The effector-independent action system: Evidence from people born without hands

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Abstract
Many parts of the visuomotor system guide daily hand actions like reaching for and grasping objects. Do these regions depend exclusively on the hand as a specific body part whose movement they guide, or are they organized for the reaching task per se, for any body part used as an effector? To address this question, we conducted a neuroimaging study with people born without upper limbs—individuals with dysplasia—who use the feet to act, as they and typically-developed controls performed reaching and grasping actions with their dominant effector. Individuals with dysplasia have no prior experience acting with hands, allowing us to control for hand motor imagery when acting with another effector (i.e. foot). Primary sensorimotor cortices showed selectivity for the hand in controls and foot in individuals with dysplasia. Importantly, we found a preference based on action type (reaching /grasping) regardless of the effector used in the association sensorimotor cortex, in the left intraparietal sulcus and dorsal premotor cortex, as well as in the basal ganglia and anterior cerebellum. These areas also showed differential response patterns between action types for both groups. Therefore, frontoparietal motor association areas showed effector-independent action-type representation. Intermediate areas along a posterior-anterior gradient in the left dorsal premotor cortex gradually transitioned from selectivity based on the body part to action type. These findings indicate that some visuomotor association areas are organized based on abstract action functions independent of specific sensorimotor parameters, suggesting a hierarchical organization from effector-dependent to effector-independent functions.

Significance statement
What are the principles of brain organization? In motor domain, separate pathways were found for reaching and grasping actions performed by the hand. To what extent is this organization specific to the hand, or based on abstract action types, regardless of which body part is performing? We tested people born without hands who perform actions with the feet. Activity in frontoparietal association motor areas show preference for an action type (reaching or grasping), regardless of performed by the foot in people born without hands, or by the hand in typically-developed controls. These findings provide evidence that some association areas are organized based on abstract functions of action types, independent of specific sensorimotor experience and parameters of specific body parts.

Introduction

Performing an action such as reaching for a ball involves planning the goal and executing it with specific body parts. This rich movement information is encoded by a wide range of motor areas. Hand kinematic and muscle synergies during reaching and grasping actions are encoded by population neural response in primary motor cortex (Gallego et al., 2017; 2018; Overduin et al., 2015; Leo et al., 2014). These are largely organized into a large-scale somatotopic organization in primary motor cortex, albeit lacking clear boundaries, with each brain area selectively representing a body part (Heed, Leone, Toni, & medendorp, 2016; Zeharia, Hertz, Flash, & Amedi, 2012; 2015; Filimon, Nelson, Huang, & Sereno, 2009; Meier, Aflalo, Kastner, & Graziano, 2008; Penfield & Boldrey, 1937). Beyond primary motor cortex, brain areas are additionally sensitive to specific action types for a given body part. For example, a dorsomedial frontoparietal network is devoted to the act of reaching towards an object with one's hand, as found in both humans and non-human primates (Batista, Buneo, Snyder, & Andersen, 1999; Chang & Snyder, 2012; Connolly, Andersen, & Goodale, 2003; Kaas, Stepniewska, & Gharbawie, 2012; Kaas, Gharbawie, & Stepniewska, 2013; Konen, Mruczek, Montoya, & Kastner, 2013; Yttri, Wang, Liu, & Snyder, 2014; Hinkley, Krubitzer, Padberg, & Disbrow, 2009). However, many common action goals can be achieved with different body parts or effectors. For example, one can reach for a ball with the hand or with the foot. Are there neural mechanisms that control each action type, independently of the effector ultimately used to perform the action?

Recent studies provide evidence that despite body-part preference, some association cortex regions can support action representations extending across body parts. During motor execution, activation patterns in premotor cortex and parietal lobe represent more abstract information, such as the target location and movement direction, regardless of which hand was performing the action (Haar, Dinstein, Shelef, & Donchin, 2017; Turella, Rumiati, & Lingnau, 2020). During motor planning, common brain areas including the dorsal premotor cortex (PMd) and intraparietal sulcus (IPS) were involved when planning to direct the hands or the eyes towards an instructed direction (Gallivan, Adam McLean, Smith, & Culham, 2011; Heed, et al., 2011; Heed, Leone, Toni, & Medendorp, 2016; Leoné, Heed, Toni, & Pieter Medendorp, 2014; Magri, Fabbri, Caramazza, & Lingnau, 2019). Moreover, two studies reported similarity in activation during pointing movements across the hand and foot (Heed et al., 2016; Heed et al., 2011). These findings suggest a more abstract organization of the motor system based on action types or goals (Graziano & Aflalo, 2007; Kaas & Garraghty, 1991; Tresilian, 1999), which may be less dependent on the effector.

One potential confound in past findings is motor imagery. In past studies, typically-developed individuals were asked to perform actions with their non-dominant limbs, e.g. foot or non-dominant hand (Heed et al., 2016; Gallivan et al., 2013; Haar et al., 2017). Because participants were less experienced in acting with these limbs, it is possible that they performed the action by imagining how the typically-used hand would perform it, engaging motor imagery processes. There is ample evidence that motor imagery engages the same sensorimotor systems as actual motor execution (Ehrsson, Geyer, & Naito, 2003; Porro et al., 1996; Solodkin, Hlustik, Chen, & Small, 2004; Hanakawa et al., 2003; Lacourse et al., 2005; Schnitzler et al., 1997). As a result,

the common activation found across effectors in prior works could reflect the shared activation of motor execution and motor imagery of the same dominant hand. This raises the question whether the common brain activation pattern across effectors truly reflect effector-independent motor representation, abstracted beyond the body part.

