Resting-State Functional Networks of Different Topographic Representations in the Somatosensory Cortex of Macaque Monkeys and Humans

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Abstract

Information processing in the brain is mediated through a complex functional network architecture whose comprising nodes integrate and segregate themselves on different timescales. To gain an understanding of the network function it is imperative to identify and understand the network structure with respect to the underlying anatomical connectivity and the topographic organization. Here we show that the previously described resting-state network for the somatosensory area 3b comprises of distinct networks that are characteristic for different topographic representations. Seed-based resting-state functional connectivity analysis in macaque monkeys and humans using BOLD-fMRI signals from the face, the hand and rest of the medial somatosensory representations of area 3b revealed different correlation patterns. Face area network had highest ipsilateral and contralateral connectivity, which included areas 3b and 4, ventral premotor area, and the secondary somatosensory cortex. The hand network included ipsilateral hand representation in area 4. The medial-most representations in area 3b showed connectivity with the rostrally adjacent ipsilateral area 4 and contralateral medial area 3b. The emergent functional network structures largely reflect the known anatomical connectivity, and were similar in both humans and macaque monkeys. Our results show that different somatotopic representations in area 3b have independent functional networks perhaps reflecting differences in the behavioral use of different body parts. The results also show that large cortical areas if considered together, do not give a complete and accurate picture of the network architecture.

Keywords

BOLD fMRI correlations; Resting-state connectivity; Area 3b; Somatotopy

Highlights

- Somatosensory resting-state functional network is not uniform across the entire area 3b.
- Different somatotopic representations have different connectivity networks.
- The bilateral somatosensory face network includes face representations in area 3b, motor cortex, S2, and PMv.
- The area 3b hand network includes primarily the hand region in ipsilateral motor cortex.
- These functional connectivity networks are similar in the two primate species, i.e. macaque monkeys and humans.

1. INTRODUCTION

Since early descriptions of the cortical areas based on cytoarchitecture (Brodmann, 1909), various anatomical, neurophysiological and neuroimaging studies have given new insights into functional segregation across brain regions (see Amunts and Zilles, 2015). Cortical parcellation combining multiple features viz. cyto-, myelo- and immuno-architecture, topography, function and connectivity analysis help better define areal and sub-areal boundaries in the cortex and understand information processing networks (Glasser et al., 2016; Jain et al., 1998; Jain et al., 1994; Kuehn et al., 2017; Preuss et al., 1997; Van Essen et al., 2012). More recently, functional connectivity, particularly the correlation of intrinsic blood oxygenation level dependent (BOLD) fMRI signals from different brain areas, which is considered to represent functional association between regions, has been utilized for parcellation of the cortex (Gordon et al., 2016).

Resting-state functional connectivity is determined from correlations in the low frequency (<0.01 Hz) fluctuations of BOLD fMRI signals between different regions in a resting brain revealing functionally related areas (Biswal et al., 1995). Such time series cross-correlation analysis between a seed region of interest (ROI) and voxels in rest of the brain reveals functional connections across different brain regions even without any explicit task paradigm (Biswal et al., 1995). The correlated sets of voxels give rise to functional 'maps', also referred to as functional connectivity networks. These have been found to be consistent within and between subjects (Choe et al., 2015; Laumann et al., 2015; Shehzad et al., 2009). The resting-state functional connectivity has been studied in a variety of species ranging from mice, ferrets, cats, and monkeys to humans (Hutchison et al., 2013; Stafford et al., 2014; Zhou et al., 2016). Seed-based resting-state fMRI (rsfMRI) analysis enables tailored investigation to delineate networks spanning entire brains. Furthermore, subject specific ROI analysis

using rsfMRI data can reveal regional differences within a cortical area, as well as individual specific variations across different subjects (Braga and Buckner, 2017).

In functional connectivity studies traditionally somatosensory and motor cortical areas have been lumped together (Beckmann et al., 2005; Hutchison et al., 2011; Mantini et al., 2013). This network includes different topographic representations in the primary somatosensory, motor and secondary somatosensory areas (Disbrow et al., 2000; Manger et al., 1996; Nelson et al., 1980; Stepniewska et al., 1993). However, it is known from anatomical connectivity studies that different body part representations form independent information processing modules. For example, the hand and face representations in the somatosensory cortex have different interconnectivity, sources of feedback connections and inter-hemispherical connections (Chand and Jain, 2015; Fang et al., 2002; Killackey et al., 1983; Liao et al., 2013). Callosal connectivity also varies widely across somatotopic representations, for example, the face and trunk representations have higher connectivity as compared to the hand and foot regions (Killackey et al., 1983).

Resting-state connectivity largely reflects direct anatomical connectivity between different brain regions (Damoiseaux and Greicius, 2009; van den Heuvel et al., 2009; Wang et al., 2013), as well as functional connectivity between areas not directly connected anatomically (Adachi et al., 2012; Vincent et al., 2007). Recent neuroimaging studies have considered differences in cortical function and functional connectivity to delineate different brain areas (Glasser et al., 2016; Gordon et al., 2016; Sohn et al., 2012). Functional connectivity studies have found topography dependent network subdivisions within the somatomotor network in humans (Power et al., 2011; Yeo et al., 2011). Utilizing *in vivo* cortical myelin mapping and resting-state analysis, Kuehn et al. (2017) showed that the functional connectivity patterns in humans

also follow the architectonic differences reiterating the importance of body part representations as an organizing principle for functional networks.

We hypothesized that different somatotopic representations within the primary somatosensory area 3b have different connectivity networks with different functionally correlating nodes. In order to test this hypothesis, we analyzed seed-based resting-state fMRI connectivity of different somatotopic representations. Further, to determine if the correlated features of these networks are evolutionarily conserved, we compared functional connectivity profiles in humans and macaque monkeys.

2. METHODS

2.1. Subjects

Five adult male macaque monkeys (*Macaca mulatta*), 8-11 years of age and weighing between 8-10 kg were used. All animal procedures were approved by the Institutional Animal Ethics Committee of National Brain Research Centre, and the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India, and conformed to NIH guidelines for care and use of animals in biomedical research. Twenty three right-handed human subjects (10 females and 13 males) between the ages of 22-39 years took part in the study. Participants had no history of neurological or psychiatric illness (self-reported). Informed consent was obtained from all the human subjects. Human study protocols were approved by the Institutional Human Ethics Committee of National Brain Research Centre.

2.2. Data acquisition

2.2.1 Macaque monkeys

For magnetic resonance data acquisition, macaque monkeys were initially anesthetized with ketamine hydrochloride (8 mg/kg, IM). Glycopyrrolate (0.015 mg/kg, IM) was administered in order to reduce the salivary secretions. When the monkeys were areflexive, they were intubated with an appropriately sized endotracheal tube and the anesthesia was switched to isoflurane (1-2% in oxygen, Surgivet CDS 2000). T1 weighted anatomical scans were acquired using 1-2% isoflurane in oxygen while the functional scans were taken using a lower isoflurane percentage (0.5-0.8% in oxygen).

MR scans were acquired by transmitting radio-frequency pulses from a quadrature body-coil inside a 3-T clinical MRI scanner (Philips Achieva, Netherlands), and receiving signals using an eight-channel phased array knee coil (MRI Device Corporation, WI, USA) and sensitivity-encoding (SENSE) parallel acquisition (Pruessmann et al., 1999). Human knee coil was used for monkeys due to a better filling factor, which improved signal-to-noise ratio and the image quality (Dutta et al., 2014). Anesthetized animals were placed in supine position inside the scanner with the head completely inside the receiver coil. Head movements inside the coil were minimized by padding the gaps between the head and the coil with polyethylene foam blocks. T1 weighted anatomical scans of the brain were acquired using a 3D multishot Turbo Field Echo sequence (TR 8.8 ms; TE 4.4 ms; flip angle 8°; 0.5 mm x 0.5 mm x 0.5 mm resolution; 250 mm x 210 mm x 56 mm field of view; 500 x 360 matrix; 112 transverse slices). Resting-state fMRI scans were acquired in oblique horizontal slice orientations, using a single-shot gradient echo echo-planar imaging (TR 2800 ms; TE 30 ms; flip angle 90°; 1.5 mm x 1.5 mm in-plane resolution; 2 mm thick slices; 96 mm x 102 mm x 54 mm field of view; 64 x 64

matrix). Each resting-state scan session consisted of 140 functional volumes acquired over approximately 13 minutes. On each scanning day, functional data acquisition was always preceded by reference and anatomical scans. This enabled similar time lag between induction of anaesthesia and the start of functional scans across different days of acquisition. During the scans, physiological condition of the monkeys was continuously monitored with a MRI-compatible pulse-oximeter (Nonin 8600FO, USA), keeping constant anesthesia level (0.5-0.8%) and the oxygen flow rate (1.5 l/min).

