<u>Differences in Motor Planning Between Intact and Prosthetic Arms</u>

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The Academic Faculty

By,

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Abstract

Amputees who have been prescribed prosthetic limbs often abandon them. They do this because learning to use them is challenging, and effective training is difficult. We propose that better training can be offered given the knowledge of how motor planning differs when the end effector is prosthetic as opposed to intact. We studied fMRI data of subjects viewing both intact and prosthetic limbs performing object manipulations to study differences in motor planning. We found that motor planning between the two conditions is functionally different and can be parsed by a machine learning classifier. These findings open the door to further developments in effective prosthetic rehabilitation and general scientific understanding of prosthetic motor planning.

1.0 Introduction

Within the United States, there are an estimated 2 million people living with amputations including loss of arms and legs as well as more distal removals like hands and feet. 1.5 in 1000 people receive an amputation every year.[1, 3] Amputees are commonly prescribed prosthetic limbs to restore the normal function of the limb before amputation. However, amputees often stop using their prosthetics after some time due to the steep learning curve of how to use the devices effectively. The International Society for Prosthetics and Orthotics studied prosthetic abandonment and found that about a quarter of adults abandon their prosthetics.[4] Amputees have cited difficulty learning to use prosthetics effectively as the primary reason for their abandonment of the devices.[4] In the case of abandonment, amputees are left with no better options and simply lose function of their lost limbs. This issue calls for innovative approaches to prosthetic training in order to reduce prosthetic abandonment rates and improve quality of life for amputees.

Developments in other subfields of neuroscience have identified closed loop neurofeedback training as a means to train people efficiently and effectively at various tasks. Closed loop neurofeedback training scans and analyzes a person's brain activity to tune a training task they are performing during the scan.[11, 18] By modulating the task difficulty, researchers can encourage changes to brain activity in specific areas of the brain. This works through conditioning as the person learns subconsciously that engaging the correct brain regions makes the task easier. This has shown promise in studies on attention in which people demonstrated sharper focus and higher brain activity in attention related brain areas after neurofeedback training.[11, 18] Based on this, using neurofeedback training to help amputees learn to use their prosthetic devices is a promising new avenue. However, it cannot be done without filling one critical gap in the literature.

Performing neurofeedback training requires researchers to know what brain regions should be encouraged to have higher or lower activity. To our knowledge, there is no literature detailing what brain regions are used to plan and perform skilled movements using prosthetics, meaning closed loop training is impossible given the current state of knowledge. Therefore, this study aims to fill the gap in the literature by analyzing brain activity before and after training with a prosthetic device. Changes in regional brain activity associated with a better understanding of prosthetic use will reveal what brain regions people must engage to operate prosthetic devices skillfully. This would be a novel discovery in the field, and further it could serve as a target for closed loop neurofeedback training.

This research will improve the quality of life for amputees by advancing understanding of how they learn to use their devices. This will facilitate the development of newer better training protocols. Improving these training techniques will help prosthetic users achieve more precise control of their devices and reduce rates of rejection.

2.0 Literature Review

2.1 Prosthetic Rejection Among Amputees

When a person loses a limb, modern medicine and technology give them the option of replacing their lost limb with a prosthetic device. These artificial limbs can be body powered devices which utilize remaining body parts to actuate the prosthesis, or they can be electric devices using motors to produce actions. Although these devices offer some comfort to many amputees, many patients in the United States suffer from a common problem; rejecting their prosthetic limb. This means that they decide to stop using their new limb. A review by the International Society of Prosthetics and Orthotics (ISPO) found the rejection rate for prosthetics among adults to be 26% for body powered devices, and 23% for electric devices.[4] This has been attributed to many reasons. Some amputees cite difficulty when operating the new limbs, difficulty learning to use the devices, and not being able to rely on their devices to perform predictably. Some say they dislike how the artificial limbs look, and in the case of unilateral amputations, some patients feel that their remaining intact limb is simply better suited for any given task.[1, 2, 3, 4, 5] In essence, with the exception of physical appearance, the general reason for subjects to abandon a prosthetic limb is that they do not feel that the device is restoring function to them. The time investment of learning to use it effectively is also substantial. The crux of this issue is a lack of effective training for users of prosthetics which limits the efficiency of the devices in practice.[2, 3] With better training methods for prosthesis users, the issues of operational impracticality, long training time, unreliability, and functional disadvantage can be minimized. This path forward is universally recognized by the field, but finding ways to improve prosthetic training has proven quite challenging.

2.2 Studying Changes in the Brain During Prosthetic Learning: Rationale, Background, Gaps

The need for robust prosthesis training is the motivation behind this study. The aim is to identify neurofeedback targets for prosthesis training. A prerequisite to performing neurofeedback is having a target brain region to optimize. There is a substantial lack of research into neural correlates of prosthetic learning. Therefore, this study seeks to bridge that gap by identifying brain regions whose activity changes as subjects' skill with prosthetic devices improves.

Although the literature surrounding brain regions in association with prosthetic learning is limited, there is an abundance of work investigating motor control and motor planning behavior in general. While not exactly the same as operating a prosthetic, the brain regions used for planning and executing movement with an intact limb are potentially conserved for operating prosthetic limbs, albeit the way they function is likely altered. In order to qualify as an acceptable candidate for neurofeedback training, this functional conservation needs to be confirmed.

Among the many brain systems, the divisions of the parietal lobe are areas with great promise in the search for targets. The first of these divisions is the inferior parietal lobule which is further divisible into the superior marginal gyrus and the angular gyrus. Together, these regions have been associated with spatial cognition and perception of space and limb location.[23] Just above the inferior parietal lobule is the superior parietal lobule. This region receives sensory information from the hand and is involved in spatial orientation cognition.[23] Anterior to both of these lobules is the somatosensory cortex. This region receives sensory inputs for the entire body, and has been implicated in a functional loop during motor behavior.[6, 7, 8] This means that sensory inputs inform subsequent motor outputs which generate more sensory feedback, a continuous process during motion.[23] Motor planning in the brain is not restricted to just the parietal lobe, the inferior frontal gyrus is also implicated. This region contains the premotor area, a region of the brain known to be active in the moments just before motor output. This suggests a role in motor planning similar to the parietal lobules and somatosensory cortex.[23] Its precise function is still under broad investigation, but it is potentially a modulator of motor planning.

All of the aforementioned functions were observed in the typical healthy population, not in prosthesis users. Due to the functional plasticity demonstrated by the human brain, loss of a limb could conceivably alter the function of these regions rendering them questionable at best when considering them as targets for training.[23] The current study aims to determine whether the functions of these regions is conserved in prosthetic motor planning. This will require measuring the neural activity of these specific brain regions while they are engaged in both intact and prosthetic motor planning. We will also correlate behavioral improvements in prosthesis skill with specific neural activity changes. Given that fMRI involves fixing subjects in place, it seems like an inappropriate tool in this study. However, related literature surrounding mirror neurons suggests otherwise.

