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Review article

Cortico-spinal modularity in the parieto-frontal system: A new perspective on action control

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ABSTRACT

Classical neurophysiology suggests that the motor cortex (MI) has a unique role in action control. In contrast, this review presents evidence for multiple parieto-frontal spinal command modules that can bypass MI. Five observations support this modular perspective: (i) the statistics of cortical connectivity demonstrate functionally-related clusters of cortical areas, defining functional modules in the premotor, cingulate, and parietal cortices; (ii) different corticospinal pathways originate from the above areas, each with a distinct range of conduction velocities; (iii) the activation time of each module varies depending on task, and different modules can be activated simultaneously; (iv) a modular architecture with direct motor output is faster and less metabolically expensive than an architecture that relies on MI, given the slow connections between MI and other cortical areas; (v) lesions of the areas composing parieto-frontal modules have different effects from lesions of MI. Here we provide examples of six cortico-spinal modules and functions they subserve: module 1) arm reaching, tool use and object construction; module 2) spatial navigation and locomotion; module 3) grasping and observation of hand and mouth actions; module 4) action initiation, motor sequences, time encoding; module 5) conditional motor association and learning, action plan switching and action inhibition; module 6) planning defensive actions. These modules can serve as a library of tools to be recombined when faced with novel tasks, and MI might serve as a recombinatory hub. In conclusion, the availability of locally-stored information and multiple outflow paths supports the physiological plausibility of the proposed modular perspective.

1. Introduction

A pervasive perspective on brain function holds that the cerebral cortex controls the body through a single output: the primary motor cortex (MI; F1). This classical view goes hand in hand with a serial processing framework, in which information flows through a unique and unidirectional pipeline; first perception, then cognition, and finally action. But this serial view is contradicted by a wealth of anatomical, physiological, and clinical data and fails to account for the highly parallel architecture of the cerebral cortex. Then why would action control still rely on a single output? We believe that seeing MI as the sole output of the cortex is an outdated view which no longer fits modern neuroscience. Maintaining this view will hamper interpretation of modern highly complex data and might even lead to a developmental *cul-de-sac* if neuroscience continues to inspire machine-learning designs.

Here we propound a modular perspective, arguing that there exist multiple parieto-frontal command modules that – depending on task demands – bypass MI and convey motor commands directly and efficiently to the body. This view is in line with the parallel nature of cortical circuits, and the notion that motor commands are encoded by distributed brain systems (Mountcastle et al., 1975; Mountcastle, 1978). Input to each module can stem from different regions, and the resulting outflow can follow different pathways, depending on the alignment between task demands and properties of the brain regions constituting a module.

This perspective explains the heterogeneity of functions of individual cortical areas (Caminiti et al., 2015; Daitch and Parvizi, 2018), their cortico-cortical relationships (Caminiti et al., 2015, 2017), and the existence of multiple cortico-spinal systems (Kuypers, 1960, 1962, 1964,

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Nomenclature

Abbreviation	Area's Name (Brodmann's area)
PARIETAL	
AIP	anterior intraparietal area
LIP	lateral intraparietal area
MIP	medial intraparietal area
Opt	occipital parietal transition area (7a)
PE	anterior parietal area PE (5)
PEc	caudal part of area PE (5)
PEip	intraparietal area PE
PF	IPL area PF (7b)
PFG	IPL area PFG (7b)
PG	IPL area PG (7a)
PGm	medial parietal area PG (7 m)
PGop	area PG op (parietal operculum)
SI	primary somatosensory area (1,2,3)
SII	secondary somatosensory area
V6	parieto-occipital visual area 6 (19)
V6A	visual Area 6 A, dorsal part of parieto-occipital area (19)
VIP	ventral intraparietal area
FRONTAL	
10	frontopolar area 10 (10)
14	area 14
11 l	lateral part of area 11 (11)
12 l/m	lateral and medial part of orbitofrontal area 12 (12)
12 l/m	lateral and medial part of orbitofrontal area 12 (12)
13a/b	areas 13a, 13b
13l	lateral part of area 13
13m	medial part of area 13
45A	area 45 A
46dc	dorso-caudal part of area 46
46dr	dorso-rostral part of area 46
46vr	ventro-rostral part of area 46
8Ad	antero dorsal part of area 8 (8)
8Av	antero-ventral part of area 8 (8)
8B	area 8B (8)
9 l	lateral part of area 9 (9)
9 m	medial part of area 9 (9)
c12r	caudal part of rostral area 12r (12)
c46vc	caudal part of area 46 ventro-caudal
DO	Dorsal Opercular area DO
F2	dorso-caudal premotor area (PMdc) (6)
F2preCD	part of F2 around the precentral dimple (6)
F2vr	ventro-rostral part of area F2 (6)
F3	Supplementary motor area (SMA) (6)
F4	Caudal ventral premotor area PMv (6)
F5	Rostral ventral anterior premotor area PMv (6)
F5a	part of F5 in the postero-ventral bank of the arcuate sulcus (area 44)
F5b	part of F5 in the postero-dorsal bank of the arcuate sulcus
F5c	posterior part of area F5
F6	pre-Supplementary motor area, (pre-SMA) (6)
F7	dorso-rostral premotor area (PMdr) (6)
F7-SEF	Supplementary Eye Field in medial F7 (6)
GrFO	Granular Frontal Opercular Area (ProM)
MI	primary motor cortex (F1) (4)
i12r	intermediate part of rostral area 12 (12)
PrCO	Precentral Opercular area
r12r	rostral part of rostral area 12 (12)
r46vc	rostral part of area 46 ventro-caudal
TEMPORAL	
EC	Entorhinal cortex
LB2	area in the lower bank of anterior part of the temporal sulcus
MST	medial superior temporal area
MT	middle temporal area
PC	perirhinal cortex
STPm	medial part of superior temporal posterior area
TEa/m	anterior and medial temporal areas TE
CINGULATE	
CMAd	dorsal Cingulate Motor Area
CMAv	ventral Cingulate Motor Area (part of 23c) (23)
24	cingulate area 24 (24)
23a	part of cingulate area 23 (23)
23b	part of cingulate area 23 (23)
24a	part of area 24 (24)
24b	part of area 24 (24)
24c	part of area 24; rostral Cingulate Motor Area (CMAr) (24)
31	retrosplenial cortical (RSC) area31
mCSv	macaque Cingulate Sulcus visual area, part of area 23c
PEci	cingulate area PE
OCCIPITAL	
V1	visual area 1, Brodmann's area (17)
V2	visual area 2 (18)
V3	visual area 3
V4	visual area 4

1981, 1982; Kuypers and Brinkman, 1970; Toyoshima and Sakai, 1982; Nudo and Masterton, 1990; Dumm and Strick, 1991; He et al., 1993; Galea and Darian-Smith, 1994; He et al., 1995; Matelli et al., 1998; Rozzi et al., 2006; for reviews see Lemon, 2008; Strick et al., 2021). It is also in line with the notion that modules exist at most scales, from cortical columns, through neural assemblies and to functional networks across hemispheres (Mountcastle, 1978, 1997; Bullmore and Sporns, 2009; Meunier et al., 2010; Innocenti et al., 2022). At each of these scales, including the scale of cortical areas that we introduce here, the modules can be defined and explained by principles of parallel processing, adaptability, information redundancy, robustness to noise, algorithmic similarity, and metabolic efficiency (Kashtan and Alon, 2005; Bullmore and Sporns, 2009; Valencia et al., 2009; Meunier et al., 2010; Bullmore and Sporns, 2012; Clune et al., 2013; Chen et al., 2021).

Recent studies have provided further evidence for this modular framework, detailing the organization of parieto-premotor anatomy (Rathelot et al., 2017; Innocenti et al., 2019; Caminiti et al., 2021), as well as lateral (Morecraft et al., 2019) and ventral (F5; Borra et al., 2010) premotor projections to the spinal cord. Studies have also characterized axon diameter, and hence conduction velocity (Hursh, 1939), of those cortico-spinal systems (Innocenti et al., 2019): Within the same descending pathway, either slow or fast axons can be recruited depending on task difficulty (Miri et al., 2017), which is ideal for a parallel, modular architecture.

We start by discussing action timings, which provide both instructive and solid evidence that the cortex is a parallel processor divided into multiple communicating modules, each of which have at least one direct outflow tract to the spinal cord.

2. Timing of action initiation supports the modular architecture of corticospinal commands

The amount of time necessary to transform motor intentions into actions depends both on task difficulty and anatomo-functional constraints, such as functional network architecture, axon diameter, synaptic efficacy, and energy costs. Therefore, the timing of motor actions is informative of those same anatomo-functional constraints, allowing us to infer functional network architecture.

For example, simple tasks such as reaching to a visual target are fast, while more complex tasks like perceptual categorization take longer. Traditionally, results from such more complex tasks were taken to indicate a steady transformation of information from input to output, where motor-related effects always come last, and action initiation only occurs after a long forward *serial* transfer of information from primary cortices. One example of such traditional reasoning comes from a Go/No-Go categorization study. While the No-Go stimulus elicited a first EEG deflection 150 ms after onset, a deflection that allegedly reflected motor preparation only emerged at about 350 ms (Thorpe et al., 1996). However, as we demonstrate in this section, neural signals that will result in action initiation often bypass much of the cortex. In practice, this means that stimulus processing and action onset largely occur in *parallel,* and without necessarily involving MI.

Evidence for this view is abundant in the non-human primate literature. Freedman et al. (2001) reported single cell responses reflecting categorical decision in the lateral prefrontal cortex (lPFC) at about 100 ms. This is surprisingly early, considering the time that would be needed for the signal to pass through all structures traditionally involved in analyzing visual images before the onset of hand movement (RT= 250–260 ms). This suggests that a fast feed-forward sweep of information is taking place, starting from the retina, passing through V1, V2, V4, posterior (PIT) and anterior (AIT) infero-temporal areas, and ending in prefrontal cortex (Thorpe and Fabre-Thorpe, 2001). Further time is necessary to 1) recruit PMd (F2) and the corticospinal tract originating in MI (MI-CST) (Lu et al., 1994); 2) pass the electromechanical delay related to hand muscle activation and movement onset (Cavanagh and Komi, 1979; Schmid et al., 2019; Novembre et al., 2018) and, finally, 3) overcome limb inertia. Other studies in monkeys have shown that even such a short forward sweep is not obligatory: During visual discrimination tasks, the earliest response in V1 occurs at approximately 50 ms, and neural activity starts predicting the animal's choice at approximately 150 ms (Ledberg et al., 2007). The recruitment time of neural activity in other areas, including PMd and MI, suggests that sensory analysis and motor outflow processing mostly overlap in time.

The parallel processing view is further supported by the theoretically shortest possible time necessary to transmit information from the retina to the cortex and finally to the musculature: This minimal time matches the latency of the earliest EMG activity after stimulus onset, indicating that very fast cortical processing needs to happen before actions can be initiated. Therefore, a full sweep across multiple cortical areas is highly unlikely to be necessary, or even possible, before action onset. At input stage, estimates of the retino-V1 delay range between 35 and 45 ms (see Novak and Bullier, 1997; Lamme and Roelfsema, 2000; Pessoa and Adolphs, 2010; Ledberg et al., 2007). The intra-cortical occipito-parietal delay is about 20 ms (Ledberg et al., 2007), while histological studies, that do not account for synaptic transmission, predict shorter delays from superior parietal (SPL) areas (such as PEc) to both MI and area F2 (about 2 and 3 ms, respectively) (Innocenti et al., 2014). At output stage there is a delay of less than 20 ms between MI and the onset of activity in hand muscles (Fetz et al., 1989). The sum of these three delays (input, intracortical and output) is 77–87 ms, and fits well with the earliest onset (~80 ms) of EMG activity in the limb muscles after presentation of a reaching target (Georgopoulos et al., 1981, 1982).

3. The modular nature of command functions

Four lines of evidence in addition to action timing support the notion of a modular and parallel parieto- premotor[1] system: 1) anatomical connectivity, 2) functional similarities between brain areas, 3) metabolic efficiency, and 4) lesion studies. We briefly introduce each of these lines of evidence here, and then expand on them one-by-one for each module in the sections below.

It is important to note that while these different lines all agree that the system is modular and parallel, not all evidence unequivocally agrees about which regions should be grouped in a module. Indeed, any modular definition will still entail considerable functional and physical overlap between modules. Therefore, we have attempted to describe a system of modules which explains as much variability in these four lines of evidence as possible, while remaining somewhat intuitively understandable. Occasionally, this means that some anatomically connected areas emerging from cluster analysis might not be considered part of the same module, due to their divergent functional properties. Unfortunately, the current state of our knowledge does not allow for irrefutably-defined modules, consistent with every possible metric. It is even unlikely that any such modules could be defined given perfect information about the brain; furthermore, it can be hypothesized that modules dynamically emerge depending on the task and their functional architecture, and interactions can be reshaped based on novel information prompting an update of the original motor intention (more on this in the "future perspectives" section).

3.1. Evidence # 1: anatomical connectivity

Statistical analysis of anatomical connections supports modularity. First, it allows defining cortical *clusters* (Averbeck et al., 2009a; Caminiti et al., 2015, 2017), which are *not* the same as modules, but do form the *basic building blocks* of modules. Clusters are composed of strongly connected cortical areas that are often spatially close (i.e., they have short path length) and share functional properties (Sporns et al., 2000; Hilgetag and Kaiser, 2004). Second, it shows that clusters are connected to each other with varying strengths. Groups of strongly connected clusters often contain at least one area that projects to the spinal cord. This is the start of how we define a *module*: areas that (a) are part of clusters strongly connected to each other, and (b) have one or more spinal projections that (c) do *not* originate from MI. These areas are more likely to be part of the same module. The criteria for labelling the cortical areas, as well as their connectivities shown in Fig. 1, are described in Caminiti et al., *e*Neuro (2017). Concerning the correspondence of parietal areas between macaque monkeys and humans, we refer to Table 1 of Caminiti et al., Neurosci and Biobehav Rev, 2015.

3.2. Evidence # 2: functional similarity

Functional similarity between areas also supports the modular organization and the definition of modules. Where statistical connectivity between clusters defines a skeleton for which areas *could* be part of a module, functional similarity allows fine tuning of the specific areas composing a module. In this way, a module is not strictly limited to

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[1] We define premotor areas as those that are anterior to M1, project to M1, and additionally project directly to the spinal cord. Under this definition, some areas that we discuss (e.g., area 46) are labelled prefrontal rather than premotor. However, given that most frontal areas of interest to this work are labelled as premotor, we will refer to the wider networks discussed in this manuscript as parieto-premotor. We also note that the original label "premotor" was functional rather than anatomical (Wise SP, The primate premotor cortex fifthy years after Fulton, Behav Brain Res,1985; 18–78–88, doi:10:01166–4328 (85)90064–6). Our definition is both anatomical and functional, and mostly based on cortical connectivity.

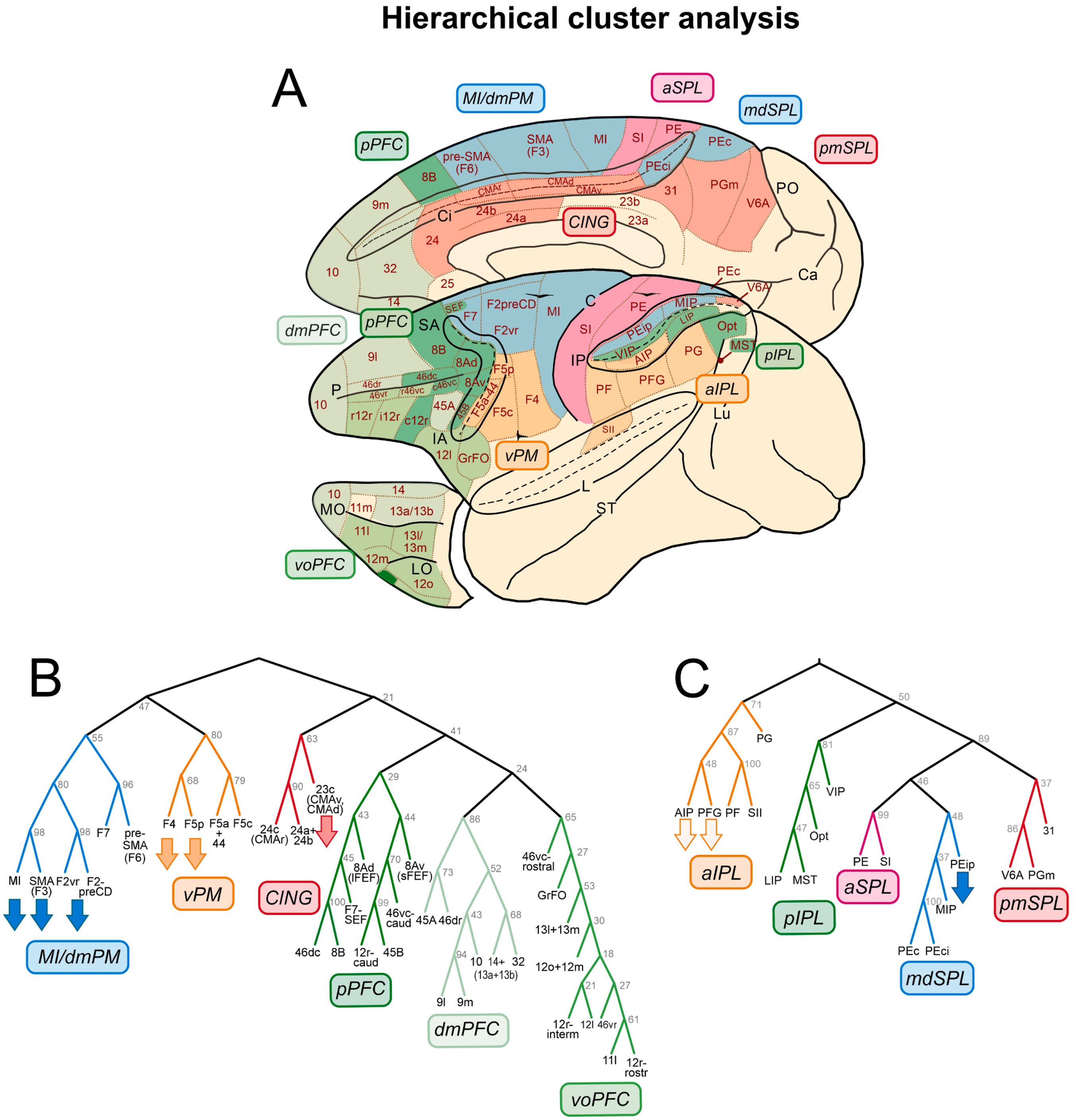


Fig. 1. A. Hierarchical cluster analysis. Brain figurine showing the location of cortical areas on the mesial, lateral and orbito-frontal aspects of the macaque cerebral cortex. Sulci are "opened", to better display the location of areas buried in their banks: Principal (P); Superior (SA) and Inferior (IA) arcuate, lateral (L), intraparietal (IP), and cingulate (CG). Sulci in the mesial aspect of the hemisphere are: parieto-occipital (PO) and fissure (Ca). In the lateral aspect of the hemisphere: Principal (P), Lu (Lunate), Superior temporal (ST). In the orbitofrontal cortex, LO and MO indicate Lateral and Medial Orbital sulcus, respectively. Cortical areas are defined on the basis of both architectonic and connectional criteria (see text). In both parietal and frontal cortex, colors indicate the location and topography of cortical clusters. B. Frontal trees generated by the cluster analysis. Numbers at each branch node indicate the number of times a cluster occurred in the 100 most likely trees. The three prefrontal (PFC) clusters, ventro-orbital *(voPFC),* dorsomedial *(dmPFC),* and posterior *(pPFC)* are indicated with different green shades, as in their location in the brain figurine (A). Similarly, red indicates the cingulate (*CING)* cluster; orange, ventral premotor (*vPM*) cluster; light blue, motor-dorsomedial premotor (*MI/dmPM)* cluster. The arrows pointing downward are located below the areas of origin of a cortico-spinal tract. C. Superior (SPL) and inferior (IPL) parietal lobule clusters generated from the 100 most likely trees of cluster analysis: red, postero-medial (*pmSPL*); light blue, medio-dorsal (*mdSPL*); magenta, anterior SPL *(aSPL)*, green, posterior IPL (*pIPL*), orange, anterior (*aIPL)*. Conventions and symbols are the same as in A and B. Frontal and parietal clusters of corresponding colors include areas preferentially connected through parieto-frontal and/or fronto-parietal connections.
Modified from Caminiti et al. (2017).

entire clusters if some areas in its hypothetical constituent clusters simply do not share sufficient functional properties with the other areas. Similarly, it allows us to occasionally include areas from clusters that are not statistically strongly connected, because they instead seem to perform almost identical roles to the rest of a module.

3.3. *Evidence # 3: metabolic efficiency*

The third line of evidence hinges on the superior metabolic efficiency of a modular system: motor commands do not need to travel far through the cortex before being sent to the spinal cord. Given that fast-descending myelinated axons are far more numerous in cortico-spinal than in cortico-cortical projections, this modular bypass of MI saves substantial energey costs by not utilising slow unmyelinated pathways (Caminiti et al., 2009; Innocenti et al., 2019; Tomasi et al., 2012). Increased metabolic costs are not only associated with *transmitting* information through unmyelinated axons, but also with *integrating* it: unmyelinated axons convey information firing rates, rather than precise and energy-efficient spike-timing (Wang et al., 2008). Finally, metabolic costs are exacerbated in larger brains, given that they scale up linearly with conduction distance (Wang et al., 2008).

3.4. *Evidence # 4: lesion studies*

The modular nature of command systems is finally supported by the fact that lesions of each module have distinct effects that are consistent within module, but not present when MI is lesioned (Krakauer and Carmichael, 2017).

In the next sections, we will focus on command modules for which the literature provides convincing evidence: congruence between anatomical, physiological, functional, and lesion studies. Besides the well-documented MI cortico-motoneuronal module devoted to hand dexterity (see Lemon, 2008; Strick et al., 2021), we identify five parieto-frontal modules (see Modules Synopsis), involved in various motor command functions. These modules also target the basal ganglia and the cerebellum, giving them a central role in action control.

4. Dorsal parieto-frontal spinal module: reaching, tool use, object construction

The dorsal parieto-fontal spinal module, alone or in synergy with other corticospinal modules, encodes functions related to motor intention for purposeful eye-hand operations in peripersonal space. These include arm reaching and hand pre-shaping before grasping, tool use and object manipulation, and construction. All these functions are impaired after posterior parietal cortex (PPC) lesion. This module's operations are rooted in PPC and its distributed system involving select frontal and cingulate areas, heavily connected to pontine nuclei and hence the cerebellum. This module is composed of areas of the *medio-dorsal SPL cluster* (PEci, PEc, MIP, PEip)**,** the *anterior IPL cluster* (area PG), and the *postero-medial SPL cluster* (V6A, PGm). The module heavily interacts with the *dorso-medial premotor cluster*, centered on F2. The dorsal partieto-frontal module's core projections to the spinal cord stem PEip, although it can also transmit information through F2.

This module projects directly to the motor centers of the spinal cord through cortico-spinal pathways stemming from both parietal and premotor areas and is influenced by nigral afferences from the basal ganglia. As for all other modules, this module also projects to – and receives input from – sub-cortical areas, providing alternative routes to the spinal cord. The sub-cortical projections of a module generally mirror the cortico-cortical connections between areas of a given module, and provide additional anatomical substrates for the modular affiliations of nearby cortical clusters. Specifically for the dorsal parieto-frontal module, area SI receives thalamic projections from different components of the Ventral Posterior (VP) and from Ventral Lateral posterior (Padberg et al., 2009) nuclei. Areas PE and PEip are targets of the Lateral Posterior (LP), Medial Dorsal (MD) and Lateral Pulvinar (PuL), while the Medial Pulvinar (PuM) projects to PE (Cappe et al., 2009). Multiple thalamic nuclei also project to AIP, including PuM, PuL, LP, VPLc, VPLo, CL, MDmf, VPI, VLc and PCn (Clower et al., 2005). Some of these nuclei (VLc, MDmf, CL) are targets of nigral and cerebellar afferents (Percheron et al., 1996) and can relay information from the substantia nigra pars reticulata (SNpr) and dentate nucleus to AIP (Clower et al., 2005). The medial parietal areas PEci, PGm (7 m) and PEc receive projections from a common set of thalamic nuclei: the anterior intralaminar nuclei (AILN), dorso-caudal MDdc, LP, and Pu (Buckwalter et al., 2008). The thalamic input to V6A stems mostly from LP and PuM (Gamberini et al., 2016; see also Impieri et al., 2018). Finally, anterior IPL areas (PF and PFG) are dominated by thalamic inputs from VPM and PO (Schmahmann and Pandya, 1990). This complex pattern of thalamic, cerebellar and basal ganglia projections suggests that a multisensory and sensorimotor interplay must occur in the terminal parietal territories of this module which is in keeping with a wealth of information accumulated over the years by physiological studies.

4.1. *Reaching*

Reaching with the hand relies on complex computations spanning multiple areas of the brain: specifying a motor plan, a trajectory, executing and controlling the movement. The entire process aims to nullify the so-called "motor error": the vector difference between the position of the hand and the target (for a review see Battaglia-Mayer et al., 2014).

4.1.1. *Anatomo-functional organization*

Reaching is mostly achieved by a network involving the *pmSPL, mdSPL, and aSPL clusters.* Area V6A receives visual input from V6 and PGm and conveys visual information to all other SPL areas of this module (PEc, MIP, PEip). Similarly, SI and PE provide somatosensory and somatomotor information, respectively, to the same parietal areas, although only SI projects directly to PEip. All above connections are reciprocal and their recursive signaling is believed to subserve early coding of eye-hand coordination and the visuomotor transformation for reaching. Area PG *(aIPL cluster)* also participates in early transformations, due to visuomotor inputs from MIP, Opt, and, to a lesser extent, PEc. PG also receives inputs from the dorsal dysgranular insula (Idd; Rozzi et al., 2006). Areas PEc, MIP, and PEip receive input from dorsal premotor cortex (F2), for example early signals of unexpected changes in the spatial location of a target. Such signals play a crucial role in the on-line control of reaching (Archambault et al., 2008; 2011). As shown in Fig. 2, in parietal cortex MI is only connected (reciprocally) to PEip, the area from which this module's parieto-spinal projection originates.

Many studies have shown that visual reaching in monkeys is encoded in spatially congruent gradients encompassing visual information about target location, as well as the position and direction of the eye and hand. Such spatial congruence within the global tuning fields (Battaglia-Mayer et al., 2000) ensures tight coordination in space and time, which is particularly important because gaze lands on the target well before hand movement onset, due to both saccade velocity and limb inertia. These combined signals modulate neural activity in clusters of parieto-occipital (V6A, 7m superior parietal (PEc, PEip, PE; MIP), and frontal (PMd, MI) areas, shaping motor intentions for reaching within a distributed network (Lacquaniti et al., 1995; Snyder et al., 1997; Mascaro et al., 2003; Pesaran et al., 2006). IPL areas also contribute to reaching (Hyvärinen and Poranen, 1974; Mountcastle al, 1975). This network operates recursively, as most connections are reciprocal (Johnson et al., 1996; Battaglia-Mayer et al., 2000, 2001; Marconi et al., 2001). The temporal delays in this network depend, at least in part, on information transfer through long oligosynaptic pathways (Johnson et al., 1996; Matelli et al., 1998) that conduct temporally dispersed action potentials and require spatial and temporal summation to discharge

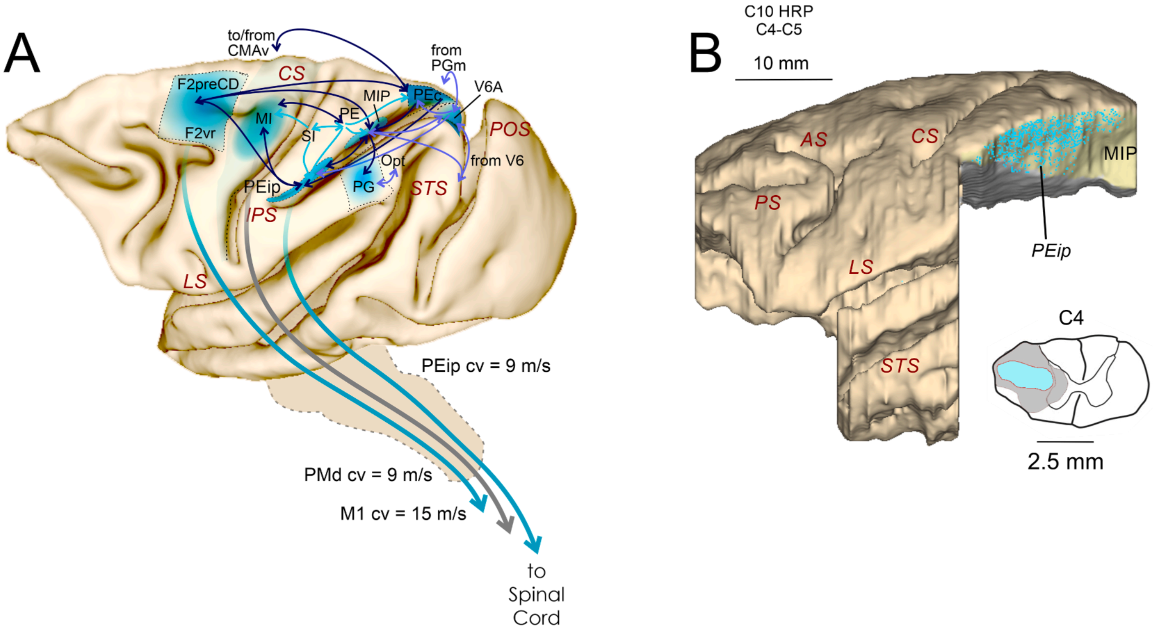


Fig. 2. Dorsal parieto-frontal spinal module: reaching, tool use, object construction. A.Macaque brain showing the cortico-cortical and cortico-spinal projections underlying hand reaching and tool use, as described in the text. Arrows indicate visual/visuomotor (violet) and somatosensory (cyan) inputs (mostly reciprocal) to the reaching-related areas V6A, PEc, MIP, PEip, PG. Input-output projections from PEip and both sectors of F2 (F2pre-CD, F2vr) are in dark blue. B. Antero-posterior distribution of the cells of origin (blue dots) of the PEip-spinal projection, after injection of a retrograde tracer (HRP) in the cervical segments (C4-C5) of the spinal cord. The image is a 3-D reconstruction of the lateral aspect of the hemisphere in which the inferior parietal lobule, including the ventral bank of the IPS, has been "removed" to show the location of parieto-spinal projecting cells, up to the border with area MIP. STS indicates the Superior Temporal Sulcus, other conventions as in Fig. 1. Here and in the following figures data on conduction velocity are from Innocenti et al. (2019).
Modified from Caminiti et al. (2017); original data on the parieto-spinal projection from Matelli et al. (1998).

post-synaptic targets.

Area F2 (Pesaran et al., 2006) receives input from SPL cells (Johnson et al., 1996), as does MI. MI therefore receives reach-related information through F2 and/or directly from SPL (Johnson et al., 1996; Caminiti et., al, 2017). However, during reach-grasp-manipulate tasks, a coupled dynamical systems model revealed that MI can drive activity in F2 (D'Aleo et al., 2022), demonstrating task-dependent interactions within this distributed network.

Parieto-occipital areas V6A and 7 m project to lateral intraparietal area (LIP), which in turn is linked to the frontal eye field (FEF, area 8). The motor outflow systems of both parietal and frontal eye-hand domains converges on the intermediate and deep layers of the superior colliculus (SC) and on the mesencephalic reticular formation (MRF), where neural activity is influenced by both eye and hand reach signals (Werner, 1993; Werner et al., 1997a, 1997b). The SPL-IPL interplay and the MRF projection to the spinal cord both play a crucial role in scaling and coordinating the onset of eye and hand movements during reaching. Additionally, the influence of wrist orientation and hand grip type in area V6A (Fattori et al., 2009, 2010) suggests that signals about both hand transport and pre-shaping are combined at an early stage of the visuomotor transformation for reaching. Finally, this reach-grasping channel seems to favor coordinating all reach-to-grasp phases (Battaglia-Mayer et al., 2000). In contrast, the lateral grasping system (see section on grasping in the lateral parieto-frontal module) might be preferentially recruited when more dexterous hand action on objects is necessary (for a review, see Borra et al., 2017).

4.1.2. *Motor output*

In macaque monkeys, parieto-spinal projections have been known for multiple decades, but several of their aspects have only recently been studied in great detail. Those relevant to reaching originates from the rostro-caudal extent of area PEip (a.k.a PEa; Fig. 2B) and includes a region characterized by large populations of reaching-related neurons (Johnson et al., 1996). The parieto-spinal axons originating from the rostral sector of PEip are addressed to the last-order interneurons of the spinal cord and their electrical stimulation evokes contralateral hand and wrist movement (Rathelot et al., 2017), as also shown in prosimians (Stepniewska et al., 2005). This function had already been described by David Ferrier (1876), who electrically stimulated the ascending parietal convolution and reported "individual and combined movements of the fingers and wrist, ending in clenching of the fist. Centers for the extensors and flexors of the individual digits could not be differentiated, but the prehensile movements of the opposite hand are evidently centralized here" (pag. 143, see fig. 29). These were not fractionated digit movements, a function typical of the "new MI" (Rathelot and Strick, 2009; Strick et al., 2021) and its monosynaptic cortico-motoneural projection, but a combined hand-wrist movement that resembles hand pre-shaping while reaching. This di-synaptic parieto-spinal projection therefore likely subserves arm reaches, given that in daily life reaching is often associated with grasping (for a review see Jeannerod et al., 1995).

This parieto-spinal projection contains axons confined to the lateral sector of the pyramid (Innocenti et al., 2019). Many axons terminate in small clusters in the pontine nuclei, forming one segment of the parieto-ponto-cerebellar system underlying action control and sensorimotor adaptation. Parieto-spinal axons in the distal internal capsule, pons, pyramid, and cervical spinal cord have very uniform size, ranging from 0.86 to 0.73 μm, with conduction velocities of about 8.79–9.58 m/s^{-1}. This parieto-spinal projection, alone or in synergy with other descending systems, can provide timely motor outflow to the functions of the parieto-spinal module. The disorders consequent to this module lesions are described in Box 1.

4.2. *Tool use*

The parietal lobe underwent significant expansion and specialization during human evolution (Caminiti et al., 2015; Goldring and Krubitzer, 2020; Bruner et al., 2017; Bruner, 2018), which is in part attributed to the emergence of tool use, making, and sensing (Stout and Hecht, 2015);

Box 1
Disorders of the Dorsal parieto-frontal spinal module: On-line control of reaching, motor intention and action perception and awareness

Reaching disorders

This module's role in reaching is supported by a classical disorder known as **optic ataxia (OA)**, caused by damage to parietal areas (lesions in humans: Perenin and Vighetto, 1988;Rossetti et al., 2019; reversible inactivation in monkeys: Battaglia-Mayer et al., 2013). OA is characterized by difficulty in accurately guiding the hand to a target and making fast online trajectory corrections when the target is displaced (Pisella et al., 2000; Gréa et al., 2002). Instead, the hand only moves to the new target location after it has arrived at the original one. Physiological studies further confirm the role of parietal cortex in online correction of reach trajectory (Archambault et al., 2009, 2011; Saberi-Moghadam et al., 2016).

OA can even occur under isometric conditions (Ferrari-Toniolo et al., 2014) and not only impairs hand movements, but also eye movement, increasing saccade RT and delaying target capture (Gaveau et al., 2008; Battaglia-Mayer et al., 2013). The breakdown of the combinatorial operation within the global tuning field of SPL neurons might be the cause of OA, leading to the collapse of the process that allows for a spatial and temporal match between information about target location, eye/hand position, and movement direction (Battaglia-Mayer and Caminiti, 2002; Mascaro et al., 2003).

In contrast to PPC lesion, reaching is not significantly affected by MI lesion (McNeal et al., 2010), and reach impairment after PMd inactivation occurs only for internally, memory-based reach sequences (Ohbayashi et al., 2016). This "resiliency" of reaching to MI lesion therefore probably rests on the parieto-spinal system stemming from intraparietal area PEip (Matelli et al., 1998; Innocenti et al., 2019; Caminiti et al., 2021), as well as the elaborate and distributed representation of reaching in the cortex (see Caminiti et al., 2017).

Motor intention disorders

The dorsal parieto-frontal module is also thought to play a role in the implicit mechanisms of motor intention. A recent cell recording study conducted on tetraplegic patients (Aflalo et al., 2022) used a variant of the Libet task (Libet et al., 1983) to examine the preconscious initiation of action: there was a sharp increase of neural activity in the superior parietal cortex hundreds of milliseconds before subjects reported an urge to move in a self-paced task. Contrary to Libet's view, Aflalo interpreted the early parietal population activity as the outcome of internal action planning operations which commence as soon as subjects decide to perform the task. This process would occur before awareness. Thus, the early parietal activity would shape an effector specific motor plan rather than an abstract motor intention (see Travers and Haggard, 2021; Travers et al., 2021). This activity is sufficient to guide patients' movement through a brain-computer interface before a subject intends to act. The construction of subjective experience, now decoupled from implicit motor planning, would rest on the neural dynamics of other areas of the parietal lobe, such as caudal IPL (Sirigu and Desmurget, 2020; Igelström and Graziano, 2017). Thus, the failure of parietal patients to predict their own actions would depend on the lack of an internal model to initiate movement.

no other species possess those capabilities to the extent humans do (Osiurak et al., 2010). Nonetheless, monkey studies have been instrumental in clarifying the neurophysiological basis of tool use.

4.2.1. *Anatomo-functional organization*

A foundational study by Iriki et al. (1996) described bimodal neurons with spatially congruent tactile (tRF) and visual (vRF) receptive fields on the arm and hand, in a parietal region encompassing areas PE and PEip. vRFs were anchored to tRFs, so that when the arm moved, the vRFs moved with it. When a monkey used a rake to retrieve food, the vRFs expanded to incorporate the rake. Neural activity related to the use of pliers has also been observed in grasping-related cells of vPM (Umiltà et al., 2008), and a set of MI corticospinal spinal neurons is also activated by tool use (Quallo et al., 2012). Finally, IPL neurons encode instantaneous force increments at the population level, providing a putative input for controlling dynamic hand force during tool use and object construction (Ferrari-Toniolo et al., 2015). This result is in keeping with the defective control of hand force in parietal patients (Ferrari-Toniolo et al., 2014), and with the involvement of anterior intraparietal cortex in the control of fine (3.8 N), rather than of large (16.6 N) fingertip forces during object manipulation (Ehrsson et al., 2001).

In humans, tool-related planning and execution activated a shared network, spanning the superior temporal, inferior frontal and ventral premotor cortex, the anterior and posterior sectors of the supramarginal gyrus, and the angular gyrus (Johnson-Frey et al., 2005). Only dorsolateral prefrontal cortex was activated uniquely during planning. Another set of studies found that a common network activates in humans and monkey when observing tool use: a bilateral system including occipitoparietal, intraparietal and ventral premotor areas. Additional tool-related activation was observed in the anterior SMG in humans only (Peeters et al., 2009; Peeters et al., 2013).

4.2.2. *Motor output*

Overall, these results suggest that the parieto-frontal spinal module plays a crucial role in tool use, given that it is based in the parietal lobe, and its spinal output stems from area PEip. This view is further strengthened by the lack of evidence for tool apraxia in monkeys or humans after MI lesion (see also Krakauer and Carmichael, 2017).

4.3. *Object construction*

Object construction is made possible by tool use (Hansell and Ruxton, 2008), and is a hallmark of human evolution (Bruner et al., 2023). Only humans are able to construct complex objects with causal understanding of the underlying process, while natural multifunctional constructions are the outcome of stereotyped action sequences, such as chimpanzee (Povinelli, 2000) and bird nests (Collias, 1964; Hansell, 2000, 2005), as well as spider webs and termite mounds (Gould and Gould, 2012).

4.3.1. *Anatomo-functional organization*

Two main processes underlie the ability to assemble complex objects: analysising the object's structure, and specifiying the necessary movement sequences (Lashley, 1951). Crowe and colleagues exploited this perspective, and elegantly demonstrated that parietal activity specifically reflects spatial analysis of object structure for construction. They recorded neural activity from inferior parietal area 7a (PG; Opt) (Chafee et al., 2005, 2007) of monkeys trained to visually explore a copy-model. The monkeys were next presented with the same model but missing a component. They then had to replace it in a choice sequence by pressing a key when the correct missing component was highlighted. Parietal activity varied in relation to the missing component, reflecting the spatial analysis necessary to guide reconstruction. The researchers were also able to identify two neural assemblies, one encoding the missing component in eye-centered, another in object-centered coordinates. The former lead the latter in time, indicating that parietal cortex can transform coordinates to be more appropriate for construction (Crowe et al., 2008).