Here we address the question of whether the sensorimotor system is organized by effector-independent motor representations, overcoming any potential hand imagery confounds, by examining a unique population: people born without hands who use the feet as the primary effector (individuals with dysplasia; IDs). We scanned the IDs while they performed reaching and grasping actions — actions that engage at least partially separable neural networks for hand movements (Culham, Cavina-Pratesi, & Singhal, 2006; Cavina-Pratesi et al., 2018, 2010; Fabbri, Strnad, Caramazza, & Lingnau, 2014). If an area is selective for an action type both when IDs perform with the foot and controls with the hand, it would indicate that this area is involved in processing that action type independently of effector. Areas showing selectivity for foot actions in IDs as compared to hand actions in controls or vice versa would be characterized as effector-dependent. This paradigm thus allows us to directly test which components of the reaching and grasping networks are effector-dependent and specific to the hand and foot respectively, and which, if any, components are based on more abstract action type processing, independent of the effector.

Results

We scanned four individuals with dysplasia (IDs), born without hands and arms, and a group of typically-developed control participants while they performed reaching (reach-to-touch) and grasping (reach-to-grasp) actions towards a centrally-located object (see schematic in **Fig. S1** and **Figure 1A**). The IDs performed the actions with their feet, the body part that they use extensively and dexterously for daily actions (Striem-Amit, Vannuscorps, & Caramazza, 2017; 2018; Vannuscorps, Wurm, Striem-Amit, Caramazza, 2019; Vannuscorps & Caramazza, 2019; Vannuscorps, Andres, & Pilon, 2014). The controls performed the actions with their hands. Here we focus on actions of the dominant effector (right hand in controls and right foot in IDs) because it is most dexterous in reaching and grasping tasks, and reaching and grasping networks are most frequently reported for the dominant (right) hand (Culham et al., 2003; Frey, Vinton, Norlund, & Grafton, 2005; Chapman et al., 2002; Cavina-Pratesi et al., 2018, 2010).

To examine the effect of action type and effector on brain activation, we first performed a random-effect (RFX) ANOVA with effector as a between-subjects factor (right foot in the IDs and right hand in the controls; the dominant effector for both), and action type (reaching and grasping) as a within-subjects factor (**Figure 1A**). Importantly, this analysis allows us to infer effector-dependent and effector-independent mechanisms in the sensorimotor system. For example, areas demonstrating a main effect of action type show preference for one action type over the other across both effectors (hand and foot in their respective groups), indicating effector-independent organization. Post-hoc analyses were then performed to investigate the direction of the main effects.

We first inspected which areas show a main effect of effector, signifying preference based on body part (i.e. stronger activation for hand movements versus foot movement or vice versa) regardless of the action type performed. We found a significant difference between hand (in controls) and foot (in IDs) actions in the medial left primary sensorimotor cortex where the foot area is located in the sensorimotor homunculus (Penfield & Boldrey, 1937), as well as in the left dorsal premotor cortex (PMd; **Figure. 1B**). Consistent with a somatotopic organization in primary sensorimotor cortex, post-hoc region-of-interest (ROI) analyses found higher activation in the foot area for foot movements in the IDs versus hand movements in the controls, and higher activation in the hand area (sampled from a motor localizer experiment, see methods) for hand movements in the controls versus foot movements in the IDs (two-tailed t-test, t(9) = 2.84, p = .020; **Fig. S2A**). This is consistent with recent evidence for somatotopic organization in primary sensorimotor cortex in IDs despite compensatory foot use, indicating it adheres to somatotopic (as opposed to function-based) organization (Striem-Amit et al., 2018). Foot movements in IDs also elicited higher activation in the left dorsal premotor cortex than hand movements in the controls (**Fig. S2A**). These findings indicate effector-selective action representation across action types in these brain areas.

