMRI data for across-subject analysis. We also found no differences in alignment and classification accuracy when a new subject is brought into alignment with a pre-established template versus creating a new template from the data of all subjects. This means that our template can be quickly and easily applied to new data in future studies. Finally, we found that the neural representations for more impaired fingers can be inferred from the data of the other hyperaligned participants. In other words, as long as the participant is able to individuate at least two of their finger movements, hyperalignment can be used to infer the neural representations for the more impaired fingers from our healthy template. Together, this work lays the foundation for the rehabilitation of finger movements in situations where identifying the neural patterns associated with the individual fingers' movements are untenable due to neurological injury. It also provides the first investigation into the use of hyperaligned templates derived from healthy individuals to target motor impairments in a neurofeedback task.

The second and third aims of this dissertation have shown that visual imagery is be a challenging, yet possible control strategy for an EEG brain-computer interface application. In aim two, we found that the action of visual imagery can be accurately identified from EEG compared to resting state. We also identified that classification of the visual imagery of specific images provided better results than category-level classification. In aim three we built upon this investigation by investigating some of the important experimental considerations when performing a visual imagery task. In this work, we found that spontaneous visual imagery following an auditory cue is a more difficult signal to decode compared to visual imagery after observation of the actual image. Since most previous studies^{81,89} involved displaying the target image directly before the imagery period, this work provides the first thorough investigation into the use of spontaneous visual imagery for an EEG BCI. We also found that visual imagery can be defined by many of the same features and brain regions as perception; however, it involves more widespread areas in the frontal regions. While the classification results from aims two and three were lower than the typical rate for effective BCI control (often set at 60% or 70% accuracy)^{87,98,99}, visual imagery may still provide a useful control paradigm for certain individuals or applications where other methods are ill suited.

FUTURE WORK

The analysis performed in the first aim of this dissertation was carried out during an offline analysis of healthy young adults. Future work is necessary to test the application of our surrogate template in individuals with mild motor impairments. This may involve healthy older adults with some minor deficits in fine motor control, or stroke individuals with mild impairments affecting the hand. One of the major considerations for the use of

this template is the level of impairment in the individual undergoing the neurofeedback task. Our analysis has shown that the neural data from at least two fingers must be intact in order to accurately align them to the surrogate temple. This procedure will not be appropriate for individuals with more severe impairments affecting the whole hand. In these individuals, it may be necessary to test alternative methods for alignment. In the case of an individual with severe impairments following a stroke or damage to one hemisphere of the brain, one potential option is to use the unimpaired hand to perform the localizer task and reflect the activity into the ipsilesional region for alignment. Another option may be to apply tactile stimulation to the fingers instead of asking the participant to perform the motor task. Since the primary somatosensory cortex is highly connected with the motor cortex, this may be enough to influence activity in this region.

From the results of the second aim on mapping the representational similarity of multiple object categories during visual imagery, further work is needed to accurately map the representational boundaries of visual imagery. We have found that aggregating the neural responses into categories did not produce a distinct signal that could be interpreted by our classifier. Future work should simplify the number of categories and investigate the representational similarity using individual images with greater amounts of training data. It may also be possible that EEG does not provide sufficient spatial resolution to accurately capture the differences between the activity associated with the various imagery categories. Future work may benefit from the use of other methods such as fMRI or fNIRS to map out the boundaries between the imagery categories.

Our final investigation into the experimental factors that can influence the ability to decode visual imagery using EEG revealed that short-term retention of an image in working memory provided better results than spontaneous mental imagery from long-term

memory. This may explain why the results from Aim two were insignificant because the participants were only presented with a written cue for the target image and had to recall the specific details from their memory. Based on the survey responses of the individuals regarding the visual imagery following the auditory cue, it appears that the participants used many different strategies that may not be optimal for performance in a visual imagery BCI application. Future work may benefit from providing more detailed instructions for how to visualize the target category. Future work should also be conducted across multiple sessions where feedback on the classifier's prediction in real-time is presented to allow the participants to adapt their strategy throughout the experiment.