Cell activity related to object construction has also been recorded and compared in dlPFC and PPC in a task where monkeys copied geometrical shapes that were drawn as sequences of movement segments (Averbeck et al., 2002; 2009b). The task involved cognitive factors related to shape analysis and segment position, as well as movement factors like hand position, direction, and speed. Both cognitive and motor variables modulated cell activity more in parietal than in dlPFC. Activation timing revealed that the sensorimotor representation in PPC was more balanced than in dlPFC: in PPC an equal number of cells lead or lagged the onset of hand velocity changes, while in dlPFC more cells lagged. Finally, while figure shape was more strongly represented in parietal than in dlPFC, both areas encoded shape, position sequence, direction, and segment length, revealing the combinatorial power of their neural activity.

There are no neural recording studies during 3D object construction in humans, but the field has been complemented by fMRI studies of drawing tasks. Despite the many differences between paradigms, most drawing tasks activate a core network that is remarkably similar to that inferred from 3D construction in macaques: BA6 (likely corresponding to F2 and SMA), BA7 (SPL), and BA40 (IPL and IPS) (Makuuchi et al., 2003; Gainotti and Trojano, 2018; Raimo et al., 2021). The IPL is particularly strongly activated during drawing as opposed to similar but non-constructional tasks such as writing (Yuan and Brown, 2015). Therefore macaque area 7a (PG; Opt) is considered the homologue of area PGa in humans (*clusters 4 and 5*; Mars et al., 2011), located in the posterior part of the SMG (Brodmann's area 40), and corresponding to the *posterior IPL cluster* PGa/PGp of Caspers et al. (2013). Lesions in this region result in constructional apraxia, as do prefrontal lesions (see Box 2).

4.3.2. Motor output

In contrast to lesions of IPL, no deficits of constructional abilities have been reported after MI lesion (Krakauer and Carmichael, 2017). This suggests that the various clusters of the SMG and potential rostral corticospinal projections might be the outflow system for IPL operations underlying constructional abilities, although these spinal outflow pathways in humans remain to be discovered.

5. Hippocampo-parieto-cingulate spinal module: spatial navigation and locomotion

The hippocampo-parieto-cingulate spinal module controls spatial navigation and locomotion, that require the transformation of spatial information between allocentric (world-centred) and egocentric (self-centred) reference frames. This module is rooted on the *postero-medial SPL cluster* (PGm; 7m) including also retrosplenial area 31. This serves as an interface between the *hippocampal formation and enthorinal cortex* on the one side, and the *cingulate cluster* (CMAd/v), as well as the *anterior IPL cluster* (PG; 7a) on the other. The module's core projection to the spinal cord stems from a sub-section of CMAv (the macaque Cingulate Sulcus visual area; mCSv). This complex organization is shown in Fig. 3.

5.1. Anatomo-functional organization

The two respective poles of the transformation between ego- and allocentric reference frames are the postero-medial parietal cortex on the one hand, and the entorhinal-hippocampal cortex on the other hand (Whitlock et al., 2008, 2012). The two-way transformations between these nodes likely occur in the brain areas that compose the hippocampo-parieto-cingulate system (Kravitz et al., 2011).

Sugiura et al. (2005) identified one particularly interesting intermediate region in humans: in the posterior cingulate and retrosplenial cortex (RSC), the ventral part of area 31 is strongly activated during exposure to familiar places over objects, while dorsal 31 is most active during presentation of familiar rather than unfamiliar objects and places. The RSC is also activated during autobiographical memory, prospective thinking, and navigation tasks (Vann et al., 2009). Human active spatial navigation is accompanied by theta oscillations in the RSC, with theta power reflecting heading changes rather than translational movement (Do et al., 2021). fMRI confirms such encoding of head-direction information in the RSC (Shine et al., 2016), which is reminiscent of similar observations in rodents: rat head-direction cells – which fire when the animal's head points in a specific direction – have been described there (Chen et al., 1994; Muller et al., 1996; Cho and Sharp, 2001). There are also head-direction cells outside of RSC, in parahyppocampal regions that are anatomically connected with RSC (Boccara et al., 2010; Sugar et al., 2011), and are targets of CA1 and subiculum, which are both involved in spatial navigation (O'Keefe and Dostrovsky, 1971; Sharp and Green, 1994).

Monkey RSC (area 31) has similar properties: it is also involved in visuomotor processing, since its neurons respond to large visual scenes (Dean et al., 2004), contraversive gaze shifts (Olson et al., 1996; Dean et al., 2004) and monitor eye movement and eye-position (Olson et al.,

Box 2
Disorders of the Dorsal parieto-frontal spinal module: Tool use and object construction

Tool use and object construction disorders

The neural substrates of tool use and object construction were first revealed through disorders in brain-damaged patients, referred to as **Tool Apraxia (TA)** and **Constructional Apraxia (CA)**, respectively (Wilson, 1909; Strauss, 1924; Kleist, 1934; Mayer Gross, 1935; Critchley, 1953; Hécaen and Assal, 1970). Patients with TA misused common tools, while those with CA were unable to produce faithful copies of model objects. Despite these impairments, patients displayed no deficits in sensory processing nor in general motor control. Therefore, apraxias are likely disorders of the cognitive aspects of motor behavior (Goldenberg, 2014; Krakauer and Carmichael, 2017). Crucially, both disorders are consequences of damage to a neural system centered on the IPL, consistent with the parieto-spinal module. For extended analysis and discussion of TA and CA, refer to Maravita and Romano (2018) and Gainotti and Trojano (2018) respectively.

The core lesion responsible for TA lies in the anterior part of the left SMG (Brodmann area 40), as evidenced by numerous fMRI studies (Orban and Caruana, 2014; Maravita and Romano, 2018). The network responsible for constructional abilities seems more distributed than the underlying one for tool use, and it also includes dlPFC (Possin et al., 2011). The reason might be that evolution of the motor system in humans has been characterized by an increased ability to construct new complex artifacts, rather than just using tools as an extended prosthetic arm. It also still remains debated whether CA is the result of left or right IPL lesion, since different aspects of constructional abilities and copying seem to be represented in different hemispheres (Chechlacz et al., 2014).

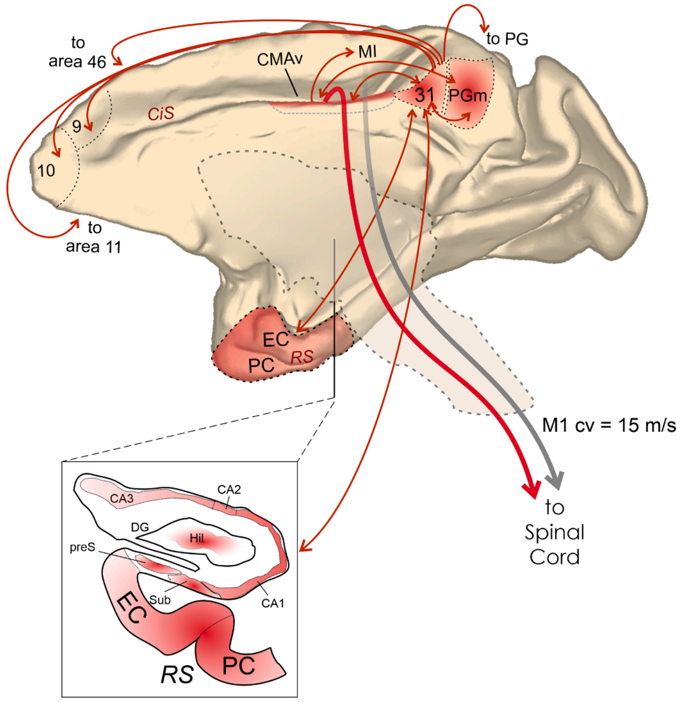


Fig. 3. Hippocampo-parietal-cingulate spinal module: Spatial Navigation and Locomotion. The core nodes of this module reside in the RSC area 31 and hippocampal formation, which includes the hippocampus, the dentate gyrus, the subiculum, presubiculum, parasubiculum, and the entorhinal cortex. RSC area 31 is recripocally connected with the hippocampal formation, the perirhinal cortex, and PGm. Major RSC projections are addressed to prefrontal areas 9, 10, 11, and 46. Additional projections are addressed to parietal area PG (7a). Area 31 and PGm project to CMAv, located in the posterior part of area 23c. CMAv, in addition to MI, projects directly to the spinal cord. The range of axon diameters, hence conduction velocities, of this cingulate-spinal projection remains to be studied. EC: entorinal cortex; PC: perirhinal cortex, Sub: subiculum preSub: presubilumum; CA1–3: hyppocampal fields; DG: dentate gyrus; Hi: hilus; RS: rhinal sulcus.

1996), the latter probably used to generate a map of the head in space. Some of these properties are shared with area 23, and suggest a relationship to the saliency of objects or locations for orienting attention, preferentially in allocentric coordinates (Dean and Platt, 2006). Therefore, area 31 might serve as an intermediate node in the transformation from allocentric maps in the hippocampus to egocentric ones in parietal cortex (Vogt et al., 1992). However, this transformation is not complete at this node, as there are neuronal populations encoding visual events in both retinocentric and egocentric coordinates (Dean and Platt, 2006). Area 31, which belongs to the *pmSPL cluster* together with PGm, receives afferents from the hippocampal formation, including the entorhinal cortex, subiculum, presubiculum and parasubiculum (Kobayashi and Amaral, 2003), as well as from parahyppocampal and perirhinal cortex. These projections are reciprocal (Kobayashi and Amaral (2007). Major RSC projections are also addressed to prefrontal areas 46 and 9, in the *posterior prefrontal cluster (pPFC)*, to area 10 (*dorso-medial prefrontal cluster, dmPFC*) and 11(*ventral orbitofrontal cluster voPFC*). Additional projections are addressed to parietal area PG *(7a; anterior IPL cluster)*. The anatomical relationships of the enthorinal cortex with hippocampus, subiculum, presubiculum, and parasubiculum in the monkey have beed studied in detail by Witter and Amaral (2021), who have outlined, among other features, a common plan of organization with nonprimate species.

Another region of interest is the mesial parietal region encompassing area PGm (7 m): it contains neurons related to virtual active navigation, and their acivity is selective for the route that monkeys track (Sato et al., 2006).

Regarding parietal maps that are used for navigation, multiple studies point to the involvement of IPL area 7a (PG). For example, Crowe et al. (2004, 2005) showed that when monkeys mentally followed a path in a maze, the neural population vector in 7a pointed towards the exit of a maze during fixation, despite no movements being made and no changes in visual input. Visual signals in 7a are in fact generally referenced to the world rather than the body (Snyder et al., 1998). Merchant et al. (2003) demonstrated a predominance of expansion over other types of visual motion, which is expected in egocentric processing of visual information for locomotion. 7a is also more responsive to changes in eye position towards extrapersonal locations than rostral IPL (Rozzi et al., 2008). Recently, Noel et al. (2022) reported this area's involvement in navigation in a closed-loop virtual navigation task aimed at studying the neural bases of the recurrent action-perception loop typical of our interaction with the environment. Neurons in area 7a encoded a mix of sensorimotor (e.g., velocity and acceleration) and latent (e.g., travelled distance and angle) variables necessary to perform the task, although 7a over-represented sensorimotor variables relative to other recorded areas (dlPFC and MSTd). 7a also predominantly coded for locations near the origin or the target of movement, further suggesting that it is involved in egocentric state transitions during navigation.

Therefore, like neural activity in the construction task, parietal cortex also contributes to covert analysis of visual input during navigation, extracting the spatial information necessary to achieve behavioural goals. All the above studies in different animal species indicate that spatial navigation is supported by a distributed system of which parietal cortex is an essential node.

Regarding the hippocampal formation, a recent study on freely moving primates during free foraging (Mao et al., 2021) demonstrated many hippocampal neurons are influenced by a broader set of spatial variables than those affecting traditional place and grid cells. Signals related to head orientation and tilt were predominant over signals concerning the animal's position and were the most realiable predictors of single neuron activity. Eye movements also strongly influenced neural activity.

These findings compliment earlier studies of the hippocampus and parahippocampal gyrus in freely moving macaques (Rolls, 1999). Those studies did not identify place cells, but instead large populations of spatial view cells, strongly influenced by visual input and the animal's direction of gaze. Rather than interpreting such activity in terms of topological maps, it was seen as encoding landmark locations, facilitating navigation from one landmark to another (see also Rolls, 2021, 2023). Importantly, the presence of eye and head postural variables does not negate the existence of topological maps in the hippocampal and enthorinal cortex. They are instead posited as essential components that modulate hippocampal activity, facilitating active sensing to guide navigation through varying environments – some requiring abstract representation, others relying on visuo-spatial information.

In all, the manner in which the transformation between allocentric and egocentric representations for spatial navigation occurs in primates remains to be fully resolved. To delve deeper, further recording experiments in freely moving macaques will be essential, during which sensory and postural variables should be quantitatively assessed. This approach might bridge the dichotomy between the representation of pure spatial maps in the hippocampus and egocentric maps in posterior parietal and retrosplenial cortex (for a review, see Zhu et al., 2023).

5.2. Motor output

This module's outflow to the motor periphery is likely to be the caudal part of area 23c (Morecraft et al., 2004), which is in part coextensive with the cingulate motor area CMAv (see Picard and Strick, 1996). In fact, this region receives significant projections from RSC area 31, and PGm (Morecraft et al., 2004).

Cingulate area CMAv is where recent studies (reviewed in Smith, 2021) locate a visually-related area, referred to as macaque Cingulate

Sulcus visual area (mCSv; Cottereau et al., 2017), whose functional properties and connectivity suggest a role in the control of locomotion. For example, mCSv activity is sensitive to optic flow and vestibular information, both of which are signals relevant to ego-motion and both probably stem from PIVC and from PEc afferents. The optic-flow inputs are selective for the focus of expansion, which is instrumental for building an invariant visual space representation during locomotion (Battaglia-Mayer et al., 2001; Raffi et al., 2002; Raffi et al., 2010). Furthermore, PEc is a potential source of somatosensory (Battaglia-Mayer et al., 2001; Breveglieri et al., 2006) and somatomotor signals (Battaglia-Mayer et al., 2001) to mCSv. Much of the module's output to mCSv probably flows through area 31 first, given their substantial interconnections.

Interestingly, mCSv is in the caudal part of CMAv, therefore within the boundaries of the leg representation, and electrical stimulation of CMAv (and CMAd) evokes not only forelimb but also hindlimb movements at relatively low threshold (Luppino et al., 1991). This is in keeping with the strong projections addressed by these areas to the spinal cord (He et al., 1995). Therefore, the signals relevant to locomotion encoded by mCSv can be conveyed to the locomotor center of the spinal cord directly by the CMAv corticospinal projection. This conclusion is further supported by the observation that control of locomotion mostly rests on the rhythmic activity of spinal locomotor centers, and that cortical control is mostly dependent on willful decisions to initiate and/or modify walking, as typical in spatial navigation (for a review see Nielsen, 2001). The conduction velocity of the CMAv-spinal projection remains to be determined. Finally, CMAv projects to motor cortex and such input might be a source of the optic flow sensitivity of MI (Merchant et al., 2001; Box 3).

6. Lateral parieto-frontal spinal module: grasping and observation of hand and mouth actions

This parieto-fontal spinal module is heavily involved in grasping, observing grasping, and observing mouth and hand-to-mouth actions, as well as in non-verbal communication. The module's operations are rooted in the parietal areas AIP and PFG, and the ventral premotor area F5a-c-p. It is further composed of the *ventral Premotor cluster (GrFO), anterior IPL cluster* (SII), and the *ventro-orbitofrontal cluster voPFC (i12r, r46vc),* as well as *infero-temporal area LB2*. This module projects to the spinal cord through one pathway from PFG, and another from F5c. There is emerging evidence that the module can additionally project through AIP.

6.1. Hand grasping

Grasping serves the purpose of interacting with daily objects and is based on complex mechanisms involving parietal, frontal, prefrontal, temporal, and insular areas.

6.1.1. Anatomo-functional organization

Grasping is encoded by a distributed system centered on inferior parietal areas AIP, PFG, and SII, all belonging to the *anterior IPL cluster*. These areas are connected to all subdivisions of ventral premotor area F5 in the *vPM cluster,* as well as prefrontal areas of the *voPFC* (Fig. 1A, C).

Parietal areas AIP and PFG are intricately connected to ventral premotor areas F5a, F5p and F5c, forming the core of a network that also includes ventral prefrontal areas (r46vc, i12r and GrFO from the *voPFC cluster),* inferior temporal areas (TEa/m) and the insular area Id. This network is central to hand grasping, often being referred to as the lateral grasping system (Bonini et al., 2010, 2011, 2012, 2014c; Borra et al., 2017). It also subserves mirror processes for hand and facial communicative actions, due to its visual inputs that can relay action observation: LIP and several superior temporal areas project to PFG (UB1, STPm, MSTd) and AIP (mostly LB2). Of these, only STPm and LB2 display consistent action observation modulation, while the others likely contribute to building such modulation in other areas without displaying it themselves. Therefore, in the mirror system for hand action observation, two main functional paths link the superior temporal area to F5, one through PFG carrying agent-related information, the other via AIP, conveying object-related signals.

F5 is also under cerebellar influence via the thalamic nuclei that target it, and are part of the cerebello-thalamic pathway: area X, the VPLo-VLc complex (Matelli et al., 1989), as well as the intralaminar nuclei and MD. Thalamic projections to AIP and PFG originate from the PuA, PuM, and LP nuclei, while SII receives projections from VPi, VPs, and PuA (Disbrow et al., 2003; Mayer et al., 2019).

Borra et al. (2017) recently proposed a model of the recursive operations occurring in the lateral grasping system. AIP and F5p extract object affordances, with F5p encoding potential action goals under the control of dorsoventral prefrontal area r46vc. Input from areas TEa/m to AIP provides information about object identity, given that TEa/m encode 3D object shape. Input from SII is essential for haptic coding of object properties, facilitating the formation of sensorimotor memories in area i12r. The distributed nature of insular input to the network (Evrard, 2019) suggests a profound influence of internal states on the grasping system.

Recent studies provide more support for this perspective, investigating the coding of grasping at network level by simultaneously recording neural activity from AIP, MI and F5. In one study (Dann et al., 2016), monkeys grasped a handle with either a precision or a power grip. The task recruited functional neural hubs of cells, strongly connected as in small-world networks (Watts and Strogatz, 1998). In a second study (Schaffelhofer and Scherberger, 2016), monkeys grasped

Box 3
Disorders of the Hippocampo-parieto-cingulate spinal module: spatial navigation

Spatial navigation is impaired by parietal disorders

In monkeys, muscimol inactivation of area PGm (7m) causes route specific navigation disorders (Sato et al., 2006). In humans, navigation tasks (Vann et al., 2009) are impaired after RSC lesion (Maguire, 2001). In rats, lesion of RSC impairs a set of tasks related to spatial memory (Sutherland et al., 1988), allocentric working memory (Vann and Aggleton, 2004), and egocentric memory (Cooper and Mizumori, 1999; Whishaw et al., 2001). Hippocampal lesions in monkeys seem to only affect allocentric navigation, leaving egocentric navigation unharmed (Lavenex et al., 2006; Rueckemann and Buffalo, 2017).

In contrast, MI lesion does not impede the spinal cord's central pattern generators, which are responsible for basic locomotor rhythms. Consequently, these patients exhibit no deficits in automatic walking or spatial navigation and orientation. Although cortical control is important for voluntary modifications of locomotion, it does not solely depend on MI. Instead, it depends on a constellation of inputs that convey optic-flow, vestibular and postural information. This reinforces the notion that the motor outputs resulting from computations underlying spatial navigation predominantly flow through the cingulate-spinal projections. Moreover, the cingulate input may drive the motivation underlying intentional choices to navigate different routes during locomotion.

either objects that looked identical but required different grasp postures, or objects that looked different but required similar hand configurations. This method dissociated visual object coding from motor grasp coding. Cells preferentially tuned to visual object properties were most prevalent in AIP, reflecting early planning of grasping. In contrast, cells related to actual motor grasping predominated in F5 and MI, reflecting later computations that execute hand movement.

Stereognosis is another function that is strongly related to grasping, defined as "the use of the moving hand to explore and identify the location, surface microstructure, size and three-dimensional form of objects" (Mountcastle, 2005; Sobinov and Bensmaia, 2021; Davare et al., 2011). Stereognosis is likely subserved by AIP, thanks to its selectivity for object shape, size and orientation (Murata et al., 2000; Durand et al., 2007; Srivastava et al., 2009).

6.1.2. *Motor output*

Dum and Strick (1991) originally described a projection from ventral premotor cortex to the pyramidal tract and demonstrated that MI contributes about ten times more to the descending output than F5. A later detailed tracing analysis showed that the F5-hand area projects to both brain stem and spinal cord (Borra et al., 2010). Axons to the brain stem terminate in the intermediate and deep layers of the superior colliculus, and in regions of the mesencephalic, pontine, and bulbar reticular formation, which in turn project to spinal cord. Direct F5 projections to the lateral part of the intermediate zone of the spinal cord were weaker and more focused than those addressed to its mid-dorsal region at C2-C5 levels. This region is a site of origin of a propriospinal system, which can directly control the hand motoneurons (Isa et al., 2007). Indeed, microstimulation of the F5 sector in area F5c elicits hand movements (Gentilucci et al., 1988; Cerri et al., 2003; Umilta et al., 2007; Schmidlin et al., 2008). Substantial amounts of information can flow through this spinal projection: F5 has been implicated in the remarkable recovery of hand dexterity after lesions confined to MI (Sasaki et al., 2004; Nishimura et al., 2007).

Therefore, the outcome of the computations underlying grasping and object manipulation is likely conveyed to the motor periphery through different parallel pathways: one direct, albeit slow pathway from F5, and an indirect albeit faster one through MI. Furthermore, a recent study has shown a corticospinal projection from AIP, which might provide early signaling about object properties to the spinal circuitry (Ribeiro Gomes et al., 2020) (Box 4).

6.2. *Observation of hand actions*

Action observation allows the recognition of another agent's actions and intentions. This function is encoded by the distributed mirror system.

6.2.1. *Anatomo-functional organization*

Mirror neurons discharge during both action execution and observation. They have been found in a widespread network that overlaps with the lateral parieto-frontal module and includes ventral premotor area F5 (Bonini et al., 2014c,b; Caggiano et al., 2016; di Pellegrino et al., 1992; Gallese et al., 1996; Kraskov et al., 2009; Papadourakis and Raos, 2017; Rizzolatti et al., 1996), IPL areas AIP and PFG (Fogassi et al., 2005; Bonini et al., 2011; Pani et al., 2014; Maeda et al., 2015), MI (Kraskov et al., 2009; Dushanova and Donoghue, 2010; Vigneswaran et al., 2013), PMd (F2; Papadourakis and Raos, 2017; 2019), ventral prefrontal cortex (Falcone et al., 2016), STPm (Nelissen et al., 2011), and infero-temporal area LB2 (Tea/m) (Rizzolatti et al., 2014; Bonini, 2017).

This mirror system influences the peripheral motor apparatus. Fadiga et al. (1995) showed a facilitation of hand motor evoked potentials (MEPs) while observing a grasping movement performed by another individual. The MEP pattern resembled muscle activity recorded when participants performed the observed actions themselves. This effect might depend on both activation of MI by F5 through cortico-cortical connections, and on direct F5 projections to the spinal cord.

6.2.2. *Motor output*

The two routes through which the mirror system can affect motor output during action observation might serve different purposes, given their different characteristics. Firstly, MI projects directly to the hand motor neurons, while F5 does not. Instead, it exerts a powerful facilitation on the hand MI cortico-spinal output, which is initially reduced and then abolished after muscimol injection in MI, suggesting that it depends on the F5-MI interaction occurring within MI itself (Shimazu et al., 2004).

A second difference is that the MI-spinal descending system is faster than the F5 one (Fig. 3), as demonstrated by two studies of mirror pyramidal tract neurons (mPTNs) projecting from F5 (Kraskov et al., 2009) and MI (Vigneswaran et al., 2013). While mPTNs represented about half of the total population studied in both areas, MI mPTNs had a much shorter activation latency (median: 1.1 ms) compared to F5 mPTNs (median: 2.6 ms).

A third difference is the proportion of suppression-type mPTNs: while most mPTNs increased their firing rate upon action observation, 25% of F5 mPTNS and 41% of MI mPTNS decreased or even ceased firing during action observation. This suppression might inhibit self-movement while observing others' actions, which is in line with the reduction of spinal glucose consumption during action observation (Stamos et al., 2010). Accordingly, action observation reduced MI mPTN activity by as much as 45 spikes/sec (Vigneswaran et al., 2013), while there was no difference in F5 facilitatory activity.

Finally, the corticospinal projection from PFG (Rozzi et al., 2006) might also be related to action observation, but no study has yet

Box 4
Disorders of the Lateral parieto-frontal spinal module: Grasping and manual exploration of objects

Grasping disorders

Inactivation of both AIP and F5p – core nodes of the lateral parieto-frontal module – produces severe grasping disorders (Gallese et al., 1994; Fogassi et al., 2001). Reversible muscimol inactivation of areas 45B, F5a, and especially F5p also results in a significant increase of grasping time. Neurons in these regions responded to various object properties during grasping, and fMRI showed that two of these three areas (F5a and 45B) were activated by electrical microstimulation of 3-D shape sensitive clusters in area AIP (Caprara and Janssen, 2021).

Astereognosia

Astereognosia is the inability to haptically explore and identify objects, and it is caused by anterior parietal lesion (Binkofski et al., 2001). This mostly perceptual disorder is frequently associated with tactile apraxia, a disturbance of hand movements for use and interaction with objects, which illustrates the importance of encoding combined perceptual and action variables in the parietal lobe (Freund, 2003).

characterized the physiological properties of PFG-spinal projecting neurons. Because PFG seems to be involved in understanding others' intentions (Fogassi et al., 2005; Bonini et al., 2011), it is possible that the PFG-spinal projection could help plan responses to others' expected behavior.

6.3. *Observation of oral actions*

An extended view of this system has been proposed based on studies about the recognition of oral actions related to communicative behavior.

6.3.1. *Anatomo-function organization*

In addition to hand actions, mirror neurons in F5c respond to mouth actions and communicative gestures, as do neurons in DO and GrFO (Ferrari et al., 2003; Maranesi et al., 2012). Some F5 and DO neurons are also modulated when monkeys vocalize (Coudé et al., 2011; Hage and Nieder, 2013). In the lateral part of area F5, populations of neurons modulated by hand and mouth actions intermingle, providing a mechanism for coordinated behavior such as eating (Gentilucci et al., 1998; Maranesi et al., 2012). The anatomical connections of this part of the mirror system, studied in detail by Gerbella et al. (2016), and reviewed by Ferrari et al. (2017), point to a network which integrates information about oral actions, facial emotions, social context, and reward.

In brief, the F5c mouth mirror region is strongly connected to the face/mouth regions of F4, and with different areas related to oral function: DO performs oral motor control, GrFO performs intraoral gustatory processing, while PrCO, PF, area 2, pre-SMA/SMA, and the mouth regions of SII perform intraoral somatosensory processing (Krubitzer et al., 1995; Rozzi et al., 2008).

Areas DO and F5c are similarly connected cortico-cortically (ventral F4, PrCo, GrFO). However, DO lacks connections with prefrontal and parietal cortex and, in contrast to F5c, it is connected with the agranular insula, allowing it to integrate oral actions with visceromotor signals. GrFO is strongly connected with area DO and PrCO, as well as with prefrontal areas 12 l, 46 v and i12r, which are involved in the conditional control of hand and mouth actions. Finally, DO can receive inputs about emotions associated with facial expression, subjective value of stimuli, and reward from several orbitofrontal areas (11, 12o, 12 m), the agranular and disgranular insular sectors, and agranular cingulate area 24.

The insula can also relay social information to the lateral parieto-frontal module through F5 (Gerbella et al., 2011), 46 vc (Gerbella et al., 2012), and pre-SMA (Luppino et al., 1993). These areas all connect to the mound and ventral dysgranular insula (Idm and Idv), which contribute to social functions (Evrard, 2019) such as approach (Jezzini et al., 2012), aggression (Rilling et al., 2004), and vocalization (Ku et al., 2011). The amygdala is involved in such social computations as well: it projects to GrFO from its basal nucleus, providing (inferotemporal input) information about others' gaze, facial identity, and expressions (Gothard et al., 2007), detection of gaze, and when a subject gazes at the eyes of a conspecific (Tazumi, 2010).

The cortical sector hosting mouth mirror neurons receives thalamic projection from VA, area X and MD, which is also a main target of prefrontal areas (46v, 12) hosting cells combining hand and mouth actions and observation (Simone et al., 2017).

6.3.2. *Motor output*

Some descending projections from F5c are addressed to the face/mouth zone of the motor putamen (Alexander and DeLong, 1985), as well as to a more rostral region involved in planning and selection of actions (Schultz and Romo, 1992) and in cognitive and motivational functions (Tremblay et al., 2015), probably related to motivational aspects of crucial forms of behavior such as foraging. The F5 descending projection is also addressed to the facial, trigeminal, and solitary tract nuclei (Morecraft et al., 2001), for the coordination of facial expression with the larynx (Jürgens, and Ehrenreich, 2007) and the respiratory nuclei. Altogether, this connectivity pattern seems ideal for the selection of appropriate hand and mouth actions by ventral premotor areas (Gerbella et al., 2016) (Box 5).

7. Medial premotor spinal module: action initiation, motor sequences, time encoding

The existence of a medial Premotor spinal module aligns with the gradually emerging realization among neurophysiologists that the medial premotor system centered on SMA is fundamentally different from the dorso-lateral one centered on dorsal premotor cortex (Schell and Strick, 1984). After all, SMA is involved in establishing probabilistic models of future action based on internal models of the world stored from past experience (Bernstein, 1967), rather than on explicit external inputs and their arbitrary association to motor outputs, which instead characterizes the dorso-lateral premotor system. Over the years, this distinction was progressively clarified through the study of anatomo-functional relationships, evolutionary considerations on cortical architecture (Sanides, 1964), and the consequences of brain lesion (see Goldberg, 1985, 1987; Nachev et. al, 2008; Passingham, 2010).

The medial premotor-spinal module is heavily involved in performing self-initiated and memorized actions and, to a lesser extent, in generating sensory-triggered movements. It is also involved in two other functions: 1) encoding the spatial and temporal aspects of serial behavior (e.g., specifying action sequences, coordinating bimanual movements, and determining action timing), and 2) encoding time during various cognitive and sensorimotor events (e.g., estimating elapsed and remaining time, and categorizing relative event durations). The central nodes of this module are SMA and pre-SMA, and its spinal projection stems from SMA. The module is also composed of selected areas of *the dorso-medial Prefrontal cluster* (F7, F7-SEF) and *the cingulate cluster* (CMAr and CMAv/d). It receives inputs from parietal (PEci) areas, as well as from the *medio-dorsal Superior Parietal Lobule cluster* (MIP, PEip, PEc), anterior *SPL cluster* (SI), and *ventral Premotor cluster* (F4, F5).

7.1. *Anatomo-functional organization*

The medial premotor spinal module is centered on SMA (F3) and pre-SMA (F6) (Fig. 1A) (Matelli et al., 1985; Matelli et al., 1991). Both belong to the frontal cluster (*MI-dmPM*) (Fig. 1B), which also contains many other areas of this module: PMdr (F7), F2v-preCD, F2-vr (i.e., the two subdivisions of PMdc, F2), and MI. Within this cluster, further structure is evident at a lower hierarchical level, distinguishing the premotor areas projecting to MI (F3, F2), from those lacking such projections (F7, F6), which instead are connected with F3, F2 and some prefrontal areas (Luppino et al., 1993). This module also includes movement-related areas in the mesial wall: dorsal (CMAd, 23c), ventral (CMAv, 23c), and rostral (CMAr, 24c) cingulate motor areas (Picard and Strick, 1996) (Fig. 1 A-B). The medial premotor module is connected to the insular areas Idd (through SMA and F5) and Idm/Idv (through pre-SMA and F5).

SMA communicates mostly with the premotor areas of its own cluster, including MI, and it is significantly influenced by the cingulate cluster. Specifically, strong frontal projections target SMA from CMAr, moderate projections from CMAv, MI, both subdivisions of F2, F4 and F5p, and weak projections arrive from pre-SMA, F7, F5a-c. Parietal projections are of moderate strength from PEci but weak from most other parietal areas.

Thalamic projection to SMA stem from VLo, and the VPLo/VLc complex, whereas those to pre-SMA stem from the nucleus ventral anterior parvocellularis (VApc) and area X of Olzewski. F7 receives thalamic input from VApc, area X, VLc and the VPLo/VLc complex; the supplementary eye field (dorsal part of F7) receives thalamic input from area X, VApc, VA, and VAmc (Matelli and Luppino, 1996). All above areas receive projections from the medial dorsal nucleus (MD).

Box 5
Disorders of the mirror system

So far there are no monkey studies on defects in understanding others' actions and intentions after inactivation of the mirror system. However, evidence is available from humans.

The development of the mirror system is likely impaired in **Autism Spectrum Disorders (ASD)**. Typically developing (TD) children differ from ASD children in their cortical dynamics during action observation, execution, and imitation. These alterations depend on various factors such as the familiarity of the agent performing the action, which have been discussed in comprehensive reviews covering the mirror system disorder hypothesis of autism (Rizzolatti and Craighero, 2004; Iacoboni and Dapretto, 2006; Rizzolatti et al., 2014). Here, we will refer only to representative results in this field.

First, ASD children seem to have difficulty in recognizing the final goal of long action chains, which is crucial to understanding another's intention. For example, ASD children do not show typical mirror effects at the beginning of an action chain (Cattaneo et al., 2007). This study investigated EMG activity of a muscle (mylohyoideus, MH) involved in mouth opening, during observation and execution of two different action chains. The first chain involved grasping a piece of chocolate and bringing it to the mouth, while the second involved grasping a piece of paper and placing it in a mouth-height container. In the first action chain, MH activated at the very beginning of the observed action in TD but not in ASD children. The same muscle was also active when observing eating in TD, but not in ASD children. This impairment in observing early planning during action chains might be responsible for the challenges that ASD children's face understanding others' intentions: while they can report *what* an action is (e.g., touch vs hold), they have difficulty in deciphering the *why* of actions (e.g., use vs move), which is often only explicitly apparent at the end of an action sequence (Boria et al., 2009). Given that early recognition of an ultimate goal might be subserved by parietal mirror neurons in area PFG (Fogassi et al., 2005), ASD might involve impaired neural dynamics of action planning in IPL, and by extension the lateral parieto-frontal module and its cortical outflows: PFG, and F5c.

Second, fMRI showed that during imitation and observation of emotional expressions, the pars opercularis of IFG was less active in ASD than in TD children (Dapretto et al., 2006). The pars opercularis is the frontal node of the human mirror system, and its level of activation was inversely related to the severity of social ASD symptoms.

Third, cortico-spinal excitability depends on autism trait severity. In one study, MEPs of low ASD trait participants were larger during action observation than during static observation, while in high ASD trait participants, no difference in MEPs was observed (Puzzo et al., 2009). Another study showed a different type of corticospinal effect by eliciting MEPs either 300 ms or 500 ms after action onset (Amoruso et al., 2018). Early MEPs were facilitated when an observed motor act was *congruent* with the environment, while late MEPs were inhibited when the motor act was incongruent with the environment. Only the strength of the late inhibition correlated with ASD traits: participants with worse social skills and more attention to detail showed less inhibition.

Finally, it must be noted that the "broken mirror theory" of autism – in which the mirror system is dysfunctional in autism – has been contentious. Critics have judged it to be premature and not supported by a solid cognitive model of social behavior (Southgate and Hamilton, 2008). The field is open for future research and debate.

Additionally, both SMA and pre-SMA project to the striatum, and receive disynaptic projections from the cerebellar dentate nucleus and from Gpi (Akkal et al., 2007). The Gpi projections to SMA stem from the sensorimotor region of the nucleus, while those to pre-SMA from its non-motor, "associative" domain, a pattern that is repeated in the organization of the cerebellar dentate projections to the cerebral cortex (Dum and Strick, 2003). Therefore, the activity of both pre-SMA and SMA are primarily determined by basal ganglia, rather than by cerebellar input. Finally, Gpi projects to the subthalamic nucleus (STN) through the hyperdirect path, thus shaping a potential substrate in the cortico-basal ganglia loop for interruption of ongoing movement by these areas (Frank et al., 2007).

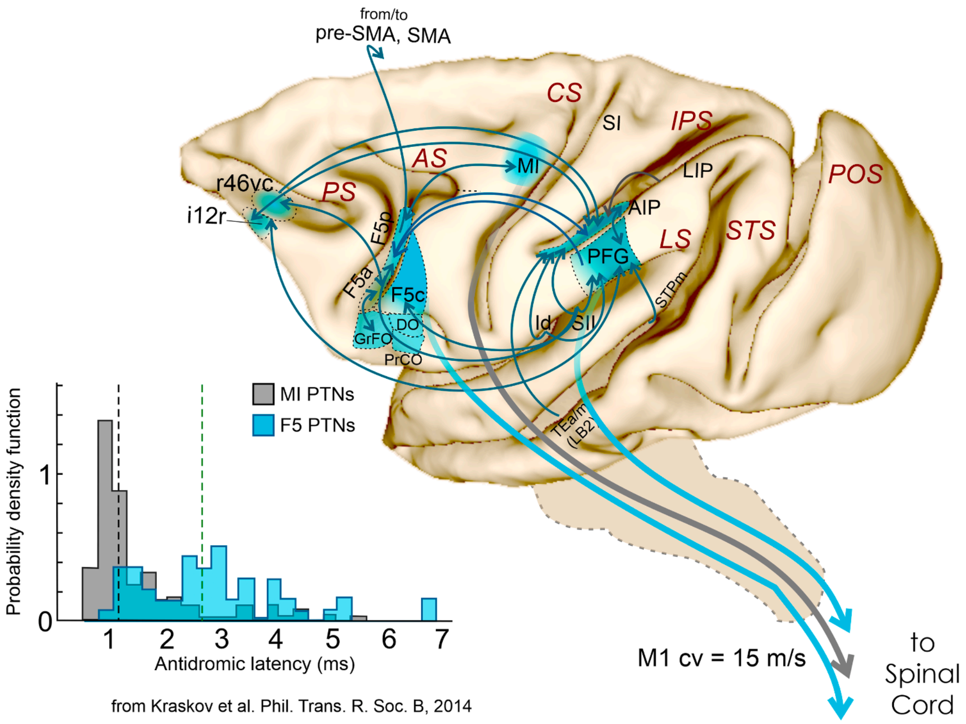
It is worth stressing that SMA and pre-SMA, once considered a single cortical area, were first distinguished on the basis of cytochrome-oxidase staining (Matelli et al., 1985) and cortico-cortical connectivity (Luppino et al., 1993). This distinction reflects their different functional properties. Therefore, in discussing SMA we will often refer to pre-SMA as well, to better understand how certain functions are distributed in the medial premotor areas.

7.1.1. *Motor output*

Depending on task demands, this module can convey relevant information to the spinal cord directly from SMA, from pre-SMA, or through the Cingulate premotor areas of the mesial wall. A recent study also documented some cortico-spinal projections stemming from F7 (Innocenti et al., 2019). SMA projects heavily, in part monosynaptically, to the spinal cord (He et al., 1995; Wise et al., 1996) (Fig. 4), through axons with mean axon diameters of 1.05 μm (median 0.87 μm) and mean conduction velocities of 10.7 m/s^{-1} (median 8.89 ms^{-1}) (Innocenti et al., 2019). Therefore, the SMA-spinal projection is the second fastest corticospinal path, after that stemming from MI (15 m/s^{-1}). The SMA synaptic boutons (mean 0.88 μm, median 0.87 μm) are smaller than those of MI (mean 1.07 μm, median 1.02 μm), but larger than in any other corticospinal path. SMA microstimulation at low intensities elicits somatotopically organized forelimb, orofacial and hindlimb movements along its antero-posterior extent. In contrast, pre-SMA projects weakly to the spinal cord and evokes movement only at high intensities (Luppino et al., 1991). CMAr and CMAd also project strongly to both MI and to spinal cord. Accordingly, electrical stimulation of these regions evokes forelimb and hindlimb movements at relatively low intensities (Luppino et al., 1991).

7.2. *The self-generated vs. externally-driven movement dichotomy*

The medial premotor module likely enacts both self-generated and externally driven actions. Over the years, there has been considerable debate on the exact balance between these two sources of action generation. Even how to distinguish between them experimentally is contended: some argue that asking a subject to perform a self-generated movement could already create a conflict between potential action choices, making it difficult to determine whether the task reflects conflict monitoring or self-paced decisions to act (Botvinick et al., 2004). However, as recently discussed by Seghezzi and Haggard (2023), "there is no unique property that demarcates voluntary actions from other actions. Rather, there appear to be a set of features, none of which are necessary, but of which some combination may be sufficient, to make an action voluntary. These include that the action be internally generated rather than externally triggered, that the action be more than merely



from Kraskov et al. Phil. Trans. R. Soc. B, 2014

Fig. 4. Lateral parieto-frontal spinal module: grasping and observation of hand and mouth actions. The central nodes of the grasping networks are the parietal areas AIP and PFG and the ventral premotor area F5a-c-p, which are linked by reciprocal cortico-cortical connections (light blue). Both parietal areas are also target of somatosensory projections from SII and insular inputs from area Id, and project/receive from areas r46vc and i12r; F5a is also target of area GrFO. F5c projects to the medial premotor complex (SMA/pre-SMA). This network is also the core of the mirror system, which benefits from visual input stemming from LIP (gray), superior temporal area STPm and anterior temporal area TEa/m(LB2), both activated by action observation. The cortico-spinal projections concerning grasping and action observation can be addressed to the spinal cord through slow F5 and/or fast MI axons (see latency of antidromic activation) (modified from Kraskov et al., 2014). Signals about intention understanding can be addressed to the motor periphery through the PFG-spinal projection. Emerging evidence suggests an additional projection stemming from area AIP (not shown). See text for more details. To date, no studies specify the range of axon diameters, and hence conduction velocities, of the F5-spinal projection. As a surrogate, we include a histogram of the latency differences obtained by recording from MI and F5 after antidromic stimulation of the bulbar pyramids (bottom left inset). The shortest latency of MI response predicts bigger and faster cortico-spinal axons, therefore shorter conduction delays from MI than from F5.

