

Distinct patterns of whole-body coding in human motor cortex and posterior parietal cortex

Highlights

- Single neurons in MC and PPC hand areas respond to movements of the whole body
- MC most strongly encodes the wrist and thumb; PPC encodes all effectors equally
- MC neurons prefer effectors within the same limb; PPC neurons mix effector preferences
- Directional tuning is shared across arbitrary effector pairs in PPC but not in MC

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In brief

Kadlec et al. record single neurons from two human brain regions long thought to control the hand and find that neurons in both areas respond to movements across the entire body. Overall effector specificity is observed in the motor cortex, while the parietal cortex represents every body part equally.

Article

Distinct patterns of whole-body coding in human motor cortex and posterior parietal cortex

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SUMMARY

Traditional views of cortical motor areas hold that movements of different parts of the body, or effectors, are represented in distinct anatomical locations. The extent of overlap in effector representations has been a topic of debate for decades. We recorded from single neurons in hand areas of the motor cortex (MC) and posterior parietal cortex (PPC) of tetraplegic humans while they attempted movements across the body. We found a population response to every movement tested in both areas; however, the hand knob of MC more selectively responded to hand movements, whereas PPC represented all effectors strongly. Single neurons in MC responded selectively to a single effector or to two effectors that were part of the same limb. In PPC, neurons exhibited mixed selectivity, responding to combinations of effectors. These findings suggest a transition from a highly effector-general representation in PPC to regional effector specificity in MC.

INTRODUCTION

Even simple movements rely on the recruitment of multiple brain areas. Understanding the functional organization of these brain areas is a classic problem in motor control. The fundamental question of how different brain regions contribute to the control of different parts of the body has provided a framework to understand how information is arranged on the cortical surface more generally. In the motor cortex (MC), results are summarized by the homunculus, an orderly representation of the body that is topographically arranged from head to toe, with this somatotopy being most rigid within the central sulcus and relaxing on the precentral gyrus toward the premotor cortex.^{1,2} In the posterior parietal cortex (PPC), results are summarized as distinct cortical regions responsible for the sensory-motor guidance of distinct effectors, such as the eyes in the lateral intraparietal area, the arm in the parietal reach region, and the hand in the anterior intraparietal area.^{3–7} However, several recent results challenge this conventional wisdom. In human MC, recent functional magnetic resonance imaging (fMRI), stereoelectroencephalography (sEEG), and intracortical recordings all show a degree of overlap in effector representations.^{8–11} Although the original topographic organization did include some overlap between neighboring effectors (e.g., the fingers¹²), the overlapping effectors in more recent findings are from head to toe. For example, single-neuron

recordings in humans from the hand knob of the precentral gyrus found a compositional code for both the hand and the entire body.¹¹ Additionally, coding for both the ipsilateral and contralateral arm/hand is found to overlap in a single hemisphere (and even within single neurons).^{13–16} In non-human primates (NHPs), long-train intracortical microstimulation (LT-ICMS) studies have revealed complex movements, suggesting that MC is organized ethologically around behaviorally relevant effectors rather than the classical homunculus.^{17–19}

In PPC, recent fMRI studies in humans show overlapping representations for effectors for similar types of movements, suggesting a functional organization of movement.^{20–23} Previously, we recorded from human PPC and found that certain variables like body part were mixed across single neurons, producing orthogonal population responses, whereas this was not the case for other variables like body side.^{24,25} We referred to this organization as partially mixed selectivity. Additionally, LT-ICMS of PPC in NHPs can evoke multi-effector movements supporting the hypothesis of functional organization.^{26,27} Further, single-neuron recordings in NHP superior parietal areas PEc and PE have revealed multi-effector representations, with neurons responding to movements of different body parts, including both upper and lower limbs.^{28–30}

These recent findings of overlapping effector representations across various brain regions raise the question of whether

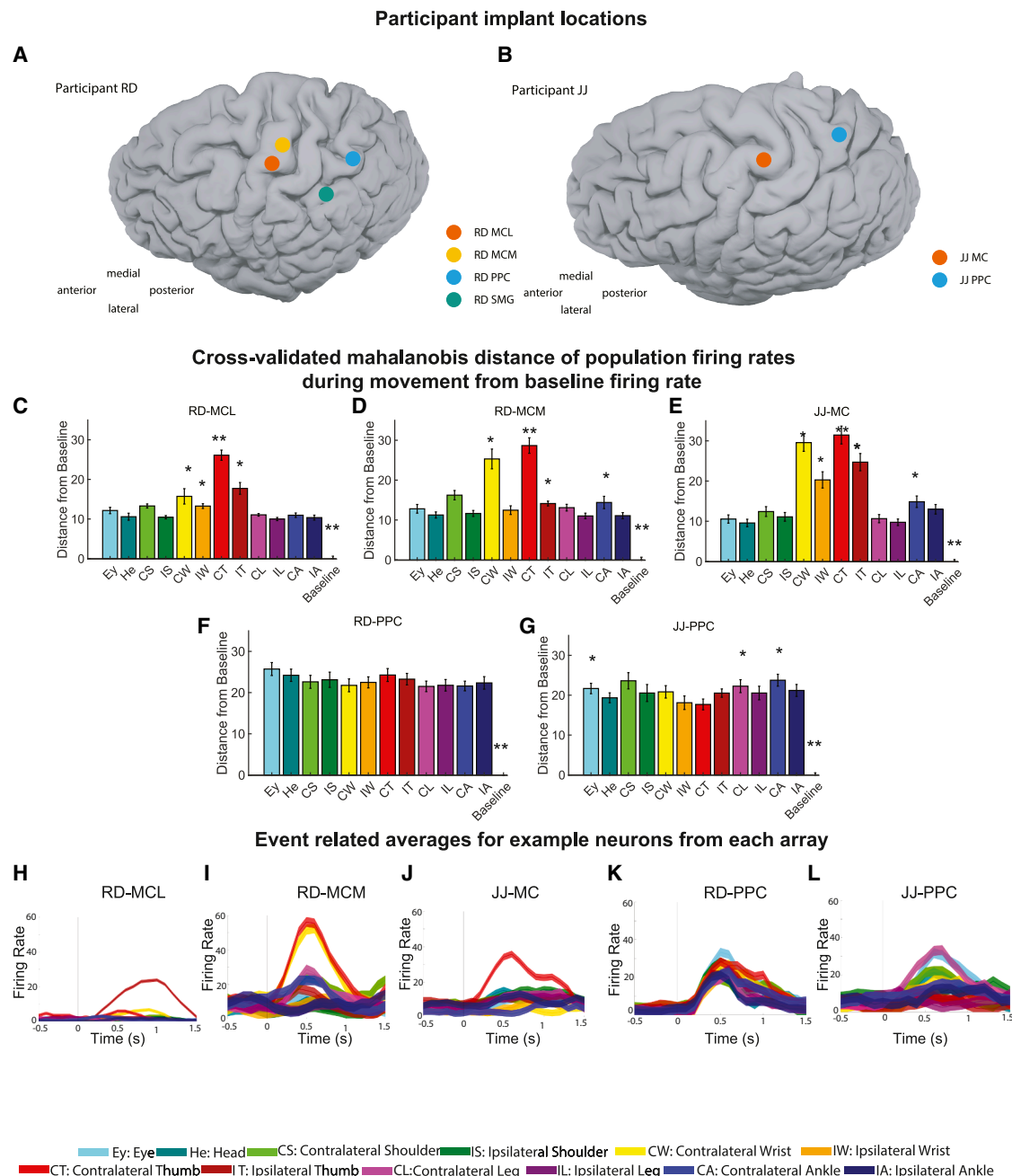


Figure 1. Whole-body coding with distinct population responses in MC and PPC

(A) RD implant locations: RD has two 64-channel Utah arrays located in the left hemisphere near the hand knob of the precentral gyrus. The array that is located more medially is referred to as RD-MCM, and the array that is more lateral is denoted RD-MCL. RD has another 64-channel array in the left hemisphere located slightly medial and posterior to the junction of the postcentral and intraparietal sulcus, denoted RD-PPC. A final 64-channel array in the left supramarginal gyrus, RD-SMG, was not included in results because only a small number of neurons recorded from this array were found to be directionally tuned.

(B) JJ implant locations: JJ has one 96-channel Utah array located in the left hemisphere near the hand knob of the precentral gyrus, denoted JJ-MC. Additionally, JJ has one 96-channel array in the left hemisphere that is located slightly medial and posterior to the junction of the postcentral and intraparietal sulcus, referred to as JJ-PPC.

(C–G) Cross-validated Mahalanobis distance of population firing rates sampled from a 500 ms window during movement execution and firing rates sampled from a 500 ms window during rest.

Error bars show the standard error of the mean. Significance was tested using a permutation test. Two stars indicate that the distance from baseline for that condition was significantly different from the distance from baseline for all other conditions. One star indicates that the distance from baseline for that condition

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different cortical areas encode movement and effectors in distinct or similar ways. Due to differences in tasks and participants in previous studies of whole-body encoding in MC and PPC, it is difficult to directly compare these studies. In this study, we had the unique opportunity to simultaneously record human PPC and MC single-neuron activity during attempted movements from head to foot in two participants. Examining these neural responses from each area in the same participant allows us to answer questions about how control of different effectors is organized in each area.

Despite targeting areas of both MC and PPC that have been classically associated with representing hand movements, we found neural responses to every part of the body; however, the pattern of this overlapping representation varied between the two brain regions. In MC, the population response for the wrist and thumb was two to three times stronger than other effectors. Most neurons were tuned to the contralateral hand, followed by the ipsilateral hand, with the fewest number of neurons being tuned to the proximal effectors. The population in PPC represented the whole body as well; however, unlike in MC, we found equivalent tuning strength across effectors. This population response was found to be driven by partially mixed selectivity within single-neuron responses, where each neuron was tuned to a mixed set of effectors. Interestingly, the structure of mixed effector and direction responses differed between the two arrays in PPC, indicating a gradient of spatial-to-effector coding within the superior parietal lobule (SPL).

