NeuroImage xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Q1 Q2

Whole brain mapping of visual and tactile convergence in the macaque monkey

Q3 Olivier Guipponi, Justine Cléry, Soline Odouard, Claire Wardak, Suliann Ben Hamed *

Q4 *Centre de Neuroscience Cognitive, CNRS UMR 5229, Université Claude Bernard Lyon I, 67 Bd Pinel, 69675 Bron cedex, France*

A R T I C L E   I N F O

Article history:
Received 17 March 2015
Accepted 8 May 2015
Available online xxxx

Keywords:
Multisensory
Monkey fMRI
Functional connectivity
Context dependent
Macaque

A B S T R A C T

The proposal that sensory processing is achieved in segregated anatomical pathways has been profoundly revisited following the description of cross-modal anatomical connections both at higher and at lower processing levels. However, an understanding of the cortical extent of these long range cross-modal functional influences has been missing. Here, we use functional magnetic resonance imaging (fMRI) to map, in the non-human primate brain, the cortical regions which are activated by both visual and tactile stimulations. We describe an unprecedented pattern of functional visuo-tactile convergence, encompassing both low-level visual and somatosensory areas and multiple higher-order associative areas. We also show that the profile of this convergence depends on the physical properties of the mapping stimuli, indicating that visuo-tactile convergence is most probably even more prevailing than what we actually describe. Overall, these observations substantiate the view that the brain is massively multisensory.

Introduction

Advances in neurosciences in the last decades have repeatedly challenged our views on the organization of cortical sensory processing. Early anatomical (Kuypers et al., 1965) and lesion studies (Massopust et al., 1965) led to the description of segregated anatomical pathways, each processing a specific sensory modality. In 1991, Felleman and Van Essen (1991) refined this view, proposing a massively parallel, hierarchical processing organization of the visual system, in which the initial sensory stages are performed by low level unimodal sensory areas, while later processing stages are performed by multisensory higher-order associative regions, such as the temporal cortex (Barraclough et al., 2005; Beauchamp et al., 2004) or the parietal cortex (Avillac et al., 2005; Duhamel et al., 1998; Guipponi et al., 2013; Schlack et al., 2005; Sereno and Huang, 2006). The subsequent description of heteromodal connection in early sensory processing areas (e.g. auditory projections onto visual cortex or vice-versa: Falchier et al., 2002; Rockland and Ojima, 2003; Cappe and Barone, 2005; somatosensory projections onto auditory cortex or vice-versa: Cappe and Barone, 2005; Budinger et al., 2006; de la Mothe et al., 2006; Smiley et al., 2007; visual projections onto somatosensory cortex: Wallace et al., 2004) further nuanced this view, suggesting that multisensory processing takes place at earlier processing stages than commonly admitted. The contribution of these heteromodal projections to the modulation of the response of early sensory neurons is confirmed both by single cell recording studies (Iurilli et al., 2012; Schroeder and Foxe, 2005; Vasconcelos et al., 2011) and functional neuroimaging studies (Amedi et al., 2001; Macaluso et al., 2000; Sathian et al., 1997). On the basis of the growing evidence for pervasive multisensory influences at all levels of cortical processing, Ghazanfar and Schroeder (2006) question, in a recent review, whether multisensory processing could actually be an essential property of neocortex.

Here, functional magnetic resonance imaging (fMRI) in the non-human primate allows us to capture the spatial pattern of visuo-tactile cortical convergence, the extent of which has been overlooked by previous studies, both in low-level visual and somatosensory areas and in multiple higher-order associative areas. In particular, we show that the profile of this visuo-tactile convergence is functionally shaped by the physical properties of the stimuli used for the sensory mapping.