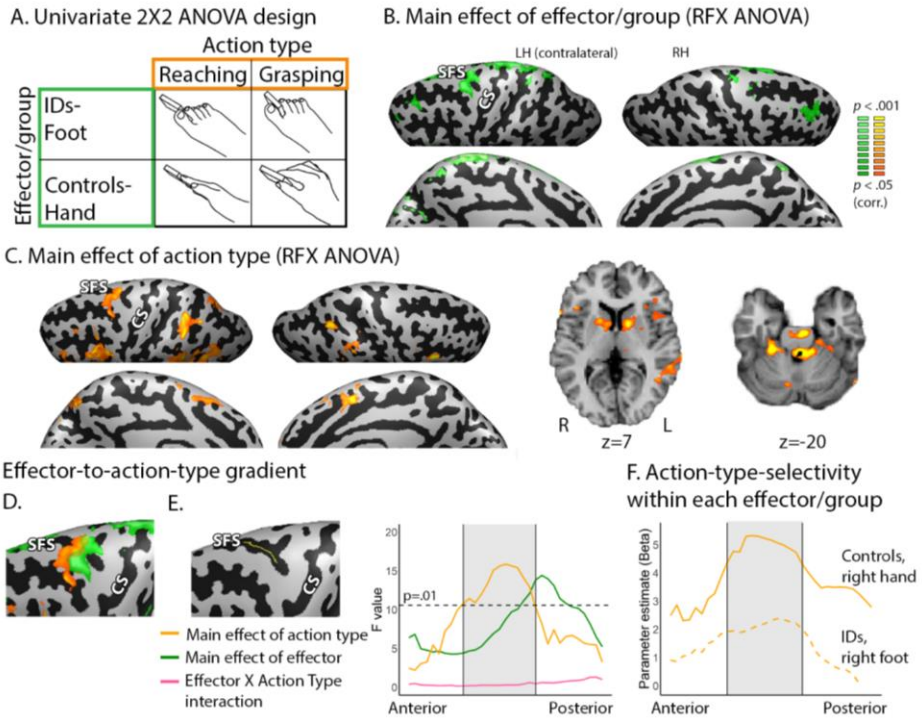

Figure 1: Effector-dependent and effector-independent action networks

Results from the random-effects (RFX) ANOVA analysis for the right hand in the controls and right foot in the IDs. **(A)** An RFX ANOVA was performed with action type as within-subject factor and effector/group as between-subject factor. (**B**) Main effect of effector/group. Difference between hand actions in controls and foot actions in IDs was found in the contralateral (left) primary sensorimotor cortex foot area and dorsal premotor cortex. An ROI analysis also revealed a difference between effectors in the primary sensorimotor hand area (**Fig. S1A**). **(C)** A main effect of action type (i.e. a consistent difference between reaching and grasping) across effectors/groups was found in contralateral (left) dorsal and ventral premotor cortex, superior parieto-occipital cortex, medial frontal gyrus (SMA and preSMA) and bilateral intraparietal sulcus. Subcortical activation was found in bilateral caudate and cerebellum (lobule I-IV and V), displayed on axial slices. **(D)** Overlaying statistical maps of both effector- and action-type main effects together revealed a posterior-anterior shift from effector- to action-type-dependent activation along dorsal premotor cortex. **(E)** A line ROI along the superior frontal sulcus (SFS) was created, along which the *F*-values of the main effect of action type and effector/group were plotted to demonstrate the selectivity gradient from effector- (green) to action-type-dependent (yellow) activation along dorsal premotor cortex. The gray window denotes spatial range showing a significant ($p < .01$) main effect of action type. **(F)** Parameter estimate (beta weights) of the GLM contrast between reaching and grasping was plotted for each group along the line ROI in SFS, from anterior to posterior voxels, showing an increase in action-type preference in both groups along SFS. The gray window denotes spatial range showing a significant ($p < .01$) main effect of action type in the ANOVA.

Next, we addressed the main question of whether there is effector-independent organization in sensorimotor cortex. Brain areas with a main effect of action type, that is, a consistent preference for an action type for both the hand-actions in controls and foot actions in IDs, would indicate effector independent representation. We found a main effect of action type, regardless of the effector used by the two groups, in a wide network of frontoparietal association sensorimotor cortices (**Figure 1C**). These included left ventral and dorsal premotor cortex (PMv and PMd respectively), supplementary and pre-supplementary motor area (SMA and preSMA respectively), middle-to-anterior intraparietal sulcus (mid-aIPS; found bilaterally), and superior parieto-occipital cortex (SPOC). Additionally, a preference based on action type was found in the basal ganglia and in the head of the caudate nucleus as well as in the anterior cerebellum (lobules I-IV and V), bilaterally. No significant interaction between effector/group and action type was found. We also performed this analysis on each ID, demonstrating the consistency of action type preference across IDs (**Fig. S3; Fig. S9**). In testing the direction of this action-based preference, an overall preference for reaching over grasping was found across both groups (**Fig. S4A**). Grasping activated the typical grasping network including premotor cortex and IPS (**Fig. S5**), consistent with past studies (Turella et al., 2020; Konen, Mruczek, Montoya, & Kastner, 2013), although it did not generate higher activation than reaching. This likely results from the absence of visuo-motor coordination (Jeannerod, Arbib, Rizzolatti, &

Sakata, 1995) in our task, as the participants could not see their moving effectors or the target object (see Discussion). Despite some variability, preference for reaching with the feet in the typical hand-reaching dorsal premotor cortex (Beurze, de Lange, Toni, & Medendorp., 2007; Crawford et al., 2011; Fabbri et al., 2014; Gallivan and Culham, 2015; Haar et al., 2017) was found consistently across the IDs **(Fig. S4C right panel, Fig. S4D**). These findings show that non-primary, association motor areas selectively represent action type for reaching, independent of specific sensorimotor parameters, such as muscle group, associated with the hand and foot, respectively.

How do these two types of representation, effector-dependent and effector-independent, relate to each other in cortical spatial organization? To investigate this question, we examined the transition areas between the two representation types. Plotting the two main effects together, we found a posterior-anterior gradient along the left dorsal premotor cortex from effector- to action-type selectivity (**Figure 1D**). This pattern is further demonstrated by a gradual shift between these main effects seen when sampling consecutive points along the posterior-anterior axis of the superior frontal sulcus (SFS; **Figure 1E**). Similar findings were found for the SFS gradient across effectors (the hand and foot) within the controls (**Fig. S6D**). Although findings from the controls cannot rule out the potential confound of hand motor imagery, these findings are also consistent with abstract representations of action type in PMd. Similar to the changes in the main effect of action type across the two groups, within each group, GLM beta estimate for the contrast between the two action types also gradually increased and decreased from posterior to anterior in the dorsal premotor cortex (**Figure 1F**). Overall, these findings suggest a hierarchical gradient of abstraction in representing actions, from body-part- to abstract action-type specificity in the dorsal premotor cortex.

