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*BODY-PLACE FIELDS AND THE SURROUNDING SPACE:
PRELIMINARY EVIDENCE FROM MULTIELECTRODE NEURAL
RECORDINGS IN THE MACAQUE PREMOTOR CORTEX*

“BODY-PLACE FIELDS” E LO SPAZIO CIRCOSTANTE: EVIDENZE
PRELIMINARI DA REGISTRAZIONI NEURALI CON MULTIELETTRODI
NELLA CORTECCIA PREMOTORIA DEL MACACO

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ABSTRACT

~ English ~

The peripersonal space is a particular sector of space, where all physical interactions between individual and the environment occur. Several studies showed that the ventral premotor cortex of macaques hosts neurons responding to tactile, visual and auditory stimuli, deemed to code the space around us in operational terms. In the current study, we recorded from premotor area F4 in order to investigate the neuronal activity when visual stimuli were moved in the space around the monkey and tactile stimuli were applied on its head and upper body. By using linear multielectrode probes, we isolated 27 single units and 192 multi-units. This preliminary analysis focused on single units. We first computed a firing rate map for each of them; next, we elaborated a linear regression model using neural responses as predictors and stimuli positions as predicted values. Thanks to the firing rate maps, it is possible to appreciate the modulation of neural discharge in an extremely detailed way. Furthermore, the data suggest that it is possible to predict stimuli position from the neural firing rate during both type of conditions, along each axis.

~ Italian ~

Lo spazio peripersonale è un particolare settore dello spazio dove avvengono tutte le interazioni fisiche tra l'individuo e l'ambiente. Vari studi hanno mostrato che la corteccia premotoria ventrale del macaco ospita neuroni che sono in grado di rispondere a stimoli tattili, visivi e uditivi, e che si ritiene codifichino lo spazio attorno a noi in termini operazionali. In questo studio abbiamo registrato dall'area premotoria F4 per indagare l'attività neurale quando stimoli visivi sono mossi nello spazio attorno alla scimmia e stimoli tattili vengono applicati sulla sua testa e sulla parte superiore del suo corpo. Usando sonde multielettrodo lineari, abbiamo isolato 27 single-unit e 196 multi-unit. Queste analisi preliminari si sono concentrate sui singoli neuroni. Abbiamo prima realizzato una "firing rate map" per ognuno di essi; dopodiché abbiamo elaborato un modello di regressione lineare usando le risposte neurali come predittori e le posizioni degli stimoli come valori predetti. Grazie alle mappe del firing rate, è possibile apprezzare la modulazione della scarica neuronale in un modo estremamente dettagliato. Inoltre i dati suggeriscono che in entrambi i tipi di condizioni, lungo ogni asse, sia possibile predire la posizione dello stimolo partendo dall'attività neurale.

1. INTRODUCTION

“Space is not a sort of ether in which all things float...”

(Merleau-Ponty, 1962)

1.1. Peripersonal space

1.1.1. A matter of definitions

Many scientist and philosophers provided a definition of *space*. In Euclidean terms, it can be described as a set of points, in a three-coordinates – x, y and z – reference system. In this perspective, space is unitary, continuous and uniform. However, an ever-growing body of evidence in neuroscience showed that we represent and perceive space in a more complex way.

We live in a complex environment, filled with conspecifics, other animals and objects. In order to *perceive* and *interact* with external stimuli, the brain needs to represent them within the space around us. To this purpose, it does not construct a single representation of space but multiple, functionally distinct representations anchored to specific reference frames, depending on the source of sensory stimulation and the nature of interaction between the individual and the environment (Serino, 2019). Amazingly, our experience of space is integrated. This appears to be referred to a more global reference frame constituting the centre of awareness, centred to a global representation of our body. One main feature of space representation is the reference to the body and its parts (Serino, 2019). The brain does not represent the space

homogenously, but three sectors of space seem to exist: the personal space (body surface), the peripersonal space (PPS, close to body) and the extrapersonal space (far from the body).

As described by Bufacchi and Iannetti (2018), a wide variety of disciplines – like ethology, neurophysiology or social science – studied the interactions within the space near the body. Many behavioural and neurophysiological responses increase as a function of the proximity of environmental stimuli to the body. Indeed, the division between near and far space was originally suggested by the British neurologist Lord Brain (1941), who noticed that lesions in parietal cortex could lead to perceptual problems limited to the near space, but not affecting the far space: for instance, his patients were unable to judge the distance and direction of objects, but they could indicate the centre of a circle or show the relative length of three lines. He also proposed the existence of a *grasping distance*, whose estimation depends upon the association pathways between the visual cortex and the motor cortex. “Awareness of [space] is not just a mere juxtaposition of sensory impressions from which some can be deduced without impairing the validity of the remainder: it is a synthesis from which springs a unity of perception corresponding to the external reality”, he suggested. In the ‘50s the Swiss biologist Heideger underlined that the individual living space of the animal is not homogeneous, but highly differentiated, and stated that there is a special zone around the body (Heideger, 1955; Heideger, 1950). At the Zurich zoo, he observed that animal behaviour changed depending on the distance between animals: especially, when a potential predator was near, the animal fled or withdrew (*flight distance*), and if it could not escape from its enemy, the animal would remain in a state of tension; also between conspecifics, a distance at which the proximity of individuals becomes no longer tolerable existed (*personal distance*). In the following years other authors emphasized this distinction, particularly Rizzolatti et al. (1981) introduced the concept of “*peripersonal*

space” to illustrate the close connection between somatosensory and visual signals in relation to specific body parts.

As illustrated by de Vignemont and Iannetti (2015), sensory events occurring in a body-centered reference system can be represented in relation to action (i.e. the body schema) or in relation to perception (i.e. the body image). In extrapersonal space, sensory events can be represented in relation to oneself (within an egocentric frame of reference) or in relation to other objects or events (within an allocentric frame of reference). The authors wonder whether there are different ways to represent object and events in the peripersonal space; but it is difficult to address this issue also because the same definition of peripersonal space remains vague in scientific literature. For instance, there are variations in terms of distance of the stimuli (more or less close to the body), relevance of the stimuli (the space of objects, preys and predators) and the potential motor action triggered by the stimuli (the space of protection action but also goal-directed action). Over the years, numerous studies in monkeys and humans, in both healthy and pathological subjects, have examined the functional features of peripersonal space, which de Vignemont and Iannetti (2015) summarised as follows:

- 1) “Bodily reference frame: the PPS is anchored to specific body parts, and moves when the body parts move.
- 2) Multisensory vigilance: the perception of objects and events occurring in PPS triggers the allocation of multisensory attention.
- 3) Sensorimotor relevance: objects and events perceived in PPS are represented in terms of possible actions.
- 4) Plasticity: the boundaries of PPS are flexible.”

Achieving consensus on a definition is extremely important for scientific progress because allows an accurate and consistent measurement across laboratories (Hunley & Lourenco, 2018). “*But what is precisely meant when referring to PPS?*” (Bufacchi and Iannetti 2018). A clear single definition does not exist and this term is essentially used with three different meanings:

- 1) “the portion of space with a given Euclidian distance from the body”;
- 2) “the space within which certain physiological or behavioural responses are larger when the stimuli eliciting them occur near the body”;
- 3) “the mechanism through which the brain represents the space near the body”.

The authors identified some problems with these definitions: for instance the first considers PPS as immutable, so it cannot explain the phenomenon that PPS can change in size (e.g., Fogassi et al., 1996). The other two definitions could appear equivalent, but we can not affirm that a modulation of the measure dependent on spatial proximity (2nd meaning) necessarily means that the brain has changed how it represents the near space (3rd meaning). Furthermore, these different meanings are often used within the same sentence, creating further conceptual misunderstandings.

According to Bufacchi and Iannetti (2018), in the past PPS was described as a “single, distance-based, in-or-out space”; nevertheless, this intuitive definition is contradicted by neurophysiological and behavioural data. First, PPS-related measures are graded with proximity (e.g., Duhamel et al., 1998; Colby et al., 1993); second, they are influenced by other factors, such as tool use or stimulus valence (e.g., Iriki et al., 1996; Taffou & Viaud-Delmon, 2014); third, many different PPS-related responses exist and each can be used to describe a different space (e.g., Cléry et al., 2015; Van der Stoep et al., 2015). In order to deal with these

issues, Bufacchi and Iannetti (2018) propose a reconceptualization of PPS as “*a set of graded fields describing behavioural relevance of actions aiming to create or avoid contact between objects and the body*” (see paragraph 1.1.4).

1.1.2. Neural basis of peripersonal space representation

Near and far space are not separated by physical boundaries in the real world, but the primate brain seems to represent PPS as separated from the far space, as if there was a distinction between what can and cannot interact with the body (Serino, 2019). For instance, in humans, neurological patients with neglect¹ selective only for the PPS have been described (e.g., Berti & Frassinetti, 2000; Halligan & Marshall, 1991), as well as cases of neglect restricted to the extrapersonal space (e.g., Cowey et al., 1994). Functional studies in humans suggest the involvement of different network in space processing: a dorsal network in the coding of near space, including the left dorsal occipital cortex, the left intraparietal cortex and the left ventral premotor cortex, and a ventral network for far space processing (e.g., Aimola et al. 2013). Fascinatingly, in 2003 Weiss and colleagues showed that, in healthy subjects, neural perceptual processes (for instance, bisection judgment task) and motor processes (for example, manual bisection task) do not display any deficit by whether the task is being performed in the near or the far space. During the years, a wide range of studies improved our understanding of the precise neural bases underlying space processing, the construction of peripersonal space representations and their relation with perception, action and body awareness. In this growing

¹ A visual-spatial disorder in which patients fail to report, respond or orient to visual, somatosensory or auditory stimuli presented in the space contralateral to the brain lesion (Vallar & Papagno, 2018).

knowledge, research with monkeys has played an important role: because of their close phylogenetic proximity to humans, studies on non-human primates allow to obtain highly detailed information about neural basis of sensory, motor and cognitive functions (e.g., Phillips, et al., 2014). Thus, since single-cell recording studies in macaque monkey (e.g., Rizzolatti et al., 1981), it has been discovered that the processing of PPS involves a network of interconnected sensorimotor areas, like parietal cortex and frontal premotor cortex, playing an important role in the control of upper body, head and arm movements (e.g., Graziano et al., 1994; Gentilucci et al. 1983).

1.1.2.1. A glimpse into the cortical parieto-frontal system for action planning and control

The traditional “sandwich model” (Hurley, 1998) that conceives perception-cognition-action as segregated and serially organized processes has dominated for decades in cognitive psychology and neuroscience. From this perspective, thinking and cognitive processes are the most relevant and interesting element of the sandwich (the filling in between the two slices of bread), whereas perception and action constitute the two separated, slave systems on the sides: the former provides the input to the cognitive processors and the latter orchestrates the commands necessary to appropriately move the body (action). According to this model, the cortical motor areas would be designated only to execute motor plans (Rizzolatti & Sinigaglia, 2006). In contrast, as illustrated by many studies so far, this is an extremely simplified conception: the cortical motor system is formed by a mosaic of anatomically and functionally distinct frontal and parietal areas, most of them strictly connected with a variety of sensory areas and is involved in more complex functions, beyond mere execution of movements. For instance,

motor areas are implicated in a series of sensory-motor transformations, such as those that transform visual information about objects and object location into the appropriate goal-directed actions to reach and grasp them (Rizzolatti & Luppino, 2001).