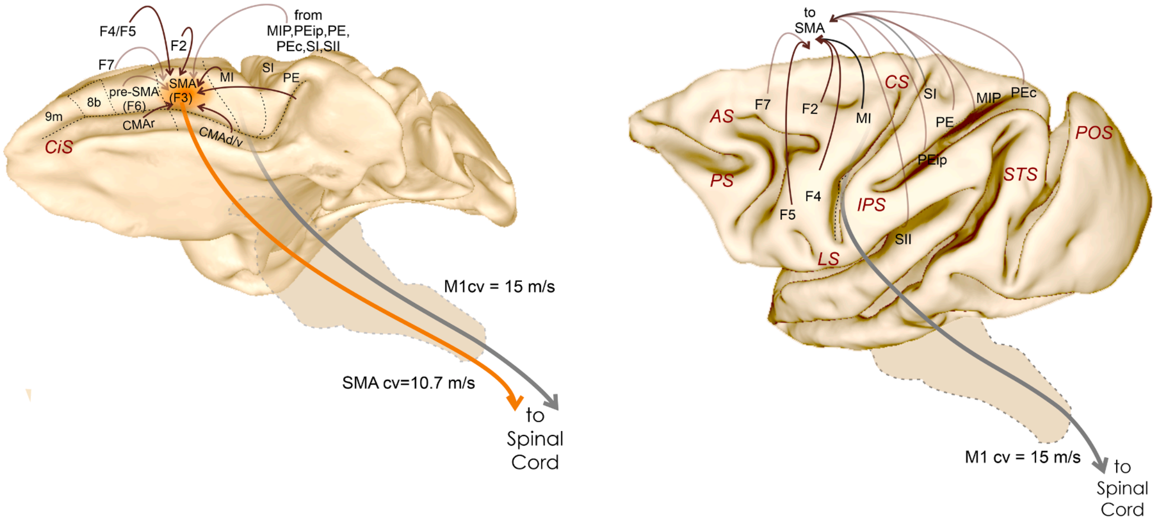


Fig. 5. Medial premotor spinal module: action initiation, motor sequences, time encoding. The central nodes of this module are SMA and pre-SMA. SMA is the target of strong projections from MI and premotor areas CMAr, CMAv, F2, F4, F5. Moderate strength input comes from F7. Parietal projections are strong from PEci, moderate from most of the SPL reaching-related areas (PEc, MIP, PEip and PE), as well as from SI. The corticospinal tract of this module stems from SMA. Left and right brain figurines illustrate the medial and lateral aspects of the macaque monkey left hemisphere. The color shading of the arrows indicates the strength of connectivity. Conventions and symbols as in previous figures.

habitual, that the action be goal-directed *reasons-responsive*, and that the action be under conscious control, or at least veto control […]. In internally generated actions participants freely generate and choose the parameters for the action, e.g., which action to perform or when to make it, in stimulus driven actions the same parameters are instructed by an external stimulus" (Haggard, 2019).

Using this definition, the medial premotor module undeniably helps initiate internally generated actions. Early research already suggested that the medial premotor complex encodes actions based on internal drives: an EEG study in humans showed a build-up of neural activity about 1 s before spontaneous or self-initiated movement onset. This negative and fast-rising potential, centered over SMA/pre-SMA (*Bereitschaftspotential*, or readiness potential, RP; Deecke and Kornhuber, 1978), was larger before self-generated than externally-triggered movements. It was interpreted as a biomarker for motor preparation and was accordingly reduced in patients with Parkinson's disease (PD; Jahanshahi et al., 1995).

However, recent work has challenged this view and proposed that the RP emerges from performing a movement-time-locked average of subthreshold random fluctuations (Schurger et al., 2012, 2021), that would trigger movement when a decision threshold is crossed, as in a stochastic leaky-accumulator model. Another set of experiments provides a more nuanced view: they suggest that SMA injects stochastic noise into a deterministic action timing signal. In other words, SMA transforms a deterministic bias into the actual – more stochastic – choice (Murakami et al., 2014, 2017). These experiments showed that cellular activity in rat M2 (corresponding to macaque SMA) fluctuated stochastically across trials, and this fluctuation was correlated with waiting time. However, M2 activity was not entirely stochastic: it also included a deterministic waiting time bias (tendency to wait short or longer) that it likely received from mPFC input. Accordingly, muscimol inactivation showed that both areas affected waiting time, but the deterministic bias was transient in M2 (SMA) and more sustained in mPFC, where it even spanned intertrial intervals. In all, current views undermine both the relevance of the RP in studies concerning movement initiation, as well as its use as a marker of unconscious initiation of action, as claimed in Libet's classical experiment (Seghezzi and Haggard, 2023).

Cell recording studies in monkeys also support the idea of a privileged role of the medial premotor module in self-initiated movements: activity in these areas can precede arm/hand movement onset (Brinkman and Porter, 1979; Tanji and Kurata, 1982) by up to 2 s. However, in addition to self-initiated tasks, monkey studies also show that the medial premotor module contributes to stimulus-cued tasks. Mushiake et al. (1991) studied cell activity in monkeys before both self- and stimulus-cued motor sequences. They found SMA cells that preceded movement onset in both memorized and visually cued trials, although their proportion was higher in the former than in the latter. PMd showed the opposite pattern (Romo and Schultz, 1987; Kurata and Wise, 1988). Romo and Schultz (1987) and Okano and Tanji (1987) also described cells firing during both self-initiated and sensory-driven movements in both SMA and PMd, although those preferring the self-driven conditions were more common in SMA. Other studies have shown that neural activities during preparatory delay-periods predominate in the anterior part of SMA, while those time-locked to movement onset are more common in its posterior part (Alexander and Crutcher, 1990; Rizzolatti et al., 1990; Matsuzaka et al., 1992). A similar predominance of cells modulated long before the onset of self-initiated movement was found in CMAr (Shima et al., 1991).

Taken together, these studies suggest that the dichotomy between internally generated and externally-triggered actions should not be considered absolute, especially because the triggers for action are more complex and elusive in the former than in the latter case (see Nachev et. al, 2008). This view has been contended by Passingham et al. (2010) but reaffirmed by Nachev and Husain (2010).

7.3. SMA, pre-SMA and the "Action Syntax" problem

The "action syntax" problem, which refers to the ability to link movements into appropriate spatial and temporal sequences, was first defined by Lashley in 1951. Since then, numerous studies have established that the sequential ordering of movements relies on a distributed system involving the cerebral cortex, basal ganglia, and cerebellum (Tanji, 2001; Hikosaka et al., 1998, 1999, 2000; Nachev et al., 2008; Passingham et al., 2010).

The medial premotor module appears to play an important role in the action syntax problem, given that many of its areas encode the temporal structure of motor behavior. For example, some neurons in SMA fire exclusively before specific sequences of button presses, remaining silent for other sequences (Mushiake et al., 1990). More than 50% of SMA cells also prefer memorized movement sequences over visually-guided ones, while in PMd roughly 50% of cells instead prefer visually-guided sequences. In MI, neural activity is not affected by either sequence (Mushiake et al., 1991). Tanji and Shima (1994) also found cells in SMA, but not in MI, that were only modulated by movement sequences arranged in a specific order. In pre-SMA, a large population of cells updates motor plans for subsequent actions sequences, while such cells are uncommon in SMA and absent in MI (Shima et al., 1996). Shima and Tanji (2000) also described more SMA and pre-SMA cells that fired before the execution of specific movement sequences, and in some cases in the interval between specific individual movements. This neural activity reflected selectivity for the chronological rank-order within the sequence. Interval-selective neural activity predominated in SMA, while rank-order selective activity was more frequent in pre-SMA.

Clower and Alexander (1998) found that SMA and pre-SMA also encode the numerical order of a motor-component in a sequence, regardless of which movements precede or follow. In a more complex experiment, Sohn and Lee (2007) varied the number of movements in a sequence across trials, dissociating the ordinal position of a movement from the number of remaining movements before reward. Neurons in both pre-SMA and SMA were more often modulated by the number of remaining movements, and therefore by the timing of expected reward. This effect was stronger in pre-SMA than in SMA. Activity in pre-SMA was also modulated more by trial parity than in SMA. Nakajima et al. (2022) recently affirmed that pre-SMA coordinates the temporal order of a motor sequence, and further disentangled the roles of pre-SMA and PMd by taking the expected reward into consideration. While pre-SMA activity was modulated when switching actions within sequences, PMd activity was modulated by a movement's proximity in time to a reward (see also Shanechi et al., 2012). Such reward proximity was interpreted as the behavioral goal,. based on previous studies showing that directionally tuned cells in PMd are modulated by the reward associated with their preferred target direction (Pastor-Bernier and Cisek, 2011), and encode reach motor goals beyond the immediate movement (Berger et al., 2020).

The roles of pre-SMA, SMA, and SEF in performance monitoring (Bonini et al., 2014a; Scangos et al., 2013), switching motor plans, and switching task rules have also been linked to the functions of anterior cingulate cortex (ACC). This complex region is regarded as a new specialization of the neocortex due to its structure and connectivity, and it plays a critical role as an interface between emotion and cognition (Allman et al., 2001), in translating motor intentions into action (Paus, 2001), in conflict monitoring and decision-making (Botvinick, 2007; Nachev et al., 2008), and in reward-guided decisions and learning (Rushworth et al., 2011). Comprehensive information comparing the ACC and the medial premotor module in their differential roles in motor cognition can be found in the above reviews, as well as more recent ones (Heilbronner and Hayden, 2016; Rolls, 2019), but such detailed comparison is out of the scope of this work.

All this motor-information about timings and sequences in the medial premotor module suggests that the module might also encode time more generally (for a review see Cona and Semenza, 2017). In the

Box 6

Disorders of the Medial premotor-spinal module: action sequences, time encoding, speech

Lesion and inactivation studies

The consequences of accidental SMA lesion have inspired both physiological investigations in humans and NHPs, as well as experiments on lesion and reversible inactivation in monkeys. Such studies paint a coherent picture of the core function of this medial premotor system in motor behavior. The literature on this issue is extensive (see Goldberg, 1985; Nachev et al., 2008; Passingham et al., 2010; Potgieser et al., 2014). Here we will recapitulate some key observations.In monkeys, several studies have investigated the behavioral consequences of lesion or reversible inactivation of SMA and or pre-SMA Theseinclude deficits in self-paced versus externally triggered actions, learning, motor sequences, and time estimation.

Brinkmann (1984) first reported that monkeys with SMA lesions had difficulty retrieving food from narrow slots in a transparent platform, when using the index finger and thumb in an ordered motor sequence. One year after surgery the bimanual problem remained, despite normal general motor behavior and only modest bilateral clumsiness of forelimb movements. However, the two hands behaved similarly instead of coordinating with each other. Callosal section abolished the deficit by preventing the inter-manual conflict. This suggests that inter-manual transfer of information depends on callosal messages between SMA of the two hemispheres. There are indeed dense callosal connections between the hand representation of SMA (Rouiller et al., 1994). None of the above deficits were observed after lesion of the dorsal and ventral premotor cortex in another animal.

Consistent with the medial premotor module's role in self-generated movements, monkeys with bilateral removal of SMA (Thaler et al., 1995) showed a paucity of self-initiated actions but no impairment of externally-triggered movements. Lesions of pre-SMA and SMA also impaired learning of motor sequences (Halsband, 1987; Passingham, 1987). Interestingly, SMA lesion generally does not impair conditional sensorimotor association tasks, as is the case after PMd lesion (see next section).

However, inactivation of SMA or pre-SMA by injecting the GABA-A agonist muscimol paints a subtly different picture about learning. Only unilateral pre-SMA inactivation, but not inactivation of SMA, caused errors when learning novel motor sequences (Nakamura et al., 1999), implying that pre-SMA plays a stronger role in the acquisition of action sequences. These results are consistent with physiological studies on the function of these areas in learning sequential procedures (Nakamura et al. (1998).

Bilateral inactivation impairs memorized motor sequences, but not when guided by visual cues (Shima and Tanji, 1998). Muscimol inactivation also does not negatively affect self-paced or sensory guided-reaching movements, suggesting that SMA inactivation specifically disrupts motor sequences, and not single movements. This has also been documented for self-paced sequential bimanual drawer pulling and grasping tasks (Kermadi et al., 1997).

Nonetheless, a complex experiment by Tanji et al. (1985) cannot be easily reconciled with such a lack of consequences of SMA lesion on conditional sensorimotor learning. The authors rapidly inactivated the medial surface of the hemisphere over SMA by cooling, while monkeys performed a Go-NoGo conditional task. On some trials an auditory tone of 300 Hz called for a hand movement (key press), if followed by a second tone of different frequency, or to withhold the movement when followed by a tactile stimulus. On other trials, a different 100 Hz tone indicated a reversal of the stimulus-response strategy: a tactile stimulus now called for hand movement, while a 300 Hz tone called for withholding movement. An overall deterioration of performance affecting reaction-times, force output and errors was observed after medial hemisphere inactivation. Interestingly, both omission and commission errors were made, as observed in human patients.

Finally, isochronous rhythmic tapping is disrupted in monkeys by systemic injections in SMA of quinpirole, a Dopamine 2-like agonist (Yc et al., 2019). This also suggests a role of the D2 system in the control of temporal precision.This summary of key results on experimental lesion and reversible perturbation of activity in the medial premotor module is consistent with the outcomes of physiological studies, and closely resembles the picture offered by clinical reports in humans.

Clinical studies in humans

In humans, **'SMA syndrome'** often occurs after tumor resection or cortical softening due to stroke. It is characterized by a constellation of symptoms that often resolve within weeks or months, most notably global akinesia (a dramatic reduction of spontaneous movement), also referred to as motor neglect (Laplane et al. (1977) in the contralateral limb, but with normal muscle tone, strength, and reflex activity.

The main persisting deficit is an impairment in alternating hand movement, which is more severe without visual guidance. This was also documented after experimental SMA lesion in monkeys (Brinkman, 1984). Other symptoms of SMA syndrome are variable. For instance, Luria's (1966) patient CH showed great difficulty with spontaneous speech but promptly replied to questions. He was also unable to perform ordered sequences of limb movements and bimanual coordination, with a strong tendency to produce symmetrical mirror movements, "as if my hands do not belong to me […] and they do not do what they should". Such difficulty in performing sequential limb movement has also been documented by Laplane et al. (1977) and Dick et al. (1986), for saccades related to complex motor programs such as head and body movement, and by Pierrot-Deseilligny et al. (1995) after SEF lesion. Similarly, a severe impairment in rhythm reproduction with alternate hand movements, in the absence of impairments in rhythm discrimination or manual dexterity, was documented by Halsband et al. (1993) in patients with SMA lesion sparing the dorso-lateral premotor cortex. Patients seemed severely impaired only when producing rhythms from memory but had no problem reproducing recently-heard rhythms.

In the language domain, SMA lesion can result in transcortical motor aphasia, characterized by reduction of self-initiated speech, involuntary vocalization, paraphasia, stuttering, speech rate changes, and agrammatical output, while language comprehension is unaffected. Most of these effects are in line with the temporal control functions of the medial premotor module. This condition should not be conflated with akinetic mutism, which results from lesion of the anterior cingulate cortex (Bangs, 1956; Barris and Schuman, 1953; for a discussion see Guenther, 2016).

Patients with SMA lesions can also experience alien-limb syndrome, in which they make unwanted movements with their contralateral hand (Della Sala et al., 1991; Feinberg et al., 1992). They often experience conflict between the alien and the healthy hand, such as when the alien hand closes an object that has just been opened by the unaffected hand. Other patients suffer from utilization behavior: a strong tendency to use nearby visible objects without any apparent purpose or need, such as putting on multiple pairs of glasses, or repeatedly pouring water into a glass and drinking it despite not being thirsty, as if visual affordances cannot be suppressed (Lhermitte, 1981, 1983).

The largest frontal lobe study on action suppression analyzed 43 patients performing the Go/NoGo task (Picton et al., 2007). It found that right-handed commission errors were significantly higher in patients with lesions in areas 6a and 8 (including SMA and pre-SMA), or in left dorsal premotor cortex, as compared to patients with other frontal lesions. By contrast, no effect was found after lesion to the right ventrolateral cortex, including the IFG.

Two rare patients with small lesions centered on SEF (J.R.) and SEF plus SMA (C.B.) showed disruptions in automatic effector-specific motor inhibition (Sumner et al. (2007)), which conflicts with the view that SMA plays a role in volition. Another patient with bilateral SMA softening due to stroke was unable to modulate or suppress unwanted actions in both hands (Boccardi et al., 2002).

Finally, patients with pre-SMA lesion have difficulty switching tasks (Nachev et al., 2007), but not in action stopping (Roberts and Husain (2015). A specific deficit related to response conflict but not in error monitoring was found in a patient with very selective lesion of SEF (Husain et al., 2003).

A combined fMRI/rTMS study performed in healthy volunteers (Rushworth et al., 2002) offers an important caveat to interpreting activity in SMA and pre-SMA. The experiment involved response switching and activated the anterior and posterior cingulate zones and pre-SMA. Then, rTMS inactivation of pre-SMA transiently impaired motor switch only at the moment of behavioral switching. In contrast, rTMS over the SMA/pre-SMA border region, which was also activated during response switching, did not impair performance, suggesting that the activation of a cortical area in different tasks does not per se imply that it exerts a crucial role in both of them.

Importantly, none of these consequences of lesion resembles those observed after lesion of MI or posterior parietal cortex. This supports the idea that the outflow of neural operations of the medial premotor module primarily address the motor periphery through the SMA-spinal pathways.

next section, we discuss this possibility.

7.4. Time encoding

The medial premotor module has been found to play a crucial role in the perception and estimation of time, necessary for the execution of movement sequences with tight temporal structure, such as playing music. This function is supported by modelling work showing remarkably similar temporal encoding schemes.

Merchant et al. (2011) first demonstrated temporal encoding in pre-SMA in monkeys, using a synchronization-continuation tapping task (SCT), where tapping was first synchronized with a metronome, and then continued after the metronome was turned off. Some neurons increased their activity as a function of the amount of time left until the next tap, while others increased activity as a function of time elapsed since the last tap. Thus, the time until the start of a new tap might depend on the interplay between two different neural chronometers. In another SCT study, Crowe et al. (2014) found that inter-tap duration and tap serial order are encoded in pre-SMA through neural trajectories: small neuronal assemblies are activated in rapid succession, passing information about the intended rhythmic behaviour between them. These neural trajectories are similar, although not identical, in subsequent inter-tap-intervals (Merchant et al., 2015). Such time-encoding trajectories were also observed in *artificial* recurrent neural networks, trained to perform time-dependent tasks: during stimulus presentation, artificial population activity travelled along stereotypical trajectories, and the distance along the trajectory encoded time since stimulus presentation (Bi and Zhou, 2020). SMA cells are also tuned to a preferred ordinal rhythmic structure. Some SMA cells were even almost invariantly tuned to the interval duration between taps, being unaffected by the number of produced intervals or the modality used to drive tapping (Merchant et al., 2013).

The medial premotor module also seems to be involved in more abstract temporal phenomena, such as judging the passage of time, and categorizing it as short or long. While categorizing time intervals recruits a widely distributed system involving putamen, medial premotor, intraparietal, and inferior parietal areas, the firing rate of a large population of pre-SMA neurons (Mendoza et al., 2018) peaked close to the subjective boundary limit between long and short, and the time at which this peak was reached predicted the categorical boundary decision. These cells' activity also reflected the selected category and the result of the decision. A resetting-drift diffusion computation model replicated the main behavioral and neural features of this rhythmic time encoding, in line with decision bound theory (Ashby and Maddox, 2005; Merchant and Averbeck, 2017). The model showed both the experimentally observed linear relations between mean and standard deviation of the interval produced by monkeys during SCT, as well as a neural population code of the elapsed time between taps.

7.4.1. Time to act

The medial premotor module also seems crucial for *deciding* when to act. Studies in humans suggested that pre-SMA is preferentially involved in selecting and suppressing stimulus-driven action. In contrast, SMA is more involved in initiating self-paced behavior (Coull et al., 2016). In monkeys, cells in both pre-SMA and SMA signal action initiation in a time-selective fashion (Mita et al., 2009). Population activity in the medial frontal cortex (which includes SMA and pre-SMA) and caudate controls the timing of motor output by altering the speed of neural population dynamics, and such speed-varying population dynamics were reproduced in a neural network model (Wang et al., 2018a), as well as in the earlier mentioned artificial neural networks of Bi and Zhou (2020). Those artificial networks additionally showed increased amplitude of their neural trajectories when producing later movements, which is remarkably reminiscent of the biological neural trajectories in macaque SMA and pre-SMA during synchronized tapping tasks (Gámez et al., 2019). Finally, the speed of these neural population dynamics in dorsal SMA and pre-SMA can in turn be controlled by adjusting the initial conditions and inputs to those brain regions (Remington et al., 2018).

During reaching, population dynamics in SMA also explicitly reflect cues concerning movement initiation timing (Lara et al., 2018), but MI dynamics do not. In fact, while population activities in both SMA and MI track progress through an extended task, they do so with distinct geometries, suggestive of different underlying computations (Russo et al., 2020) despite their mutual connections. These results align with the proposal that SMA exerts proactive control by establishing the response threshold for initiating an action (Chen et al., 2010a), and participates in performance monitoring (Scangos et al., 2013; Stuphorn and Emeric, 2012).

However, an elegant study in monkeys (Khalighinejad et al., 2020) has challenged this idea, showing that a distributed basal forebrain-cingulate system is instead responsible for decisions on whether and when to act. Disrupting this system with transcranial ultrasound changes decisions about when to act. We also note that another important factor about the time of the next action is the timing of past ones (Murakami et al., 2014, 2017).

The above findings about temporal processing have interesting implications from an evolutionary perspective. They suggest that the medial premotor also participates in complex auditory-motor processing and imagery, necessary for functions such as speech, vocalizations, and music (see Mendoza and Merchant, 2014; Lima et al., 2016). Music for example, a traditionally 'higher order' domain, has been studied across species (Hoeschele et al., 2015), including both non-human primates and humans (Merchant et al., 2015). More recent studies confirm that macaques and humans share common mechanisms for maintaining internal rhythms without sensory stimuli or motor action (García-Garibay et al., 2016), as well for encoding the periodicity of complex sounds (Ayala et al., 2017).

7.5. Social cognition

The medial premotor module is also implicated in social cognition, particularly in processing other people's actions and intentions. In pre-SMA, some cells selectively encode others' actions, while other cells are modulated by a task-partner's errors (Yoshida et al., 2011; Yoshida et al., 2012). Livi et al. (2019) described pre-SMA neurons that encode not only a monkey's own actions, but also another agent's actions, as well as neurons related to the intention, either from the self or another, to grasp an object. By analyzing population activity over time, they found that pre-SMA neurons may encode a shared agent-based representation of objects and actions during action performance, which depends on their location in the space near the observer's body. This suggests an "object-mirroring" mechanism that allows observers to predict others' impending actions (Box 6).

8. Dorsal premotor spinal module: conditional motor association and learning, action plan switching and inhibition

The Dorsal premotor-spinal module is central to conditional motor learning and behavior. It plays a key role in online movement control, action switching, and inhibiting ongoing movements, both voluntarily and when externally instructed. This module has also been implicated in reward-based decision making about action initiation and suppression, as well as in encoding choice difficulty during logical decisions. Finally, this module is recruited when observing and rehearsing familiar actions, when estimating time duration, and in social cognition. It is important to note that the functions of this module, as well as the consequences of its breakdown, are distinct from those of MI. This module's core area is F2 of the *dorso-medial premotor cluster*, from which it projects to the spinal cord. The module is strongly connected to areas of the *dorso-medial premotor cluster* (F7, SMA), the *cingulate cluster* (CMAr, 24a-b), *ventral premotor cluster* (F4, F5), *medio-dorsal SPL cluster* (PEc, MIP, PEip), and *postero-medial SPL cluster* (V6A).

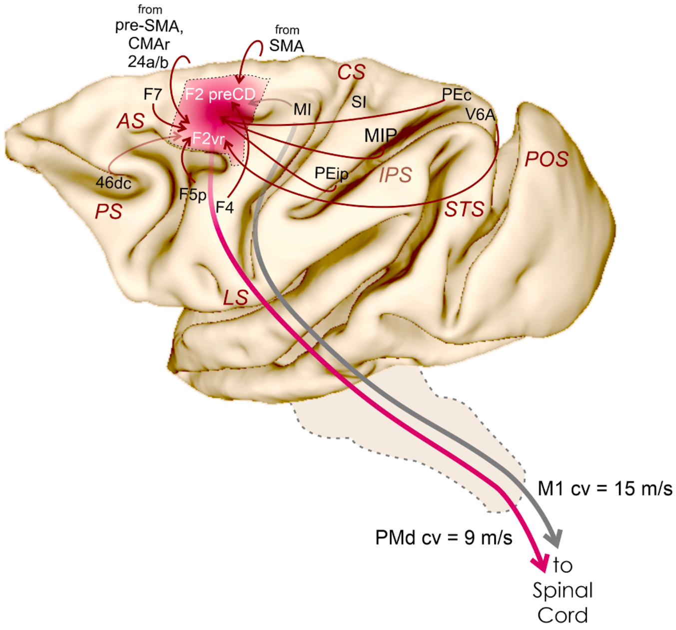


Fig. 6. Dorsal premotor spinal module: conditional motor association and learning, action plan switching and inhibition. The central node of this module is dorsolateral premotor area F2, with both its components (F2-preCD and F2-vr). Cortical projections to both components are shown at their putative border and stem for the reaching-related visuomotor areas PEc, MIP, PEip, from pre-SMA, CMAr, and from 24a-b. Projections addressed only to F2vr stem from V6A, F5p, and F7; weaker projections come from prefrontal area 46dc; the input from SMA, ventral premotor area F4 and MI are addressed only to F2-preCD. This dorsal premotor module projects directly to the last-order interneurons of the spinal cord. Intensity of color shading illustrates strength of connectivity. Conventions and symbols as in previous figures.

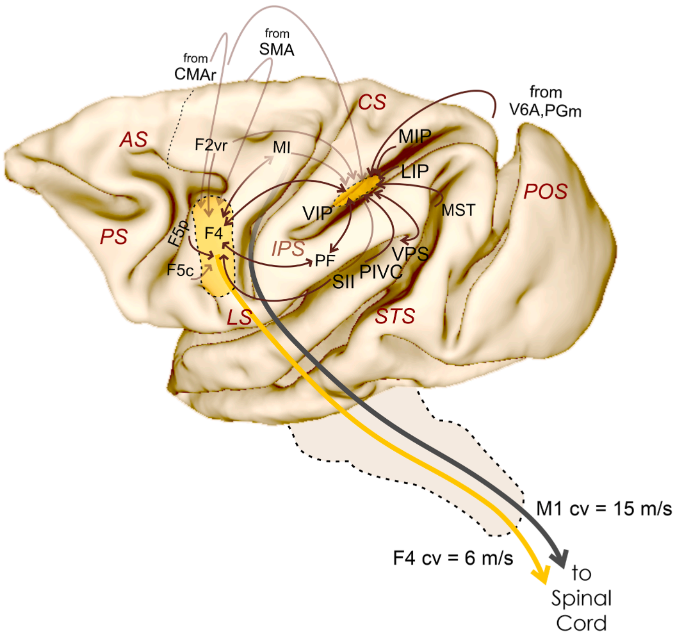


Fig. 7. Ventral premotor spinal module: binding features for defensive behaviour. The central nodes of this module are the parietal area VIP and the ventral promotor area F4, which are strongly and reciprocally connected in a direct fashion, as well as indirectly through area PF. The main inputs to VIP come from the vestibular (PIVC, VPS) and motion-related (MST) areas. Strong projections also stem for the visuomotor areas V6A, PGm, MIP, as well as from the visual and eye-movement related area LIP. Area F4 receives strong inputs from SII, PF, from F5c and MI. The reciprocal F4 to MI projection is weak. Additional weak inputs come from dorso-medial (CMAr, SMA) and dorsolateral (F2vr) premotor areas. The cortico-spinal projection of this module originates from F4 and consists of small and slow conducting axons. Conventions and symbols as in previous figures.

8.1. Anatomo-functional organization

The central hub of the dorsal premotor-spinal module is the dorsal premotor area F2, which belongs to the *MI-dmPM cluster* (Fig. 1B). F2 is subdivided into a dorsal region around the precentral dimple (F2-preCD) and a more ventral one closer to the spur of the arcuate sulcus (F2vr), based on the differential local and long cortico-cortical connectivity. The two F2 subdivisions are strongly interconnected. They share most of their external connections with other cingulate, frontal, and parietal areas, although with different strengths. Connections to only one subdivision are very rare.

The strongest frontal inputs to F2 stem from cingulate areas 24a/b, medial premotor areas CMAr, SMA, ventral premotor areas F4 and F5, pre-SMA, and dorso-rostral premotor area F7. A moderate input originates from MI. The premotor areas generally send a strong connection to one of the F2 subdivisions and a weaker one (not shown in Fig. 5) to the other. Prefrontal area 46dc, and cingulate areas 23a/b provide weak inputs to F2 vr (not shown in the figure). There are also strong parietal projections to F2, originating from reaching-related SPL areas V6A, PEc, MIP, and PEip.

Dorso-rostral premotor area F7 (Fig. 1A) is also relatively important to the dorsal premotor module and belongs to a different branch of the *MI-dmPM cluster,* when compared to F2 (Fig. 1B). Unlike F2, F7 is not connected to MI, while it is strongly linked to pre-SMA, CMAr, F2vr, 46dc, and F7-SEF. F7-SEF is the F7 subdivision receiving strong inputs from FEF, area 45a/b and 8B, and LIP, all devoted to the control of eye movement. F7 has strong connections with parietal areas V6A, PGm and 31, all belonging to the *pmSPL cluster.* The F7 connections are not shown in Fig. 5.

The dorsal premotor module has multiple connections with the insular mound and ventral disgranular areas (Idm and Idv): areas 24a/b, F5 and pre-SMA (Evrard, 2019). In terms of sub-cortical connections, PMdc (F2) receives most of its thalamic afferents from the VPLo/VLc complex, VLc and VLo (Matelli and Luppino, 1996; Kurata, 1994). The thalamic input from VLo can be a source of pallidal influences (Schell and Strick, 1984), contrasting that of ventral premotor cortex (area X, VPLo), which is dominated by cerebellar afferents. PMdr (F7) is target of the VApc, VLc, the VPLo/VLc complex, and area X. F7-SEF is target mostly of VApc, area X and the VPLo/VL complex. The mediodorsal nuclus (MD) projects heavily to all above areas. Therefore, F2 is target of the motor basal ganglia circuit and of cerebellar afferents from dorso-rostral sectors of the dentate and interpositus nuclei. In contrast, F7 receives input from the basal ganglia complex circuit and from the dentate (Matelli and Luppino, 1996).

8.2. *Motor output*

The dorsal premotor-spinal module conveys information to the spinal cord through a disynaptic F2 projection to the last order interneurons of the intermediate zone (Fig. 5; Dum and Strick, 1991; He et al., 1993; Strick, 2021). The projections arising at the F2/F7 border conduct action potentials at about 9.80 msec^{-1} (Innocenti et al., 2019). Information transfer along this pathway is context-dependent, since profound modulations of neural activity have been described in PMd in absence of muscle activity (Tanji et al., 1988), and this is at odds with what is commonly observed in MI. Accordingly, electric stimulation of PMd does evoke limb movements, but at higher thresholds than MI (Wise, 1996). The operations encoded by the Dorsal Premotor-Spinal Module can influence the motor periphery through this pathway, alone or in association with MI.

8.3. *Conditional visuomotor association and learning*

Conditional visuomotor association and learning refers to linking non-spatial visual cues to action, which can be observed in everyday situations such as stopping at a red traffic light and proceeding at a green light. This type of association is also known as conditional motor behavior, or arbitrary visuomotor mapping (Passingham, 1993; Wise et al., 1997; Wise and Murray, 2000).

The ability to perform conditional motor behavior relies on a distributed network, including PMd (Wise et al., 1997), prefrontal cortex (Asaad et al., 1998), the hippocampal formation, and striatum (Petrides, 1982, 1985; Gaffan and Harrison, 1988, 1989; Toni and Passingham, 1999; Wise and Murray, 2000; Makino et al., 2016). During learning, activity in the different nodes of this network changes in a graded manner, with an increase of learning-dependent activity and a decrease of learning-selective activity (Mitz et al., 1991; Cahusac et al., 1993; Asaad et al., 1998; Tremblay et al., 1998; Xiang and Brown, 1999; for a review see Wise and Murray, 2000). In this interplay, the striatum forms early arbitrary associations, prefrontal neural circuits monitor the evolution of training, and the hippocampus is responsible for long-term memory storage and recall of new associations (Pasupathy and Miller, 2005).

In neurophysiological monkey studies, PMd neurons show activity that depends on the motor significance of non-spatial visual signals (Boussaoud and Wise, 1993; Kermadi and Boussaoud, 1995), and reflects the learning stage of arbitrary stimulus-response associations (Mitz et al., 1991). The instructional value of a stimulus can also influence PMd activity (di Pellegrino and Wise, 1993), both at single cell and population level (Wise et al., 1996). For example, cue location signals that instruct an animal whether to reach toward a stimulus or away from it, also influence early neural activity in PMd (Crammond and Kalaska (1994). During reach-selection tasks in which two potential reach directions are possible, neural activity in PMd specifies both directions simultaneously, until a non-spatial cue indicates the correct choice (Cisek and Kalaska, 2005). When the correct choice is specified, its PMd encoding strength increases, while neural activity related to the non-selected direction is suppressed. These results have been interpreted as neural competitions between affordances, whose outcome is biased by prefrontal influences (Cisek, 2006, 2007).

PMd activity also reflects the level of difficulty of memory tasks, which are important for forming arbitrary visuomotor associations. This was shown in a study based on transitive inference (Mione et al., 2020), requiring subjects to create a mental number line (e.g., A>B>C>D>E > F) by using fragmented information (e.g., A>B, B>C, C>D, D>E, E > F) learned and stored independently. As task difficulty increased, so did PMd activity (see Moyer and Landauer, 1967).

However, it must be stressed that neural activity in PMd is also modulated by self-initiated movements, even in the absence of external cues (Romo and Schultz, 1987; Kurata and Wise, 1988). The extent to which PMd activity reflects strictly stimulus-driven visuomotor associations over the internal decision to move is therefore not always clear.

Other studies have shown PMd's involvement in mental rehearsal of familiar action during observation, thanks to the similarity of neural activity during action observation and execution (Cisek and Kalaska, 2004).

8.4. *Time perception*

While temporal encoding in PMd seems more conditional than that in SMA (see section 7.4 above), certain temporal mechanisms have been found in PMd, using a duration-discrimination task (Genovesio et al., 2009). Two stimuli were presented, followed by two delays periods, and the animals compared stimulus durations. PMd encoded both the duration of individual stimuli and their relative duration. The encoding of stimulus duration depended on stimulus features and order of presentation, while the encoding of relative duration mostly indicated which stimulus was shorter or longer. Relative encoding also only emerged from population activity as the time of behavioral report approached, suggesting that the short-term temporal information in PMd might work in synergy with the intermediate-term temporal coding of the hippocampus, to also support episodic memory.

8.5. *Social cognition*

PMd is involved in mechanisms of social cognition related to between-subject action coordination (Ferrari-Toniolo et al., 2019). Populations of “joint-action cells” in PMd fire only or preferentially when two monkeys coordinate their hand actions in a common task, compared to when they perform the same task individually. PMd's role in both solo and joint action is further highlighted by the fact that neural dynamics are similar during solo, joint-action and observation of the partner's action (Pezzulo et al., 2022). In this study, the largest components of the population dynamics, traditionally attributed to the transition from action planning to execution (Churchland et al., 2012), actually encoded the covert representation (Jeannerod, 2006) of actions and goals, shared across contexts in which a movement is either required (solo and joint-action) or not (action observation). Despite this overall shared representation of action goals, there exists a minority of PMd neurons that encode what others will do in tasks where the monkeys observe an experimenter choosing between two targets (Falcone et al., 2016). The key role of dorsal premotor cortex (PMd) in guiding movement when acting with others is also suggested by a TMs study in

Box 7
Disorders of the Dorsal premotor spinal module: conditional visuomotor association and learning, action suppression

Lesion and inactivation studies.

In monkeys, lesion and inactivation of prefrontal cortex and PMd severely impairs the use of non-spatial visual information for action control (Gaffan and Harrison, 1988; Petrides, 1982; Passingham, 1993; Kurata and Hoffman, 1994). In contrast, MI and PPC lesions cause no such effects. Moreover, reversible inactivation of PMd neurons which were active during both visually-guided and memorized movement sequences, impairs only internally generated sequences, suggesting that arbitrary motor-to-motor mapping might also be encoded in PMd (Ohbayashi et al., 2016). This conclusion is consistent with a meta-analysis of motor learning studies in humans (Hardwick et al., 2013).

Lesion of PMd also results in an increased frequency of impulsive and uncontrolled reaching movements (Moll and Kuypers, 1977), which is in keeping with the impaired ability to withhold movements after muscimol inactivation (Sawaguchi et al., 1996). LFPs recorded from dorsal prefrontal cortex and its rostro-ventral corner also showed that these two regions are involved in action inhibition during Go/No-Go tasks (Sasaki and Gemba, 1986). Given that pre-SMA neurons suppress ongoing automatic and unwanted actions when switching to desired and controlled ones (Isoda and Hikosaka, 2007), a frontal network including prefrontal cortex, PMd and pre-SMA likely inhibits potential actions. Lesions to this entire network can impair action control, resulting in commission errors (for a review see Battaglia-Mayer et al., 2014).

In humans, defective conditional visuomotor learning can occur after lesions of the distributed PMd system. For example, PMd-lesion patients were unable to learn associations between simple sensory stimuli and arm movements but had no issues associating spatial cues with those same arm movements (Halsband and Freund, 1990).

As mentioned when discussing action stopping, Picton et al. (2007) showed that right-handed commission errors were significantly higher after either lesion of SMA and pre-SMA, or of left dorsal premotor cortex. In contrast, no effect was found after lesion to the right ventrolateral prefrontal cortex, including the IFG.

Finally, decreased motor inhibition has been reported in children with attentional disorders (Nigg, 2001), with substance abuse disorders (Zhang et al., 2018; Wang et al., 2018b), and in aging adults (Hu et al., 2019;Yang et al., 2019; Hsieh and Lin, 2017a,b; Lee and Hsieh, 2017). Such conditions are all associated with impaired PMd function.

humans, which showed that PMd modulates stopping performance during joint action (Cardellicchio et al., 2021).

8.6. Action suppression

The premotor-spinal module also plays an important role in action suppression, which involves halting a movement either deliberately or in response to an unexpected event. Such inhibitory control is an important function thas been studied through two main paradigms: the Go/No-Go task and the Stop-task (i.e., countermanding; for a review see Battaglia-Mayer et al., 2014), which explore different aspects of explicit action suppression, both producing commission errors. The Go/No-Go paradigm requires subjects to stop a potential action which has not yet started, while the Stop-task requires halting an ongoing action and measures the so-called Stop Signal Reaction Time (SSRT; Logan and Cowan, 1984; Schall and Godlove, 2012), i.e., the speed of the action interruption process.

PMd's involvement in action stopping is supported by the effects of inactivating PMd. For example, monkeys with PMd lesion suffer from impulsive and uncontrolled reaching (Moll and Kuypers, 1977). Injections of the GABA-A antagonist muscimol in PMd also reduce monkeys' ability to withhold movements (Sawaguchi et al., 1996). For more effects of inactivations, see Box 7. This stopping can emerge from the outcome of two independent neural events: action execution and suppression (Boucher et al., 2007; Salinas and Stanford, 2013; Verbruggen and Logan, 2009).