REFERENCES

1. WHO, G. *Global health estimates*. (World Health Organization Geneva, 2012).
2. Stewart, J. C. & Cramer, S. C. Patient-reported measures provide unique insights into motor function after stroke. *Stroke* **44**, 1111–1116 (2013).
3. Heller, A. *et al.* Arm function after stroke: measurement and recovery over the first three months. *J. Neurol. Neurosurg. Psychiatry* **50**, 714–719 (1987).
4. Sunderland, A., Tinson, D., Bradley, L. & Hower, R. L. Arm function after stroke. An evaluation of grip strength as a measure of recovery and a prognostic indicator. *J. Neurol. Neurosurg. Psychiatry* **52**, 1267–1272 (1989).
5. Cramer, S. C. *et al.* Harnessing neuroplasticity for clinical applications. *Brain* **134**, 1591–1609 (2011).
6. Takeuchi, N. & Izumi, S.-I. Maladaptive plasticity for motor recovery after stroke: mechanisms and approaches. *Neural Plast.* **2012**, (2012).
7. Bulárka, S. & Gontean, A. Brain-Computer Interface review. in *2016 12th IEEE International Symposium on Electronics and Telecommunications (ISETC)* 219–222 (2016). doi:10.1109/ISETC.2016.7781096.
8. Nicolas-Alonso, L. F. & Gomez-Gil, J. Brain Computer Interfaces, a Review. *Sensors* **12**, 1211–1279 (2012).
9. Wolpaw, J. R. *et al.* Brain-computer interface technology: a review of the first international meeting. *IEEE Trans. Rehabil. Eng.* **8**, 164–173 (2000).

10. Abiri, R., Borhani, S., Sellers, E. W., Jiang, Y. & Zhao, X. A comprehensive review of EEG-based brain–computer interface paradigms. *J. Neural Eng.* **16**, 011001 (2019).
11. Wolpaw, J. R., Birbaumer, N., McFarland, D. J., Pfurtscheller, G. & Vaughan, T. M. Brain–computer interfaces for communication and control. *Clin. Neurophysiol.* **113**, 767–791 (2002).
12. Nijholt, A. BCI for Games: A ‘State of the Art’ Survey. in *Entertainment Computing - ICEC 2008* (eds. Stevens, S. M. & Saldamarco, S. J.) 225–228 (Springer, 2009). doi:10.1007/978-3-540-89222-9_29.
13. Wolpaw, J. & Wolpaw, E. W. *Brain-Computer Interfaces: Principles and Practice*. (Oxford University Press, 2012).
14. Chaudhary, U., Birbaumer, N. & Ramos-Murguialday, A. Brain–computer interfaces for communication and rehabilitation. *Nat. Rev. Neurol.* **12**, 513–525 (2016).
15. Lu, H.-Y. *et al.* Multi-scale neural decoding and analysis. *J. Neural Eng.* **18**, 045013 (2021).
16. Buxton, R. B. *Introduction to Functional Magnetic Resonance Imaging: Principles and Techniques*. (Cambridge University Press, 2009).
17. Sitaram, R. *et al.* Closed-loop brain training: the science of neurofeedback. *Nat. Rev. Neurosci.* **18**, 86 (2017).

18. Takeuchi, N. & Izumi, S.-I. Noninvasive brain stimulation for motor recovery after stroke: mechanisms and future views. *Stroke Res. Treat.* **2012**, (2012).
19. Webster, B. R., Celnik, P. A. & Cohen, L. G. Noninvasive brain stimulation in stroke rehabilitation. *NeuroRx* **3**, 474–481 (2006).
20. Kubis, N. Non-invasive brain stimulation to enhance post-stroke recovery. *Front. Neural Circuits* **10**, 56 (2016).
21. Butler, A. J. *et al.* A meta-analysis of the efficacy of anodal transcranial direct current stimulation for upper limb motor recovery in stroke survivors. *J. Hand Ther.* **26**, 162–171 (2013).
22. Wolpaw, J. R. The negotiated equilibrium model of spinal cord function. *J. Physiol.* **596**, 3469–3491 (2018).
23. Reinkensmeyer, D. J., Guigon, E. & Maier, M. A. A computational model of use-dependent motor recovery following a stroke: optimizing corticospinal activations via reinforcement learning can explain residual capacity and other strength recovery dynamics. *Neural Netw.* **29**, 60–69 (2012).
24. Schieber, M. H. & Hibbard, L. S. How somatotopic is the motor cortex hand area? *Science* **261**, 489–492 (1993).
25. Yokoi, A., Arbuckle, S. A. & Diedrichsen, J. The role of human primary motor cortex in the production of skilled finger sequences. *J. Neurosci.* **38**, 1430–1442 (2018).