2.2.2 Humans

Data from human subjects were acquired using the same 3-T MRI scanner but with an 8 channel SENSE headcoil. Anatomical T1 weighted image was acquired for each subject using 3D multishot TFE sequence (TR= 8.4 ms; flip angle= 8°; FOV= 250 mm x 230 mm x150 mm; 252 x 211 matrix; 150 slices) before the functional scanning sessions. Resting-state functional scans were acquired with a T_2* weighted gradient echo EPI sequence (TR = 2000 ms; TE= 30ms; flip angle= 70°; 3 mm x 3 mm in plane resolution; slice thickness 4 mm; FOV = 230 mm x 242 mm x 132 mm; 33 slices). Two hundred functional volumes were acquired during which the participants lay in supine position with palms facing downwards. They were instructed not to intentionally move any body part, keep their eyes closed and try not to indulge in any active thought process.

Of the twenty three subjects, the data from two subjects (both females) were discarded due to excessive head motion and self-reported sleepiness during the resting scans. Data from additional four subjects (2 females, 2 males) were not considered due to involuntary hand movements during the acquisition.

Data from the remaining seventeen subjects (6 females, 11 males) were used for further analyses.

Resting-state fMRI scans were acquired over multiple sessions for both human participants and monkeys. For humans data is from 34 scans acquired from seventeen participants, and for monkeys from 32 scans acquired from five monkeys across different sessions.

2.3. Pre-processing

Monkey and human data were processed using statistical parametric mapping (SPM8) software (http://www.fil.ion.ucl.ac.uk/spm/software/spm8) operating in Matlab 2013a platform (MathWorks Inc., MA, USA). The acquired structural images were aligned in the anterior commissure-posterior commissure (AC-PC) plane with coordinates of AC set to zero. After removal of the dummy scans, the functional images were slice time corrected to remove the time lag between slices within a volume. These slice-time corrected functional volumes were head motion corrected using a six-parameter affine 'rigid body' transformation to minimize differences between each successive scan and the reference scan (the first scan in the time series). Motion corrected functional volumes of monkeys were co-registered with the corresponding high-resolution subject specific structural images. For humans, structural images were normalized to the standard template (ICBM 2009a Nonlinear Symmetric template; Fonov et al., 2009). Images were then visually inspected to check the registration and were smoothed with a 2 mm (macaques) or 8 mm (humans) Full Width at Half Maximum Gaussian kernels.

Functional connectivity for both macaques and humans was determined using CONN toolbox (version 15.e) for SPM (Whitfield-Gabrieli and Nieto-Castanon, 2012). Nuisance covariates of cerebrospinal fluid and white-matter

signals were modeled and removed following CompCor strategy (Behzadi et al., 2007), as implemented in CONN. Linear regression was performed where signals from the white matter and the cerebrospinal fluid, along with the global signal and the motion parameters were taken as covariates of no interest. This was followed by a temporal band pass filtering (0.008 - 0.09 Hz) to reduce low frequency drifts and the high frequency physiological noise. Before calculating bivariate correlation coefficients across brain regions, the processed data were despiked with hyperbolic tangent squash function and linearly detrended to remove low drift scanner noise.

2.4. Regions of Interest (ROIs)

For determining resting-state functional connectivity of different somatosensory representations, we demarcated boundaries of the face (face3b), hand (hand3b) and rest of the medial region (med3b) in area 3b (Fig. 1), and other regions of interest (ROIs) for both monkeys (MK) and humans (HU) as described below.

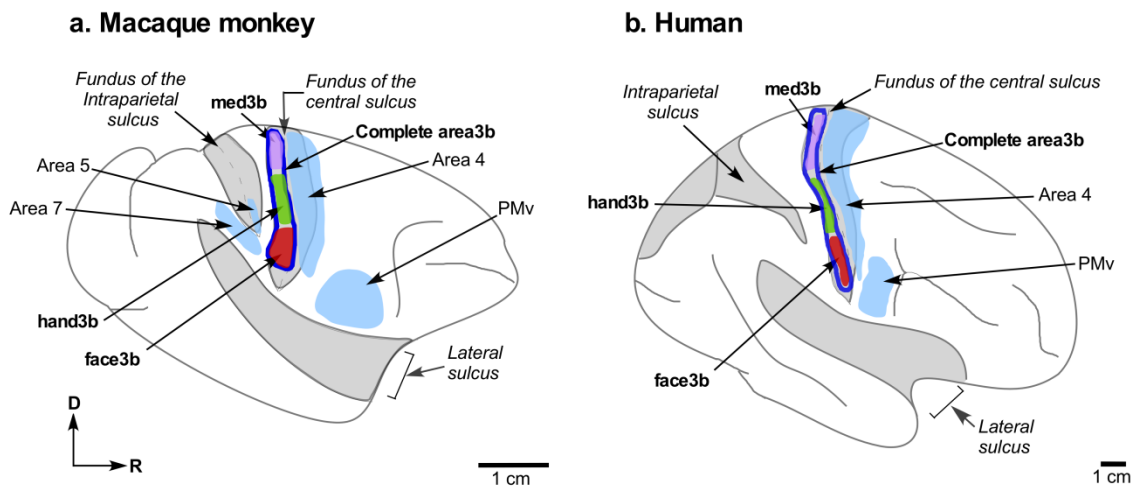

Fig. 1. Regions of interests (ROI's) used for the seed-based resting-state functional connectivity analysis of the somatosensory cortex in (**a**) macaque monkeys and (**b**) humans.

Complete area 3b ROI (dark blue outline; area3b), and somatotopy specific ROIs - face3b (red), hand3b (green) and med3b (violet). The target ROI's are light blue. The ROI's are shown on outline drawings of the partially inflated cortical surface. The major sulci are labelled in *italics* for reference. Some of the sulci are shown opened (grey shading). S2 ROI is not visible in this view. PMv, Premotor Ventral Area; D, dorsal; R, rostral.

2.4.1 Macaque monkeys

The ROI were drawn (Fig. 1a) for both the hemispheres on subject specific high resolution T1 images. The entire medio-lateral extent of the primary somatosensory area 3b in the post central gyrus, excluding the medial wall was taken as the complete area 3b seed ROI (area3b). Care was taken to restrict the ROI within the dorso-ventral boundaries of the area 3b based upon the cytoarchitectonic and electrophysiology studies (Chand and Jain, 2015; Nelson et al., 1980). A perpendicular from the tip of the intraparietal sulcus to the central sulcus on the surface of the brain was considered as the hand-face border, i.e. the medial limiting boundary of the face ROI (Chand and Jain, 2015; Jain et al., 2008; Manger et al., 1997). Intra-oral representations were excluded from the face ROI (Manger et al., 1996). The hand ROI was restricted to 7 mm distance medial from the hand-face border (Jain et al., 2008; Nelson et al., 1980). This included the hand representation i.e., digits and palm, but excluded other forelimb representations. In addition, the fMRI activation loci in response to the chin and hand stimulation were matched to confirm the accuracy of ROIs (Dutta et al., 2014, and our unpublished fMRI results from the same monkeys; Fig. 2a).

The remaining medial region of area 3b excluding the medial wall was considered together as the third ROI termed med3b. This included representations of the shoulder, trunk, foot and parts of the leg that are on the dorsal surface (Nelson et al., 1980). This ROI also included medial-most parts

of the upper arm representation. Due to the uncertainties in demarcating boundaries between these representations, the combined ROI was used.

