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Neuronal encoding of multisensory motion features in the rat associative parietal cortex

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Abstract

Motion perception is facilitated by the interplay of various sensory channels. In rodents, the cortical areas involved in multisensory motion coding remains to be identified. Using voltage-sensitive-dye imaging, we revealed a visuo-tactile convergent region which anatomically corresponds to the associative parietal cortex (APC). Single unit responses to moving visual gratings or whiskers deflections revealed a specific coding of motion characteristics strikingly found in both sensory modalities. The heteromodality of this region was further supported by a large proportion of bimodal neurons and by a classification procedure revealing that APC carries information about motion features, sensory origin and multisensory direction-congruency. Altogether, the results point to a central role of APC in multisensory integration for motion perception.

Introduction

Our ability to extract and process motion information is crucial to navigate in and enable interactions with the environment. Combining information from several sensory modalities facilitates motion

perception by providing precisions about the characteristics of the movement or by disambiguating incongruent sensory cues to distinguish object- from self-motion (Chancel et al., 2016; Landy et al., 2012; Prsa et al., 2012).

In the specific context of motion perception, neurons sensitive to the direction of visual cues have been located in the nonhuman primate, in the mediotemporal areas MT and MST. These areas have thus been traditionally considered as visual motion areas (for a review: Born and Bradley, 2005a; Dubner and Zeki, 1971; Lagae et al., 1993). Other cortical areas have been proposed to be involved in visual motion processing. Area V3, for instance, contains “real-motion” cells (Galletti et al., 1990), and its perturbation by inhibitory rTMS induces deficits in speed discrimination (McKeefry et al., 2008) ; area V6 (for a review in macaque and human: (Fattori et al., 2009)) could be involved in distinguishing object- from self-motion (Pitzalis et al., 2010); area 7a containing neurons with specialized tuning to several aspects of motion flow (Siegel and Read, 1997) in macaques has been proposed to bring a new representation of motion beyond MT and MST or parietal areas (VIP, LIP, etc) (Bremmer et al., 2002; Duhamel et al., 1998).

Motion perception, arising frequently from multisensory inputs, should be considered in a global sensory framework, in which neuronal populations process and integrate multiple information. While early views of sensory processing proposed the segregation of sensory information, especially in primary areas, the studies of multisensory integration mechanisms have been tackling this parcellation concept in the past decade (Cappe et al., 2009; Cappe and Barone, 2005; Ghazanfar and Schroeder, 2006; Klemen and Chambers, 2012; Wallace et al., 2004). In particular, the MT/MST complex, initially classified as part of the visual system, has more recently been found to host multisensory integrative mechanisms. Several studies demonstrated that dorsal MST is not only involved in the processing of visual cues but also of vestibular information for self-motion perception (Fetsch et al., 2012; Gu, 2006; Gu et al., 2008). In humans, several neuroimaging studies consistently found that hMT+, the human cortical complex comprising areas MT and MST, was activated when an

illusory movement of self-body was elicited by an optic flow (Deutschländer et al., 2004; Kovacs et al., 2008; Previc et al., 2000; Wall and Smith, 2008). Interestingly, hMT+ was also found to be sensitive to multisensory stimuli (Blake et al., 2004; Saldern and Noppeney, 2013; Van Kemenade et al., 2014). Other regions appear to be specifically associated with the sensation of body movement: the intraparietal sulcus (Kovacs et al., 2008; Wall and Smith, 2008), the homologue of the multisensory VIP area in monkeys whose neurons are sensitive to moving vestibular and somatosensory stimuli (Bremmer et al., 2002; Duhamel et al., 1998) and the parieto-temporal retro-insular region (Previc et al., 2000). Specifically, visuo-tactile convergence is generally reported to occur in both low-level processing visual and somatosensory areas and higher-order areas including the posterior and anterior parietal cortex, the superior temporal sulcus and area MST (Guipponi et al., 2015). Overall, both macaques and humans studies stress that movement coding must take place in heteromodal regions that can integrate several sensory cues, congruent with the multisensory experience of motion in the environment.

A first investigation in rats using c-Fos immunoreactivity revealed the selective responsiveness of the associative parietal cortex (APC) to visual motion (Montero and Jian, 1995) compared to static visual stimuli, similarly to MT/MST. Later, the APC was functionally explored in mice in which neuronal modulations to visual moving stimuli was reported (Andermann et al., 2011; Juavinett and Callaway, 2015; Marshel et al., 2011). However, none of these previous studies have investigated the putative direction selectivity of APC neurons to moving visual stimuli which would provide a strong evidence to designate APC as a motion processing area. The location of this cortical region, although not well delimited anatomically in the rat – partly due to the multiple ways used to divide the parietal cortex - could favor multisensory integration as it is located at the junction of all major primary sensory areas (Brett-Green et al., 2003; Toldi et al., 1986; Wallace et al., 2004). APC is also anatomically connected to the primary sensory areas, as it receives inputs from the auditory, visual and somatosensory cortices (Miller and Vogt, 1984; Sanderson et al., 1991; Wang et al., 2012, 2011 ; for a review see : Wilber et al., 2015 ; Olsen and Witter, 2016). Even though these anatomical characteristics designate

APC a good candidate as a heteromodal region of multisensory integration processing, the available functional evidence is still scarce.

Two main studies give important clues about the processing of visual and somatosensory information in APC (Lippert et al., 2013; Olcese et al., 2013). While they provide a fertile ground for the exploration of heteromodal processing in APC, they did not search for essential neuronal features defining a multisensory motion area. Indeed, any movement is defined by its direction and speed, and neurons displaying motion sensitivity should exhibit response selectivity to these attributes. Moreover, multiunit recording techniques used in the above-mentioned studies did not allow the characterization of individual neurons' responses and thus could not provide conclusive information about the bimodality of APC neurons. Furthermore, individual neuron responses to concomitant moving visuo-tactile stimuli have never been investigated so far in APC.

Therefore, the present study was designed to find out in the rat whether visual and tactile inputs converge onto the APC and whether it processes motion specifically, by testing the individual neurons' responses to characteristics relevant to motion processing. Our purpose was to search for APC neurons responding to both visual and somatosensory moving stimuli and characterize their response properties. We used Voltage-Sensitive-Dye imaging (VSDI) to identify the cortical zone of functional convergence of tactile and visual inputs within the APC, and single-unit recordings to investigate the uni- and bi-modal processing of these sensory inputs. Rats were exposed to moving visual gratings and to air puffs deflecting bilaterally all the whiskers, in the antero-posterior or postero-anterior direction, to mimic motion evoked during the animal's whole-body self-displacement. When delivered simultaneously, visual and tactile stimuli could be either in the same or opposite direction (congruent or incongruent). Our study provides the first single-unit evidence of direction tuning of both visual and tactile neurons within the APC, demonstrating the contribution of APC to the encoding of multisensory features of movement. Moreover, in the population of recorded cells, an important proportion of bimodal neurons was characterized by a visual and/or tactile

directional selectivity, among which the potential integrative function was evidenced by a decoding approach.

Materials and Methods

Animals

All experiments were performed in compliance with the recommendations of Laboratory Animal Care and in accordance with Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes.

Male Long-Evans rats housed in a naturalistic environment were used in this study. This environment consisted of 1 m³ cages, each housing six rats, with sets of objects enabling exploration.

Surgery and recordings

We used voltage-sensitive dye imaging to locate the APC in 5 rats, but only images acquired in two animals were usable, due to technical issues (low or loss of fluorescence, low signal-to-noise ratio or animal physiology). The electrophysiological recordings were performed in 10 rats to characterize the response properties of single neurons. Anesthesia was induced with intraperitoneal injection of ketamine (Ketamine 1000; 25 mg/kg; Virbac, France) and medetomidine (Domitor; 0.25 mg/kg; Orion Corporation, Finland). The level of anesthesia was monitored by testing the hindpaw reflex to pinch and maintained using half of the initial dose. A local anesthetic (Xylocaïne, Xylovet, France) was applied on the scalp and to the external auditory canal to minimize pain generated by the ear-bars. The animal head was secured to a stereotaxic apparatus and a unilateral craniotomy was performed in the right hemisphere to expose a region encompassing the associative parietal cortex and a part of the primary visual and somatosensory areas (AP : -3 mm to -8 mm, ML : 3 mm to 8 mm from Bregma; (Paxinos and Watson, 2013). The dura was removed to expose the cortical area of interest. Body temperature was controlled and kept constant (around 38 °C) using a probe and a thermoregulated

heating blanket. Hydration was maintained with a subcutaneous injection of glucose (5%, 0.25 ml) and sodium chloride (NaCl, 0.25 ml). At the completion of experiment, the animal received a lethal dose of embutramide (T61, Med'Vet, France).