The motor cortex formed the caudal sector of frontal lobe and, histologically, is characterized by the lack of granular cortical layer. This agranular frontal cortex is cytoarchitecturally heterogeneous and constituted of several distinct areas (Figure 1).

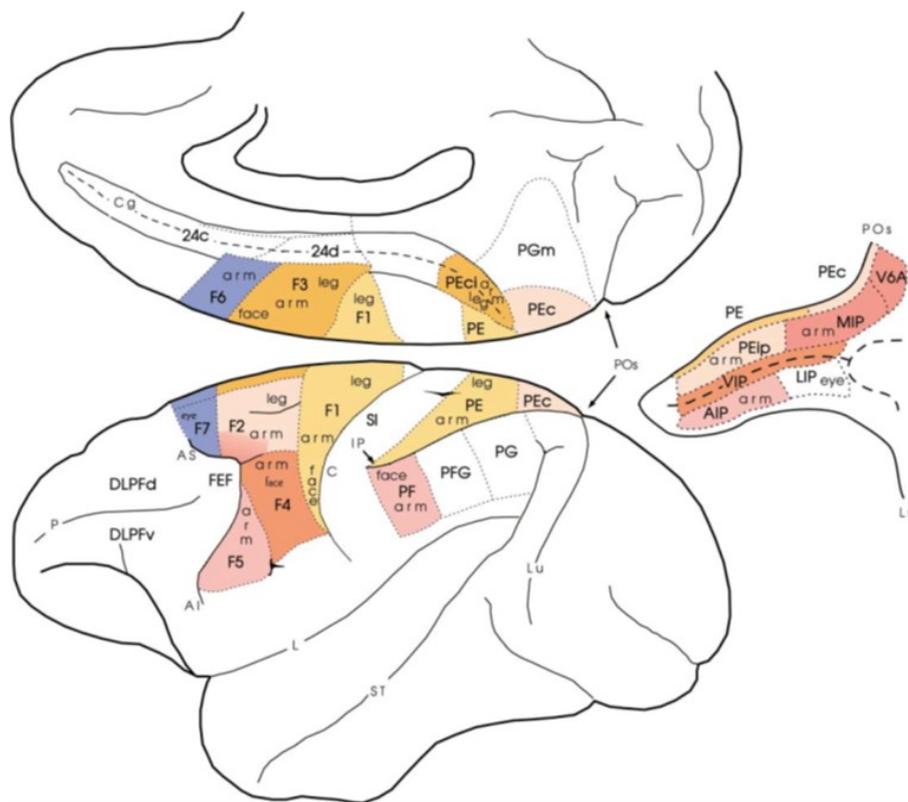


Figure 1. Mesial and lateral views of the monkey brain showing the parcellation of the parieto-frontal motor system, including frontal, posterior parietal, and cingulate cortices. The areas located within the intraparietal sulcus are shown in an unfolded view of the sulcus in the right part of the figure. The posterior motor areas and the parietal areas that are the source of their major cortical afferents are indicated with the same colour. The anterior areas are indicated in blue. AI, inferior arcuate sulcus; AS, superior arcuate sulcus; C, central sulcus; Cg, cingulate sulcus; DLPFd, dorsolateral prefrontal cortex, dorsal; DLPFv, dorsolateral prefrontal cortex, ventral; L, lateral fissure; Lu, lunate sulcus; P, principal sulcus; POs, parieto-occipital sulcus; ST, superior temporal sulcus. (Luppino & Rizzolatti, 2000)

F1 corresponds to Brodmann area 4 (primary motor cortex), while the other motor areas (F2-F7) lie inside Brodmann area 6. Areas F3 and F6 constitute the mesial premotor cortex (pre-supplementary motor area and supplementary motor area); areas F2 and F7 form the dorsal premotor cortex; areas F4 and F5 identify the ventral premotor cortex. Each area hosts different somatotopic maps and electrophysiological properties: for instance, F4 and F5 are both electrically excitable, but the former responds to intracortical microstimulation (ICMS) by showing axial, forelimb and face movements, whereas the latter represents mainly mouth and hand/wrist movements. More recently Graziano et al. (e.g., Graziano et al., 2005) used long ICMS trains (≥ 500 ms), which approximate the duration of ethologically-relevant actions, rather than shorter ICMS trains of electrical pulses, which evoke only muscle twitches as in classical mapping studies (e.g., Penfield & Boldrey, 1937; Woolsey et al., 1952). Thus, the movements evoked during these long stimulation trains involved many joints in coordination and often resemble meaningful actions, such as making a defensive gesture to protect the body against an impending impact.

Each area is connected to other motor areas (*intrinsic* connections), to cortical areas outside the agranular frontal cortex (*extrinsic* connections), and to subcortical structures and spinal cord (*descending* connections). According to Rizzolatti and Luppino (2001), the anterior motor area – area F6 and F7 – do not send fiber to F1, but have diffuse connections with the other motor areas. In contrast, the posterior motor areas – areas F2-F5 – are connected with F1 as well as to downstream subcortical regions exerting more direct influence on the motor output. Regarding extrinsic connections, areas F1-F5 receive their main cortical connections from the parietal lobe, whereas areas F6 and F7 receive their main cortical input from the prefrontal

cortex. Finally, concerning descending projections, areas F1, F2, F3, part of F4, and the part of F5 buried in the inferior arcuate sulcus directly contribute to the cortico-spinal tract, while areas F6 and F7 project to the brainstem structures only.

1.1.2.2. Studying the peripersonal space in macaque monkey

The spatial extent of multisensory receptive fields² (RFs) appears to be of great interest in the research about peripersonal space. From the early 1980s, many studies have described various type of multisensory neurons, that is neurons “*with a tactile receptive field centred on a body part, and with a visual and/or an auditory receptive field anchored to the same body part, and extending in space for a given distance, variable among the different neurons and depending on environmental contexts*” (Serino, 2019). Neurons with such features have been found in some regions of motor system: a) the frontal cortex, in particular in the ventral premotor cortex (e.g., Rizzolatti et al., 1981); b) the posterior parietal cortex, in particular between the superior parietal and the inferior parietal lobule along the rostro-caudal unfolding of the the intraparietal sulcus (IPS) (e.g., Duhamel et al., 1998); c) in the putamen (Graziano & Gross, 1993).

In the macaque monkey, the premotor area F4 is located in the caudal part of inferior BA 6, just rostral to BA 4 (area F1). It receives a strong input from the inferior parietal lobule (e.g., Matelli et al., 1986) and from ventral intraparietal area (area VIP), located in the depth of the intraparietal sulcus. F4 contains a representation of head, trunk, arm and mouth movements (Gentilucci et al., 1988). Proximal, axials and arm movements tend to be represented dorsally, whereas mouth movements are represented mostly in its ventral part. F4 contains also neurons

² We can define *receptive field* as the whole of stimuli’s characteristics, such a position or colour, that active a neuron.

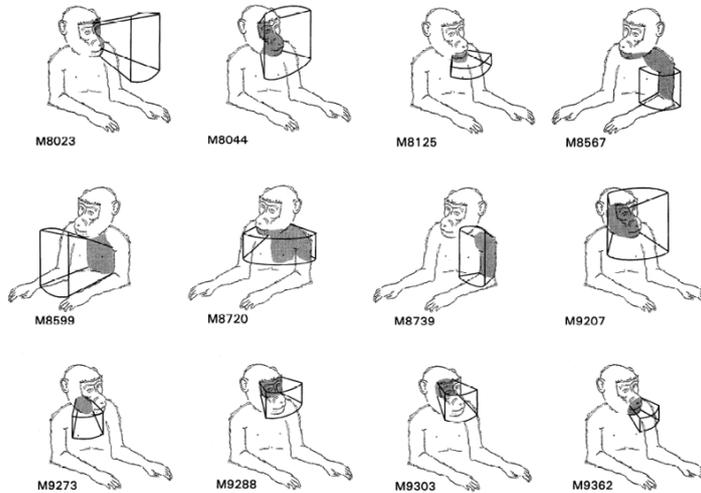


Figure 2. Different types of tactile and visual RFs of F4 bimodal neurons. Shaded areas: tactile RFs. Solids around different body parts: visual RFs. Neurons M8023-M8125 and neurons M9207-M9362 were recorded from the left hemisphere; neurons M8567-M8739 were recorded from the right hemisphere. (Fogassi et al. 1996)

that respond to tactile stimulation. Their tactile receptive fields are relatively large and located primarily on the monkey's face, neck, arm and hand or both hands (Rizzolatti et al., 1981). A wide proportion of neurons in area F4 discharges in response to both tactile and visual stimuli, and they are

defined as *bimodal* (Figure 2). Differently from classical visual neurons, F4 neurons are poorly triggered by visual stimuli far from the animal, but they respond strongly to real three-dimensional objects moving near the animal (e.g., Gentilucci et al., 1983). Some F4 neurons encode also auditory information about the location of objects near the monkey (Graziano et al., 1999), suggesting that a multimodal representation of nearby space is created in area F4 (Figure 3). The visual RF location is independent from eye movements, i.e., it remains in the same position of the PPS regardless of gaze deviation (e.g., Fogassi et al., 1996). Moreover, for bimodal visual-tactile neurons with tactile RFs on the arm or hand, the visual RF is “anchored” to the tactile RF: this means that displacements of the monkey's limb cause a shift in the location of the visual RF (Graziano et al., 1994). These results suggest that F4 neurons do not represent the space in retino-centric coordinates, rather, they operate in body-centered coordinates,

encoding the location of visual stimuli with respect to the face, arm, hand or other body parts. Furthermore, F4 neurons seem to encode space not only in response to external stimuli, but also as a consequence of internally generated signals, based on working memory (Graziano et al., 1997b). In this study a subset of F4 neurons that were triggered by visual stimuli in PPS continued to respond when lights were turned off and the previously presented object was silently removed. Such neurons exhibit “object permanence” – a concept emphasized by Jean Piaget (1952) that denotes the awareness that objects continue to exist even though they can no longer be seen, heard or touched –

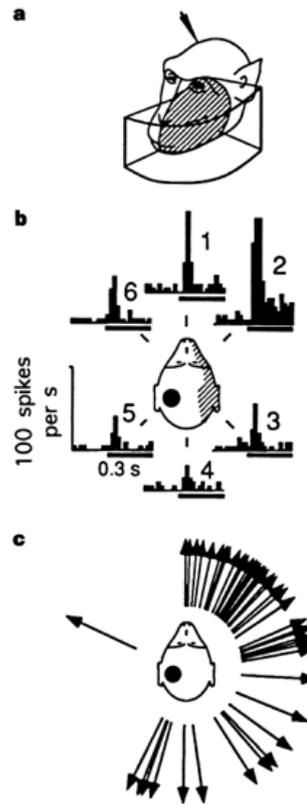


Figure 3. Responses of bimodal and trimodal neurons in ventral premotor cortex. a) Receptive fields of a typical bimodal, visual-tactile neuron (shaded: tactile RF; boxed: visual RF). b) Responses of a typical trimodal, visual-tactile-auditory neuron. c) The calculated preferred direction of the auditory response for 43 trimodal neurons. (Graziano et al. 1999)

encoding the presence of an object that is no longer visible, and may play a role in the ability to reach toward or avoid objects that are no longer visible, such as object occluded, behind the animal, or no longer fixated. In 1999 Graziano showed that the position of the arm is represented in the premotor cortex by means of a convergence of visual cues and proprioceptive onto the same neurons. These bimodal, visual-tactile neurons responded to the felt position of the arm

when the arm is out of sight, but they were also triggered by visual objects presented near a fake arm placed in a realistic posture (Graziano, 1999).