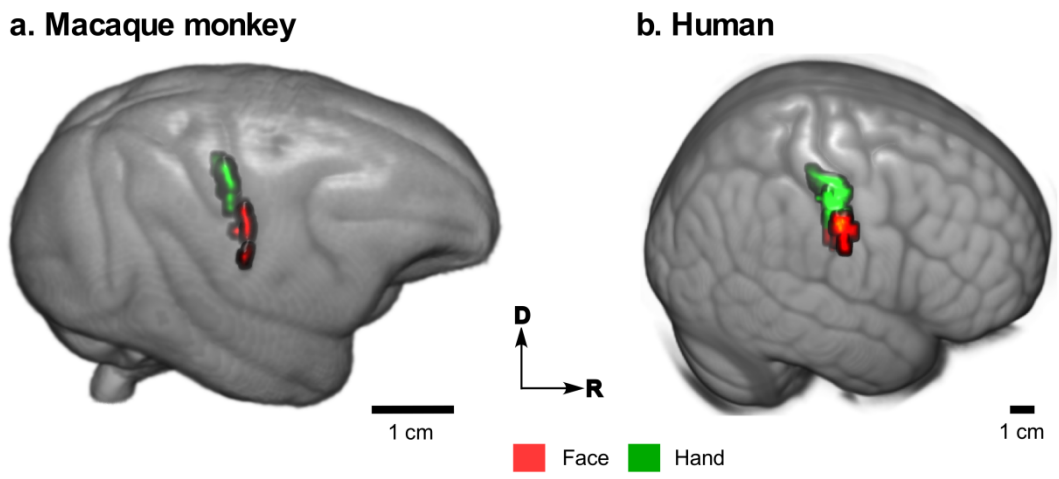

Fig. 2. Voxels activated in fMRI scans of **(a)** macaque monkeys (n = 5) and **(b)** humans (n = 5) when the hand, i.e. digits and palm (green) or the face (red) was undergoing tactile stimulation. The voxels are rendered on respective standard brain template images. Statistical t- maps are at $p<0.005$ (uncorrected) for monkeys and $p<0.05$ (FWER corrected) for humans. D, dorsal; R, rostral.

Other ROIs, the primary motor cortex (area4), ventral premotor cortex (PMv) and secondary somatosensory cortex (S2) were drawn with reference to the published anatomical and electrophysiological data and the macaque monkey brain atlas (Barbas and Pandya, 1987; Burton et al., 1995; Krubitzer et al., 1995; Paxinos et al., 2000; Saleem and Logothetis, 2006). ROIs were drawn for the topographic representations in area 4 to demarcate the face (face4), the hand (hand4) and the remaining medial region (med4) in accordance with the published reports (Stepniewska et al., 1993)

2.4.2 Humans

The complete area 3b ROI (area3b) included the area 3b within the entire medio-lateral extent of the post central gyrus (Fig. 1b). The hand (hand3b) and the face (face3b) ROIs were then delineated on the standard brain template. The inverted Ω shaped knob was taken as suggestive of the motor hand area (Yousry et al., 1997). The somatosensory hand representation was drawn on the post central gyrus with the 'knob' as a guide (Blankenburg et al., 2003; Maldjian et al., 1999; Nakamura et al., 1998). Face ROI was drawn lateral to the hand ROI taking care to exclude the intra-oral representations (Miyamoto et al., 2006). Dorsoventral extent of the face3b and hand3b were drawn according to the published anatomical studies (Geyer et al., 1999; Geyer et al., 2000). Similar to monkeys, med3b in humans comprised of parts of area 3b medial to the hand representation up to the location where central sulcus meets the midline sulcus, and excluded the medial wall representations. We also acquired fMRI data while stimulating the entire hand (i.e. glabrous digits and palm) or the chin, and matched the regions of activation with ROI's to confirm their accuracy (Fig. 2b).

Other ROIs - area4, PMv and S2 were also drawn on the standard ICBM template. ROI's for area 4 (the primary motor cortex) and PMv (ventral premotor cortex) were drawn with reference to the available anatomical data (Geyer et al., 1996; Geyer et al., 1999; Geyer et al., 2000). Secondary somatosensory ROI, which included both S2 and PV, was drawn using SPM-Anatomy toolbox referring the existing literature on S2 topography (Blatow et al., 2007; Disbrow et al., 2000; Eickhoff et al., 2007; Ferretti et al., 2004).

ROIs were drawn for the topographic sub-divisions of the primary motor cortex to demarcate the face (face4), the hand (hand4) and the remaining medial

region (med4) in accordance with the published reports (Geyer et al., 1996; Schieber, 2001).

2.5. Connectivity analysis

For both monkeys and humans, seed-to-voxel connectivity was determined using CONN toolbox. For analysis, both the successive sessions for each human subject, acquired on the same day were concatenated, whereas each session of the monkeys was considered separately. To construct connectivity maps and to perform ROI analysis, complete area 3b, face3b, hand3b and med3b were used as seed regions for independent analysis. While performing linear regression in CONN, motion parameters were taken as regressors. Resultant *beta* maps, which were Fisher-z transformed correlation value maps, were used for further statistical analysis.

To perform group analysis for monkeys, *beta* maps were transformed to standard INIA19 template space (Rohlfing et al., 2012) using transformation matrix. The transformation matrix was generated using FSL's linear and non-linear registration tool FLIRT and FNIRT respectively, registering subject specific high resolution T1 image to INIA19 template space (Jenkinson et al., 2002). Transformed *beta* maps in the template space were statistically tested using one sample t-test with null hypothesis of no correlation at $p<0.01$ with False Discovery Rate (FDR) correction. Resultant group level statistical maps were then mapped on inflated brain surface using CARET (ver. 5.616; Van Essen et al., 2001).

For human subjects, Fisher-z transformed seed-to-voxel correlations were calculated for area3b, face3b, hand3b, and med3b seeds using CONN. Group analysis was performed using one-sample t-test with null hypothesis of no correlation and statistical threshold at $p<0.05$, with more stringent Family-Wise

Error Rate (FWER) correction. The thresholded statistical maps were mapped on inflated standard template brain surface using BrainNet Viewer (Xia et al., 2013) and were displayed on slices using MRIcron software (ver. 1; Rorden and Brett, 2000).

To calculate the effect size of highly correlating ROIs, specific ROI-ROI Fisher-z transformed correlations were calculated between different ROI's using CONN. One sample t-test was performed with null hypothesis of no correlation with a threshold for significance set for monkeys at $p<0.01$, and humans at $p<0.00001$. The thresholds were decided empirically referring to the connectivity networks reported for the somatomotor cortex (Biswal et al., 1995; Kuehn et al., 2017; Mantini et al., 2013; Power et al., 2011; Yeo et al., 2011). All ROI-ROI statistical tests were performed in MATLAB.

3. RESULTS

We determined resting-state functional connectivity networks of different topographic representations in area 3b of macaque monkeys and humans. Exploratory seed to voxel correlation analysis was first done to reveal functionally connected regions in the brain. The networks thus defined were further analyzed by ROI-ROI correlation analysis. We describe below our results for macaque monkeys and humans together for ease of comparison.

3.1. Somatosensory resting-state networks: seed to voxel correlation analysis

Resting-state network organization was determined taking the entire area 3b and different somatotopic representations as seeds for an exploratory

correlation analysis. The networks were broadly similar for both humans and monkeys (Fig. 3 and 4).

The network of complete area 3b in both the primate species comprised of contralateral area 3b, and other areas bilaterally that included area 4, second somatosensory area (S2), premotor ventral area (PMv), and insula (Fig. 4). In monkeys the area 3b network also included in both the hemispheres - area 7, putamen, and area 5 (Fig. 4).