Does the differentiation based on action type across groups and effectors also manifest in the regional pattern of activation? We performed multivariate pattern analysis (MVPA) to investigate whether action-related brain regions' activity pattern represents information regarding action type (see methods), i.e. if we can decode what action is performed. We specifically tested whether we can decode foot action type in IDs in areas previously shown to represent action-type information for the hand (Gallivan, McLean, Flanagan, & Culham, 2013; see methods for detailed information). It was previously reported that response pattern in left PMd and aIPS differed between planned action types (reaching and grasping) for either hand (Gallivan et al., 2013). Here we further show that response pattern in aIPS and PMd also differed between action types performed by the foot (**Figure 2A**). In addition, we successfully decoded foot action types in areas that were previously reported to represent action type only for the contralateral hand (motor cortex and SMA; Gallivan et al., 2013). Finally, response pattern in the left hand-selective primary sensorimotor cortex could be used to decode action types for the foot in IDs (**Figure 2B**). Therefore, action type representation for foot actions in IDs manifests in activity pattern in typical frontoparietal hand-action areas.

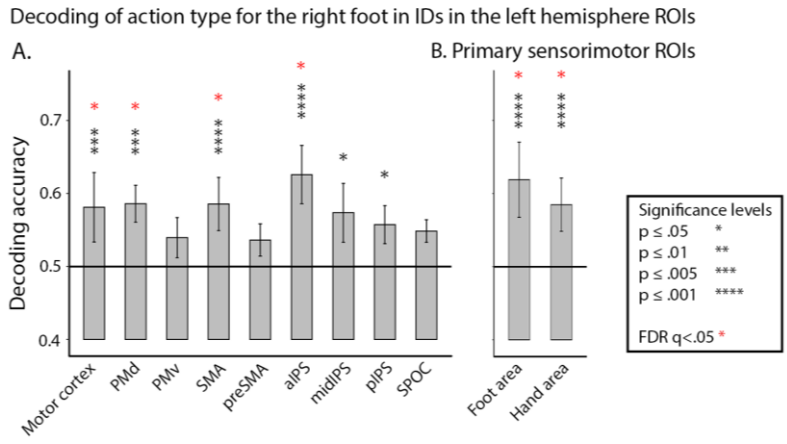

Figure 2: **Effector-independent action-type decoding**

Decoding of action type for foot actions in IDs was significant in action peak ROIs defined on past literature (Gallivan et al., 2013; **A**) as well as body-part-selective ROIs defined from a control motor experiment (**B**). Horizontal lines at 0.5 denote chance level. Error bars denote standard error. Asterisks denote significance (red: FDR corrected for multiple comparisons).

Discussion

Manual reaching and grasping actions were reported to engage partially separable neural pathways, indicating an organization of the sensorimotor network based on action type (Culham et al., 2006; Cavina-Pratesi et al., 2010; 2018; Fabbri et al., 2014). We examined individuals born without hands who act with their feet to investigate to what extent this organization is specific to the hand, or based on preference to the action type regardless of specific effectors. We found that frontal and parietal association sensorimotor areas, including contralateral PMd, PMv, SMA/preSMA, mid-aIPS and SPOC, preferentially responded to an action type (reaching /grasping), regardless of whether it is performed by the hand in typically-developed controls or by the foot in IDs. Moreover, using MVPA we found that in areas known to have distinct patterns for hand actions, distinct patterns of foot actions exist as well. These findings indicate that in these association areas, motor representations are based on action type without specified sensorimotor parameters, encoding information at a more abstract level than the effector-dependent computation.

Effector-independence action-based organization in sensorimotor cortices

Studying IDs and their foot use allowed us to extend past findings on effector-independent action representation. There is evidence that response patterns in aIPS, midIPS, PMd, and preSMA can differentiate planning or execution of reaching and grasping actions for both hands (Gallivan, et al., 2013; Haar et al., 2017; Turella et al., 2020). Given that the two hands share highly homologous muscle structures, it is possible that the abstraction level found in previous studies was hand-side-independent, but still specific to the biomechanical structure of the hands (Haar et al.2017) and does not generalize to the foot. Our findings indicate effector-independence across biomechanical structures, i.e. between the hand and foot. Moreover, in aIPS specifically, evidence for effector-independence has also been shown beyond the hands: although aIPS is hand-selective (Heed et al., 2016; Leone et al., 2014), it has also been implicated in shared representation of actions of the hand and eyes, when planning to move either the hand (in reaching) or eye (in performing saccades) towards external locations (Heed et al., 2011; Magri et al., 2019). One possibility is that these common motor representations are abstracted during hand-eye coordination in performing visually-guided hand actions; whereas effector-independent motor organization in individuals born without hands precludes an account of hand-based coordination. Finally, a few studies reported that areas in posterior parietal cortex, including aIPS and anterior superior parietal lobule, were equally activated by hand and foot pointing movements (Heed et al., 2011; Heed et al., 2016; Leone et al., 2014). Although supporting effector-independent organization, it is possible that performing foot actions involved mental imagery of analogous hand actions, a process that also engages hand-action execution network (Ehrsson et al., 2003; Porro et al., 1996; Solodkin et al., 2004; Hanakawa et al., 2003; Lacourse et al., 2005; Schnitzler et al., 1997). In contrast, by studying individuals born without hands, who do not have prior experience with hand movements, our results are not confounded by manual motor (kinesthetic) imagery. Although IDs can still imagine viewing other people perform hand actions, visual action imagery does not reliably involve motor-associated areas and instead more strongly engages visual areas (Guillot et al., 2008; Stinear et al., 2005; Neuper et al., 2005). Furthermore, action observation in ventral premotor areas and inferior parietal lobule are associated primarily with action-execution and motor imagery functions (Gallese et al., 1996; Fabbri-Destro & Rizzolatti, 2008). Therefore, excluding kinesthetic motor imagery by testing individuals with dysplasia reveals the core role of these regions in action execution, and expand on previous findings in showing effector independence beyond aIPS to additional regions, including the premotor cortex, basal ganglia and cerebellum (see below).