2.3 Mirror Neurons to Study Motor Planning in the Absence of Motor Output

Mirror neurons are neurons in the mammalian brain which show similar activation when a person performs an action as well as when that person observes someone else perform the same action.[12, 13] These neurons were first observed in monkeys, but in recent years studies in humans have revealed neurons with mirror like properties.[12, 13, 14, 15, 16] Mirror neurons therefore enable us to study motor output behavior without actually performing the motor functions associated with that cortical activity. This presents an exciting opportunity, as removing the need for motor output brings fMRI into the conversation as a way to measure neural activity before and after prosthesis training. This study will build on this foundation by testing subjects before and after prosthetic training to correlate differences in neural activity with prosthetic skill. This analysis will fill the gap in understanding what brain regions could be targeted to increase prosthetic learning rate.

This study has two aims. First, we want to identify whether the observation of prosthesis use and sound limbs engages distinct or overlapping brain areas. Second, we seek to understand if motor training leads to a change in the brain areas encoding prosthesis use compared to sound limbs. Our findings will pave the way for a new approach to making more effective training schemes through closed loop neurofeedback. To begin this process, we investigated what brain regions showed activity predictive of motor planning with prosthetic devices. Building on these findings will lead to improved training methods that could lower prosthesis rejection rates and improve overall quality of life for hundreds of thousands of amputees.

3.0 Methods

We studied differences in motor planning in humans when the end effector being used is an intact limb versus a prosthetic one. Using fMRI to study this is an effective strategy thanks to the action of mirror neurons in the mammalian brain.[10, 20, 21] We implemented a machine learning classification paradigm which allowed for the differentiation of distinct neural patterns of activity between the prosthetic and intact conditions.[11, 18]

3.1 Participants

Fifteen participants (female = 10, male = 5, age range 18-47, all right handed) were recruited for this study. Preliminary subject surveys included gathering basic demographics like age, sex, and handedness, as well as a list of neuropathies and other MRI contraindications that would eliminate subjects from consideration.[24] The fifteen recruited and discussed here were neurologically healthy and showed no contraindications. All methods used were approved by the Georgia Tech Institutional Review Board.

3.2 Scanning Stimuli

The scanning stimuli studied here was developed and reported on previously.[25] Subjects were scanned using fMRI four times in runs lasting approximately seven minutes each. Within each run, twenty sets of stimuli were shown on a video screen within the scanner. Each stimuli set consisted of a fixation cross presented for eight seconds, followed by ready text (the word "Ready!") for two seconds, then a prompt describing the action that was about to occur for three seconds, and finally four concatenated videos of a hand performing the action (each two seconds in length, comprising a concatenated length of eight seconds). This sequence is visualized in Figure 1. Within the videos, the hand, or end effector, could be an intact limb, meaning a healthy human hand. Alternatively, it could be a prosthetic limb performing the same action. For each subject, half the videos were an intact limb and half were prosthetic. The identity of the end effector as intact or prosthetic defined the two groups classified by a machine learning classifier. Consistent differences in BOLD activation between these two conditions would allow the classifier to differentiate and effectively learn which condition is represented by distinct brain activity patterns. Differences in activity within motor planning regions of the brain would suggest that subjects differently plan motion based on the identity of the end effector.

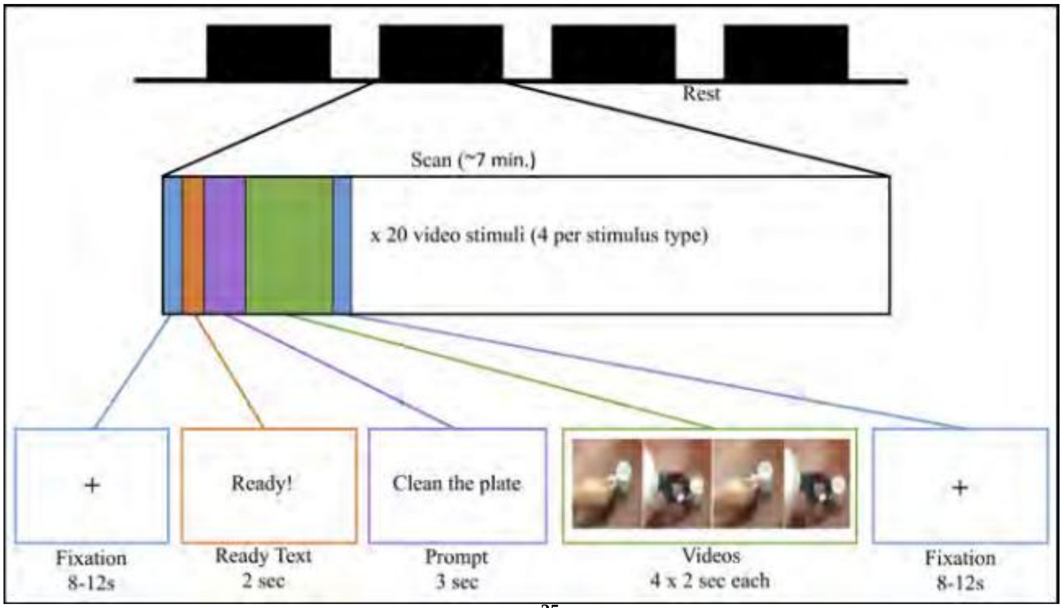

Figure 1: Visualization of scanning stimuli.[25] Sequence of visual prompts shown to subjects during fMRI scanning. 4 runs were taken per subject as shown by the black bars with rest intervals in between. Within each scan, 20 sequences of video stimuli were shown. Videos of intact and prosthetic limbs were presented in equal amounts. This figure was generated by and borrowed from John Johnson's doctoral dissertation, as we used the same source data.[25]

3.3 Data Collection

Data was collected at the Georgia Tech/Georgia State University Center for Advanced Brian Imaging (CABI). A Siemens TrioTim 3T scanner with a twelve-channel head coil was used to gather structural and functional images. Structural images were gathered as T1 weighted images using an MPRAGE sequence (Echo time of 4ms, Repetition time of 2.25s, Interval time of 850ms, flip angle of 9 degrees, 256mm by 256mm FOV).[25] Functional images were gathered as T2 weighted images generated by a gradient-echo echo-planar-imaging sequence (echo time of 30ms, repetition time of 2s, 90 degree flip angle, 204mm, 68x68 in-plane matrix FOV)[25] Data gathered was converted from the native DICOM format to NifTI format as previously described.[26] This format changed no information but allowed easier integration with MATLAB. Raw fMRI scans were motion and slice time corrected using the SPM toolbox before being projected into standardized MNI space.[26]

3.4 Prosthetic Training

Two subjects were trained to use a prosthetic arm simulator following their initial scans. This training consisted of learning how to perform basic object manipulations using the prosthetic like grasping and moving objects. The exact training protocol was reported on previously.[27, 28, 29] They were then scanned again with similar stimuli presented to them. Theoretically, their novel understanding of how to execute actions with the prosthetic should strengthen their ability to plan movements with prosthetics, and so these classifications should show stronger activity in motor planning regions post-training. Behavioral measures of prosthetic skill were also taken to correlate with changes in BOLD activity as reported previously.[27, 28, 29] Unfortunately, the timing of data collection for this project just preceded lockdown associated with the Covid-19 pandemic. Therefore, only these two subjects could be given this training and rescanned. This specific part of the study is therefore underpowered and serves as case studies for potential hypothesis generation. Their results will be reported on and discussed, but no definitive conclusions may be drawn from such limited data.