The posterior parietal lobe, particularly areas PF/PFG (Rozzi et al. 2008) and VIP (Duhamel et al., 1998; Avillac et al., 2007) – heavily linked to area F4 (e.g., Matelli et al., 1986) – contains bimodal, visuo-tactile neurons with proprieties similar to those of neurons in the ventral premotor cortex. In area 7b, these neurons have tactile RFs distributed over the face, arm and hand, showing a somatotopic organization with considerable overlap between the representation of different body parts (e.g., Graziano & Gross, 1995; Hyvarinen, 1981; Leinonen et al., 1979). Most of these neurons respond to visual stimuli moving toward the monkey, within about 20 cm of the tactile RF, and their tactile and visual RFs are aligned in a spatially congruent manner (Graziano & Gross, 1995). Testing bimodal neurons with tactile

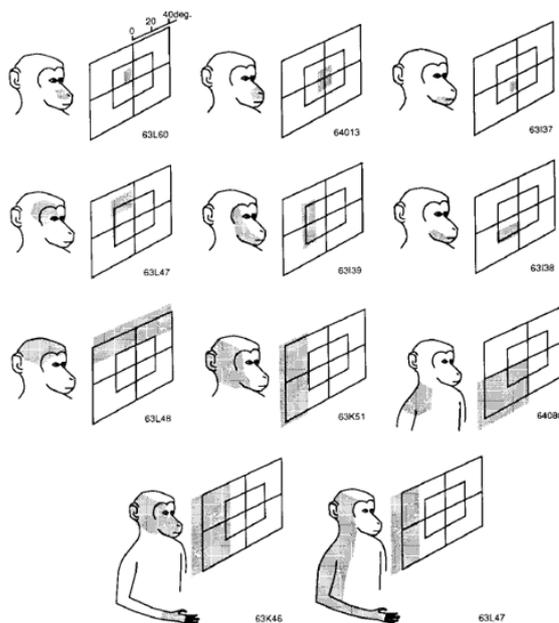


Figure 4. Somatosensory and visual receptive fields in area VIP. Schematic representation of somatosensory and visual receptive fields of 11 representative bimodal ventral intraparietal area neurons. Shaded areas on the monkey and screen represent tactile and visual RF surfaces. (Duhamel et al. 1998)

RFs on the arm by moving the monkey's upper limb to different position, Graziano and Gross (1995) showed that, unlike in ventral premotor cortex, visual responses in area 7b appeared to be independent of the position of the arm.

Area VIP contains two main categories of neurons triggered by sensorial stimuli: visual neurons and bimodal,

visuo-tactile neurons (Colby et al. 1993; Duhamel et al. 1998) (Figure 4). Concerning the distribution of somatosensory RF locations, head and face representation are selectively emphasized in area VIP. Visual and auditory receptive fields usually refers to upper part of space, covering a distance of 10-60 cm from the body surface, almost always on the same side of the tactile receptive field (e.g., Duhamel et al., 1997; Schlack et al., 2005). Area VIP seems to be involved in the generation of a multisensory, head-centered representation of nearby space (Duhamel et al., 1998).

In 1993 Graziano and Gross discovered that also the putamen – a subcortical region of the primate brain that receives projections from area 6 and area 7b (e.g., see Matelli et al., 1986) – represents the space near the body. It contains neurons that respond to somatosensory stimuli such as light touch or deep muscle pressure. In the face and arm regions of its somatotopic map, the authors found neurons that responded to visual stimuli: some of them were bimodal, while others were purely somatosensory or visual. The visual and tactile RFs in the putamen are spatially aligned, with the visual RFs anchored to the tactile ones. Consequently, bimodal neurons with the tactile RFs on the arm respond visually when the arm is within the monkey's field of view, but do not respond when the arm is moved out of view (Graziano & Gross, 1995).

Not only neurophysiological studies but also studies of the behavioural effects of focal brain lesions have supported the existence of a selective representation of the space near the body (di Pellegrino & Làdavas, 2015). In 1983 Rizzolatti and colleagues carried out a study on the frontal cortex of macaques, showing a double dissociation between peripersonal and extrapersonal space. After unilateral surgical ablations of the postarcuate cortex (area 6), monkeys exhibited a failure to grasp food with the mouth when presented contralaterally to the lesion, a reluctance to use the contralateral hand and a severe hemi-inattention, in both the

somatosensory and visual modalities. Nonetheless, the deficits were limited to the peripersonal space. Even when motor and attentional deficits improved, the animals tended to use the ipsilateral hand and, when presented with two stimuli, they preferred the one ipsilateral to the lesioned side. In control experiments, area 8 (the frontal eye fields; i.e., peri-arcuate cortex facing area F4, across the arcuate sulcus) was ablated unilaterally and a reduction of eye movements toward the space sector contralateral to the lesion and a neglect of the contralateral hemispace were observed. However, no somatosensory deficit was found and the visual neglect was more prominent for far space than for that near the animal.

Over the past few years, some studies have explored how a mirror-like mechanism might reflect and encode the PPS of other individuals (di Pellegrino & Làdavas, 2015). Indeed, in monkey, the brain areas involved in encoding PPS are adjacent to regions containing mirror neurons – a class of motor neurons that respond during both action execution and action observation (di Pellegrino et al., 1992; Gallese et al., 1996). The study carried out by Caggiano et al. in 2009 is an intriguing example: they found mirror neurons with a different modulation according to the location in space of the observed motor acts relative to the monkey. These neurons encode differentially peripersonal and extrapersonal space and, moreover, a portion of these neurons encoded space in metric terms, whereas other neurons encoded space according to an operational framework, changing their properties according to the possibility that the monkey will or not interact with the object. When the continuous between near and far space is made more clear-cut (Bonini et al. 2014; Maranesi et al, 2017), the preference of mirror neurons response for the peripersonal space increases considerably, suggesting a strong pragmatic valence of space coding in the ventral premotor cortex.

Bufacchi and Iannetti (2018) highlight that, in single neuron studies of bimodal representations of tactile and visual stimuli, neurons were often described as demarcating zones of space, represented as “bubbles” with clear boundaries. However, in many cases the neuronal response did not appear as a step-like function, but as a gradual proximity function linking the object and the subject (Colby et al., 1993). Moreover, some neurons exhibit a receptive field that extends further than the distance commonly reported (reaching distance), even to the end of the room (e.g., Graziano et al., 1997a). Finally, in premotor and parietal cortex, some neurons respond more strongly to visual stimuli slightly further away in space than to visual stimuli near their somatosensory receptive field (e.g., Rizzolatti et al., 1981; Colby et al., 1993). These limits can be found also in psychological literature: using behavioural measures – such as line bisection or visuotactile extinction – most experiments would often test only near versus far conditions. Furthermore, authors often use simple summary statistics, such as the point of first increase over baseline activity (e.g., Sambo & Iannetti, 2013). Simplification in experimental paradigm and analysis is understandable, but the binary experimental designs preclude a more complete conceptual understanding of PPS (Bufacchi & Iannetti, 2018). Taken together, these empirical data suggest that a step-like proximity function appears inadequate to describe PPS and emphasize the complexity behind the representation of PPS.

1.1.3. Plasticity and influence on peripersonal space

Accumulating evidence in monkeys and humans suggest that PPS is extremely plastic and dynamic (di Pellegrino & Làdavas, 2015) and several factors can influence its neural representation (Figure 5). Cléry et al. (2015) distinguished two types of changes in peripersonal space: “plastic changes”, that occur following training or learning, and “dynamic changes”, due

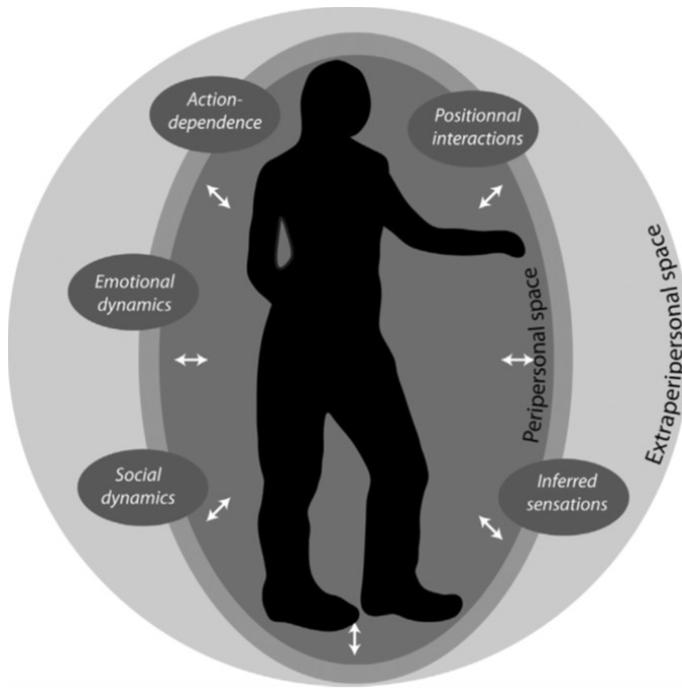


Figure 5. Influence on peripersonal space. The boundary between far and near space representations is plastic and dynamic, under the influence of a variety of endogenous and exogenous factors. (Cléry et al. 2015)

to a correlated change in the environment or in the internal state of the individual, like emotional state changes. In 2018 Cléry and Ben Hamed introduced another classification, identifying a bottom-up driven reorganization of PPS (produced by stimuli like threatening stimuli) and a top-down driven reorganization of PPS (for instance, associated to social factors such as the presence of an observer).

In monkey, the visual RFs of neurons involved in PPS processing are dynamic and shaped by sensorimotor experience and many factors can influence PPS measures, like stimuli features. For instance, increasing the speed of approaching stimuli, Fogassi and colleagues (1996) observed an online expansion in depth in most F4 neurons visual field. Furthermore, the majority of VIP neurons discharge more than twice stronger if stimuli move along a preferred direction (Colby et al., 1993). Some bimodal neurons in area VIP respond preferentially to receding objects and their tactile response are observed when tactile stimuli are removed from the RF rather than applied to it (Duhamel et al., 1998). This area is involved in decoding self-motion and heading direction relative to environment (Chen et al., 2011; Bremmer et al., 2002), but not in heading perception (Chen et al., 2016). Other stimulus features that can influence the

representation of PPS are the size, the direction/rotation, the active and passive joint movements or even the semantic value of the stimulus (e.g, Rizzolatti et al., 1981; Graziano et al., 1997a; Fogassi et al., 1996; Graziano et al., 2002).