26. Wang, T., Mantini, D. & Gillebert, C. R. The potential of real-time fMRI neurofeedback for stroke rehabilitation: A systematic review. *cortex* **107**, 148–165 (2018).
27. Shibata, K., Watanabe, T., Sasaki, Y. & Kawato, M. Perceptual learning incepted by decoded fMRI neurofeedback without stimulus presentation. *science* **334**, 1413–1415 (2011).
28. Ruiz, S., Birbaumer, N. & Sitaram, R. Abnormal neural connectivity in schizophrenia and fMRI-brain-computer interface as a potential therapeutic approach. *Front. Psychiatry* **4**, 17 (2013).
29. Cordes, J. S. *et al.* Cognitive and neural strategies during control of the anterior cingulate cortex by fMRI neurofeedback in patients with schizophrenia. *Front. Behav. Neurosci.* **9**, 169 (2015).
30. Linden, D. E. *et al.* Real-time self-regulation of emotion networks in patients with depression. *PloS One* **7**, e38115 (2012).
31. Young, K. D. *et al.* Real-time FMRI neurofeedback training of amygdala activity in patients with major depressive disorder. *PloS One* **9**, e88785 (2014).
32. Subramanian, L. *et al.* Real-time functional magnetic resonance imaging neurofeedback for treatment of Parkinson's disease. *J. Neurosci.* **31**, 16309–16317 (2011).

33. Zilverstand, A. *et al.* fMRI neurofeedback training for increasing anterior cingulate cortex activation in adult attention deficit hyperactivity disorder. An exploratory randomized, single-blinded study. *PloS One* **12**, e0170795 (2017).
34. Megan, T. deBettencourt, Cohen, J. D., Lee, R. F., Norman, K. A. & Turk-Browne, N. B. Closed-loop training of attention with real-time brain imaging. *Nat. Neurosci.* **18**, 470–475 (2015).
35. DeCharms, R. C. *et al.* Control over brain activation and pain learned by using real-time functional MRI. *Proc. Natl. Acad. Sci.* **102**, 18626–18631 (2005).
36. Hartwell, K. J. *et al.* Individualized real-time fMRI neurofeedback to attenuate craving in nicotine-dependent smokers. *J. Psychiatry Neurosci. JPN* **41**, 48 (2016).
37. Li, X. *et al.* Volitional reduction of anterior cingulate cortex activity produces decreased cue craving in smoking cessation: a preliminary real-time fMRI study. *Addict. Biol.* **18**, 739–748 (2013).
38. Lioi, G. *et al.* A Multi-Target Motor Imagery Training Using Bimodal EEG-fMRI Neurofeedback: A Pilot Study in Chronic Stroke Patients. *Front. Hum. Neurosci.* **14**, 37 (2020).
39. Liew, S.-L. *et al.* Improving motor corticothalamic communication after stroke using real-time fMRI connectivity-based neurofeedback. *Neurorehabil. Neural Repair* **30**, 671–675 (2016).

40. Sitaram, R. *et al.* Acquired control of ventral premotor cortex activity by feedback training: an exploratory real-time fMRI and TMS study. *Neurorehabil. Neural Repair* **26**, 256–265 (2012).
41. Lewis-Peacock, J. A. & Norman, K. A. Multi-voxel pattern analysis of fMRI data. *Cogn. Neurosci.* **911**, 920 (2013).
42. Haxby, J. V. *et al.* Distributed and Overlapping Representations of Faces and Objects in Ventral Temporal Cortex. *Science* **293**, 2425–2430 (2001).
43. Norman, K. A., Polyn, S. M., Detre, G. J. & Haxby, J. V. Beyond mind-reading: multi-voxel pattern analysis of fMRI data. *Trends Cogn. Sci.* **10**, 424–430 (2006).
44. Kriegeskorte, N., Mur, M. & Bandettini, P. Representational similarity analysis - connecting the branches of systems neuroscience. *Front. Syst. Neurosci.* **2**, 4 (2008).
45. Kriegeskorte, N. *et al.* Matching Categorical Object Representations in Inferior Temporal Cortex of Man and Monkey. *Neuron* **60**, 1126–1141 (2008).
46. Cichy, R. M., Pantazis, D. & Oliva, A. Resolving human object recognition in space and time. *Nat. Neurosci.* **17**, 455–462 (2014).
47. Kaneshiro, B., Guimaraes, M. P., Kim, H.-S., Norcia, A. M. & Suppes, P. A Representational Similarity Analysis of the Dynamics of Object Processing Using Single-Trial EEG Classification. *PLOS ONE* **10**, e0135697 (2015).
48. Sulzer, J. *et al.* Real-time fMRI neurofeedback: progress and challenges. *Neuroimage* **76**, 386–399 (2013).