We also sought to understand whether this overlap has functionally useful characteristics, for example, shared spatial information between effectors, which has been suggested to facilitate the transfer of learned motor skills from one limb to another. The extent to which information is shared is expected to vary between lower and higher cognitive areas, leading to a prediction that in MC, spatial coding would be shared between specific effectors, such as the left and right hand, while in PPC, arbitrary effectors would be able to share information.^{24,25} Our results confirm this prediction. These results point to clearly distinct organization of effector representations in MC and PPC and allow for a greater understanding of the different functional roles of each area and how each area contributes to motor control.

RESULTS

As part of an ongoing clinical study, two participants were implanted with microelectrode Utah arrays. Participant RD is tetraplegic (C3/C4) and was implanted with four 64-channel arrays in the left hemisphere: two in the hand knob of the precentral gyrus (RD-MCL and RD-MCM), one in the left SPL of PPC (RD-PPC),

and one in the supramarginal gyrus (see [methods](#) for exclusion rationale) ([Figure 1A](#)). Participant JJ is tetraplegic (C4/C5) and was implanted with two 96-channel arrays in the left hemisphere, one in the hand knob of the precentral gyrus (JJ-MC) and the other in SPL (JJ-PPC, [Figure 1B](#)). Implant locations within each brain area were selected by finding the regions of peak activation in response to the participants performing grasping imagery for hand and arm movements during functional magnetic resonance imaging (see [Table S1](#) for Montreal Neurological Institute (MNI) coordinates, Guan et al.³¹ for localization task details).

We asked the participants to attempt to move twelve effectors in five directions using a center-out paradigm where the effector to be moved was instructed on the screen ([Figure S1](#)). For each movement, the direction was indicated by one of five targets changing color from gray to red. A 1.5 s inter-trial interval (ITI) followed each movement during which the participant was at rest. Array recordings were made simultaneously as the participants attempted movements of the eyes, head, contralateral/ipsilateral shoulder, wrist, thumb, leg, and ankle. For both participants, attempted movements of the eyes, head, and shoulders resulted in overt movements of that effector. Attempted movements of the wrists, thumbs, legs, and ankles did not result in overt movement. Recorded signals were spike sorted before analysis (see [Table S2](#) for array neuron counts).

Overlapping whole-body representations with differing population preferences in MC and PPC

Is there an effector-specific movement code implemented in MC or PPC? We examined the population responses for effector preferences. The strength of representation across the body was determined by finding the cross-validated distance between population firing rates during movements for each condition (effector-direction pairing) and firing rates during rest (during the ITI). In both participants, both MC and PPC showed population responses that were distinct from the baseline for all 12 effectors ([Figures 1C–1G](#), permutation test, $p < 0.05$ for MC and PPC); however, the relative strengths of these representations across effectors were different between the two brain areas.

In RD-MCL, RD-MCM, and JJ-MC, the contralateral thumb was significantly more strongly encoded than other effectors (aside from the contralateral wrist in RD-MCM and JJ-MC, permutation test, $p < 0.05$) ([Figures 1C–1E](#)). In RD-MCL the next strongest response was to the ipsilateral thumb, and in RD-MCM it was to the contralateral wrist ([Figures 1C and 1D](#)). In JJ-MC, the contralateral wrist, ipsilateral thumb, and ipsilateral wrist all evoked responses stronger than any of the non-hand effectors ([Figure 1E](#); permutation test, $p < 0.05$). By contrast, the population responses from both RD-PPC and JJ-PPC generally did not show significant coding strength differences between

was significantly different from that for select other conditions listed below. $p < 0.05$. (C) Results for RD-MCL. CT > all; IT > EY, HE, CS, IS, IW, CL, IL, CA, IA, CW; CW > HE, IS, CL, IL, IA; IW > HE, IS, CL, IL, IA; CS > HE, IS, CL, IL, CA, IA.

(D) RD-MCM. CT > all; CW > EY, HE, CS, IS, IW, IT, CL, IL, CA, IA; CS > HE, IS, IW, CL, IL, IA; IT > HE, IS, IL, IA; CA > IL.

(E) JJ-MC. CT > all; CW > EY, HE, CS, IS, IW, IT, CL, IL, CA, IA; IT > EY, HE, CS, IS, CL, IL, CA, IA; IW > EY, HE, CS, IS, CL, IL, CA, IA; CA > EY, HE, IS, IL.

(F) RD-PPC. No significant differences other than all conditions from baseline.

(G) JJ-PPC. CA > IW, CT; CS > CT.

(H–L) Event-related averages for an example neuron from each array. Neurons selected are representative of the population. Colors show responses to different effectors. Mean and 95% confidence intervals are shown. (H) RD-MCL, (I) RD-MCM, (J) JJ-MC, (K) RD-PPC, and (L) JJ-PPC.

effectors (exceptions noted in the figure caption, permutation test, $p > 0.05$) (Figures 1F and 1G).

To help qualitatively understand the population results, we visualized exemplar single-neuron firing rates during each neuron's preferred direction, grouped by effector. In the single-neuron examples for RD-MCL, RD-MCM, and JJ-MC, the neurons respond strongly to the contralateral thumb, followed by the ipsilateral thumb and contralateral wrist (Figures 1H–1J). In the single-neuron examples for RD-PPC and JJ-PPC, the neurons respond to one, two, several, and even all effectors. The chosen examples show a neuron in RD-PPC that is tuned across all twelve effectors and one in JJ-PPC that is tuned to half of the effectors (Figures 1K and 1L, more examples in Figure S2).

Next, we sought to understand the relationship between effector representations within the population by examining neural distance between pairs of effectors. In the MC arrays, this further emphasized the population effector preference, with small distances between most effectors except the contralateral wrist and thumb (and ipsilateral in JJ-MC) (Figures S3A–S3C). In PPC, results differed between the two arrays. In RD-PPC, distances between effectors are smaller than distances between effectors and baseline. However, in JJ-PPC we observed similar distances between each effector as those observed between effector movement and baseline (Figures S3D and S3E, baseline distances shown in Figures 1C–1G). To address how these distances might map to anatomically relevant effector groupings, we compared the distances between (1) effectors on the same side of the body and those on opposite sides, (2) effectors within the same limb or not, (3) matched bilateral effector pairs and non-matched pairs, and (4) within proximal, within distal, and across proximal-distal pairs. This revealed that in both RD-PPC and JJ-PPC, there were significantly smaller distances between effectors on the same side of the body than those on opposing sides. Interestingly, in JJ-PPC there were also smaller distances between pairs of the same effector on opposing sides compared with non-same pairs (e.g., contralateral and ipsilateral wrist), hinting at an underlying structure of mixed single-neuron selectivity.

To directly evaluate how the patterns of effector distances observed compared with the patterns expected for anatomical distance between effectors, we simulated a distance matrix based on body topography and anatomically guided principles (e.g., somatotopy, laterality, and single effector coding; see Figure S4). We then performed a Mantel test to determine the correlation between our observed distance matrices from each array and those we simulated. The distance matrices from the MC arrays were statistically most similar to a distance matrix for a hand-centered somatotopy, although with notably low explained variance and weak effect size ($p < 0.05$; Figures S4B–S4D). None of the anatomical organization schemes tested were statistical matches for PPC (Figures S4E and S4F).

This distinction between RD-PPC and JJ-PPC motivated us to compare the population structure in two additional ways. First, we examined how distances between effectors compared with distances between movement directions. This revealed similar distances between directions compared with effectors within both RD-PPC and JJ-PPC (Figures 2A and 2B). Next, we trained a classifier using linear discriminant analysis on the effector and

direction labels and found the cross-validated accuracy for each variable. This further illustrated the differences in effector representations between the two arrays, with poorer effector classification in RD-PPC compared with JJ-PPC (26% vs. 70%, chance $\approx 8\%$, Figures 2C and 2D). In RD-PPC the highest accuracy was found for the eyes and head, followed by the thumbs, with the legs and ankles demonstrating the lowest accuracy and greatest confusion. In JJ-PPC, the most common confusion was between bilateral pairs of the same effector, followed by confusion between the wrists and ankles within a side of the body and the legs and ankles across body sides. By contrast, direction classification accuracy was highest in RD-PPC (96%), although still well above chance in JJ-PPC (85%, chance = 20%, Figures 2E and 2F).

Single neurons respond to multiple effectors in both the MC and PPC with distinct patterns of overlap

We next sought to better understand the neural architecture that supports coding for multiple body parts in each area. Here, we focus on two aspects of functional organization at the single-neuron level. First, was there evidence for a systematic relationship between different effectors, e.g., if the preferred effector is the contralateral wrist, is it more likely that the neuron is tuned to the ipsilateral wrist? Second, if a neuron is tuned to multiple effectors, are the spatial tuning preferences similar?

We calculated the directional modulation strength of single-neuron firing rates during movements of each effector. The strength was determined by subtracting a neuron's firing rate in its worst direction (lowest firing rate) from the firing rate in its best direction (highest firing rate). Only neurons that were significantly directionally tuned to at least one effector were included in the results (shuffle test, $p < 0.05$). First, we found each neuron's most preferred effector, or the effector that resulted in the strongest modulation of that neuron's firing rate (Figures 3A–3E). In each of the three MC arrays, around 40% of units preferred the contralateral thumb, in line with the population results (Figures 3A–3C, RD-MCL: 53%, RD-MCM: 40%, JJ-MC: 38%). We explored how these effector preferences mapped onto the channels of each array in order to evaluate potential somatotopy within the array (Figure S5). We performed autocorrelation analysis (Moran's I and join count) on the channel effector preferences to identify any spatial organization. This revealed no significant spatial clustering for any effector. However, both contralateral and ipsilateral wrists showed marginally significant Moran's I value on the JJ-MC array ($p < 0.05$, uncorrected), consistent with a loose spatial concentration of wrist-tuned channels that did not form tight adjacent clusters.

In the PPC arrays, neural preferences were spread across effectors, with between 4% and 18% of neurons best tuned to each effector (Figures 3D and 3E). In both arrays the eyes stand out as being slightly more preferred than other effectors, and likewise for the contralateral ankle in JJ-PPC; however, this is only a significant difference for a few of the conditions (one-way ANOVA, $p < 0.05$). We mapped the effector preferences across the PPC arrays as we did for MC. Both visual inspection and autocorrelation analysis reveal no clear pattern in effector organization (Figure S5).