By using tools³, primates can exceed the physical limits of their body and reach targets beyond them. Iriki and colleagues explored the neural bases of peripersonal space remapping induced by tool use, both in “proximal” neurons, whose tactile receptive field was on the skin of the shoulder, and in “distal” neurons, whose tactile RF was on the skin of the hand (Iriki et al., 1996; Maravita & Iriki, 2004). In 1996, Iriki et al. trained monkeys to retrieve distant objects using a rake and recorded neuronal activity in the intraparietal region, where the somatosensory and visual signals converge. During tool use, they noticed an elongation of the visual RFs of hand-related neurons: they included the entire length of the rake or covered the expanded accessible space. The tool was thus incorporated into the modified body schema. Moreover, even if monkey was holding the rake unmovingly, the expanded visual RFs shrank back to their original size after a short time of rest in tool activity.

Also human experiments have shown that the use of tools can change the way in which individuals interacts with stimuli in far space. The study carried out by Berti and Frassinetti (2000) is a relevant example: a patient suffered from neglect apparent in near space, but not in far space, when line bisection task was performed with a projection lightpen. Nonetheless, when the patient performed in the far space bisection with a stick, using it to trace the line, the neglect was transferred to the far space. The authors supposed that, via tool-use, the extension of the

³ Beck (1980) defined *tool use* as “the external employment of an unattached environmental object to alter more efficiently the form, position, or condition of another object, another organism, or the user itself when the user holds or carries the tool during or just prior to use and is responsible for the proper and effective orientation of the tool”.

patient's body caused the remapping of far space including it into the near space. Later, Serino and colleagues took an interest in cases where a tool is used every day and for long time periods and in 2007 they investigated audio-tactile interaction in the space around the hand and in extrapersonal space in blind cane users and in a control group of sighted, blinded-folded subjects. Whereas in controls subjects the auditory PPS is limited to the region surrounding the hand, in blind individuals it is immediately extended as soon as they hold their cane, even without any active temporary use of the tool. Thus, a long-term experience with the cane appears to induce a durable extension of the peripersonal space.

Finally, as Serino (2019) noticed, everyday humans use a variety of tools allowing them to interact with objects and with others, including virtual interactions. Thus, the study about the manner in which tools can modulate the peripersonal space has extended to digital technologies. For instance, Bassolino et al. (2010) found that when individuals held a computer mouse in the hand that normally used to operate it, sounds near to computer screen, but far from their hand, improved their tactile reactions time. This effect was evident even when subjects were holding the mouse, while a cursor moved on the screen, but it was not observed when they sat in front of the computer, without holding the mouse. Also the control and use of robot devices has been investigated in peripersonal space research. For example, Canzoneri et al. (2013) showed that when patients performed a tactile distance perception task without prosthesis, the PPS around amputated limb shrank, as compared to their healthy limb and to healthy controls. Instead, when participants were wearing the prosthesis, the perceived length of the stump increased and the PPS boundaries extended so as to include the prosthetic hand as well. Together, this data suggest that also technological artefacts can plastically reshape PPS representations.

The space around us is a privileged region for interacting with other individuals. Accordingly, abundant literature dealt with how social information can modulate PPS processing (di Pellegrino & Làdavas, 2015). For instance, it has been shown that some neurons respond to visuo-tactile stimulation not only within one's own PPS but also in the PPS of others. In 2010 Ishida and colleagues recorded bimodal neurons in area VIP, some of which also exhibited responses to visual stimuli presented near the corresponding body parts of the experimenter (for instance, an arm). The majority of these neurons responded depending on the position of the experimenter with respect to the monkey. This study suggests that individuals might encode the body parts of others using a representation of their own body parts, just as mirror neurons encode one's own action and the actions of others. Brozzoli et al. (2013) identified neuronal populations in the human ventral premotor cortex that encode the space near both one's own hand and another person's hand. These findings suggest the existence of a shared peripersonal space representation of the space near oneself and other people, which could support social interactions by coding sensory events, actions, and cognitive processes in a common spatial reference frame. Heed et al. (2010) showed that crossmodal processing in PPS can be reduced for perceptual events that another person act upon. In their behavioural study, participants performed a visuo-tactile interference task in which they had to respond to the elevation (up or down) of tactile stimuli applied on the hand, ignoring visual distractor near or far from the tactile stimuli. The task was performed both alone and with a partner who responded to the visual distractors. Responses were more accurate and fast when the visual distractor occurred near the tactile stimulus. This crossmodal congruency effect was reduced when performing the task with the partner, but only if the partner occupied the participant's PPS and if he responded to all of the visual distractors. Thus, according to the authors, other's

action can modulate the multisensory integration in PPS in a top-down fashion, and this phenomenon could serve to guide voluntary action – rendering the visual stimuli less likely as action targets for the participant – and to allow others’ action in a space of self-defence – because the partner’s engagement with the visual distractors may have decreased their potential threat in peripersonal space. Teneggi and colleagues (2013) extended this view, using the audio-tactile interaction task and investigating how the nature of social relationship with others can shape PPS representations. They found that PPS boundaries shrink when the far space is occupied by another person, as compared to a mannequin. Furthermore, they showed that, after playing an economic game with another individual – a modified version of the mutual advantage game (McCabe et al., 1996) – , there are no detectable PPS boundaries between the self and the other, but only if the other behaved cooperatively. Indeed, after an unfair interaction, participants generically responded to tactile stimuli faster, independently from the position of concurrent sounds in space; whereas, after a fair interaction, subjects were faster than before game only at the farthest sound distances, thus at the space occupied by the other participant.

To recapitulate, a great number of factors can modulate PPS processing and, according to Bufacchi and Iannetti (2018), from a functional perspective, stimulus proximity not necessarily is more important to PPS measures than any other factor. The authors notice that this relevance to space has been applied also to the functional interpretation of place and grid cells. These neurons were discovered by O’Keefe’s group in rat hippocampus in the ‘70s (O’Keefe & Dostrovsky, 1971), and they have been supposed to code the position of an animal relative to the environment. However, some studies have shown that place and grid cells are not only sensitive to spatial information and has led to idea that these cells could code a value

of a given state (Stachenfeld et al., 2017). All that is relevant also because the hippocampus and parieto-premotor loop likely cooperate to plan and coordinate actions (Whitlock et al., 2008).

1.1.4. Functions of peripersonal space representation

Di Pellegrino and Làdavas (2015) describe PPS representations as “multisensory-motor interfaces, which serve to encode the location of nearby sensory stimuli to generate suitable motor acts”. Allowing the motor system to compute the position of the stimulus relative to the head, the hand or both, the body-centered PPS representation could provide an effective mechanism to guide actions directed at objects (or away from object). Moreover, PPS processing is modulated by voluntary action themselves, so that a dynamic and bidirectional links between PPS representations and actions exists.

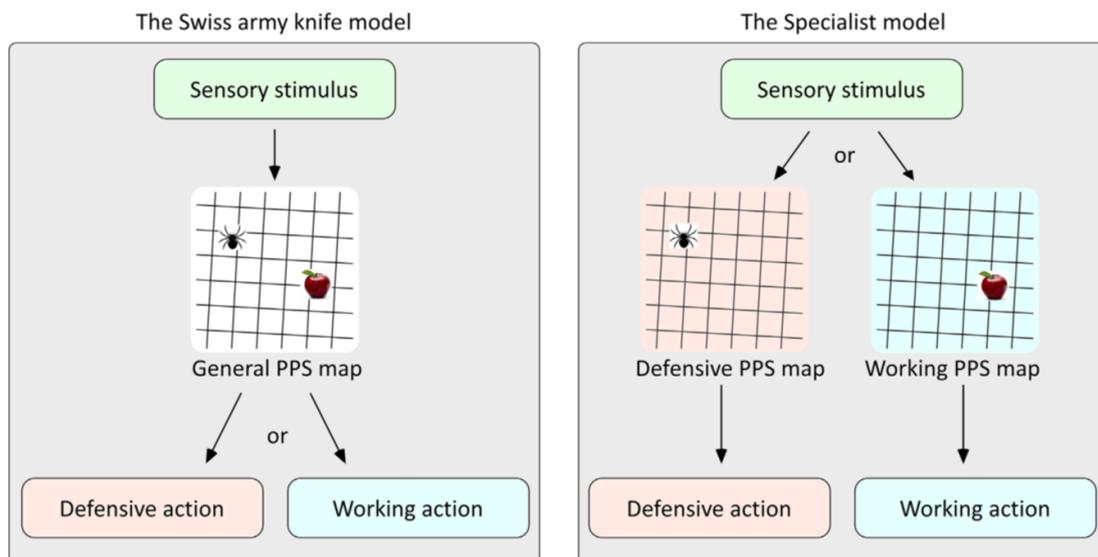


Figure 6. How many peripersonal spaces? Two model to describe how peripersonal space is represented in our brain (de Vignemont & Iannetti, 2014).

Dealing with functions of PPS representations, de Vignemont and Iannetti (2014) wonder how the brain encodes the available sensory information, and they introduce two explanatory models: “Swiss army-knife model” and “Specialist model” (Figure 6). According to the first model, a single cortical map representing the PPS exists and, as a Swiss army-knife, it subserves several functions (particularly object grasping and body protection), depending on the context. The authors use an apple and a spider such as example: both an apple that one wants to eat and a spider coming close to the body are mapped on the same PPS representation, although the contexts are different and the stimuli trigger different response. In compliance with the second model, peripersonal representations are functionally defined, just as a specialist has a unique expertise to which fully dedicate him or her; especially, the representation of PPS could be involved in goal-direction action (*working space*) and in the protection of the body (*protective or defensive space*). The authors specify that this type of model does not preclude multiple representations of the same stimulus on the two maps or interactions between them. They argue in favour of a dual representation of PPS, state that non-defensive behaviours are organized quite distinctly from defensive behaviours. Differences can be found in a) repertoire of motor responses – generally, goal-directed actions are largely organized toward an object, whereas defensive actions are geared away from an object; b) spatial organization – the two types of PPS give priority to different body parts in the allocation of attentional and motor resources; c) automaticity – most movements within working space are voluntary, while the majority of movements within the protective space are largely automatic; d) level of motor precisions – for example, goal-directed actions, such as grasping an object, require slow, precise motor guidance, whereas protective actions must be rapid, in order to keep the threat away from the body. We could ask if there are more than two functions. De Vignemont and Iannetti (2015)

explain that the Specialist model does not lead to an infinite multiplication of PPS, but it is parsimonious and plausible to assume the existence of only these two types of PPS.

Bodily Self Consciousness can be defined as “*the experience of the self as a subject of the experience grounded into a body that is felt as one’s own (self-identification), which occupies a specific location in space (self-location) and which faces the world from a specific perspective (first-person perspective)*” (Serino, 2019). By integrating multisensory cues related to the body, it has been proposed that the PPS processing also plays a key role in the sense of body ownership and other components of bodily self-consciousness, thus suggesting that the PPS system is involved in the underlying subjective experience.