Method details

Voltage-Sensitive-Dye Imaging

For the VSDI experiments, a tracheotomy was performed before the craniotomy as the animal was subsequently maintained under artificial ventilation. The electrocardiogram was also monitored by placing subcutaneous electrodes. To avoid the intratracheal secretions and bradycardia, atropine sulfate (0.05mg/kg, Aguetant, France) was injected at the induction and during the maintenance of anesthesia.

Voltage-sensitive dye (RH1691) was dissolved in artificial cerebrospinal fluid (1 mg in 1 ml). A sponge soaked with this mix was placed on the cortical surface for 2 hours, including a dye re-soaking after one hour. The cortex was then washed abundantly with an isotonic saline solution (20 ml). Finally, agar gel (1%) was deposited on the cortex to avoid desiccation, while preserving transparency during recording of the optical signals. As respiration and heartbeat generate movements of the cortex, the signal acquisition was synchronized to both the start of inspiration and heart beats to improve image stability and signal-to-noise ratio during acquisition. A recording session consisted of blocs in which trials were acquired every 10 seconds. In each trial, 256 images of 100*100 pixels were captured with a sampling rate of 3 ms using a high-speed CMOS based camera (MiCAM Ultima, SciMedia; Japan). Each trial acquired after a stimulation, a trial "stim", was followed by a trial acquired after no stimulation, a trial "blank", serving as a reference. Each bloc consisted of trials of visual and/or somatosensory stimulations, presented in a pseudo-random order. Given the set of lenses used, the fluorescence emitted in the cortical zone investigated images of 5x5 mm, with a spatial resolution of 50 μ m.

Electrophysiology

Neural activity was acquired using a 16-channels tungsten microelectrode array (MEA, Alpha-Omega; Israël). Two neighboring electrodes were separated by 250 μm . The 2 rows of 8 electrodes were also separated by 250 μm . Reference and ground electrodes were respectively located near electrode 1 and 8 of the array, reducing the uncertainty about the source location of the recorded LFP signal (Kajikawa and Schroeder, 2011). The position of the microelectrode array was adjusted using a motorized micromanipulator to reach the stereotaxic coordinates of the associative parietal cortex (Paxinos and Watson, 2013). The signal was amplified, filtered and digitized with a commercially available neurophysiological system (multichannel acquisition processor, MAP system, Plexon; TX, USA). LFPs (1 to 200 Hz at 1 kHz) and spiking activity (400 Hz-5000 Hz at 22000 kHz) were stored. Isolation of single units and discrimination of waveforms were performed online, then refined offline using principal component analysis with commercially available software (Offline Sorter, Plexon, TX, USA). We checked that the neurons, were single units on the basis of interspikes-interval measurement and waveform analysis (Figure S6).

In this study, the two recording techniques (VSDI and electrophysiological recordings) were used separately in different animals.

Sensory stimulations

Visual stimuli were presented for 500 ms on a screen (monitor size: 34*28 cm, frequency: 60Hz, resolution: 1024*920, pixel resolution: 33 μm) placed laterally at 15 cm from the animal's head. They consisted in moving visual sinusoidal gratings (contrast: 250/1) in two opposite directions, with two motion speeds (5 and 10 cycles/second) and a period of 0.05 cycles/degree. A uniformly grey screen was always shown between the visual stimulations, with a mean luminance of 46 candela/m², corresponding to that of the gratings.

The whisker stimulations consisted of continuous puffs of pressurized air (3.5-4 bars, 500 ms) deflecting bilaterally all the whiskers either in the antero-posterior (backward) or postero-anterior (forward) direction, to mimic passive whisker movement during the animal's motion. We used four custom-designed funneled-air-nozzles (length: 4cm, width: 1.2 cm, 3 rows of 12 holes; diameters of holes: 3 mm; see Figure S1) which size allowed the deflection of all the whiskers. This set-up was fixed on a frame enabling the appropriate and independent orientation and stability of all 4 air-puffs. The air puffs delivery system was positioned for each animal to assess visually that all whiskers were systematically deflected and remained in the deflected position throughout the stimulation duration. We also checked that the whiskers came back to their original position when the stimulus was stopped. We ensured that the air puffs did not induce any auditory evoked response by positioning the air puffs so that they did not provide any somatosensory stimulation, by putting them upwards towards the ceiling. When doing so, we did not find any evoked neuronal response. The whiskers were stimulated in total darkness - except when visual and whisker stimuli were presented simultaneously. The anesthesia prevented the contamination of the sensory-evoked neuronal responses by spontaneous whisking.

The choice of using only two visual and tactile directions intended to reproduce ecologically-valid sensory stimulations. Visual and tactile stimuli were delivered either separately or concurrently, in a congruent (same direction) or incongruent (opposite direction) manner. Both sensory stimulations were pseudo-randomly presented. As VSDI was devoted to the localization of APC, all conditions in each modality were pooled together in the same analyses.

Quantification and Statistical Analysis

VSDI analyses

To reveal the spatial convergence of visual and tactile inputs, we used VSDI which has been shown to capture mostly sub-threshold activity in the superficial cortical layers 2/3 (Ferezou et al., 2006). The

matrices of the 256 images composing each trial were extracted and reconstructed. A gaussian filter with a 1 pixel-wide standard deviation was then applied on these matrices, resulting in an image filtered in all directions. To obtain a sequence of images corresponding to the evoked response, the evoked fluorescence of each “stim” trial was divided by the filtered fluorescence values of the following “blank” trial, pixel by pixel (DF/F). Only intra-subject analyses were performed on the VSDI acquisitions. For each block, the images obtained for all the trials in each stimulation condition were then averaged. For each region of interest (ROI), the mean responses (DF/F) to each stimulus were computed in a temporal window of 0 to 500 ms following the stimulus. The distribution of the optical response across trials (not the average activity) for each sensory-evoked response was compared to the distribution of the baseline signal (-100 to 0ms). Since the Kolmogorov-Smirnov test showed that the distributions were not normal, we performed non-parametric Wilcoxon tests. The significance of the evoked fluorescence (“stim” trials divided by “blank” trials) was tested against baseline in the ROIs using Wilcoxon test with a significant level set at $p < 0.05$.

Maximum Fluorescence Maps. To determine the spatial location of the evoked responses, the maximum DF/F recorded, regardless of the time of occurrence within the trial, were extracted for unimodal visual (max v) and tactile (max t) stimulations. These values were then normalized with respect to the maximum between these conditions.

Selectivity Maps. To highlight the regions in which one of the unimodal evoked response was greater than the other, a contrast of selectivity by condition was computed: visual contrast = $\frac{\max v - \max t}{\max t}$, somatosensory contrast = $\frac{\max t - \max v}{\max v}$. Then, to determine the regions showing a fluorescence modulation for both sensory modalities, we defined a selectivity map computed by adding the absolute values of the previously obtained contrasts: selectivity index = |visual contrast| + |tactile contrast|. The selectivity index was zero for a pixel which had exactly the same fluorescence amplitude for both unimodal stimulations. The more a cortical region was selective to one modality, the more the value of the selectivity index increased.

Units' analyses

All analyses were performed using home-made programs (MATLAB, Mathworks). For each neuron recorded, and for each trial, the action potentials were realigned on the stimulations. As the response latencies to the somatosensory and visual stimuli were different, a sliding window test (window size: 40 ms, window step: 20 ms, time tested: 0-600 ms from stimulus onset) was performed on each neuron to determine, using Student t-tests (Bonferroni correction for multiple comparisons), whether it responded significantly to the different stimulation conditions. When the baseline activity was different from zero (t-test vs. 0, $p < 0.05$), a two-sampled t-test was performed to compare the post-stimulus spiking activity to baseline. If baseline was not significantly different from zero, we used a one-sampled t-test. This sliding test allowed the extraction of the timing of the evoked response for each neuron in each stimulation condition. This approach allowed us to define the uni- and bimodal neurons and to quantify their proportions, which we further confirmed using a receiver operating characteristic (ROC) analysis (Figure S5). Latencies of bimodal neurons to unimodal stimuli were compared using a Wilcoxon-Mann-Whitney rank-sum test. A neuron was considered as selective to the direction of visual stimulation if it responded exclusively to one of the stimulus directions presented. The same classification was applied for visual speed selectivity and whisker deflection direction selectivity. The selectivity to direction in visual and somatosensory conditions allowed us to define the neurons' coherencies. A neuron was classified as coherent when selective to the same direction of motion in both sensory modalities.