3.5 Machine Learning Classification

Once all data was gathered, corrected, and normalized, multivariate pattern analysis was performed within each subject to classify whether the subject was viewing (a) intact limbs or (b) prosthetic ones within each run. Successful classification indicates the neural pattern for the two is systematically different. How accurate and confident the classifier is quantifies how strong and reliable that difference is between the two types of action perception. The use of machine learning classifiers such as this to interpret complex patterns of neural activity is well established.[11, 18, 26] In order to isolate differences in motor planning behavior, a broad brain mask encompassing bilateral angular gyrus, inferior frontal gyrus, inferior parietal lobule, somatosensory cortex, superior parietal lobule, and marginal gyrus was used, as shown in figure 2.[11, 18, 23] Models were trained using the Princeton MVPA lite toolbox in MATLAB and the LibLinear classifier. Classifiers were validated with 8 fold leave one out validation, L2 loss, and an overfitting penalty parameter of 1.5. Input data was normalized across the run such that voxels deeper in the brain were not incorrectly weighted as less intense. This often happens in fMRI studies due to the scanner being unable to pick up larger magnitude of signals from deeper brain regions.[26] This classification process resulted in a classification accuracy per subject and a set of importance maps which show what voxels, and therefore brain regions, the classifier learned to use to predict viewing of intact or prosthetic limbs.

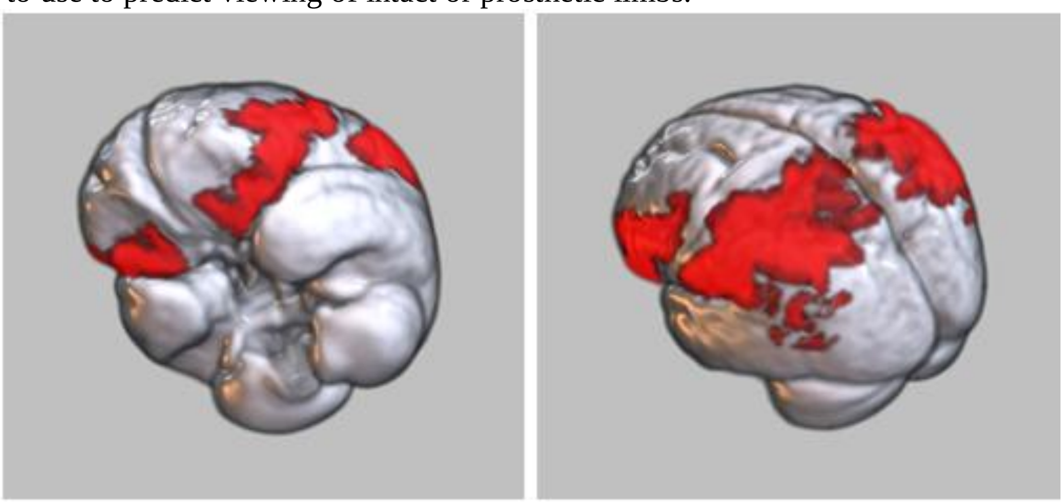

Figure 2: Masked region used in MVPA classification. The red highlights represent voxels considered in classification between intact and prosthetic viewing conditions. The regions are symmetrical across the midsagittal plane. Visualization was generated using MRIcroGL.

3.6 Statistical Analysis

The nature of MVPA classification is that the model will only be able to differentiate the conditions if there is a qualitative difference between the neural patterns associated with either condition.[10] Therefore, to understand if there was a difference in motor planning activity, a paired t-test was performed based on the classification accuracy of the models compared to chance performance. To determine chance performance for each subject, random permutation tests were performed per subject. This means randomly scrambling the labels of the training data to abstract any possible learning by the model and force the models to make uninformed guesses. A significance threshold of .05 was used. A significant result would mean that the neural pattern activity between intact and prosthetic conditions was different enough to let the classifier predict above chance levels. We also reported the change in classification accuracy after training for the limited subjects who underwent training, but due to the poor sample size, no statistics were performed for this part of the study. Finally, importance maps were generated and visually inspected to see any differences in the spatial location of voxels used to predict intact or prosthetic conditions.

4.0 Results

4.1 Classification of intact versus prosthetic viewing conditions in naive subjects.

We scanned 15 subjects while they watched videos of both intact and prosthetic limbs performing object manipulation tasks. MVPA classifiers were trained on the fMRI data of these subjects' motor planning brain regions. Above chance classification would mean that these brain regions contain some information that the classifiers can use to make informed decisions. In other words, it would imply that the brain regions are functionally different in these cases. In practice, classifiers performed significantly above chance and were able to distinguish between the intact and prosthetic viewing conditions ($p = 0.0000043$; Mean Accuracy = 0.5974; St. Dev = 0.05907).

4.2 Confusion matrices for Intact versus Prosthetic predictions.

In addition to raw predictive accuracies for all subjects, confusion matrices were generated to see how the classifier was performing within the individual conditions of intact and prosthetic. These matrices reveal more nuanced information about how accurate the classifiers are within class. The average confusion matrix across all 15 subjects is provided in Table 1. The models on average had much higher confusion predicting the intact condition, with a true positive rate of 53.86% and a false negative rate of 46.15%. The model was far more adept at predicting when the trial was a prosthetic trial with a true positive rate of 65.84% and a false negative rate of 34.16%.

	Guess_Int	Guess_Pros
True Intact	0.5386	0.4615
True Prosthetic	0.3416	0.6584

Table 1: Average Confusion Matrix for Intact Versus Prosthetic Predictions. The confusion matrix represents the proportion of classifier predictions in each category split out by what the true label should have been. The values on the main diagonal (top left and bottom right) represent true positives (correct classifications) while the off diagonal (bottom left and top right) represents false negatives (incorrect classifications).