As reported above, Bufacchi and Iannetti (2018) propose a reconceptualization of PPS: “*a set of continuous fields describing physiological or perceptual responses that reflect the behavioural relevance of actions aiming to create or avoid contact between objects and the body*”. This formulation includes several essential concepts: the term *field* – used in the same sense of modern Physics, i.e. a quantity with a magnitude for each point in space and time, in agreement with the evidence that PPS measures change gradually; the expression *set of fields* – compatible with the observation that different PPS measures show different response profiles; the *contact-related behavioural relevance* – in particular, they propose that the values of PPS field reflects the relevance of potential actions. Thus, the brain estimates the value of external events differently for the behaviour triggered by these events, take into consideration the context, because it can define the range of action choice of an animal (for instance, depending on the presence of environmental factors such as tree or a cave, an animal could decide to escape from a predator or face it). Moreover, this reconceptualization overcome the distinction between *appetitive* PPS and *defensive* PPS (like in de Vignemont and Iannetti, 2015): both grasping and

defensive actions determine whether contact is created or avoided between a body part and an object. Such a definition attempts to capture the complexity of PPS and its multifaceted nature.

2. AIMS OF THE STUDY

In this study, we employed a simple visuo-tactile stimulation task in order to explore the modulation of neuronal activity in premotor area F4 when visual stimuli moved in space around and in contact with the monkeys' head and upper body were presented. By leveraging multielectrode recordings of single unit activity we will investigate body-centred somatosensory and visual place fields with a standard stimulation protocol, allowing us to finally explore the possibility to decode the position of a stimulus in the space near the body by exploiting the neural activity readout.

3. MATERIALS AND METHODS

3.1. Subject

The study involved one male macaque monkey, *Macaca mulatta* (13 kg). Before recordings, the monkey was habituated to sit in a primate chair and to interact with the experimenter; then it was habituated to a visuo-tactile task. Subsequently, it underwent surgery in deep anaesthesia and aseptic conditions to implant a headpost and a chamber for neural recordings (Bruni et al., 2015). The coordinates of the chamber were determinate using magnetic resonance images.

All experimental protocols complied with the European law on the humane care and use of laboratory animals (directives 86/609/EEC, 2003/65/CE, and 2010/63/EU), they were approved by the Veterinarian Animal Care and Use Committee of the University of Parma (Prot. 52/OPBA/2018) and authorized by the Italian Ministry of Health (D.M. Aut. Min. 802/2018-PR).

3.2. Apparatus and experimental paradigm

During the experiments, the monkey (head-fixed) was sitting in a primate chair at the centre of a transparent plexiglas enclosure (Width: 208 cm; Height: 205 cm; Depth: 181 cm) (Figure 7). A system of 8 video cameras were located at each corner of the enclosure (4 in the upper part and 4 in the lower part). Dual Gigabit Ethernet Machine vision cameras (mvBlueCOUGAR-

XD, Matrix Vision) with a resolution of 1936×1214 set to 50 frame-per-second acquisition rate were used. The cameras are equipped with a global shutter with sensor size 1/2” format (5.86 μm pixel), a manual C-Mount Lenses with 5 mm focal length (CCTV Lens, KowaOptical Products Co., Ltd) and LEDs ring lights. Each camera has two RJ-45 Gigabit Ethernet connectors with screw-locking and two Industry standard 12-pin locking connectors to provide transmission of images and signals to the



Figure 7. The plexiglas enclosure.

Windows computer, and to synchronize all cameras through a synchronization box connected to both cameras and computer. They fed their signal to a computer with the dedicated software (Simi Motion), necessary for the video recording of the experimental sessions and for tracking the marker’s position (see paragraph 3.4.1.).

The experimental session included two type of stimulation: 1) tactile and 2) visual. Tactile stimulation of the skin was carried out with a short stick (length: 40 cm). Visual stimulation was performed with a long stick (length: 100 cm). In both cases, a IR reflective sphere was positioned at the end of each stick: a small one (1 cm diameter) in the case of the short stick, and a bigger one (6 cm diameter) for the long stick.

The experimental protocol included a phase of tactile stimulation, performed on the monkey’s face (Figure 8A) and upper body (Figure 8B). Monkey’s face was ideally divided into six sectors, as shown in Figure 8. Each sector, from 1 to 6, underwent 270 stimulations

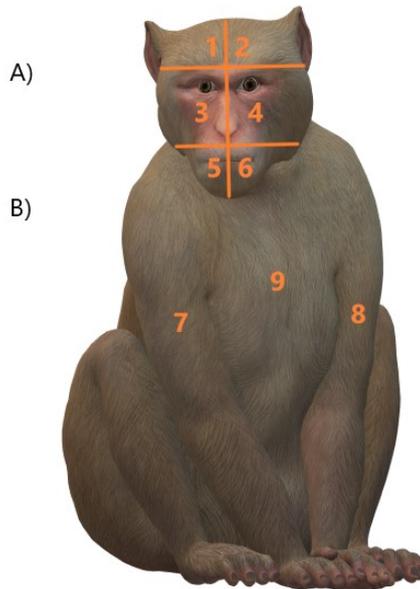


Figure 8. Tactile stimulation protocol. A) Sectors of monkey's face used to perform the tactile stimulation with uniform coverage of the skin surface. B) Sectors of the monkey's upper body used to perform the tactile stimulation with uniform coverage of the skin surface.

while monkey's eyes were closed with small opaque goggles. In each sector, the 90 tactile stimulations were first subdivided in five categories, depending on the stimulation plan or the type of stimulus: a) horizontal, b) vertical, c) tapping, d) diagonal (left-right), e) diagonal (right-left). Then, the same stimulations were repeated on the adjacent sector. Finally, the same protocol was applied to a territory encompassing two adjacent sectors. The right forelimb was tested with 100 random stimulations, likewise the left forelimb and the trunk.

During visual stimulation, the experimenter was outside the enclosure and performed a total of 1050 stimulations at seven possible distances from it: 10 cm, 20 cm, 30 cm, 40 cm, 50 cm, 60 cm, 70 cm. Five were the types of visual stimulations for each hemifield (first contralateral hemifield – i.e., right –, then ipsilateral hemifield – i.e., left) and 210 stimuli per category were applied: a) horizontal, b) vertical, c) diagonal bottom-up (from left to right); d) diagonal top-down (from left to right); e) in depth (see Table 2). The visual stimulation for each hemifield lasted approximately 20 minutes.

Following tables (Table 1 and Table 2) summarise experimental paradigm.

Table 1. Tactile stimulation.

<i>Condition</i>	<i>Stimulation type</i>	<i>Position in body</i>
Tactile – Face	Horizontal, vertical, tapping, diagonal l/r, diagonal r/l., n=270	Each sector and across pairs of adjacent sectors
Tactile – Upper Body	N=300, random	Right and left forelimb, trunk

Table 2. Visual stimulation.

<i>Condition</i>	<i>Stimulation type</i>	<i>Position in plexiglas enclosure</i>
Visual – contralateral hemifield (r.)	Horizontal, vertical, diagonal bottom-up, diagonal top-down, in depth, n=1050	From 10 cm to 70 cm (n=140 per category); then from 70 cm to 10 cm (n=70 per category)
Visual – ipsilateral hemifield (l.)	Horizontal, vertical, diagonal bottom-up, diagonal top-down, in depth, n=1050	From 10 cm to 70 cm (n=140 per category); then from 70 cm to 10 cm (n=70 per category)

3.3. Neural recording procedures

Neural recordings were performed using eight 16-channel linear silicon probes (shaft length: 8 mm; shaft width: 140 μm ; shaft thickness: 100 μm). Probes were implanted into the ventral premotor cortex of the left hemisphere by estimating the angle of penetration with MRI-based reconstruction of the outline of the spur (arcuate sulcus) at the selected site of insertion. The probe shaft was attached to a highly flexible polyimide (PI)-based ribbon cable with a zero-insertion-force (ZIF) connector that was electrically connected through OMNETICS A79025 connectors to the acquisition board of the electrophysiology platform Open Ephys (<https://open->

ophys.org/). The latter is connected to the host computer, which in turn is connected to the computer with Simi Motion software. In these ways, it is possible to monitor and synchronize various signals during the whole session. The signal from 96 channels (two slots were non-functional) was amplified and sampled at 30 kHz with three 32-channel Intan amplifier boards (Intan Technologies, Los Angeles, CA, USA), controlled in parallel via the Open Ephys. All formal signal analyses were performed off-line with fully automated software (MountainSort, Chung et al., 2017), using a -3.0 standard deviations of the signal-to-noise ratio of each channel as threshold for detecting units. Units were distinguished into single and multi-units using the noise overlap, a parameter that can vary between 0 and 1, with units with value below 0.1 considered as a single. Single unit isolation was further verified using standard criteria (ISI distribution, refractory period > 1 ms, and absence of cross-correlated firing with time-lag of ≈ 0 relative to other isolated units, to avoid oversampling). Possible artefacts were removed and all the remaining waveforms that could not be classified as single units formed the multi-unit activity.

3.4. Analysis

We analysed three types of data: the neuronal activity, the stick positions and possible monkey behaviours. Particularly, data connected with monkey behaviours were preliminary identified and blanked-out from further analysis of the relationship between stimulation and neuronal firing rate, to avoid confounding the neuronal activity associated with stick positions with that caused by the monkey's behaviour. As a preliminary data analysis, we focused on single-units.

The tracking of the IR reflective marker fixed to the tip of the stick used for testing was achieved by means of the Simi Motion software. Behavioural data analysis was obtained with

the software BORIS (*Behavioral Observation Research Interactive Software*). Then, the firing rate of single-unit was assessed by correlating it with the positions of the marker during valid period (no confounds from active monkey's behaviour). Later, a firing rate map was produced for each single unit with customized code in Matlab (MATLAB version R2020b). Eventually, a linear regression model was created using spikes as predictors and marker's positions as predicted values.

3.4.1. Marker tracking

Simi Motion (<http://www.simi.com/en/>) was used for data capture and analysis. The software detected and tracked IR reflective markers place on one extremity of the stick used for the tests. By detecting the markers in time bins of 20 ms (corresponding to a rate of the video monitoring system of 50 Hz) it was possible to extract 3D-coordinates of instantaneous marker's position and then recreating the trajectory of the tip of the stick in 3D.

Firstly, it is necessary to turn off ambient lighting and to switch on video cameras and their LEDs ring lights. In this way, the odds that Simi Motion will capture an exaggerate number of glare (i.e., markers in general) are reduced considerably. Calibrating video cameras and creating a new project are following steps. Now it is possible to video record experimental session, and then to start automatic tracking into an area of interest (for example, face and upper body in tactile stimulation). In this way, Simi Motion detects every contrasted signal identified as a marker, including some glares of the plexiglas walls of the enclosure. By appropriate pre-processing operations, it is possible to identify the marker of interest and limit the automatic detection of the software, which subsequently allowed us to extract the stick 3D-coordinates.