This effector-independent organization suggests that at least for the non-primary sensorimotor system, their organization may be better defined by action types rather than by body-part topography. A proposal of an action-type-based organization principle for the motor system has been made previously based on studies in non-human primates. Long-train (~500ms) microstimulation in premotor cortex appear to generate coordinated actions that extend beyond a single body part to complete an ethological goals (e.g. grasping, feeding; Graziano, Taylor, & Moore, 2002; Graziano, Aflalo, & Cooke, 2005; Kaas et al., 2013; Baldwin, Cooke, Goldring, & Krubitzer, 2017). Despite their theoretical interest, these works were criticized stating that long stimulation may lead to spread of activation and non-local recruitment (Jankowska, Padel, & Tanaka, 1975). Here, using whole-brain neuroimaging, by showing distinct

activation level and spatial patterns between reaching and grasping, our findings lend support to a motor organization based on action-type, and extend the level of abstraction across effectors.

Relationship between different abstraction levels

While we found a large-scale dissociation between effector-dependence in primary sensorimotor cortex and effector-independence in association areas, our results also support a proposal that multiple organization principles, for body-parts and for action-types, co-exist in some motor areas (Graziano & Aflalo, 2007). First, we found a gradient between effector-dependent and effector-independent preferences in the sensorimotor system, along the left dorsal premotor cortex. Although these two seemingly discrete clusters allow us to draw a line between more anterior areas whose activity is action-type-dependent and more posterior areas whose activity is effector-dependent, they may also be interpreted as a gradient of overlapping distributions, which includes transition voxels selective to both properties (see interaction of these two main effects in the controls; **Fig. S3C,D**). Second, primary motor area, while showing clear preference for a specific body part (**Fig. 1B**, **Fig. S1A**), also showed distinct multivoxel response patterns for reaching and grasping actions in the IDs, indicating co-existence of representation at different abstraction levels. This apparent effector-invariance contrasts with past findings that during movement execution, the decoding between action types in the primary motor hand area is limb-specific – only for the contralateral hand and not for the ipsilateral hand (Gallivan et al., 2013; Turella et al., 2020). However, a recent study reported differential responses to individual toes in IDs in the missing *hand* area of primary sensorimotor cortex, indicating this region also receives meaningful information about the foot in these individuals (Dempsey Jones, Wesselink, Friedman, & Makin, 2019). Therefore, the role of early sensorimotor cortex in effector-invariant action processing remains open to future explorations. Taken together, our findings suggest that instead of having discrete areas each representing action at a specific abstraction level, there may be multiple organization principles co-existing in sensorimotor areas, consistent with the proposal from past studies (Aflalo & Graziano, 2006; Graziano & Aflalo, 2007; Graziano, 2016).

Effector-independence in subcortical areas

Our findings show effector-independent action-type preference not only in in cortical frontoparietal areas but also in the cerebellum and basal ganglia (peaking in the caudate). A somatotopic organization in anterior cerebellum is well characterized in humans, with an anterior-posterior distribution from lobule IV to VI between foot, hand, and lip movements (Rijntjes, Buechel, Kiebel, & Weiller, 1999; Nitschke, Kleinschmidt, Wessel, & Frahm, 1996; Boillat, Bazin, van der Zwaag, 2020). We found a main effect of action type in lobule IV to V, falling between typical hand- and foot-movement areas (see **Fig. S6**). Importantly, the role of cerebellum extends beyond simple movements to various domains of motor control, including performing reaching and grasping actions (Jacobs, Danielmeier, & Frey, 2009; Grafton, Fagg, Woods, & Arbib, 1996; Fu, Flament, Coltz, & Ebner, 1997; Kitazawa, Kimura, & Yin, 1998; Espinoza & Smith, 1990; Dugas & Smith, 1992) and motor learning (Imamizu et al., 2000; Doyon

& Benali, 2005; Penhune, & Doyon, 2005). Although these cerebellar responses generally overlap with the cerebellar hand area, it remains a question whether these functions are specific to the hand or operates at an effector-independent level. Interestingly, a recent study investigated cerebellar organization in people born with one hand and found that the cerebellar missing hand area is activated by multiple body parts (Hahamy and Makin, 2018). Although body-part selectivity in the cerebellum for compensatory effectors was not investigated in that case, it is also consistent with our evidence for function-based organization near the somatotopic hand area. Overall, our findings suggest that the cerebellum may also have effector-independent organization for action types, adding important insights on the understanding of the topography and motor hierarchy of cerebellum.