Material and methods

Ethical statement

All procedures were in compliance with the guidelines of the European Community on animal care (European Community Council, Directive No. 86–609, November 24, 1986). All the protocols used in this experiment were approved by the animal care committee (Department of Veterinary Services, Health & Protection of Animals, permit number 69 029 0401) and the Biology Department of the University Claude Bernard Lyon 1. The animals' welfare and the steps taken to ameliorate suffering were in accordance with the recommendations of the Weatherall report, "The use of non-human primates in research". The study involved two rhesus monkeys (*Macaca mulatta*, a male, 7 kg, age

* Corresponding author at: Centre de Neuroscience Cognitive, CNRS UMR 5229, Université Claude Bernard Lyon I, 67 Bd Pinel, 69675 Bron cedex, France.
E-mail address: benhamed@isc.cnrs.fr (S. Ben Hamed).

http://dx.doi.org/10.1016/j.neuroimage.2015.05.022
1053-8119/© 2015 Published by Elsevier Inc.

7 and a female, 5 kg, age 5), as accepted in non-human primate fMRI studies. The animals were housed in twin cages (2 m^2 by 2 m height in total). The twin cages could be separated in two individual cages or connected to form a unique housing for a pair of monkeys thus offering the monkeys a socially enriched environment. This last configuration was the norm. Twin cages communicated with a larger play cage (4 × 1.5 × 2 m^3) to which the monkeys were granted access on days on which they were not involved in experiments. Light was switched on and off at fixed hours (on: 7.30 a.m and off: 8 p.m), all year round. Monkeys had free access to food pellets. They were also given fresh fruits and nuts. During week days, monkeys had access to water during the training sessions. Additional water and fruits were given in order to achieve a minimum of 30–40 ml/kg of daily water intake. Animals had free access to water starting from Friday late afternoon to Sunday night. All cages were enriched with mirrors, hanging ropes, balls and foraging baskets. No procedure that might cause discomfort or pain was undertaken without adequate analgesia or anesthesia. The specific surgical procedures are detailed below. The general health status of the animals was monitored every day by competent and authorized personal. In agreement with the 3R 'reduction' recommendation, the two animals involved in the present study were enrolled later in another experiment.

Subjects and materials

Two rhesus monkeys (female M1, male M2, 5–7 years old, 5–7 kg) participated in the study. The animals were implanted with a custom-made PEI plastic MRI compatible headset covered by dental acrylic. The anesthesia during surgery was induced by Zoletil (Tiletamine-Zolazepam, Virbac, 15 mg/kg) and followed by Isoflurane (Belamont, 1–2%). Post-surgery analgesia was ensured thanks to Temgesic (buprenorphine, 0.3 mg/ml, 0.01 mg/kg). During recovery, proper analgesic and a full antibiotic coverage was provided (long action Terramycin, one injection during the surgery and one 5 days later, 0.1 ml/kg, i.m.). The surgical procedures conformed to the European and National Institutes of Health guidelines for the care and use of laboratory animals.

During the scanning sessions, monkeys sat in a sphinx position in a plastic monkey chair positioned within a horizontal magnet (1.5-T MR scanner Sonata; Siemens, Erlangen, Germany) facing a translucent screen placed 90 cm from the eyes. Their head was restrained and equipped with MRI-compatible headphones customized for monkeys (MR Confon GmbH, Magdeburg, Germany). A radial receive-only surface coil (10-cm diameter) was positioned above the head. Eye position was monitored at 120 Hz during scanning using a pupil-corneal reflection tracking system (Iscan®, Cambridge, MA). Monkeys were rewarded with liquid dispensed by a computer-controlled reward delivery system (Crist®) thanks to a plastic tube coming to their mouth. The task, all the behavioral parameters as well as the sensory stimulations were controlled by two computers running with Matlab® and Presentation®. The fixation point the monkeys were instructed to fixate, as well as the visual stimuli, were projected onto a screen with a Canon XEED SX60 projector. Tactile stimulations were delivered through Teflon tubing and 6 articulated plastic arms connected to istant air pressure electro-valves. Monkeys were trained in a mock scan environment approaching to the best the actual MRI scanner setup.

Task and stimuli

The animals were trained to maintain fixation on a red central spot (0.24° × 0.24°) while stimulations (visual or tactile) were delivered. The monkeys were rewarded for staying within a 2° × 2° tolerance window centered on the fixation spot. The reward delivery was scheduled to encourage long fixation without breaks (i.e. the interval between successive deliveries was decreased and their amount was increased, up to a fixed limit, as long as the eyes did not leave the window). The two sensory modalities were tested in independent interleaved runs (see below for the organization of the runs). Stimulation strength was maximized in order to saturate the evoked neuronal response and induce an unambiguously strong percept for all types of stimuli.