Figure 9 shows some examples of a track of marker.

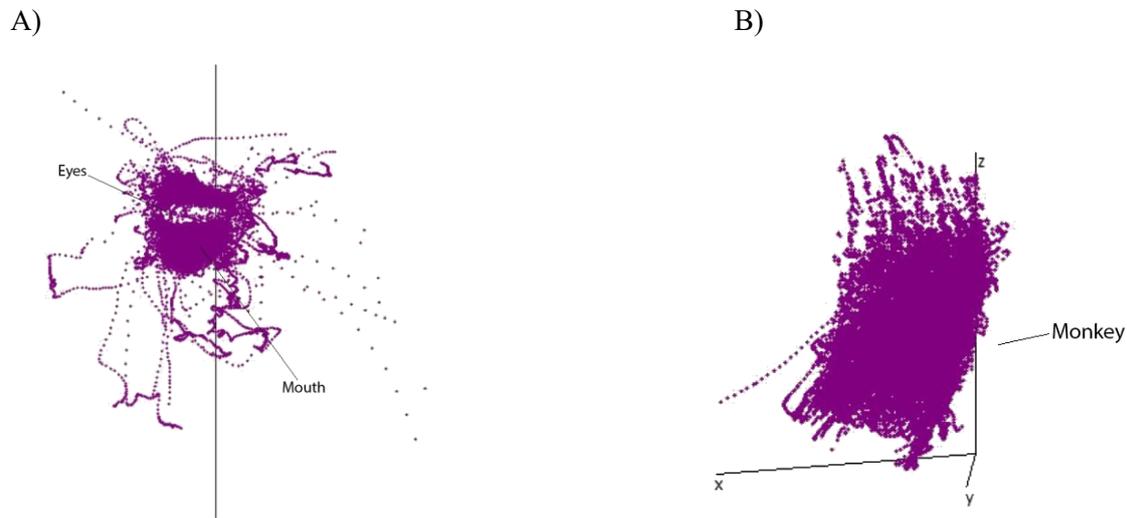


Figure 9. Marker tracking. The purple lines recreate the raw marker's position during tactile stimulation on the face (A) and during visual stimulation of the surrounding space (B).

3.4.2. Behavioural data analysis and blanking of epochs in which the monkey moved

BORIS (*Behavioral Observation Research Interactive Software*, <http://www.boris.unito.it/>) is a free, open-source event-logging software for video or audio coding and live observation of primates' behaviour (Friard & Gamba, 2016). A BORIS project file includes all information related to a set of observations, like the ethogram (list of behaviours), the independent variables and the subjects. First of all, it is necessary to define an ethogram. The behaviour type can be definite as a *point event* (without duration) or a *state event* (with duration). For each behaviour, an elevated number of modifiers can be added, so as to simplify the behavioural coding. It is possible analyse each step in the video easily and with high accuracy because BORIS can be slowed down and switched on and off to a frame-by-frame mode. Behavioural scoring data of monkey movements and states during an experimental session were used to remove intervals

when unwanted behaviours occurred, and the firing rate analyses were carried out on the remaining parts.

3.4.3. Firing Rate Maps

Three-dimensional firing rate maps were constructed using a similar approach to that reported in Grieves et al. (2020). Firing rate was calculated as

$$f(x) = \frac{\sum_{i=1}^n g(S_i - x)}{\int_0^T g(y(t) - x)}$$

where

- $g(x) = e^{-0.5\left(\frac{x-x < d}{\sigma}\right)^2}$
- d is the distance threshold of the truncated Gaussian function ($g(x)$), which was set to 1.5 voxels;
- σ is the standard deviation of the truncated Gaussian function ($g(x)$), which was set to 1 voxel width;
- S_i refers to the position of every recorded spike;
- x is the voxel centre;
- $[0T]$ is the recording session time period;
- $y(t)$ is the position of the stick at time t . If the stimulation lasted less than 1 s in a certain voxel, that voxel was considerate unstimulated.

So, firing rate maps were created in following way: in each voxel (10 x 10 x 10 mm in tactile condition; 50 x 50 x 50 mm in visual condition) the distance from the voxel centre to every recorded spike in the neighbouring voxels was calculated. Then it was divided by the distance to every stimulation position data in these voxels. At last, these distances were weighted with a truncated Gaussian function; consequently, spikes and stimulation position data closer to a voxel's centre had more influence on the voxel's firing rate and outside the neighbouring voxels had no influence on the firing rate.

3.4.4. From neural response to marker's position: a linear regression model

A linear regression model was used to determine if we could decode the marker's position from neuronal activity (bin width = 200 ms). We examined marker's position on the x, y and z axes, during the tactile stimulation on face and the visual stimulation. This procedure was applied to every single unit, recorded in two different days. Formally,

$$\hat{Y}_i = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 X_5 + \dots + \beta_n X_n + \varepsilon$$

where

- \hat{Y}_i is the predicted value of marker's position (on x, y or z axes);
- β_0 describes the intercept of the regression line;
- β_i represents the effect of each single unit;
- X_i is the firing rate of each single unit;
- ε estimates the residual.

Later, a scatter plot for each axis (x, y and z) was created with real values of marker's position along the horizontal axis and predicted values along the vertical axis, both for the visual condition and the tactile condition. Then, the coefficient of determination (R^2) was calculated in order to provide a measure of model accuracy. Regarding the visual condition, we examined the ability to predict marker's position in a more specific way, repeating this procedure with the neural activity during horizontal, vertical, and depth stimulations alone.

4. RESULTS

The neuronal activity was recorded from premotor area F4, during two conditions while the monkey was sitting on a primate chair (head-fixed): 1) tactile stimulations on its face and its upper body, and 2) visual stimulations along both contralateral and ipsilateral hemispace. We obtained 27 single units (single-unit, SU) and 192 multi-units (MU). Next, for each SU, three-dimensional firing rate maps were created, in order to explore how neuronal activity was modulated in the peripersonal space. Finally, a linear regression was used to determine whether we could predict marker's position from neural activity, for x, y and z axes (see Figure 10 for axes orientation).

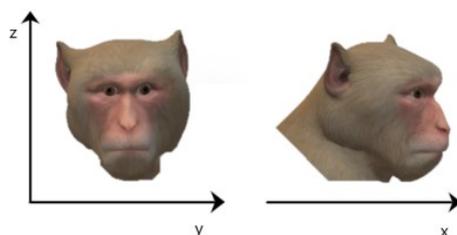


Figure 10. Reference frame used in tactile and visual conditions.

4.1. Neural activity during tactile and visual stimulations

Example of firing rate maps during tactile stimulations are shown in Figure 11. The single neuron in Figure 11A exhibits a greater discharge during tactile stimulation of upper body, but a suppression of its spontaneous discharge during tactile stimulations of the face. The single

unit in Figure 11B shows a different activation pattern with apparently bilateral facilitated activity along a diagonal of the face (from top left to lower right part) surrounded by an inhibitory region. Figure 11C illustrates an example of single unit with an overall weak response during tactile stimulation.

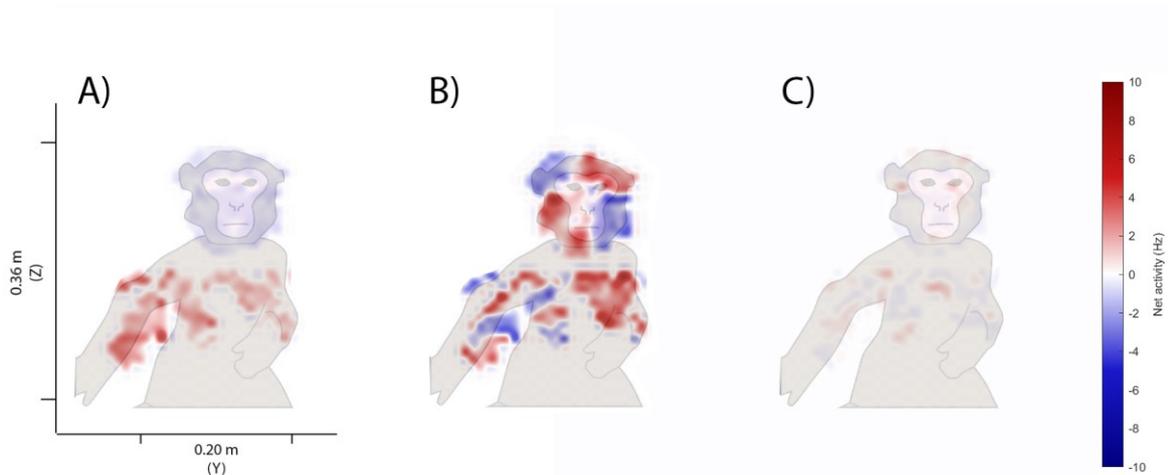


Figure 11. Examples of the Firing Rate Maps of single unit during tactile condition. A) Example unit with a facilitated response during tactile stimulation of the upper body; B) single unit with multiple body-place field; C) single unit with no body-place field. The horizontal axis (Y) shows the width of monkey's trunk (20 cm), while the vertical axis (Z) represents monkey's height from head to trunk (36 cm). The color bar depicts the range of neuronal activity in relation to the average firing rate. The different hues describe the neuronal activity with reference to the average firing rate: blue indicates lower discharge, red greater discharge.

Some example of firing rate maps during visual stimulations are shown in Figure 12. The single unit in Figure 12A exhibits a strong response to visual stimulations in the contralateral hemispace, but a suppression in the ipsilateral hemispace. The response of single unit represented in Figure 12B seems to depict a cone in front of the monkey. An example of single neuron without a spatially well-defined response is presented in Figure 12C.

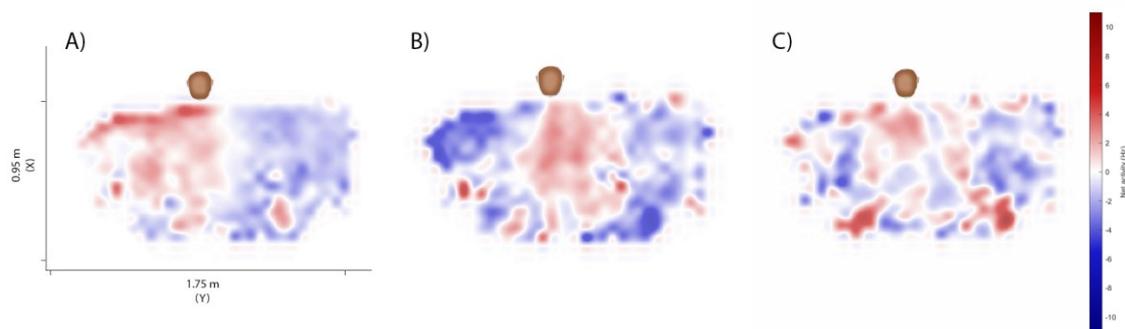


Figure 12. The Firing Rate Maps of a single unit in visual condition. A) Example unit with a facilitated response during visual stimulation of the contralateral hemispace; B) single unit with facilitated response when the visual stimulation was performed in front of monkey; C) single unit with no a spatially well-defined response. The horizontal axis (Y) shows the width of stimulations' space (95 cm), while the vertical axis (X) represents their depth (175 cm). The color bar depicts the range of neuronal activity in relation to average firing rate. The different hues describe the neuronal activity with reference to the average firing rate: blue indicates lower discharge, red greater discharge.