There are several possible neurophysiological mechanisms underlying suppression of movement, which all involve PMd. First, PMd cells projecting to MI might convey feed-forward intracortical inhibition to MI (Ghosh and Porter, 1988; Tokuno and Nambu, 2000; Coxon et al., 2006), either directly or through selective targeting of interneurons (Ghosh and Porter, 1988; Tokuno and Nambu, 2000). Second, PMd corticospinal projections could target inhibitory interneurons at the level of the spinal cord (Dum and Strick, 1991; Johnson et al., 1996; Johnson and Ferraina, 1996; Innocenti et al., 2019) thanks to their disynaptic connection with motoneurons. This could also occur at movement onset (Reynolds and Ashby, 1999). Both these views are supported by the modulation of activity of two different neural assemblies in PMd, one for which activity decreases during stop trials, and the other whose activity increases (Mirabella et al., 2011). This scheme is compatible with the interactive race model proposed for the inhibitory control of eye movements (Boucher et al., 2007), where Go and Stop processes are non-independent.

A more elaborate view proposes that the source of action lies in cortical attractor dynamics of neural populations (Mattia et al., 2013; Shenoy et al., 2013). In this view, motor plans are metastable states of activity that evolve into overt action when external controllers are released. Therefore, if neural variability is high before movement, reaction times will be long, because the population is unlikely to be near the attractor state from which movement can start. This has been shown to be the case: recent task history influences both the monkey's behavioural performance and neural variability in PMd, with reaction times correlating to neural variability (Marcos et al., 2013). During and before movement tasks, two subspaces can even be identified in the dynamics of cell populations: a first one for position holding and active inhibition, and a second, orthogonal space in which transitions from the first subspace can form the final motor plan if neural activity passes a threshold (Pani et al., 2022). Therefore, this view is compatible with the interactive race model, but moves it into the more detailed framework of attractor dynamics.

The neural substrates of action suppression have been a topic of great interest in cognitive control of executive functions (Aron, 2007; Logan et al., 2014; Logan and Cowan, 1984). Early fMRI studies showed that the inferior prefrontal gyrus (IFG, consisting of areas F5a (area 44) – a node of this dorsal premotor module – and 45) is activated during action inhibition (Konishi et al., 1998, 1999; Garavan et al., 1999; Rubia et al., 1999 Menon et al., 2001; Bunge et al., 2002). Congruent with these results, in a foundational neuropsychological study, Aron et al. (2003) showed that lesions in the same region disrupt action stop signalling, particularly in the *pars triangularis* (Brodmann area 45). Aron and Poldrack (2006) also suggested the involvement of the STN in silencing the "direct" fronto-striatal pathway, that is physiologically activated by action initiation. Since then, neuropsychological studies on action suppression have been controversial, due to the limited number of patients studied and variability of lesion size. A large frontal lobe study analyzed 43 patients performing the Go/NoGo task (Picton et al., 2007), and showed that right-handed commission errors were significantly higher after either lesions of areas 6a and 8 (including SMA and pre-SMA), or lesions of left dorsal premotor cortex, than in patients with other frontal lesions. By contrast, no effect was found after lesion to the right ventrolateral cortex, including the IFG. Hampshire et al. (2010) similarly showed that the right IFG was always recruited when salient cues were detected, regardless of whether inhibition, generation, or no motor response at all followed. Then again, Cai et al. (2014) showed that both the IFG and the insula participate in action suppression, with the latter more involved in saliency detection, the former in inhibitory control. In their survey of the field, Aron et al. (2014) offered an updated theory on the role of the right IFG in pausing or inhibiting motor responses under different contexts, that is after salient external stimuli, or internal intentions, also discussing the disruption of action inhibition in brain damaged patients. This theory was reaffirmed in a rebuttal to the criticisms raised by two different studies (Swick and Chatham, 2014; Erika-Florence et al., 2014).

However, there are more factors to consider when assessing action inhibition. Besides salient stimuli and internal intentions, PMd activity can also influence and halt motor programs based on the motivational value of cues. Giamundo et al. (2021) varied the rewards offered for correctly moving or stopping across trials in a countermanding task. They showed that PMd activity reflected those rewards, and appropriately updated motor plans to maximise expected reward. Furthermore, other methods of analysis imply that even larger networks are involved in action stopping. For example, Hsu et al. (2020) used resting state fMRI analysis and graph-theoretical approaches in a very large cohort of subjects performing a stop-signal task. They found significant correlations with connectivity in the dorsal and ventral attention and saliency networks, together with interactions with the frontal, cingulate and parietal areas.

Given the many open issues in understanding action inhibition, it comes as little surprise that the entire field has recently been reassessed by Hannah and Aron (2021). While stressing the central role of the prefrontal-basal ganglia circuits, they have combined information gained from different neuroscience disciplines. They offered an extended view of the action stopping scenario, by including tasks of increasing “real-worldness”, moving beyond the classic laboratory action stopping paradigms, which were mostly based on the analysis of the Stop Signal Reaction Time (Verbruggen and Gordon, 2008). In this new view, automatic forms of movement – such as postural control, gait, balance, and verbal communication – can be temporarily brought under voluntary control, and also inhibited. The relevance of these studies for movement abnormalities, such as shuddering, tics, freezing of gait, are also discussed. An interesting new arena for discussion has opened for this decade of studies on action stopping.

8.7. Motor output

The motor output for action suppression mostly resembles the default outflow of the Dorsal Premotor-Spinal Module: either through a direct pathway from F2 to spinal cord, or through a circuit additionally involving the basal ganglia and MI. Indeed, the action stopping function of PMd is supported by observations that the PMd projection to the STN in monkeys is stronger than that of MI (Borgognon et al., 2020). This opens a window on the possibility of a dorsal premotor influence on the hyperdirect cortical-basal ganglia pathway. Interestingly, the ventral portion of the STN in monkeys seems to be related to rapid action-stopping (Pasquereau and Turner, 2017).

In humans, the cortical outflow allowing action stopping might be subtly expanded. The model by Hannah and Aron discussed above predicts that action stopping signals would additionally be addressed by pre-SMA to the rIFG, where the stop-unit is located. This excites the STN, whose output in turn excites the GPi/SNr when movement suppression is required. The net results will be an augmented inhibition of the thalamic tonic excitatory influence on MI, which would reduce the probability of action initiation. This model also tentatively predicts an involvement of the “hyperdirect” pathway in action stopping, interpreted as an emergency-system that stops ongoing actions in a global fashion.

9. Ventral premotor spinal module: binding features for defensive behaviour

The Ventral Premotor Spinal module, centered on parietal area VIP and ventral premotor area F4, receives somatosensory, visual, auditory, and vestibular signals from parietal, temporal and frontal areas. Some neurons in this module display body-part centered receptive fields to visual or auditory stimuli. These peripersonal response fields, have been implicated in impact prediction and threat avoidance. This module has also been suggested to be involved in estimating numerosity, which can be relevant to approach or avoidance behavior. There is some evidence that the module might contribute to bodily ownership. The corticospinal tract of this module originates in ventral premotor area F4, which is a central node of the module, together with VIP. This module further communicates with the *posterior IPL cluster (LIP, MST),* the *ventral Premotor cluster* (F5c), the *anterior IPL cluster* (PF, SII), *the postero-medial SPL cluster* (V6A, PGm), the *medio-dorsal SPL cluster* (MIP), as well as vestibular areas (PIVC, VPS) that fall outside of our pre-defined parieto-premotor clusters.

9.1. Anatomo-functional organization

This module is rooted on a complex distributed system of parietal and frontal areas, whose core nodes are the ventral intraparietal area (VIP; Fig. 1a), which belongs to the posterior IPL cluster (*pIPL;* Fig. 1C), and ventral premotor area F4 in the ventral premotor cluster *(vPM;* Fig. 1B*)*.

F4 receives its strongest frontal inputs from MI, and ventral premotor area F5p**.** Weaker inputs originate from SMA, CMAr, F2vr, and F5a/c. F4 also receives strong afferents from parietal areas VIP, PF, and SII**.** VIP receives strong frontal projections from F4, modest input from MI, dorsal premotor F2vr, and CMAr. VIP is also target of strong parietal visuomotor inputs from eye (LIP), and reach (V6A, PGm, VIP) related areas, the motion sensitive area MST, the visual parietal Sylvian area (VPS), the parietoinsular vestibular area (PIVC), as well as from IPL area PF.

VIP is a classical multisensory area (i.e., an area containing neurons responding to stimuli of more than one sensory modality, even when presented in isolation) generally related to the processing of visual stimuli moving relative to the head and face (Colby et al., 1993; Duhamel et al., 1998; for a recent review see Foster et al., 2022). VIP’s bimodal neurons integrate visual motion inputs, originating in the superior temporal area MT/MST, with tactile signals from the head and face, probably stemming from PF and PFG. In addition, VIP receives visuomotor information from PGm and V6/V6A. VIP also receives vestibular input from PIVC (Grüsser et al., 1990) and combined optic flow/vestibular information from VPS (Chen et al., 2011). This convergence of information creates multiple reference frames that are simultaneously available in VIP (Foster et al., 2022).

Ventral premotor area F4 shares some crucial functional properties with VIP. These include bimodal neurons with 3-D visual and tactile receptive fields located on the face and head (Fogassi et al., 1996; Gentilucci et al., 1988). Another feature shared with VIP, is that long-lasting electrical stimulation of F4 results in complex movement sequences resembling defensive actions (see Graziano, 2006). Beyond shaping defensing behavior, some authors proposed that this cortico-cortical network is recruited for other ethologically relevant actions, such as reaching for and bringing food to the mouth (Fogassi et al., 1996; Gentilucci et al., 1988). Interestingly, after electrical stimulation in the monkey, D. Ferrier (1876) described "in the ascending frontal convolution, at the bend or knee of the anterior parietal sulcus (that is, central sulcus), *supination and flexion of the forearm*, by which the hand is raised to the mouth" (pag 143; see his Fig. 29, stimulation site 6). Ethologically critical actions, resembling self-feeding, have been elicited after electrical stimulation of similar sensory-motor regions in humans (Desmurget et al., 2014). However, other authors reported a possibly surprising lack of VIP activation during reaching (Graziano, 2017).

The egocentric and multisensory response properties that prevail in the ventral premotor module are also reflected in its insular connectivity: the module makes connections with the dorsal dysgranular area Idd through SII and F5 (Mesulam and Mufson, 1982; Friedman et al., 1986; Gerbella et al., 2011), and Idd is highly involved in processing information about one's own body (Evrard, 2019). PIVC meanwhile is connected to the posterior Granular insula (Ig; Mesulam and Mufson, 1982; Friedman et al., 1986; Guldin et al., 1992), which integrates vestibular, proprioceptive, visual motion, and auditory inputs (Chen et al., 2010b; Schinder and Newlands, 2014), all of which are necessary to create egocentric responses.

Finally, F4 receives strong thalamic input from VLo, and additional projections from area X and VPLo-VLc complex. The intralaminar nuclei, posterior thalamus and MD also project to F4 (Matelli et al., 1989; Kurata, 1994). Because VLo receives pallidal input, and area X and VPLo-VLc receive cerebellar input, F4 is under the influence of both basal ganglia and cerebellum. The thalamic input to VIP has not yet been studied in detail.

9.2. *Motor output*

The ventral premotor module likely conveys information to the spinal cord through F4. Defensive movements can be elicited by electrical stimulation of F4, and at much lower intensities than those necessary to elicit movements from VIP (see below). One would after all expect the region closest to the motor outflow to be the most easily and consistently excitable. In this view, the spinal projection from F4 might be used to predominantly pass defensive motor signals to the periphery.

However, given the short path length of the fibers connecting F4 and MI and the faster corticospinal projections from MI (Innocenti et al., 2019), it is plausible that fast reactions for defensive behavior, which generally rely on parieto-frontal interactions (Cooke et al., 2003; Graziano and Cooke, 2006; Kaas and Stepniewska, 2016), might involve MI (Cooke and Graziano, 2004; Kaas and Stepniewska, 2016). The F4 descending projection might then (additionally) play an auxiliary role in more complex decisions on how to act in the face of threatening stimuli. It can likely maintain neural dynamics in the output-null space typical of action preparation and freezing responses. Subsequently, it could bias activity towards the output-potent space when action must be taken. Such dynamics have been postulated for both motor and premotor cortex (Kaufman et al., 2013, 2014).

9.3. *Defensive behavior as a binding feature for diverse module function*

We have previously proposed (Caminiti et al., 2019) that VIP, F4, and their connections might be the substrates of a system for threat avoidance (Bufacchi and Iannetti, 2018; Battaglia-Mayer and Caminiti, 2019). Many body-part centered receptive fields in F4 and VIP likely indicate the value of performing defensive actions: when objects are nearer to body parts, defensive actions become more important, and so neurons that code for defensive actions will display body-part centered, or peripersonal fields (Bufacchi et al., 2022).

In this section, we will first present evidence for the defensive functions of the ventral premotor module (see Cléry et al., 2015 for a more expansive breakdown). In the following sub-sections, we will then argue that the other functional properties of this module emerge from encoding of defensive or avoidance behavior.

9.3.1. *Defense*

The strongest evidence for the defensive nature of this module comes from chemical manipulation and electrical activation. Defensive actions are more likely to occur when either VIP or F4 are more active (Graziano, 2006). Specifically, bicuculine activation of area F4 increased defensive response strength and probability, while inactivation with muscimol decreased them (Cooke and Graziano, 2004; for more details, see Box 9). Similarly, long-lasting electrical stimulation of both F4 and VIP evokes a constellation of movements resembling defensive actions aimed at protecting the head and upper body (Graziano et al., 2002; Cooke et al., 2003). Both areas elicit ear folding, eye closing, grimacing, shoulder shrugging, retracting of the face from contralateral space, and raising the contralateral arm so as to protect the head. F4 stimulation can also elicit retraction of the hand. Such movements are in line with the predominant receptive fields of F4 and VIP neurons: they are primarily centered around the head and the face, although F4 also shows more receptive fields around the hands and upper limbs than VIP (Gentilucci et al., 1983; Colby et al., 1993; Graziano et al., 1994; Fogassi et al., 1996; Duhamel et al., 1998). These results are not exclusive to macaques: similar types of defensive movements can be elicited from the fundus of the IPS in prosimian galagos (Stepniewska et al., 2005). VIP neurons are also part of a distributed network devoted to the estimation of numerosity in the visual scene (Nieder and Miller, 2004; Nieder and Dehaene, Nieder, 2009, 2016), which might be related to the need for different approaching and defensive reactions when faced with different numbers of threats (Caminiti et al., 2019).

Additional support for the existence and function of the ventral premotor-spinal module can be gleaned from several interesting *differences* between defensive movements elicited from VIP and F4 (Graziano and Cooke, 2006). First, the electrical thresholds for eliciting movements from F4 (~20 μA) are substantially lower than those for VIP (~100 μA). Second, motor responses elicited from VIP are more strongly inhibited by anesthesia than those elicited from F4. Third, while actions elicited from both areas interrupt behavior, after stimulation of F4 finishes, the ongoing behavior is usually resumed without delay. In contrast, after stimulation of VIP ends, the elicited movements often continue. Finally, VIP habituates to stimulation more strongly than F4 does. Taken together, these differences suggest that VIP might constitute a more flexible, context-dependent part of the defensive module, which may also be more involved in constructing environmental perception. F4, meanwhile, seems more related to enacting, modulating, and delaying fast motor responses aimed at immediately defending the body (Cléry et al., 2015).

9.3.2. *Impact prediction and visuo-tactile integration*

Defensive actions implicitly take into account the probability that a stimulus might contact the body: Defending oneself is meaningless if the body is unlikely to be damaged. If VIP and F4 are indeed hubs of defensive action, it should then come as no surprise that they have also frequently been linked to impact prediction (Cléry et al., 2015, 2017, 2018). We have recently demonstrated this emergent property of the need for defense: the neural network controlling an artificial agent to defend itself will also implicitly encode impact prediction (Bufacchi et al., 2022). Such a network will also perform visuo-tactile multisensory integration – another property often associated with F4 and VIP (Làdavas and Farnè, 2004; Dijkerman and Medendorp, 2021) – because both multisensory integration and impact prediction entail the same computation: they both use visual or auditory input to compute the probability of touch, but the prediction occurs at different timescales (Bufacchi and Iannetti, 2021).

Neural correlates of time to contact have in fact been found in many species and have often been related to defensive function. For example, locusts (Schlotterer, 1977; Rind and Simmons, 1992; Gabbiani et al., 1999) and flies (de Vries and Clandin, 2012) both have neurons that are tuned to looming objects on a collision course and are important for efficiently initiating escapes. Similarly, neurons in the pingeon's nucleus rotundus activate at specific times before predicted collision, regardless of stimulus size and velocity (Wang and Frost, 1992). While various other features of impending impact are also encoded by these neurons, their fixed-time discharge initiates avoidance responses (Wu et al., 2005). Zebrafish larvae also have loom-sensitive retinal-ganglion cells which are causally involved initiating escape responses (Temizer et al., 2015). Activity of all these neurons can be approximated using only velocity information, without acceleration.

However, we know from human experiments that at least one type of acceleration is taken into account when estimating time to impact: gravitational cues. Gravity is probably the only consistently predictable form of acceleration in the natural world. Consequently, humans use an internal model of gravity to catch objects (McIntyre et al., 2001), and even modulate some defensive reflexes (Bufacchi and Iannetti, 2016). In contrast, humans do not properly account for non-gravitational accelerations (Delle Monache et al., 2021). Furthermore, astronauts only partially un-learn their gravitational model while in space: even after a long time in orbit, they still catch objects as if there were some gravitational influences (McIntyre et al., 2001). These facts are useful functional tools to identify areas involved in impact prediction and object interception: such areas should also combine gravitational cues from vestibular and visual signals. Indeed, experiments in monkeys suggest that a distributed network contributes to intercepting objects (Merchant et al., 2004) and judging impact, in part because position history and current velocity seem to affect object interception differently (Merchant et al., 2003). The vestibular network (Indovina et al., 2020; Delle Monache et al., 2021) is similar in humans and monkeys, with core nodes in VIP, VPS and PIVC (and their human homologues), all of which are part of the Ventral Premotor Module. Accordingly, lesions to the human homologues of VPS and PIVC often cause vestibular symptoms like vertigo, dizziness, and postural instability (Marsden et al., 2005; Eguchi et al., 2019; Di Stefano et al., 2021). Damage to the wider area surrounding those regions prevents detecting mismatches between sensory gravitational cues and stored models of gravity (Maffei et al., 2016).

Therefore, the Ventral Premotor Module underlying defensive action naturally overlaps with a network involved in impact prediction and time to collision judgement. While impact prediction can be an emergent property of the need for defense, this second network might contribute to both appetitive and defensive actions, as we explain in the section below.

9.3.3. Egocentric spatial coding

The fact that impact prediction is implicitly encoded in a network performing defensive action suggests that such a network has a second emergent property: it can provide a statistical model of the world near the body. Specifically, we recently suggested (Bufacchi et al., 2022) that if a simple *in silico* agent is taught to avoid a stimulus by moving its limbs, it can effectively 'recycle' the value functions that it learns: if the agent has learned enough ways to avoid a stimulus, that set of action values can be used as building blocks, predictive features, of how the world near the agent works in general. When the agent is then exposed to a novel situation in which there is an appetitive stimulus instead of a threatening one, the agent can re-use its collection of defensive value functions to appropriately grab the appetitive stimulus. Therefore, the representation (and even perception) of the environment space near the body might be partially built up of defensive motor schemata in VIP and F4 (Graziano and Cooke, 2006; Rizzolatti et al., 1997; Berthoz, 2000; Colby, 1998). In line with this notion, VIP neurons also encode heading direction (Schlack et al., 2002, 2005; Britten, 2008; Chen et al., 2011, 2013, 2016).

However, we do not see this ventral premotor module as the main hub for *allocentric* navigation (a function assigned to the separate hippocampo-parieto-cingulate module), because the self-motion information in VIP does not causally contribute to heading perception (Chen et al., 2016). Nonetheless, egocentric-to-allocentric transformations

Box 8
Disorders of the Ventral premotor spinal module: defensive behaviour, body ownership

Lesion and inactivation studies

There exists a limited literature concerning impairments of defensive behavior in monkeys and/or humans after brain lesions. In monkeys, only one study has addressed the problem by chemical manipulation of the ventral premotor-spinal module.

Cooke and Graziano (2004) altered defensive behavior by enhancing and depressing neural activity in ventral premotor area F4 with the GABA antagonist bicuculline and the GABA agonist muscimol respectively. After bicuculine injection, the monkey reacted in an exaggerated manner to air puffs delivered to the contralateral cheek. The enhanced movements were typical of defensive reactions to threatening stimuli moving toward the face: a facial squint and blink, which are considered the most reliable signs of defensive reactions across species (Strauss, 1929; Landis and Hunt, 1939; Schiff et al., 1962; King et al., 1992). In contrast, after muscimol injection, an opposite and reduced effect was observed in the contralateral side of the face. In both cases, the observed effects depended on modulating the motor output of F4 neurons, rather than on sensory modulation or sensory neglect, because sensory modulation would affect contralateral sensory processing, and so also influence defensive behavior ipsilateral to the modulation.

Studies in humans.

Somatoparaphrenia is a condition of relevance to studying disorders of defensive behavior. It involves a sense of disownership towards contralesional paralyzed body parts of brain damaged patients, and is characterized by delusional belief that one's body part belongs to someone else (for reviews seeVallar and Ronchi, 2009; Gandola et al., 2012; Vallar and Calzolari, 2018; Ronchi et al., 2018). This condition is mostly associated with spatial neglect and right parieto-temporal lesions, but it can also occur with inferior frontal lesions, as well as with lesion of a large subcortical network including thalamus, basal ganglia, and the posterior limb of the internal capsule (Romano et al., 2014).

Romano et al. (2014) showed that somatoparaphrenia might be associated with an impairment of the network responsible for defensive behavior. They measured the skin conductance response to noxious stimuli approaching either the affected or the unaffected hand, using two possible stimuli: a painful needle and a neutral cotton swab; both stimuli could either touch the hand or stop just before contact, creating an anticipatory response. The anticipatory responses were significantly reduced when stimuli were directed toward the contralesional affected hand, as compared to the ipsilesional one. Skin conductance responses were not reduced in control subjects, nor in patients with anosognosia for the somatosensory deficit and in patients with motor neglect. However, it should be noted that the two stimuli differed along many dimensions, making it difficult to ascribe the observed effect purely to differences in the threatening value of the stimuli (see Mouraux and Iannetti, 2018 for a discussion on this topic).

involving some other PPC areas must causally contribute to allocentric spatial navigation (Whitlock et al., 2008; Gramann et al., 2010; Wilber et al., 2014; Wang et al., 2020). Therefore, while this module contains egocentric information that *could* be used to create allocentric navigational maps, the egocentric information that *is* actually used for allocentric navigation likely stems from the PPC areas of the hippocampo-parieto-cingulate module. Indeed, VIP encodes a task-dependent reference frame (Sasaki et al., 2020), which seems unsuitable for robust navigation.

9.3.4. Bodily ownership

Peripersonal fields and neural activity in VIP and F4 have also been tentatively linked, albeit inconclusively, to the perception of ownership and location of body parts, and even the whole body (Blanke et al., 2015; Noel et al., 2015; Guterstam et al., 2019). The reasoning behind this link often follows roughly the following steps: first, tactile input defines an interaction with one's body. Second, vision defines one's environment. Third, one can only define the self and ownership of body parts in relation to the things that are not the self. Fourth, since VIP and F4 integrate touch with vision, they can contrast and integrate sensations which must come from the self (via the touch), with those coming from the environment (through vision). Hence VIP and F4 might contribute to one's perception of ownership and location of body parts in the world. This line of reasoning often draws on the rubber-hand-illusion literature (Serino, 2019; Bertoni et al., 2021), although the direct links between that literature and VIP/F4 activity remain up for debate (e.g., Graziano and Cooke, 2001). Perhaps more convincingly, lesions to the ventral premotor module and the surrounding white matter result in both reduced feelings of ownership and diminished defensive responses (see Box 8 below).

We propose an alternative, although non-mutually exclusive, perspective on the link between this module and the feeling of body-part ownership. This speculative link relies on defensive function: the value of defensive actions can be an excellent indicator of ownership over a body part. Specifically, and from an entropic perspective, defensive actions are those which counteract a *very fast, very large* increase in an animal's entropy (Friston et al., 2022): they prevent the body from becoming quickly and extremely disordered, i.e., damaged or dismembered. Such actions differ from others, which instead either stave off a gradual increase in entropy, or simply reduce entropy, such as eating, foraging, seeking shelter, urinating etc. In other words, if the brain aims to determine what 'belongs to the body', it could identify actions that prevent a sharp increase of entropy, and associate ownership to the areas which would experience that increase. This possibility is especially appealing, given that interrupting the outflow of information from VIP by damaging the surrounding gray matter prevents feelings of ownership over body parts (see Box 9 below). Furthermore, a recent fMRI study showed neural representations of body ownership in IPS and PMv that are equally active whether participants are being touched or are themselves moving (Sonobe et al., 2023). This indicates that VIPs relationship to bodily ownership is probably not purely visuo-tactile.

10. Summary and future perspectives

10.1. Summary

The existence of several cortico-spinal systems has long been known. However, no systematic attempts have been made to discuss their organization nor potential functions within a coherent conceptual framework. This was our goal. Several lines of evidence, not available few years ago, now indicate that different cortico-spinal modules underlie different forms of motor behavior. These modules are composed of clusters of parietal and frontal areas that share functional properties, afferent connectivity, and corticofugal pathways. Such modular architecture is supported by (1) the statistics of parieto-frontal connectivity, (2) the similar functional properties of neurons across the clusters of each module, (3) energy saving considerations, and (4) the effects of clinical and experimental lesions of different modules.

Modules can directly target the motor periphery, with or without the involvement of MI. This avoids the use of long oligosynaptic, and energetically expensive, unmyelinated cortico-cortical connections. Such unmyelinated axons, instead, more likely play modulatory roles during learning and when performing new tasks (Battaglia-Mayer and Caminiti, 2019; Innocenti et al., 2022). In this view, each module targets spinal interneurons and motoneurons privately, using fewer and faster descending myelinated axons. Such axons transfer information more accurately through precise spike-timing rather than only using spike-rate. The efficiency of bypassing MI in this way is further supported by 1) the different ranges of axon diameters available to cortico-cortical vs. corticospinal communication, and by 2) the fact that metabolic costs scale-up linearly with conduction distance and therefore become prohibitive in the primate brain. The fact that the size of recruited corticospinal axons depends on task demand and difficulty (Miri et al., 2017) suggests that the accurate selection of heterogeneous axons is a major result of evolution.

Here we posited the existence of at least six corticospinal modules by combining anatomical, histological, physiological, metabolic, and clinical information. The cortico-spinal modules and functions discussed here include modules for: 1) arm reaching, tool use and object construction; 2) spatial navigation and locomotion; 3) grasping and observation of hand and mouth actions; 4) action initiation, motor sequences, time encoding; 5) conditional, arbitrary sensorimotor association and learning, action plan switching and action inhibition, social cognition; 6) defensive actions.

10.2. Future perspectives

10.2.1. Across-module interactions in novel tasks, and the role of MI

We now face the challenge of understanding the interaction between modules in novel tasks. Current computational research – most recently on hierarchical reinforcement learning – suggests that modules offer a library of tools that can be dynamically recombined to solve novel tasks (Kashtan and Alon, 2005; Barreto et al., 2017, 2018, 2020). As an agent progresses in learning a new task, such rough re-combinations of activity from separate modules could slowly be replaced by more task-dedicated, cross-module networks. Recent work in rodents supports this hypothesis: mice that learned two hierarchical sub-tasks were able to quickly recombine the neural activity underlying both, to effectively learn a new composite task. Their performance was substantially better than the mice who had not learned the sub-tasks, and importantly, the neural activity supporting each sub-task was localized to separate parieto-premotor module-like networks (Makino, 2023). After the mice gained more experience with the composite task, the neural activity in the original networks became less distinguishable, indicating that a new task-specific functional sub-network was formed.

Another set of studies showed similar results, and even suggested where the early binding of modules might take place: while MI inactivation impaired forelimb movements during early and middle stages of motor learning, it had no effect in the late stage (Hwang et al., 2019). In fact, MI disengagement positively correlated with task performance after learning: the less MI was involved in a task, the better the task was performed (Kawai et al., 2015; Hwang et al., 2021). A similar effect is seen in humans: MI activity contralateral to the used hand decreases as fast learning progresses, as does activity in the dorsal pole and ipsilateral dlPFC (Kami et al. 1995; Floyer-Lea and Matthews, 2004, 2005). Meanwhile, activity in the premotor cortex, SMA, PPC, and cerebellum increases Floyer-Lea and Matthews (2004, 2005), indicating the shaping of more task-specific networks.

Therefore, MI might be a major hub that brings parallel modules together, in the specific context of novel tasks. Once an animal is exposed to a particular task for long enough, a dedicated network is formed that bypasses MI. This would be reflected in the increased activity of the other motor areas, and simultaneous decrease in coupling with MI. Functional connectivity in humans shows exactly that pattern: dPMC, SMA and pre-SMA are more strongly coupled to MI during early rather than late sequence learning (Sun et al., 2007). Other studies confirm that during early learning a circuit focused on MI progressively decreases its activity (MI-premotor-parietal-cerebellar), while another circuit – not including MI – becomes more active (PPC-premotor) (Hikosaka et al., 2002; Kincses et al., 2008). As dedicated networks form for similar tasks, we can then imagine how modules might originate. Even sleep-dependent improvements of early learning coincide with decreases in BOLD MI activity (Fischer et al., 2005). This suggests that the recombinatory pattern learned in MI is used to consolidate the MI-bypassing network during sleep, weakening the MI representation in the process. Such a mechanism parallels the way hippocampal sequences are used to consolidate memories into the cortex, while simultaneously weakening the sequence in the hippocampus (Klinzing et al., 2019). The concept of MI functioning as an early recombinatory hub also aligns with the faster conduction velocities of its spinal tract: Given that transmitting and recombining the activity from other modules are time-consuming processes, MI's recombined signals must 'catch up' with those sent to the spinal cord along other cortico-spinal tracts. This ensures that more coherent commands are delivered to the muscles.

However, the role of MI cannot purely be one of early recombination: the classical view of MI function has considerable empirical support, emphasizing its role in the control and recovery of fine finger movements and hand dexterity (Passingham et al., 1983; Rouiller et al., 1998; Liu and Rouiller, 1999; Rouiller and Olivier, 2004; Kaeser et al., 2010; Bashir et al., 2012; Hoogewoud et al., 2013; Murata et al., 2008; Lemon, 2008; Darling et al., 2021; Strick et al., 2021), as well as its contribution to other tasks such as reaching and locomotion (Georgopoulos and Grillner, 1989; Nielsen, 2001). These traditional functions of MI are more in line with *slow* learning of motor skills, especially sequences of finger movements: after the decrease in MI activity during fast learning, MI activity actually progressively increases over the course of weeks to months, specifically for dextrous movements (Kami et al., 1995; Kleim et al., 2004; Floyer-Lea and Matthews, 2005).

Therefore, we envision a dual role for MI in the recombination and reshaping of parieto-premotor modules. First, during early learning in novel situations, MI acts as a recombinatory hub, sticking together activity from multiple modules to create a decent action policy on the fly. As this early learning continues, the importance of MI decreases and a more task-specific network starts to form and take over. Second, once early learning has progressed, more fine-grained alterations can be made to the new task-specific network. In this second stage, MI can be reincorporated into the network, *if the task demands are suited to the specialties of MI*. In other words, MI plays a permissive role only for dextrous learned behaviors, while it plays an instructive role in the early acquisition of new motor skills and in adapting subcortical networks to meet behavioral demands (Grillner and Wallén, 2004). Given the direct cortical control that (human) MI has over finger movements, we should therefore see MI re-emerge as an important node in many of the finger-based tasks performed in human experiments. The slow, fine-grained alterations to task-specific networks that we envision also have considerable empirical support: long-term learning increases both gray and white matter volume in regions specific to the learned task (Draganski et al., 2004; Bengtsson et al., 2005; Bermudez and Zatorre, 2005; Cannonieri et al., 2007; Han et al., 2009; Scholz et al., 2009). Interestingly, the magnitude and timing of changes in gray and white matter show little correlation. They might therefore represent different stages in the recombination-to-refinement trajectory that we have outlined here. We consider this an important and interesting direction for future studies. We also note that our view of slow learning is subtly different from the traditional views in which motor control progressively moves from frontal to parietal areas: we instead claim that the refined task-specific networks will utilize the brain regions which have most efficient access to the information necessary for the task. Therefore, over the course of a lifetime, we can end up with the modules described in this work, which are biased to frontal or parietal areas, depending on the functions that they subserve.

Finally, we do not claim that MI should be the only or ultimate recombiner of modular activity in novel environments. For example, while we postulate that control over complex actions moves from MI to parieto-premotor modules, in mice the basal ganglia often end up controlling the detailed kinematics of learned motor skills somewhat independently of cortex (Dhawale et al., 2021). Sub-cortical structures in primates inarguably also have considerable roles in shaping motor responses. In fact, it seems like the associative striatum could perform a complementary role to what we propose for MI during early learning, recombining activity from multiple modules (Albouy et al., 2008; Ashby et al., 2010). The sensorimotor striatum meanwhile seems like it would be the outflow for the consolidated task-specific networks (Ashby et al., 2010). Other cortical regions might contribute to the reweighting as well, although probably not as gatekeepers to direct spinal access. For example, the orbitofrontal and prefrontal cortex provide information about reward and decision variables, such as the comparative reward offered by objects (see Schultz, 2015, 2016 for reviews). Such information is crucial for estimating the weight with which to combine modules (Barreto et al., 2018).

10.2.2. *Modular interactions that are stable across tasks*

We must also look for consistencies in how modules interact across tasks and timescales. Subcortical regions such as the brainstem, basal ganglia and thalamus probably play a role in coordinating information from and to parallel modules. For example, the dorsal striatum combines information from various cortical sources in order to act and make decisions (Balleine et al., 2007). It could therefore, as mentioned above, integrate motor commands from the parallel parieto-premotor modules. The thalamus on the other hand shares rather than integrates information between modules, possibly improving coordination and preventing competition (Sherman, 2016; Halassa and Kastner, 2017). For example, the cortico-thalamic projections from parietal areas PE and PEip (PEa) project both to nucleus LP territories from which they receive information, as well as to LP territories that in turn project to dorsal premotor cortex (PMd; F2; Cappe et al., 2009). This provides a trans-thalamic loop (Guillery and Sherman, 2002) for between-module coordination (see Battaglia-Mayer and Caminiti, 2009). Cortically, the insula might play a similar role in concert with the ACC, sharing information across modules, albeit at substantially higher levels of abstraction than the thalamus (Dosenbach et al., 2006; Menon and Uddin, 2010; Uddin, 2015; Evrard, 2019). The insula is after all strongly interconnected with all considered modules. The cerebellum, finally, could both integrate and share task-relevant information across modules, including information arriving directly from the sensory peripehery, thanks to the cortico-ponto-cereballar pathways and the reentrant cerebello-thalamo-cortical systems. Such systems confer the parieto-frontal modules additional sensorimotor adaptation and flexibility (see Areshenkoff et al., 2022).

However, explicit regulatory hubs might not always be necessary to balance between-module dynamics. Artificial modular neural networks display the characteristic robustness and coordination of biological modular networks as emergent properties, without requiring a dedicated coordination module (Chen et al., 2021). Similarly, artificial agents trained to intercept certain objects and avoid others automatically form sub-networks dedicated to responding to the different object types. These sub-networks have an inherent dynamic balance between them, given that the agent responds appropriately to different stimuli, with different sub-networks varying their activation as appropriate (Bufacchi et al., 2022). Much of the dynamic balance between modules might therefore be regulated by the interconnections between the modules themselves, possibly through inter-module communication in output-null spaces (Kaufman et al., 2014).

10.2.3. *Cross-module functions*

A third challenge is posed by functions which feature prominently in more than one module, such as social cognition and time estimation. A possible explanation is that these cross-module functions are in some ways closer to world states than specific tasks: social considerations can be important in almost any environment and for any action, as is keeping track of time. Despite the experiments in which social or time-keeping tasks are carefully designed to isolate exactly these elements, there are likely few situations or tasks in real life which would shape time- or social- specific modules.

If so, the particular aspects of social cognition and time encoding should vary between modules, in line with the broader function of the module. We argue that this is precisely what we observe, and take social cognition as an example. The lateral parieto-frontal module encodes facial emotions of others, as well as social context, which is in line with its ability to perform movements that require coordination between the hand and the face. The medial premotor module instead seems to contain more information about the intentions of others, including whether their actions match those intentions. Such functions are in line with the module's emphasis on longer-term goals and intentions, and the sequences of actions necessary to achieve them. The dorsal premotor module finally is more involved in joint action and coordination. These are functions for which one needs to be able to form arbitrary associations between stimuli and action, as well as appropriately inhibit one's own actions: precisely the type of operations with which this module is concerned.

In this view, actions conveying important social information should be controlled by a cross-module network involving the modules mentioned here. That is in fact the case, and we provide the example of facial expressions (for recent reviews see Müri, 2016; Ferrari et al., 2017; Cattaneo and Pavesi, 2014). In macaque monkeys, at least five cortical regions are involved in producing these expressions, which all project to the facial nucleus of the pons: MI, dorso-lateral and ventrolateral premotor cortex, and two regions of the cingulate gyrus: one in area 24, the M3 of Morecraft et al. (2001), probably including CMAr, and a second, more posterior area (M4), likely encompassing CMAd/v. In the same vein, the amygdala and its distributed connections provide a substrate for social perception, since neural activity in monkeys is tuned to specific parts of faces and in humans to the internal states evoked by viewing faces (Rutishauser et al., 2015). These areas are part of the dorsal premotor, ventral premotor, medial premotor and dorsal parieto-frontal modules, constituting a cross-module network. The existence of certain cross-module functions is therefore not a counterpoint to the perspective that we propose, although there is clearly more ground for investigating and defining a firmer distinction between inter- and intra-modular functions.

10.2.4. *Clinical implications*

An important final question is whether the modularity of command systems can provide an anatomical substrate and physiological mechanism for facilitating the recovery of cognitive-motor functions after lesions in parieto-frontal areas, or their descending systems. There is indeed evidence that the dorsal premotor spinal module participates in the recovery of motor functions in patients with stroke or focal lesion affecting the MI-CST (Johansen-Berg et al., 2002; Fridman et al., 2004; Darling et al., 2011), and that spike-timing dependent plasticity of non-MI descending projections can attenuate the clinical consequences of lesions affecting the MI descending outflow (Bunday and Perez, 2012; see also commentary by Lemon, 2012). Moreover, the F5 spinal projection has been implicated in the remarkable recovery of hand dexterity after lesion limited to the hand area of MI (Sasaki et al., 2004; Nishimura et al., 2007), thanks to its influence on the C3-C4 propriospinal system stemming from the mid-dorsal sector of the intermediate zone (Isa et al., 2006). These phenomena can be interpreted within the context of the homeostatic plasticity and regulation of cortical networks (Turrigiano, 1999; Marder and Goaillard, 2006; Keck et al., 2013) and convey an important evolutionary implication, since they mitigate the dramatic consequences of brain lesions.

Only a sustained research effort integrating basic neurophysiology, neuropsychology, and computational modelling can answer these questions. Modelling approaches now benefit from extensive knowledge on axon diameters and conduction velocities of cortico-cortical and cortico-spinal systems and can thereby help analyze how conduction delays influence the temporal dynamics of cortical networks. This also has translational value, given that different brain diseases can result from the preferential impairment of axons of a particular diameter.

MODULES SYNOPSIS.

	Function	Anatomy	Motor output	Lesions
DORSAL PARIETO-FRONTAL SPINAL MODULE	This module encodes functions including arm reaching (Mountcastle et al., 1975; Johnson et al., 1996; Snyder et al., 1997;Battaglia-Mayer et al., 2000) and its online control (Archambault et al., 2009, 2011), eye-hand coordination (Battaglia-Mayer et al., 2000, 2001; Marconi et al., 2001), tool use (Iriki et al., 1996; Peeters et al., 2013), and object construction (Chafee et al., 2005).	The module's core areas are intraparietal areas PEip and MIP. The module further consists of clusters of parietal areas of the *medio-dorsa*l (areas PEci, PEc), *postero-medial* (V6A, PGm, area 31), *and inferior parietal* (area PG) clusters. Beyond PPC, this module's operations depend on a distributed system of premotor (F2) and cingulate areas, and on subcortical relations with pontine nuclei and, therefore, cerebellum.	The spinal output of his module stems from superior parietal area PEip (Rathelot et al., 2017; Innocenti et al., 2019), although it can also transmit information through F2.	Posterior parietal lesions of this module result in optic ataxia, which includes impaired online control of hand reaching, tool apraxia and constructional apraxia. See Boxs 1–2.
HIPPOCAMPO-PARIETO-CINGULATE SPINAL MODULE	This module underpins spatial navigation and locomotion through multisensory and sensorimotor integration, transforming spatial information between allocentric (world-centered) and egocentric (self-centred) reference frames.	The two poles of this circuit are the hippocampal formation on one side (O'Keefe and Dostrovsky (1971); Fyhn et al., 2004; Moser et al., 2008) and on the other side retrosplenial (area 31;Vann et al., 2009), postero-medial area PGm (Sato et al., 2006), and inferior parietal area PG (7a);Crowe et al. (2004);Noel et al. (2022)).	Motor commands from this module likely reach the periphery through the strong direct cortico-spinal pathway stemming from the cingulate motor area CMAv (He et al., 1995; Luppino et al., 1991), which in turn receives from area 31 (Picard and Strick, 1996), and PGm (Morecraft et al., 2004)	Lesions of these hippocampal, retrosplenial and parietal areas impair various forms of spatial navigation and memory, across species (rodents, macaques and humans;Maguire, 2001; Sutherland et al., 1988; Lavenex et al., 2006; Rueckemann and Buffalo, 2017) See Box 3.