Visual stimulations

Large field (32° × 32°) visual stimulations consisted of white bars (3.2° × 24.3°, horizontal, vertical, or 45° oblique) or white random dots on a black background (Fig. 1A). Three conditions were tested in blocks of 10 pulses (TR = 2.08 s): 1) *coherent movement*, with bars moving in one of the 8 cardinal directions or expanding or contracting random dots pattern (with 5 possible optic flow origins: center, upper left (−8°, 8°), upper right, lower left and lower right); each coherent movement sequence lasted 850 ms and 24 such sequences were pseudo-randomly presented in a given coherent movement block; 2) *scrambled movement*, in which the different frames of a given coherent movement sequence were randomly reorganized; 3) *static*, in which individual frames randomly picked from the coherent movement visual stimuli sequences, were presented for 250 ms. As a result, within a given block, 850 ms portions of the different stimuli (bars/dots/directions/origins) of the same category (coherent/scrambled/static) were pseudo-randomly interleaved. The movement related activations were reported for the parietal cortex in a previous paper (Guipponi et al., 2013). In the present paper, we focus on the static stimulations, so that in all analyses, the visual stimulation vs. fixation contrast corresponds to static visual stimuli compared to the fixation, except in the analysis presented in Figs. 4 and 5.

Tactile stimulations

They consisted of air puffs delivered to three different locations on the left and the right of the animals' body (Fig. 1B): 1) *center* of the face, close to the nose and the mouth; 2) *periphery* of the face, above the eyebrows; 3) *shoulders* (cf. Guipponi et al. (2013)). The intensity of the stimulations ranged from 0.5 bars (center/periphery) and 1 bar (shoulders), to adjust for the larger distance between the extremity of the stimulation tubes and the skin, as well as for the difference in hair density. The inter-stimulus interval for air-puff presentation was random (mean of 1210 ms, s.d. of 148 ms). Though the air-puff delivery system produced a weak noise at air-puff production, the entire system was placed outside the MRI room and the noise could thus not reach the

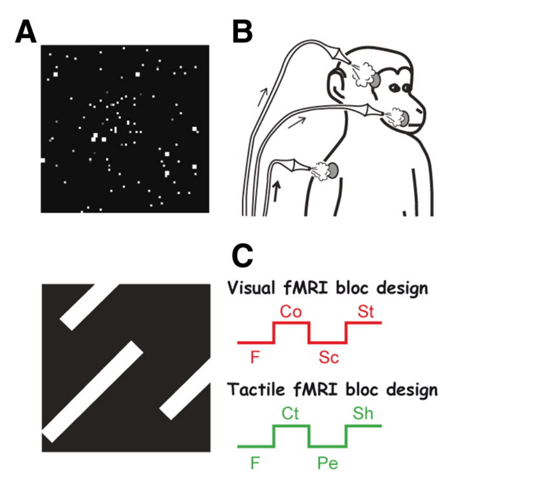

Fig. 1. Stimulation fMRI protocol. A. Two examples of whole field visual stimuli: optic flows and large-field bars. These stimuli were assembled to evoke either static, coherent movement or scrambled dynamic visual stimulation. B. Tactile stimulations: air-puffs were delivered to the center of the face, the periphery of the face, or the shoulders, simultaneously on the left and right sides of the monkeys. C. fMRI block design. Visual runs consisted of a pseudorandom association of fixation blocks (F), coherent visual movement blocks (Co), scrambled visual movement blocks (Sc) and static visual stimulation blocks (St). Tactile runs consisted of a pseudorandom association of fixation blocks (F), center of the face tactile stimulations (Ct), periphery of the face tactile stimulations (Pe) and shoulder tactile stimulations (Sh).

Please cite this article as: Guipponi, O., et al., Whole brain mapping of visual and tactile convergence in the macaque monkey, NeuroImage (2015), http://dx.doi.org/10.1016/j.neuroimage.2015.05.022