49. Lang, C. E. & Schieber, M. H. Reduced muscle selectivity during individuated finger movements in humans after damage to the motor cortex or corticospinal tract. *J. Neurophysiol.* **91**, 1722–1733 (2004).
50. Li, S., Latash, M. L., Yue, G. H., Siemionow, V. & Sahgal, V. The effects of stroke and age on finger interaction in multi-finger force production tasks. *Clin. Neurophysiol.* **114**, 1646–1655 (2003).
51. Rademacher, J., Caviness Jr, V. S., Steinmetz, H. & Galaburda, A. M. Topographical variation of the human primary cortices: implications for neuroimaging, brain mapping, and neurobiology. *Cereb. Cortex* **3**, 313–329 (1993).
52. Frost, M. A. & Goebel, R. Measuring structural–functional correspondence: spatial variability of specialised brain regions after macro-anatomical alignment. *Neuroimage* **59**, 1369–1381 (2012).
53. Grachev, I. D. *et al.* A method for assessing the accuracy of intersubject registration of the human brain using anatomic landmarks. *NeuroImage* **9**, 250–268 (1999).
54. Cox, D. D. & Savoy, R. L. Functional magnetic resonance imaging (fMRI) “brain reading”: detecting and classifying distributed patterns of fMRI activity in human visual cortex. *Neuroimage* **19**, 261–270 (2003).
55. Al-Wasity, S., Vogt, S., Vuckovic, A. & Pollick, F. E. Hyperalignment of motor cortical areas based on motor imagery during action observation. *Sci. Rep.* **10**, 1–12 (2020).

56. Haxby, J. V. *et al.* A common, high-dimensional model of the representational space in human ventral temporal cortex. *Neuron* **72**, 404–416 (2011).
57. Taschereau-Dumouchel, V. *et al.* Towards an unconscious neural reinforcement intervention for common fears. *Proc. Natl. Acad. Sci.* **115**, 3470–3475 (2018).
58. Oblak, E. F., Sulzer, J. S. & Lewis-Peacock, J. A. A simulation-based approach to improve decoded neurofeedback performance. *NeuroImage* **195**, 300–310 (2019).
59. Guntupalli, J. S., Feilong, M. & Haxby, J. V. A computational model of shared fine-scale structure in the human connectome. *PLoS Comput. Biol.* **14**, e1006120 (2018).
60. Guntupalli, J. S. *et al.* A model of representational spaces in human cortex. *Cereb. Cortex* **26**, 2919–2934 (2016).
61. Schönemann, P. H. A generalized solution of the orthogonal procrustes problem. *Psychometrika* **31**, 1–10 (1966).
62. Haxby, J. V., Connolly, A. C. & Guntupalli, J. S. Decoding neural representational spaces using multivariate pattern analysis. *Annu. Rev. Neurosci.* **37**, 435–456 (2014).
63. Mak, J. N. & Wolpaw, J. R. Clinical Applications of Brain-Computer Interfaces: Current State and Future Prospects. *IEEE Rev. Biomed. Eng.* **2**, 187–199 (2009).
64. Frisoli, A. *et al.* A New Gaze-BCI-Driven Control of an Upper Limb Exoskeleton for Rehabilitation in Real-World Tasks. *IEEE Trans. Syst. Man Cybern. Part C Appl. Rev.* **42**, 1169–1179 (2012).

65. Kilmarx, J., Abiri, R., Borhani, S., Jiang, Y. & Zhao, X. Sequence-based manipulation of robotic arm control in brain machine interface. *Int. J. Intell. Robot. Appl.* **2**, 149–160 (2018).
66. Tariq, M., Trivailo, P. M. & Simic, M. EEG-Based BCI Control Schemes for Lower-Limb Assistive-Robots. *Front. Hum. Neurosci.* **12**, 312 (2018).
67. Krusienski, D. J., Sellers, E. W., McFarland, D. J., Vaughan, T. M. & Wolpaw, J. R. Toward enhanced P300 speller performance. *J. Neurosci. Methods* **167**, 15–21 (2008).
68. Birbaumer, N. Breaking the silence: Brain–computer interfaces (BCI) for communication and motor control. *Psychophysiology* **43**, 517–532 (2006).
69. Kaplan, A. Y., Shishkin, S. L., Ganin, I. P., Basyul, I. A. & Zhigalov, A. Y. Adapting the P300-Based Brain–Computer Interface for Gaming: A Review. *IEEE Trans. Comput. Intell. AI Games* **5**, 141–149 (2013).
70. Ahn, M., Lee, M., Choi, J. & Jun, S. C. A Review of Brain-Computer Interface Games and an Opinion Survey from Researchers, Developers and Users. *Sensors* **14**, 14601–14633 (2014).
71. Borhani, S. *et al.* Clash of minds: A BCI car racing game in simulated virtual reality environment. in *2018 Biomedical Engineering Society (BMES) Annual Meeting* (2018).
72. Polich, J. Updating P300: An integrative theory of P3a and P3b. *Clin. Neurophysiol.* **118**, 2128–2148 (2007).