4.2. Predicting the marker's position

As reported above, a linear regression model was created with the firing rate of single neurons as predictors and marker's positions as predicted values, decomposing their coordinates into x, y and z axes (see Figure 9 for axes orientation). Thus, we examined the possibility of predicting marker's positions on x, y and z axes, starting from neurons firing rate. Then real marker's positions and predicted values were plotted to provide comparative evidence of prediction accuracy (see Figures 13 and 14). Concerning the visual condition, this procedure was next repeated using as predictors the neural activity only during the horizontal stimulations, then only during the vertical stimulations, eventually only during the stimulations in depth (see Figures 15 and 16). Overall, the results are consistent between the two neurons groups, both for the tactile condition and for the visual condition. It seems that greater accuracy is obtained in the tactile (e.g., Figure 13A) than in the visual (e.g., Figure 13D) condition, although along the y axis the values of R^2 are higher in the visual condition. Concerning the tactile condition, the

greater accuracy is achieved along z axis (the hole in the graphs could coincide with the eye positions). As far as the visual condition during whole stimulations is concerned, we can find a better ability to predict marker's position along y axis. Furthermore, it seems that a greater accuracy could be observed when visual stimulations were performed in ipsilateral hemisphere (e.g., Figure 13E). The lowest values of R^2 can be found for the whole visual stimulations, if we compare these with the several type of visual stimulations. If we compare the single type of visual stimulations (horizontal, vertical and in depth), we can notice a better prediction ability along y axis for each type of stimulations. It seems that a greater accuracy during stimulations in depth is present in the first set of neurons, whereas this effect is unclear in the second set.

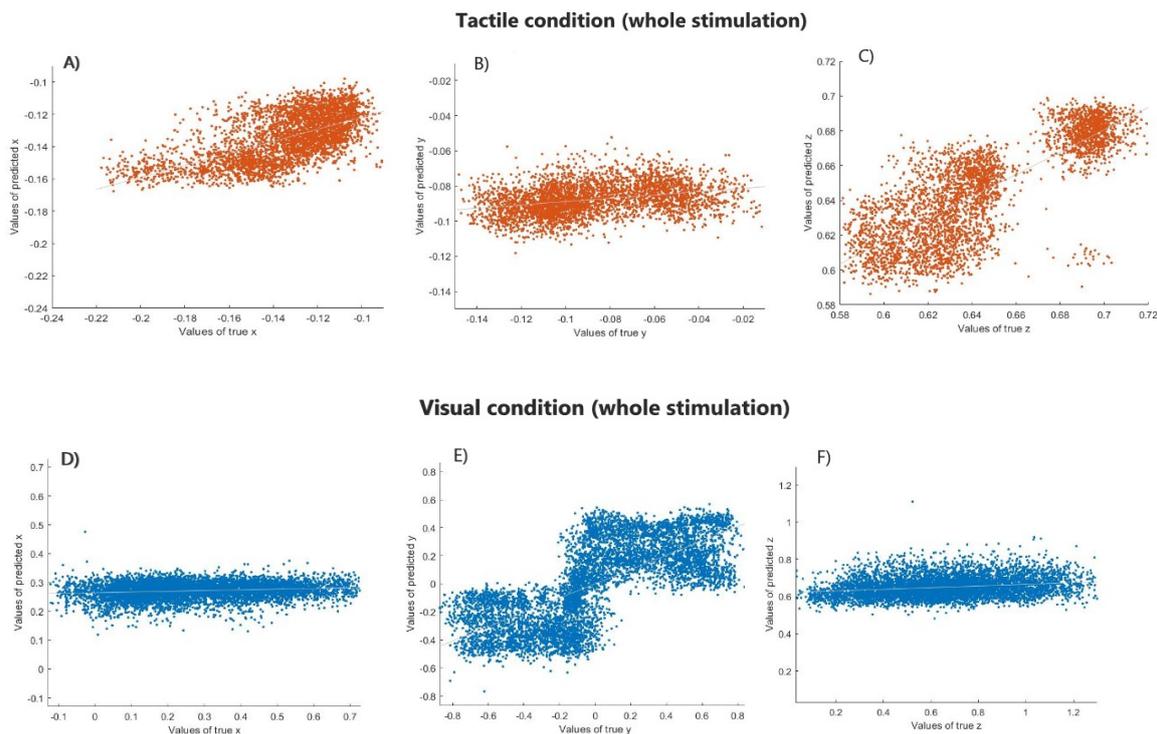


Figure 13. Prediction of marker's position, starting from firing rate (first neurons group). The decoding of marker's position in tactile condition (face) is shown in A, B and C, respectively for axis x, y and z (A) $R^2 = .37$; B) $R^2 = .09$; C) $R^2 = .64$). D, E and F display the prediction of marker's position in visual condition, respectively for axis x, y and z (D) $R^2 = .03$; E) $R^2 = .50$; F) $R^2 = .04$). In each scatter plot, the horizontal axis represents the real positions, whereas the vertical axis shows the predicted positions by the linear regression model.

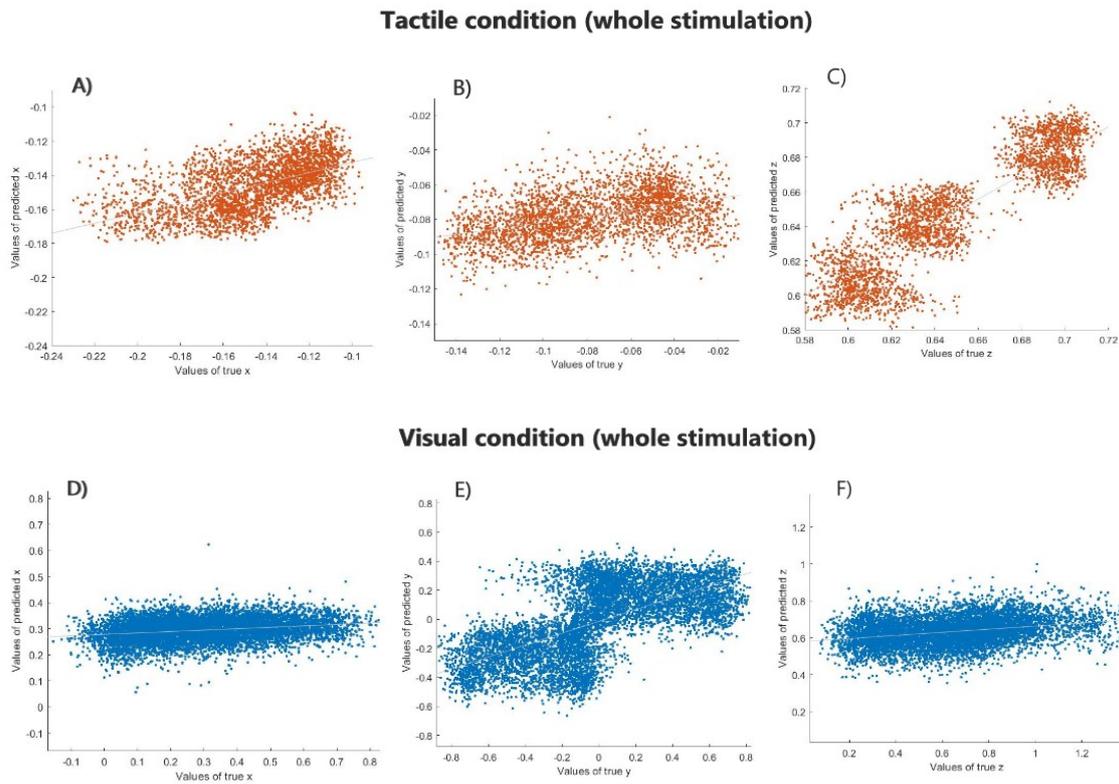


Figure 14. Prediction of marker's position, starting from firing rate (second neurons group). The decoding of marker's position in tactile condition (face) is shown in A, B and C, respectively for axis x, y and z (A) $R^2 = .30$; B) $R^2 = .17$; C) $R^2 = .70$). D, E and F display the prediction of marker's position in visual condition, respectively for axis x, y and z (D) $R^2 = .05$; E) $R^2 = .41$; F) $R^2 = .08$). In each scatter plot, the horizontal axis represents the real positions, whereas the vertical axis shows the predicted positions by the linear regression model.