We performed a decoding analysis to classify between the two unimodal conditions (visual and somatosensory) in the two different directions (forward and backward). This analysis queried whether the bimodal neurons code for the modality (visual vs. somatosensory) and/or the direction of the stimulus (forward vs. backward). To this end, our classifier takes a set of training data and training labels (2 visual and 2 somatosensory directions) and learns a model of the relationship between the training data and the labels from the different classes. The training data are spikes that

are counted in 100 ms-bins that advance with a step size of 50 ms; and this from -100 ms to 700 ms relative to stimulus onset. Once this model has been learned, the classifier was then used to make predictions about what labels were present in a new set of 'test data' (Meyers, 2013). The information contained in the trained data set changes over time, the trained model was then different for each time point. We used a maximal correlation coefficient classifier (MCC) as implemented in the neural decoding toolbox (ndt) developed by (Meyers, 2013). The MCC learns a mean population vector for each category of the training set. The classifier is tested by calculating a Pearson's correlation coefficient between a test point and the templates learned from the training set, and the class with the highest correlation value is returned as the predicted label. The MCC computed a mean template \bar{x}_i for each condition and assigned the condition $i^* = \text{argmax}_i \text{corr}(x^*, \bar{x}_i)$ for test trial x^* . The decision values returned by the classifier are the correlation coefficients between all test points and all templates. We used a 10-fold cross-validation; for each repetition, 10 trials from each condition were randomly chosen from each neuron. One trial from each condition was used for testing and the remaining 9 were used for training the algorithm. All possibilities were tested, and this process was repeated 100 times with different groups of trials, resulting in a total of 1000 runs. We estimated the null distribution by repeating the described procedure after shuffling the labels of the conditions. For a given time bin, the classifier gives us its prediction regarding the stimulus label. We then compared this prediction to the real label corresponding to the trained trial. The percentage in the confusion matrix corresponds to the percentage of correct predictions made by the classifier. The percentage of classification accuracies from the MCC classifier were extracted for each time bins. The significance of the classification accuracies for each label, at each time point, was compared to the distribution of the shuffled accuracies using Wilcoxon non-parametric tests, with a multiple-comparison Bonferroni correction (Figure 3E). A peri-stimulus time matrix was constructed to determine the relevant time bins for which individual confusion matrices were derived. In order to extract the time windows for which the classification accuracy was larger than those of the shuffled data, we compared the distribution of classification accuracies from the data to the classification

accuracy from the shuffled data from each cross-validation for each time bin (Wilcoxon non-parametric test, Bonferroni corrected).

This classification algorithm was also used to decode the uni- and bi-modality congruency (congruent and incongruent) of the stimuli, based on the neuronal firing of the bimodal neurons. In fact, this classification approach was performed on the unimodal visual and somatosensory neurons but did not yield significant decoding accuracies (Figure S7).

As the unimodal results emphasized the importance of the neuron's direction selectivity, we took this property into account by only testing the bimodal neurons with a direction selectivity in the modality of interest. We thus performed two separate decoding analyses: one based on the direction selectivity in the visual modality (Figure 4B), the other in the somatosensory modality (Figure 4F). Only the neurons preferring either the forward or the backward direction were included in each analysis. This choice was made to take out the dependency of the neuron's response on the neuron's direction selectivity. For instance, in the visual-direction-based decoding, for a bimodal neuron preferring visual backward, the congruent condition is visual backward and somatosensory backward, and the incongruent condition is visual backward and somatosensory forward. We thus compared the neuron's response to its preferred unimodal direction and its responses to the corresponding bimodal congruent and incongruent stimulation. The training labels were thus "unimodal – preferred direction", "congruent", and "incongruent". We assigned these new labels depending on the unimodal preferred direction of each neuron. These analytical choices allowed to reveal congruency effects linked to the addition of another sensory motion information to the preferred direction for a given sensory modality.

Results

Convergence of visual and somatosensory inputs onto the APC

The VSDI acquisitions revealed that the unimodal stimulations evoked focal increases in relative fluorescence change (DF/F) with well differentiated time windows between modalities (visual: 150-350 ms, somatosensory: 59-90 ms) in the anterior and posterior regions of the acquisition window (Figure 1A). These regions fall into the whisker area of the primary somatosensory cortex (S1) and to the primary visual cortex (V1), respectively, as anatomically delineated based on the craniotomy's coordinates (Paxinos and Watson, 2013). Typically, the latency of the responses evoked by the whisker stimulation was shorter (mean medians \pm s.e.m.: 59 ± 4.24 ms) than that induced by the visual stimulation (152 ± 8.48 ms) (Figure 1B). While the whisker stimulation evoked a sharp response, the visual response was delayed and of longer duration. The activations then spread laterally and medially for the somatosensory condition (Figure 1A, upper row), and anteriorly for the visual condition (Figure 1A, lower row).

To disclose a potential zone of convergence of the unimodal stimuli, a map of maximum response and a map of selectivity were extracted for each unimodal stimulation (Figure 1C-D). The selectivity computed for each pixel yielded a mesh map that reflected whether the evoked DF/F was high for both sensory stimuli (i.e. the pixel value revealed a low selectivity) or whether only one modality induced an activation of the pixel (i.e. highest selectivity). This analysis highlighted a strong unimodal selectivity within V1 and S1 for visual and somatosensory stimulation, respectively (Figure 1D; Rat 1: S1: 1.05 ± 0.25 , V1: 0.98 ± 0.07 , Rat 2: S1: 0.96 ± 0.08 , V1: 0.82 ± 0.07). Nevertheless, the visual stimulus also evoked a significant response, as compared to baseline (-100 to 0 ms) in S1 (within the visual response time window : 140-330ms; Wilcoxon test: $p < 0.0001$) while the somatosensory stimulus evoked a significant response in V1 (within the somatosensory response time window: 20-140ms, $p < 0.001$) (Figure 1E).

The selectivity-index was significantly lower in a localized narrow strip than in S1 and V1 (Student's t test and Hedges'g for effect size, Rat 1: 0.09 ± 0.06 vs. V1 $p < 0.0001$ $g = 14.04$, vs. S1 t-test $p < 0.0001$ $g = 6.48$; Rat 2: 0.10 ± 0.07 vs. V1 t-test $p < 0.0001$ $g = 11.35$, vs. S1 t-test $p < 0.0001$ $g = 12.37$) (Figure 1D), thus indicating responses of similar intensity in this non-selective bimodal cortical field. It is also worth mentioning that this narrow non-selective area, located at the interface of S1 and V1, seems to correspond anatomically to the associative parietal cortex (APC, Paxinos and Watson, 2013).

Motion-specific characteristics found in visual neurons.

Targeting the convergence zone based on our VSDI analyses, on topographical data from anatomical framework (Paxinos and Watson, 2013) and on previous studies of this area (Lippert et al., 2013; Olcese et al., 2013), we recorded electrophysiological responses of 914 single neurons (Figure S2). Among them, 124 responded only to visual stimulation (14%; t-test $p < 0.05$) (Figure 2A-C, J), with a median latency of 81 ms. These visual neurons were mainly located in the posterior part of the APC, spatially closer to a cortical zone referred to as V1 (pink; Figure 2A, K ; Paxinos and Watson, 2013). We found that 51% (63/124 neurons) of these visual neurons were selective to the grating motion direction (Figure 2B), i.e. the neurons responded to only one of the two directions tested: backward vs forward, each direction being equally represented in the neuronal population tested (33/124: 27% and 30/124: 24%, respectively). Figure 2C shows an example of a visual neuron only responding to the backward visual motion direction. The remaining 61 visual neurons (61/124; 49% of the visual neuronal population) responded significantly to both directions of the gratings. In addition, 35 visual cells were tested with two grating speeds (5 and 10cycles/seconds). We found that among them, 21 neurons (21/35; 60%) were selective to one of the speeds of the visual stimulus (17/35 to 5c/s; 4/35 to 10c/s). The visual neurons thus present selectivity to motion parameters.