73. Johnson Jr., R. On the neural generators of the P300 component of the event-related potential. *Psychophysiology* **30**, 90–97 (1993).
74. Farwell, L. A. & Donchin, E. Talking off the top of your head: toward a mental prosthesis utilizing event-related brain potentials. *Electroencephalogr. Clin. Neurophysiol.* **70**, 510–523 (1988).
75. Fazel-Rezai, R. *et al.* P300 brain computer interface: current challenges and emerging trends. *Front. Neuroengineering* **5**, 14 (2012).
76. McCane, L. M. *et al.* Brain-computer interface (BCI) evaluation in people with amyotrophic lateral sclerosis. *Amyotroph. Lateral Scler. Front. Degener.* **15**, 207–215 (2014).
77. Vialatte, F.-B., Maurice, M., Dauwels, J. & Cichocki, A. Steady-state visually evoked potentials: Focus on essential paradigms and future perspectives. *Prog. Neurobiol.* **90**, 418–438 (2010).
78. Volosyak, I., Valbuena, D., Luth, T., Malechka, T. & Graser, A. BCI Demographics II: How Many (and What Kinds of) People Can Use a High-Frequency SSVEP BCI? *IEEE Trans. Neural Syst. Rehabil. Eng.* **19**, 232–239 (2011).
79. An, W. W. *et al.* Decoding Music Attention from “EEG Headphones”: A User-Friendly Auditory Brain-Computer Interface. in *ICASSP 2021 - 2021 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP)* 985–989 (2021). doi:10.1109/ICASSP39728.2021.9414492.

80. An, W. W. *et al.* Decoding auditory and tactile attention for use in an EEG-based brain-computer interface. in *2020 8th International Winter Conference on Brain-Computer Interface (BCI)* 1–6 (IEEE, 2020). doi:10.1109/BCI48061.2020.9061623.
81. Kosmyna, N., Lindgren, J. T. & Lécuyer, A. Attending to Visual Stimuli versus Performing Visual Imagery as a Control Strategy for EEG-based Brain-Computer Interfaces. *Sci. Rep.* **8**, 13222 (2018).
82. Simanova, I., van Gerven, M., Oostenveld, R. & Hagoort, P. Identifying Object Categories from Event-Related EEG: Toward Decoding of Conceptual Representations. *PLoS ONE* **5**, e14465 (2010).
83. Gemblér, F., Stawicki, P. & Volosyak, I. Exploring the possibilities and limitations of multitarget SSVEP-based BCI applications. in *2016 38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)* 1488–1491 (2016). doi:10.1109/EMBC.2016.7590991.
84. Volosyak, I., Gemblér, F. & Stawicki, P. Age-related differences in SSVEP-based BCI performance. *Neurocomputing* **250**, 57–64 (2017).
85. Pfurtscheller, G. & Lopes da Silva, F. H. Event-related EEG/MEG synchronization and desynchronization: basic principles. *Clin. Neurophysiol.* **110**, 1842–1857 (1999).
86. Wolpaw, J. R., McFarland, D. J., Neat, G. W. & Forneris, C. A. An EEG-based brain-computer interface for cursor control. *Electroencephalogr. Clin. Neurophysiol.* **78**, 252–259 (1991).

87. Ahn, M. & Jun, S. C. Performance variation in motor imagery brain–computer interface: A brief review. *J. Neurosci. Methods* **243**, 103–110 (2015).
88. Pereira, J., Ofner, P., Schwarz, A., Sburlea, A. I. & Müller-Putz, G. R. EEG neural correlates of goal-directed movement intention. *Neuroimage* **149**, 129–140 (2017).
89. Lee, S.-H., Lee, M. & Lee, S.-W. Neural Decoding of Imagined Speech and Visual Imagery as Intuitive Paradigms for BCI Communication. *IEEE Trans. Neural Syst. Rehabil. Eng.* **28**, 2647–2659 (2020).
90. Abiri, R. *et al.* A Usability Study of Low-Cost Wireless Brain-Computer Interface for Cursor Control Using Online Linear Model. *IEEE Trans. Hum.-Mach. Syst.* **50**, 287–297 (2020).
91. Bradberry, T. J., Gentili, R. J. & Contreras-Vidal, J. L. Fast attainment of computer cursor control with noninvasively acquired brain signals. *J. Neural Eng.* **8**, 036010 (2011).
92. Bobrov, P. *et al.* Brain-Computer Interface Based on Generation of Visual Images. *PLOS ONE* **6**, e20674 (2011).
93. Wang, L., Zhang, X., Zhong, X. & Zhang, Y. Analysis and classification of speech imagery EEG for BCI. *Biomed. Signal Process. Control* **8**, 901–908 (2013).
94. Min, B., Kim, J., Park, H. & Lee, B. Vowel Imagery Decoding toward Silent Speech BCI Using Extreme Learning Machine with Electroencephalogram. *BioMed Res. Int.* **2016**, e2618265 (2016).