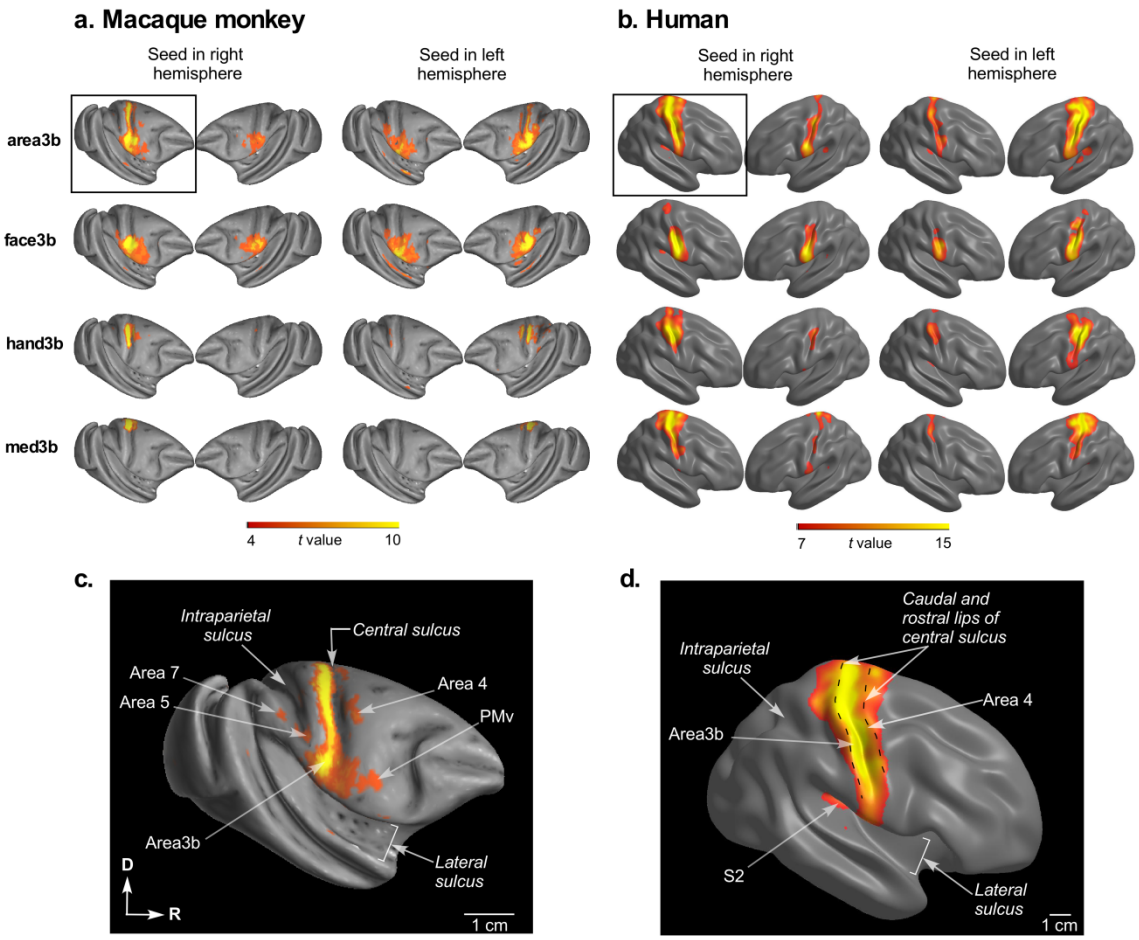

Fig. 3. Seed to voxel resting-state functional connectivity of the somatosensory cortex of (**a** and **c**) macaque monkeys and (**b** and **d**) humans. (**a** and **b**) Bi-hemispherical views of the somatosensory network on partially inflated cortical surfaces are shown when the seed was complete area 3b (area3b; top row), face representation in area 3b (face3b; second row), hand representation (hand3b; third row), or the medial part of area 3b (med3b; bottom row). To illustrate symmetrical nature of the network, data are shown when the seed was either in the left or the right hemisphere (see labels on top). The 't- values' correspond to statistical

significance of p<0.01 (FDR corrected) in monkeys and p<0.05 (FWER corrected) in humans; see the colour scale bars at the bottom. (**c**) and (**d**) show enlarged view of the boxed figurines in (a) and (b) respectively to illustrate the details. D, dorsal; R, rostral; orientation arrows shown in **'c'** also apply to **'d'**.

Further analysis of somatotopy specific connectivity revealed that each individual body part representations in area 3b had a distinct connectivity pattern as described below.

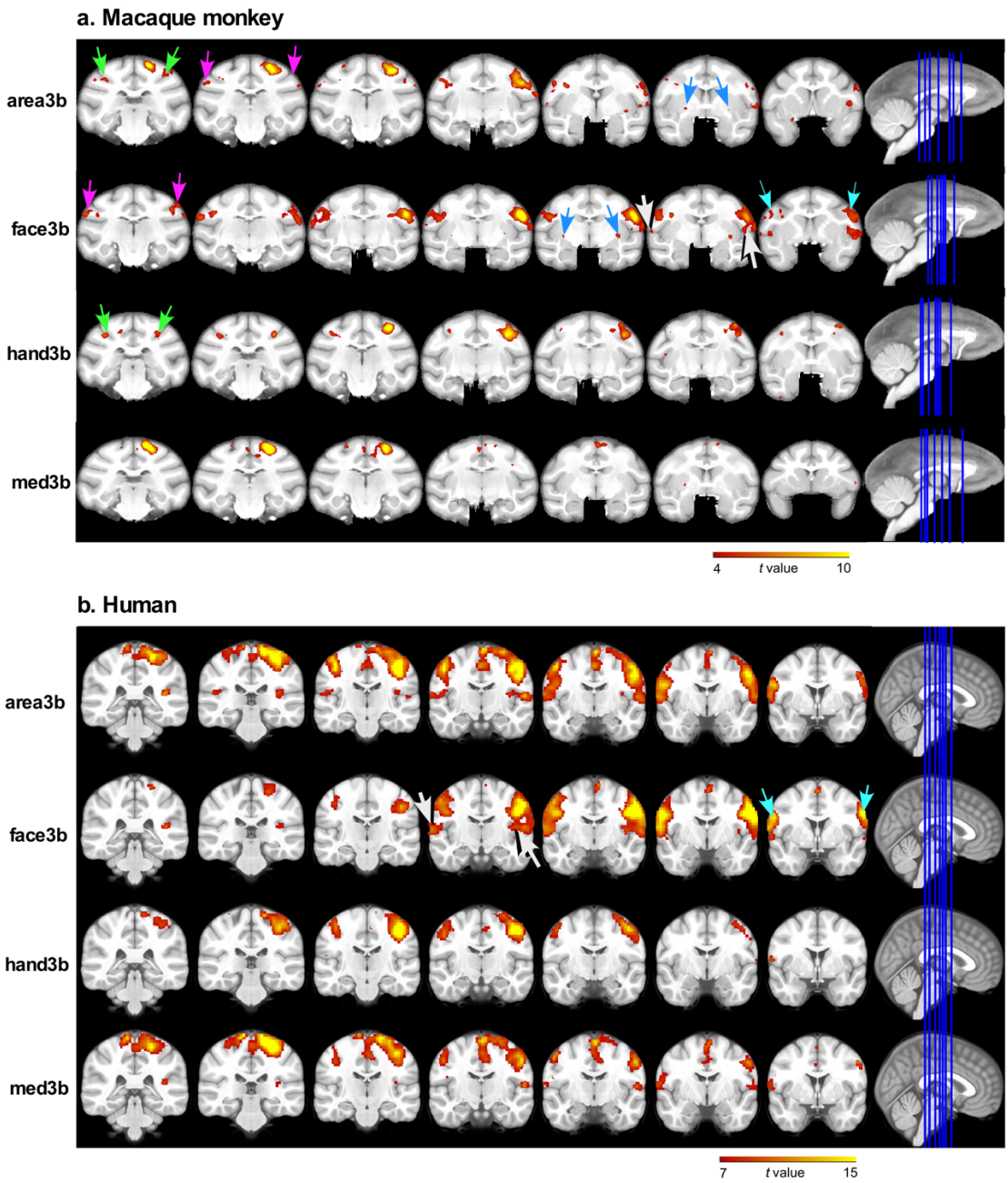

Fig. 4. Seed to voxel correlations in area 3b of the right hemisphere of (a) monkeys and (b) humans shown in a series of coronal sections. The slices are arranged in the caudal to rostral order from left

to right. The right-most column shows parasagittal sections of the brain with the blue lines marking the plane from which the coronal slices are taken. Correlations with area 7 (Pink arrows), area 5 (Green arrows) and putamen (Blue arrows) were observed only in monkeys (Panel 'a'). Locations of S2 (White arrows) and PMv (Cyan arrows) are also marked. M, medial; R, rostral. Other conventions as for Figure 3.