Motion tuning also found in APC somatosensory neurons

We further examined whether motion sensitivity properties were met in the somatosensory modality. From the sampled population recorded in APC, 135 neurons (135/914; 15%) responded only to the somatosensory stimulations (Figure 2D-F, J), with a median latency of 21.5ms. Within this population, 44 neurons (33%) responded to both whisker deflection directions (Figure 2E). An example of somatosensory neuron responding to both directions is shown in Figure 2F. A motion-direction selectivity was thus found in the remaining 67% (91/135) of the neurons (Figure 2E) with a higher number of cells responding selectively to the backward deflection (79/135; 58%), as compared to the forward deflection (12/135; 9%). Spatially, the somatosensory population was concentrated in the anterior part of the APC, closer to the anatomical localization of S1 (Figure 2D,K).

APC population greatly represented by bimodal neurons

In the population recorded in this region of visuo-tactile convergence, 42% of single cells (388/914) (Figure 2G-I, J), located at the interface of the two unisensory populations (Figure 2G, K), responded significantly to both visual and somatosensory stimulations. Among the bimodal neurons, 34% (132/388) showed a selectivity to the visual motion directions tested and 40% (155/388) to the whisker motion directions (Figure 2H). Among the bimodal neurons tested with two visual speeds, 28% (31/112) were selective to 5c/s and 11% (12/112) to 10c/s. Our latency analysis confirmed what was found for unimodal neurons, i.e., that the bimodal neurons' latencies to the unimodal stimuli were significantly different: the latency to whisker deflection was shorter (34 ± 39.2 ms; mean median \pm std) than that to visual grating motion (75 ± 51.9 ms) (Wilcoxon-Mann-Whitney rank-sum test, $p < 0.001$).

To illustrate the cortical localization of the populations recorded (visual, somatosensory and bimodal), we determined 95% confidence ellipses based on each of the population's neurons' position projected on a 2-D space, by performing an eigen decomposition (Figure 2K). By realigning

all the ellipses obtained in each animal on their own bimodal ellipse, a clear spatial organization emerged where the visual neurons recorded were mostly located in the posterior part of the convergence region, while the somatosensory neurons were at the anterior part and the bimodal neurons confined at the interface of both unimodal populations.

Bi-selective bimodal neurons in APC

In the bimodal population, visual and somatosensory motion selectivity were first studied independently. Therefore, we asked whether a bimodal neuron could show congruent visual and somatosensory direction-selectivity. In the bimodal population recorded, 65 neurons (65/388) were indeed direction-selective in both sensory modalities. Among them, 46% (30/65) were selective to the same direction of motion in both modalities, defined as directionally coherent (forward: 11%, backward: 35%). Inversely, 54% (35/65) had opposite direction-selectivity (e.g. visual selectivity to the forward direction and somatosensory selectivity to the backward direction) and were defined as directionally incoherent (forward: 17%, backward: 37%; Figure 2L, middle). A majority of the bi-selective neurons (47/65, 72%) responded only to the backward whisker deflection, while the remaining (18/65, 28%) responded to the forward whisker deflection. However, when taken separately depending on their selectivity to the somatosensory direction (Figure 2L, left and right), roughly similar proportions displayed directionally coherent and incoherent responses.

Information on direction of motion in both sensory modalities carried by APC's neuronal activity

We assessed whether APC neurons' firing contained information about motion direction in both modalities. The decoding analysis was performed over time, as the neurons' unimodal responses' latencies were separated in time. The 520 neurons tested in the 4 relevant conditions (visual / somatosensory x forward/backward) were selected for this analysis.

The global accuracy, including the four conditions, presented an abrupt increase at 50ms, remaining significant for 300ms and dropping at longer latencies (Figure 3A-B). The confusion matrices were computed at each time bin to reveal the nature of the information encoded in the neurons' firing across time (Figure 3C). The classification accuracy outreached above-chance level (25%, Figure 3D) and was significantly different from shuffled accuracies (Figure 3E) for all four conditions starting at the 50-150ms time bin. Note however, that at this time bin, the classifier was able to decode the modality of the stimulus but could only decode the direction in the somatosensory modality. Indeed, the direction of the visual stimulus could be decoded only starting at the 200-300ms bin. This is consistent with the recorded neuronal response latency differences to visual and somatosensory stimulation. After 200ms, the classifier was able to decode both the stimulus' modality and its direction. To ensure that this performance was not only due to the unimodal neurons that intrinsically carry information about the modality, and for the direction-selective cells, about the direction of the stimulus, we also carried this analysis on the bimodal sub-population of APC (Figure S9). We reveal that the classifier is able to decode, such as described above for the whole population, based only on the bimodal neurons' responses.

Multisensory responses to congruent and incongruent visuo-tactile stimuli in APC

Among the neuronal population recorded, the analysis of neurons' activity to concurrent visuotactile stimulations revealed a variety of pattern responses as exemplified in Figure 4A, which illustrates three examples of neurons' spiking activity to unimodal and bimodal stimuli. Left and right plots depict neurons responding to only one of the unimodal stimulations. However, when the other modality is added, these neurons display a modulation of their neuronal activity, even in the response time window of the modality they are not sensitive to when presented alone. Left plot shows a unimodal somatosensory neuron that decreases its spiking probability in the congruent condition, and slightly enhances it in the visual response time window. Right plot illustrates a unimodal visual neuron displaying an enhanced response in the somatosensory response time

window and a decrease in the visual one, when an incongruent somatosensory stimulus is added. On the other hand, middle plot shows a bimodal neuron that increases its response in the somatosensory response time window while decreasing it in the visual one, for both congruent and incongruent bimodal conditions. Note that these are only a subset of integrative neuronal patterns that can be observed in the population.

Due to the separated timing of the neuronal responses to each sensory modality and the great diversity in response patterns, classical indices of multisensory integration did not seem adapted. To study whether APC neurons perform multisensory integration, we therefore separately considered the different time windows of visual and somatosensory unimodal responses and compared them to their bimodal counterpart. The classification algorithm was trained to differentiate the population patterns related to the different conditions (unimodal, bimodal congruent, bimodal incongruent), taking into account the preferred direction of each neuron. This allowed to specifically test the influence of adding a stimulus in a second modality (e.g., somatosensory), with the same or opposite direction, to the response to the preferred motion direction in the first modality (e.g., visual). The previous analyses revealing a strong direction selectivity, it enabled to highlight potential congruency effects independent from this direction selectivity. The decoding performed on the bimodal population was found significant (Figure 4), unlike the decoding performed on the unimodal populations (visual and somatosensory; Figure S8). The analysis on bimodal neurons revealed that the algorithm was able to decode, in the visual time window, for a given visual direction, whether the stimulus was only visual or accompanied by a congruent or incongruent somatosensory stimulus (Figure 4B-D, statistics in Figure S7). This demonstrates that there is an integration of the visual and somatosensory stimuli at the later “visual” latencies (150-300ms). The same analysis was performed with the neuronal responses to the preferred somatosensory direction (Figure 4E-G). In the somatosensory time window, the classifier was not able to decode whether the stimulus was unimodal or bimodal, showing that the combination of tactile and visual stimulations overall did not change the spiking activity in the early “somatosensory” time window (50-200ms).

Discussion

At the interface of V1 and S1: a visuo-tactile convergence zone containing a large bimodal population

We showed the convergence of visual and tactile information, both in layer II/III as revealed by VSDI, and in layer IV as demonstrated by single-unit recordings. The VSDI results revealed a narrow strip of visual and somatosensory convergence, corresponding to the APC. The rather sharp transition from pixels exhibiting a modality preference to those showing no modality preference suggests a short spatial gradient in modality selectivity.