The role of basal ganglia in motor control is extensively studied: activity in the caudate nucleus was associated with skilled limb movements including reaching, grasping, and self-feeding in animal models (Dolbakyan, Hernandez-Mesa, & Bures, 1977; Buser, Pouderoux, & Mereaux, 1974). Functional neuroimaging studies on human reported basal ganglia activity during motor learning and transferring (Jueptner, Frith, Brooks, Frackowiak, & Passingham, 1997; Lehericy et al., 2005; Seidler, Noll, & Chintalapati, 2006). Interestingly, literature on motor sequence learning proposed a division between anterior (associative) and posterior (sensorimotor) areas of the striatum (Lehericy et al., 2005). Whereas learning of new motor sequences activated associative (anterior) areas including caudate and anterior putamen, execution of overlearned movements activated sensorimotor (posterior) putamen areas (Jueptner et al., 1997; Lehericy et al., 2005). Our finding of a main effect of action type supports the anterior striatal areas engagement in encoding abstract movement rules, showing it can also support effector-independent abstract action representation.

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Effector-independence across motor domains

Whereas we examined ethological actions (e.g. reaching, grasping; Graziano, 2016; Kaas et al., 2013), effector-independent action representation has also been demonstrated in other domains, including motor timing (Bengtsson et al., 2005) and writing (Rapp and Caramazza, 1997; Rijntjes et al., 1999; Kadmon Harpas et al., 2014). For example, common activation in PMd and PMv was found when individuals signed their names with either the index finger or big toe, although not controlling for motor hand imagery (Rijntjes et al., 1999). Moreover, studies on motor learning and transferring also indicate some effector-independent transference. There is evidence that when individuals learn a motor sequence or visuomotor adaptation with one hand, learning is transferred to the other hand (Perez et al., 2007; Schulze, Lüders, & Jäncke, 2002; Van Mier & Petersen, 2006; Wiestler, Waters-Metenier, & Diedrichsen, 2014; Kovacs, Mühlbauer, & Shea, 2009), or between proximal (shoulder-elbow) and distal (wrist-index finger) effector systems either unilaterally or bilaterally (Vangheluwe, Puttemans, Wenderoth, Van Baelen, & Swinnen, 2004; Aune, Aune, Ingvaldsen, & Vereijken, 2017). The ability to transfer motor skills from a trained effector to a novel effector indicates that movements are represented not only in terms of specific muscle patterns, but also in more abstract forms that can be flexibly translated into alternative muscle patterns. Consistent with our findings, such learning transference relies on the frontal motor areas and parietal lobe

(Kumar, Panthi, Divakar, & Mutha, 2020; Wiestler et al., 2014; Perez et al., 2007). Whereas these domains differ in time scale, from evolutionarily-old (e.g. grasping) to more recent (e.g. writing) and to newly trained visuo-motor perturbations, studies on different domains indicate that effector-independent motor representation may be a common mechanism that supports flexible motor execution and learning across effectors.

Study limitations

It could be argued that the effects reported here could be unique to the IDs, resulting from a unique reorganization in their brains due to the absence of hands, undermining their usefulness in informing theories of the typically-developed brain. However, overall the IDs' brain has shown remarkable consistency with typical organization for other visuomotor properties, including action observation network (Striem-Amit et al., 2017; Vannuscorps et al., 2019). Furthermore, the controls in our study also showed difference between reaching and grasping in SMA/preSMA, SPOC, PMv, and PMd for the right foot (**Fig. S8**), indicating that action type affects responses also for foot actions even in typically developed participants. Therefore, together with past evidence of effector-invariance in association sensorimotor cortex in typically-developed individuals (Gallivan, et al., 2013; Haar et al., 2017; Turella et al., 2020), it is likely that these areas are organized in an effector-invariant manner. Taken together, our findings indicate that effector-independence may be an innate organization principle of the sensorimotor system.

Our task emphasis on motor pattern rather than on visuomotor coordination generated some differences from past literature. Past studies which employed visually-guided reaching and grasping reported a larger network across posterior parietal cortex (PPC) activated by reaching and grasping actions (Culham et al., 2003; Gallivan et al., 2013; Konen et al., 2013). Some of these were not found in our motor-driven task, which did not provide the participants with view of the objects and effector. This design was created to match the inability to see foot action in the scanner environment and isolate the motor reach and grasp component. The lack of PPC involvement in our design is therefore likely due to reduced need of transforming object location from an eye-centered reference frame to an effector-based reference frame (Batista et al., 1999; Desmurget et al., 1999; Graziano, 2001; Snyder, Batista, & Andersen, 1997). Similarly, whereas we found preference for reaching in PMd and SPOC, consistent with past findings (Cavina-Pratesi et al., 2010; Connolly et al., 2003; Culham et al., 2006; Konen et al., 2013), no preference for grasping was found in aIPS and PMv (Binkofski et al., 1998; Cavina-Pratesi et al., 2010; Culham et al., 2006, 2003). Notably, preference for grasping vs. reaching has only been reported when visual information was available (Culham et al., 2003; Cavina-Pratesi et al., 2010; Cavina-Pratesi et al., 2018) and has not been widely studied when visual information is removed from sighted individuals (Turella et al., 2020; Ariani et al., 2015). Our results hence do not contradict past findings and instead likely reflect modulation of visual information on the reaching and grasping networks and tasks; for example, by affecting visuo-motor coordination (Jeannerod, Arbib, Rizzolatti, & Sakata, 1995). Importantly, these differences do not influence our conclusion of effector-independent action network. By removing common visual object representation between hand and foot actions, our findings demonstrate effector-independent

action-type representation across muscle patterns that were not driven by shared visual representation mechanisms. Finally, we recognize that our findings may be limited in revealing the complete scale of effector-invariance organization given the study power and sample size. Therefore, while our study found reliable effector invariance based on motor coding in some regions, future studies may also reveal similar properties for visuomotor transformation processes and their neural substrates.