The face representation (face3b), in both monkeys and humans showed strong connectivity with the face representation in contralateral area 3b. Face3b also showed bilateral connectivity with the face representation in area 4 (face4), PMv, S2, and insula (Fig. 3 and 4). However, only in monkeys, similar to the network of complete area 3b, face3b showed bilateral connectivity with area 7 and putamen (Fig. 4).

The other two ROIs i.e. hand3b and med3b revealed a network with fewer correlating nodes than face3b. In monkeys the hand3b network included area 5 and hand representation in area 4 (hand4) in both the hemispheres. The human hand3b showed connectivity to the contralateral hand3b and the ipsilateral hand4 (Fig. 3 and 4). Med3b in both monkeys and humans showed connections to the rostrally adjacent medial part of area 4 (med4) and the contralateral med3b (Fig. 4).

The results show that the functional connectivity network of area 3b is not similar for individual somatotopic representations. It is also apparent from our results that seed-ROIs placed in either of the hemispheres had generally similar connectivity patterns, other than the differences described below, suggesting that the networks are broadly laterality independent (Fig. 3).

3.2. Different topographic representations in area 3b contribute differentially to complete area 3b functional connectivity: ROI-ROI correlations

For a detailed investigation of the results from the seed-to-voxel analysis described above, ROI to ROI analysis was performed using ROIs drawn in the seed as well as the target networked areas viz. primary somatosensory and motor areas, and S2 and PMv. In order to determine the extent of connectivity between correlated regions BOLD signals from all the voxels in each ROI were averaged and time series correlations of this averaged signals were determined for each ROI-ROI pair. Color coded connectivity matrices were constructed using averaged Fisher-z transformed correlation coefficients (CC_Z) for ROI-ROI pairs in both humans and macaque monkeys to illustrate the results (Fig. 5).

Analysis of connectivity of the ROI encompassing entire area 3b in either of the hemisphere revealed significant connections with the contralateral area 3b. Area 3b seed in the right hemisphere also revealed significant bilateral correlations with area 4, S2, and PMv in both monkeys and humans (Fig. 5). In contrast when area 3b seed was in the left hemisphere, correlations were observed with ipsilateral area 4 in monkeys, and the ipsilateral S2 and PMv in humans (Fig. 5).

In both the species face3b ROI showed significant connections with the contralateral face3b, and bilateral connectivity with - S2, PMv and face representation in area 4. Whereas, hand3b and med3b had significant connectivity with homotopic representations in area 3b and area 4 (one sample *t*-test, for *p*-values see Tables 1 and 2, appended at the end).

ROI-ROI analysis also showed that face3b has more widespread and complex functional network than med3b and hand3b. The network of complete area 3b ROI is simply the sum of all the three representation specific networks viz. face3b, hand3b and med3b. Some of the salient features of the functional networks are described below.

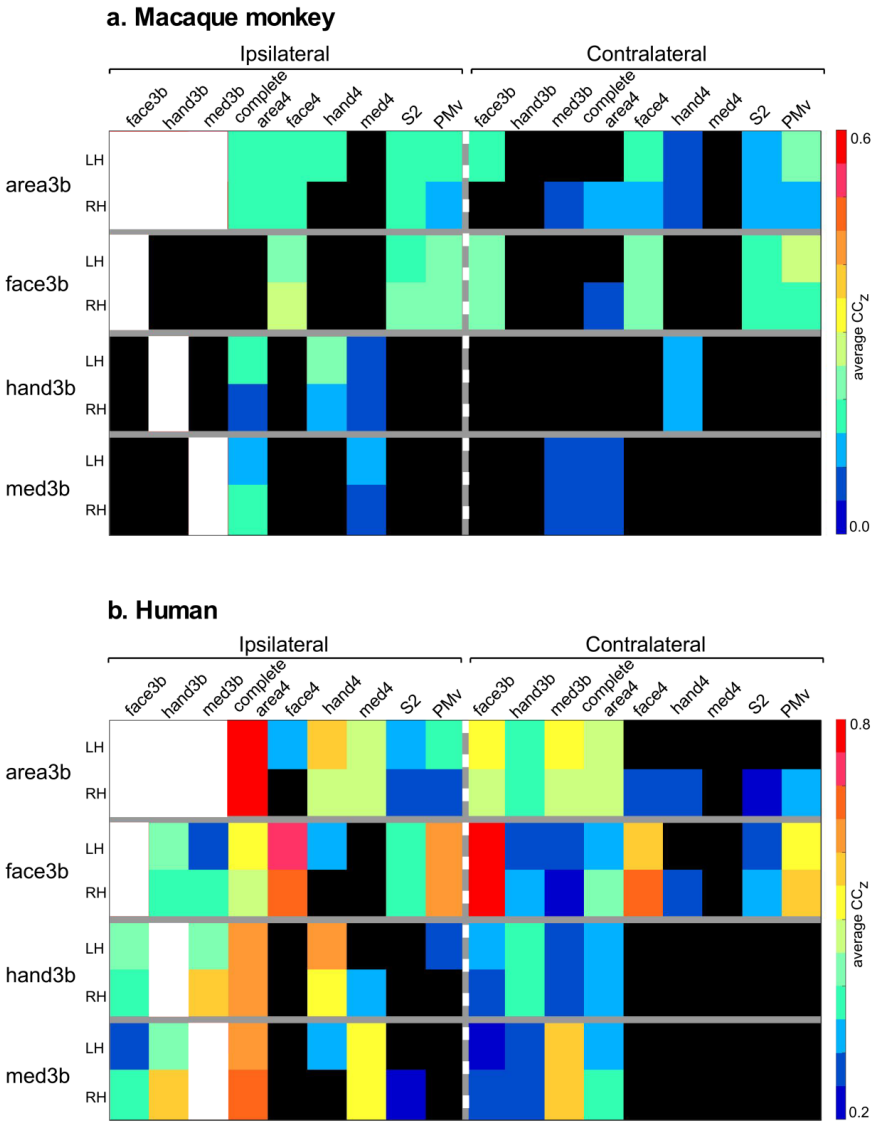

Fig. 5. Correlation matrices showing ROI-ROI resting state functional connectivity between different ROI's in ipsilateral (left of the dashed white line) and contralateral hemispheres (right of the dashed white line) of (a) monkeys and (b) humans. The seed regions are shown on the y-axis, and the target regions on top. Each colour coded value denotes averaged Fisher-z transformed correlations (CCz) acquired from different subjects. For colour codes, see the bars on the right. Statistically nonsignificant correlations are shown in black and autocorrelations are in white ($p \leq 0.01$ for monkeys; $p \leq 0.00001$ for humans; one sample t-test). 3b, area 3b; 4, area 4; 'face', 'hand', 'med' prefixes denote the face, hand and the medial part of area 3b or 4. LH, left hemisphere; RH, right hemisphere.

3.2.1 Bilateral connectivity

Networks of different somatotopic representations showed differences in the extent of connectivity with homotopic representations in the contralateral hemisphere. All somatotopy based ROI's in both the species showed significant bilateral connectivity except for the hand3b in monkeys (Fig. 5). Average Fisher's z-transformed correlation coefficient (CCz) values in both species showed that the highest inter-hemispherical strength of correlations was for face3b followed by med3b (Fig. 6; face3b: macaque, p=1.0 x 10^{-3}; human, p=6.7 x 10^{-10}; med3b: macaque, p= 1.9 x 10^{-3}; human, p=2.3 x 10^{-9}; one sample t-test). In humans the hand3b had lesser bilateral connectivity than med3b, while in monkeys hand3b had no significant connections to the contralateral hand3b (Fig. 6; p=4.03 x 10^{-7}, one sample t-test).

The interhemispheric connectivity of all the three ROI's -face3b, hand3b and med3b with non-homotopic ROI's in contralateral area 3b was significant only in humans (Fig. 5; one-sample t-test, see Table 2 for p-values).