4.3 Importance maps generated by classifiers.

In order to gain insight into how the classifiers are making their decisions, we generated importance maps for each predictive model. These maps are visual representations of how much specific voxels contributed to the models' decision making process. The numerical value is the product of the parameter weight of the voxel and the average activity in that voxel. Here we report an example of one subject's individual importance maps (Figure 3) followed by a representation of the average importance map across all subjects (Figure 4). At the individual level, we expect and observe complimentary maps because a voxel predictive of one condition cannot be predictive of the other. At the group level however, there is no guarantee that a voxel used in one subject to predict one condition will also be used by every other subject to predict the same condition. Therefore, calculating the average importance maps allows us to examine whether or not there are common regions used to predict between intact and prosthetic conditions. In the maps we generated, the average map has significant overlap between both conditions. This means that in our masked region using these classifiers, there was no specific region or regions which consistently informed the models about subject viewing conditions. Despite this, models still performed above chance in the average case.

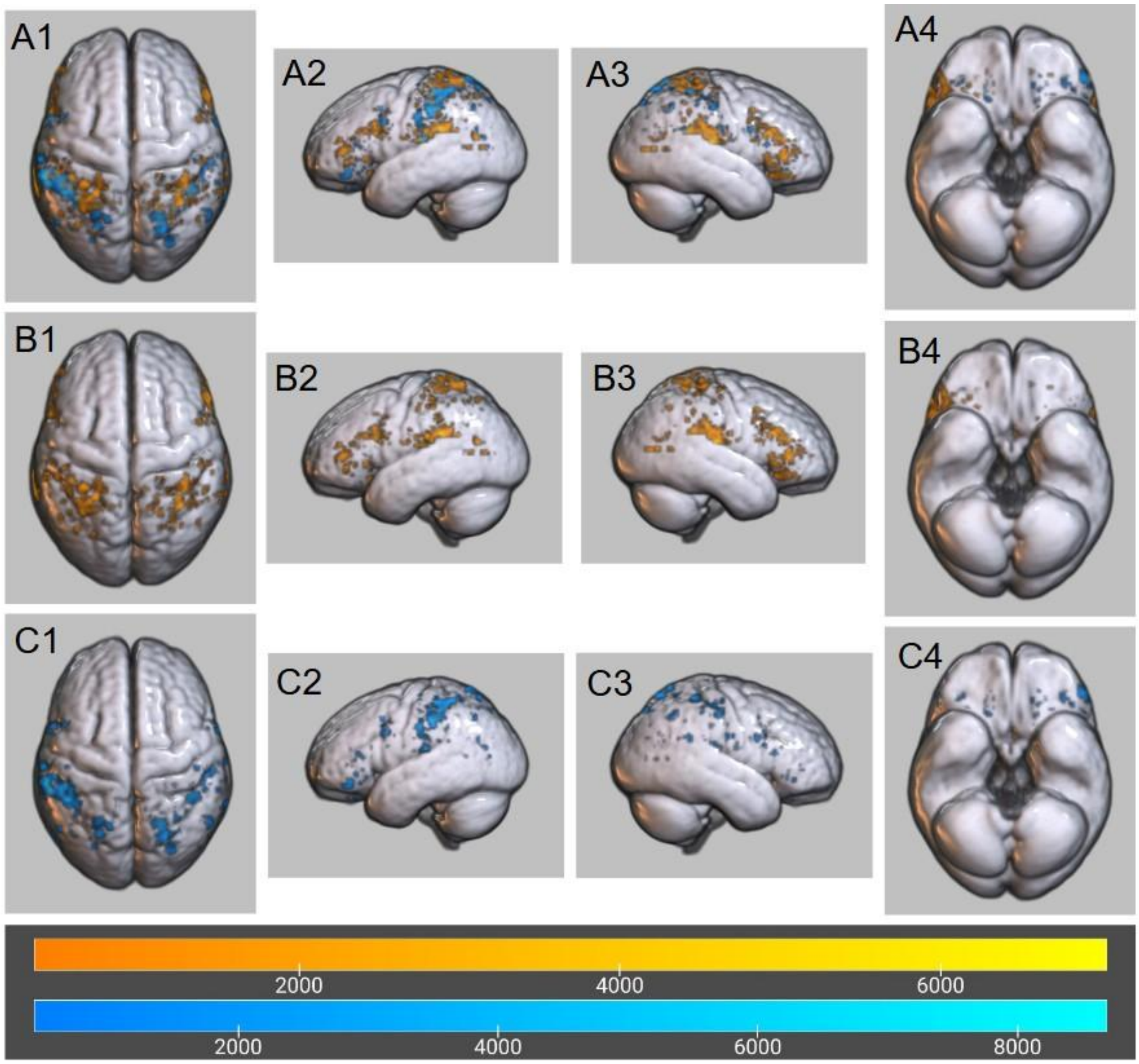

Figure 3: Importance maps for an individual subject. Visualized importance maps used by the classifier to predict intact versus prosthetic viewing conditions for subject 1. For clarity, only the top 95% most important voxels are pictured. The bottom 5% have predictive contributions near zero, but still show up in visualization normally. Voxels in orange represent voxels predictive of the subject viewing an intact end effector. Blue voxels represent those predictive of viewing prosthetic conditions. (A1) through (A4) show the two maps superimposed with each other.(B1) through (B4) isolate the intact condition. (C1) through (C4) isolate the prosthetic condition. The color bars indicate the range of importance values calculated by the classifiers. Visualizations were created using MRIcroGL.