Implications for brain organization principles

Beyond addressing motor system organization and action representations, our findings also have broader implications on brain organization and plasticity. Specifically, our results add to past findings from blind and deaf individuals that showed typical functional specificity of the visual and auditory association cortices despite sensory deprivation (Heimler et al., 2015). Such findings, of processing domain- and category-specific computations in the ventral and dorsal steams of the visual cortex in people born blind (Bi, Want, & Caramazza, 2016; Cecchetti et al., 2016; Heimler et al., 2015; Renier, De Volder, & Rauschecker., 2014; Ricciardi et al., 2013), suggested that the visual cortex organization is independent of visual features and experience, and can support a representation abstracted from such elements (Heimler et al., 2015; Pascual-Leone and Hamilton, 2001; Bi, Wang, & Caramazza, 2016; Peelen and Downing, 2017). Visual association cortices also appear to be independent from motor experience for relevant visual percepts, as shown for hand and action perception areas in people born without hands (Striem-Amit et al., 2017; Vannuscorps et al., 2019). Importantly, comparable findings of processing for localization, identity and communication signals in the auditory cortex in deafness (Bola et al., 2017; Cardin et al., 2015; Lomber, 2017; Newman et al., 2015; Benetti et al., 2017; Cardin et al., 2013) indicate that this principle of sensory-modality independence is applicable to the association sensory cortex at large. Here we extend the same principle to the motor domain. We provide evidence that similar to sensory-independence, some parts of the association motor system are effector-independent, representing actions regardless of specific motor outputs on which the computation is carried out. Taken together, these findings suggest a common organization principle in association areas across multiple domains in cortex organization.

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In summary, by examining individuals with dysplasia, we provide evidence that the association sensorimotor cortex represents abstract action types, reaching and grasping, regardless of performed by hands or feet. The current study extends past literature on effector-independent representation by controlling for potential manual motor imagery, and identifies a level of abstraction beyond homologous muscle structure between the two hands. Effector-independent representation in motor domain adds to research in the domains of visual and auditory perception that the organization principle in association areas is based on abstract function and computation, regardless of specific sensory inputs or motor effectors, for both perception and action.

Methods

Participants: Four individuals born with severely shortened or completely absent upper limbs (individuals with upper limb dysplasia), and nine typically developed control participants, matched for age (no group difference; $P < 0.29$), participated in the experiment. The IDs' data in a series of behavioral and neuroimaging experiments have been reported previously (Striem-Amit et al., 2017; 2018; Vannuscorps et al., 2019). For the correspondence of participant codes across studies see **Supplementary materials**. The causes of dysplasia were genetic, ototoxic medications (thalidomide), or unknown. See **Supplementary materials** for a summary of the characteristics of the IDs. None of the IDs had a history of phantom limb sensations or movements, and all were adept at performing everyday actions with their feet. Two control participants were excluded from analyses due to missing data for technical reasons.

Experimental Design and Procedure: The experiment was conducted in a block design, with each type of effector (feet in the IDs, hands and feet in the controls) tested in two runs of 255 TRs each. The order of hand and foot runs was randomized across control participants. Each run began with a baseline period of 10 TRs, followed by reaching and grasping trials. Participants began with the legs rested naturally on a triangular support pillow and the hands resting on the sides of the abdomen. A foam bar (1 cm wide, 4cm tall, 6cm deep) was placed ~30 cm centrally in front of the hands or feet, equidistant from both sides (**Fig. S1**). Each trial started with an auditory instruction on the effector side and action type (e.g. "right reach"). At the end of the two-second instruction, participants began to perform the instructed action four times at auditory cues (metronome) spaced by 1.5s intervals. At each auditory cue, participants completed the movement and returned the limb to the starting position. In each reaching movement, participants reached towards and touched the foam bar with the tips of the fingers (with the hand flat open) or toes (see **Figure 1A**). In each grasping movement, participants reached towards and grasped the foam bar between digit 1 and digit 2 of the hand or foot (**Figure 1A**; thumb and index finger for the hand). Trials were spaced by 4 seconds. Twenty-five percent of the trials were followed by a prolonged 16-second rest period to better model the baseline. Each combination of side and action type was repeated in eight trials within each run, with trial order pseudo-randomized. All trials were visually-inspected by an experimenter during their execution to make sure they were accurately performed.

Functional Imaging: The blood oxygen level-dependent (BOLD) fMRI measures were obtained in a Siemens Trio 3T scanner at the Center for Brain Science at Harvard University. For acquisition details, see **Supplementary Methods**. Data that support the findings of this study are available from the corresponding authors upon reasonable request.
Data analyses were performed using the Brain Voyager QX 21.4 software package (Brain Innovation, Maastricht, Netherlands) using standard preprocessing procedures. The first two images of each scan (during the first baseline rest condition) were excluded from the analysis because of non-steady state magnetization. Functional MRI data preprocessing included head motion correction, slice scan time correction and high-pass filtering (cutoff frequency: 3 cycles/scan) using temporal smoothing in the frequency domain to remove drifts and to

improve the signal to noise ratio. No data included in the study showed translational motion exceeding 2 mm in any given axis, or had spike-like motion of more than 1 mm in any direction.