In particular, both whisker deflections and visual moving gratings evoked activations in the APC, with similar levels, reflecting the convergence of equally weighted visual and somatosensory information. This result is in agreement with previous findings analyzing current source density (Lippert et al., 2013) or using calcium imaging (Olcese et al., 2013), which described this region as heteromodal (Takagaki et al., 2008). However, these studies did not perform extracellular single-unit recordings and could not ascertain whether this area processes both inputs independently in separate neuronal populations, or whether it contains heteromodal neurons as candidates for multisensory integrative processing. In our study, we more specifically targeted the APC zone of multisensory convergence based on the spatial localization evidenced by VSDI, to provide an electrophysiological characterization of individual units' spiking activity, thus supplying additional information to the previous studies (Lippert et al., 2013; Olcese et al., 2013). The noteworthy finding is that the majority of the cells recorded in the APC were bimodal (42 %, out of 914 cells recorded) and precisely located at the interface of the regions spatially close to V1 and S1 in which neurons displayed unimodal visual (14%) or somatosensory (13%) responses, respectively. The existence of bimodal neurons strongly points to a potential role of the APC in heteromodal sensory integration. The proportions of neuronal types of response observed in our study are comparable to those found using multiunit recordings in

the mouse Rostro-Lateral (RL) visual area (visual: 16%, somatosensory: 19% and bimodal: 63% ; Olcese et al., 2013). However, the similarity between the mouse RL and the rat APC is limited, as RL probably corresponds only to a sub-part of APC. Indeed, not clearly delineated anatomically in the rat, the APC may correspond in mice to a region including the areas Antero-Lateral (AL) and Rostro-Lateral (RL) (Juavinett and Callaway, 2015; Marshel et al., 2011). Thus, one cannot exclude that some units were recorded either in a rat homolog of RL or in other subregions of the APC. The lack of anatomical studies (see however (Olsen and Witter, 2016; Wilber et al., 2014) in the rat prevents a precise description of the functional localization of electrode penetrations. Moreover, this associative cortex also contains other uni- and multisensory neural populations that were not targeted in our study. Indeed, at the border of V1 and A1, audio-visual facilitation was observed in the APC (Hirokawa et al., 2008), which actually contains bimodal audio-visual neurons (Xu et al., 2014). Therefore, the rodent APC can be seen as a cortical region in which converge multiple sensory information from the neighboring primary sensory areas that importantly contributes to multisensory integration guiding purposeful behavior. Our results go beyond the anatomical descriptions of the APC first made by Krieg in 1946 who proposed this area as a “meeting ground for somesthetic and visual sensations”. They are more relevant to later anatomical studies showing that the APC receives inputs from the auditory, visual and somatosensory cortices (Coogan and Burkhalter, 1993; Miller and Vogt, 1984; Sanderson et al., 1991). Our findings sustain the view that multisensory cortical regions containing heteromodal neurons and located at the interface of unisensory areas act as transitional zones where the information from multiple senses are integrated (Wallace et al., 2004).

Visual and somatosensory coding of motion in the APC

An area dedicated to the processing of motion, regardless of sensory modality, can play a pivotal role for the central nervous system to integrate the information flow brought concurrently by various senses to elaborate a coherent percept.

Visual motion coding

By analyzing the single neuron's responses to different directions, we provide the first evidence in rats of unitary spiking activity in the APC selective to visual motion parameters, direction and speed, shared features with the non-human primates' area MT (Albright, 1984; Born and Bradley, 2005b; Maunsell and Van Essen, 1983). Indeed, we found that 51% of the visual neurons recorded in the cortical region identified as APC are selective to the direction of moving visual gratings. The proportion of visual neurons recorded in the present study is higher than that found by Juavinett and Callaway (Juavinett and Callaway, 2015) in the mice RL area (18-27%), but lower than that reported in previous primate studies in which nearly all of the 100 MT recorded neurons were found to be selective to the motion direction (Albright, 1984; Maunsell and Van Essen, 1983; Mikami et al., 1986; Rust et al., 2006). Although these proportions differ, the existence of neurons selective to the stimulus direction is in favor of a specific visual motion coding in the APC. These differences with our findings could not be explained by a bias in unit location, as our neurons were recorded within the whole extent of the cortical territory between S1 and V1 (Figure S2), but rather by the fact that only two opposite gratings directions (forward and backward) were used to define the direction selectivity. Thus, a neuron that, for instance, responded only to the presentation of a downward stimulus would not be classified in our population, and would be considered as non-responsive, while it could have contributed to increase the percentage of direction selective neurons if the appropriate direction had been tested. We tested this hypothesis by recording the response of a few APC neurons (n=91) in 4 directions (upward, downward, forward and backward) of the visual moving gratings and observed that about 10% (9/91) were selective to the upward or the downward directions (Figure S3).

The selectivity to the speed of the grating motion observed in the visual neurons (27%) is an additional argument for characterizing the APC as a visual motion area. In mice, preference to particular ranges of stimulus velocity has been described by Andermann et al. (2011), with AL

neurons tuned to high speeds (20-1000°/s) and Posterior-Median neurons tuned to low speeds (1-40°/s), possibly reflecting specialization in self-motion and external motion cues, respectively. The limited range of velocities (5 and 10 c/s, see however tunings using 4 speeds in Figure S4) used in the present study did not allow to assess such spatial discrimination of the neurons recorded in the APC. We revealed a higher percentage of neurons selective to 5 c/s than to 10 c/s. A possible explanation for such a difference could be that, in ecological conditions, faster visual velocities are less frequent.

In the present study, the stimulation parameters used for both sensory modalities, were chosen to induce behaviorally relevant motion cues, but did not cover all possible directions and speeds. Thus, future studies should investigate whether a wider range of stimuli specifications like speed, direction and spatial frequencies of gratings would reveal neurons selective to other directions and speeds. Nevertheless, the characteristics of responses of the neurons recorded herein strongly suggest that the rat APC contributes to the cortical processing of visual motion and, to that extent, could be considered as a homolog of the primate areas MT and/or MST.

Somatosensory motion coding

We also investigated whether motion was coded in the somatosensory modality with selectivity features, as it was the case in the visual modality. We provide in this study the first evidence for a direction selectivity to whisker stimulation in the APC, for 61% of the somatosensory neurons. Thus, motion features were found to be extracted in either visual or somatosensory modalities by unimodal neurons. Nevertheless, an asymmetry of direction-selectivity was found in the somatosensory neurons (i.e. greater proportions were selective to the backward whisker deflection) but not in the visual neurons. This asymmetry was also observed for the biselective bimodal neurons. A potential explanation for this observation could lie in the fact that in ecological conditions, the most frequently encountered external stimulation of the whiskers is in the backward direction, as the animal moves forward.

Of particular relevance is the directional selectivity found in bimodal neurons for both sensory stimuli. We showed that similar percentages of the bimodal population recorded were selective to the direction of visual and somatosensory stimulus motion. This homogenous repartition of direction-selective cells in both modalities could suggest that there is no prevalence of one modality over the other in terms of neuronal proportions assigned to each sense.

Distinct and specific coding of motion and modality by APC neurons

Using a maximal correlation coefficient procedure as a decoding method on the bimodal neurons' response, we were able to demonstrate that information on direction of motion was contained in the spike count of populations' responses. The trained classifier was able to correctly sort out the modality and the direction of the presented stimulus, providing evidence for the APC as a heteromodal motion-coding area. Future studies should tackle this matter, for instance by modulating sensory cue reliability, to understand whether APC neurons weight sensory inputs depending on their relevance, as was shown for MST neurons (Fetsch et al., 2012).

Interestingly, the decoding accuracy was time-dependent and closely related to the neuronal response latencies. The two recording techniques used in the present study (VSDI and unit extracellular recordings) showed that the somatosensory stimulations evoked earlier responses than did the visual stimulations, both in the supragranular and granular layers. This temporal dissociation was also previously observed using current-source density (Lippert et al., 2013) and could reveal a functional purpose whereby whisker deflection, which is perceptually prominent for rodents, would exert a triggering role in the multisensory processing of motion cues during the animals' displacement, while visual inputs would confirm or rebut body motion information.

Interestingly, a recent investigation using an orientation detection task based on visual or whisker discrimination in alert rats described a different type of visual-tactile cooperation (Nikbakht et al., 2018). This study reported single units recorded in the posterior parietal cortex that displayed

identical response profiles to visual, tactile and visual-tactile orientation cues, suggesting a modality-free coding in this association area. In particular, the animals' orientation judgment was similar under these two unimodal sensory conditions. The fact that we found equivalent proportions of motion-selective neurons in the two sensory modalities could relate to this behavioral observation: both sensory modalities can be used to judge the orientation or direction of stimuli.