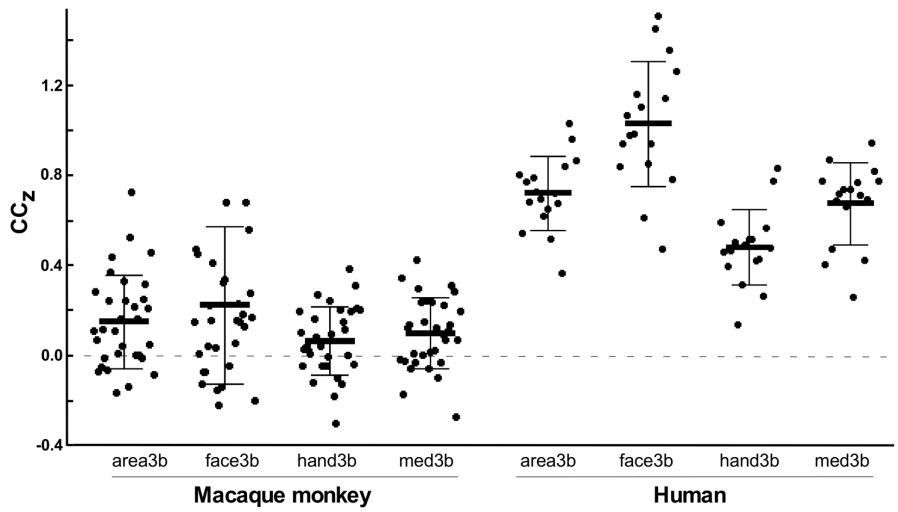

Fig. 6. Inter-hemispheric homotopic functional connectivity of area 3b, and the somatotopic ROI's – face3b, hand3b and med3b, in macaque monkeys and humans. Each dot denotes Fisher-z transformed correlation value (CC_Z) for a single session in monkeys and a single subject in humans. The thick horizontal lines mark the mean, and the thin lines, ±SD.

3.2.2 Functional connectivity with S2 and PMv

In both monkeys and humans only face3b had significant connectivity with areas other than the primary somatosensory and motor ROI's (Fig. 5 and 7). The face3b, in the left hemisphere (LH) as well as the right hemisphere (RH) had significant connectivity with S2 and PMv (for S2 in LH see Fig. 7a, top; macaque, $p = 9.5 \times 10^{-5}$; human, $p = 3.1 \times 10^{-6}$; for S2 in RH see Fig. 7a, bottom; macaque, $p = 1.1 \times 10^{-6}$; human, $p = 1.0 \times 10^{-8}$; for PMv in LH see Fig. 7b, top; macaque, $p = 3.0 \times 10^{-7}$; human, $p = 4.7 \times 10^{-9}$; for PMv in RH see Fig. 7b, bottom; macaque, $p = 4.9 \times 10^{-6}$, human, $p = 8.8 \times 10^{-9}$; one sample *t*-test). In humans hand3b in the left hemisphere also showed significant connectivity with PMv (Fig. 7b, top; one sample *t*-test, $p = 8.4 \times 10^{-6}$), and med3b of right hemisphere had significant bilateral connections with S2 (see Table 2 for *p*-values). In monkeys, hand3b or med3b did not show any connectivity with S2 or PMv.

The data suggested that in both the species connectivity observed for entire area 3b with S2 and PMv was primarily a reflection of the face3b correlations with these areas.

3.2.3 Connectivity with homotopic representations in area 4

We compared the correlations of different topographic representations in area 3b with the homotopic body part representation in motor area 4. All three ROIs - face3b, hand3b and med3b showed strong connectivity with the corresponding representation in the ipsilateral primary motor cortex in both macaque monkeys and humans (Fig. 5). The mean correlation strength of face3b with face4 was significantly higher than the correlation between face3b and hand3b (see Fig. 8a, left, for LH, , macaque, $p = 5.4 \times 10^{-3}$; humans, $p = 4.0 \times 10^{-3}$; see Fig. 8a, right, for RH; macaque, $p = 5.2 \times 10^{-4}$; humans, $p = 2.7 \times 10^{-3}$; paired *t*-test) or face3b and med3b (see Fig. 8a, left. for LH; macaque, $p = 2.4 \times$

10^{-4}; humans $p = 1.5 \times 10^{-4}$; see Fig. 8a, right, for RH; macaque, $p = 1.7 \times 10^{-3}$; human, $p = 2.0 \times 10^{-3}$; paired *t*-test). Thus, for face connectivity with face representation in area 4 was stronger than for other ROI's in area 3b.

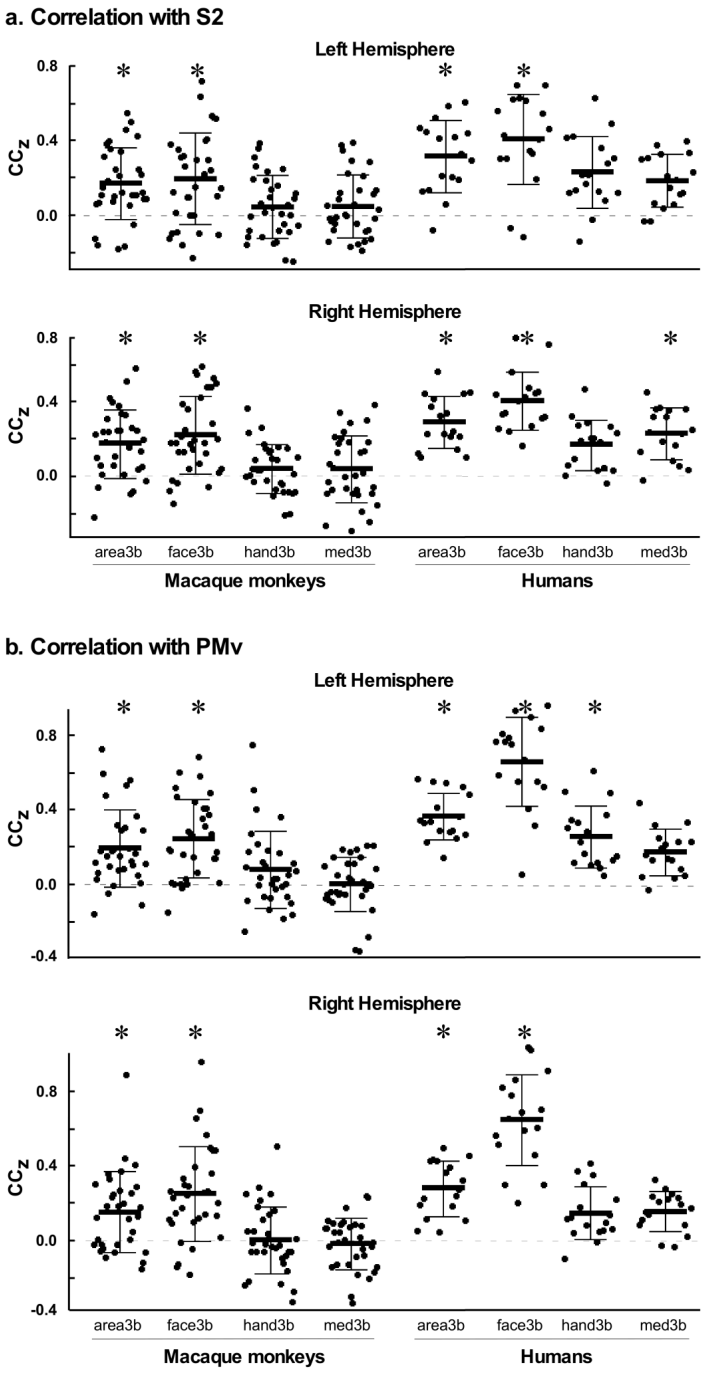

Fig. 7. Correlation coefficients (CCz) of somatosensory ROIs with ipsilateral (a) S2 and (b) PMv in macaque monkeys and humans. Each dot denotes Fisher-z transformed correlation value (CCz) for a single session in monkeys and a single subject in humans. Asterisk* denote statistical significant difference ($p < 0.01$ in monkeys; $p < 0.00001$ in humans; one sample t-test). Other conventions as for Fig. 6.