Functional and anatomical datasets for each participant were aligned and fit to standard Talairach space (Talairach & Tournoux, 1988). Anatomical cortical reconstruction procedures included segmentation of the white matter using a grow-region function embedded in Brain Voyager. Analyses were conducted in the volumetric space and then superimposed to cortical space. Single-subject data were spatially smoothed by a 6mm full-width-half-maximum (FWHM) Gaussian kernel for the univariate analyses, and a 3mm FWHM Gaussian kernel for MVPA.

Univariate analyses: We first performed random-effects (RFX) ANOVAs to examine the main effect of effector/group and action type. We then performed GLM contrasting between reaching and grasping within each group, using RFX GLM analyses (Friston et al., 1999) for the control group, and fixed-effect GLM for the IDs due to the sample size. These were complemented by additional probabilistic mapping of the overlap of significant activation across individuals (**Fig. S4D**) and presentation of single subject data for the various ROIs (**Fig. S9**), to illustrate the consistency of the findings within this group. Activation maps were thresholded at $p < .01$ and corrected for multiple-comparison at $p < .05$ level using the spatial extent method, a set-level statistical inference correction (Forman et al., 1995; Friston et al., 1993), implemented in Brainvoyager.

To investigate the effector-dependence of the sensorimotor hand area, which did not appear at a whole-brain group-level analysis, we sampled the sensorimotor cortex ROI using a functional ROI from a simple motor localizer conducted on the same participants (Striem-Amit et al., 2018). The typically developed controls performed simple flexing/contraction movements of different body parts, including the right and left hand, foot and shoulder as well as the bilateral mouth and abdomen in separate blocks. Data was analyzed using standard preprocessing as performed here, and analyzed in RFX GLM analysis. For full detail of the experimental design and analysis see Striem-Amit et al., 2018. For the purpose of the current analysis, a contrast was computed for right hand flexing as compared to the right foot, shoulder, and bilateral mouth and abdomen, at $p<0.05$ corrected for multiple comparisons, to define the hand-selective ROI in the left cortex. A foot-selective ROI was also defined for each group separately for the multivariate analyses (see below). For the controls, the foot ROI was computed by a contrast of right foot flexing vs. flexing the right hand, shoulder, and bilateral mouth and abdomen, thresholded at $p<.001$ to obtain a cluster constrained within the primary sensorimotor cortex. For the IDs, we calculated a contrast of right foot flexing vs. flexing of bilateral mouth and abdomen, thresholded at $p<1e-20$, to achieve a similarly sized ROI.

Multivariate analyses: Whole-brain searchlight MVPA were performed using a linear support-vector machine classifier implemented in the CoSMoMVPA toolbox (Oosterhof, Connolly, & Haxby, 2016; Vannuscorps et al., 2019), with each spherical searchlight containing 200 voxels. First, z-normalized β weights were estimated for each trial using Brain Voyager. For within-effector decoding, classification accuracies were calculated using leave-one-trial-pair-out N-fold cross-validation (Gallivan et al., 2013): In each iteration, one trial from each action type was left

out as the testing dataset, and the classifier was trained on the remaining dataset. The final decoding accuracy was the average across all iterations. For each participant, 100 null maps were generated for each analysis by randomly shuffling action-type labels across trials. These chance-accuracy maps were then used at group level for multiple-comparison correction for ROI MVPA (10000 simulation iterations; Oosterhof et al., 2016; Vannuscorps et al., 2019).
To investigate if specific brain regions represent action-type information, we performed ROI MVPA. To assess hand-action regions independently from our experimental data, we sampled ROIs used to investigate action representation across hands in a previous study, based on reported peak Talairach coordinates (Gallivan et al., 2013; **Figure 2A**; see **Table S2** for ROI list and coordinates). Each ROI was an 8mm-radium sphere centered on the coordinate reported in **Table S2**. Centers of the ROIs were shifted from the coordinates reported in the original study (Gallivan et al., 2013) within one standard deviation when necessary to prevent overlapping between ROIs. Body-part-selective ROIs sampled based on the control motor experiment were also examined (**Figure 2B**). Within each ROI, decoding accuracy of each voxel was extracted from the searchlight MVPA results and then averaged across voxels. For each group and ROI, an average accuracy was calculated by averaging across all individuals. To determine the significance level of the decoding accuracy, a bootstrap permutation method was used. In each iteration, one of the null maps from each individual was sampled, then a new decoding accuracy was calculated for each group and ROI based on the null maps. The sampling procedure was repeated for 10000 iterations, resulting in 10000 decoding accuracies under the null hypothesis. Significance level was calculated by counting the number of null decoding accuracies that surpassed the actual decoding accuracy, with less than 5% ($p<.05$) deemed significant. For each effector-side and group, significance level of decoding accuracy was corrected for the number of ROIs at FDR $q<.05$.

Control for magnetic field distortion: Performing arm movements in the scanner may distort the magnetic field and induce artifacts that occur instantaneously at the time of movement (Culham et al., 2003). To verify such movement-induced artifacts could not have driven our results, we re-analyzed our data by explicitly modelling instantaneous movement-induced artifacts using box-car functions. All regions showing a main effect of action type retained their effects after regressing out artifacts, indicating that our reported results reflects action hemodynamic response and not field distortions (**Fig. S9**). Additionally, we conducted a control experiment in which a phantom was scanned while an experimenter performed the same reaching and grasping actions in the scanner. If our findings were results of movement-induced artifacts, we would also see an effect of action type on the phantom. We show that this is not the case (**Fig. S10**), confirming that our results cannot be accounted for by such artifacts.

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