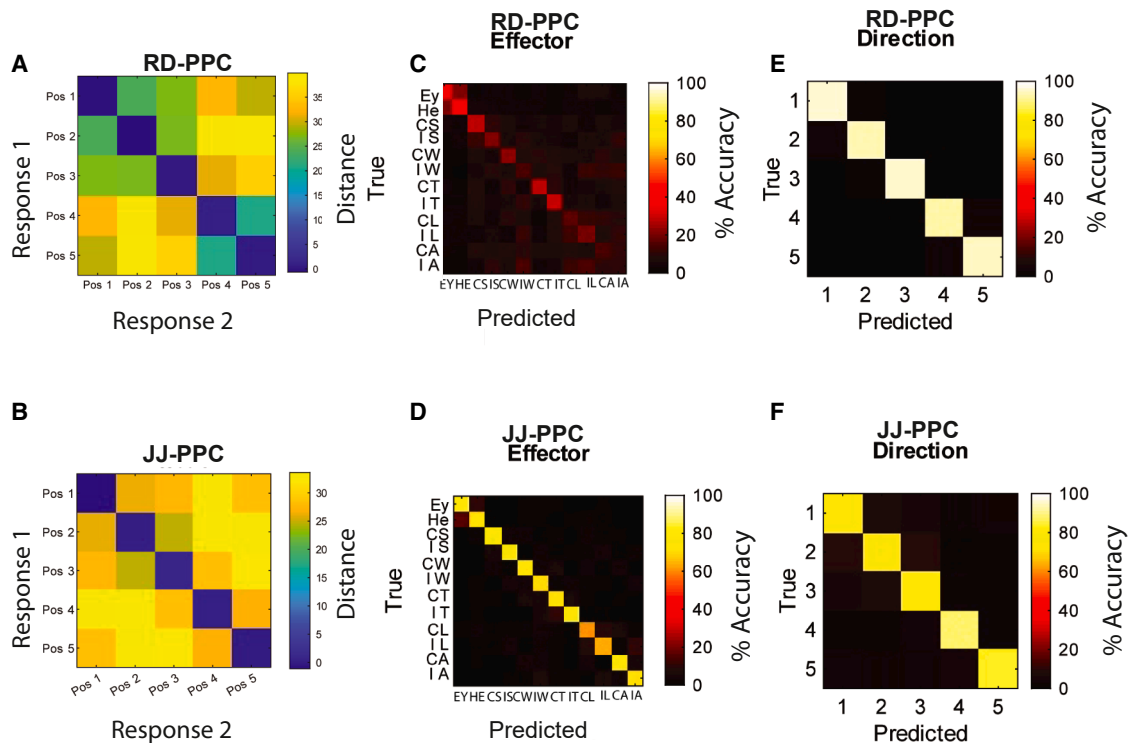


Figure 2. Effector, not direction, discriminability differs between PPC arrays

(A and B) Cross-validated Mahalanobis distance matrices between the five movement directions (Pos 1–5) for each PPC array (A, RD-PPC; B, JJ-PPC). Warmer colors indicate greater distances between direction representations.

(C–F) Cross-validated linear discriminant analysis (LDA) classification confusion matrices for effector identity (12-class, left) and movement direction (5-class, right) in RD-PPC (C and E) and JJ-PPC (D and F). Warmer colors along the diagonal indicate higher classification accuracy.

(C) Effector classification accuracy was 26% in RD-PPC, with the highest accuracy found for the eyes and head, followed by the thumbs, with the legs and ankles demonstrating the lowest accuracy and greatest confusion.

(D) Effector classification accuracy was 70% in JJ-PPC. The most common confusion was between bilateral pairs of the same effector, followed by confusion between the wrists and ankles within a side of the body.

(E) Direction classification accuracy was highest in RD-PPC (96%).

(F) 85% direction classification accuracy in JJ-PPC (chance = 20%). Confusion matrices were averaged across sessions.

Next, we examined how the strengths computed for each neuron compared across all twelve effectors. The normalized strength of each neuron's response is plotted with neurons sorted by two characteristics: their most preferred effector (from eyes to ankle) and the number of other effectors tuned (shuffle test, $p < 0.05$; Figures 3F–3J). To ensure these effects were truly driven by single neurons, we applied a stricter criterion for spike quality to rule out any potential signals from multi-unit activity and found the same pattern of results (Figure S6). The qualitative difference for MC and PPC is notable. To better understand the tuning of a single neuron across different effectors, we separated the neurons by their most preferred effector and then summarized what other effectors those neurons were tuned to in pie charts (Figures 3K–3O and S7). As shown in Figures 3D and 3E, there are a similar number of neurons that prefer each effector in PPC, but in MC there are very few neurons that prefer an effector other than the contralateral thumb or wrist ($n < 10$). Thus, to compare single-neuron tuning across effectors using a similar number of neurons recorded from arrays in both MC and PPC, the pie charts for neurons that most preferred the

contralateral wrist and thumb are shown (Figures 3K–3O, pie charts for other effectors Figure S7).

In all three arrays in MC, most neurons are tuned to one effector, and a smaller portion of single neurons are tuned to multiple effectors (Figures 3F–3H and S8A–S8C). In the RD-MCL and RD-MCM arrays, less than 10% of neurons are tuned to multiple effectors (Figures S8A and S8B). In RD-MCL only a single neuron that preferred the contralateral thumb was tuned to another effector (contralateral shoulder) (Figure 3K). There were only 5 total neurons that preferred the contralateral wrist in RD-MCL, with one of these neurons also coding for the contralateral shoulder and another for the contralateral thumb. In RD-MCM, less than 10% of neurons that prefer the contralateral thumb were tuned to additional effectors, and this included the ipsilateral thumb and contralateral wrist (Figure 3L). In RD-MCM, only six neurons that preferred the contralateral wrist were tuned to other effectors, and two of these were tuned to the contralateral thumb (Figure 3L).

In JJ-MC, the most apparent effector overlap for single neurons is between corresponding ipsilateral and contralateral effectors, in

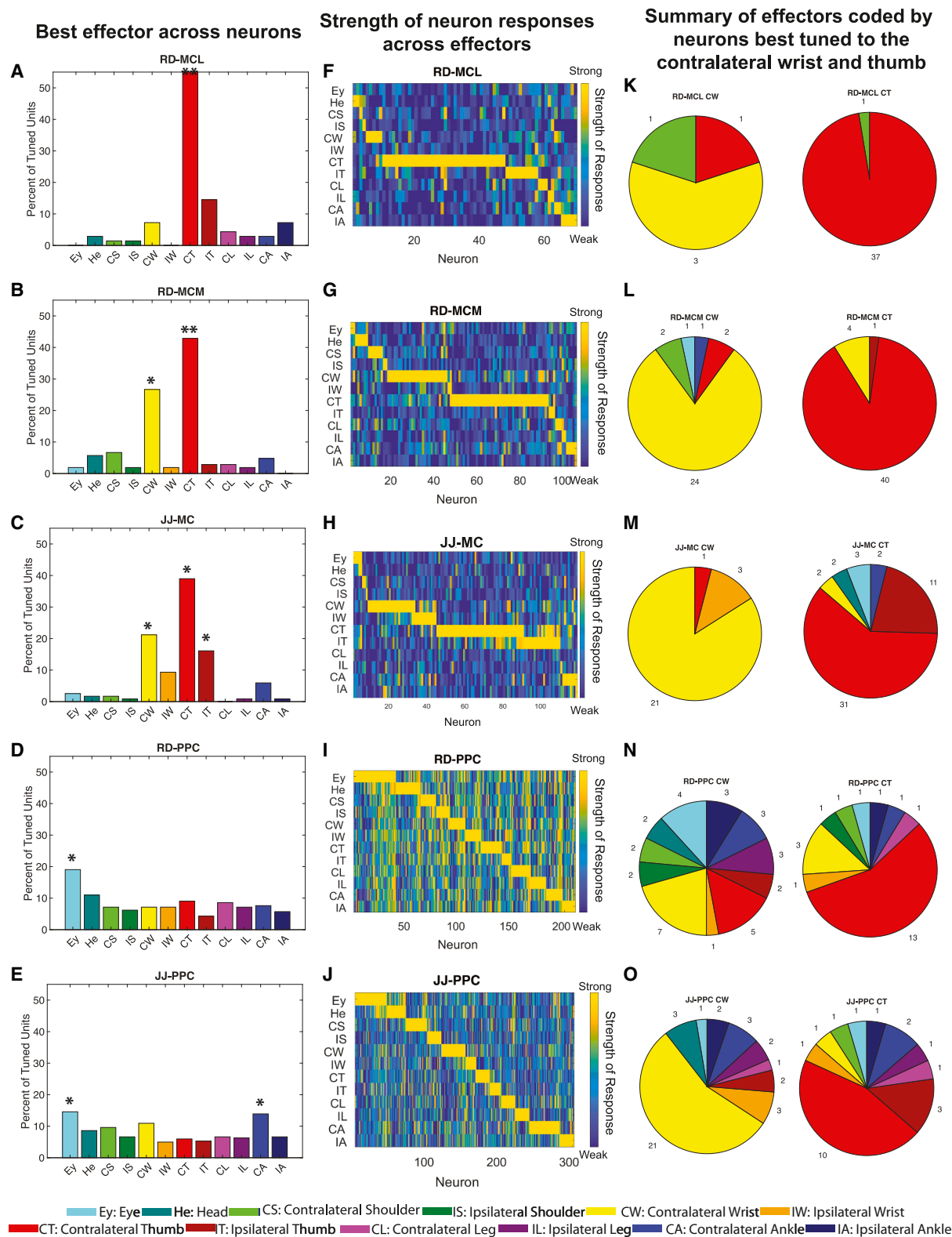


Figure 3. Single-neuron responses show distinct patterns of overlapping representations across effectors in MC and PPC

(A–O) The strength of single-neuron responses across effectors was found by determining each neuron's best-tuned direction and worst-tuned direction and then subtracting the firing rate during movements in the worst from the best for each condition. (A–E) The best effector for each neuron was the effector that evoked the

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particular the wrist and thumb (Figures 3H and 3M). Around 40% of the neurons that were best tuned to the contralateral thumb were tuned to additional effectors. Of these, just under 50% are tuned to the ipsilateral thumb. Two of the three neurons that prefer the contralateral wrist and are tuned to multiple effectors are tuned to the ipsilateral wrist, with the third neuron tuned to the contralateral thumb (Figure 3M). Overall, across all MC arrays, tuning across multiple effectors by a single neuron was largely restricted within a single limb with few exceptions.