95. García-Salinas, J. S., Villaseñor-Pineda, L., Reyes-García, C. A. & Torres-García, A. A. Transfer learning in imagined speech EEG-based BCIs. *Biomed. Signal Process. Control* **50**, 151–157 (2019).
96. Hortal, E. *et al.* SVM-based Brain–Machine Interface for controlling a robot arm through four mental tasks. *Neurocomputing* **151**, 116–121 (2015).
97. Vidaurre, C. & Blankertz, B. Towards a cure for BCI illiteracy. *Brain Topogr.* **23**, 194–198 (2010).
98. Wierzgała, P., Zapala, D., Wojcik, G. M. & Masiak, J. Most Popular Signal Processing Methods in Motor-Imagery BCI: A Review and Meta-Analysis. *Front. Neuroinformatics* **12**, 78 (2018).
99. Guger, C., Edlinger, G., Harkam, W., Niedermayer, I. & Pfurtscheller, G. How many people are able to operate an EEG-based brain-computer interface (BCI)? *IEEE Trans. Neural Syst. Rehabil. Eng.* **11**, 145–147 (2003).
100. Thompson, M. C. Critiquing the Concept of BCI Illiteracy. *Sci. Eng. Ethics* **25**, 1217–1233 (2019).
101. Allison, B. *et al.* BCI Demographics: How Many (and What Kinds of) People Can Use an SSVEP BCI? *IEEE Trans. Neural Syst. Rehabil. Eng.* **18**, 107–116 (2010).
102. Knauff, M., Kassubek, J., Mulack, T. & Greenlee, M. W. Cortical activation evoked by visual mental imagery as measured by fMRI. *NeuroReport* **11**, 3957–3962 (2000).

103. Potter, M. C., Wyble, B., Haggmann, C. E. & McCourt, E. S. Detecting meaning in RSVP at 13 ms per picture. *Atten. Percept. Psychophys.* **76**, 270–279 (2014).
104. Vogel, D. R., Dickson, G. W. & Lehman, J. A. Persuasion and the role of visual presentation support: The UM/3M study. (1986).
105. Shenoy, P. & Tan, D. S. Human-aided computing: Utilizing implicit human processing to classify images. in *Proceedings of the SIGCHI Conference on Human Factors in Computing Systems* 845–854 (2008).
106. Llorella, F. R., Azorín, J. M. & Patow, G. Black hole algorithm with convolutional neural networks for the creation of brain-computer interface based in visual perception and visual imagery. *Neural Comput. Appl.* **35**, 5631–5641 (2023).
107. Pupillometric measures of cognitive and emotional processes. *Int. J. Psychophysiol.* **52**, 1–6 (2004).
108. Kamper, D. G. & Rymer, W. Z. Impairment of voluntary control of finger motion following stroke: role of inappropriate muscle coactivation. *Muscle Nerve Off. J. Am. Assoc. Electrodiagn. Med.* **24**, 673–681 (2001).
109. Lang, C. E. & Schieber, M. H. Differential impairment of individuated finger movements in humans after damage to the motor cortex or the corticospinal tract. *J. Neurophysiol.* **90**, 1160–1170 (2003).
110. Hummel, F. *et al.* Effects of non-invasive cortical stimulation on skilled motor function in chronic stroke. *Brain* **128**, 490–499 (2005).

111. Ward, N. S., Brown, M. M., Thompson, A. J. & Frackowiak, R. S. J. Neural correlates of outcome after stroke: a cross-sectional fMRI study. *Brain* **126**, 1430–1448 (2003).
112. Ejaz, N., Hamada, M. & Diedrichsen, J. Hand use predicts the structure of representations in sensorimotor cortex. *Nat. Neurosci.* **18**, 1034 (2015).
113. Kolasinski, J. *et al.* Investigating the stability of fine-grain digit somatotopy in individual human participants. *J. Neurosci.* **36**, 1113–1127 (2016).
114. Wiestler, T. & Diedrichsen, J. Skill learning strengthens cortical representations of motor sequences. *Elife* **2**, e00801 (2013).
115. Bray, S., Shimojo, S. & O’Doherty, J. P. Direct instrumental conditioning of neural activity using functional magnetic resonance imaging-derived reward feedback. *J. Neurosci.* **27**, 7498–7507 (2007).
116. Blefari, M. L., Sulzer, J., Hepp-Reymond, M.-C., Kollias, S. & Gassert, R. Improvement in precision grip force control with self-modulation of primary motor cortex during motor imagery. *Front. Behav. Neurosci.* **9**, 18 (2015).
117. Oblak, E. F., Lewis-Peacock, J. A. & Sulzer, J. S. Differential neural plasticity of individual fingers revealed by fMRI neurofeedback. *bioRxiv* (2020).
118. Xu, J. *et al.* Separable systems for recovery of finger strength and control after stroke. *J. Neurophysiol.* **118**, 1151–1163 (2017).
119. Kriegeskorte, N. & Kievit, R. A. Representational geometry: integrating cognition, computation, and the brain. *Trends Cogn. Sci.* **17**, 401–412 (2013).