It is noteworthy however that, in contrast with this study, we found that the tactile response latency was twice shorter than the visual one. Such a difference can be explained by the fact that in the Nikbakht et al. study (2018), rats performed whisker palpation to discriminate various orientations, whereas in our study whisker movement resulted from passive deflection. Considering the two studies, it seems that the neuronal coding of visual and tactile motion cues and their potential functional contribution critically depends upon the perceptual context in which these sensory channels operate.

Bimodal neurons: the pivotal population for multisensory integrative processing

Strikingly, among the bimodal population recorded in the APC, 15% of the bimodal neurons showed a selectivity to both modalities, revealing directionally coherent and incoherent subpopulations. Beyond such experimentally-defined congruency, these two subpopulations might subservise distinct roles depending on the behavioral context and whether or how the animal moves (e.g., backward whisker deflection can occur together with forward visual motion as congeners are passing by while the animal is in locomotion), so that the messages generated would contribute to a contextually defined perceptual coherence. For each possible combination of visuo-tactile stimuli, one subpopulation of bi-selective APC neurons may be activated and thus convey a specific message. In addition, APC neurons may contribute to detect and integrate the motion information provided by the different sensory channels and yield "error" messages whenever the so-called incoherent neurons are activated. Nikbakht et al. (2018) provided a first substantive step in answering this questioning as they revealed that not only do the posterior cortex neurons contain information on

both stimulus orientation and modality, but the rats' perceptual judgment can be predicted by the neuronal activity. This is in favor of APC playing an important role in building up a supramodal representation of perceptual objects. Nevertheless, the available evidence left open the question of the role of APC in the more global network involved in multisensory motion perception.

Multisensory integration is usually defined as a process generating “a statistically significant difference between the number of impulses evoked by a crossmodal combination of stimuli and the number evoked by the most effective of these stimuli individually” (Stein and Meredith, 1993). Complex multisensory interactions and integrative mechanisms have been described at several levels of the nervous system, especially in the superior colliculi and several cortical regions in cats (for a review: (Stein and Stanford, 2008)). A recent study conducted in the superior colliculi of the rat also provided evidence of visuo-tactile interactions (Gharaei et al., 2018). Using concentric luminous stimulations and a mesh contacting the whiskers, the latter authors revealed bimodal neurons in the colliculi but with mainly suppressive interactions, which they attributed to the low ecological significance of these stimuli in combination. Nevertheless, while many other parameters differ, the present study provides evidence in the parietal cortex of multisensory integration of moving visual and whisker signals that are ecologically relevant. In fact, in the present study, the complexity of the neuronal activity recorded was not compatible with the classical analyses of multisensory integration. Using a decoding approach, allowing for a more global way of exploring whether and when integration occurred, we provide here the first evidence of multisensory integration in the APC that is dependent on the direction and congruency of motion cues in the visual and tactile modalities. Predictably, due to clearly separated timing of the neuronal responses to each sensory stimulation, the decoding varies across time and is significant only at certain time bins. This *machine learning* approach also allowed us to reveal that the integration of the visuo-tactile motion stimuli relies predominantly on the bimodal population as performing this decoding on the unimodal neurons did not unveil accuracies above chance (Figure S8). One cannot rule out that other integrative mechanisms might be at work in the neurons for which no direction selectivity was found.

It must be reminded that some other directions, speeds, and sensory modality could have also generated responses in the neurons that we recorded, thus leading to other population classification and other integration results.

APC and self-motion in the environment

The present work was focused on the processing of motion information in the APC and provides the very first evidence of bimodality for single units as well as direction selectivity in both the visual and somatosensory modalities in this area. Interestingly, the APC sends projections back to the visual and somatosensory cortices but also to the entorhinal cortex in mice (Wang et al., 2011). In this context, the APC could play a major role in spatial navigation by processing multisensory information to send a unified message to the entorhinal cortex related to self-body motion. Save and Poucet (2000) revealed the importance of the APC for idiothetic navigation, as rats with a lesion to this area displayed impaired performance during proximal landmarks processing. Compatibly with our findings, they proposed that the APC could provide a combined egocentric information, via multisensory integration, to the hippocampus, where the frame of reference would evolve into an allocentric one (Save et al., 1998). Several studies exploring the parietal cortex more generally point out to a role of this cortical region in translating and integrating egocentric and allocentric sensory cues, a critical role for goal-directed behaviors and trajectory adjustments during locomotion (humans: (Matthew B. Wall and Smith, 2008) ; non-human primates: (Avillac et al., 2005; Cléry et al., 2018, 2015; Zhang and Britten, 2004) ; mice: (Minderer et al., 2019) ; rats: (McNaughton et al., 1994; Nitz, 2006; Whitlock et al., 2012; Wilber et al., 2014)). The stimuli used in our studies are external stimuli that could yield self-motion perception, had we used them in awake rats. In line with previous work in rodents, non-human primates (Bremmer et al., 2002) and humans (for a comparative study: (Bremmer et al., 2001); humans: (Kovacs et al., 2008; Schindler and Bartels, 2018)), our results also argue in favor of the parietal cortex involvement in multisensory self-motion perception. Bringing together both the anatomical and functional available evidences, the APC could be seen as a hub in

which multisensory motion information converge and are integrated to contribute to the elaboration of a supramodal percept useful for interacting and navigating in one's surroundings.

Conclusion

By combining VSDI and single unit recordings, this study revealed that at the border of S1 and V1, the APC is a convergence zone of visual and tactile inputs. The neuronal population of APC is heteromodal, as it contains visual, somatosensory as well as bimodal neurons processing motion information. Functionally, the present results demonstrate that the APC hosts multisensory integrative processing that may relay perceptually coherent self-motion information to navigation-specialized areas. Such purpose could be translated to primate studies as the building up of a coherent multisensory percept of self- and external motion was traditionally found related to posterior parietal cortex.

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Authors Contribution

Conceptualization, N.C., J.C.-G., J.C., Y.Z.-A., A.K. and C.X.; Methodology, J.C.-G., J.C., N.C., Y.Z.-A. and C.X.; Software, J.C.-G., N.C.; Validation, J.C.-G., J.C., N.C., Y.Z.-A., A.K. and C.X.; Formal analysis, J.C.-G. and N.C.; Investigation, J.C.-G., N.C., Y.Z.-A. and C.X.; Writing – Original draft, J.C.-G.; Writing – Review and Editing, N.C., J.C.-G., J.C., Y.Z.-A., C.X. and A.K.; Visualization, J.C.-G and N.C.; Supervision, N.C., A.K., Y.Z.-A., and C.X. .

Competing Interests

The authors declare no competing interests.

References

- Albright, T.D., 1984. Direction and orientation selectivity of neurons in visual area MT of the macaque. *Journal of Neurophysiology* 52, 1106–1130. <https://doi.org/10.1152/jn.1984.52.6.1106>
- Andermann, M.L., Kerlin, A.M., Roumis, D.K., Glickfeld, L.L., Reid, R.C., 2011. Functional specialization of mouse higher visual cortical areas. *Neuron* 72, 1025–1039. <https://doi.org/10.1016/j.neuron.2011.11.013>
- Avillac, M., Denève, S., Olivier, E., Pouget, A., Duhamel, J.-R., 2005. Reference frames for representing visual and tactile locations in parietal cortex. *Nat. Neurosci.* 8, 941–949. <https://doi.org/10.1038/nn1480>
- Blake, R., Sobel, K. V., James, T.W., 2004. Neural synergy between kinetic vision and touch. *Psychological Science* 15, 397–402. <https://doi.org/10.1111/j.0956-7976.2004.00691.x>
- Born, R.T., Bradley, D.C., 2005a. STRUCTURE AND FUNCTION OF VISUAL AREA MT. *Annu. Rev. Neurosci.* 28, 157–189. <https://doi.org/10.1146/annurev.neuro.26.041002.131052>
- Born, R.T., Bradley, D.C., 2005b. Structure and Function of Visual Area Mt. *Annual Review of Neuroscience* 28, 157–189. <https://doi.org/10.1146/annurev.neuro.26.041002.131052>
- Bremmer, F., Klam, F., Duhamel, J.-R., Ben Hamed, S., Graf, W., 2002. Visual-vestibular interactive responses in the macaque ventral intraparietal area (VIP): Visual-vestibular interaction in primate parietal cortex. *European Journal of Neuroscience* 16, 1569–1586. <https://doi.org/10.1046/j.1460-9568.2002.02206.x>
- Bremmer, F., Schlack, A., Shah, N.J., Zafiris, O., Kubischik, M., Hoffmann, K., Zilles, K., Fink, G.R., 2001. Polymodal motion processing in posterior parietal and premotor cortex: a human fMRI study strongly implies equivalencies between humans and monkeys. *Neuron* 29, 287–296. [https://doi.org/10.1016/s0896-6273\(01\)00198-2](https://doi.org/10.1016/s0896-6273(01)00198-2)
- Brett-Green, B., Fifková, E., Larue, D.T., Winer, J.A., Barth, D.S., 2003. A multisensory zone in rat parietotemporal cortex: Intra- and extracellular physiology and thalamocortical connections. *Journal of Comparative Neurology* 460, 223–237. <https://doi.org/10.1002/cne.10637>
- Cappe, C., Barone, P., 2005. Heteromodal connections supporting multisensory integration at low levels of cortical processing in the monkey. *European Journal of Neuroscience* 22, 2886–2902. <https://doi.org/10.1111/j.1460-9568.2005.04462.x>
- Cappe, C., Rouiller, E.M., Barone, P., 2009. Multisensory anatomical pathways 1–9. <https://doi.org/10.1016/j.heares.2009.04.017>
- Chancel, M., Blanchard, C., Guerraz, M., Montagnini, A., Kavounoudias, A., 2016. Optimal visuotactile integration for velocity discrimination of self- hand movements 1522–1535. <https://doi.org/10.1152/jn.00883.2015>
- 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>
- 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>
- Coogan, T., Burkhalter, A., 1993. Hierarchical organization of areas in rat visual cortex. *The Journal of Neuroscience* 13, 3749–3772. <https://doi.org/10.1523/JNEUROSCI.13-09-03749.1993>