(*continued on next page*)

(*continued*)

	Function	Anatomy	Motor output	Lesions
LATERAL PARIETO-FRONTAL SPINAL MODULE	This module encodes observation (Rizzolatti et al., 2014), and planning and execution of grasping (Mountcastle et al., 1975; Jeannerod et al., 1995; Dann et al., 2016; Schaffelhofer and Scherberger, 2016; Borra et al., 2017), as well as extended functions involving mouth and hand-to-mouth actions, and communicative gestures (Ferrari et al., 2003; Maranesi et al., 2012).	This module's core areas are AIP, PFG, and F5a-c-p. The module consists also of areas of the *ventral premotor (GrFO), anterior IPL* (SII), and *ventro-orbitofrontal (i12r, r46vc) clusters,* as well as infero-temporal area LB2. The module's inputs from the insula and inner perisylvian regions contribute to high-level social functions (approach, aggression, vocalization; Evrard, 2019; Jezzini et al., 2012), while those from amygdala contribute to more basic social computations (i.e., information from other's gaze, facial identity and expressions).	The module projects directly to the spinal cord through two pathways. The first stems from area PFG (Rozzi et al., 2006), and probably pre-informs the spinal centers about others' intentions and potential actions. The second originates from F5c and includes mirror pyramidal tract neurons (Kraskov et al., 2009), which might suppress one's own actions during action observation. The F5 descending projection to the facial, trigeminal, and solitary tract nuclei (Morecraft et al., 2001) underlies the selection of combined hand and mouth actions by ventral premotor areas (Gerbella et al., 2016).	Some alterations of the mirror system have been related to the Autism Spectrum Disorder (Rizzolatti et al., 2014). See Boxs 4–5.
MEDIAL PREMOTOR SPINAL MODULE	This module encodes self-initiated (Brinkman and Porter, 1979; Tanji and Kurata, 1982), and memorized actions (Roland, 1987; 1980), to a lesser extent, sensory-triggered movements (Romo and Schultz, 1987). It has two additional major functions: 1) encoding the spatial and temporal aspects of serial order of behavior (Lashley, 1951), in concert with basal ganglia and cerebellum (Tanji, 2001; Hikosaka et al., 1998, 2000), and 2) encoding time during various cognitive and sensorimotor events (e.g., estimating elapsed and remaining time, and categorizing relative event durations, temporal decision making; MIta et al., 2009; Merchant et al., 2011, 2013; Bi and Zou, 2020).	The central nodes of this module are SMA and pre-SMA. The module is further composed of the *dorso-medial Premotor* (F7, F7-SEF), and *cingulate* (CMAr and CMAv/d) *clusters*. It receives input from the *medio-dorsal SPL cluster* (MIP, PEip, PEc), *ventral premomotor vPM cluster* (F4, F5), and from parietal area PEci.	This module's spinal projection stems from SMA, which has monosynaptic connections with spinal motoneurons (He et al., 1995; Innocenti et al., 2019).	Lesions of this module are associated with various deficits, including impaired self-generated movements, learningcccccccf and remembering motor sequences, sequential limb and eye movements problems (SMA and SEF respectively), increased omission and commission errors, and improper isochronous tapping. Clinical studies in humans confirm such findings, with additional phenomena such as alien hand syndrome, reduction of self-initiated speech, involuntary vocalization, changes in speech rate, agrammatical output, impairments in producing rhythms from memory, and difficulty in task switching. See Box 6.
DORSAL PREMOTOR SPINAL MODULE:	This module is central to conditional motor learning and behavior (Passingham, 1993; Wise et al., 1997; Wise and Murray, 2000).The module also participates in the online control of reaching (Archambault et al., 2011), reach-direction selection (Cisek and Kalaska, 2005), reward-based decision making about action initiation and suppression (Schultz et al., 2015;Giamundo et al., 2021), encoding choice difficulty during logical decisions (Mione et al., 2020), and switching and inhibiting ongoing movements (Mirabella et al., 2011). Finally, the module is recruited when observing and rehearsing familiar actions (Cisek and Kalaska, 2004), and during social cognition concerning joint-action with another agent (Ferrari-Toniolo et al., 2019; Pezzulo et al., 2022).	This module's core area is F2 of the *the dorso-medial premotor cluster*, The module is strongly connected to other areas at different hierarchical level of *the same cluster* (F7, SMA), and to parts of *the cingulate* (CMAr, 24a-b), *ventral premotor* (F4, F5), *medio-dorsal SPL* (PEc, MIP, PEip), and *postero-medial SPL* (V6A) *clusters.*	The module's motor output to the spinal cord stems from area F2 (Dum and Strick, 1991; He et al., 1993; Innocenti et al., 2019; Strick, 2021)	Lesions and inactivation of prefrontal cortex and PMd in monkeys impair action suppression, the use of non-spatial cues for movement control (Gaffan and Harrison, 1988; Petrides, 1982; Passingham, 1993; Kurata and Hoffman, 1994), and internally-generated memorized motor sequences (Ohbayashi et al., 2016). This is consistent with a meta-analysis of motor learning studies in humans (Hardwick et al., 2013). inactivation of PMd aPMd lesionesion here results in commission errors (Picton et al., 2007). Decreased motor inhibition, dependent on PMd impairment, has been documented in children with attentional disorders (Nig, 2001), and substance abuse disorders (Zang et al., 2018,Wang et al., 2018b). See Box 7.
VENTRAL PREMOTOR SPINAL MODULE	This module is involved in defense of the body (Graziano, 2006; Cléry et al., 2015; Bufacchi et al., 2022), impact prediction (Cléry et al., 2017, 2018; Bertoni et al., 2021), visuo-tactile multisensory integration (Làdavas and Farnè, 2004; Dijkerman and Medendorp, 2021), egocentric spatial coding (Colby, 1998; Chen et al., 2011; Foster et al., 2022) and bodily ownership (Blanke et al., 2015; Noel et al., 2015; Guterstam et al., 2019; Serino, 2019; Bertoni et al., 2021).	The module's core areas are VIP and F4. It further communicates with areas of the posterior IPL cluster (LIP, MST), ventral Premotor cluster (F5c), anterior IPL cluster (PF, SII), postero-medial SPL cluster (V6A, PGm), medio-dorsal SPL cluster (MIP), and parieto-vestibular areas PIVC and VPS.	The module's spinal projections stem from F4. The short path length from F4 to MI suggests that MI might also be actively involved in fast, short-latency defensive reactions to sudden stimuli.	Lesion studies of the module are limited. Chemical suppression of F4 results in decreased defensive responses, while activation of F4 strengthens defensive reactions (Cooke and Graziano, 2004). In humans, damage to areas of this module can result in somatoparaphrenia, a condition characterized by the belief that one's body part belongs to someone else (Ronchi et al., 2018). This condition seems to be associated with impaired defensive behaviour (Romano et al., 2014). See Box 8.

CRediT authorship contribution statement

Conception and design of the manuscript: R. Caminiti. Drafting of the paper, all authors. Organization of the paper: R. Caminiti ideated and produced the first draft of the ms; all authors contributed to its final version and organization., Revising paper critically for important intellectual content: all authors, Final approval of the submitted version: all authors.

Declaration of Competing Interest

None.

Data availability

No data was used for the research described in the article.

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References

Aflalo, T., Zhang, C., Revechkis, B., Rosario, E., Pouratian, N., Andersen, R.A., 2022. Implicit mechanisms of intention. Curr. Biol. 32 (9), 2051–2060. https://doi.org/10.1016/j.cub.2022.03.047.

Akkal, D., Dum, R.P., Strick, P.L., 2007. Supplementary motor area and presupplementary motor area: targets of basal ganglia and cerebellar output. J. Neurosci. 27 (40), 10659–10673. https://doi.org/10.1523/JNEUROSCI.3134-07.2007.

Albouy, G., Sterpenich, V., Balteau, E., Vandewalle, G., Desseilles, M., Dang-Vu, T., Darsaud, A., Ruby, P., Luppi, P.H., Degueldre, C., Peigneux, P., 2008. Both the hippocampus and striatum are involved in consolidation of motor sequence memory. Apr 24 Neuron 58 (2), 261–272. https://doi.org/10.1016/j.neuron.2008.02.008.

Alexander, G.E., Crutcher, M.D., 1990. Preparation for movement: neural representations of intended direction in three motor areas of the monkey. J. Neurophysiol. 64 (1), 133–150. https://doi.org/10.1152/jn.1990.64.1.133.

Alexander, G.E., DeLong, M.R., 1985. Microstimulation of the primate neostriatum. II. Somatotopic organization of striatal microexcitable zones and their relation to neuronal response properties. J. Neurophysiol. 53 (6), 1417–1430. https://doi.org/10.1152/jn.1985.53.6.1417.

Allman, JM, Hakeem, A, Erwin, JM, Nimchinsky, E, Hof, P, 2001. The anterior cingulate cortex. The evolution of an interface between emotion and cognition. Ann N Y Acad Sci 935, 107–117.

Amoruso, L., Finisguerra, A., Urgesi, C., 2018. Autistic traits predict poor integration between top-down contextual expectations and movement kinematics during action observation. Published 2018 Nov 1. doi Sci. Rep. 8 (1), 16208. https://doi.org/10.1038/s41598-018-33827-8.

Archambault, P.S., Caminiti, R., Battaglia-Mayer, A., 2009. Cortical mechanisms for online control of hand movement trajectory: the role of the posterior parietal cortex. Cereb. Cortex 19 (12), 2848–2864. https://doi.org/10.1093/cercor/bhp058.

Archambault, P.S., Ferrari-Toniolo, S., Battaglia-Mayer, A., 2011. Online control of hand trajectory and evolution of motor intention in the parietofrontal system. J. Neurosci. 31 (2), 742–752. https://doi.org/10.1523/JNEUROSCI.2623-10.2011.

Areshenkoff, et al., 2022. eLife 11, e74591. DOI: https:// doi. org/ 10. 7554/ eLife.74591.

Aron, A.R., 2007. The neural basis of inhibition in cognitive control. Neuroscientist 13 (3), 214–228. https://doi.org/10.1177/1073858407299288.

Aron, A.R., Poldrack, R.A., 2006. Cortical and subcortical contributions to Stop signal response inhibition: role of the subthalamic nucleus. J. Neurosci. 26, 2424–2433. https://doi.org/10.1523/JNEUROSCI.4682-05.2006.

Aron, A.R., Fletcher, P.C., Bullmore, E.T., Sahakian, B.J., Robbins, T.W., 2003. Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. Nat. Neurosci. 6 (2), 115–116 (Feb).

Aron, A.R., Robbins, T.W., Poldrack, R.A., 2014. Inhibition and the right inferior frontal cortex: one decade on. Trends Cogn. Sci. 18 (4), 177–185 doi: 10.1016/j.tics.2013.12.003. Epub 2014 Jan 15. PMID: 24440116.

Asaad, W.F., Rainer, G., Miller, E.K., 1998. Neural activity in the primate prefrontal cortex during associative learning. Neuron 21 (6), 1399–1407. https://doi.org/10.1016/s0896-6273(00)80658-3.

Ashby, F.G., Maddox, W.T., 2005. Human category learning. Annu Rev. Psychol. 56, 149–178 doi: 10.1146/annurev.psych.56.091103.070217. PMID: 15709932.

Ashby, F.G., Turner, B.O., Horvitz, J.C., 2010. Cortical and basal ganglia contributions to habit learning and automaticity. May 1 Trends Cogn. Sci. 14 (5), 208–215. https://doi.org/10.1016/j.tics.2010.02.001.

Averbeck, B.B., Battaglia-Mayer, A., Guglielmo, C., Caminiti, R., 2009a. Statistical analysis of parieto-frontal cognitive-motor networks. J. Neurophysiol. 102 (3), 19111920. https://doi.org/10.1152/jn.00519.2009.

Averbeck, B.B., Chafee, M.V., Crowe, D.A., Georgopoulos, A.P., 2002. Parallel processing of serial movements in prefrontal cortex. Proc. Natl. Acad. Sci. Usa. 99 (20), 13172–13177. https://doi.org/10.1073/pnas.162485599.

Averbeck, B.B., Crowe, D.A., Chafee, M.V., Georgopoulos, A.P., 2009b. Differential contribution of superior parietal and dorsal-lateral prefrontal cortices in copying. Cortex 45 (3), 432–441. https://doi.org/10.1016/j.cortex.2008.02.007.

Ayala, Y.A., Lehmann, A., Merchant, H., 2017. Monkeys share the neurophysiological basis for encoding sound periodicities captured by the frequency-following response with humans. Sci. Rep. 7 (1), 16687. Published 2017 Nov 30. doi:10.1038/s41598-017-16774-8.

Balleine, B.W., Delgado, M.R., Hikosaka, O., 2007. The role of the dorsal striatum in reward and decision-making. Aug 1 J. Neurosci. 27 (31), 8161–8165. https://doi.org/10.1523/JNEUROSCI.1554-07.2007.

Bangs, W.J., 1956. Bilateral lesions of the anterior cingulate gyri; report of case. Bull. Los Angel Neuro Soc. 21 (3), 149–151.

Barreto, A., Dabney, W., Munos, R., Hunt, J.J., Schaul, T., van Hasselt, H.P., Silver, D., 2017. Successor features for transfer in reinforcement learning. Adv. Neural Inf. Process. Syst. 30.

Barreto A., Borsa D., Quan J., Schaul T., Silver D., Hessel M., Mankowitz D., Zidek A., Munos R. Transfer in Deep Reinforcement Learning Using Successor Features and Generalised Policy Improvement. Proceedings of the 35th International Conference on Machine Learning, PMLR, 2018; 80:501–510, 2018.

Barreto A., Hou S., Borsa D., Silver D., Precup D. Fast reinforcement learning with generalized policy updates. Proceedings of the National Academy of Sciences, 2020 Dec 1;117(48):30079–30087. doi:10.1073/pnas.1907370117.

Barris, R.W., Schuman, H.R., 1953. Bilateral anterior cingulate gyrus lesions. Syndrome of the anterior cingulate gyri. Neurology 3, 44–52. https://doi.org/10.1212/WNL.3.1.44.

Bashir, S., Kaeser, M., Wyss, A., Hamadjida, A., Liu, Y., Bloch, J., Brunet, J.F., Belhaj-Saif, A., Rouiller, E.M., 2012. Short-term effects of unilateral lesion of the primary motor cortex (M1) on ipsilesional hand dexterity in adult macaque monkeys. Brain Struct. Funct. 217 (1), 63–79 (Jan).

Battaglia-Mayer, A., Caminiti, R., 2002. Optic ataxia as a result of the breakdown of the global tuning fields of parietal neurones. Brain 125 (Pt 2), 225–237. https://doi.org/10.1093/brain/awf034.

Battaglia-Mayer, A., Caminiti, R., 2019. Corticocortical Systems Underlying High-Order Motor Control. J. Neurosci. 39 (23), 4404–4421. https://doi.org/10.1523/JNEUROSCI.2094-18.2019.

Battaglia-Mayer, A., Ferraina, S., Mitsuda, T., et al., 2000. Early coding of reaching in the parietooccipital cortex. J. Neurophysiol. 83 (4), 2374–2391. https://doi.org/10.1152/jn.2000.83.4.2374.

Battaglia-Mayer, A., Ferraina, S., Genovesio, A., et al., 2001. Eye-hand coordination during reaching. II. An analysis of the relationships between visuomanual signals in parietal cortex and parieto-frontal association projections. Cereb. Cortex 11 (6), 528–544. https://doi.org/10.1093/cercor/11.6.528.

Battaglia-Mayer, A., Ferrari-Toniolo, S., Visco-Comandini, F., Archambault, P.S., Saberi-Moghadam, S., Caminiti, R., 2013. Impairment of online control of hand and eye movements in a monkey model of optic ataxia. Cereb. Cortex 23 (11), 2644–2656. https://doi.org/10.1093/cercor/bhs250.

Battaglia-Mayer, A., Buiatti, T., Caminiti, R., Ferraina, S., Lacquaniti, F., Shallice, T., 2014. Correction and suppression of reaching movements in the cerebral cortex: physiological and neuropsychological aspects. Neurosci. Biobehav Rev. 42, 232–251 (May).

Bengtsson, S.L., Nagy, Z., Skare, S., Forsman, L., Forssberg, H., Ullén, F., 2005. Extensive piano practicing has regionally specific effects on white matter development. Sep 1 Nat. Neurosci. 8 (9), 1148–1150. https://doi.org/10.1038/nn1516.

Berger, M., Agha, N.S., Gail, A., 2020. Wireless recording from unrestrained monkeys reveals motor goal encoding beyond immediate reach in frontoparietal cortex. In: Elife, 9, e51322 doi: 10.7554/eLife.51322. Erratum in: Elife. 2021 Apr 13;10: PMID: 32364495; PMCID: PMC7228770.

Bermudez, P., Zatorre, R.J., 2005. Differences in gray matter between musicians and nonmusicians (Dec). Ann. N. Y. Acad. Sci. 1060 (1), 395–399. https://doi.org/10.1196/annals.1360.057.

Bernstein N.A. The coordination and regulation of movements. Pergamon Press e, Oxford, New York, 1967.

Berthoz, A., 2000. The Brain's Sense of Movement. Harvard Univ Press,. ISBN-10: ↱0674801091;ISBN-13: 978-0674801097.

Bertoni, T., Magosso, E., Serino, A., 2021. From statistical regularities in multisensory inputs to peripersonal space representation and body ownership: Insights from a neural network model. Eur. J. Neurosci. 53 (2), 611–636. https://doi.org/10.1111/ejn.14981.

Bi, Z., Zhou, C., 2020. Understanding the computation of time using neural network models. Proc. Natl. Acad. Sci. Usa. 117 (19), 10530–10540. https://doi.org/10.1073/pnas.1921609117.

Binkofski, F., Kunesch, E., Classen, J., Seitz, R.J., Freund, H.J., 2001. Tactile apraxia: unimodal apractic disorder of tactile object exploration associated with parietal lobe lesions. Brain 124 (Pt 1), 132–144. https://doi.org/10.1093/brain/124.1.132.

Blanke, O., Slater, M., Serino, A., 2015. Behavioral, Neural, and Computational Principles of Bodily Self-Consciousness. Neuron 88 (1), 145–166. https://doi.org/10.1016/j.neuron.2015.09.029.

Boccara, C.N., Sargolini, F., Thoresen, V.H., et al., 2010. Grid cells in pre- and parasubiculum. Nat. Neurosci. 13 (8), 987–994. https://doi.org/10.1038/nn.260.

Boccardi, E., Della Sala, S., Motto, C., Spinnler, H., 2002. Utilisation behaviour consequent to bilateral SMA softening. Cortex 38 (3), 289–308. https://doi.org/10.1016/s0010-9452(08)70661-0.

Bonini, L., 2017. The Extended Mirror Neuron Network: Anatomy, Origin, and Functions. Neuroscientist 23 (1), 56–67. https://doi.org/10.1177/1073858415626400.

Bonini, F., Burle, B., Liégeois-Chauvel, C., Régis, J., Chauvel, P., Vidal, F., 2014a. Action monitoring and medial frontal cortex: leading role of supplementary motor area. Science 343 (6173), 888–891. https://doi.org/10.1126/science.1247412.

Bonini, L., Maranesi, M., Livi, A., Fogassi, L., Rizzolatti, G., 2014b. Space-dependent representation of objects and other's action in monkey ventral premotor. grasping neurons. J. Neurosci. 34, 4108–4119. https://doi.org/10.1523/JNEUROSCI.4187-13.2014.

Bonini, L., Maranesi, M., Livi, A., Fogassi, L., Rizzolatti, G., 2014c. Ventral premotor neurons encoding representations of action during self and others' inaction. Curr. Biol. 24 (14), 1611–1614. https://doi.org/10.1016/j.cub.2014.

Bonini, L., Rozzi, S., Serventi, F.U., Simone, L., Ferrari, P.F., Fogassi, L., 2010. Ventral premotor and inferior parietal cortices make distinct contribution to action organization and intention understanding. Cereb. Cortex 20, 1372–1385. https://doi.org/10.1093/cercor/bhp200.

Bonini, L., Ugolotti Serventi, F., Simone, L., Rozzi, S., Ferrari, P.F., Fogassi, L., 2011. Grasping neurons of monkey parietal and premotor cortices encode action goals at distinct levels of abstraction during complex action sequences. J. Neurosci. 31, 5876–5886. https://doi.org/10.1523/JNEUROSCI.5186-10.2011.

Bonini, L., Ugolotti Serventi, F., Bruni, S., Maranesi, M., Bimbi, M., Simone, L., Rozzi, S., Ferrari, P.F., Fogassi, L., 2012. Selectivity for grip type and action goal in macaque inferior parietal and ventral premotor grasping neurons. J. Neurophysiol. 108, 1607–1619. https://doi.org/10.1152/jn.01158.2011.

Borgognon, S., Cottet, J., Badoud, S., Bloch, J., Brunet, J.F., Rouiller, E.M., 2020. Cortical Projection From the Premotor or Primary Motor Cortex to the Subthalamic Nucleus in Intact and Parkinsonian Adult Macaque Monkeys: A Pilot Tracing Study. Oct 26 Front Neural Circuits 14, 528993. https://doi.org/10.3389/fncir.2020.528993.

Boria, S., Fabbri-Destro, M., Cattaneo, L., et al., 2009. Intention understanding in autism [published correction appears in PLoS One. 2009;4(6). doi: 10.1371/annotation/3f865d29-8d14-4f15-86dc-061631ff6d78]. PLoS One 4 (5), e5596 doi:10.1371/journal.pone.0005596.

Borra, E., Belmalih, A., Gerbella, M., Rozzi, S., Luppino, G., 2010. Projections of the hand field of the macaque ventral premotor area F5 to the brainstem and spinal cord. J. Comp. Neurol. 518 (13), 2570–2591. https://doi.org/10.1002/cne.22353.

Borra, E., Gerbella, M., Rozzi, S., Luppino, G., 2017. The macaque lateral grasping network: A neural substrate for generating purposeful hand actions. Neurosci. Biobehav Rev. 75, 65–90. https://doi.org/10.1016/j.neubiorev.2017.01.017.

Botvinick, M.M., 2007. Conflict monitoring and decision making: reconciling two perspectives on anterior cingulate function. Cogn. Affect Behav. Neurosci. 7 (4), 356–366. https://doi.org/10.3758/cabn.7.4.356.

Botvinick, M.M., Cohen, J.D., Carter, C.S., 2004. Conflict monitoring and anterior cingulate cortex: an update. Trends Cogn. Sci. 8 (12), 539–546. https://doi.org/10.1016/j.tics.2004.10.003.

Boucher, L., Palmeri, T.J., Logan, G.D., Schall, J.D., 2007. Inhibitory control in mind and brain: an interactive race model of countermanding saccades. Psychol. Rev. 114 (2), 376–397. https://doi.org/10.1037/0033-295X.114.2.376.

Boussaoud, D., Wise, S.P., 1993. Primate frontal cortex: effects of stimulus and movement. Exp. Brain Res 95 (1), 28–40. https://doi.org/10.1007/BF00229651.

Breveglieri, R., Galletti, C., Gamberini, M., Passarelli, L., Fattori, P., 2006. Somatosensory cells in area PEc of macaque posterior parietal cortex. In: J Neurosci, 26, pp. 3679–3684 doi: 10.1523/JNEUROSCI.4637-05.2006. Erratum in: J Neurosci. 2006 Apr 19;26(16):4452.

Brinkman, C., 1984. Supplementary motor area of the monkey's cerebral cortex: short- and long-term deficits after unilateral ablation and the effects of subsequent callosal section. J. Neurosci. 4 (4), 918–929. https://doi.org/10.1523/JNEUROSCI.04-04-00918.1984.

Brinkman, C., Porter, R., 1979. Supplementary motor area in the monkey: activity of neurons during performance of a learned motor task. J. Neurophysiol. 42 (3), 681–709 (May).

Britten, K.H., 2008. Mechanisms of self-motion perception. Annu Rev. Neurosci. 31, 389–410. https://doi.org/10.1146/annurev.neuro.29.051605.112953.

Bruner, E., 2018. Human paleoneurology and the evolution of the parietal cortex. Brain Behav. Evol. 91, 136–147. https://doi.org/10.1159/000488889.

Bruner, E., Preuss, T.M., Chen, X., Rilling, J.K., 2017. Evidence for expansion of the precuneus in human evolution. Brain Struct. Funct. 222, 1053–1060. https://doi.org/10.1007/s00429-015-1172-y.

Bruner, E., Battaglia-Mayer, A., Caminiti, R., 2023. The parietal lobe evolution and the emergence of material culture in the human genus. Brain Struct. Funct. 228 (1), 145–167. https://doi.org/10.1007/s00429-022-02487-w. Epub 2022 Apr 22.

Buckwalter, J.A., Parvizi, J., Morecraft, R.J., van Hoesen, G.W., 2008. Thalamic projections to the posteromedial cortex in the macaque. J. Comp. Neurol. 507 (5), 1709–1733 doi: 10.1002/cne.21647. PMID: 18253938; PMCID: PMC3757573.

Bufacchi, R.J., Iannetti, G.D., 2016. Gravitational cues modulate the shape of defensive peripersonal space. Nov 7 Curr. Biol. 26 (21), R1133–R1134. https://doi.org/10.1016/j.cub.2016.09.025.

Bufacchi, R.J., Iannetti, G.D., 2018. An action field theory of peripersonal space. Trends Cogn. Sci. 22 (12), 1076–1090. https://doi.org/10.1016/j.tics.2018.09.004.

Bufacchi, R.J., Iannetti, G.D., 2021. What do 'peripersonal space measures' really reflect? The action field perspective. The World at Our Fingertips: A Multidisciplinary Exploration of Peripersonal Space. Oxford University Press,, pp. 155–180. https://doi.org/10.1093/oso/9780198851738.003.0009.

Bufacchi, R.J., Somervail, R., Fitzpatrick, A.M., Caminiti, R., Iannetti, G.D., 2022. Egocentric value maps of the near-body environment. BioRxiv. https://doi.org/10.1101/2022.08.18.504456.

Bullmore, E., Sporns, O., 2009. Complex brain networks: Graph theoretical analysis of structural and functional systems. Nat. Rev. Neurosci. 10 (3), 186–198. https://doi.org/10.1038/nrn2575.

Bullmore, E.D., Sporns, O., 2012. The economy of brain network organization. Nat. Rev. Neurosci. 13, 336–349. https://doi.org/10.1038/nrn3214.

Bunday, K.L., Perez, M.A., 2012. Motor recovery after spinal cord injury enhanced by strengthening corticospinal synaptic transmission [published correction appears in Curr Biol. 2013 Jan 7;23(1):94]. Curr. Biol. 22 (24), 2355–2361. https://doi.org/10.1016/j.cub.2012.10.046.

Bunge, S.A., Dudukovic, N.M., Thomason, M.E., Vaidya, C.J., Gabrieli, J.D., 2002. Immature frontal lobe contributions to cognitive control in children: evidence from fMRI. Jan 17 Neuron 33 (2), 301–311. https://doi.org/10.1016/s0896-6273(01)00583-9.

Caggiano, V., Fleischer, F., Pomper, J.K., Giese, M.A., Thier, P., 2016. Mirror Neurons in Monkey Premotor Area F5 Show Tuning for Critical Features of Visual Causality Perception. Curr. Biol. 26 (22), 3077–3082. https://doi.org/10.1016/j.cub.2016.10.007.

Cahusac, P.M., Rolls, E.T., Miyashita, Y., Niki, H., 1993. Modification of the responses of hippocampal neurons in the monkey during the learning of a conditional spatial response task. Hippocampus 3 (1), 29–42. https://doi.org/10.1002/hipo.450030104.

Cai, W., Ryali, S., Chen, T., Li, C.S., Menon, V., 2014. Dissociable roles of right inferior frontal cortex and anterior insula in inhibitory control: evidence from intrinsic and task-related functional parcellation, connectivity, and response profile analyses across multiple datasets. Oct 29 J. Neurosci. 34 (44), 14652–14667. https://doi.org/10.1523/JNEUROSCI.3048-14.2014.

Caminiti, R., Ghaziri, H., Galuske, R., Hof, P.R., Innocenti, G.M., 2009. Evolution amplified processing with temporally dispersed slow neuronal connectivity in primates. Proc. Natl. Acad. Sci. Usa. 106 (46), 19551–19556. https://doi.org/10.1073/pnas.0907655106.

Caminiti, R., Innocenti, G.M., Battaglia-Mayer, A., 2015. Organization and evolution of parieto-frontal processing streams in macaque monkeys and humans. Neurosci. Biobehav Rev. 56, 73–96. https://doi.org/10.1016/j.neubiorev.2015.06.014.

Caminiti, R., Borra, E., Visco-Comandini, F., Battaglia-Mayer, A., Averbeck, B.B., Luppino, G., 2017. Computational Architecture of the Parieto-Frontal Network Underlying Cognitive-Motor Control in Monkeys. eNeuro 4 (1). ENEURO.0306-16.2017. Published 2017 Feb 27. doi:10.1523/ENEURO.0306-16.2017.

Caminiti R., G.D. Iannetti, A. Battaglia-Mayer (2019) How the Senses Guide Goal-Directed and Defensive Actions: Common Principles of Organization. In "The Senses: A Comprehensive Reference 2nd Ed." Eds. {C}{C}Krubitzer L. and Kaas J.{C}{C} https://doi.org/10.1016/B978–0-12–809324-5.23893–5.

Caminiti, R., Girard, G., Battaglia-Mayer, A., Borra, E., Schito, A., Innocenti, G.M., Luppino, G., 2021. The Complex Hodological Architecture of the Macaque Dorsal Intraparietal Areas as Emerging from Neural Tracers and DW-MRI Tractography. eNeuro 8 (4). ENEURO.0102-21.2021. ⟨https://doi.org/10.1523/ENEURO.0102-21.2021⟩.

Cannonieri, G.C., Bonilha, L., Fernandes, P.T., Cendes, F., Li, L.M., 2007. Practice and perfect: length of training and structural brain changes in experienced typists. Jul 2 Neuroreport 18 (10), 1063–1066. https://doi.org/10.1097/WNR.0b013e3281a030e5.

Cappe, C., Morel, A., Barone, P., Rouiller, E.M., 2009. The thalamocortical projection systems in primate: an anatomical support for multisensory and sensorimotor interplay. Cereb. Cortex 19 (9), 2025–2037. https://doi.org/10.1093/cercor/bhn228.

Caprara, I., Janssen, P., 2021. The causal role of three frontal cortical areas in grasping. Cereb. Cortex 31 (9), 4274–4288. https://doi.org/10.1093/cercor/bhab085.

Cardellicchio, P., Dolfini, E., D'Ausilio, A., 2021. The role of dorsal premotor cortex in joint action stopping. Iscience 24 (11).

Caspers, S., Schleicher, A., Bacha-Trams, M., Palomero-Gallagher, N., Amunts, K., Zilles, K., 2013. Organization of the human inferior parietal lobule based on receptor architectonics. Cereb. Cortex 23 (3), 615–628. https://doi.org/10.1093/cercor/bhs048.

Cattaneo, L., Pavesi, G., 2014. The facial motor system. Neurosci. Biobehav Rev. 38, 135–159. https://doi.org/10.1016/j.neubiorev.2013.11.002.

Cattaneo, L., Fabbri-Destro, M., Boria, S., Pieraccini, C., Monti, A., Cossu, G., Rizzolatti, G., 2007. Impairment of actions chains in autism and its possible role in intention understanding. Proc. Natl. Acad. Sci. Usa. 104 (45), 17825–17830 doi: 10.1073/pnas.0706273104. Epub 2007 Oct 26.

Cavanagh, P.R., Komi, P.V., 1979. Electromechanical delay in human skeletal muscle under concentric and eccentric contractions. Eur. J. Appl. Physiol. Occup. Physiol. 42 (3), 159–163. https://doi.org/10.1007/BF00431022.

Cerri, G., Shimazu, H., Maier, M.A., Lemon, R.N., 2003. Facilitation from ventral premotor cortex of primary motor cortex outputs to macaque hand muscles. J. Neurophysiol. 90 (2), 832–842. https://doi.org/10.1152/jn.01026.2002.

Chafee, M.V., Crowe, D.A., Averbeck, B.B., Georgopoulos, A.P., 2005. Neural correlates of spatial judgement during object construction in parietal cortex. Cereb. Cortex 15, 1393–1413. https://doi.org/10.1093/cercor/bhi021.

Chafee, M.V., Averbeck, B.B., Crowe, D.A., 2007. Representing spatial relationships in posterior parietal cortex: single neurons code object-referenced position. Cereb. Cortex 17, 2914–2932. https://doi.org/10.1093/cercor/bhm017.

Chechlacz, M., Novick, A., Rotshtein, P., Bickerton, W.L., Humphreys, G.W., Demeyere, N., 2014. The neural substrates of drawing: a voxel-based morphometry analysis of constructional, hierarchical, and spatial representation deficits. J. Cogn. Neurosci. 26 (12), 2701–2715. https://doi.org/10.1162/jocn_a_00664.

Chen, A., DeAngelis, G.C., Angelaki, D.E., 2010b. Macaque parieto-insular vestibular cortex: responses to self-motion and optic flow. J. Neurosci. 30, 3022–3042. https://doi.org/10.1523/jneurosci.4029-09.2010.

Chen, A., DeAngelis, G.C., Angelaki, D.E., 2011. A comparison of vestibular spatiotemporal tuning in macaque parietoinsular vestibular cortex, ventral intraparietal area, and medial superior temporal area. J. Neurosci. 31 (8), 3082–3094. https://doi.org/10.1523/JNEUROSCI.4476-10.2011.

Chen, A., DeAngelis, G.C., Angelaki, D.E., 2013. Functional specializations of the ventral intraparietal area for multisensory heading discrimination. J. Neurosci. 33 (8), 3567–3581. https://doi.org/10.1523/JNEUROSCI.4522-12.2013.

Chen, A., Gu, Y., Liu, S., DeAngelis, G.C., Angelaki, D.E., 2016. Evidence for a Causal Contribution of Macaque Vestibular, But Not Intraparietal, Cortex to Heading Perception. J. Neurosci. 36 (13), 3789–3798. https://doi.org/10.1523/JNEUROSCI.2485-15.2016.

Chen, G., Kang, B., Lindsey, J., Druckmann, S., Li, N., 2021. Modularity and robustness of frontal cortical networks. Jul 8 Cell 184 (14), 3717–3730. https://doi.org/10.1016/j.cell.2021.05.026.

Chen, L.L., Lin, L.H., Green, E.J., Barnes, C.A., McNaughton, B.L., 1994. Head-direction cells in the rat posterior cortex. I. Anatomical distribution and behavioral modulation. Exp. Brain Res 101 (1), 8–23. https://doi.org/10.1007/BF00243212.

Chen, X., Scangos, K.W., Stuphorn, V., 2010a. Supplementary motor area exerts proactive and reactive control of arm movements. J. Neurosci. 30 (44), 14657–14675. https://doi.org/10.1523/JNEUROSCI.2669-10.2010.

Cho, J., Sharp, P.E., 2001. Head direction, place, and movement correlates for cells in the rat retrosplenial cortex. Behav. Neurosci. 115 (1), 3–25. https://doi.org/10.1037/0735-7044.115.1.3.

Churchland, M., Cunningham, J., Kaufman, M., et al., 2012. Neural population dynamics during reaching. Nature 487, 51–56. https://doi.org/10.1038/nature11129.

Cisek, P., 2006. Integrated neural processes for defining potential actions and deciding between them: a computational model. J. Neurosci. 26 (38), 9761–9770. https://doi.org/10.1523/JNEUROSCI.5605-05.2006.

Cisek, P., 2007. Cortical mechanisms of action selection: the affordance competition hypothesis. Philos. Trans. R. Soc. Lond. B Biol. Sci. 362 (1485), 1585–1599. https://doi.org/10.1098/rstb.2007.2054.

Cisek, P., Kalaska, J.F., 2004. Neural correlates of mental rehearsal in dorsal premotor cortex. Nature 431 (7011), 993–996. https://doi.org/10.1038/nature03005.

Cisek, P., Kalaska, J.F., 2005. Neural correlates of reaching decisions in dorsal premotor cortex: specification of multiple direction choices and final selection of action. Neuron 45 (5), 801–814. https://doi.org/10.1016/j.neuron.2005.01.027.

Cléry, J., Guipponi, O., Wardak, C., Ben Hamed, S., 2015. Neuronal bases of peripersonal and extrapersonal spaces, their plasticity and their dynamics: knowns and unknowns. Neuropsychologia 70, 313–326. https://doi.org/10.1016/j.neuropsychologia.2014.10.022.

Cléry, J., Guipponi, O., Odouard, S., Pinède, S., Wardak, C., Hamed, S.B., 2017. The prediction of impact of a looming stimulus onto the body is subserved by multisensory integration mechanisms. J. Neurosci. 37, 10656–10670. https://doi.org/10.1523/JNEUROSCI.0610-17.2017.

Cléry, J., Guipponi, O., Odouard, S., Wardak, C., Ben Hamed, S., 2018. Cortical networks for encoding near and far space in the non-human primate. Neuroimage 176, 164–178. https://doi.org/10.1016/j.neuroimage.2018.04.036.

Clower, D.M., Dum, R.P., Strick, P.L., 2005. Basal ganglia and cerebellar inputs to 'AIP'. Cereb. Cortex 15 (7), 913–920. https://doi.org/10.1093/cercor/bhh190.

Clower, W.T., Alexander, G.E., 1998. Movement sequence-related activity reflecting numerical order of components in supplementary and presupplementary motor areas. J. Neurophysiol. 80 (3), 1562–1566. https://doi.org/10.1152/jn.1998.80.3.1562.

Clune, J., Mouret, J.B., Lipson, H., 2013. The evolutionary origins of modularity. Proc. R. Soc. B. 280, 20122863. https://doi.org/10.1098/rspb.2012.2863.

Colby, C.L., 1998. Action-oriented spatial reference frames in cortex. Neuron 20 (1), 15–24 (Jan).

Colby, C.L., Duhamel, J.R., Goldberg, M.E., 1993. Ventral intraparietal area of the macaque: anatomic location and visual response properties. J. Neurophysiol. 69 (3), 902–914. https://doi.org/10.1152/jn.1993.69.3.902.

Collias, N.E., 1964. The evolution of nests and of nests-building in birds. Am. Zool. 4, 175–190. https://doi.org/10.1093/icb/4.2.175.

Cona, G., Semenza, C., 2017. Supplementary motor area as key structure for domain-general sequence processing: a unified account. Neurosci Biobehav Rev. 72, 28–42.

Cooke, D.F., Graziano, M.S., 2004. Super-flinchers and nerves of steel: defensive movements altered by chemical manipulation of a cortical motor area. Neuron 43 (4), 585–593. https://doi.org/10.1016/j.neuron.2004.07.029.

Cooke, D.F., Taylor, C.S., Moore, T., Graziano, M.S., 2003. Complex movements evoked by microstimulation of the ventral intraparietal area. Proc. Natl. Acad. Sci. Usa. 100 (10), 6163–6168. https://doi.org/10.1073/pnas.1031751100.

Cooper, B.G., Mizumori, S.J., 1999. Retrosplenial cortex inactivation selectively impairs navigation in darkness. Neuroreport 10 (3), 625–630. https://doi.org/10.1097/00001756-199902250-00033.

Cottereau, B.R., Smith, A.T., Rima, S., et al., 2017. Processing of Egomotion-Consistent Optic Flow in the Rhesus Macaque Cortex. Cereb. Cortex 27 (1), 330–343. https://doi.org/10.1093/cercor/bhw412.

Coudé, G., Ferrari, P.F., Rodà, F., Maranesi, M., Borelli, E., Veroni, V., Monti, F., Rozzi, S., Fogassi, L., 2011. Neurons controlling voluntary vocalization in the macaque ventral premotor cortex. PLoS One 6. :e26822.22073201.

Coull, J.T., Vidal, F., Burle, B., 2016. When to act, or not to act: that's the SMA's question. Curr. Opin. Behav. Sci. Volume 8, 14–21. https://doi.org/10.1016/j.cobeha.2016.01.003.

Coxon, J.P., Stinear, C.M., Byblow, W.D., 2006. Intracortical inhibition during volitional inhibition of prepared action. J. Neurophysiol. 95 (6), 3371–3383. https://doi.org/10.1152/jn.01334.2005.

Crammond, D.J., Kalaska, J.F., 1994. Modulation of preparatory neuronal activity in dorsal premotor cortex due to stimulus-response compatibility. J. Neurophysiol. 71 (3), 1281–1284. https://doi.org/10.1152/jn.1994.71.3.1281.

Critchley, M., 1953. The Parietal Lobes. Hafner Press New York,.