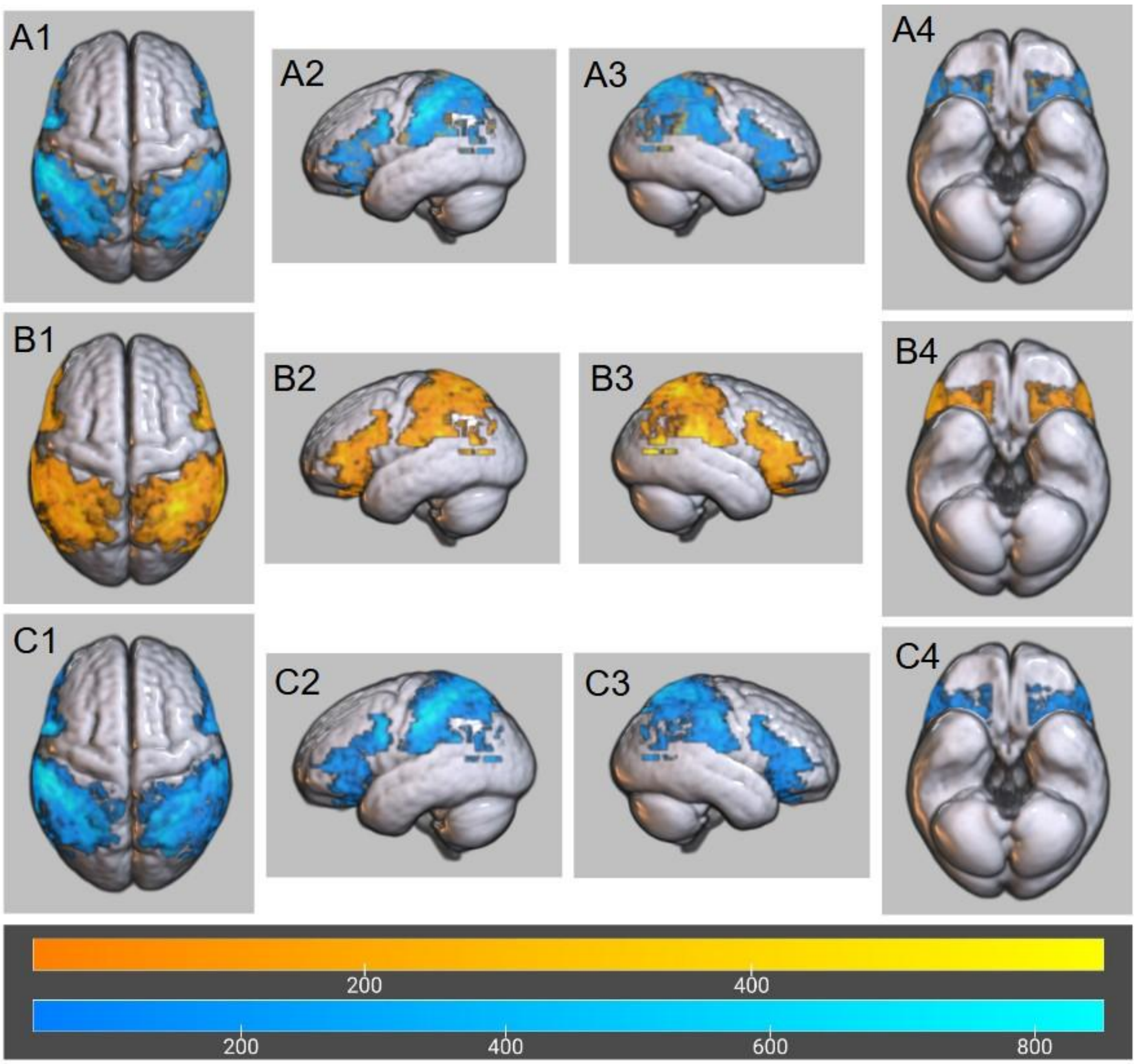

Figure 4: Average Importance maps across subjects. Visualizations of the average importance maps used by the classifier to predict intact versus prosthetic across subjects. For clarity, only the top 95% most important voxels are pictured. The bottom 5% have predictive contributions near zero, but still show up in visualization normally. Voxels in orange represent voxels predictive of the subject viewing an intact end effector. Blue voxels represent those predictive of viewing prosthetic conditions. (A1) through (A4) show the two maps superimposed with each other.(B1) through (B4) isolate the intact condition. (C1) through (C4) isolate the prosthetic condition. Note that unlike the individual case, overlap between the two conditions is possible and present. This is because a voxel predictive of one condition in some subjects could be predictive of the other in other subjects. The color bars indicate the range of importance values calculated by the classifiers. Visualizations were created using MRIcroGL.

4.4 Results from Prosthetic Training Subjects.

To reiterate, only 2 subjects underwent prosthetic training and were rescanned. Results reported in this section are therefore akin to a case study**.** In one of the subjects who underwent training, classification accuracy increased by a minor amount from 58.44% to 61.47% (+ 3.03%). The largest contributor to this shift in accuracy was a decrease in confusion within the intact condition. This subject showed quicker task completions in the translation task with shorter durations, faster peak reach velocities, and lower error after training. In rotation, this subject similarly got quicker, but made more errors. The other training subject experienced a more dramatic increase in accuracy, going from 48.2% to 71.98% (+23.78%). Their confusion matrices show large improvements in both intact and prosthetic accuracy. Similar to the previous subject, this subject showed marked speed increases and additionally scored lower error in both rotation and translation tasks. Changes in model confusion are summarized in table 2. Behavioral results are summarized in table 3. We also visualized the changes in importance values by voxel in each subject. In these maps, colored voxels are those which changed in importance after training. The difference maps for subject 21 are shown in figure 5. There is a gain in importance values visible most distinctly in the superior and inferior parietal lobules for subject 21.

Subject 20 pre-training

Total Performance: .5844

Confusion Matrix

	Guess_Int	Guess_Pros
Intact	.5625	.4375
Prosthetic	.3858	.6142

Subject 20 post-training

Total Performance: .6147

Confusion Matrix

	Guess_Int	Guess_Pros
Intact	.6016	.3984
Prosthetic	.3701	.6299

Subject 21 pre-training

Total Performance: .4820

Confusion Matrix

	Guess_Int	Guess_Pros
Intact	.4766	.5234
Prosthetic	.5118	.4882

Subject 21 post-training

Total Performance: .7198

Confusion Matrix

	Guess_Int	Guess_Pros
Intact	.7734	.2266
Prosthetic	.3386	.6614

Table 2: Confusion matrices for training subjects before and after training. These matrices are exactly like Table 1. Confusion matrices represents the proportion of classifier predictions in each category split out by what the true label should have been. The values on the main diagonal (top left and bottom right) represent true positives (correct classifications) while the off diagonal (bottom left and top right) represents false negatives (incorrect classifications). The top 2 matrices correspond to Subject 20, and the bottom two to Subject 21.

Participant	Day	Task	Duration w/o Drops	Duration w/ Drops	Peak Velocity w/ Drops	Error w/ Drops
20	1	Translation	3469.18 ms	765.65 ms	0.700 m/s	0.776
20	5	Translation	3198.76 ms	684.66 ms	0.834 m/s	0.710
21	1	Translation	5290.90 ms	965.79 ms	0.629 m/s	0.790
21	5	Translation	4137.30 ms	910.00 ms	0.714 m/s	0.696
20	1	Rotation	4837.54 ms	821.94 ms	0.608 m/s	0.147
20	5	Rotation	4531.74 ms	667.70 ms	0.733 m/s	0.222
21	1	Rotation	7130.16 ms	873.10 ms	0.547 m/s	0.556
21	5	Rotation	6204.07 ms	856.71 ms	0.587 m/s	0.222

Table 3: Summary of Behavioral Outcomes From Training Subjects. This table summarizes the average measurements from training subjects performing translation and rotation tasks on day 1 and day 5 of training with a prosthesis simulator. Columns labeled w/o drops specifically report trials in which the subjects did not drop the item they were manipulating. Error was defined as failure to complete the task, with a full failure constituting an error of 3, near completion 1, and full completion 0. For more details about the task implemented, see previous reports.[27, 28, 29]