120. Rathelot, J.-A. & Strick, P. L. Muscle representation in the macaque motor cortex: an anatomical perspective. *Proc. Natl. Acad. Sci.* **103**, 8257–8262 (2006).
121. Rathelot, J.-A. & Strick, P. L. Subdivisions of primary motor cortex based on cortico-motoneuronal cells. *Proc. Natl. Acad. Sci.* **106**, 918–923 (2009).
122. Witham, C. L., Fisher, K. M., Edgley, S. A. & Baker, S. N. Corticospinal inputs to primate motoneurons innervating the forelimb from two divisions of primary motor cortex and area 3a. *J. Neurosci.* **36**, 2605–2616 (2016).
123. Maier, M. A., Bennett, K. M., Hepp-Reymond, M. C. & Lemon, R. N. Contribution of the monkey corticomotoneuronal system to the control of force in precision grip. *J. Neurophysiol.* **69**, 772–785 (1993).
124. Keizer, K. & Kuypers, H. Distribution of corticospinal neurons with collaterals to the lower brain stem reticular formation in monkey (*Macaca fascicularis*). *Exp. Brain Res.* **74**, 311–318 (1989).
125. Porro, C. A. *et al.* Primary motor and sensory cortex activation during motor performance and motor imagery: a functional magnetic resonance imaging study. *J. Neurosci.* **16**, 7688–7698 (1996).
126. Yoo, S.-S. & Jolesz, F. A. Functional MRI for neurofeedback: feasibility study on a hand motor task. *Neuroreport* **13**, 1377–1381 (2002).
127. Dayan, E. & Cohen, L. G. Neuroplasticity subserving motor skill learning. *Neuron* **72**, 443–454 (2011).

128. Hardwick, R. M., Rottschy, C., Miall, R. C. & Eickhoff, S. B. A quantitative meta-analysis and review of motor learning in the human brain. *Neuroimage* **67**, 283–297 (2013).
129. Kilmarx, J. *et al.* Investigating Visual Imagery as a BCI Control Strategy: A Pilot Study. in *2022 10th International Winter Conference on Brain-Computer Interface (BCI)* 1–6 (2022). doi:10.1109/BCI53720.2022.9734919.
130. Friedrich, E. V. C., Scherer, R. & Neuper, C. The effect of distinct mental strategies on classification performance for brain–computer interfaces. *Int. J. Psychophysiol.* **84**, 86–94 (2012).
131. Allison, B. Z. & Neuper, C. Could Anyone Use a BCI? in *Brain-Computer Interfaces: Applying our Minds to Human-Computer Interaction* (eds. Tan, D. S. & Nijholt, A.) 35–54 (Springer, 2010). doi:10.1007/978-1-84996-272-8_3.
132. Li, J. & Zhang, L. Active training paradigm for motor imagery BCI. *Exp. Brain Res.* **219**, 245–254 (2012).
133. Faul, F., Erdfelder, E., Buchner, A. & Lang, A.-G. Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. *Behav. Res. Methods* **41**, 1149–1160 (2009).
134. Hong, K.-S. & Khan, M. J. Hybrid Brain–Computer Interface Techniques for Improved Classification Accuracy and Increased Number of Commands: A Review. *Front. Neurorobotics* **11**, 35 (2017).

135. Combrisson, E. & Jerbi, K. Exceeding chance level by chance: The caveat of theoretical chance levels in brain signal classification and statistical assessment of decoding accuracy. *J. Neurosci. Methods* **250**, 126–136 (2015).
136. Xie, S., Kaiser, D. & Cichy, R. M. Visual Imagery and Perception Share Neural Representations in the Alpha Frequency Band. *Curr. Biol.* **30**, 2621-2627.e5 (2020).
137. D'Esposito, M. & Postle, B. R. The Cognitive Neuroscience of Working Memory. *Annu. Rev. Psychol.* **66**, 115–142 (2015).
138. Ganis, G., Thompson, W. L. & Kosslyn, S. M. Brain areas underlying visual mental imagery and visual perception: an fMRI study. *Cogn. Brain Res.* **20**, 226–241 (2004).
139. Lee, S.-H., Lee, M., Jeong, J.-H. & Lee, S.-W. Towards an EEG-based Intuitive BCI Communication System Using Imagined Speech and Visual Imagery. in *2019 IEEE International Conference on Systems, Man and Cybernetics (SMC)* 4409–4414 (2019). doi:10.1109/SMC.2019.8914645.
140. Randolph, A. B. Not All Created Equal: Individual-Technology Fit of Brain-Computer Interfaces. in *2012 45th Hawaii International Conference on System Sciences* 572–578 (2012). doi:10.1109/HICSS.2012.451.
141. Randolph, A. B., Jackson, M. M. & Karmakar, S. Individual Characteristics and Their Effect on Predicting Mu Rhythm Modulation. *Int. J. Human–Computer Interact.* **27**, 24–37 (2010).