Crowe, D.A., Chafee, M.V., Averbeck, B.B., Georgopoulos, A.P., 2004. Neural activity in primate parietal area 7a related to spatial analysis of visual mazes. Cereb. Cortex 14 (1), 23–34. https://doi.org/10.1093/cercor/bhg088.

Crowe, D.A., Averbeck, B.B., Chafee, M.V., Georgopoulos, A.P., 2005. Dynamics of parietal neural activity during spatial cognitive processing. Neuron 47, 885–891. https://doi.org/10.1016/j.neuron.2005.08.005.

Crowe, D.A., Averbeck, B.B., Chafee, M.V., 2008. Neural ensemble decoding reveals a correlate of viewer- to object-centered spatial transformation in monkey parietal cortex. J. Neurosci. 28, 5218–5228. https://doi.org/10.1523/JNEUROSCI.5105-07.200.

Crowe, D.A., Zarco, W., Bartolo, R., Merchant, H., 2014. Dynamic representation of the temporal and sequential structure of rhythmic movements in the primate medial premotor cortex. J. Neurosci. 34 (36), 11972–11983. https://doi.org/10.1523/JNEUROSCI.2177-14.2014.

Daitch, A.L., Parvizi, J., 2018. Spatial and temporal heterogeneity of neural responses in human posteromedial cortex. Proc. Natl. Acad. Sci. Usa. 115, 4785–4790. https://doi.org/10.1073/pnas.1721714115.

D'Aleo, R., Rouse, A.G., Schieber, M.H., Sarma, S.V., 2022. Cortico-cortical drive in a coupled premotor-primary motor cortex dynamical system. Dec 20 Cell Rep. 41 (12), 111849. https://doi.org/10.1016/j.celrep.2022.111849.

Dann, B., Michaels, J.A., Schaffelhofer, S., Scherberger, H., 2016. Uniting functional network topology and oscillations in the fronto-parietal single unit network of behaving primates. eLife 5, e15719. https://doi.org/10.7554/eLife.15719.

Dapretto, M., Davies, M.S., Pfeifer, J.H., et al., 2006. Understanding emotions in others: mirror neuron dysfunction in children with autism spectrum disorders. Nat. Neurosci. 9 (1), 28–30. https://doi.org/10.1038/nn1611.

Darling, W.G., Pizzimenti, M.A., Morecraft, R.J., 2011. Functional recovery following motor cortex lesions in non-human primates: experimental implications for human stroke patients (Sep). J. Integr. Neurosci. 10 (3), 353–384. https://doi.org/10.1142/S0219635211002737.

Darling, W.G., Pizzimenti, M.A., Rotella, D.L., Ge, J., Stilwell-Morecraft, K.S., Morecraft, R.J., 2021. Greater Reduction in Contralesional Hand Use After Frontoparietal Than Frontal Motor Cortex Lesions in Macaca mulatta. Mar 18 Front Syst. Neurosci. 15, 592235. https://doi.org/10.3389/fnsys.2021.592235.

Davare, M., Kraskov, A., Rothwell, J.C., Lemon, R.N., 2011. Interactions between areas of the cortical grasping network. Curr. Opin. Neurobiol. 21 (4), 565–570. https://doi.org/10.1016/j.conb.2011.05.021.

Dean, H.L., Platt, M.L., 2006. Allocentric spatial referencing of neuronal activity in macaque posterior cingulate cortex. J. Neurosci. 26 (4), 1117–1127. https://doi.org/10.1523/JNEUROSCI.2497-05.2006.

Dean, H.L., Crowley, J.C., Platt, M.L., 2004. Visual and saccade-related activity in macaque posterior cingulate cortex. J. Neurophysiol. 92 (5), 3056–3068 (Nov).

Deecke, L., Kornhuber, H.H., 1978. An electrical sign of participation of the mesial 'supplementary' motor cortex in human voluntary finger movement. Brain Res 159 (2), 473–476. https://doi.org/10.1016/0006-8993(78)90561-9.

Della Sala, S., Marchetti, C., Spinnler, H., 1991. Right-sided anarchic (alien) hand: a longitudinal study. Neuropsychologia 29 (11), 1113–1127. https://doi.org/10.1016/0028-3932(91)90081-i.

Delle Monache, S., Indovina, I., Zago, M., Daprati, E., Lacquaniti, F., Bosco, G., 2021. Watching the Effects of Gravity. Vestibular Cortex and the Neural Representation of "Visual" Gravity. Front Integr. Neurosci. 15, 793634. Dec 1.

Desmurget, M., Richard, N., Harquel, S., et al., 2014. Neural representations of ethologically relevant hand/mouth synergies in the human precentral gyrus. Proc. Natl. Acad. Sci. USA 111 (15), 5718–5722. https://doi.org/10.1073/pnas.1321909111.

Dhawale, A.K., Wolff, S.B., Ko, R., Ölveczky, B.P., 2021. The basal ganglia control the detailed kinematics of learned motor skills (Sep). Nat. Neurosci. 24 (9), 1256–1269. https://doi.org/10.1101/825810.

di Pellegrino, G., Wise, S.P., 1993. Visuospatial versus visuomotor activity in the premotor and prefrontal cortex of a primate (Mar). J. Neurosci. 13 (3), 1227–1243. https://doi.org/10.1523/JNEUROSCI.13-03-01227.1993.

di Pellegrino, G., Fadiga, L., Fogassi, L., Gallese, V., Rizzolatti, G., 1992. Understanding motor events: a neurophysiological study. Exp. Brain Res 91 (1), 176–180. https://doi.org/10.1007/BF00230027.

Di Stefano, V., De Angelis, M.V., Montemitro, C., Russo, M., Carrarini, C., di Giannantonio, M., et al., 2021. Clinical presentation of strokes confined to the insula: a systematic review of literature. Neurol. Sci. 42, 1697–1704. https://doi.org/10.1007/s10072-021-05109-1.

Dick, J.P., Benecke, R., Rothwell, J.C., Day, B.L., Marsden, C.D., 1986. Simple and complex movements in a patient with infarction of the right supplementary motor area. Mov. Disord. 1 (4), 255–266. https://doi.org/10.1002/mds.870010405.

Dijkerman, H.C., Medendorp, W.P., 2021. Visuotactile Predictive Mechanisms of Peripersonal Space. In Oxford University Press. Oxford University Press,, Oxford.

Disbrow, E., Litinas, E., Recanzone, G.H., Padberg, J., Krubitzer, L., 2003. Cortical connections of the second somatosensory area and the parietal ventral area in macaque monkeys. J. Comp. Neurol. 462 (4), 382–399. https://doi.org/10.1002/cne.10731.

Do, T.N., Lin, C.T., Gramann, K., 2021. Human brain dynamics in active spatial navigation. Sci. Rep. 11 (1), 13036. Published 2021 Jun 22. doi:10.1038/s41598-021-92246-4.

Dosenbach, N.U., Visscher, K.M., Palmer, E.D., Miezin, F.M., Wenger, K.K., Kang, H.C., Burgund, E.D., Grimes, A.L., Schlaggar, B.L., Petersen, S.E., 2006. A core system for the implementation of task sets. Jun 1 Neuron 50 (5), 799–812. https://doi.org/10.1016/j.neuron.2006.04.031.

Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., May, A., 2004. Changes in grey matter induced by training. Jan 22 Nature 427 (6972), 311–312. https://doi.org/10.1038/427311a.

Duhamel, J.R., Colby, C.L., Goldberg, M.E., 1998. Ventral intraparietal area of the macaque: congruent visual and somatic response properties. J. Neurophysiol. 79 (1), 126–136. https://doi.org/10.1152/jn.1998.79.1.126.

Dum, R.P., Strick, P.L., 1991. The origin of corticospinal projections from the premotor areas in the frontal lobe. J. Neurosci. 1991 11 (3), 667–689. https://doi.org/10.1523/JNEUROSCI.11-03-00667.1991.

Dum, R.P., Strick, P.L., 2003. An unfolded map of the cerebellar dentate nucleus and its projections to the cerebral cortex. J. Neurophysiol. 89 (1), 634–639. https://doi.org/10.1152/jn.00626.2002.

Durand, J.B., Nelissen, K., Joly, O., et al., 2007. Anterior regions of monkey parietal cortex process visual 3D shape. Neuron 55 (3), 493–505. https://doi.org/10.1016/j.neuron.2007.06.040.

Dushanova, J., Donoghue, J., 2010. Neurons in primary motor cortex engaged during action observation. Eur. J. Neurosci. 31 (2), 386–398 (Jan).

Eguchi, S., Hirose, G., Miaki, M., 2019. Vestibular symptoms in acute hemispheric strokes. J. Neurol. 266 (8), 1852–1858. https://doi.org/10.1007/s00415-019-09342-9.

Ehrsson, H.H., Fagergren, E., Forssberg, H., 2001. Differential fronto-parietal activation depending on force used in a precision grip task: an fMRI study. J. Neurophysiol. 85 (6), 2613–2623. https://doi.org/10.1152/jn.2001.85.6.2613.

Erika-Florence, M., Leech, R., Hampshire, A., 2014. A functional network perspective on response inhibition and attentional control. Nat. Commun. 5, 4073. https://doi.org/10.1038/ncomms5073.

Evrard, E.C., 2019. The organization of the primate insular cortex. art. 43 Front. Neuroanat. vol. 13. https://doi.org/10.3389/fnana.2019.00043.

Fadiga, L., Fogassi, L., Pavesi, G., Rizzolatti, G., 1995. Motor facilitation during action observation: a magnetic stimulation study. J. Neurophysiol. 73 (6), 2608–2611. https://doi.org/10.1152/jn.1995.73.6.2608.

Falcone, R., Brunamonti, E., Ferraina, S., Genovesio, A., 2016. Neural Encoding of Self and Another Agent's Goal in the Primate Prefrontal Cortex: Human-Monkey Interactions. Cereb. Cortex 26 (12), 4613–4622. https://doi.org/10.1093/cercor/bhv224.

Fattori, P., Breveglieri, R., Marzocchi, N., Filippini, D., Bosco, A., Galletti, C., 2009. Hand orientation during reach-to-grasp movements modulates neuronalactivity in the medial posterior parietal area V6A. J. Neurosci. 29, 1928–1936. https://doi.org/10.1523/JNEUROSCI.4998-08.2009.

Fattori, P., Raos, V., Breveglieri, R., Bosco, A., Marzocchi, N., Galletti, C., 2010. The dorsomedial pathway is not just for reaching: grasping neurons in themedial-parieto-occipital cortex of the macaque monkey. J. Neurosci. 30, 342–349. https://doi.org/10.1523/jneurosci.3800-09.2010.

Feinberg, T.E., Schindler, R.J., Flanagan, N.G., Haber, L.D., 1992. Two alien hand syndromes. Neurology 42 (1), 19–24. https://doi.org/10.1212/wnl.42.1.19.

Ferrari, P.F., Gallese, V., Rizzolatti, G., Fogassi, L., 2003. Mirror neurons responding to the observation of ingestive and communicative mouth actions in the monkey ventral premotor cortex. Eur. J. Neurosci. 17 (8), 1703–1714. https://doi.org/10.1046/j.1460-9568.2003.02601.x.

Ferrari, P.F., Gerbella, M., Coudé, G., Rozzi, S., 2017. Two different mirror neuron networks: The sensorimotor (hand) and limbic (face) pathways. Neuroscience 358, 300–315. Sep 1.

Ferrari-Toniolo, S., Papazachariadis, O., Visco-Comandini, F., et al., 2014. A visuomotor disorder in the absence of movement: does optic ataxia generalize to learned isometric hand action. Neuropsychologia 63, 59–71. https://doi.org/10.1016/j.neuropsychologia.2014.07.029.

Ferrari-Toniolo, S., Visco-Comandini, F., Papazachariadis, O., Caminiti, R., Battaglia-Mayer, A., 2015. Posterior Parietal Cortex Encoding of Dynamic Hand Force Underlying Hand-Object Interaction. J. Neurosci. 35 (31), 10899–10910. https://doi.org/10.1523/JNEUROSCI.4696-14.2015.

Ferrari-Toniolo, S., Visco-Comandini, F., Battaglia-Mayer, A., 2019. Two brains in action: joint-action coding in the primate frontal cortex. J. Neurosci. 39 (18), 3514–3528. https://doi.org/10.1523/JNEUROSCI.1512-18.2019.

Ferrier, D., 1876. Functions of the Brain. Smith, Elder & Co.,, London.

Fetz, E.E., Cheney, P.D., Mewes, K., Palmer, S., 1989. Control of forelimb muscle activity by populations of corticomotoneuronal and rubromotoneuronal cells. Prog. Brain Res 80, 437-430. https://doi.org/10.1016/s0079-6123(08)62241-4.

Fischer, S., Nitschke, M.F., Melchert, U.H., Erdmann, C., Born, J., 2005. Motor memory consolidation in sleep shapes more effective neuronal representations. Dec 7 J. Neurosci. 25 (49), 11248–11255. https://doi.org/10.1523/JNEUROSCI.1743-05.2005.

Floyer-Lea, A., Matthews, P.M., 2004. Changing brain networks for visuomotor control with increased movement automaticity (Oct). J. Neurophysiol. 92 (4), 2405–2412. https://doi.org/10.1152/jn.01092.2003.

Floyer-Lea, A., Matthews, P.M., 2005. Distinguishable brain activation networks for short-and long-term motor skill learning (Jul). J. Neurophysiol. 94 (1), 512–518. https://doi.org/10.1152/jn.00717.2004.

Fogassi, L., Gallese, V., Fadiga, L., Luppino, G., Matelli, M., Rizzolatti, G., 1996. Coding of peripersonal space in inferior premotor cortex (area F4. J. Neurophysiol. 76 (1), 141–157. https://doi.org/10.1152/jn.1996.76.1.141.

Fogassi, L., Gallese, V., Buccino, G., Craighero, L., Fadiga, L., Rizzolatti, G., 2001. Cortical mechanism for the visual guidance of hand grasping movements in the monkey: A reversible inactivation study. Brain 124 (Pt 3), 571–586. https://doi.org/10.1093/brain/124.3.571.

Fogassi, L., Ferrari, P.F., Gesierich, B., Rozzi, S., Chersi, F., Rizzolatti, G., 2005. Parietal lobe: from action organization to intention understanding. Apr 29 Science 308 (5722), 662–667. https://doi.org/10.1126/science.1106138.

Foster C., Sheng W.A., Heed T., Ben Hamed S. The macaque ventral intraparietal area has expanded into three homologue human parietal areas. Prog Neurobiol., 2022 Feb; 209:102185. doi: 10.1016/j.pneurobio.2021.102185. Epub 2021 Nov 11. Erratum in: Prog Neurobiol. 2022 Jan 3;209:102210. PMID: 34775040.

Frank, M.J., Samanta, J., Moustafa, A.A., Sherman, S.J., 2007. Hold your horses: impulsivity, deep brain stimulation, and medication in parkinsonism. In: Science, 318, pp. 1309–1312. https://doi.org/10.1126/science.1146157.

Freedman, D.J., Riesenhuber, M., Poggio, T., Miller, E.K., 2001. Categorical representation of visual stimuli in the primate prefrontal cortex. Sci. (N. Y., N. Y.) 291 (5502), 312–316. https://doi.org/10.1126/science.291.5502.312.

Freund, H.J., 2003. Somatosensory and motor disturbances in patients with parietal lobe lesions. Adv. Neurol. 93, 179–193.

Fridman, E.A., Hanakawa, T., Chung, M., Hummel, F., Leiguarda, R.C., Cohen, L.G., 2004. Reorganization of the human ipsilesional premotor cortex after stroke. Brain 127 (Pt 4), 747–758. https://doi.org/10.1093/brain/awh082.

Friedman, D.P., Murray, E.A., O'Neill, J.B., Mishkin, M., 1986. Cortical connections of the somatosensory fields of the lateral sulcus of macaques: evidence for a corticolimbic pathway for touch. J. Comp. Neurol. 252, 323–347. https://doi.org/10.1002/cne.902520304.

Friston, K., Sajid, N., Heins, C., Pavliotis, G.A., & Parr, T., 2022, The free energy principle made simpler but not too simple. 1–42.https://doi.org/10.48550/arXiv.2201.06387.

Fyhn, M., Molden, S., Witter, M.P., Moser, E.I., Moser, M.B., 2004. Spatial representation in the entorhinal cortex. Science 305 (5688), 1258–1264. https://doi.org/10.1126/science.1099901.

Gabbiani, F., Krapp, H.G., Laurent, G., 1999. Computation of object approach by a wide-field, motion-sensitive neuron. J. Neurosci. 19 (3), 1122–1141. https://doi.org/10.1523/JNEUROSCI.19-03-01122.1999.

Gaffan, D., Harrison, S., 1988. Inferotemporal-frontal disconnection and fornix transection in visuomotor conditional learning by monkeys. Behav. Brain Res 31 (2), 149–163. https://doi.org/10.1016/0166-4328(88)90018-6.

Gaffan, D., Harrison, S., 1989. A comparison of the effects of fornix transection and sulcus principalis ablation upon spatial learning by monkeys. Behav. Brain Res 31 (3), 207–220. https://doi.org/10.1016/0166-4328(89)90003-x.

Gainotti, G., Trojano, L., 2018. Constructional apraxia. Handb. Clin. Neurol. 151, 331–348. https://doi.org/10.1016/B978-0-444-63622-5.00016-4.

Galea, M.P., Darian-Smith, I., 1994. Multiple corticospinal neuron populations in the macaque monkey are specified by their unique cortical origins, spinal terminations, and connections. Cereb. Cortex 4 (2), 166–194. https://doi.org/10.1093/cercor/4.2.166.

Gallese, V., Murata, A., Kaseda, M., Niki, N., Sakata, H., 1994. Deficit of hand preshaping after muscimol injection in monkey parietal cortex. Neuroreport 5 (12), 1525–1529. https://doi.org/10.1097/00001756-199407000-00029.

Gallese, V., Fadiga, L., Fogassi, L., Rizzolatti, G., 1996. Action recognition in the premotor cortex (Apr). Brain 119 (Pt 2), 593–609. https://doi.org/10.1093/brain/119.2.593.

Gamberini, M., Bakola, S., Passarelli, L., et al., 2016. Thalamic projections to visual and visuomotor areas (V6 and V6A) in the Rostral Bank of the parieto-occipital sulcus of the Macaque. Brain Struct. Funct. 221 (3), 1573–1589. https://doi.org/10.1007/s00429-015-0990-2.

Gámez, J., Mendoza, G., Prado, L., Betancourt, A., Merchant, H., 2019. The amplitude in periodic neural state trajectories underlies the tempo of rhythmic tapping. PLoS Biol. 17 (4), e3000054. Published 2019 Apr 8. doi:10.1371/journal.pbio.3000054.

Gandola, M., Invernizzi, P., Sedda, A., et al., 2012. An anatomical account of somatoparaphrenia. Cortex 48 (9), 1165–1178. https://doi.org/10.1016/j.cortex.2011.06.012.

Garavan, H., Ross, T.J., Stein, E.A., 1999. Right hemispheric dominance of inhibitory control: an event-related functional MRI study. Proc Natl Acad Sci U S A 96 (14), 8301–8306. https://doi.org/10.1073/pnas.96.14.8301.

García-Garibay, O., Cadena-Valencia, J., Merchant, H., de Lafuente, V., 2016. Monkeys Share the Human Ability to Internally Maintain a Temporal Rhythm. Front Psychol. 7, 1971.

Gaveau, V., Pélisson, D., Blangero, A., et al., 2008. Saccade control and eye-hand coordination in optic ataxia. Neuropsychologia 46 (2), 475–486. https://doi.org/10.1016/j.neuropsychologia.2007.08.028.

Genovesio, A., Tsujimoto, S., Wise, S.P., 2009. Feature- and order-based timing representations in the frontal cortex. Neuron 63 (2), 254–266 doi: 10.1016/j.neuron.2009.06.018. PMID: 19640483; PMCID: PMC2803114.

Gentilucci, M., Scandolara, C., Pigarev, I.N., Rizzolatti, G., 1983. Visual responses in the postarcuate cortex (area 6) of the monkey that are independent of eye position. Exp. Brain Res. 50 (2–3), 464–468. https://doi.org/10.1007/BF00239214.

Gentilucci, M., Fogassi, L., Luppino, G., Matelli, M., Camarda, R., Rizzolatti, G., 1988. Functional organization of inferior area 6 in the macaque monkey. I. Somatotopy and the control of proximal movements. Exp. Brain Res 71 (3), 475–490. https://doi.org/10.1007/BF00248741.

Georgopoulos, A.P., Grillner, S., 1989. Visuomotor coordination in reaching and locomotion. Sep 15 Science 245 (4923), 1209–1210. https://doi.org/10.1126/science.2675307.

Georgopoulos, A.P., Kalaska, J.F., Massey, J.T., 1981. Spatial trajectories and reaction times of aimed movements: effects of practice, uncertainty, and change in target location. J. Neurophysiol. 46 (4), 725–743. https://doi.org/10.1152/jn.1981.46.4.725.

Georgopoulos, A.P., Kalaska, J.F., Caminiti, R., Massey, J.T., 1982. On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. J. Neurosci. 2 (11), 1527–1537. https://doi.org/10.1523/JNEUROSCI.02-11-01527.1982.

Gerbella, M., Belmalih, A., Borra, E., Rozzi, S., Luppino, G., 2011. Cortical connections of the anterior (F5a) subdivision of the macaque ventral premotor area F5. Brain Struct. Funct. 216, 43–65. https://doi.org/10.1007/s00429-010-0293-6.

Gerbella, M., Borra, E., Tonelli, S., Rozzi, S., Luppino, G., 2012. Connectional heterogeneity of the ventral part of the Macaque Area 46. Cereb. Cortex. 23 (4), 967–987. https://doi.org/10.1093/cercor/bhs096.

Gerbella, M., Borra, E., Rozzi, S., Luppino, G., 2016. Connections of the macaque Granular Frontal Opercular (GrFO) area: a possible neural substrate for the contribution of limbic inputs for controlling hand and face/mouth actions. Brain Struct. Funct. 221 (1), 59–78. https://doi.org/10.1007/s00429-014-0892-8.

Ghosh, S., Porter, R., 1988. Corticocortical synaptic influences on morphologically identified pyramidal neurones in the motor cortex of the monkey. J. Physiol. 400, 617–629. https://doi.org/10.1113/jphysiol.1988.sp017139.

Giamundo, M., Giarrocco, F., Brunamonti, E., Fabbrini, F., Pani, P., Ferraina, S., 2021. Neuronal Activity in the Premotor Cortex of Monkeys Reflects Both Cue Salience and Motivation for Action Generation and Inhibition. J. Neurosci. 41 (36), 7591–7606. https://doi.org/10.1523/JNEUROSCI.0641-20.2021.

Goldberg, G., 1985. Supplementary motor area structure and function: review and hypotheses. Behav. Brain Res. 8, 567–588.

Goldberg, G., 1987. From intent to action: evolution and function of the premotor systems of the frontal lobe. In: Perecman, E. (Ed.), In The Frontal Lobes Revisited. IRBN Press, pp. 273–306.

Goldenberg, G., 2014. Apraxia – the cognitive side of motor control. Cortex 57, 270–274. https://doi.org/10.1016/j.cortex.2013.07.016.

Goldring, A.B., Krubitzer, L.A., 2020. Evolution of parietal cortex in mammals: from manipulation to tool use. Evolutionary Neuroscience. Elsevier,, pp. 627–656.

Gothard, K.M., Battaglia, F.P., Erickson, C.A., Spitler, K.M., Amaral, D.G., 2007. Neural responses to facial expression and face identity in the monkey amygdala. J. Neurophysiol. 97, 1671–1683. https://doi.org/10.1152/jn.00714.2006.

Gould, J.L., Gould, C.G., 2012. Animal Architects: Building and the Evolution of Intelligence. Paperback 1. publ. Basic Books,, New York.

Gramann, K., Onton, J., Riccobon, D., Mueller, H.J., Bardins, S., Makeig, S., 2010. Human brain dynamics accompanying use of egocentric and allocentric reference frames during navigation. Dec 1 J. Cogn. Neurosci. 22 (12), 2836–2849. https://doi.org/10.1162/jocn.2009.21369.

Graziano, M., 2006. The organization of behavioral repertoire in motor cortex. Annu Rev. Neurosci. 29, 105–134. https://doi.org/10.1146/annurev.neuro.29.051605.112924.

Graziano, M., 2017. The Spaces Between Us: A Story of Neuroscience, Evolution, and Human Nature. Oxford University Press,.

Graziano, M.S., Cooke, D.F., 2006. Parieto-frontal interactions, personal space, and defensive behavior. Neuropsychologia 44 (6), 845–859. https://doi.org/10.1016/j.neuropsychologia.2005.09.009.

Graziano, M.S., Yap, G.S., Gross, C.G., 1994. Coding of visual space by premotor neurons. Sci. (N. Y., N. Y.) 266 (5187), 1054–1057. https://doi.org/10.1126/science.7973661.

Graziano, M.S., Taylor, C.S., Moore, T., 2002. Complex movements evoked by microstimulation of precentral cortex. Neuron 34 (5), 841–851. https://doi.org/10.1016/s0896-6273(02)00698-0.

Graziano, M.S.A., & Cooke, F.F. (2001). Coding the Location of the Arm by Sight. May 2014. https://doi.org/10.1126/science.290.5497.1782.

Gréa, H., Pisella, L., Rossetti, Y., Desmurget, M., Tilikete, C., Grafton, S., Prablanc, C., Vighetto, A., 2002. A lesion of the posterior parietal cortex disrupts on-line adjustments during aiming movements. Neuropsychologia 40 (13), 2471–2480. https://doi.org/10.1016/s0028-3932(02)00009-x.

Grillner, S., Wallén, P., 2004. Innate versus learned movements–a false dichotomy? Prog. Brain Res 143, 3–12. https://doi.org/10.1016/s0079-6123(03)43001-x.

Grüsser, O.J., Pause, M., Schreiter, U., 1990. Localization and responses of neurones in the parieto-insular vestibular cortex of awake monkeys (Macaca fascicularis). J. Physiol. 430, 537–557. https://doi.org/10.1113/jphysiol.1990.sp018306.

Guenther, F.H., 2016. Neural Control of Speech. MIT Press,, Cambridge, MA.

Guillery, R.W., Sherman, S.M., 2002. Thalamic relay functions and their role in corticocortical communication: generalizations from the visual system. Neuron 33 (2), 163–175. https://doi.org/10.1016/s0896-6273(01)00582-7.

Guldin, W.O., Akbarian, S., Grusser, O.J., 1992. Cortico-cortical connectionsand cytoarchitectonics of the primate vestibular cortex: a study in squirrel monkeys (Saimiri sciureus). J. Comp. Neurol. 326, 375–401. https://doi.org/10.1002/cne.903260306.

Guterstam, A., Collins, K.L., Cronin, J.A., Zeberg, H., Darvas, F., Weaver, K.E., Ojemann, J.G., Ehrsson, H.H., 2019. Direct Electrophysiol. Correl. Body Ownersh. Hum. Cereb. Cortex (November 2018), 1328–1341. https://doi.org/10.1093/cercor/bhy285.

Hage, S.R., Nieder, A., 2013. Single neurons in monkey prefrontal cortex encode volitional initiation of vocalizations. Nat. Commun. 4, 2409. https://doi.org/10.1038/ncomms3409.

Haggard, P., 2019. The Neurocognitive Bases of Human Volition. Annu Rev. Psychol. 70, 9–28. Jan 4.

Halassa, M.M., Kastner, S., 2017. Thalamic functions in distributed cognitive control (Dec). Nat. Neurosci. 20 (12), 1669–1679. https://doi.org/10.1038/s41593-017-0020-1.

Halsband, U., 1987. Higher disturbances of movement in monkeys (Macaca mulatta). In: Gantchev, G.N., et al. (Eds.), Motor Control. Plenum Press, pp. 79–85.

Halsband, U., Freund, H.J., 1990. Premotor cortex and conditional motor learning in man. Brain 113 (Pt 1), 207–222. https://doi.org/10.1093/brain/113.1.207.

Halsband, U., Ito, N., Tanji, J., Freund, H.J., 1993. The role of premotor cortex and the supplementary motor area in the temporal control of movement in man. Brain 116 (Pt 1), 243–266. https://doi.org/10.1093/brain/116.1.243.

Hampshire, A., Chamberlain, S.R., Monti, M.M., Duncan, J., Owen, A.M., 2010. The role of the right inferior frontal gyrus: inhibition and attentional control. Neuroimage 50 (3), 1313–1319. https://doi.org/10.1016/j.neuroimage.2009.12.109.

Han, Y., Yang, H., Lv, Y.T., Zhu, C.Z., He, Y., Tang, H.H., Gong, Q.Y., Luo, Y.J., Zang, Y. F., Dong, Q., 2009. Gray matter density and white matter integrity in pianists' brain: a combined structural and diffusion tensor MRI study. Jul 31 Neurosci. Lett. 459 (1), 3–6. https://doi.org/10.1016/j.neulet.2008.07.056.

Hannah, R., Aron, A.R., 2021. Towards real-world generalizability of a circuit for action-stopping. Nat. Rev. Neurosci. 22 (9), 538–552 (Sep).

Hansell, M., 2000. Bird Nests and Construction Behaviour, 1st edn..,. Cambridge University Press,.

Hansell, M., Ruxton, G., 2008. Setting tool use within the context of animal construction behaviour. Trends Ecol. Evol. 23, 73–78. https://doi.org/10.1016/j.tree.2007.10.006.

Hansell, M.H., 2005. Animal Architecture. Oxford University Press,, Oxford; New York.

Hardwick, R.M., Rottschy, C., Miall, R.C., Eickhoff, S.B., 2013. A quantitative meta-analysis and review of motor learning in the human brain. Neuroimage 67, 283–297. Feb 15.

He, S.Q., Dum, R.P., Strick, P.L., 1993. Topographic organization of corticospinal projections from the frontal lobe: motor areas on the lateral surface of the hemisphere. J. Neurosci. 13 (3), 952–980. https://doi.org/10.1523/JNEUROSCI.13-03-00952.1993.

He, S.Q., Dum, R.P., Strick, P.L., 1995. Topographic organization of corticospinal projections from the frontal lobe: motor areas on the medial surface of the hemisphere. J. Neurosci. 15 (5 Pt 1), 3284–3306. https://doi.org/10.1523/JNEUROSCI.15-05-03284.1995.

Hécaen, H., Assal, G., 1970. A comparison of constructive deficits following right and left hemispheric lesions. Neuropsychologia 8, 289–303. https://doi.org/10.1016/0028-3932(70)90075-8.

Heilbronner, S.R., Hayden, B.Y., 2016. Dorsal anterior cingulate cortex: a bottom-up view. Annu Rev. Neurosci. 39, 149–170. https://doi.org/10.1146/annurev-neuro-070815-013952.

Hikosaka, O., Miyashita, K., Miyachi, S., Sakai, K., Lu, X., 1998. Differential roles of the frontal cortex, basal ganglia, and cerebellum in visuomotor sequence learning. Neurobiol. Learn. Mem. 70, 137–149. https://doi.org/10.1006/nlme.1998.3844.

Hikosaka, O., Nakahara, H., Rand, M.K., Sakai, K., Lu, X., Nakamura, K., Miyachi, S., Doya, K., 1999. Parallel neural networks for learning sequential procedures. Trends Neurosci. 22 (10), 464–471. 〈https://doi.org/10.1016/s0166-2236〉(99)01439-3 Erratum 1999. Trends Neurosci. 22(12):569.

Hikosaka, O., Takikawa, Y., Kawagoe, R., 2000. Role of the basal ganglia in the control of purposive saccadic eye movements. Physiol. Rev. 80 (3), 953–978. https://doi.org/10.1152/physrev.2000.80.3.953.

Hikosaka, O., Nakamura, K., Sakai, K., Nakahara, H., 2002. Central mechanisms of motor skill learning. Apr 1 Curr. Opin. Neurobiol. 12 (2), 217–222. https://doi.org/10.1016/S0959-4388(02)00307-0.

Hilgetag, C.C., Kaiser, M., 2004. Clustered organization of cortical connectivity. Neuroinform 2, 353–360. https://doi.org/10.1385/NI:2:3:353.

Hoeschele, M., Merchant, H., Kikuchi, Y., Hattori, Y., ten Cate, C., 2015. Searching for the origins of musicality across species. Philos. Trans. R. Soc. B 370, 20140094. https://doi.org/10.1098/rstb.2014.0094.

Hoogewoud, F., Hamadjida, A., Wyss, A.F., Mir, A., Schwab, M.E., Belhaj-Saif, A., Rouiller, E.M., 2013. Comparison of functional recovery of manual dexterity after unilateral spinal cord lesion or motor cortex lesion in adult macaque monkeys. Jul 22 Front Neurol. 4, 101. https://doi.org/10.3389/fneur.2013.00101.

Hsieh, S., Lin, Y.C., 2017a. Strategies for stimulus selective stopping in the elderly. Acta Psychol. 173, 122–131. https://doi.org/10.1016/j.actpsy.2016.12.011.

Hsieh, S., Lin, Y.C., 2017b. Stopping ability in younger and older adults: Behavioral and event-related potential. Cogn. Affect Behav. Ne. 17 (2), 348–363. https://doi.org/10.3758/s13415-016-0483-7.

Hsu, H.M., Yao, Z.-F., Hwang, K., Hsieh, S., 2020. Between-module functional connectivity of the salient ventral attention network and dorsalattention network is associated with motor inhibition. PLoS ONE 15 (12), e0242985 https:// doi.org/10.1371/journal.pone.0242985.

Hu, S.E., Job, M., Jenks, S.K., Chao, H.H., Li, C.S.R., 2019. Imaging the effects of age on proactive control in healthy adults. Brain Imaging Behav. 13 (6), 1526–1537. https://doi.org/10.1007/s11682-019-00103-w.

Hursh, J.B., 1939. The Properties of Growing Nerve Fibers. Am. J. Physiol. – Leg. Content 127, 140–153.

Husain, M., Parton, A., Hodgson, T.L., Mort, D., Rees, G., 2003. Self-control during response conflict by human supplementary eye field. Nat. Neurosci. 6 (2), 117–118. https://doi.org/10.1038/nn1005.

Hwang, E.J., Link, T.D., Hu, Y.Y., Lu, S., Wang, E.H., Lilascharoen, V., Aronson, S., O'Neil, K., Lim, B.K., Komiyama, T., 2019. Corticostriatal flow of action selection bias. Dec 18 Neuron 104 (6), 1126–1140. https://doi.org/10.1016/j.neuron.2019.09.028.

Hwang, E.J., Dahlen, J.E., Mukundan, M., Komiyama, T., 2021. Disengagement of motor cortex during long-term learning tracks the performance level of learned movements. Aug 18 J. Neurosci. 41 (33), 7029–7047. https://doi.org/10.1523/JNEUROSCI.3049-20.2021.

Hyvärinen, J., Poranen, A., 1974. Function of the parietal associative area 7 as revealed from cellular discharges in alert monkeys. Brain 97 (4), 673–692. https://doi.org/10.1093/brain/97.1.673.

Iacoboni, M., Dapretto, M., 2006. The mirror neuron system and the consequences of its dysfunction. Nat. Rev. Neurosci. 7 (12), 942–951. https://doi.org/10.1038/nrn2024.

Igelström, K.M., Graziano, M.S.A., 2017. The inferior parietal lobule and temporoparietal junction: A network perspective. Neuropsychologia 105, 70–83. https://doi.org/10.1016/j.neuropsychologia.2017.01.001.

Impieri, D., Gamberini, M., Passarelli, L., Rosa, M.G.P., Galletti, C., 2018. Thalamo-cortical projections to the macaque superior parietal lobule areas PEc and PE. J. Comp. Neurol. 526 (6), 1041–1056. https://doi.org/10.1002/cne.24389.

Indovina, I., Bosco, G., Riccelli, R., Maffei, V., Lacquaniti, F., Passamonti, L., Toschi, N., 2020. Structural connectome and connectivity lateralization of the multimodal vestibular cortical network. Neuroimage 222, 117247. Nov 15.

Innocenti, G.M., Vercelli, A., Caminiti, R., 2014. The diameter of cortical axons depends both on area of origin and target. Cereb. Cortex. 24, 2178–2188. The diameter of cortical axons depends both on area of origin and target. doi:10.1093/cercor/bht070.

Innocenti, G.M., Caminiti, R., Rouiller, E.M., Knott, G., Dyrby, T.B., Descoteaux, M., Thiran, J.P., 2019. Diversity of Cortico-descending Projections: Histological and Diffusion MRI Characterization in the Monkey. Cer Cortex 29, 788–801. https://doi.org/10.1093/cercor/bhx363.

Innocenti, G.M., Schmidt, K., Milleret, C., Fabri, M., Knyazeva, M.G., Battaglia-Mayer, A., Aboitiz, F., Ptito, M., Caleo, M., Marzi, C.A., Barakovic, M., Lepore, F., Caminiti, R., 2022. The functional characterization of callosal connections. Prog. Neurobiol. 208, 102186 https://doi.org/10.1016/j.pneurobio.2021.102186.

Iriki, A., Tanaka, M., Iwamura, Y., 1996. Coding of modified body schema during tool use by macaque postcentral neurones. Neuroreport 7, 2325–2330. https://doi.org/10.1097/00001756-199610020-00010.

Isa, T., Ohki, Y., Seki, K., Alstermark, B., 2006. Properties of propriospinal neurons in the C3-C4 segments mediating disynaptic pyramidal excitation to forelimb motoneurons in the macaque monkey. J. Neurophysiol. 95 (6), 3674–3685. https://doi.org/10.1152/jn.00103.2005.

Isoda, M., Hikosaka, O., 2007. Switching from automatic to controlled action by monkey medial frontal cortex. Nat. Neurosci. 10 (2), 240–248. https://doi.org/10.1038/nn1830.

Jahanshahi, M., Jenkins, I.H., Brown, R.G., Marsden, C.D., Passingham, R.E., Brooks, D. J., 1995. Self-initiated versus externally triggered movements. I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. Brain 118 (Pt 4), 913–933. https://doi.org/10.1093/brain/118.4.913.

Jeannerod, M., 2006. Motor Cognition. Oxford University Press,.

Jeannerod, M., Arbib, M.A., Rizzolatti, G., Sakata, H., 1995. Grasping objects: the cortical mechanisms of visuomotor transformation. Trends Neurosci. 18 (7), 314–320 (Jul).

Jezzini, A., Caruana, F., Stoianov, I., Gallese, V., Rizzolatti, G., 2012. Functional organization of the insula and inner perisylvian regions. Proc. Natl. Acad. Sci. 109 (25), 10077–10082. https://doi.org/10.1073/pnas.1200143109.

Johansen-Berg, H., Rushworth, M.F., Bogdanovic, M.D., Kischka, U., Wimalaratna, S., Matthews, P.M., 2002. The role of ipsilateral premotor cortex in hand movement after stroke. Proc. Natl. Acad. Sci. Usa. 99 (22), 14518–14523. https://doi.org/10.1073/pnas.222536799.

Johnson, P.B., Ferraina, S., Bianchi, L., Caminiti, R., 1996. Cortical networks for visual reaching: intrinsic frontal lobe connectivity. Eur. J. Neurosci. 8 (7), 1358–1362. https://doi.org/10.1111/j.1460-9568.1996.tb01598.x.

Johnson, P.B., Ferraina, S., Bianchi, L., Caminiti, R., 1996. Cortical networks for visual reaching: physiological and anatomical organization of frontal and parietal lobe arm regions. Cereb. Cortex 6 (2), 102–119. https://doi.org/10.1093/cercor/6.2.102.

Johnson-Frey, S.H., Newman-Norlund, R., Grafton, S.T., 2005. A distributed left hemisphere network active during planning of everyday tool use skills. Cereb. cortex (N. Y., N. Y.: 1991), 15(6), 681–695. https://doi.org/10.1093/cercor/bhh169.

Jürgens, U., Ehrenreich, L., 2007. The descending motorcortical pathway to the laryngeal motoneurons in the squirrel monkey. Brain Res. 1148, 90–95. https://doi.org/10.1016/j.brainres.2007.02.020.

Kaas, J.H., Stepniewska, I., 2016. Evolution of posterior parietal cortex and parietal-frontal networks for specific actions in primates. J. Comp. Neurol. 524 (3), 595–608. https://doi.org/10.1002/cne.23838.

Kaeser, M., Wyss, A.F., Bashir, S., Hamadjida, A., Liu, Y., Bloch, J., Brunet, J.F., Belhaj-Saif, A., Rouiller, E.M., 2010. Effects of unilateral motor cortex lesion on ipsilesional hand's reach and grasp performance in monkeys: relationship with recovery in the contralesional hand. J. Neurophysiol. 103 (3), 1630–1645 (Mar).

Kami, A., Meyer, G., Jezzard, P., Adams, M.M., Turner, R., Ungerleider, L.G., 1995. Functional MRI evidence for adult motor cortex plasticity during motor skill learning. Sep 14 Nature 377 (6545), 155–158. https://doi.org/10.1038/377155a0.

Kashtan, N., Alon, U., 2005. Spontaneous evolution of modularity and network motifs. Proc. Nat. Ac. Sci. 102 (39), 13773–13778. https://doi.org/10.1073/pnas.0503610102.