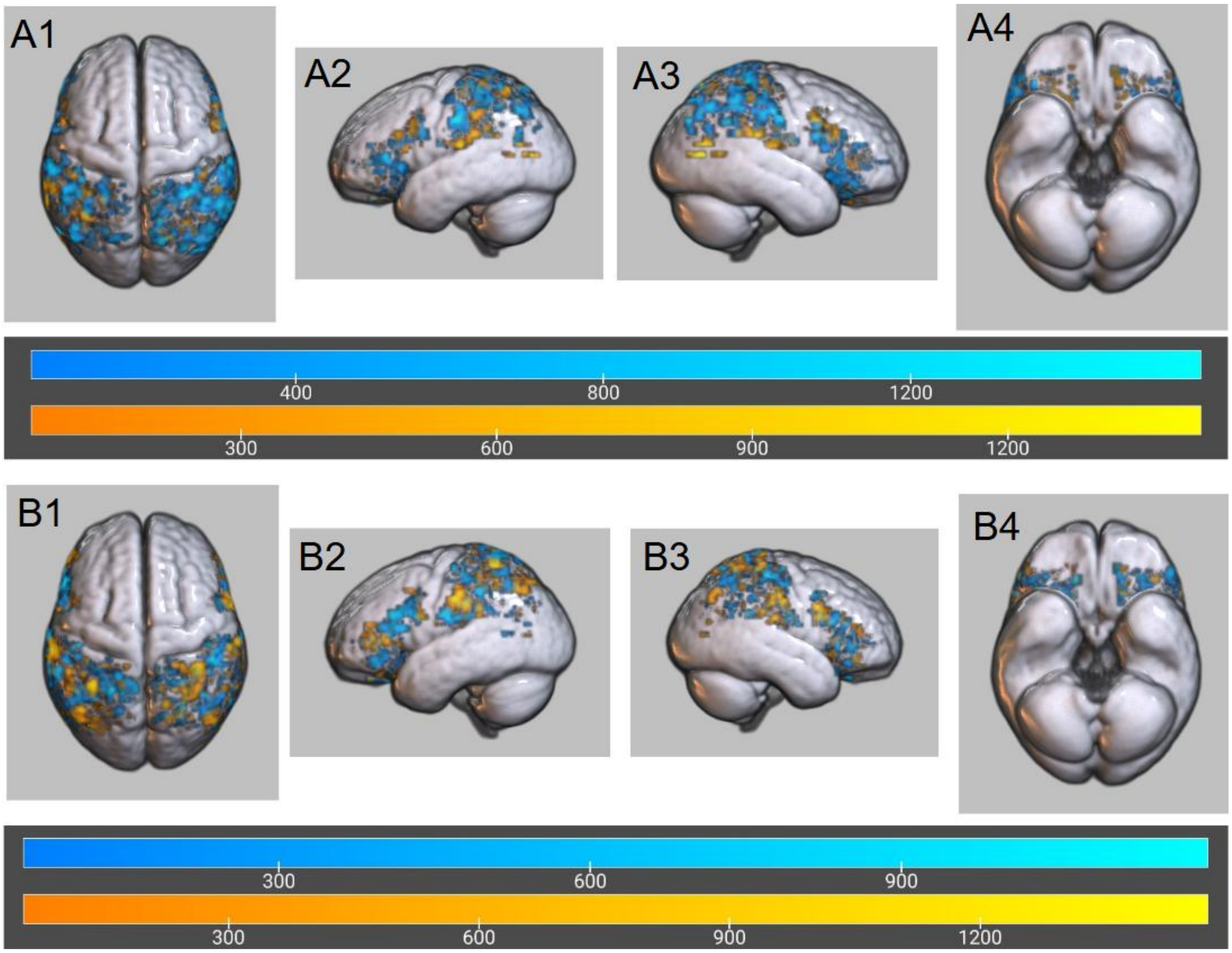

Figure 5: Voxels changed in Subject 21 after prosthetic training. These visualizations show changes in predictive importance values for subject 21 after training compared to their values before training. The top row (A1 through A4) shows differences in intact predictions with warm colors corresponding to increases in predictive importance and cool voxels representing decreases in importance. The bottom row represents the same for the prosthetic condition. Note that while this looks similar to Figures 3 and 4, it is displaying a *change* in importance rather than the *absolute* importance.

5.0 Discussion

5.1 Classification Results.

In our classifier data, we found significantly above chance predictions (59.74% accuracy, p=4.3e-6) when classifying between prosthetic and intact conditions. This shows that classifiers were able to extract some meaningful information about the type of action being viewed from subject fMRI signals. This aligns with existing literature which similarly finds that predictive models can be reliably trained using motor planning signals.[30, 31, 32] The exact nature of this information is difficult to interpret. Above chance classification could be due to extraneous factors like biases in the data, random chance, and differences in variance. Some of these effects are controlled for by using techniques of normalization and balancing during model training, but there is always the chance for alternative explanations to observed trends. This is why we produced confusion matrices and importance map visualizations. These additional visualizations allow us to better understand how the models make their decisions. Our confusion matrices reveal a key insight into this data; the models on average were much better at determining the identity of true prosthetic trials (65% true positive rate) versus intact trials (53% true positive rate). This suggests that intact trials are potentially more variable and hard to identify using a specific characteristic. In comparison, prosthetic trials likely have a more unique feature about them which allows the classifier to more reliably recognize them. This means that the brain is processing prosthetic motor planning in a fundamentally different way to intact motor planning. This is significant to therapeutic efforts aimed at amputees. This implies that treating a new prosthetic limb as if it were an intact limb may be counter to what the brain wants to do. An alternative explanation could be that the brain's familiarity with the intact case allows it to pick up more subtle details which end up looking like noise to the classifier. The prosthetic by comparison is more novel and the brain would only be able to focus on more general information. If there is a different modality by which the brain plans movements with a prosthetic, understanding what that mode is can guide better treatment aimed at improving skill in that specific mode.

5.2 Importance Visualizations

We generated and visualized importance maps to show which voxels the models used most to make their decisions. At the individual level, we see clear separable areas where models can use local activity to predict either condition. We also tend to see broader variance in signal intensity within the prosthetic condition. At the group level, there is no specific region which is exclusive to either condition. Rather, the average maps reveal that any given voxel could be used to predict prosthetic in one subject and intact in another. This contributes to the average signal intensity being an order of magnitude smaller than in the individual case. If a voxel is predictive of intact only half the time, it's average intensity should be zero since the values from all the intact predictors will cancel out the prosthetic predictors. That being said, our average values are not zero. There are some regions where predictions of one condition over the other are strong enough to pull the average towards that condition. For example, we see some biased areas of the parietal lobe for the prosthetic condition. Similar biased areas are sparser in the intact condition. This offers a possible explanation for why the model struggled with the intact condition more than the prosthetic condition. In prosthetic trials, those high signal areas can be used to predict prosthetic fairly reliably. But in intact trials, there are no corollary high signal areas to rely on. These prosthetic areas are roughly in the area containing Brodmann areas 2, 7, and 40. These are the primary somatosensory cortex, superior parietal lobule, and supramarginal gyrus respectively. These regions are broadly related to visuomotor coordination and spatial perception.[33] It therefore makes sense that they would be active during the current experiment. This finding is in alignment with EEG results which also found that activity in parietal areas could train reliable classifiers of movement.[34] This finding suggests a potential target for closed loop neurofeedback training. Stronger activity in these spatial areas could allow people to more skillfully use their prosthetic limbs.