- Deutschländer, A., Bense, S., Stephan, T., Schwaiger, M., Dieterich, M., Brandt, T., 2004. Rollvection Versus Linearvection : Comparison of Brain Activations in PET Angela Deutschla 153, 143–153. <https://doi.org/10.1002/hbm.10155>
- Dubner, R., Zeki, S.M., 1971. Response properties and receptive fields of cells in an anatomically defined region of the superior temporal sulcus in the monkey. *Brain Research* 35, 528–532. [https://doi.org/10.1016/0006-8993\(71\)90494-X](https://doi.org/10.1016/0006-8993(71)90494-X)
- Duhamel, J.-R., Colby, C.L., Goldberg, M.E., 1998. Ventral Intraparietal Area of the Macaque: Congruent Visual and Somatic Response Properties. *Journal of Neurophysiology* 79, 126–136. <https://doi.org/10.1152/jn.1998.79.1.126>
- Fattori, P., Pitzalis, S., Galletti, C., 2009. The cortical visual area V6 in macaque and human brains. *J. Physiol. Paris* 103, 88–97. <https://doi.org/10.1016/j.jphysparis.2009.05.012>
- Ferezou, I., Bolea, S., Petersen, C.C.H., 2006. Visualizing the Cortical Representation of Whisker Touch: Voltage-Sensitive Dye Imaging in Freely Moving Mice. *Neuron* 50, 617–629. <https://doi.org/10.1016/j.neuron.2006.03.043>
- Fetsch, C.R., Pouget, A., Deangelis, G.C., Angelaki, D.E., 2012. Neural correlates of reliability-based cue weighting during multisensory integration. *Nature Neuroscience* 15, 146–154. <https://doi.org/10.1038/nn.2983>
- Galletti, C., Battaglini, P.P., Fattori, P., 1990. “Real-motion” cells in area V3A of macaque visual cortex. *Exp Brain Res* 82. <https://doi.org/10.1007/BF00230838>
- Gharaei, S., Arabzadeh, E., Solomon, S.G., 2018. Integration of visual and whisker signals in rat superior colliculus. *Sci Rep* 8, 16445. <https://doi.org/10.1038/s41598-018-34661-8>
- Ghazanfar, A.A., Schroeder, C.E., 2006. Is neocortex essentially multisensory? *Trends in Cognitive Sciences* 10, 278–285. <https://doi.org/10.1016/j.tics.2006.04.008>
- Gu, Y., 2006. Visual and Nonvisual Contributions to Three-Dimensional Heading Selectivity in the Medial Superior Temporal Area. *Journal of Neuroscience* 26, 73–85. <https://doi.org/10.1523/JNEUROSCI.2356-05.2006>
- Gu, Y., Angelaki, D.E., DeAngelis, G.C., 2008. Neural correlates of multisensory cue integration in macaque MSTd. *Nature Neuroscience* 11, 1201–1210. <https://doi.org/10.1038/nn.2191>
- Guipponi, O., Cléry, J., Odoard, S., Wardak, C., Ben Hamed, S., 2015. Whole brain mapping of visual and tactile convergence in the macaque monkey. *NeuroImage* 117, 93–102. <https://doi.org/10.1016/j.neuroimage.2015.05.022>
- Hirokawa, J., Bosch, M., Sakata, S., Sakurai, Y., Yamamori, T., 2008. Functional role of the secondary visual cortex in multisensory facilitation in rats. *Neuroscience* 153, 1402–1417. <https://doi.org/10.1016/j.neuroscience.2008.01.011>
- Juavinett, A.L., Callaway, E.M., 2015. Pattern and Component Motion Responses in Mouse Visual Cortical Areas. *Current Biology* 25, 1759–1764. <https://doi.org/10.1016/j.cub.2015.05.028>
- Kajikawa, Y., Schroeder, C.E., 2011. How local is the local field potential? *Neuron* 72, 847–858. <https://doi.org/10.1016/j.neuron.2011.09.029>
- Klemen, J., Chambers, C.D., 2012. Current perspectives and methods in studying neural mechanisms of multisensory interactions. *Neuroscience & Biobehavioral Reviews* 36, 111–133. <https://doi.org/10.1016/j.neubiorev.2011.04.015>
- Kovacs, G., Raabe, M., Greenlee, M.W., 2008. Neural Correlates of Visually Induced Self-Motion Illusion in Depth. <https://doi.org/10.1093/cercor/bhm203>
- Krieg, W.J.S., 1946. Connections of the cerebral cortex. I. The albino rat. B. Structure of the cortical areas. *Journal of Comparative Neurology* 84, 277–323. <https://doi.org/10.1002/cne.900840302>
- Lagae, L., Raiguel, S., Orban, G.A., 1993. Speed and direction selectivity of macaque middle temporal neurons. *Journal of Neurophysiology* 69, 19–39. <https://doi.org/10.1152/jn.1993.69.1.19>
- Landy, M.S., Banks, M.S., Knill, D.C., 2012. Ideal-Observer Models of Cue Integration. *Sensory Cue Integration* 5–29. <https://doi.org/10.1093/acprof:oso/9780195387247.003.0001>