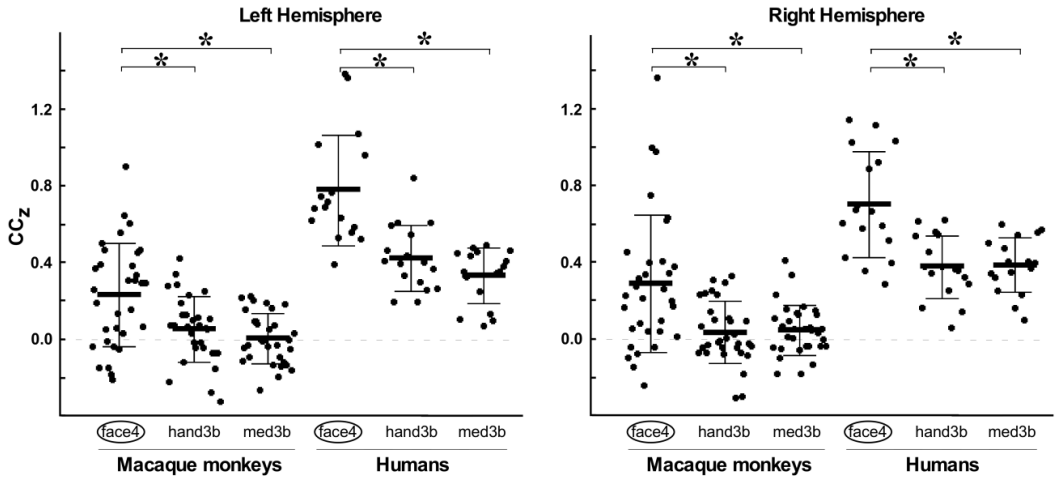

Fig. 8. Functional correlations of the somatosensory face3b ROI with rostrally adjacent motor representation in area 4 (face4) in both hemispheres of macaque monkeys and humans. Each dot denotes Fisher-z transformed correlation value (CCz) for a single session in monkeys and a single subject in humans. The homotopic area 4 representation in marked by the oval. Asterisk* denotes statistical significance with p<0.01, paired t-test. Other conventions as for Fig. 6.

In the left hemisphere of monkeys the connectivity of hand3b with hand4 was significantly higher (not shown) than between hand3b and face3b (paired *t*-test, $p = 7.4 \times 10^{-5}$) or hand3b and med3b (paired *t*-test, $p=2.7 \times 10^{-6}$). In the right hemisphere the connectivity of hand3b with hand4 was higher, but not statistically different from that between hand3b and face3b (paired *t*-test, $p=4.5 \times 10^{-2}$) or hand3b and med3b (paired *t*-test, $p=2.8 \times 10^{-1}$). In humans, the connectivity of hand3b with hand4 in both the hemispheres was stronger, but was not significantly higher than between hand3b and face3b (paired *t*-test, $p=1.3 \times 10^{-2}$, LH; $p=1.7 \times 10^{-2}$, RH) or hand3b and med3b (paired *t*-test, $p=1.1 \times 10^{-2}$, LH; $p=6.9 \times 10^{-1}$, RH).

For med3b, connectivity with med4 in humans was significantly higher than with face3b, but only in the left hemisphere ($p = 9.3 \times 10^{-3}$, paired *t*-test).

The mean connectivity of med3b with med4 in the right hemisphere of both species was higher than with face3b (macaque, $p = 1.8 \times 10^{-1}$; human, $p = 1.5 \times 10^{-1}$; paired *t*-test) or med3b and hand3b (macaque, $p = 3.0 \times 10^{-1}$; human, $p = 5.7 \times 10^{-1}$; paired *t*-test) but the difference was not statistically significant.

3.3. Comparison of the functional connectivity in monkeys and humans

The functional networks of entire area 3b and the somatotopic ROI's were similar in both macaque monkeys and humans (Fig. 3 and 9). The network of the entire area 3b in both the species simply shows the nodes of networks of face3b, hand3b and med3b. In both monkeys and humans, the face3b has widespread bilateral functional connectivity network with correlating regions both within and outside the primary somatosensory cortex. Only the face3b was functionally connected to secondary sensory cortex and premotor areas in both the species (Fig. 7). The hand3b and med3b, in both species showed network connectivity restricted to area 3b and area 4 (Fig. 9).

However, there were few notable differences in the functionally connected regions and their connectivity strengths between the two species. Face3b connections in macaque monkeys showed significant bilateral correlations with parietal area 7b and putamen, which were not observed in humans (Fig. 4). The face3b network in monkeys did not show any connections with the regions on the medial wall at the border of area 4 and the supplementary motor area, which was seen in humans (Fig. 4).

In monkeys hand3b showed significant bilateral functional connectivity with hand4, but not in humans (Fig. 5 and 9; RH, $p=2.7 \times 10^{-5}$, LH, $p=1.01 \times 10^{-4}$, one sample *t*-test. The inter-hemispheric connectivity of the hand representations in area 3b was also different between the two species. Only in

humans, hand3b showed significant connection with the hand representation in contralateral area 3b (one sample *t*-test, p=3.0 x 10^{-2}, MK; p=4x 10^{-7}, HU). In addition, med3b showed significantly higher bilateral connectivity in humans than macaque monkeys (p=2.4x10^{-11}, two sample *t*-test). Finally, the significant connectivity between different somatotopic representations within area 3b i.e. face, hand and medial regions was observed only in humans (Fig. 5 and 9).

4. DISCUSSION

We performed seed-based correlation analysis to determine resting-state connectivity of different somatotopic representations in area 3b of macaque monkeys and humans. Previously both somatosensory and motor areas have been lumped together for connectivity analysis. Our results show that there is a characteristic somatosensory network for each somatotopic representation, which is largely similar in macaque monkeys and humans. Some of the main observations from our ROI-ROI and ROI-voxel analyses are discussed below. The results are summarized in Figure 9.

4.1 Understanding brain connectivity using resting-state correlations

Resting-state functional connectivity networks, which are determined from the time-series correlation of different brain regions in a task free condition have been described for different mammalian species including humans, monkeys, cats, ferrets, rats and mice (Biswal et al., 1995; Lu et al., 2012; Popa et al., 2009; Stafford et al., 2014; Vincent et al., 2007; Zhou et al., 2016). Resting-state networks have been used to delineate functional brain networks such as somatomotor, visual and auditory networks, the dorsal and ventral attention systems, the fronto-opercular salience region, and what is known as default mode network (Biswal et al., 1995; Cordes et al., 2000; De Luca et al., 2005; Fox et al.,

2006; Fox et al., 2005; Greicius et al., 2003; Lowe et al., 1998; Raichle et al., 2001; Seeley et al., 2007). The latter has been proposed to support emotional processing and self-referential activity (Gusnard et al., 2001; Simpson et al., 2001). The resting-state networks also predict brain areas that would be active during stimulus driven activation and during various cognitive tasks (De Luca et al., 2005; Hampson et al., 2006; Seeley et al., 2007; Tavor et al., 2016; Vincent et al., 2006). Changes in intrinsic functional connectivity have also been used as biomarkers for diseased brains (Greicius, 2008; Zhang and Raichle, 2010), and more recently for determining the location and extent of cortical areas (Glasser et al., 2016; Gordon et al., 2016).

We determined resting-state network connectivity for different topographic representations in the somatosensory cortex of macaque monkeys and humans. Previous reports in macaque monkeys described the resting-state network considering all the somatomotor areas as a single ROI (Beckmann et al., 2005; Hutchison et al., 2011), or at the most after dividing the somatomotor areas into dorsal and ventral subdivisions (Mantini et al., 2013; Vincent et al., 2007). We show here that each somatotopic representation in area 3b has its own distinct network, which is different from that for other body parts. Network of the entire area 3b simply reflects sum of all individual networks. The somatosensory network for complete area 3b described here is generally similar to as those for the 'somatomotor networks' described in previous studies (Long et al., 2014; Mantini et al., 2013; Power et al., 2011; Yeo et al., 2011). However, some of the nodes such as area 5, 7, putamen, and insula are revealed only when area 3b was considered separately as seed ROI, suggesting importance area specific ROI's for connectivity analysis.