In both RD-PPC and JJ-PPC, a large portion of neurons are tuned to multiple effectors (Figures 3I, 3J, S8D, and S8E, 49% in RD-PPC, 35% in JJ-PPC). Additionally, there is no single rule that describes the relationship between the effectors to which a single neuron in PPC is tuned. Rather, neurons exhibit mixed selectivity for combinations of effectors. This includes neurons that are selective for clear anatomical features like body side or body part and others for which an anatomical description is less tangible (e.g., contralateral shoulder and ipsilateral ankle). In both RD-PPC and JJ-PPC, neurons that preferred either the contralateral wrist or contralateral thumb were tuned to the full range of effectors from head to ankle (Figures 3N and 3O; Figure S7 shows the same pattern across all effectors, and Figure S9 shows well-isolated neurons). Comparing the strength of single-neuron responses across all effectors in each brain area, we found a trend toward stronger representation across all effectors in PPC than MC (Figure S10).

Next, we compared the directional tuning properties of neurons across effectors. We asked whether single neurons used the same spatial code for different effectors. We found the linear regression coefficients for each neuron and used those coefficients to determine the angle between the directions coded in the response for each effector (see Figure S11 for radial tuning plots). An angle of zero implies that the neuron used the same directional tuning across effectors. This comparison was done for the most and second-most preferred effector for each neuron (determined using the criterion from Figures 3A–3E). Few neurons from RD-MCL and RD-MCM were tuned to more than one effector, meaning no strong claims can be made about the directional tuning of these neurons (Figures 4A and 4B, $n = 6$ for RD-MCL and $n = 13$ for RD-MCM). In JJ-MC, RD-PPC, and JJ-PPC, we found most neurons are tuned to the same direction across effectors, meaning zero angle of difference (Rayleigh test for uniformity, $p < 0.05$; circular mean JJ-MC = -8.8° , RD-PPC = -1.0° , JJ-PPC = -3.2° ; Figures 4C–4E). Figure S12 shows the mean angle of difference for individual effector pairs in each array.

Finally, we asked what reference frame neurons used to encode direction. Spatial information can be represented intrinsically, relative to the location of our body and joints, or extrinsically, relative to location in the external world. Here, we leveraged the fact extrinsic vs. intrinsic coordinates are naturally dissociated between the left and right sides of the body (see Figures 5A and 5B for examples). We compared the linear regression coefficients found above for ipsilateral and contralateral pairs of effectors to determine the reference frame used by each neuron. Again, in RD-MCL and RD-MCM, there were too few neurons to determine the reference frame this way ($n \leq 2$). In JJ-MC, there was a significant negative correlation between the coefficients for pairs of contralateral and ipsilateral effectors, demonstrating an intrinsic reference frame (Figure 5C, Pearson correlation = -0.75 , $p < 0.001$). By contrast, RD-PPC shows a positive correlation between contralateral and ipsilateral coefficients, suggesting an extrinsic reference frame (Figure 5D, Pearson correlation, $r = 0.94$, $p < 0.001$). Finally, in JJ-PPC there was no trend toward a positive or negative relationship, implying a mixture of both intrinsic and extrinsic reference frames (Figure 5E, Pearson correlation, $r = -0.10$, $p = 0.6$).

Spatial coding transfers between specific effectors in MC and all effectors in PPC

How might MC and PPC be using these overlapping effector representations? One possible explanation discussed in motor literature is that this provides a shared architecture through which learned motor skills can be transferred across limbs.^{11,24,32} At the level of effector preference, we report clear distinctions between representations in MC and PPC. While these differences in the structure and extent of overlap in effector representation give some intuition, they do not answer the question of how efficiently information can be shared across effectors in either area. We call the extent to which information is shared between effectors the transfer efficiency. If the neural code has high transfer efficiency across effectors, information is shared between two effectors regardless of their location on the body or function in movement. Another possibility is that high transfer efficiency only exists between specific effectors, for example, effectors that are more likely to be moved together, such as the contralateral wrist and the contralateral thumb, or the contralateral and ipsilateral wrist for bimanual tasks.

To assess how information was shared across effectors in MC and PPC, we trained a partial least squares linear regression (PLSR) model to find a directional coding subspace that was shared for two effectors and not the rest (Figure 6A). In other

strongest response or had the greatest difference in firing rates. Conditions are along the x axis, and the y axis is the percent of neurons. A one-way ANOVA was used to test for significant differences between the number of neurons best tuned to each effector. Two stars indicate that there were significantly more neurons best tuned to that effector than all other effectors. One star indicates that there were significantly more neurons best tuned to that effector than neurons best tuned to specific other effectors listed below. $p < 0.05$.

(A) RD-MCL: CT > all.

(B) RD-MCM: CT > all; CW > all but CT.

(C) JJ-MC: CT > EY, HE, CS, IS, IW, CL, IL, CA, IA; CW > EY, HE, CS, IS, CL, IL, IA; IT > EY, HE, CS, IS, CL, IL, IA.

(D) RD-PPC: EY > all but HE.

(E) JJ-PPC: EY > IS, IW, IT, CT; CA > IS, IW, CT, IT, IL.

(F–J) The strength of a neuron's response, with neurons sorted by their best effector and then by the number of effectors they coded. The strength of neural responses was normalized to the strongest response from each array. Each column shows a single neuron's response across all 12 effectors.

(K–O) Breakdown of effectors coded by neurons best tuned to the contralateral wrist (left) and the contralateral thumb (right).

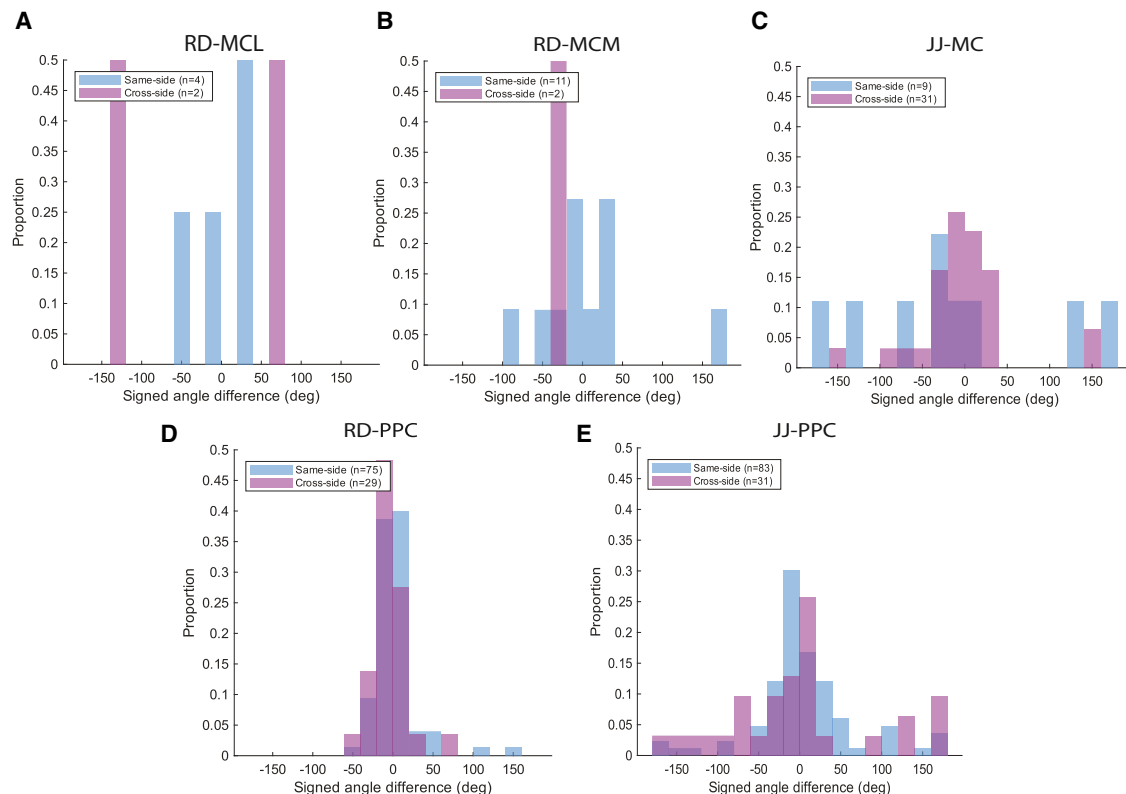


Figure 4. Preserved directional tuning across effectors within single neurons

(A–E) The angle between the direction vectors coded for the most preferred and second most preferred effector of single neurons. Pairs on the same side of the body are shown in blue; opposite body-side effector pairs are shown in purple.

(A) RD-MCL circular mean (cm) = 2.5°. Rayleigh test for uniformity $p < 0.05$.

(B) RD-MCM cm = -11.7°. Rayleigh test for uniformity $p < 0.05$.

(C) JJ-MC cm = -8.8°. Rayleigh test for uniformity $p < 0.05$.

(D) RD-PPC cm = -1.0°. Rayleigh test for uniformity $p < 0.05$.