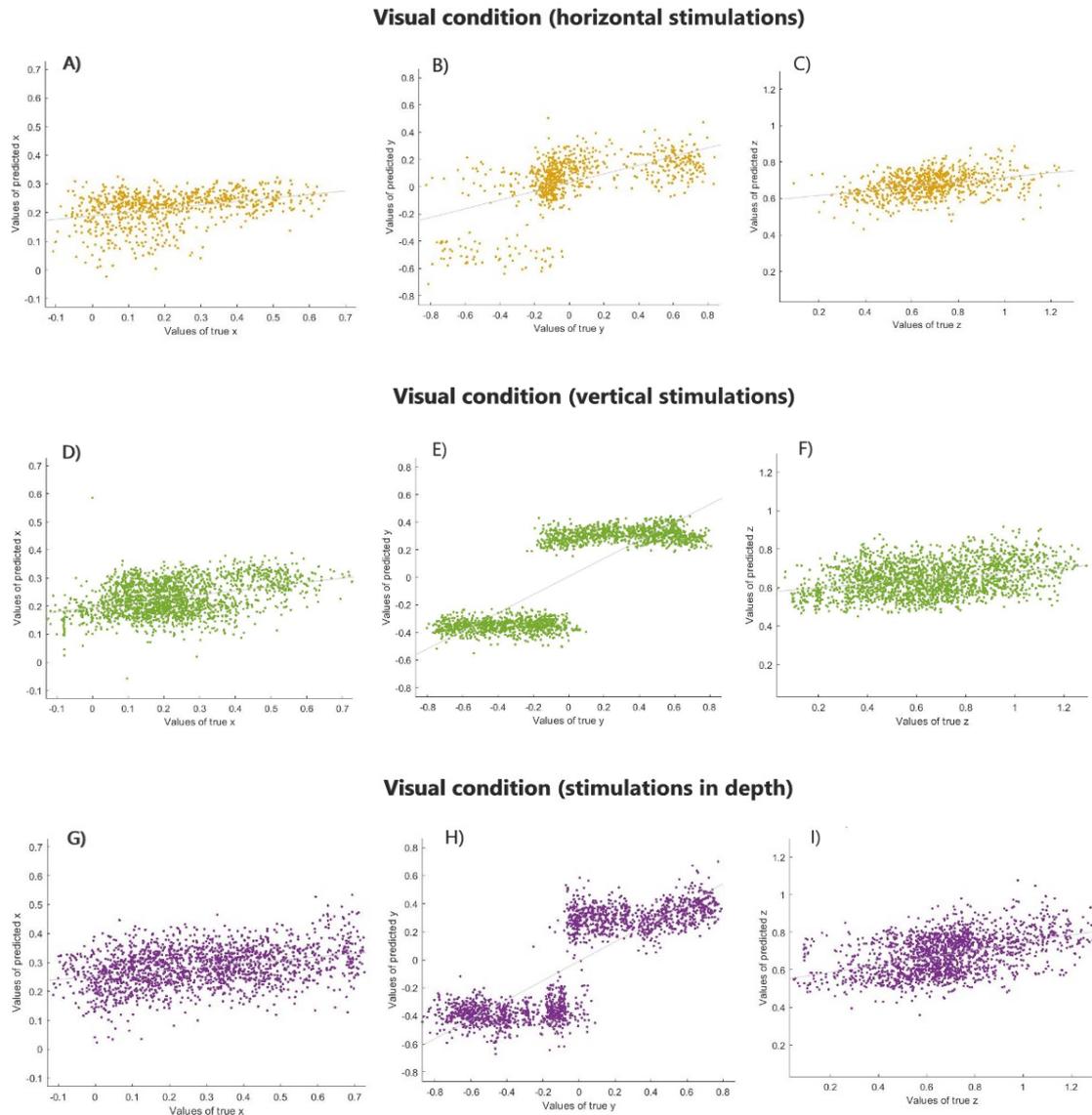


Figure 15. Prediction of marker's position during visual condition, starting from firing rate (first neurons group). The decoding of marker's position during the horizontal stimulations is shown in A, B and C, respectively for axis x, y and z (A) $R^2 = .12$; B) $R^2 = .32$; C) $R^2 = .12$). D, E and F display the prediction of marker's position during the vertical stimulations, respectively for axis x, y and z (D) $R^2 = .15$; E) $R^2 = .65$; F) $R^2 = .11$). Finally, the prediction of marker's position during the stimulations in depth is shown in G, H and I, respectively for axis x, y and z (D) $R^2 = .11$; E) $R^2 = .69$; F) $R^2 = .20$). In each scatter plot, the horizontal axis represents the real positions, whereas the vertical axis shows the predicted positions by the linear regression model.

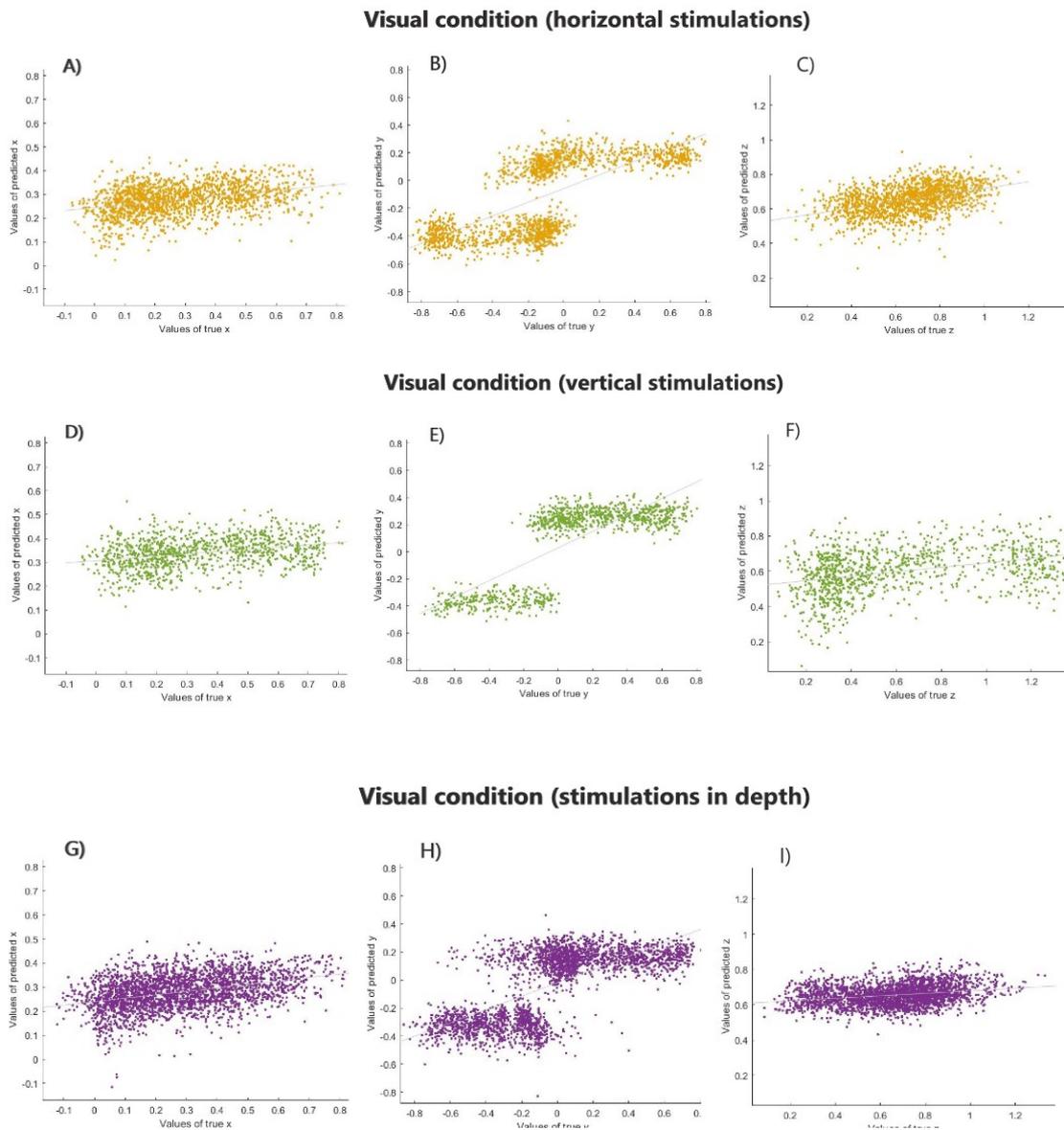


Figure 16. Prediction of marker's position during visual condition, starting from firing rate (second neurons group). The decoding of marker's position during the horizontal stimulations is shown in A, B and C, respectively for axis x, y and z (A) $R^2 = .12$; B) $R^2 = .49$; C) $R^2 = .19$). D, E and F display the prediction of marker's position during the vertical stimulations, respectively for axis x, y and z (D) $R^2 = .09$; E) $R^2 = .61$; F) $R^2 = .13$). Finally, the prediction of marker's position during the stimulations in depth is shown in G, H and I, respectively for axis x, y and z (D) $R^2 = .14$; E) $R^2 = .47$; F) $R^2 = .07$). In each scatter plot, the horizontal axis represents the real positions, whereas the vertical axis shows the predicted positions by the linear regression model.

5. DISCUSSION

“... a World Full of Action Choices”

(Cisek & Kalaska, 2010)

We live in a complex world and our brain needs to represent external stimuli within the space around us, so as to perceive and interact with them. Although our experience of space appears unitary, uniform and continuous, a collection of multiple spatial representations is held in our brain: the personal space (body surface), the peripersonal space (close to body) and the extrapersonal space (far from the body). Particularly, the PPS constitutes a relevant sector of space, because all physical interactions between the individual and the environment occurs within it; however, defining the peripersonal space is a strenuous challenge, due to the complexity of this construct. Multisensory neurons appear to play a key role in the peripersonal space representation and, surprisingly, they were found in some regions of the motor system, like the ventral premotor area F4 (e.g., Rizzolatti et al., 1981).

In the current study, we recorded the activity of single single-units and multi-units from area F4 with multielectrode array, while a macaque monkey was sitting on a primate chair (head-fixed) and two type of stimulations were performed by experimenter: tactile stimulations on monkey's face and its upper body, and visual stimulations along both contralateral and ipsilateral hemispace. To investigate the relationship between stimulation and neuronal activity, we first built a firing rate map for each single unit; then, we created a linear regression model using neural responses as predictors and object positions as predicted values.

By evaluating the firing rate maps, we found that our data are in line with previous work showing that area F4 hosts neurons with somatosensory and visual response properties (e.g., Graziano et al. 1994; Fogassi et al., 1996). Indeed, the recorded neurons discharge to the tactile stimulation of the face, forelimbs or trunk; they also responded during visual stimulations, up to 70 cm. The firing rate maps show that the neural activity changes gradually along the three spatial dimensions, as emerged from other studies (e.g., Graziano et al., 1997a; Duhamel et al. 1998).

We next examined how the recorded neurons might form a population-level representation of visuo-tactile stimulations. Thanks to a decoding model, it is sought to predict stimulus properties (in this case its position) with a linear combination of neural responses. For instance, the neural decoding finds considerable applications in Brain Machine Interface, like neural prosthesis (Hatsopoulos & Donoghue, 2009). Our results suggest that neural ensembles encode object positions both during tactile stimulations and during visual stimulations. A better accuracy seems to be achieved in the decoding of tactile stimuli, particularly when the stimulation occurs along z axis. Concerning the visual condition, it appears more difficult to predict the stimuli position in the course of the whole stimulations instead of during a single type of stimulation, likely due to a wider range of possible movements. It is not completely clear which kind of visual stimulations yield the best decoding accuracy, but increasing the data set may certainly help to get more precise and reliable results. We observed a greater ability to predict the object position along the horizontal axis, in agreement with previous studies emphasizing that “the terrestrial life needs more horizontal scanning than vertical scanning” (Kobayashi & Kohshima, 2001).

These data arise from preliminary analysis of multielectrode neural recordings in the macaque premotor cortex. Only single-units are considered, but next steps may consider to use multi-unit activity as well. It could also be interesting to compare the tactile and the visual properties of each single and multi-unit, examining a possible visuo-tactile matching, as reported by previous studies (Fogassi et al., 1996). Furthermore, control conditions could be added, in order to avoid confounding factors associated with the nature of the object used for the stimulation or the type of stimulation applied (e.g. by placing a different object at the end of the stick).

The apparatus employed in this study reflects classical laboratory settings (for example, the use of a primate chair). However, the findings obtained in this setting can be compared with those collected on the same neurons recorded during freely behaving sessions in which the monkey move spontaneously and actively during active exploration of the environment (Bonini, 2019), thereby increasing the ecological validity of the findings and comparing passive stimulations with active changes in the body-object positions because of monkey's active movement.

The values of PPS fields likely correspond with the relevance of potential motor actions in relation to the stimuli (Bufacchi and Iannetti 2018), suggesting that “contact-related behavioural relevance” refers to the perspective of interactive behaviour: according to this theoretical framework, “interaction with the environment involves continuous and simultaneous processes of sensorimotor control and action selection from among the distributed representations of a limited number of response options” (Cisek & Kalaska, 2010). The parietal and premotor cortices – the cortical regions thought to underlie the peripersonal space representation – appear to take on great relevance the potential actions' specification (e.g.,

Whitlock et al., 2008). Future studies will be crucial to elucidate how the mechanisms so far revealed in constrained behavioural conditions may apply or work in a different way during unconstrained, active interactions of a subject with its physical and social environment.

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