142. Hammer, E. M. *et al.* Psychological predictors of SMR-BCI performance. *Biol. Psychol.* **89**, 80–86 (2012).
143. Burde, W. & Blankertz, B. Is the locus of control of reinforcement a predictor of brain-computer interface performance? in (2006).
144. Halder, S. *et al.* Neural mechanisms of brain–computer interface control. *NeuroImage* **55**, 1779–1790 (2011).
145. Blankertz, B. *et al.* Neurophysiological predictor of SMR-based BCI performance. *NeuroImage* **51**, 1303–1309 (2010).
146. Ahn, M., Cho, H., Ahn, S. & Jun, S. C. High Theta and Low Alpha Powers May Be Indicative of BCI-Illiteracy in Motor Imagery. *PLOS ONE* **8**, e80886 (2013).
147. Guillot, A. *et al.* Functional neuroanatomical networks associated with expertise in motor imagery. *NeuroImage* **41**, 1471–1483 (2008).
148. Halder, S. *et al.* Prediction of brain-computer interface aptitude from individual brain structure. *Front. Hum. Neurosci.* **7**, 105 (2013).
149. Kilmarx, J., Oblak, E., Sulzer, J. & Lewis-Peacock, J. Towards a common template for neural reinforcement of finger individuation. *Sci. Rep.* **11**, 1–11 (2021).
150. Marks, D. F. Visual Imagery Differences in the Recall of Pictures. *Br. J. Psychol.* **64**, 17–24 (1973).
151. Rozado, D., Duenser, A. & Howell, B. Improving the Performance of an EEG-Based Motor Imagery Brain Computer Interface Using Task Evoked Changes in Pupil Diameter. *PLOS ONE* **10**, e0121262 (2015).

152. Wen, D., Liang, B., Zhou, Y., Chen, H. & Jung, T.-P. The Current Research of Combining Multi-Modal Brain-Computer Interfaces With Virtual Reality. *IEEE J. Biomed. Health Inform.* **25**, 3278–3287 (2021).
153. Winn, M. B., Wendt, D., Koelewijn, T. & Kuchinsky, S. E. Best practices and advice for using pupillometry to measure listening effort: An introduction for those who want to get started. *Trends Hear.* **22**, 2331216518800869 (2018).
154. Mathôt, S. & Vilotjević, A. Methods in cognitive pupillometry: Design, preprocessing, and statistical analysis. *Behav. Res. Methods* 1–23 (2022).
155. Miller, E. K. & Cohen, J. D. An Integrative Theory of Prefrontal Cortex Function. *Annu. Rev. Neurosci.* **24**, 167–202 (2001).
156. Macaluso, E., Eimer, M., Frith, C. D. & Driver, J. Preparatory states in crossmodal spatial attention: spatial specificity and possible control mechanisms. *Exp. Brain Res.* **149**, 62–74 (2003).
157. Cabeza, R. *et al.* Attention-related activity during episodic memory retrieval: a cross-function fMRI study. *Neuropsychologia* **41**, 390–399 (2003).
158. Courtney, S. M., Ungerleider, L. G., Keil, K. & Haxby, J. V. Object and Spatial Visual Working Memory Activate Separate Neural Systems in Human Cortex. *Cereb. Cortex* **6**, 39–49 (1996).
159. Faillenot, I., Decety, J. & Jeannerod, M. Human Brain Activity Related to the Perception of Spatial Features of Objects. *NeuroImage* **10**, 114–124 (1999).

160. Göbel, S., Walsh, V. & Rushworth, M. F. S. The Mental Number Line and the Human Angular Gyrus. *NeuroImage* **14**, 1278–1289 (2001).
161. Mellet, E. *et al.* Neural basis of mental scanning of a topographic representation built from a text. *Cereb. Cortex* **12**, 1322–1330 (2002).
162. Ishai, A., Haxby, J. V. & Ungerleider, L. G. Visual Imagery of Famous Faces: Effects of Memory and Attention Revealed by fMRI. *NeuroImage* **17**, 1729–1741 (2002).