(E) JJ-PPC cm = -3.2°. Rayleigh test for uniformity $p < 0.05$.

words, we looked for a subspace where the spatial code was approximately the same for two effectors but distinct from other effectors. This was done for the 66 possible pairings of effectors. To evaluate the transfer efficiency of information between these effector pairs, we found the correlation matrix for actual vs. model-predicted position. Pairs with high transfer efficiency will have high R^2 values, and the average R^2 across pairs gives a sense of the population's overall transfer efficiency. To determine significance, this R^2 value was compared with a null distribution of R^2 values that was generated for each pair by shuffling the firing rates for trials with one effector to mimic a population where no information is shared between effectors. Finally, to evaluate how distinct this spatial representation was from that used by other effector pairs, we computed the principal angles between direction vectors for each pair of effectors and those for other pairs of effectors. We found that only specific pairs of effectors significantly share directional coding in MC (Figures 6B–6D). In RD-MCL and RD-MCM, the highest transfer efficiency between two effectors was between the contralateral thumb and wrist, and in JJ-MC, for the contralateral and ipsilateral thumbs. The fewest pairs were found to share information in

RD-MCL, with only three effector pairs sharing spatial information. In RD-MCM, the contralateral thumb shares information with most contralateral effectors, and most contralateral effectors share with each other (with a few exceptions). In JJ-MC, the contralateral wrist, thumb, and ankle shared information with each other and with their ipsilateral counterparts. The shared information between the thumb and other hand effectors was somewhat expected based on the other results seen in MC thus far, but finding the ankle also shared with other effectors was more surprising. Previous work has shown that certain motor skills like writing can be transferred from the hands to the feet. Perhaps this shared spatial information reflects the functional organization that has also been reported alongside somatotopy in MC.¹⁰ The interpretation of this finding will be expanded on further in the discussion.

In RD-PPC and JJ-PPC, shared directional coding is found for every set of effectors (Figures 6E and 6F). All effector pairs seem to share information relatively equally, especially in RD-PPC. Although significant sharing is found for all pairs in JJ-PPC as well, more variation is noticeable across pairs. This could be a result of the mixed intrinsic and extrinsic reference frames

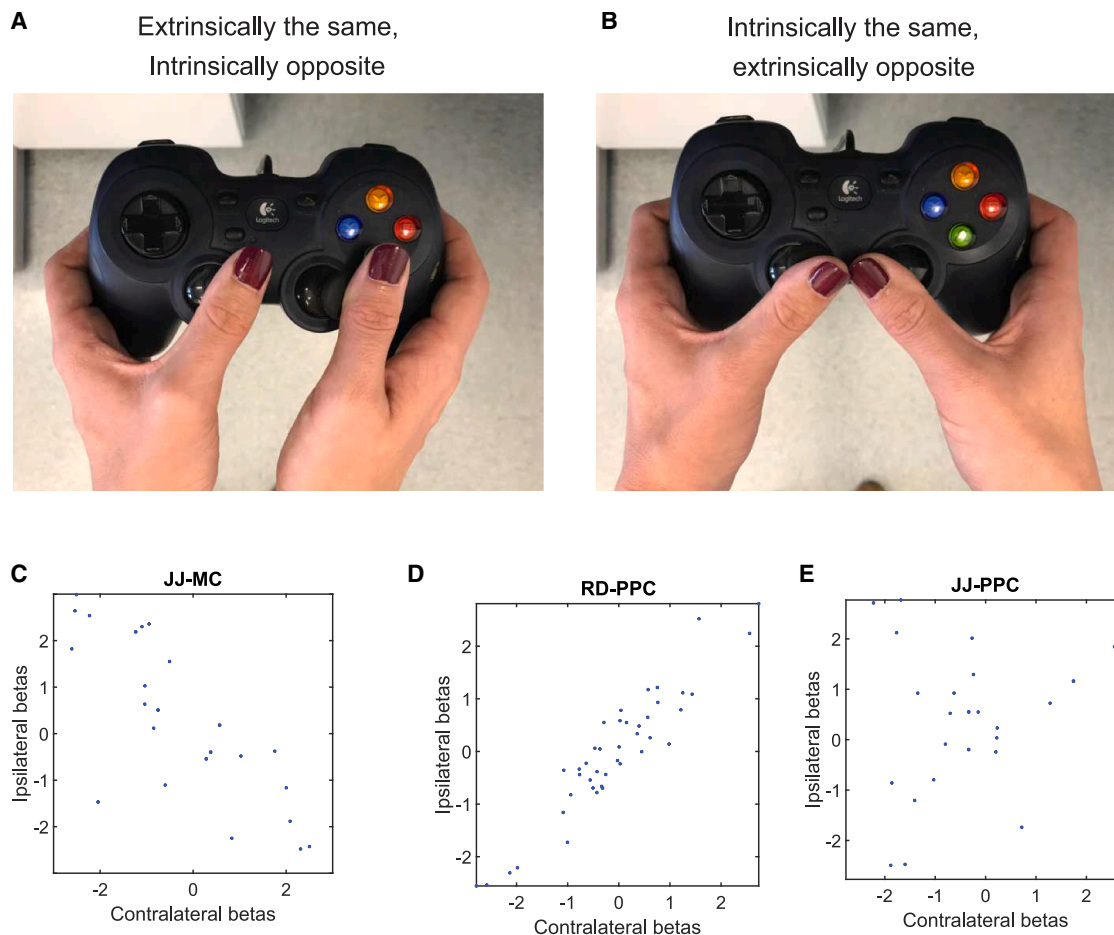


Figure 5. Extrinsic vs. intrinsic reference frames

(A) An example of thumb movements that are both extrinsically in the same direction, to the right, but require movements in opposite directions relative to the joint of the thumb or intrinsically opposite directions.

(B) An example of movements that are in extrinsically opposite directions (ipsilateral thumb to the right, contralateral thumb to the left); they require movement in the same direction relative to the thumb joint and are intrinsically the same.

(C–E) The resulting betas for linear regressions for contralateral and ipsilateral pairs of effectors.

(C) JJ-MC $r = -0.75$, $p < 0.001$.

(D) RD-PPC $r = 0.94$, $p < 0.001$.

(E) JJ-PPC shows no correlation.

used, which were not fully accounted for in this analysis. The two arrays also differed in how distinct the spatial codes for individual effector pairs were from one another, with greater separation between direction subspaces in JJ-PPC compared with RD-PPC (Figure S13). Principal angle analysis shows near-orthogonality in JJ-PPC direction coding between most effector pairs, highlighting the complexity of its neural response space.

DISCUSSION

We found that the entire body is represented within small patches of hand areas in human MC and PPC. These results add to the growing body of work that illustrates a more complex organization of motor areas than initially expected.^{8,9,11,20,24} Importantly, we found clear differences in the structure of these representations in each area. In MC, single neurons showed

effector-specific coding dominated by the contralateral hand, with multi-effector tuning largely confined within a limb and an intrinsic (body-centered) reference frame. In PPC, neurons exhibited mixed selectivity across combinations of effectors. These patterns align with and extend previous notions of distinct functional organization within low- and high-level motor areas.

MC

In the lower-level MC, we found a clear dominant effector, the contralateral thumb. In addition, the pattern of overlapping effector representations seen also fits with a broader somatotopic organization. For example, the prominent population response to the contralateral wrist supports a gradual transition between coding for neighboring parts of the body. Further, neurons tuned to the contralateral thumb were more likely to be tuned to the contralateral wrist than most other effectors.

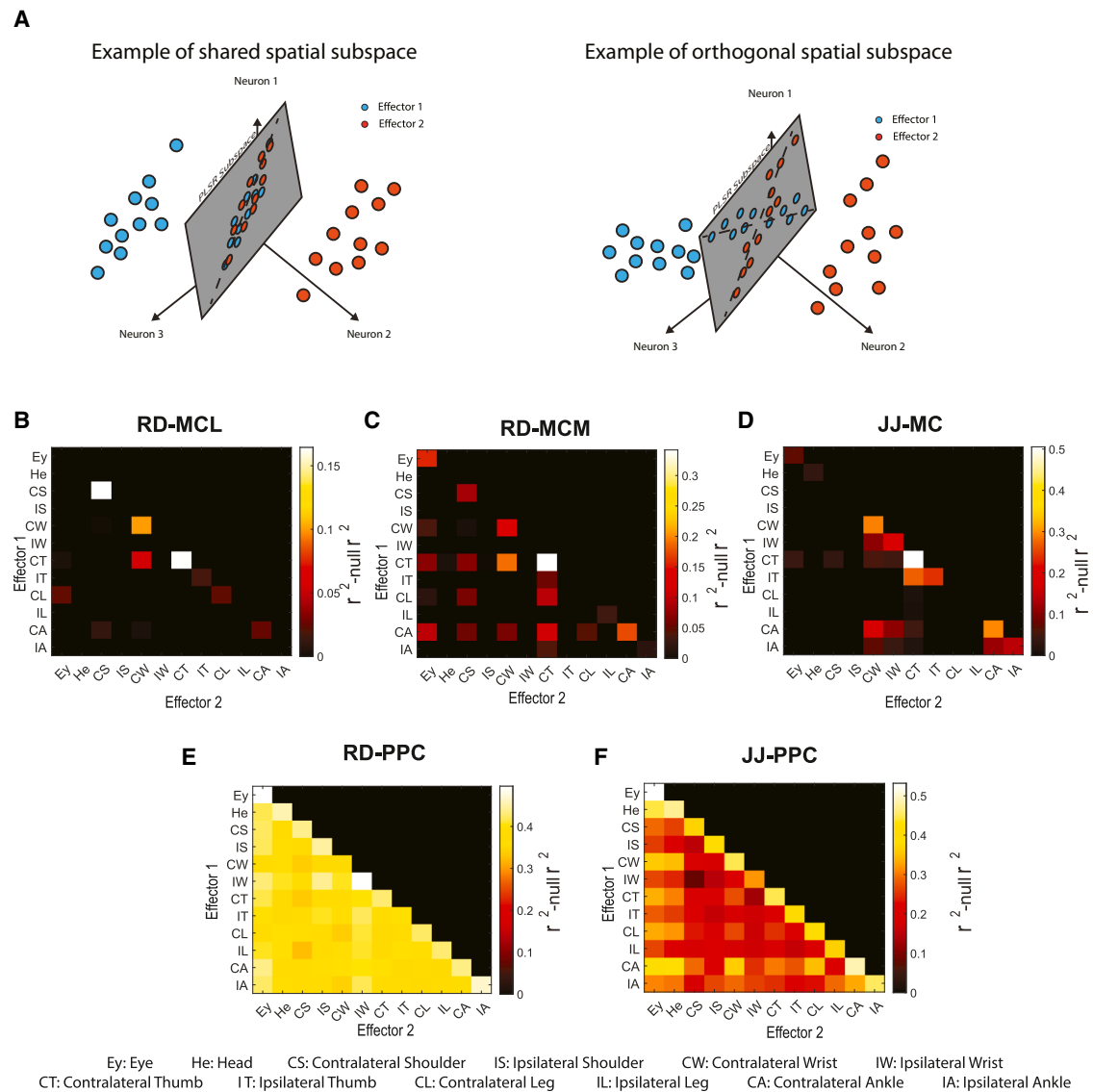


Figure 6. Evaluating shared information between effectors

A PLSR model was trained using firing rates from all neurons and position information for two effectors for each possible pairing of effectors. The positions predicted by the model were then correlated with the original input position values to determine whether spatial information had been shared between the two effectors. This same process was done for a matrix of shuffled firing rates to obtain a null distribution to compare these models' performances with for significance.