Kaufman, M.T., Churchland, M.M., Shenoy, K.V., 2013. The roles of monkey M1 neuron classes in movement preparation and execution. J. Neurophysiol. 110 (4), 817–825. https://doi.org/10.1152/jn.00892.2011.

Kaufman, M.T., Churchland, M.M., Ryu, S.I., Shenoy, K.V., 2014. Cortical activity in the null space: permitting preparation without movement. Nat. Neurosci. 17 (3), 440–448. https://doi.org/10.1038/nn.3643.

Kawai, R., Markman, T., Poddar, R., Ko, R., Fantana, A.L., Dhawale, A.K., Kampff, A.R., Ölveczky, B.P., 2015. Motor cortex is required for learning but not for executing a motor skill. May 6 Neuron 86 (3), 800–812. https://doi.org/10.1016/j.neuron.2015.03.024.

Keck, T., Keller, G.B., Jacobsen, R.I., Eysel, U.T., Bonhoeffer, T., Hübener, M., 2013. Synaptic scaling and homeostatic plasticity in the mouse visual cortex in vivo. Neuron 80 (2), 327–334. https://doi.org/10.1016/j.neuron.2013.08.018.

Kermadi, I., Boussaoud, D., 1995. Role of the primate striatum in attention and sensorimotor processes: comparison with premotor cortex. Neuroreport 6 (8), 1177–1181.

Kermadi, I., Liu, Y., Tempini, A., Rouiller, E.M., 1997. Effects of reversible inactivation of the supplementary motor area (SMA) on unimanual grasp and bimanual pull and grasp performance in monkeys. Somatosens. Mot. Res. 14 (4), 268–280. https://doi.org/10.1080/08990229770980.

Khalighinejad, N., Bongioanni, A., Verhagen, L., et al., 2020. A Basal Forebrain-Cingulate Circuit in Macaques Decides It Is Time to Act. e8 Neuron 105 (2), 370–384. https://doi.org/10.1016/j.neuron.2019.10.030.

Kincses, Z.T., Johansen-Berg, H., Tomassini, V., Bosnell, R., Matthews, P.M., Beckmann, C.F., 2008. Model-free characterization of brain functional networks for motor sequence learning using fMRI. Feb 15 Neuroimage 39 (4), 1950–1958. https://doi.org/10.1016/j.neuroimage.2007.09.070.

King, S.M., Dykeman, C., Redgrave, P., Dean, P., 1992. Use of a distracting task to obtain defensive head movements to looming visual stimuli by human adults in a laboratory setting. Perception 21 (2), 245–259. https://doi.org/10.1068/p210245.

Kleim, J.A., Hogg, T.M., VandenBerg, P.M., Cooper, N.R., Bruneau, R., Remple, M., 2004. Cortical synaptogenesis and motor map reorganization occur during late, but not early, phase of motor skill learning. Jan 21 J. Neurosci. 24 (3), 628–633. https://doi.org/10.1523/JNEUROSCI.3440-03.2004.

Kleist K. (1934). Gehirnpathologie. Barth, Leipzig.

Klinzing, J.G., Niethard, N., Born, J., 2019. Mechanisms of systems memory consolidation during sleep (Oct). Nat. Neurosci. 22 (10), 1598–1610. https://doi.org/10.1038/s41593-019-0467-3.

Kobayashi, Y., Amaral, D.G., 2003. Macaque monkey retrosplenial cortex: II. Cortical afferents. J. Comp. Neurol. 466 (1), 48–79. https://doi.org/10.1002/cne.10883.

Kobayashi, Y., Amaral, D.G., 2007. Macaque monkey retrosplenial cortex: III. Cortical efferents. J. Comp. Neurol. 502 (5), 810–833. https://doi.org/10.1002/cne.21346.

Konishi, S., Nakajima, K., Uchida, I., Sekihara, K., Miyashita, Y., 1998. No-go dominant brain activity in human inferior prefrontal cortex revealed by functional magnetic resonance imaging (Mar). Eur. J. Neurosci. 10 (3), 1209–1213. https://doi.org/10.1046/j.1460-9568.1998.00167.x.

Konishi, S., Nakajima, K., Uchida, I., Kikyo, H., Kameyama, M., Miyashita, Y., 1999. Common inhibitory mechanism in human inferior prefrontal cortex revealed by event-related functional MRI (May). Brain 122 (Pt 5), 981–991. https://doi.org/10.1093/brain/122.5.981.

Krakauer, J.W., Carmichael, S.T., 2017. Broken Mov.: Neurobiol. Mot. Recovery Stroke. https://doi.org/10.7551/mitpress/9310.001.0001.

Kraskov, A., Dancause, N., Quallo, M.M., Shepherd, S., Lemon, R.N., 2009. Corticospinal neurons in macaque ventral premotor cortex with mirror properties: a potential mechanism for action suppression. Neuron 64 (6), 922–930. https://doi.org/10.1016/j.neuron.2009.12.010.

Kravitz, D., Saleem, K., Baker, C.I., Mishkin, M., 2011. A new neural framework for visuospatial processing. Nat. Rev. Neurosci. 2011 12, 217–230. https://doi.org/10.1038/nrn3008.

Krubitzer, L., Clarey, J., Tweedale, R., Elston, G., Calford, M., 1995. A redefinition of somatosensory areas in the lateral sulcus of macaque monkeys. J. Neurosci. 15, 3821–3839. ⟨http://www.ncbi.nlm.nih.gov/pubmed/7751949.7751949⟩.

Ku, S.P., Tolias, A.S., Logothetis, N.K., Goense, J., 2011. fMRI of the face processing network in the ventral temporal lobe of awake and anesthetized macaques. Neuron 70, 352–362. https://doi.org/10.1016/j.neuron.2011.02.048.

Kurata, K., 1994. Site of origin of projections from the thalamus to dorsal versus ventral aspects of the premotor cortex of monkeys. Neurosci. Res 21 (1), 71–76. https://doi.org/10.1016/0168-0102(94)90069-8.

Kurata, K., Hoffman, D.S., 1994. Differential effects of muscimol microinjection into dorsal and ventral aspects of the premotor cortex of monkeys. J. Neurophysiol. 71 (3), 1151–1164 (Mar).

Kurata, K., Wise, S.P., 1988. Premotor and supplementary motor cortex in rhesus monkeys: neuronal activity during externally- and internally-instructed motor tasks. Exp. Brain Res 72 (2), 237–248. https://doi.org/10.1007/BF00250247.

Kuypers, H.G., 1982. A new look at the organization of the motor system. Prog. Brain Res 57, 381–403 doi:10.1016/S0079-6123(08)64138-2 doi:10.1016/S0079-6123(08)64138-2.

Kuypers, H.G., Brinkman, J., 1970. Precentral projections to different parts of the spinal intermediate zone in therhesus monkey. Nov 11 Brain Res 24 (1), 29–48. https://doi.org/10.1016/0006-8993(70)90272-6.

Kuypers, H.G.J.M., 1960. Central cortical projections to motor and somato-sensory cell groups. An experimental study in the rhesus monkey. Brain 83, 161–184. https://doi.org/10.1126/science.132.3418.38.

Kuypers, H.G.J.M., 1962. Corticospinal connections: postnatal development in the rhesus monkey. Science 138 (3541), 678–680. https://doi.org/10.1126/science.138.3541.678.

Kuypers, H.G.J.M., 1964. The Descending Pathways to the Spinal Cord, Their Anatomy and Function. Prog. Brain Res 11, 178–202. https://doi.org/10.1016/s0079-6123(08)64048-0.

Kuypers, H.G.J.M., 1981. Anatomy of the descending pathways. In: Brooks, V.B. (Ed.), Handbook of Physiology, Section 1. The nervous system, vol. II. Motor Control. American Physiological Society, Bethesda, MD, pp. 597–666.

Lacquaniti, F., Guigon, E., Bianchi, L., Ferraina, S., Caminiti, R., 1995. Representing spatial information for limb movement: role of area 5 in the monkey. Cereb. cortex (N. Y., N. Y.: 1991) 5 (5), 391–409. https://doi.org/10.1093/cercor/5.5.391.

Làdavas, E., Farnè, A., 2004. Visuo-tactile representation of near-the-body space. J. Physiol., Paris 98 (1–3), 161–170. https://doi.org/10.1016/j.jphysparis.2004.03.007.

Lamme, V.A., Roelfsema, P.R., 2000. The distinct modes of vision offered by feedforward and recurrent processing. Trends Neurosci. 23 (11), 571–579. https://doi.org/10.1016/s0166-2236(00)01657-x.

Landis, C., Hunt, W.A., 1939. The Startle Pattern. Farrar and Rinhart Inc.,, New York.

Laplane, D., Talairach, J., Meininger, V., Bancaud, J., Orgogozo, J.M., 1977. Clinical consequences of corticectomies involving the supplementary motor area in man. J. Neurol. Sci. 34 (3), 301–314. https://doi.org/10.1016/0022-510x(77)90148-4.

Lara, A.H., Cunningham, J.P., Churchland, M.M., 2018. Different population dynamics in the supplementary motor area and motor cortex during reaching. Nat. Commun. 9 (1), 2754. Published 2018 Jul 16. doi:10.1038/s41467-018-05146-z.

Lashley, K.S., 1951. The problem of serial order in behavior. In: Jeffress, L.A. (Ed.), Cerebral Mechanisms in Behavior; The Hixon Symposium. Wiley, pp. 112–146.

Lavenex, P.B., Amaral, D.G., Lavenex, P., 2006. Hippocampal lesion prevents spatial relational learning in adult macaque monkeys. J. Neurosci. 26 (17), 4546–4558. https://doi.org/10.1523/JNEUROSCI.5412-05.2006.

Ledberg, A., Bressler, S.L., Ding, M., Coppola, R., Nakamura, R., 2007. Large-scale visuomotor integration in the cerebral cortex. Cereb. Cortex 17 (1), 44–62. https://doi.org/10.1093/cercor/bhj123.

Lee, H.H., Hsieh, S., 2017. Resting-State fMRI Associated with Stop-Signal Task Performance in Healthy Middle-Aged and Elderly People. Front Psychol. 8, 766. https://doi.org/10.3389/fpsyg.2017.00766.

Lemon, R., 2012. Spinal cord injury: harnessing spike timing to induce plastic change. Curr. Biol. 22 (24), R1039–R1040. https://doi.org/10.1016/j.cub.2012.11.004.

Lemon, R.N., 2008. Descending pathways in motor control, 2008 Annu Rev. Neurosci. 31, 195–218. https://doi.org/10.1146/annurev.neuro.31.060407.125547.

Lhermitte, F., 1981. Le "comportement d'utilisation" et ses relations avec les lésions del lobes frontaux. Rev. Neurol. 137, 846–847.

Lhermitte, F., 1983. Utilization behaviour' and its relation to lesions of the frontal lobes. Brain 106 (Pt 2), 237–255. https://doi.org/10.1093/brain/106.2.237.

Libet, B., Gleason, C.A., Wright, E.W., Pearl, D.K., 1983. Time of conscious intention to act in relation to onset of cerebral activity (readiness-potential). The unconscious initiation of a freely voluntary act. Brain 106 (Pt 3), 623–642. https://doi.org/10.1093/brain/106.3.623.

Lima, C.F., Brancatisano, O., Fancourt, A., et al., 2016. Impaired socio-emotional processing in a developmental music disorder. Sci. Rep. 6, 34911. Published 2016 Oct 11. doi:10.1038/srep34911.

Liu, Y., Rouiller, E.M., 1999. Mechanisms of recovery of dexterity following unilateral lesion of the sensorimotor cortex in adult monkeys. Exp. Brain Res 128 (1–2), 149–159 (Sep).

Livi, A., Lanzilotto, M., Maranesi, M., Fogassi, L., Rizzolatti, G., Bonini, L., 2019. Agent-based representations of objects and actions in the monkey pre-supplementary motor area. Proc. Natl. Acad. Sci. Usa. 116 (7), 2691–2700. https://doi.org/10.1073/pnas.1810890116.

Logan, G.D., Cowan, W.B., 1984. On the Ability to Inhibit Thought and Action—a Theory of an Act of Control. Psychol. Rev. 91 (3), 295–327. https://doi.org/10.1037/0033-295x.91.3.295.

Logan, G.D., Van Zandt, T., Verbruggen, F., Wagenmakers, E.J., 2014. On the ability to inhibit thought and action: general and special theories of an act of control. Psychol. Rev. 121 (1), 66–95. https://doi.org/10.1037/a0035230.

Lu, M.T., Preston, J.B., Strick, P.L., 1994. Interconnections between the prefrontal cortex and the premotor areas in the frontal lobe. J. Comp. Neurol. 341 (3), 375–392. https://doi.org/10.1002/cne.903410308.

Luppino, G., Matelli, M., Camarda, R.M., Gallese, V., Rizzolatti, G., 1991. Multiple representations of body movements in mesial area 6 and the adjacent cingulate cortex: an intracortical microstimulation study in the macaque monkey. J. Comp. Neurol. 311 (4), 463–482. https://doi.org/10.1002/cne.903110403.

Luppino, G., Matelli, M., Camarda, R., Rizzolatti, G., 1993. Corticocortical connections of area F3 (SMA-proper) and area F6 (pre-SMA) in the macaque monkey. J. Comp. Neurol. 338 (1), 114–140. https://doi.org/10.1002/cne.903380109.

Luria, A.R., 1966. Human Brain and Psychological Processes. Harper & Row,, New York.

Maeda, K., Ishida, H., Nakajima, K., Inase, M., Murata, A., 2015. Functional properties of parietal hand manipulation-related neurons and mirror neurons responding to vision of own hand action. J. Cogn. Neurosci. 27 (3), 560–572 (Mar).

Maffei, V., Mazzarella, E., Piras, F., Spalletta, G., Caltagirone, C., Lacquaniti, F., Daprati, E., 2016. Processing of visual gravitational motion in the peri-sylvian cortex: Evidence from brain-damaged patients (May). Cortex 78, 55–69. https://doi.org/10.1016/j.cortex.2016.02.004.

Maguire, E.A., 2001. The retrosplenial contribution to human navigation: a review of lesion and neuroimaging findings. Scand. J. Psychol. 42 (3), 225–238 (Jul).

Makino, H., 2023. Arithmetic value representation for hierarchical behavior composition (Jan). Nat. Neurosci. 26 (1), 140–149. https://doi.org/10.1038/s41593-022-01211-5.

Makino, H., Hwang, E.J., Hedrick, N.G., Komiyama, T., 2016. Circuit Mechanisms of Sensorimotor Learning. Neuron 92 (4), 705–721. https://doi.org/10.1016/j.neuron.2016.10.029.

Makuuchi, M., Kaminaga, T., Sugishita, M., 2003. Both parietal lobes are involved in drawing: a functional MRI study and implications for constructional apraxia. Cogn. Brain Res. 16, 338–347. https://doi.org/10.1016/s0926-6410(02)00302-6.

Mao, D., Avila, E., Caziot, B., Laurens, J., Dickman, J.D., Angelaki, D.E., 2021. Spatial modulation of hippocampal activity in freely moving macaques. e6 Neuron 109 (21), 3521–3534. https://doi.org/10.1016/j.neuron.2021.09.032.

Maranesi, M., Rodà, F., Bonini, L., Rozzi, S., Ferrari, P.F., Fogassi, L., Coudé, G., 2012. Anatomo-functional organization of the ventral primary motor and premotor cortex in the macaque monkey. Eur. J. Neurosci. 36 (10), 3376–3387. https://doi.org/10.1111/j.1460-9568.2012.08252.x.

Maravita, A., Romano, D., 2018. The parietal lobe and tool use. Handbook of Clinical Neurology. Elsevier,, pp. 481–498.

Marconi, B., Genovesio, A., Battaglia-Mayer, A., et al., 2001. Eye-hand coordination during reaching. I. Anatomical relationships between parietal and frontal cortex. Cereb. Cortex 11 (6), 513–527. https://doi.org/10.1093/cercor/11.6.513.

Marcos, E., Pani, P., Brunamonti, E., Deco, G., Ferraina, S., Verschure, P., 2013. Neural variability in premotor cortex is modulated by trial history and predicts behavioral performance. Neuron 78 (2), 249–255. https://doi.org/10.1016/j.neuron.2013.02.006.

Marder, E., Goaillard, J.M., 2006. Variability, compensation and homeostasis in neuron and network function. Nat. Rev. Neurosci. 7 (7), 563–574. https://doi.org/10.1038/nrn1949.

Mars, R.B., Jbabdi, S., Sallet, J., et al., 2011. Diffusion-Weighted Imaging Tractography-Based Parcellation of the Human Parietal Cortex and Comparison with Human and Macaque Resting-State Functional Connectivity. J. Neurosci. 31, 4087–4100. https://doi.org/10.1523/JNEUROSCI.5102-10.2011.

Marsden, J.F., Playford, D.E., Day, B.L., 2005. The vestibular control of balance after stroke (May). J. Neurol. Neurosurg. Psychiatry 76 (5), 670–678. https://doi.org/10.1136/jnnp.2004.046565.

Mascaro, M., Battaglia-Mayer, A., Nasi, L., Amit, D.J., Caminiti, R., 2003. The eye and the hand: neural mechanisms and network models for oculomanual coordination in parietal cortex. Cereb. Cortex 13 (12), 1276–1286. https://doi.org/10.1093/cercor/bhg075.

Matelli, M., Luppino, G., 1996. Thalamic input to mesial and superior area 6 in the macaque monkey. J. Comp. Neurol. 372 (1), 59–87 doi:10.1002/(SICI)1096-9861(19960812)372:1<59:AID-CNE6>3.0.CO;2-L.

Matelli, M., Luppino, G., Rizzolatti, G., 1985. Patterns of cytochrome oxidase activity in the frontal agranular cortex of the macaque monkey. Behav. Brain Res 18 (2), 125–136. https://doi.org/10.1016/0166-4328(85)90068-3.

Matelli, M., Luppino, G., Fogassi, L., Rizzolatti, G., 1989. Thalamic input to inferior area 6 and area 4 in the macaque monkey. J. Comp. Neurol. 280 (3), 468–488. https://doi.org/10.1002/cne.902800311.

Matelli, M., Luppino, G., Rizzolatti, G., 1991. Architecture of superior and mesial area 6 and the adjacent cingulate cortex in the macaque monkey. J. Comp. Neurol. 311, 445–462.

Matelli, M., Govoni, P., Galletti, C., Kutz, D.F., Luppino, G., 1998. Superior area 6 afferents from the superior parietal lobule in the macaque monkey. J. Comp. Neurol. 402 (3), 327–352. Dec 21.

Matsuzaka, Y., Aizawa, H., Tanji, J., 1992. A motor area rostral to the supplementary motor area (presupplementary motor area) in the monkey: neuronal activity during a learned motor task. J. Neurophysiol. 68 (3), 653–662. https://doi.org/10.1152/jn.1992.68.3.653.

Mattia, M., Pani, P., Mirabella, G., Costa, S., Del Giudice, P., Ferraina, S., 2013. Heterogeneous attractor cell assemblies for motor planning in premotor cortex. J. Neurosci. 33 (27), 11155–11168. https://doi.org/10.1523/JNEUROSCI.4664-12.2013.

Mayer, A., Lewenfus, G., Bittencourt-Navarrete, R.E., Clasca, F., Franca, J.G.D., 2019. Thalamic Inputs to Posterior Parietal Cortical Areas Involved in Skilled Forelimb Movement and Tool Use in the Capuchin Monkey. Cereb. Cortex 29 (12), 5098–5115. https://doi.org/10.1093/cercor/bhz051.

Mayer Gross, W., 1935. Some observation on apraxia. Proc. R. Soc. Med 28, 1203–1212.

McIntyre, J., Zago, M., Berthoz, A., Lacquaniti, F., 2001. Does the brain model Newton's laws? (Jul). Nat. Neurosci. 4 (7), 693–694. https://doi.org/10.1038/89477.

McNeal, D.W., Darling, W.G., Ge, J., et al., 2010. Selective long-term reorganization of the corticospinal projection from the supplementary motor cortex following recovery from lateral motor cortex injury. J. Comp. Neurol. 518 (5), 586–621. https://doi.org/10.1002/cne.22218.

Mendoza, G., Merchant, H., 2014. Motor system evolution and the emergence of high cognitive functions. Prog. Neurobiol. 122, 73–93. https://doi.org/10.1016/j.pneurobio.2014.09.001.

Mendoza, G., Méndez, J.C., Pérez, O., Prado, L., Merchant, H., 2018. Neural basis for categorical boundaries in the primate pre-SMA during relative categorization of time intervals. Nat. Commun. 9 (1), 1098. Published 2018 Mar 15. doi:10.1038/s41467-018-03482-8.

Menon, V., Uddin, L.Q., 2010. Saliency, switching, attention and control: a network model of insula function (Jun). Brain Struct. Funct. 214, 655–667. https://doi.org/10.1007/s00429-010-0254-0.

Menon, V., Adleman, N.E., White, C.D., Glover, G.H., Reiss, A.L., 2001. Error-related brain activation during a Go/NoGo response inhibition task (Mar). Hum. Brain Mapp. 12 (3), 131–143. https://doi.org/10.1002/1097-0193(200103)12:3<131::aid-hbm1010>3.0.co;2-c.

Merchant, H., Averbeck, B.B., 2017. The Computational and Neural Basis of Rhythmic Timing in Medial Premotor Cortex. J. Neurosci. 37 (17), 4552–4564. https://doi.org/10.1523/JNEUROSCI.0367-17.2017.

Merchant, H., Battaglia-Mayer, A., Georgopoulos, A.P., 2001. Effects of optic flow in motor cortex and area 7a. J Neurophysiol 86 (4), 1937–1954. https://doi.org/10.1152/jn.2001.86.4.1937.

Merchant, H., Battaglia-Mayer, A., Georgopoulos, A.P., 2003. Interception of real and apparent motion targets: psychophysics in humans and monkeys. Exp. Brain Res. 152 (1), 106–112 (Sep).

Merchant, H., Battaglia-Mayer, A., Georgopoulos, A.P., 2004. Neural responses during interception of real and apparent circularly moving stimuli in motor cortex and area 7a. Cereb. Cortex 14 (3), 314–331. https://doi.org/10.1093/cercor/bhg130.

Merchant, H., Zarco, W., Pérez, O., Prado, L., Bartolo, R., 2011. Measuring time with different neural chronometers during a synchronization-continuation task. Proc. Natl. Acad. Sci. Usa. 108 (49), 19784–19789. https://doi.org/10.1073/pnas.1112933108.

Merchant, H., Pérez, O., Zarco, W., Gámez, J., 2013. Interval tuning in the primate medial premotor cortex as a general timing mechanism. J. Neurosci. 33 (21), 9082–9096. https://doi.org/10.1523/JNEUROSCI.5513-12.2013.

Merchant, H., Pérez, O., Bartolo, R., et al., 2015. Sensorimotor neural dynamics during isochronous tapping in the medial premotor cortex of the macaque. Eur. J. Neurosci. 41 (5), 586–602. https://doi.org/10.1111/ejn.12811.

Mesulam, M.M., Mufson, E.J., 1982. Insula of the old world monkey. III: Efferent cortical output and comments on function. J. Comp. Neurol. 212, 38–52. https://doi.org/10.1002/cne.902120104.

Meunier, D., Lambiotte, R., Bullmore, E.T., 2010. Modular and hierarchically modular organization of brain networks. Front. Neurosci. 4, 200. https://doi.org/10.3389/fnins.2010.00200.

Mione, V., Brunamonti, E., Pani, P., Genovesio, A., Ferraina, S., 2020. Dorsal premotor cortex neurons signal the level of choice difficulty during logical decisions. Cell Rep. 32 (4), 107961. Jul 28.

Mirabella, G., Pani, P., Ferraina, S., 2011. Neural correlates of cognitive control of reaching movements in the dorsal premotor cortex of rhesus monkeys. J. Neurophysiol. 106 (3), 1454–1466. https://doi.org/10.1152/jn.00995.2010.

Miri, A., Warriner, C.L., Seely, J.S., Elsayed, G.F., Cunningham, J.P., Churchland, M.M., Jessell, T.M., 2017. Behaviorally Selective Engagement of Short-Latency Effector Pathways by Motor Cortex. e11 Neuron 95 (3), 683–696. https://doi.org/10.1016/j.neuron.2017.06.042.

Mita, A., Mushiake, H., Shima, K., Matsuzaka, Y., Tanji, J., 2009. Interval time coding by neurons in the presupplementary and supplementary motor areas. Nat. Neurosci. 12 (4), 502–507. https://doi.org/10.1038/nn.2272.

Mitz, A.R., Godschalk, M., Wise, S.P., 1991. Learning-dependent neuronal activity in the premotor cortex: activity during the acquisition of conditional motor associations. J. Neurosci. 11 (6), 1855–1872. https://doi.org/10.1523/JNEUROSCI.11-06-01855.1991.

Moll, L., Kuypers, H.G., 1977. Premotor cortical ablations in monkeys: contralateral changes in visually guided reaching behavior. Science 198 (4314), 317–319. https://doi.org/10.1126/science.410103.

Moser, E.I., Kropff, E., Moser, M.B., 2008. Place cells, grid cells, and the brain's spatial representation system. Annu Rev Neurosci 31, 69–89. https://doi.org/10.1146/annurev.neuro.31.061307.090723.

Morecraft, R.J., Louie, J.L., Herrick, J.L., Stilwell-Morecraft, K.S., 2001. Cortical innervation of the facial nucleus in the non-human primate: a new interpretation of the effects of stroke and related subtotal brain trauma on the muscles of facial expression. Brain 124 (Pt 1), 176–208. https://doi.org/10.1093/brain/124.1.176.

Morecraft, R.J., Cipolloni, P.B., Stilwell-Morecraft, K.S., Gedney, M.T., Pandya, D.N., 2004. Cytoarchitecture and cortical connections of the posterior cingulate and adjacent somatosensory fields in the rhesus monkey. J. Comp. Neurol. 469 (1), 37–69. Jan 26.

Morecraft, R.J., Ge, J., Stilwell-Morecraft, K.S., Rotella, D.L., Pizzimenti, M.A., Darling, W.G., 2019. Terminal organization of the corticospinal projection from the lateral premotor cortex to the cervical enlargement (C5-T1) in rhesus monkey. J. Comp. Neurol. 527 (16), 2761–2789. https://doi.org/10.1002/cne.24706.

Mountcastle, V.B., 1978. An organizing principle for cerebral function: the unit model and the distributed system. In: Mountcastle, V.B., Edelmann, G. (Eds.), The Mindful Brain. MIT Press, Cambridge, pp. 7–50.

Mountcastle, V.B., 1997. The columnar organization of the neocortex. Brain 120 (4), 701–722. https://doi.org/10.1093/brain/120.4.701.

Mountcastle, V.B., 2005. The Sensory Hand. Harvard University Press,, Cambridge, Massachusetts, and London, England.

Mountcastle, V.B., Lynch, J.C., Georgopoulos, A., Sakata, H., Acuna, C., 1975. Posterior parietal association cortex of the monkey: command functions for operations within extrapersonal space. J. Neurophysiol. 38, 871–908. https://doi.org/10.1152/jn.1975.38.4.871.

Mouraux, A., Iannetti, G.D., 2018. The search for pain biomarkers in the human brain. Brain 141 (12), 3290–3307. Dec 1.

Moyer, R.S., Landauer, T.K., 1967. Time required for judgements of numerical inequality. Nature 215 (5109), 1519–1520. https://doi.org/10.1038/2151519a0.

Muller, R.U., Ranck Jr, J.B., Taube, J.S., 1996. Head direction cells: properties and functional significance. Curr. Opin. Neurobiol. 6 (2), 196–206. https://doi.org/10.1016/s0959-4388(96)80073-0.

Murakami, M., Vicente, M.I., Costa, G.M., Mainen, Z.F., 2014. Neural antecedents of self-initiated actions in secondary motor cortex. Nat. Neurosci. 17 (11), 1574–1582. https://doi.org/10.1038/nn.3826.

Murakami, M., Shteingart, H., Loewenstein, Y., Mainen, Z.F., 2017. Distinct Sources of Deterministic and Stochastic Components of Action Timing Decisions in Rodent Frontal Cortex. e7 Neuron 94 (4), 908–919. https://doi.org/10.1016/j.neuron.2017.04.040.

Murata, A., Gallese, V., Luppino, G., Kaseda, M., Sakata, H., 2000. Selectivity for the shape, size, and orientation of objects for grasping in neurons of monkey parietal area AIP. J. Neurophysiol. 83 (5), 2580–2601. https://doi.org/10.1152/jn.2000.83.5.2580.

Murata, Y., Higo, N., Oishi, T., Yamashita, A., Matsuda, K., Hayashi, M., Yamane, S., 2008. Effects of motor training on the recovery of manual dexterity after primary motor cortex lesion in macaque monkeys. J. Neurophysiol. 99 (2), 773–786 (Feb).

Müri, R.M., 2016. Cortical control of facial expression. J Comp Neurol 524 (8), 1578–1585. https://doi.org/10.1002/cne.23908.

Mushiake, H., Inase, M., Tanji, J., 1990. Selective coding of motor sequence in the supplementary motor area of the monkey cerebral cortex. Exp. Brain Res 82 (1), 208–210. https://doi.org/10.1007/BF00230853.

Mushiake, H., Inase, M., Tanji, J., 1991. Neuronal activity in the primate premotor, supplementary, and precentral motor cortex during visually guided and internally determined sequential movements. J. Neurophysiol. 66 (3), 705–718. https://doi.org/10.1152/jn.1991.66.3.705.

Nachev, P., Husain, M., 2010. Action and the fallacy of the 'internal': Comment on Passingham et al. Trends Cogn. Sci. 14 (5), 192–194. https://doi.org/10.1016/j.tics.2010.03.002.

Nachev, P., Kennard, C., Husain, M., 2008. Functional role of the supplementary and pre-supplementary motor areas. Nat. Rev. Neurosci. 9 (11), 856–869. https://doi.org/10.1038/nrn2478.

Nakajima, T., Hosaka, R., Mushiake, H., 2022. Complementary roles of primate dorsal premotor and pre-supplementary motor areas to the control of motor sequences. J. Neurosci. 42 (36), 6946–6965. Jul 29.

Nakamura, K., Sakai, K., Hikosaka, O., 1998. Neuronal activity in medial frontal cortex during learning of sequential procedures. J. Neurophysiol. 80 (5), 2671–2687. https://doi.org/10.1152/jn.1998.80.5.2671.

Nakamura, K., Sakai, K., Hikosaka, O., 1999. Effects of local inactivation of monkey medial frontal cortex in learning of sequential procedures. J. Neurophysiol. 82 (2), 1063–1068. https://doi.org/10.1152/jn.1999.82.2.1063.

Nelissen, K., Borra, E., Gerbella, M., et al., 2011. Action observation circuits in the macaque monkey cortex. J. Neurosci. 31 (10), 3743–3756. https://doi.org/10.1523/JNEUROSCI.4803-10.2011.

Nieder, A., 2016. The neuronal code for number. Nat. Rev. Neurosci. 17 (6), 366–382. https://doi.org/10.1038/nrn.2016.40.

Nieder, A., Dehaene, S., 2009. Representation of number in the brain. Annu Rev. Neurosci. 32, 185–208. https://doi.org/10.1146/annurev.neuro.051508.135550.

Nieder, A., Miller, E.K., 2004. A parieto-frontal network for visual numerical information in the monkey. Proc. Natl. Acad. Sci. Usa. 101 (19), 7457–7462. https://doi.org/10.1073/pnas.0402239101.

Nielsen J.B. Human Spinal Motor Control. Annu Rev Neurosci. 2016 Jul 8;39:81–101. doi: 10.1146/annurev-neuro-070815–013913.

Nigg, J.T., 2001. Is ADHD a disinhibitory disorder? Psychol Bull 127 (5), 571–598. https://doi.org/10.1037/0033-2909.127.5.571.

Nishimura, Y., Onoe, H., Morichika, Y., Perfiliev, S., Tsukada, H., Isa, T., 2007. Time-dependent central compensatory mechanisms of finger dexterity after spinal cord injury. Science 318 (5853), 1150–1155. https://doi.org/10.1126/science.1147243.

Noel, J.P., Pfeiffer, C., Blanke, O., Serino, A., 2015. Peripersonal space as the space of the bodily self. Cognition 144, 49–57. https://doi.org/10.1016/j.cognition.2015.07.012.

Noel, J.P., Balzani, E., Avila, E., et al., 2022. Coding of latent variables in sensory, parietal, and frontal cortices during closed-loop virtual navigation. Published 2022 Oct 25 Elife 11, e80280. https://doi.org/10.7554/eLife.80280.

Novak, L.G., Bullier, J., 1997. The timing of information transfer in the visual system. In: Rockland, K., Kaas, J.H., Peters, A. (Eds.), In Cerebral Cortex, vol. 12: "Extrastriate cortex in primates" Chapter: 5. Plenum,Publishing Corporation, pp. 205–241.

Novembre, G., Pawar, V.M., Bufacchi, R.J., et al., 2018. Saliency Detection as a Reactive Process: Unexpected Sensory Events Evoke Corticomuscular Coupling. J Neurosci 38 (9), 2385–2397. https://doi.org/10.1523/JNEUROSCI.2474-17.2017.

Nudo, R.J., Masterton, R.B., 1990. Descending pathways to the spinal cord, III: Sites of origin of the corticospinal tract. J. Comp. Neurol. 296 (4), 559–583. https://doi.org/10.1002/cne.902960405.

O'Keefe, J., Dostrovsky, J., 1971. The hippocampus as a spatial map. Preliminary evidence from unit activity in the freely-moving rat. Brain Res 34, 171–175.

Ohbayashi, M., Picard, N., Strick, P.L., 2016. Inactivation of the Dorsal Premotor Area Disrupts Internally Generated, But Not Visually Guided, Sequential Movements. J. Neurosci. 36 (6), 1971–1976. https://doi.org/10.1523/JNEUROSCI.2356-15.2016.

Okano, K., Tanji, J., 1987. Neuronal activities in the primate motor fields of the agranular frontal cortex preceding visually triggered and self-paced movement. Exp. Brain Res 66 (1), 155–166. https://doi.org/10.1007/BF00236211.

Olson, C.R., Musil, S.Y., Goldberg, M.E., 1996. Single neurons in posterior cingulate cortex of behaving macaque: eye movement signals. J Neurophysiol 76 (5), 3285–3300. https://doi.org/10.1152/jn.1996.76.5.3285.

Orban, G.A., Caruana, F., 2014. The neural basis of human tool use. Published 2014 Apr 9 Front Psychol. 5, 310. https://doi.org/10.3389/fpsyg.2014.00310.

Osiurak, F., Jarry, C., Le Gall, D., 2010. Grasping the affordances, understanding the reasoning: Toward a dialectical theory of human tool use. Psychol. Rev. 117, 517–540. https://doi.org/10.1037/a0019004.

Padberg, J., Cerkevich, C., Engle, J., et al., 2009. Thalamocortical connections of parietal somatosensory cortical fields in macaque monkeys are highly divergent and convergent. Cereb. Cortex 19 (9), 2038–2064. https://doi.org/10.1093/cercor/bhn229.

Pani, P., Theys, T., Romero, M.C., Janssen, P., 2014. Grasping execution and grasping observation activity of single neurons in the macaque anterior intraparietal area. J. Cogn. Neurosci. 26 (10), 2342–2355 (Oct).

Pani, P., Giamundo, M., Giarrocco, F., Mione, V., Fontana, R., Brunamonti, E., Mattia, M., Ferraina, S., 2022. Neuronal population dynamics during motor plan cancellation in nonhuman primates. Proc. Natl. Acad. Sci. USA 119 (28), e2122395119. https://doi.org/10.1073/pnas.2122395119.

Papadourakis, V., Raos, V., 2017. Evidence for the representation of movement kinematics in the discharge of F5 mirror neurons during the observation of transitive and intransitive actions. J. Neurophysiol. 118 (6), 3215–3229. https://doi.org/10.1152/jn.00816.201.

Pasquereau, B., Turner, R.S., 2017. A selective role for ventromedial subthalamic nucleus in inhibitory control. Dec 4 Elife 6, e31627. https://doi.org/10.7554/eLife.31627.

Passingham, R.E., 1987. Two cortical systems for directing movements. In: Porter, R. (Ed.), In Motor Areas of the Cerebral Cortex. Wiley, pp. 151–164.

Passingham, R.E., 1993. The Frontal Lobes and Voluntary Action. Oxford Univ. Press,, Oxford.

Passingham, R.E., Perry, V.H., Wilkinson, F., 1983. The long-term effects of removal of sensorimotor cortex in infant and adult rhesus monkeys (Sep). Brain 106 (Pt 3), 675–705. https://doi.org/10.1093/brain/106.3.675.

Passingham, R.E., Bengtsson, S.L., Lau, H.C., 2010. Medial frontal cortex: from self-generated action to reflection on one's own performance. Trends Cogn. Sci. 14 (1), 16–21. https://doi.org/10.1016/j.tics.2009.11.001.

Passingham, R.E., Bengtsson, S.L., Lau, H.C., 2010. Medial frontal cortex: from self-generated action to reflection on one's own performance. Trends Cogn. Sci. 14 (1), 16–21 (Jan).

Pastor-Bernier, A., Cisek, P., 2011. Neural correlates of biased competition in premotor cortex. J. Neurosci. 31 (19), 7083–7088. May 11.

Pasupathy, A., Miller, E.K., 2005. Different time courses of learning-related activity in the prefrontal cortex and striatum. Nature 433 (7028), 873–876. https://doi.org/10.1038/nature03287.

Paus, T., 2001. Primate anterior cingulate cortex: where motor control, drive and cognition interface. Nat. Rev. Neurosci. 2 (6), 417–424. https://doi.org/10.1038/35077500.

Peeters, R., Simone, L., Nelissen, K., Fabbri-Destro, M., Vanduffel, W., Rizzolatti, G., Orban, G.A., 2009. The representation of tool use in humans and monkeys: common and uniquely human features. J. Neurosci.: Off. J. Soc. Neurosci. 29 (37), 11523–11539. https://doi.org/10.1523/JNEUROSCI.2040-09.2009.

Peeters, R.R., Rizzolatti, G., Orban, G.A., 2013. Functional properties of the left parietal tool use region. NeuroImage 78, 83–93. https://doi.org/10.1016/j.neuroimage.2013.04.023.

Percheron, G., François, C., Talbi, B., Yelnik, J., Fénelon, G., 1996. The primate motor thalamus. Brain Res Brain Res Rev. 22 (2), 93–181.

Perenin, M.T., Vighetto, A., 1988. Optic ataxia: a specific disruption in visuomotor mechanisms. I. Different aspects of the deficit in reaching for objects. Brain 111 (Pt 3), 643–674. https://doi.org/10.1093/brain/111.3.643.

Pesaran, B., Nelson, M.J., Andersen, R.A., 2006. Dorsal premotor neurons encode the relative position of the hand, eye, and goal during reach planning. Neuron 51 (1), 125–134. https://doi.org/10.1016/j.neuron.2006.05.025.

Pessoa, L., Adolphs, R., 2010. Emotion processing and the amygdala: from a 'low road' to 'many roads' of evaluating biological significance. Nat. Rev. Neurosci. 11 (11), 773–783. https://doi.org/10.1038/nrn2920.

Petrides, M., 1982. Motor conditional associative-learning after selective prefrontal lesions in the monkey. Behav. Brain Res 5 (4), 407–413. https://doi.org/10.1016/0166-4328(82)90044-4.

Petrides, M., 1985. Deficits on conditional associative-learning tasks after frontal- and temporal-lobe lesions in man. Neuropsychologia 23 (5), 601–614. https://doi.org/10.1016/0028-3932(85)90062-4.

Pezzulo, G., Donnarumma, F., Ferrari-Toniolo, S., Cisek, P., Battaglia-Mayer, A., 2022. Shared population-level dynamics in monkey premotor cortex during solo action, joint action and action observation. Prog. Neurobiol. 210, 102214 https://doi.org/10.1016/j.pneurobio.2021.102214.

Picard, N., Strick, P.L., 1996. Motor areas of the medial wall: a review of their location and functional activation. Cereb. Cortex 6 (3), 342–353. https://doi.org/10.1093/cercor/6.3.342.

Picton, T.W., Stuss, D.T., Alexander, M.P., Shallice, T., Binns, M.A., Gillingham, S., 2007. Effects of focal frontal lesions on response inhibition. Cereb. Cortex 17 (4), 826–838. https://doi.org/10.1093/cercor/bhk031.

Pierrot-Deseilligny, C., Rivaud, S., Gaymard, B., Müri, R., Vermersch, A.I., 1995. Cortical control of saccades. Ann. Neurol. 37 (5), 557–567. https://doi.org/10.1002/ana.410370504.

Pisella, L., Gréa, H., Tilikete, C., et al., 2000. An 'automatic pilot' for the hand in human posterior parietal cortex: toward reinterpreting optic ataxia. Nat. Neurosci. 3 (7), 729–736. https://doi.org/10.1038/76694.