5.3 Training Subjects

An additional arm of this study investigated the effects of prosthetic training on neural activity. However, as discussed previously, this training was halted preemptively due to the covid lockdown. With the understanding that these results are effectively a case study, we discuss here the results of our 2 subjects who underwent training. In one subject, training had little effect on classification accuracy. However, in the other, accuracy climbed from 48.2% to 71.98% as a result of training. In this subject, the strength of the high signal parietal areas (BA 2, 7, and 40) observed in prosthetic trials increased. This suggests that not only did training cause a change in neural pattern activity, but further that these parietal areas are involved in the long term effects of learning with a prosthetic. The finding of neural patterns changing with learning has been similarly observed in a study focused on visual memory representations.[35] This study found that new visual stimuli were initially represented by a mixture of higher order and lower order cortical signals. Over time they distributed their representations into more stable higher order networks. This paradigm offers an explanation to our observed changes in prosthetic learning. Naive or untrained prosthetic users do not possess higher order representations of the procedural knowledge required to use a prosthetic. As they learn, these patterns emerge in their cortex, and classifiers can learn these patterns. An alternative explanation could be that a prosthetic is less like a limb and more like a tool or extension of the body. In fact, the literature surrounding tool use does find that similar left parietal brain regions are involved in using hand tools.[36] This explanation is plausible given that modern prosthetic technology cannot deliver the same kind of sensory feedback that an intact limb can. The way a prosthetic user interfaces with their device may, in some respect, be more like swinging a hammer than using their arm. Further exploration of this idea is highly desirable, as this too would be a clear distinction by which to tailor prosthetic training and rehabilitation. If a prosthetic is truly more akin to a tool than a limb, then training to use it as if it were a limb could hold patients back.

5.4 Limitations & Future Directions

The current study was not able to study enough subjects throughout a prosthetic training program to characterize how neural representations change with increasing prosthetic skill. Additionally, fMRI is not an ideal scanning method, as it restricts movement during a motor planning task. Future work should explore other scanning methods like EEG or fNIRS to measure a cohort of subjects during prosthetic training. These extended works will solidify our understanding of how the brain adapts to prosthetic limbs. This will also reveal ways in which we can optimize rehabilitation efforts for amputees new to prosthetics.

The current study used able bodied subjects to study prosthetics. In an ideal world, amputees should be directly studied so that results are more likely to generalize to them. However, as was the case with the present work, this can prove challenging. It remains to be seen how well these neural pattern differences are conserved between able bodied people and amputees. Finally, the idea of a prosthetic being represented by the brain as a tool rather than a limb should be explored. This could be the case consciously or unconsciously, and if it is true it could explain some of our observations. It would also guide rehabilitation efforts in a more accurate direction.

Conclusion

The present work explored differences in neural pattern activity between motor planning with intact and prosthetic limbs. Our analyses revealed left parietal areas associated with prosthetic motor planning and opened the path to many future works. Continued investigation should focus on dynamic neural patterns as a result of learning and better characterization of underlying networks controlling prosthetic motor planning. This work will guide rehabilitative efforts to assist amputees in using their prosthetic limbs most effectively.

References

1. Carey, S. L., Lura, D. J., & Highsmith, M. J. (2015). Differences in myoelectric and body-powered upper-limb prostheses: Systematic Literature Review. *Journal of Rehabilitation Research and Development*, *52*(3), 247–262. https://doi.org/10.1682/jrrd.2014.08.0192
2. Resnik, L., Borgia, M., Cancio, J., Heckman, J., Highsmith, J., Levy, C., & Webster, J. (2021). Upper limb prosthesis users: A longitudinal cohort study. *Prosthetics & Orthotics International*, *45*(5), 384–392. https://doi.org/10.1097/pxr.0000000000000034
3. Das, N., Nagpal, N., & Bankura, S. S. (2018). A review on the advancements in the field of upper limb prosthesis. *Journal of Medical Engineering & Technology*, *42*(7), 532–545. https://doi.org/10.1080/03091902.2019.1576793
4. Biddiss, E. A., & Chau, T. T. (2007). Upper limb prosthesis use and abandonment. *Prosthetics & Orthotics International*, *31*(3), 236–257. https://doi.org/10.1080/03093640600994581
5. Chadwell, A., Kenney, L., Thies, S., Head, J., Galpin, A., & Baker, R. (2021). Addressing unpredictability may be the key to improving performance with current clinically prescribed myoelectric prostheses. *Scientific Reports*, *11*(1). https://doi.org/10.1038/s41598-021-82764-6
6. Chen, S., Liu, Y., Wang, Z. A., Colonell, J., Liu, L. D., Hou, H., Tien, N.-W., Wang, T., Harris, T., Druckmann, S., Li, N., & Svoboda, K. (2024). Brain-wide neural activity underlying memory-guided movement. *Cell*, *187*(3). https://doi.org/10.1016/j.cell.2023.12.035
7. Gao, Z., Davis, C., Thomas, A. M., Economo, M. N., Abrego, A. M., Svoboda, K., De Zeeuw, C. I., & Li, N. (2018). A cortico-cerebellar loop for motor planning. *Nature*, *563*(7729), 113–116. https://doi.org/10.1038/s41586-018-0633-x
8. Svoboda, K., & Li, N. (2018). Neural mechanisms of movement planning: Motor Cortex and beyond. *Current Opinion in Neurobiology*, *49*, 33–41. https://doi.org/10.1016/j.conb.2017.10.023
9. Andersen, R. A., Hwang, E. J., & Mulliken, G. H. (2010). Cognitive neural prosthetics. *Annual Review of Psychology*, *61*(1), 169–190. https://doi.org/10.1146/annurev.psych.093008.100503
10. Johnson, J. T., de Mari, D., Doherty, H., Hammond, F. L., & Wheaton, L. A. (2022). Alpha-band activity in PARIETOFRONTAL Cortex predicts future availability of vibrotactile feedback in prosthesis use. *Experimental Brain Research*, *240*(5), 1387–1398. https://doi.org/10.1007/s00221-022-06340-8
11. Sherwood, M. S., Weisend, M. P., Kane, J. H., & Parker, J. G. (2016). Combining real-time fmri neurofeedback training of the DLPFC with N-back practice results in neuroplastic effects confined to the Neurofeedback Target Region. *Frontiers in Behavioral Neuroscience*, *10*. https://doi.org/10.3389/fnbeh.2016.00138
12. Cook, R., Bird, G., Catmur, C., Press, C., & Heyes, C. (2014). Mirror neurons: From origin to function. *Behavioral and Brain Sciences*, *37*(2), 177–192. https://doi.org/10.1017/s0140525x13000903
13. Bonini, L., Rotunno, C., Arcuri, E., & Gallese, V. (2022). Mirror neurons 30 years later: Implications and applications. *Trends in Cognitive Sciences*, *26*(9), 767–781. https://doi.org/10.1016/j.tics.2022.06.003