(A) Schematic showing how the PLSR model identifies shared (left) vs. orthogonal (right) spatial coding subspaces between neurons. The gray plane is the subspace identified by the model.

(B–F) Performance of models trained for each effector pair. The x and y axes are the two effectors used in the pair. The diagonal is made up of a single effector rather than a pair of effectors. The threshold for significance determined by the null r^2 distribution is marked on the color bar. Only the lower triangle is shown because the matrices are symmetric. (B) RD-MCL, (C) RD-MCM, (D) JJ-MC, (E) RD-PPC, and (F) JJ-PPC.

Another pattern that emerged in both population and single-neuron preferences was overlapping representation of the contralateral and ipsilateral sides for both the wrist and thumb. Although this strays somewhat from a classic somatotopic view, coding for both sides of the body has also been reported in NHPs.^{13–16} More work on bimanual coordination is needed to further understand the role of ipsilateral hand representations in both NHPs and humans.

An important consideration is the precise location of our recording sites. Our arrays were placed on the crown of the precentral gyrus at the hand knob, a region that likely includes premotor cortex (area 6) in addition to primary MC (area 4a).^{33,34} Effector representations are known to be more inter-mixed in the premotor cortex than in the primary MC.^{11,19} Recent fMRI work reveals a further possible explanation for the overlap in effector representations we observe. Gordon

et al.⁸ described a somato-cognitive action network (SCAN) with inter-effector zones that alternate with effector-specific regions across the precentral gyrus. Our MC arrays may overlap with these inter-effector zones, which could contribute to the whole-body responses we observe. Overall, our recordings show a clear dominant preference for the contralateral hand, consistent with the classical hand knob identity, and multi-effector tuning by individual neurons remained largely constrained within a single limb.

Examination of the spatial layout of effector preferences across electrode positions within an array revealed hints of somatotopic organization in MC (Figure S5), with some clustering of wrist-preferring neurons on the medial array in RD and on a portion of the JJ-MC array. While these observations are consistent with local somatotopic structure, the small spatial extent of each array (4×4 mm) limits the conclusions that can be drawn about large-scale topographic organization. Our results suggest that despite complexity at the level of single-neuron responses, MC still follows a broadly somatotopic organization where different parts of the body are emphasized in different cortical locations. These findings do not rule out the possibility of other parts of MC demonstrating more functional organization, as fMRI work suggests that some locations within MC show more anatomically specialized representations than others.^{8,10}

PPC

In higher-level PPC, we observed an equal strength in representation across effectors, although not to the extent of an effector-agnostic representation. Initial work in PPC of NHPs established separate anatomical patches for coding eye, hand, and arm movements; however, subsequent single-neuron recordings in areas PEc and PE revealed multi-effector representations that challenge this strict segregation.^{28–30,35,36} In more recent fMRI work in humans, such effector-specific regions have remained elusive.^{37–39} Further, studies that compare hand and foot movements report areas in PPC that are activated equivalently by both movements.^{20,23} Overlap between effectors has also been found in single neurons, where previous recordings in human PPC from our lab found the contralateral and ipsilateral hand and shoulder encoded in the same, small patch of cortex.²⁴ The present findings tie these results together and reveal an important insight about the initial interpretation from fMRI studies. Instead of a purely effector or functional organization within PPC, when recording from the single-neuron level, we found that individual effectors are mixed. This ultimately results in an equal strength of coding across effectors within the population, which appears as an effector-agnostic population code when observed with the spatial resolution of fMRI. Importantly, the degree to which individual effectors are discriminable from the population varied between our two PPC arrays, with the more anterior JJ-PPC showing substantially higher effector classification accuracy than RD-PPC (70% vs. 26%).

An unexpected finding of this study is that the two PPC arrays, while both located in the SPL, exhibited meaningfully different coding properties. In RD-PPC, effector classification accuracy was relatively low, the between-effector Mahalanobis distances were smaller than effector-vs-baseline distances, and the reference frame was predominantly extrinsic (world-centered). This

pattern suggests that RD-PPC primarily encodes the spatial goal of movement in an extrinsic reference frame, with relatively weak modulation by effector identity. By contrast, JJ-PPC showed substantially higher effector classification accuracy, larger between-effector distances that approached the magnitude of effector-vs-baseline distances, and a mixed intrinsic/extrinsic reference frame.

These differences between RD-PPC and JJ-PPC are likely attributable to the precise cortical location of each array along a gradient of reference frame coding in PPC, from more extrinsic in posterior SPL to more intrinsic toward motor areas (MNI coordinates reported in Table S1). Notably, the same pre-surgical fMRI localizer, a grasping imagery task, was used to target the implant locations within cortical patches preferentially involved in hand movements.³¹ Critically, these results caution against treating PPC as a homogeneous region and suggest that even small differences in implant location can meaningfully influence the balance of effector vs. spatial coding observed. In particular, our results are consistent with a transition from a spatial code that is effector modulated in posterior SPL to distinguishable codes for both direction and effector as one moves anteriorly. More evidence is needed to fully disentangle true cortical architecture from individual differences.

Shared spatial subspaces

What is the functional purpose of the overlapping effector representations seen in each area? In motor literature, it has been suggested that this could facilitate the transfer of motor skills from one limb to another.^{11,24} Transfer of motor skills can occur between limbs in motor-intact individuals, and not only are skills transferable, but often an individual's movement characteristics are preserved from one body part to the next.⁴⁰ An example of this is in handwriting, where it has been found that writing produced by the digits, wrist, arm, and foot all share common characteristics.⁴¹ Further, both amputees and individuals born without hands show great dexterity with the feet when used in place of the hands.³² This suggests that at least some motor brain areas could contain a shared substrate for multiple effectors. PPC has been identified as an area of particular importance for such a process from fMRI evidence both in amputees and motor-intact individuals.²³ For example, one fMRI study comparing finger and foot movements during name signing and zig-zag motions found increased activation of SPL regardless of effector or condition.⁴²

Our PLSR analysis of shared directional coding subspaces revealed a striking dissociation between MC and PPC. In MC, only specific pairs of effectors shared spatial information, including the contralateral thumb and wrist, and in JJ-MC, corresponding ipsilateral and contralateral effectors. Interestingly, the contralateral ankle also shared spatial coding with hand effectors in JJ-MC, which may reflect functional organization alongside somatotopy and parallels the behavioral finding that motor skills like writing can transfer from hands to feet.^{10,41} An important consideration for interpreting the MC results is that single-effector spatial decoding accuracy was poor for many non-hand effectors in MC. Thus, the restricted transfer we observe in MC is partly a consequence of weak underlying spatial signals for non-hand effectors.

In both PPC arrays, shared directional coding was found for every pair of effectors. This broad transfer efficiency was relatively uniform in RD-PPC, while JJ-PPC showed more variation across pairs, likely reflecting the mixed intrinsic/extrinsic reference frame in that array, which was not fully accounted for in this analysis. The different structures of spatial codes in each PPC array were further demonstrated by the finding that in RD-PPC effector pairs implemented similar spatial codes, while in JJ-PPC the broad sharing does not rely on a single common spatial subspace for all effectors. This further supports the trend that as one moves anteriorly in SPL, the population starts to support effector-specific representations rather than collapsing all effectors into a single spatial code.

Another likely function of overlapping representations is coordinating movements of multiple effectors. It has been proposed that during hand-eye coordination, information about the direction of both hand and eye movements is combined through global tuning fields, or the shared directional coding of individual cells in the PPC for the hand and eyes.⁴³ While in this study we do not explicitly test coordinated movements, the common spatial tuning used by single neurons across effectors appears to extend the concept of global tuning fields to humans and to effectors across the entire body.

Another potential role for the coding structure observed is computational efficiency. PPC has previously been shown to implement a framework called partially mixed selectivity, in which some task variables are coded with structure (e.g., preserved directional tuning across effectors) while others are mixed nonlinearly (e.g., which effectors a neuron responds to).^{24,44–48} In our results, single neurons in PPC code for mixed combinations of effectors, and no single anatomical or functional structure emerged to explain the relationship between effectors to which a neuron responded. Yet a given neuron tends to use the same spatial/directional code across the effectors it encodes. This partially mixed selectivity has been proposed to provide a computationally efficient way of representing high-dimensional information in areas involved in higher cognitive functions, consistent with PPC implementing a higher-level representation of motor control.^{46,48,49} Additionally, the finding that PPC encodes similar activity during overt, observed, and imagined movements further supports its role as a higher-order motor planning region.^{50–54} Given the variety of information PPC represents, from motor control to semantics to action observation, there is still much to explore regarding its computational functions.^{55–57}

Limitations of the study

Several limitations should be noted. First, our recordings are from individuals with chronic tetraplegia who were attempting, rather than executing, movements. Evidence from fMRI work in motor-intact individuals largely supports that attempted-movement representations mirror overt-movement representations, but this cannot be directly confirmed in our participants.^{8,10,20,23}

On a related note, we have limited insight into the posture and kinematics of attempted movements for which no overt movement occurred (i.e., below the level of spinal cord injury). For example, participants were instructed to move their thumb toward targets displayed on a screen, and it is plausible that this

instruction also engaged wrist pronation-supination planning. The overlap between thumb and wrist representations in MC may therefore partly reflect shared motor planning for coordinated hand movements rather than purely overlapping somatotopic representations.