- Lippert, M.T., Takagaki, K., Kayser, C., Ohl, F.W., 2013. Asymmetric Multisensory Interactions of Visual and Somatosensory Responses in a Region of the Rat Parietal Cortex. *PLoS ONE* 8. <https://doi.org/10.1371/journal.pone.0063631>
- Marshel, J.H., Garrett, M.E., Nauhaus, I., Callaway, E.M., 2011. Functional specialization of seven mouse visual cortical areas. *Neuron* 72, 1040–1054. <https://doi.org/10.1016/j.neuron.2011.12.004>
- Maunsell, J.H., Van Essen, D.C., 1983. Functional properties of neurons in middle temporal visual area of the macaque monkey. I. Selectivity for stimulus direction, speed, and orientation. *Journal of Neurophysiology* 49, 1127–1147. <https://doi.org/10.1152/jn.1983.49.5.1127>
- McKeefry, D.J., Burton, M.P., Vakrou, C., Barrett, B.T., Morland, A.B., 2008. Induced Deficits in Speed Perception by Transcranial Magnetic Stimulation of Human Cortical Areas V5/MT+ and V3A. *Journal of Neuroscience* 28, 6848–6857. <https://doi.org/10.1523/JNEUROSCI.1287-08.2008>
- McNaughton, B.L., Mizumori, S.J.Y., Barnes, C.A., Leonard, B.J., Marquis, M., Green, E.J., 1994. Cortical Representation of Motion during Unrestrained Spatial Navigation in the Rat. *Cereb Cortex* 4, 27–39. <https://doi.org/10.1093/cercor/4.1.27>
- Meyers, E.M., 2013. The neural decoding toolbox. *Front Neuroinform* 7, 8. <https://doi.org/10.3389/fninf.2013.00008>
- Mikami, A., Newsome, W.T., Wurtz, R.H., 1986. Motion selectivity in macaque visual cortex. I. Mechanisms of direction and speed selectivity in extrastriate area MT. *Journal of Neurophysiology* 55, 1308–1327. <https://doi.org/10.1152/jn.1986.55.6.1308>
- Miller, M.W., Vogt, B.A., 1984. Direct connections of rat visual cortex with sensory, motor, and association cortices. *Journal of Comparative Neurology* 226, 184–202. <https://doi.org/10.1002/cne.902260204>
- Minderer, M., Brown, K.D., Harvey, C.D., 2019. The Spatial Structure of Neural Encoding in Mouse Posterior Cortex during Navigation. *Neuron* 102, 232–248.e11. <https://doi.org/10.1016/j.neuron.2019.01.029>
- Montero, V.M., Jian, S., 1995. Induction of c-fos protein by patterned visual stimulation in central visual pathways of the rat. *Brain Research* 690, 189–199. [https://doi.org/10.1016/0006-8993\(95\)00620-6](https://doi.org/10.1016/0006-8993(95)00620-6)
- Nikbakht, N., Tafreshiha, A., Zoccolan, D., Diamond, M.E., 2018. Supralinear and Supramodal Integration of Visual and Tactile Signals in Rats: Psychophysics and Neuronal Mechanisms. *Neuron* 1–14. <https://doi.org/10.1016/j.neuron.2018.01.003>
- Nitz, D.A., 2006. Tracking route progression in the posterior parietal cortex. *Neuron* 49, 747–756. <https://doi.org/10.1016/j.neuron.2006.01.037>
- Olcese, U., Iurilli, G., Medini, P., 2013. Cellular and synaptic architecture of multisensory integration in the mouse neocortex. *Neuron* 79, 579–593. <https://doi.org/10.1016/j.neuron.2013.06.010>
- Olsen, G.M., Witter, M.P., 2016. Posterior parietal cortex of the rat: Architectural delineation and thalamic differentiation. *J. Comp. Neurol.* 524, 3774–3809. <https://doi.org/10.1002/cne.24032>
- Paxinos, G., Watson, C., 2013. *The Rat Brain in Stereotaxic Coordinates*, 7th editio. ed. Academic Press.
- Pitzalis, S., Sereno, M.I., Committeri, G., Fattori, P., Galati, G., Patria, F., Galletti, C., 2010. Human v6: the medial motion area. *Cereb. Cortex* 20, 411–424. <https://doi.org/10.1093/cercor/bhp112>
- Previc, F.H., Liotti, M., Blakemore, C., 2000. Functional imaging of brain areas involved in the processing of coherent and incoherent wide field-of-view visual motion. <https://doi.org/10.1007/s002219900298>
- Prsa, M., Gale, S., Blanke, O., 2012. Self-motion leads to mandatory cue fusion across sensory modalities. *Journal of Neurophysiology* 108, 2282–2291. <https://doi.org/10.1152/jn.00439.2012>
- Rust, N.C., Mante, V., Simoncelli, E.P., Movshon, J.A., 2006. How MT cells analyze the motion of visual patterns. *Nature Neuroscience* 9, 1421–1431. <https://doi.org/10.1038/nn1786>

- Saldern, S. Von, Noppeney, U., 2013. Sensory and Striatal Areas Integrate Auditory and Visual Signals into Behavioral Benefits during Motion Discrimination 33, 8841–8849. <https://doi.org/10.1523/JNEUROSCI.3020-12.2013>
- Sanderson, K.J., Dreher, B., Gayer, N., 1991. Proencephalic connections of striate and extrastriate areas of rat visual cortex. *Experimental Brain Research* 85, 324–334. <https://doi.org/10.1007/BF00229410>
- Save, E., Poucet, B., 2000. Involvement of the hippocampus and associative parietal cortex in the use of proximal and distal landmarks for navigation. *Behavioural Brain Research* 109, 195–206. [https://doi.org/10.1016/S0166-4328\(99\)00173-4](https://doi.org/10.1016/S0166-4328(99)00173-4)
- Save, E., Poucet, B., Foreman, N., Thinus-Blanc, C., 1998. The contribution of the associative parietal cortex and hippocampus to spatial processing in rodents 153–161. <https://doi.org/10.3758/BF03330603>
- Schindler, A., Bartels, A., 2018. Integration of visual and non-visual self-motion cues during voluntary head movements in the human brain. *NeuroImage* 172, 597–607. <https://doi.org/10.1016/j.neuroimage.2018.02.006>
- Siegel, R.M., Read, H.L., 1997. Analysis of optic flow in the monkey parietal area 7a. *Cereb. Cortex* 7, 327–346. <https://doi.org/10.1093/cercor/7.4.327>
- Stein, B. E. & Meredith, M. A. (1993). *The merging of the senses*. Cambridge, MA: MIT Press.
- Stein, B.E., Stanford, T.R., 2008. Multisensory integration: current issues from the perspective of the single neuron. *Nature Reviews Neuroscience* 9, 255–266. <https://doi.org/10.1038/nrn2331>
- Takagaki, K., Zhang, C., Wu, J.Y., Lippert, M.T., 2008. Crossmodal propagation of sensory-evoked and spontaneous activity in the rat neocortex. *Neuroscience Letters* 431, 191–196. <https://doi.org/10.1016/j.neulet.2007.11.069>
- Toldi, J., Fehér, O., Wolff, J.R., 1986. Sensory interactive zones in the rat cerebral cortex. *Neuroscience* 18, 461–465. [https://doi.org/10.1016/0306-4522\(86\)90166-1](https://doi.org/10.1016/0306-4522(86)90166-1)
- Van Kemenade, B.M., Seymour, K., Wacker, E., Spitzer, B., Blankenburg, F., Sterzer, P., 2014. Tactile and visual motion direction processing in hMT+/V5. *NeuroImage* 84, 420–427. <https://doi.org/10.1016/j.neuroimage.2013.09.004>
- Wall, Matthew B., Smith, A.T., 2008. The Representation of Egomotion in the Human Brain. *Current Biology* 18, 191–194. <https://doi.org/10.1016/j.cub.2007.12.053>
- Wall, Matthew B, Smith, A.T., 2008. Report The Representation of Egomotion in the Human Brain 191–194. <https://doi.org/10.1016/j.cub.2007.12.053>
- Wallace, M.T., Ramachandran, R., Stein, B.E., 2004. A revised view of sensory cortical parcellation. *Proceedings of the National Academy of Sciences* 101, 2167–2172. <https://doi.org/10.1073/pnas.0305697101>
- Wang, Q., Gao, E., Burkhalter, A., 2011. Gateways of Ventral and Dorsal Streams in Mouse Visual Cortex. *Journal of Neuroscience* 31, 1905–1918. <https://doi.org/10.1523/JNEUROSCI.3488-10.2011>
- Wang, Q., Sporns, O., Burkhalter, A., 2012. Network Analysis of Corticocortical Connections Reveals Ventral and Dorsal Processing Streams in Mouse Visual Cortex. *Journal of Neuroscience* 32, 4386–4399. <https://doi.org/10.1523/JNEUROSCI.6063-11.2012>
- 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, 789–802. <https://doi.org/10.1016/j.neuron.2011.12.028>
- Wilber, A.A., Clark, B.J., Demecha, A.J., Mesina, L., Vos, J.M., McNaughton, B.L., 2014. Cortical connectivity maps reveal anatomically distinct areas in the parietal cortex of the rat. *Front Neural Circuits* 8, 146. <https://doi.org/10.3389/fncir.2014.00146>
- Xu, J., Sun, X., Zhou, X., Zhang, J., Yu, L., 2014. The cortical distribution of multisensory neurons was modulated by multisensory experience. *Neuroscience* 272, 1–9. <https://doi.org/10.1016/j.neuroscience.2014.04.068>

Zhang, T., Britten, K.H., 2004. Clustering of selectivity for optic flow in the ventral intraparietal area. *Neuroreport* 15, 1941–1945. <https://doi.org/10.1097/00001756-200408260-00022>