14. Thompson, E. L., Bird, G., & Catmur, C. (2022). Mirror neuron brain regions contribute to identifying actions, but not intentions. *Human Brain Mapping*, *43*(16), 4901–4913. https://doi.org/10.1002/hbm.26036
15. Dapretto, M., Davies, M. S., Pfeifer, J. H., Scott, A. A., Sigman, M., Bookheimer, S. Y., & Iacoboni, M. (2005). Understanding emotions in others: Mirror neuron dysfunction in children with autism spectrum disorders. *Nature Neuroscience*, *9*(1), 28–30. https://doi.org/10.1038/nn1611
16. Schmidt, S. N. L., Sojer, C. A., Hass, J., Kirsch, P., & Mier, D. (2020). FMRI adaptation reveals: The Human Mirror Neuron system discriminates emotional valence. *Cortex*, *128*, 270–280. https://doi.org/10.1016/j.cortex.2020.03.026
17. Fuelscher, I., Caeyenberghs, K., Enticott, P. G., Kirkovski, M., Farquharson, S., Lum, J., & Hyde, C. (2019). Does fMRI repetition suppression reveal mirror neuron activity in the human brain? insights from univariate and multivariate analysis. *European Journal of Neuroscience*, *50*(5), 2877–2892. https://doi.org/10.1111/ejn.14370
18. deBettencourt, M. T., Cohen, J. D., Lee, R. F., Norman, K. A., & Turk-Browne, N. B. (2015). Closed-loop training of attention with real-time brain imaging. *Nature Neuroscience*, *18*(3), 470–475. https://doi.org/10.1038/nn.3940
19. Cortese, A., Tanaka, S. C., Amano, K., Koizumi, A., Lau, H., Sasaki, Y., Shibata, K., Taschereau-Dumouchel, V., Watanabe, T., & Kawato, M. (2021). The DECNEF collection, fmri data from closed-loop decoded neurofeedback experiments. *Scientific Data*, *8*(1). https://doi.org/10.1038/s41597-021-00845-7
20. Sinke, M., Chadwell, A., & Smit, G. (2022). State of the art of prosthesis simulators for the upper limb: A narrative review. *Annals of Physical and Rehabilitation Medicine*, *65*(6), 101635. https://doi.org/10.1016/j.rehab.2022.101635
21. Romkema, S., Bongers, R. M., & van der Sluis, C. K. (2013). Intermanual transfer in training with an upper-limb myoelectric prosthesis simulator: A mechanistic, randomized, pretest-posttest study. *Physical Therapy*, *93*(1), 22–31. https://doi.org/10.2522/ptj.20120058
22. Logothetis, N. K. (2008). What we can do and what we cannot do with fmri. Nature, 453(7197), 869–878. https://doi.org/10.1038/nature06976
23. Kandel, E. R., & Mack, S. (2014). *Principles of Neural Science*. McGraw-Hill Medical.
24. Oldfield, R. C. (1971). The assessment and analysis of Handedness: The Edinburgh Inventory. *Neuropsychologia*, *9*(1), 97–113. https://doi.org/10.1016/0028-3932(71)90067-4
25. Johnson, J.T. (2022). *The neurobehavioral effects of sensorimotor dissonance during observation and execution with upper-extremity prostheses*[Doctoral Dissertation, Georgia Institute of Technology]. Georgia Tech Library Repository. https://repository.gatech.edu/entities/publication/a56071c0-dd77-4aa7-9d68-f522237304e6
26. Cox, D. D., & Savoy, R. L. (2003). Functional magnetic resonance imaging (fmri) “Brain reading”: Detecting and classifying distributed patterns of fmri activity in human visual cortex. *NeuroImage*, *19*(2), 261–270. https://doi.org/10.1016/s1053-8119(03)00049-1
27. Alterman, B. L., Keeton, E., Ali, S., Binkley, K., Hendrix, W., Lee, P. J., Wang, S., Kling, J., Johnson, J. T., & Wheaton, L. A. (2022). Partial-hand prosthesis users show improved reach-to-grasp behaviour compared to transradial prosthesis users with increased task

complexity. *Journal of Motor Behavior*, *54*(6), 706–718. https://doi.org/10.1080/00222895.2022.2070122

28. Alterman, B. L., Ali, S., Keeton, E., Binkley, K., Hendrix, W., Lee, P. J., Johnson, J. T., Wang, S., Kling, J., Gale, M. K., & Wheaton, L. A. (2024). Grasp posture variability leads to greater ipsilateral sensorimotor beta activation during simulated prosthesis use. *Journal of Motor Behavior*, *56*(5), 579–591. https://doi.org/10.1080/00222895.2024.2364657
29. Alterman, B.L. (2022). *Neuroplasticity and Upper-limb Loss: Towards Predicting and Improving Functional Rehabilitation Outcomes* [Doctoral Dissertation, Georgia Institute of Technology]. Georgia Tech Library Repository.
30. Shenoy, K., Meeker, D., Cao, S., Kureshi, S., Pesaran, B., Buneo, C., Batista, A., Mitra, P., Burdick, J., & Andersen, R. (2003). Neural prosthetic control signals from plan activity. Neuro Report, 14(4). https://doi.org/https://doi.org/10.1097/00001756-200303240-00013
31. Kumar, N., & Michmizos, K. P. (2022). A neurophysiologically interpretable deep neural network predicts complex movement components from brain activity. Scientific Reports, 12(1). https://doi.org/10.1038/s41598-022-05079-0
32. Schwartz, A. B. (2004). Cortical neural prosthetics. Annual Review of Neuroscience, 27(1), 487–507. https://doi.org/10.1146/annurev.neuro.27.070203.144233
33. Kandel, E. R., Koester, J., Mack, S., & Siegelbaum, S. (2021). Principles of Neural Science. McGraw Hill.
34. Johnson, J. J., Breault, M. S., Sacre, P., Kerr, M. S., Johnson, M., Bulacio, J., Gonzalez-Martinez, J., Sarma, S. V., & Gale, J. T. (2017). The role of nonmotor brain regions during Human Motor Control. 2017 39th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), 2498–2501. https://doi.org/10.1109/embc.2017.8037364
35. Zohar, E., Kozak, S., Abeles, D., Shahar, M., & Censor, N. (2024). Convolutional neural networks uncover the dynamics of human visual memory representations over time. Cerebral Cortex, 34(11). https://doi.org/10.1093/cercor/bhae447
36. Randerath, J., Goldenberg, G., Spijkers, W., Li, Y., & Hermsdörfer, J. (2010). Different left brain regions are essential for grasping a tool compared with its subsequent use. NeuroImage, 53(1), 171–180. https://doi.org/10.1016/j.neuroimage.2010.06.038