Also of note is that the precise implant location influences the coding properties observed. Perhaps most importantly, both MC and PPC recordings that have emphasized effector separation have typically been within the sulcus (central and intraparietal, respectively), whereas our recordings are on the cortical surface. That said, recent fMRI and sEEG work has revealed highly overlapping representations within the central sulcus as well, and fMRI work in human PPC has generally revealed more flexibility than specificity in effector coding.^{8,9,37,39} The differences between RD-PPC and JJ-PPC further underscore this point, as despite targeting hand regions in SPL, the two arrays appear to sample different positions along a gradient of spatial-to-effector coding (MNI coordinates: [Table S1](#)).

Finally, the task design prioritized testing many effectors to address the primary question of whole-body representation, which limited us to six repetitions per direction per effector per session. While this provided adequate signal for the analyses reported here, the limited repetition count constrains more nuanced comparisons in both the effector and spatial response spaces. For example, we are limited in our ability to distinguish between true nonlinear, random mixing of effectors and a more structured response. It is possible that with sufficient observations on a tighter continuum of effectors along the body, anatomical or functional structure would emerge. At the population level, some hint at laterality being observed in the between-effector Mahalanobis distance analysis and classification confusion patterns; however, laterality alone is insufficient to describe the pattern of responses seen. Future studies with more repetitions per condition are needed to fully explore this point. We also did not test coordinated movements, which will be a critical future direction in elucidating the functional role of overlapping effector representations.

Conclusions

This study presents the first single-neuron evidence for encoding of effectors across the body in human PPC. In addition, we recorded from MC and PPC simultaneously, allowing us to compare the encoding of movement variables in distinct neural populations. The results reveal a fundamental difference in how these regions represent the body. MC implements effector-specific coding with somatotopic structure and an intrinsic reference frame, while PPC implements effector-modulated spatial coding with mixed selectivity. These distinct coding strategies suggest that the transition from PPC to MC involves a shift from goal-directed spatial representations that generalize across effectors to effector-specific motor commands.

These results have implications for evaluating the use of different brain areas in the control of therapeutic devices with brain-machine interfaces for those with impaired movement. In MC, strong representation of single effectors supports its usefulness in biomimetic control. In PPC, equal representation across

effectors highlights its potential to be used flexibly across several applications. Overall, the surprising variety of whole-body responses seen within hand motor areas contributes to the growing notion that use of simplified and highly controlled experiments around predefined cortical maps may limit our understanding of the more complex coding properties of different areas of the cortex.^{58,59}

RESOURCE AVAILABILITY

Lead contact

Further information and requests for resources should be directed to, and will be fulfilled by, the lead contact, Kelly Kadlec (kelly.kadlec@ucsf.edu).

Materials availability

This study did not generate any new, unique reagents.

Data and code availability

- De-identified, preprocessed neural and behavioral data supporting the analyses in this paper have been deposited at CaltechData and are publicly available as of the date of publication. Raw broadband neural recordings are not included in the deposit. The DOI is listed in the [key resources table](#).
- All original code has been deposited at Zenodo and is publicly available as of the date of publication. The DOI is listed in the [key resources table](#).
- Any additional information required to reanalyze the data reported in this paper is available from the [lead contact](#) upon request.

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AUTHOR CONTRIBUTIONS

K.K., J.G., T.A., and R.A.A. designed the study. K.K. developed the experimental task. K.K., J.G., T.A., and C.G. collected data and had unrestricted access to all data. K.K. and J.G. analyzed the results. K.K., J.G., and T.A. interpreted the results. K.K. wrote the paper. K.K., J.G., C.G., and R.A. reviewed and edited the paper, including the original draft. E.R.R. and K.P. coordinated regulatory requirements of clinical trials. A.B. and N.P. performed the surgery to implant the microelectrode arrays. R.A.A. supervised the study.

DECLARATION OF INTERESTS

The authors declare no competing interests.

STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- [KEY RESOURCES TABLE](#)
- [EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS](#)
 - Study participants
- [METHOD DETAILS](#)
 - Experimental procedures
 - Implant locations
 - Neural signal recording and preprocessing
- [QUANTIFICATION AND STATISTICAL ANALYSIS](#)
 - Cross-validated Mahalanobis distance

- Classification analysis
- Event related averages
- Strength of single unit responses
- Autocorrelation analysis of array maps
- Spatial tuning across effectors
- Intrinsic vs extrinsic coordinates
- Shared directional subspaces (PLSR)

● ADDITIONAL RESOURCES

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at <https://doi.org/10.1016/j.neuron.2026.09.030>.

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STAR★METHODS

KEY RESOURCES TABLE

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Deposited data		
De-identified data used for analysis	This paper	CaltechData: 10.22002/d1y63-g3f65
Software and algorithms		
Original analysis code	This paper	github.com/kkadlec/analysis-for-whole-body-study ; 10.5281/zenodo.21443150
MATLAB 2019b	MathWorks	http://www.mathworks.com
CircStat toolbox	Berens, 2009	https://www.mathworks.com/matlabcentral/fileexchange/10676-circular-statistics-toolbox-directional-statistics
Other		
NeuroPort Utah electrode array (64 ch, 96 ch)	Blackrock Microsystems	https://blackrockneurotech.com/
NeuroPort Neural Signal Processor	Blackrock Microsystems	https://blackrockneurotech.com/

EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

Study participants

The present data were collected from two participants enrolled in a BMI clinical study ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01958086) Identifier: NCT01958086). The main goal of the trial is to obtain scientific knowledge of visuomotor transformations in PPC and MC to advance the development of neural prosthetics. The central hypothesis of the trial is that PPC and MC will encode visuomotor parameters in both similar and different ways, and that algorithms can be developed to leverage those complimentary signals to improve prosthetic range and performance. The institutional review boards of California Institute of Technology, Casa Colina Hospital and Centers for Healthcare, and University of California, Los Angeles approved study procedures including informed consent, implant surgery, and experiment design. Participant RD is a right-handed male (39) with a C3/C4 level spinal cord injury that occurred approximately ten years before his enrollment in the study. RD can move his eyes, head, and shoulders (he can move his shoulder but cannot stabilize the arm). In addition, RD shows weak residual movements (twitches) of the wrist and thumbs. Participant JJ is a right-handed male (51), with a C4/C5 level spinal cord injury that occurred approximately three years before his enrollment in the study. JJ can move his eyes, head, and shoulder.

METHOD DETAILS

Experimental procedures

An adaptation of a traditional center-out task was used. The task was displayed on a screen in front of the participant. Participants were instructed to attempt movements as though they were motor-intact. At the start of each trial, participants were asked to have the effector that was going to be moved in a neutral position and their eyes fixed in the center of the screen. The participants were instructed to attempt movements of twelve different effectors (head, eyes, right/left shoulders, wrist, thumbs, legs, and ankles) in five different directions, 72 degrees apart. The direction of the movement was instructed by one of five targets on the screen changing color from gray to red as a “go” cue ([Figure S1A](#)). The participants were asked to make the instructed movement and then relax. They moved one effector to each of the five targets before the instructed effector changed to the next. Fixation was kept at the center except during trials for the eyes. Between each trial was an inter-trial interval (ITI) during which time the participant was at rest. Each ITI was 1.5s and each go phase was 2s. A total of 7 sessions were collected for JJ and 6 for RD. Three runs of the task with two repetitions for each movement were collected for each session. Before each session, movements were demonstrated by a researcher to help ensure the same movement profile of attempted movements across days.

Implant locations

Participant RD was implanted with four 64-channel NeuroPort Utah electrode arrays in his left hemisphere on July 20, 2023 ([Figure 1A](#)). Two arrays were placed near the hand knob of left precentral gyrus, with one slightly more lateral and the other slightly more medial (denoted RD-MCL and RD-MCM respectively). A third array was placed in the superior parietal lobule (RD-PPC). A final fourth array was placed in the supramarginal gyrus, however results from this array are excluded from the present study because only a limited number of tuned single neurons were recorded. Data from participant RD was collected ranging from three to six months

after implant surgery. Participant JJ was implanted with two 96-channel NeuroPort Utah electrode arrays in his left hemisphere on December 7, 2018 (Figure 1B). One array was placed near the hand knob of the left precentral gyrus and is referred to as motor cortex or “JJ-MC”. The second array was implanted in the left superior parietal lobule and is denoted “JJ-PPC”. Data from JJ was largely collected 20–22 months after surgery (along with one session 13 months and a final session 27 months post implant). A presurgical functional MRI during which each participant performed a grasping imagery task showed substantial neural response in regions of each implant location. During this task the participants were asked to imagine making the hand shape required to grasp an object from varying angles (for details see Guan et al.³¹).

Neural signal recording and preprocessing

Microelectrode arrays in each participant were recorded simultaneously. Neural signals were amplified, bandpass filtered (0.3 Hz–7.5 kHz) and digitized (30 kHz, 16 bits/sample) (NeuroPort Neural Signal Processors, Blackrock Microsystems Inc.). To detect action potentials, the signal was then band-pass filtered from 50 to 250 Hz and thresholded at -3.5 times the root-mean-square voltage (for each electrode). We used the k-medoids clustering method along with the gap criterion in order to identify single neurons and the total number of waveforms respectively.⁶⁰ This was done for the first four principal components (selected to account for 95% of waveform variance). Example waveforms can be found in Figure S14.

For analysis of each behavioral epoch during the 12-effector task, we calculated firing rates from neural activity over a 500ms window of neural activity. The movement execution (‘Go’ or ‘move’) analysis window was defined as the 500ms window starting 250ms after the Go cue. Similarly, the 500ms ITI window used in the distance analysis began 250ms into the ITI phase.

Neurons with an average firing rate of less than 1 Hz across the entire task were excluded from the analysis as noise. Additionally, all analysis was repeated on well-isolated neurons to avoid influences from multi-unit clustering. We classified neurons that corresponded to the lowest third of L-ratio values as well-isolated.⁶¹

QUANTIFICATION AND STATISTICAL ANALYSIS

Cross-validated Mahalanobis distance

The cross-validated Mahalanobis distance^{62,63} was used to compare the population level neural activity during movements of each effector as well as during rest (baseline, defined as a window during the inter-trial interval). With high-dimensional neural populations, Mahalanobis distance provides a statistically principled way to measure the separation between population states while accounting for the covariance structure of neural responses. Distances were estimated using repeated random split-half cross-validation. On each iteration (5,000 total), four trial indices were sampled without replacement and applied to both conditions being compared. Two indices formed one split and the remaining two formed an independent split.