Possin, K.L., Laluz, V.R., Alcantar, O.Z., et al., 2011. Distinct neuroanatomical substrates and cognitive mechanisms of figure copy performance in Alzheimer's disease and behavioral variant frontotemporal dementia. Neuropsychologia 49, 43–48. https://doi.org/10.1016/j.neuropsychologia.2010.10.026.

Potgieser, A.R., de Jong, B.M., Wagemakers, M., Hoving, E.W., Groen, R.J., 2014. Insights from the supplementary motor area syndrome in balancing movement initiation and inhibition [published correction appears in Front Hum Neurosci. 2015; 9:19]. Front Hum. Neurosci. 8, 960. Published 2014 Nov 28. doi:10.3389/fnhum.2014.00960.

Povinelli, D., 2000. Folk Physics for Apes: The Chimpanzee's theory of how the world works. Oxford University Press,.

Puzzo, I., Cooper, N.R., Vetter, P., Russo, R., Fitzgerald, P.B., 2009. Reduced cortico-motor facilitation in a normal sample with high traits of autism. Neurosci. Lett. 467 (2), 173–177. https://doi.org/10.1016/j.neulet.2009.10.033.

Quallo, M.M., Kraskov, A., Lemon, R.N., 2012. The Activity of Primary Motor Cortex Corticospinal Neurons during Tool Use by Macaque Monkeys. J. Neurosci. 32, 17351–17364. https://doi.org/10.1523/JNEUROSCI.1009-12.2012.

Raffi, M., Squatrito, S., Maioli, M.G., 2002. Neuronal responses to optic flow in the monkey parietal area PEc. Cereb. Cortex 12 (6), 639–646. https://doi.org/10.1093/cercor/12.6.639.

Raffi, M., Carrozzini, C., Maioli, M.G., Squatrito, S., 2010. Multimodal representation of optic flow in area PEc of macaque monkey. Neuroscience 171 (4), 1241–1255. https://doi.org/10.1016/j.neuroscience.2010.09.026.

Raimo, S., Santangelo, G., Trojano, L., 2021. The Neural Bases of Drawing. A Meta-analysis and a Systematic Literature Review of Neurofunctional Studies in Healthy Individuals. Neuropsychol. Rev. 31 (4), 689–702. https://doi.org/10.1007/s11065-021-09494-4.

Rathelot, J.A., Dum, R.P., Strick, P.L., 2017. Posterior parietal cortex contains a command apparatus for hand movements. Proc. Natl. Acad. Sci. Usa. 2017 114 (16), 4255–4260. https://doi.org/10.1073/pnas.1608132114.

Rathelot, J.A., Strick, P.L., 2009. Subdivisions of primary motor cortex based on cortico-motoneuronal cells. Proc. Natl. Acad. Sci. 106 (3), 918–923. https://doi.org/10.1073/pnas.0808362106. Epub 2009 Jan 12. PMID: 19139417;.

Remington, E.D., Narain, D., Hosseini, E.A., Jazayeri, M., 2018. Flexible Sensorimotor Computations through Rapid Reconfiguration of Cortical Dynamics. e5 Neuron 98 (5), 1005–1019. https://doi.org/10.1016/j.neuron.2018.05.020.

Reynolds, C., Ashby, P., 1999. Inhibition in the human motor cortex is reduced just before a voluntary contraction. Neurology 53 (4), 730–735. https://doi.org/10.1212/wnl.53.4.730.

Ribeiro Gomes, A.R., Olivier, E., Killackey, H.P., et al., 2020. Refinement of the Primate Corticospinal Pathway During Prenatal Development. Cereb. Cortex 30 (2), 656–671. https://doi.org/10.1093/cercor/bhz116.

Rilling, J.K., Winslow, J.T., Kilts, C.D., 2004. The neural correlates of mate competition in dominant male rhesus macaques. Biol. Psychiatry 56, 364–375. https://doi.org/10.1016/j.biopsych.2004.06.027.

Rind, F.C., Simmons, P.J., 1992. Orthopteran DCMD neuron: a reevaluation of responses to moving objects. I. Selective responses to approaching objects. J. Neurophysiol. 68 (5), 1654–1666. https://doi.org/10.1152/jn.1992.68.5.1654.

Rizzolatti, G., Craighero, L., 2004. The mirror-neuron system. Annu Rev. Neurosci. 27, 169–192. https://doi.org/10.1146/annurev.neuro.27.070203.144230.

Rizzolatti, G., Gentilucci, M., Camarda, R.M., et al., 1990. Neurons related to reaching-grasping arm movements in the rostral part of area 6 (area 6a beta). Exp. Brain Res 82 (2), 337–350. https://doi.org/10.1007/BF00231253.

Rizzolatti, G., Fadiga, L., Gallese, V., Fogassi, L., 1996. Premotor cortex and the recognition of motor actions (Mar). Brain Res Cogn. Brain Res 3 (2), 131–141. https://doi.org/10.1016/0926-6410(95)00038-0.

Rizzolatti, G., Fadiga, L., Fogassi, L., Gallese, V., 1997. The space around us. Jul 11 Science 277 (5323), 190–191. https://doi.org/10.1126/science.277.5323.190.

Rizzolatti, G., Cattaneo, L., Fabbri-Destro, M., Rozzi, S., 2014. Cortical mechanisms underlying the organization of goal-directed actions and mirror neuron-based action understanding. Physiol. Rev. 94 (2), 655–706. https://doi.org/10.1152/physrev.00009.2013.

Roberts, R.E., Husain, M., 2015. A dissociation between stopping and switching actions following a lesion of the pre-supplementary motor area. Cortex 63, 184–195 (Feb).

Roland, P.E., 1987. Metabolic mapping of sensorimotor integration in the human brain. Ciba Found. Symp. 132, 251–268. https://doi.org/10.1002/9780470513545.ch15.

Roland, P.E., Larsen, B., Lassen, N.A., Skinhøj, E., 1980. Supplementary motor area and other cortical areas in organization of voluntary movements in man (Jan). J. Neurophysiol. 43 (1), 118–136. https://doi.org/10.1152/jn.1980.43.1.118.

Rolls, E.T., 1999. Spatial view cells and the representation of place in the primate hippocampus. Hippocampus 9 (4), 467–480. https://doi.org/10.1002/(SICI)1098-1063(1999)9:4<467::AID-HIPO13>3.0.CO;2-F.

Rolls, E.T., 2019. The cingulate cortex and limbic systems for action, emotion, and memory. Handb. Clin. Neurol. 166, 23–37. https://doi.org/10.1016/B978-0-444-64196-0.00002-9.

Rolls, E.T., 2021. Neurons including hippocampal spatial view cells, and navigation in primates including humans. Hippocampus 31 (6), 593–611. https://doi.org/10.1002/hipo.23324.

Rolls, E.T., 2023. Hippocampal spatial view cells for memory and navigation, and their underlying connectivity in humans. Hippocampus 33 (5), 533–572. https://doi.org/10.1002/hipo.23467.

Romano, D., Gandola, M., Bottini, G., Maravita, A., 2014. Arousal responses to noxious stimuli in somatoparaphrenia and anosognosia: clues to body awareness. Brain 137 (Pt 4), 1213–1223. https://doi.org/10.1093/brain/awu009.

Romo, R., Schultz, W., 1987. Neuronal activity preceding self-initiated or externally timed arm movements in area 6 of monkey cortex. Exp. brain Res. 67 (3), 656–662. https://doi.org/10.1007/BF00247297.

Ronchi, R., Park, H.D., Blanke, O., 2018. Bodily self-consciousness and its disorders. Handb. Clini Neurol. 151, 313–330. https://doi.org/10.1016/B978-0-444-63622-5.00015-2.

Rossetti, Y., Pisella, L., McIntosh, R.D., 2019. Definition: Optic ataxia. Cortex 121, 481. https://doi.org/10.1016/j.cortex.2019.09.004.

Rouiller, E.M., Olivier, E., 2004. Functional recovery after lesions of the primary motor cortex. Prog. Brain Res 143, 467–475 doi: 10.1016/S0079-6123(03)43044-6.

Rouiller, E.M., Babalian, A., Kazennikov, O., Moret, V., Yu, X.H., Wiesendanger, M., 1994. Transcallosal connections of the distal forelimb representations of the primary and supplementary motor cortical areas in macaque monkeys. Exp. Brain Res. 102, 227–243.

Rouiller, E.M., Yu, X.H., Moret, V., Tempini, A., Wiesendanger, M., Liang, F., 1998. Dexterity in adult monkeys following early lesion of the motor cortical hand area: the role of cortex adjacent to the lesion (Feb). Eur. J. Neurosci. 10 (2), 729–740. https://doi.org/10.1046/j.1460-9568.1998.00075.x.

Rozzi, S., Calzavara, R., Belmalih, A., et al., 2006. Cortical connections of the inferior parietal cortical convexity of the macaque monkey. Cereb. Cortex 16 (10), 1389–1417. https://doi.org/10.1093/cercor/bhj076.

Rozzi, S., Ferrari, P.F., Bonini, L., Rizzolatti, G., Fogassi, L., 2008. Functional organization of inferior parietal lobule convexity in the macaque monkey: electrophysiological characterization of motor, sensory and mirror responses and their correlation with cytoarchitectonic areas. Eur. J. Neurosci. 28 (1569–1588), 2008. https://doi.org/10.1111/j.1460-9568.2008.06395.x.

Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S.C., Simmons, A., Bullmore, E.T., 1999. Hypofrontality in attention deficit hyperactivity disorder during higher-order motor control: a study with functional MRI. Am. J. Psychiatry 156 (6), 891–896 (Jun).

Rueckemann, J.W., Buffalo, E.A., 2017. Spatial responses, immediate experience, and memory in the monkey hippocampus. Curr. Opin. Behav. Sci. 17, 155–160. https://doi.org/10.1016/j.cobeha.2017.08.008.

Rushworth, M.F., Hadland, K.A., Paus, T., Sipila, P.K., 2002. Role of the human medial frontal cortex in task switching: a combined fMRI and TMS study. J. Neurophysiol. 87 (5), 2577–2592. https://doi.org/10.1152/jn.2002.87.5.2577.

Rushworth, M.F., Noonan, M.P., Boorman, E.D., Walton, M.E., Behrens, T.E., 2011. Frontal cortex and reward-guided learning and decision-making. Neuron 70 (6), 1054–1069. https://doi.org/10.1016/j.neuron.2011.05.014.

Russo, A.A., Khajeh, R., Bittner, S.R., et al., 2020. Neural trajectories in the supplementary motor area and motor cortex exhibit distinct geometries, compatible with different classes of computation. e6 Neuron 107 (4), 745–758. https://doi.org/10.1016/j.neuron.2020.05.020.

Rutishauser, U., Mamelak, A.N., Adolphs, R., 2015. The primate amygdala in social perception - insights from electrophysiological recordings and stimulation. Trends Neurosci 38 (5), 295–306. https://doi.org/10.1016/j.tins.2015.03.001.

Saberi-Moghadam, S., Ferrari-Toniolo, S., Ferraina, S., Caminiti, R., Battaglia-Mayer, A., 2016. Modulation of Neural Variability in Premotor, Motor, and Posterior Parietal Cortex during Change of Motor Intention. J. Neurosci. 36 (16), 4614–4623. https://doi.org/10.1523/JNEUROSCI.3300-15.2016.

Salinas, E., Stanford, T.R., 2013. The countermanding task revisited: fast stimulus detection is a key determinant of psychophysical performance. J. Neurosci. 33 (13), 5668–5685. https://doi.org/10.1523/JNEUROSCI.3977-12.2013.

Sanides, F., 1964. The cyto-myeloarchitecture of the human frontal lobe and its relation to phylogenetic differentiation of the cerebral cortex. J. Hirnforsch. 7, 269–282.

Sasaki, K., Gemba, H., 1986. Electrical activity in the prefrontal cortex specific to no-go reaction of conditioned hand movement with colour discrimination in the monkey. Exp. Brain Res 64 (3), 603–606. https://doi.org/10.1007/BF00340499.

Sasaki, R., Anzai, A., Angelaki, D.E., DeAngelis, G.C., 2020. Flexible coding of object motion in multiple reference frames by parietal cortex neurons (Aug). Nat. Neurosci. 23 (8), 1004–1015. https://doi.org/10.1038/s4159302006560.

Sasaki, S., Isa, T., Pettersson, L.G., et al., 2004. Dexterous finger movements in primate without monosynaptic corticomotoneuronal excitation [published correction appears in J Neurophysiol. 2005 Mar;93(3):1821]. J. Neurophysiol. 92 (5), 3142–3147. https://doi.org/10.1152/jn.00342.2004.

Sato, N., Sakata, H., Tanaka, Y.L., Taira, M., 2006. Navigation-associated medial parietal neurons in monkeys. Proc. Natl. Acad. Sci. Usa. 103 (45), 17001–17006. https://doi.org/10.1073/pnas.0604277103.

Sawaguchi, T., Yamane, I., Kubota, K., 1996. Application of the GABA antagonist bicuculline to the premotor cortex reduces the ability to withhold reaching movements by well-trained monkeys in visually guided reaching task. J. Neurophysiol. 75 (5), 2150–2156. https://doi.org/10.1152/jn.1996.75.5.2150.

Scangos, K.W., Aronberg, R., Stuphorn, V., 2013. Performance monitoring by presupplementary and supplementary motor area during an arm movement countermanding task. J. Neurophysiol. 109 (7), 1928–1939. https://doi.org/10.1152/jn.00688.2012.

Schaffelhofer, S., Scherberger, H., 2016. Object vision to hand action in macaque parietal, premotor, and motor cortices. eLife 5, e15278. https://doi.org/10.7554/eLife.15278.

Schall, J.D., Godlove, D.C., 2012. Current advances and pressing problems in studies of stopping. Curr. Opin. Neurobiol. 22 (6), 1012–1021. https://doi.org/10.1016/j.conb.2012.06.002.

Schell, G.R., Strick, P.L., 1984. The origin of thalamic inputs to the arcuate premotor and supplementary motor areas. J. Neurosci. 4 (2), 539–560. https://doi.org/10.1523/JNEUROSCI.04-02-00539.1984.

Schiff, W., Caviness, J.A.S., Gibson, J.J., 1962. Persistent fear responses in rhesus monkeys to the optical stimulus of "looming". Science 136 (3520), 982–983 doi: 10.1126science.136.3520.982.

Schlack, A., Hoffmann, K.P., Bremmer, F., 2002. Interaction of linear vestibular and visual stimulation in the macaque ventral intraparietal area (VIP. Eur. J. Neurosci. 16 (10), 1877–1886. https://doi.org/10.1046/j.1460-9568.2002.02251.x.

Schlack, A., Sterbing-D'Angelo, S.J., Hartung, K., Hoffmann, K.P., Bremmer, F., 2005. Multisensory space representations in the macaque ventral intraparietal area. J. Neurosci. 25 (18), 4616–4625. https://doi.org/10.1523/JNEUROSCI.0455-05.2005.

Schlotterer, G.R., 1977. Response of the locust descending movement detector neuron to rapidly approaching and withdrawing visual stimuli. Can. J. Zool. 55, 1372–1376. https://doi.org/10.1139/z77-179.

Schmahmann, J.D., Pandya, D.N., 1990. Anatomical investigation of projections from thalamus to posterior parietal cortex in the rhesus monkey: a WGA-HRP and fluorescent tracer study. J. Comp. Neurol. 295 (2), 299–326. https://doi.org/10.1002/cne.902950212.

Schmid, L., Klotz, T., Siebert, T., Röhrle, O., 2019. Characterization of Electromechanical Delay Based on a Biophysical Multi-Scale Skeletal Muscle Model. Front. Physiol. 10, 1270. https://doi.org/10.3389/fphys.2019.01270.

Schmidlin, E., Brochier, T., Maier, M.A., Kirkwood, P.A., Lemon, R.N., 2008. Pronounced reduction of digit motor responses evoked from macaque ventral premotor cortex after reversible inactivation of the primary motor cortex hand area [published correction appears in J Neurosci. 2008 Dec 17;28(51):2 p following 13951]. J. Neurosci. 28 (22), 5772–5783. https://doi.org/10.1523/JNEUROSCI.0944-08.2008.

Scholz, J., Klein, M.C., Behrens, T.E., Johansen-Berg, H., 2009. Training induces changes in white-matter architecture (Nov). Nat. Neurosci. 12 (11), 1370–1371. https://doi.org/10.1038/nn.2412.

Schultz, W., 2015. Neuronal Reward and Decision Signals: From Theories to Data. Physiol. Rev. 95 (3), 853–951. https://doi.org/10.1152/physrev.00023.2014.

Schultz, W., 2016. Dopamine reward prediction-error signalling: a two-component response. Nat. Rev. Neurosci. 17 (3), 183–195. https://doi.org/10.1038/nrn.2015.26.

Schultz, W., Romo, R., 1992. Role of primate basal ganglia and frontal cortex in the internal generation of movements. I. Preparatory activity in the anterior striatum. Exp. brain Res. 91 (3), 363–384. https://doi.org/10.1007/BF00227834.

Schurger, A., Sitt, J.D., Dehaene, S., 2012. An accumulator model for spontaneous neural activity prior to self-initiated movement. Proc. Natl. Acad. Sci. USA 109 (42), E2904–E2913. https://doi.org/10.1073/pnas.1210467109.

Schurger, A., Hu, P.', Pak, J., Roskies, A.L., 2021. What Is the Readiness Potential. Trends Cogn. Sci. 25 (7), 558–570. https://doi.org/10.1016/j.tics.2021.04.001.

Seghezzi, S., Haggard, P., 2023. Volition and "free will". SAGE Handb. Cogn. Syst. Neurosci. Ch. 25 Vol. 2.

Serino, A., 2019. Peripersonal space (PPS) as a multisensory interface between the individual and the environment, defining the space of the self. Neurosci. Biobehav. Rev. https://doi.org/10.1016/J.NEUBIOREV.2019.01.016.

Shanechi, M.M., Hu, R.C., Powers, M., Wornell, G.W., Brown, E.N., Williams, Z.M., 2012. Neural population partitioning and a concurrent brain-machine interface for sequential motor function. Nat. Neurosci. 15 (12), 1715–1722. https://doi.org/10.1038/nn.3250.

Sharp, P.E., Green, C., 1994. Spatial correlates of firing patterns of single cells in the subiculum of the freely moving rat. J. Neurosci. 14 (4), 2339–2356. https://doi.org/10.1523/JNEUROSCI.14-04-02339.1994.

Shenoy, K.V., Sahani, M., Churchland, M.M., 2013. Cortical control of arm movements: a dynamical systems perspective. Annu Rev. Neurosci. 36, 337–359. https://doi.org/10.1146/annurev-neuro-062111-150509.

Sherman, S.M., 2016. Thalamus plays a central role in ongoing cortical functioning (Apr). Nat. Neurosci. 19 (4), 533–541. https://doi.org/10.1038/nn.4269.

Shima, K., Tanji, J., 1998. Both supplementary and presupplementary motor areas are crucial for the temporal organization of multiple movements. J. Neurophysiol. 80 (6), 3247–3260. https://doi.org/10.1152/jn.1998.80.6.3247.

Shima, K., Tanji, J., 2000. Neuronal activity in the supplementary and presupplementary motor areas for temporal organization of multiple movements. J. Neurophysiol. 84 (4), 2148–2160. https://doi.org/10.1152/jn.2000.84.4.2148.

Shima, K., Aya, K., Mushiake, H., Inase, M., Aizawa, H., Tanji, J., 1991. Two movement-related foci in the primate cingulate cortex observed in signal-triggered and self-paced forelimb movements (Feb). J. Neurophysiol. 65 (2), 188–202. https://doi.org/10.1152/jn.1991.65.2.188.

Shima, K., Mushiake, H., Saito, N., Tanji, J., 1996. Role for cells in the presupplementary motor area in updating motor plans. Proc. Natl. Acad. Sci. Usa. 93 (16), 8694–8698. https://doi.org/10.1073/pnas.93.16.8694.

Shimazu, H., Maier, M.A., Cerri, G., Kirkwood, P.A., Lemon, R.N., 2004. Macaque ventral premotor cortex exerts powerful facilitation of motor cortex outputs to upper limb motoneurons. J. Neurosci. 24 (5), 1200–1211. https://doi.org/10.1523/JNEUROSCI.4731-03.2004.

Shinder, M.E., Newlands, S.D., 2014. Sensory convergence in the parieto-insular vestibular cortex. J. Neurophysiol. 111 (12), 2445–2464. https://doi.org/10.1152/jn.00731.2013.

Shine, J.P., Valdés-Herrera, J.P., Hegarty, M., Wolbers, T., 2016. The Human Retrosplenial Cortex and Thalamus Code Head Direction in a Global Reference Frame. J. Neurosci. 36 (24), 6371–6381. https://doi.org/10.1523/JNEUROSCI.1268-15.2016.

Simone, L., Bimbi, M., Rodà, F., Fogassi, L., Rozzi, S., 2017. Action observation activates neurons of the monkey ventrolateral prefrontal cortex. Sci. Rep. 7, 44378. 〈http://www.nature.com/articles/srep44378.28290511〉.

Sirigu, A., Desmurget, M., 2020. The sensorimotor posterior parietal cortex: From intention to action. The Senses: a Comprehensive Reference. Elsevier,, pp. 349–358. https://doi.org/10.1016/B978-0-12-809324-5.24205-3.

Smith, A.T., 2021. Cortical visual area CSv as a cingulate motor area: a sensorimotor interface for the control of locomotion. Brain Struct. Funct. 226 (9), 2931–2950. https://doi.org/10.1007/s00429-021-02325-5.

Snyder, L., Grieve, K., Brotchie, P., Anderson, A., 1998. Separate body- and world-referenced representations of visual space in parietal cortex. Nature 1998 394, 887–891. https://doi.org/10.1038/29777.

Snyder, L.H., Batista, A.P., Andersen, R.A., 1997. Coding of intention in the posterior parietal cortex. Nature 386 (6621), 167–170. https://doi.org/10.1038/386167a0.

Sobinov, A.R., Bensmaia, S.J., 2021. The neural mechanisms of manual dexterity. Nat. Rev. Neurosci. 22 (12), 741–757. https://doi.org/10.1038/s41583-021-00528-7.

Sohn, J.W., Lee, D., 2007. Order-dependent modulation of directional signals in the supplementary and presupplementary motor areas. J. Neurosci. 27 (50), 13655–13666. https://doi.org/10.1523/JNEUROSCI.2982-07.2007.

Sonobe, Y., Yamagata, T., Yang, H., Haruki, Y., Ogawa, K., 2023. Supramodal Representation of the Sense of Body Ownership in the Human Parieto-Premotor and Extrastriate Cortices. eNeuro 10 (2). ENEURO.0332-22.2023. Published 2023 Feb 10. doi:10.1523/ENEURO.0332-22.2023.

Southgate, V., Hamilton, A.F., 2008. Unbroken mirrors: challenging a theory of Autism. Trends Cogn. Sci. 12 (6), 225–229. https://doi.org/10.1016/j.tics.2008.03.005.

Sporns, O., Tononi, G., Edelman, G.M., 2000. Theoretical neuroanatomy: relating anatomical and functional connectivity in graphs and cortical connection matrices (Feb). Cereb. Cortex 10 (2), 127–141. https://doi.org/10.1093/cercor/10.2.127.

Srivastava, S., Orban, G.A., De Mazière, P.A., Janssen, P., 2009. A distinct representation of three-dimensional shape in macaque anterior intraparietal area: fast, metric, and coarse. J. Neurosci. 29 (34), 10613–10626. https://doi.org/10.1523/JNEUROSCI.6016-08.2009.

Stamos, A.V., Savaki, H.E., Raos, V., 2010. The spinal substrate of the suppression of action during action observation. J. Neurosci. 30 (35), 11605–11611. https://doi.org/10.1523/JNEUROSCI.2067-10.2010.

Stepniewska, I., Fang, P.C., Kaas, J.H., 2005. Microstimulation reveals specialized subregions for different complex movements in posterior parietal cortex of prosimian galagos. Proc. Natl. Acad. Sci. Usa. 102 (13), 4878–4883. https://doi.org/10.1073/pnas.0501048102.

Stout, D., Hecht, E., 2015. Neuroarchaeology. In: Bruner, E. (Ed.), Human Paleoneurology. Springer International Publishing, Cham, pp. 145–175.

Strauss, H., 1924. Über konstruktive Apraxie. pp. 65–84. Eur. Neurol. 56 (2–3), 65–84.

Strauss, H., 1929. Das Zusammenschrecken. J. Psychol. U. Neurol. 39, 111–231.

Strick, P.L., Dum, R.P., Rathelot, J.A., 2021. The Cortical Motor Areas and the Emergence of Motor Skills: A Neuroanatomical Perspective. Annu Rev. Neurosci. 44, 425–447. https://doi.org/10.1146/annurev-neuro-070918-050216.

Stuphorn, V., Emeric, E.E., 2012. Proactive and reactive control by the medial frontal cortex. Front Neuroeng. 5, 9. Published 2012 Jun 19. doi:10.3389/fneng.2012.00009.

Sugar, J., Witter, M.P., van Strien, N.M., Cappaert, N.L., 2011. The retrosplenial cortex: intrinsic connectivity and connections with the (para)hippocampal region in the rat. An interactive connectome. Front Neuroinform. 5, 7. Published 2011 Jul 27. doi:10.3389/fninf.2011.00007.

Sugiura, M., Shah, N.J., Zilles, K., Fink, G.R., 2005. Cortical representations of personally familiar objects and places: functional organization of the human posterior cingulate cortex. J. Cogn. Neurosci. 17 (2), 183–198 (Feb).

Sumner, P., Nachev, P., Morris, P., et al., 2007. Human medial frontal cortex mediates unconscious inhibition of voluntary action. Neuron 54 (5), 697–711. https://doi.org/10.1016/j.neuron.2007.05.016.

Sun, F.T., Miller, L.M., Rao, A.A., D'Esposito, M., 2007. Functional connectivity of cortical networks involved in bimanual motor sequence learning. May 1 Cereb. cortex 17 (5), 1227–1234. https://doi.org/10.1093/cercor/bhl033.

Sutherland, R.J., Whishaw, I.Q., Kolb, B., 1988. Contributions of cingulate cortex to two forms of spatial learning and memory. J. Neurosci. 8 (6), 1863–1872. https://doi.org/10.1523/JNEUROSCI.08-06-01863.1988.

Swick, D., Chatham, C.H., 2014. Ten year sof inhibition revisited. Front. Hum. Neurosci. 8, 329. https://doi.org/10.3389/fnhum.2014.00329.

Tanji, J., 2001. Sequential organization of multiple movements: involvement of cortical motor areas. Annu Rev. Neurosci. 24, 631–651. https://doi.org/10.1146/annurev.neuro.24.1.631.

Tanji, J., Kurata, K., 1982. Comparison of movement-related activity in two cortical motor areas of primates. J. Neurophysiol. 48 (3), 633–653 (Sep).

Tanji, J., Shima, K., 1994. Role for supplementary motor area cells in planning several movements ahead. Nature 371 (6496), 413–416. https://doi.org/10.1038/371413a0.

Tanji, J., Kurata, K., Okano, K., 1985. The effect of cooling of the supplementary motor cortex and adjacent cortical areas. Exp. Brain Res 60 (2), 423–426.

Tanji, J., Okano, K., Sato, K.C., 1988. Neuronal activity in cortical motor areas related to ipsilateral, contralateral, and bilateral digit movements of the monkey. J. Neurophysiol. 60 (1), 325–343. https://doi.org/10.1152/jn.1988.60.1.325.

Tazumi, T., Hori, E., Maior, R.S., Ono, T., Nishijo, H., 2010. Neural correlates to seen gaze-direction and head orientation in the macaque monkey amygdala. Neurosci. 169 (1), 287–301. https://doi.org/10.1016/j.neuroscience.2010.04.028.

Temizer, I., Donovan, J.C., Baier, H., Semmelhack, J.L., 2015. A Visual Pathway for Looming-Evoked Escape in Larval Zebrafish. Curr. Biol. 25 (14), 1823–1834. https://doi.org/10.1016/j.cub.2015.06.002.

Thaler, D., Chen, Y.C., Nixon, P.D., Stern, C.E., Passingham, R.E., 1995. The functions of the medial premotor cortex. I. Simple learned movements. Exp. Brain Res 102 (3), 445–460. https://doi.org/10.1007/BF00230649.

Thorpe, S., Fize, D., Marlot, C., 1996. Speed of processing in the human visual system. Nature 381 (6582), 520–522. https://doi.org/10.1038/381520a0.

Thorpe, S.J., Fabre-Thorpe, M., 2001. Neuroscience. Seeking categories in the brain. Science 291 (5502), 260–263. https://doi.org/10.1126/science.1058249.

Tokuno, H., Nambu, A., 2000. Organization of nonprimary motor cortical inputs on pyramidal and nonpyramidal tract neurons of primary motor cortex: An electrophysiological study in the macaque monkey. Cereb. Cortex 10 (1), 58–68. https://doi.org/10.1093/cercor/10.1.58.

Tomasi, S., Caminiti, R., Innocenti, G.M., 2012. Areal differences in diameter and length of corticofugal projections. Cereb. Cortex 22 (6), 1463–1472. https://doi.org/10.1093/cercor/bhs011.

Toni, I., Passingham, R.E., 1999. Prefrontal-basal ganglia pathways are involved in the learning of arbitrary visuomotor associations: a PET study. Exp. Brain Res 127 (1), 19–32. https://doi.org/10.1007/s002210050.

Toyoshima, K., Sakai, H., 1982. Exact cortical extent of the origin of the corticospinal tract (CST) and the quantitative contribution to the CST in different cytoarchitectonic areas. A study with horseradish peroxidase in the monkey. J. Hirnforsch. 23 (3), 257–269.

Travers, E., Haggard, P., 2021. The Readiness Potential reflects the internal source of action, rather than decision uncertainty. Eur. J. Neurosci. 53 (5), 1533–1544. https://doi.org/10.1111/ejn.15063.

Travers, E., Friedemann, M., Haggard, P., 2021. The Readiness Potential reflects planning-based expectation, not uncertainty, in the timing of action. Cogn. Neurosci. 12 (1), 14–27. https://doi.org/10.1080/17588928.2020.1824176.

Tremblay, L., Hollerman, J.R., Schultz, W., 1998. Modifications of reward expectation-related neuronal activity during learning in primate striatum. J. Neurophysiol. 80 (2), 964–977. https://doi.org/10.1152/jn.1998.80.2.964.

Tremblay, L., Worbe, Y., Thobois, S., Sgambato-Faure, V., Féger, J., 2015. Selective dysfunction of basal ganglia subterritories: From movement to behavioral disorders. Mov. Disord. 30 (9), 1155–1170. https://doi.org/10.1002/mds.26199.

Turrigiano, G.G., 1999. Homeostatic plasticity in neuronal networks: the more things change, the more they stay the same. Trends Neurosci. 22 (5), 221–227. https://doi.org/10.1016/s0166-2236(98)01341-1.

Uddin, L.Q., 2015. Salience processing and insular cortical function and dysfunction (Jan). Nat. Rev. Neurosci. 16 (1), 55–61. https://doi.org/10.1038/nrn3857.

Umilta, M.A., Brochier, T., Spinks, R.L., Lemon, R.N., 2007. Simultaneous recording of macaque premotor and primary motor cortex neuronal populations reveals different functional contributions to visuomotor grasp. J. Neurophysiol. 98 (1), 488–501. https://doi.org/10.1152/jn.01094.2006.

Umiltà, M.A., Escola, L., Intskirveli, I., Grammont, F., Rochat, M., Caruana, F., Jezzini, A., Gallese, V., Rizzolatti, G., 2008. When pliers become fingers in the monkey motor system. Proc. Natl. Acad. Sci. Usa. 105 (6), 2209–2213. Feb 12.

Valencia, M., Pastor, M.A., Fernández-Seara, M.A., Artieda, J., Martinerie, J., Chavez, M., 2009. Complex modular structure of large-scale brain networks. Chaos 19 (2), 023119. https://doi.org/10.1063/1.3129783.

Vallar, G., Calzolari, E., 2018. Unilateral spatial neglect after posterior parietal damage. Handb. Clin. Neurol. 151, 287–312. https://doi.org/10.1016/B978-0-444-63622-5.00014-0.

Vallar, G., Ronchi, R., 2009. Somatoparaphrenia: a body delusion. A review of the neuropsychological literature. Exp. Brain Res 192 (3), 533–551. https://doi.org/10.1007/s00221-008-1562-y.

Vann, S.D., Aggleton, J.P., 2004. Testing the importance of the retrosplenial guidance system: effects of different sized retrosplenial cortex lesions on heading direction and spatial working memory. Behav. Brain Res 155 (1), 97–108. https://doi.org/10.1016/j.bbr.2004.04.005.

Vann, S.D., Aggleton, J.P., Maguire, E.A., 2009. What does the retrosplenial cortex do. Nat. Rev. Neurosci. 10 (11), 792–802. https://doi.org/10.1038/nrn2733.

Verbruggen, F., Gordon, D. Logan, 2008. Response inhibition in the stop-signal paradigm. Trends Cogn. Sci. 12 (11), 418–424.

Verbruggen, F., Logan, G.D., 2009. Models of response inhibition in the stop-signal and stop-change paradigms. Neurosci. Biobehav Rev. 33 (5), 647–661. https://doi.org/10.1016/j.neubiorev.2008.08.014.

Vigneswaran, G., Philipp, R., Lemon, R.N., Kraskov, A., 2013. M1 corticospinal mirror neurons and their role in movement suppression during action observation. Curr. Biol. 23 (3), 236–243. https://doi.org/10.1016/j.cub.2012.12.006.

Vogt, B.A., Finch, D.M., Olson, C.R., 1992. Functional heterogeneity in cingulate cortex: the anterior executive and posterior evaluative regions. Cereb. Cortex 2 (6), 435–443. https://doi.org/10.1093/cercor/2.6.435-a.

de Vries, S.E., Clandin, T.R., 2012. Loom-sensitive neurons link computation to action in the Drosophila visual system. Curr. Biol. 22 (5), 353–362. https://doi.org/10.1016/j.cub.2012.01.007.

Wang, C., Chen, X., Knierim, J.J., 2020. Egocentric and allocentric representations of space in the rodent brain. Feb 1 Curr. Opin. Neurobiol. 60, 12–20. https://doi.org/10.1016/j.conb.2019.11.005.

Wang, J., Narain, D., Hosseini, E.A., Jazayeri, M., 2018a. Flexible timing by temporal scaling of cortical responses. Nat. Neurosci. 21 (1), 102–110. https://doi.org/10.1038/s41593-017-0028-6.

Wang, S.S., Shultz, J.R., Burish, M.J., Harrison, K.H., Hof, P.R., Towns, L.C., Wagers, M. W., Wyatt, K.D., 2008. Functional trade-offs in white matter axonal scaling. J. Neurosci. 28 (15), 4047–4056. Apr 9.

Wang, W., Worhunsky, P.D., Zhang, S., Le, T.M., Potenza, M.N., Li, C.S.R., 2018b. Response inhibition and fronto-striatal-thalamic circuit dysfunction in cocaine addiction. Drug Alcohol Depen. 192, 137–145. https://doi.org/10.1016/j.drugalcdep.2018.07.037.

Wang, Y., Frost, B.J., 1992. Time to collision is signalled by neurons in the nucleus rotundus of pigeons. Nature 356 (6366), 236–238 doi: 10.1038/356236a0. PMID: 1552942.

Watts, D.J., Strogatz, S.H., 1998. Collective dynamics of 'small-world' networks. Nature 393 (6684), 440–442. https://doi.org/10.1038/30918.

Werner, W., 1993. Neurons in the primate superior colliculus are active before and during arm movements to visual targets. Eur. J. Neurosci. 5 (4), 335–340. https://doi.org/10.1111/j.1460-9568.1993.tb00501.x.

Werner, W., Dannenberg, S., Hoffmann, K.P., 1997a. Arm-movement-related neurons in the primate superior colliculus and underlying reticular formation: comparison of neuronal activity with EMGs of muscles of the shoulder, arm and trunk during reaching. Exp. Brain Res 115 (2), 191–205. https://doi.org/10.1007/pl00005690.

Werner, W., Hoffmann, K.P., Dannenberg, S., 1997b. Anatomical distribution of arm-movement-related neurons in the primate superior colliculus and underlying reticular formation in comparison with visual and saccadic cells. Exp. Brain Res 115 (2), 206–216. https://doi.org/10.1007/pl00005691.

Whishaw, I.Q., Maaswinkel, H., Gonzalez, C.L., Kolb, B., 2001. Deficits in allothetic and idiothetic spatial behavior in rats with posterior cingulate cortex lesions. Behav. Brain Res 118 (1), 67–76. https://doi.org/10.1016/s0166-4328(00)00312-0.

Whitlock, J.R., Sutherland, R.J., Witter, M.P., Moser, M.B., Moser, E.I., 2008. Navigating from hippocampus to parietal cortex. Proc. Natl. Acad. Sci. Usa. 105 (39), 14755–14762. https://doi.org/10.1073/pnas.0804216105.

Whitlock, J.R., Pfuhl, G., Dagslott, N., Moser, M.B., Moser, E.I., 2012. Functional split between parietal and entorhinal cortices in the rat. Neuron 73 (4), 789–802. https://doi.org/10.1016/j.neuron.2011.12.028.

Wilber, A.A., Clark, B.J., Forster, T.C., Tatsuno, M., McNaughton, B.L., 2014. Interaction of egocentric and world-centered reference frames in the rat posterior parietal cortex. Apr 16 J. Neurosci. 34 (16), 5431–5446. https://doi.org/10.1523/JNEUROSCI.0511-14.2014.

Wilson, S.A.K., 1909. A contribution to the study of apraxia with a review of the literature. Brain 31, 164–216.

Wise, S.P., 1996. Corticospinal efferents of the supplementary sensorimotor area in relation to the primary motor area. Adv. Neurol. 70, 57–69.

Wise, S.P., Murray, E.A., 2000. Arbitrary associations between antecedents and actions. Trends Neurosci. 23 (6), 271–276. https://doi.org/10.1016/s0166-2236(00)01570-8.

Wise, S.P., di Pellegrino, G., Boussaoud, D., 1996. The premotor cortex and nonstandard sensorimotor mapping. Can. J. Physiol. Pharm. 74 (4), 469–482. https://doi.org/10.1139/cjpp-74-4-469.

Wise, S.P., Boussaoud, D., Johnson, P.B., Caminiti, R., 1997. Premotor and parietal cortex: corticocortical connectivity and combinatorial computations. Annu Rev. Neurosci. 20, 25–42. https://doi.org/10.1146/annurev.neuro.20.1.25.

Witter, M.P., Amaral, D.G., 2021. The entorhinal cortex of the monkey: VI. Organization of projections from the hippocampus, subiculum, presubiculum, and parasubiculum. J. Comp. Neurol. 529 (4), 828–852. https://doi.org/10.1002/cne.24983.

Wu, L.Q., Niu, Y.Q., Yang, J., Wang, S.R., 2005. Tectal neurons signal impending collision of looming objects in the pigeon. Eur. J. Neurosci. 22 (9), 2325–2331. https://doi.org/10.1111/j.1460-9568.2005.04397.x.

Xiang, J.Z., Brown, M.W., 1999. Differential neuronal responsiveness in primate perirhinal cortex and hippocampal formation during performance of a conditional visual discrimination task. Eur. J. Neurosci. 11 (10), 3715–3724. https://doi.org/10.1046/j.1460-9568.1999.00790.x.

Yang, M.H., Yao, Z.F., Hsieh, S., 2019. Multimodal neuroimaging analysis reveals age-associated common and discrete cognitive control constructs. Hum. Brain Mapp. https://doi.org/10.1002/hbm.24550.

Yc, K., Prado, L., Merchant, H., 2019. The scalar property during isochronous tapping is disrupted by a D2-like agonist in the nonhuman primate. J. Neurophysiol. 121 (3), 940–949. https://doi.org/10.1152/jn.00804.2018.

Yoshida, K., Saito, N., Iriki, A., Isoda, M., 2011. Representation of others' action by neurons in monkey medial frontal cortex. Curr. Biol. 21 (3), 249–253. https://doi.org/10.1016/j.cub.2011.01.004.

Yoshida, K., Saito, N., Iriki, A., Isoda, M., 2012. Social error monitoring in macaque frontal cortex. Nat. Neurosci. 15 (9), 1307–1312. https://doi.org/10.1038/nn.3180.

Yuan, Y., Brown, S., 2015. Drawing and writing: An ALE meta-analysis of sensorimotor activations. Brain Cogn. 98, 15–26. https://doi.org/10.1016/j.bandc.2015.05.004.

Zhang, Y.H., Zhang, S., Ide, J.S., Hu, S.E., Zhornitsky, S., Wang, W.Y., et al., 2018. Dynamic network dysfunction in cocaine dependence: Graph theoretical metrics and stop signal reaction time. NeuroImage-Clin. 18, 793–801. https://doi.org/10.1016/j.nicl.2018.03.016.

Zhu, S.L., Lakshminarasimhan, K.J., Angelaki, D.E., 2023. Computational cross-species views of the hippocampal formation. Hippocampus 33 (5), 586–599. https://doi.org/10.1002/hipo.23535.