For each neuron n , weights were constructed from the pooled within-condition variance. Responses for each condition were mean-centered and concatenated across all conditions and time points. The standard deviation for each neuron was then computed across this pooled set of residuals and squared to obtain a variance estimate:

$$\sigma n^2 = \text{Var}(\text{ukrk}, i - \bar{r}k).$$

To ensure numerical stability, a lower bound of 1 was imposed on the standard deviation estimates prior to squaring (equivalent to a variance floor of 1). Neurons with zero variance across the pooled residuals were excluded from the analysis. Neuron-wise weights were then defined as:

$$wn = \frac{1}{\sigma n^2}.$$

The cross-validated squared distance between two conditions A and B was computed as the weighted inner product between independent difference vectors from the two splits. Let (a_1, a_2) denote responses from condition A and (b_1, b_2) denote responses from condition B , drawn from the two independent splits. The distance was computed as:

$$dcv = \sum nwn(a1, n - b1, n)(a2, n - b2, n).$$

This procedure was repeated 5,000 times and averaged to obtain the mean cross-validated squared distance. The final reported distance was defined as a signed square-root transform:

$$D = \text{sign}(\bar{dcv}) \cdot \sqrt{|\bar{dcv}|}.$$

A permutation test with 10,000 shuffles was used to determine whether there was a significant difference between the distances of firing rates from baseline during movements of each effector (distances averaged across sessions).

For comparisons between effectors, pairwise distances were grouped according to predefined anatomical and functional categories: (1) same-side versus opposite-side effectors, (2) within-limb versus across-limb pairs, (3) matched bilateral pairs versus non-matched pairs, and (4) proximal–proximal, distal–distal, and proximal–distal pairs. Group differences were assessed using the same session-level permutation procedure described above (10,000 shuffles).

Classification analysis

To quantify how well effector identity and movement direction could be discriminated from population activity in each array, we performed linear discriminant analysis (LDA) classification. Two classification tasks were evaluated: (1) effector classification (12-class: which effector was being moved) and (2) direction classification (5-class: which target direction, pooling across all effectors). For each task, a linear discriminant model was fit using firing rates from all neurons as features. Classification accuracy was assessed using k-fold cross-validation (10-fold for effector and direction classification). Predictions from all held-out folds were aggregated to compute overall accuracy and to construct confusion matrices. The analysis was run independently for each recording session and the resulting confusion matrices were averaged across sessions. Chance-level performance was 8.3% (1/12) for effector classification and 20% (1/5) for direction classification.

Event related averages

Firing rates for each neuron were computed in 100ms bins across a 2s window, smoothed with a 400ms moving-average filter, and averaged across trials of each effector moving in the neuron's preferred direction to obtain the mean and standard error of the mean.

Strength of single unit responses

For each neuron and effector, a cross-validated best-minus-worst direction difference was computed. On each of 1,000 iterations, 5 of 6 trials were used to identify the directions with the maximum and minimum mean firing rate, and the difference was evaluated on the held-out 6th trial:

$$\Delta r_e = r_{\hat{d}_{\max}} - r_{\hat{d}_{\min}},$$

where $\hat{d}_{\max}$ and $\hat{d}_{\min}$ are the best and worst directions estimated from the training set. This was averaged across iterations and normalized by the pooled standard deviation across all conditions and directions:

$$\text{Response strength}_e = \frac{\Delta r_e}{\sigma_{\text{pooled}}}.$$

To evaluate whether the response to an effector was significant, the same measure was performed with shuffled firing rates to find a null distribution for that neuron to compare the strength of response for each effector (>95 percentile). The best effector for each neuron was then determined by finding the largest difference in firing rates between best and worst direction. Neural responses were normalized to the maximum response strength within each array. Neural responses were then sorted first by best effector and then the number of effectors to which that neuron was tuned (least to most).

Autocorrelation analysis of array maps

We calculated the spatial autocorrelation of channels with neurons tuned to a specific effector. We created a binary map for each effector, with channels that had at least one neuron identified as its preferred effector during any session as a 1, and 0 otherwise. We calculated Moran's I according to the following formula:

$$I = \frac{n \sum_{i=1}^n \sum_{j=1}^n w_{ij} (x_i - \bar{x})(x_j - \bar{x})}{\left(\sum_{i=1}^n \sum_{j=1}^n w_{ij} \right) \sum_{i=1}^n (x_i - \bar{x})^2},$$

where n is the number of channels, and x_i are the values at coordinates i and j , $\bar{x}$ is the mean of the values and w_{ij} is the weight matrix, that had a value of 1 for immediate neighbors of each channel and 0 for all other channels. Moran's I values range from -1 to 1. -1 indicates a spatially dispersed pattern (checkerboard pattern), 0 indicates a random spatial distribution of values, and 1 indicates clustering of similar values. To ensure interpretability, effectors represented on fewer than 5 channels were excluded. Statistical significance was assessed via a permutation test with 10,000 random permutations of the original spatial values and comparing the simulated I's with the original value obtained. The threshold for significance for Moran's I was $p < 0.01$.

Using the same channel effector maps as in Moran's I, we calculated join count statistics. Join count evaluates the frequency of neighboring pairs that share the same or different attributes. The two main statistics are:

$$BB = \frac{1}{2} \sum_{i,j,i \neq j} w_{i,j} x_i x_j, \text{ and}$$

$$BW = \frac{1}{2} \sum_{i,j,i \neq j} w_{i,j} (x_i - x_j)^2,$$

where BB indicates the number of elements next to elements of the same type (1), and BW counts the number of elements next to elements of a different type (0).

A p -value was calculated creating 10,000 random permutations of the spatial data and creating a distribution of BB and BW simulated values. We considered BB and BW significant if they had a $p < 0.01$.

Spatial tuning across effectors

The spatial tuning of each neuron was determined independently for the most preferred and second most preferred effector for each significantly tuned neuron (most preferred, second most preferred, and test for significance described in the above section). This was done by performing an ordinary least squares regression using target location on the screen as independent variables and neural firing rates as response variables. The coefficients from this regression give the directional vector coded by each neuron. The direction vector for effector e is $v_e = [\beta_x, \beta_y]$. The signed angle between the direction vectors of the best and second-best effectors was computed as:

$$\theta = \arccos\left(\frac{v_1 \cdot v_2}{\|v_1\| \|v_2\|}\right) \times \text{sign}((v_1 \times v_2)_z).$$

Finally, the MATLAB toolbox CircStat was used to calculate the circular mean and confidence intervals for each distribution, and to perform the Rayleigh test for uniformity.

Intrinsic vs extrinsic coordinates

To determine whether neurons were encoding space in a body-centered, or intrinsic reference frame, or a world-centered, or extrinsic reference frame, linear regression was used to find the direction vector coded by each neuron for pairs of contralateral and ipsilateral effectors (described in the section above). Then the correlation coefficient values from these regressions were correlated for each pair of effectors. A positive correlation indicated extrinsic coding, a negative correlation indicated intrinsic coding and no correlation implies some combination of the two. We found a significant negative correlation in JJ-MC that implies intrinsic coding of direction (Figure 5). Thus, in any of the analyses where we want to compare between directional coding of the contralateral and ipsilateral sides of the body, we must adjust the position information to be the same in intrinsic rather than extrinsic coordinates (Figures 4 and 5). This can be achieved by switching the position information for movements to the left and right targets. This was only done for JJ-MC, because no such intrinsic relationship was found in the other arrays.

Shared directional subspaces (PLSR)

We evaluated the structure of the neural population code using a cross-validated partial least squares regression (PLSR) model to find shared directional subspaces between pairs of effectors, for each possible combination of effectors (Figure 6). A series of models for each effector pair were trained using neural firing rates across all units as predictor variables and the target position information for the two effectors as the response variable for a subset of the trials. For each model, up to 10 latent components were considered, and the optimal number of components was selected using cross-validated mean squared error. The PLSR model takes the form

$$\hat{Y} = 1\beta_0T + XB,$$

where X is the $n \times p$ matrix of neural firing rates (n trials, p units), $\hat{Y}$ is the $n \times q$ matrix of predicted target position labels, B is the $p \times q$ matrix of regression coefficients, β_0 is the intercept vector, and 1 is an n -vector of ones. To control for effects of training dataset size, these subsets were created by randomly choosing fifteen trials for each of the effectors in the pair but using all thirty trials for the models trained on a single effector. The model output was the predicted position information. The performance of each model was evaluated by taking the bootstrapped correlation between the input labels and those predicted by the model. The mean value of the correlation of the models of 200 randomized subsets was calculated for each effector pair. To determine whether the r^2 values were driven by shared information or a single effector, a null r^2 distribution was generated. The null r^2 distribution was found using the same general steps, but with randomly shuffled firing rates for trials for one of the effectors for pairs of effectors, or half of the trials for the single effector cases. This was done to mimic an effector pair where one effector may have spatial information, but that information is not shared between the two effectors. The threshold for significance for shared information was $p < 0.01$. Each effector pair generated two r^2 values (for each order of pairing), and to be considered significant, we strictly required $p < 0.01$ for both orderings. In addition, effector pairs where one or both effectors did not significantly share information within itself were excluded for their lack of spatial information. Both models were k -fold cross-validated over 6 folds. To account for the intrinsic reference frame in JJ-MC, the position information for right and left targets were switched for ipsilateral effectors.

We calculated the principal angles between the beta coefficients of the models to measure the degree of orthogonality between subspaces. This allowed us to determine whether the subspaces obtained from the PLSR models across effector pairs were different. The principal angles were calculated using the singular value decomposition of the inner product of the orthonormalized beta coefficients of each of the two models as follows.

$$\beta_1^T \beta_2 = U \Sigma V^T,$$

where β_1 and β_2 are the beta coefficients of the models, and the diagonal of Σ contains the singular values. To obtain the principal angles we calculated the arccosine of these singular values. Finally, we averaged the principal angles of target position.

ADDITIONAL RESOURCES

This study was conducted as part of a clinical trial ([ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT01958086) Identifier: NCT01958086).