4.2 Functional connectivity reflects anatomical connections

The resting-state functional networks reflect anatomical connections as determined using neuroanatomical tracers or lesion studies. Relationship between functional connectivity and direct anatomical connectivity has been emphasized (van den Heuvel et al., 2009; Wang et al., 2013). Our results show that area 3b has connectivity with areas 1, 2, 4, 5, 7, S2/PV, PMv and insula, the areas that are known to have anatomical connections with area 3b (Burton et al., 1995; Darian-Smith et al., 1993; Jones and Powell, 1969a; Pons and Kaas, 1986). Differences in the ipsilateral and contralateral resting-state connectivity observed for different somatotopic ROIs- face3b, hand3b, and med3b reflects differences in the underlying anatomical connectivity of these somatotopic representations (Jones and Powell, 1969b; Killackey et al., 1983). For example, we found that face3b network has the largest number of bilateral nodes which include face4, S2/PV, PMv and insular cortex, and the contralateral face3b. This reflects anatomical connectivity of face representation in area 3b. Face representation in area 3b is known to receive direct projections from area 3a, 1, 2, 4, S2/PV, PMv and Insula (Cerkevich et al., 2014; Disbrow et al., 2003). Connectivity of area3b is also seen with areas 3a, 1 and 2 (see Fig. 3 and 4) but is not separately analyzed here because of difficulties in placing ROI's that are clearly distinct from area 3b.

In macaque monkeys, the face representation also showed significant correlation with the posterior parietal area 7b and putamen in the ROI to voxel analysis. Neuroanatomical studies have shown connectivity of the face representation in area 3b with the rostro-lateral part of area 7b (Burton et al., 1995; Lewis and Van Essen, 2000), and large parts of area 7b has somatosensory responses to mouth and face (Hyvarinen, 1981). In monkeys topographic projections from the somatosensory cortex to the putamen have been seen using anatomical tracers (Jones et al., 1977; Kunzle, 1977) as well as lesion studies (Kemp and Powell, 1970). The voxels in the lateral putamen

correlating with face3b are in a similar location as the somatosensory projections to putamen (Kunzle, 1977).

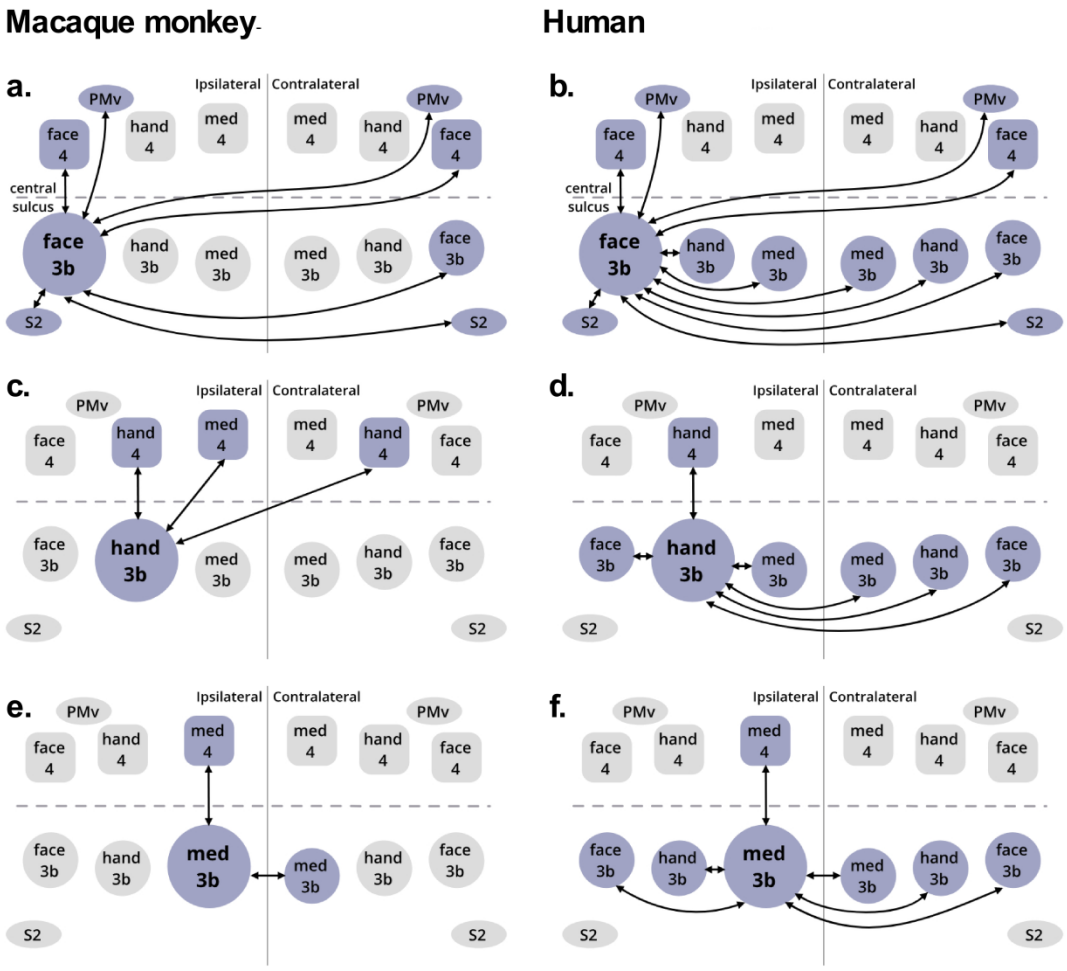

Fig. 9. A schematic showing resting state functional connectivity in macaque monkeys (left panels) and humans (right panels) for different somatotopic ROI's (enclosed with large circles) – (**a** and **b**) face3b, (**c** and **d**) hand3b, and (**e** and **f**) med3b with different areas and topographic representations in the ipsilateral and contralateral hemispheres. Spheres represent topographic representations in area 3b, rounded squares in area 4; and ovals represent areas other than the primary somatosensory and motor cortical areas. Blue shaded regions connected by double headed arrows show areas with statistically significant ROI - ROI correlations. The regions filled with light grey did not have any significant correlations. One sample t-test, $p<0.01$ (monkeys), $p<0.00001$ (humans). Arrows in the schematic do not imply any directionality.

As compared to face3b, the network of other ROIs i.e., hand3b and med3b had fewer nodes, which were largely confined to the primary somatosensory and motor cortices (see Results, and Fig. 9). In monkeys, hand3b was functionally connected to the hand representation in contralateral area 4, but not the hand representation in contralateral area 3b. This reflects the lack of homotopic callosal connections of the hand representation in area 3b (Killackey et al., 1983), and the presence of callosal connectivity, although weak, of primary motor cortex (Fang et al., 2008; Rouiller et al., 1994). In monkeys, bilateral correlation of hand3b with area 5 was observed. In area 5 there is a magnification of the hand representation with neurons having large receptive fields on the forelimb and hand (Padberg et al., 2005; Seelke et al., 2012).

Differences in the functional connectivity of the face and hand representations in area 3b with PMv also reflect differences in the anatomical connectivity. Although the strongest projections from area 3b to PMv are from the face representation, PMv also has minor inputs from the hand representation (Dancause et al., 2006). In humans we observed hand3b to PMv connectivity in the left hemisphere.

The functional connections of med3b were found to be restricted to the rostrally adjacent area 4 and the contralateral homotopic med3b. This is in agreement with the known callosal connectivity of area 3b representations, where face and trunk representations have more callosal connections as compared to the hand representation (Killackey et al., 1983; Pandya and Vignolo, 1969). Thus, the functional connectivity of different somatotopic representations reflects anatomical connectivity.

However, we did not observe any significant resting state correlations of hand representation in area 3b with S2 in spite of their direct anatomical connectivity (Eickhoff et al., 2007; Krubitzer et al., 1995). This might be due to

relatively smaller representation of hand within S2, which does not emerge as significant in the averaged correlation measures.

4.3 Functional connectivity is not always dependent upon direct structural connectivity

It has been suggested that functional connectivity is not necessarily constrained by absence of direct structural connectivity (Raichle, 2015). The functional connectivity networks are not only driven by monosynaptic connections but also polysynaptic connections (Honey et al., 2009; Vincent et al., 2007). Thus resting state coherence observed between areas that lack monosynaptic connections likely reflects emergent cortical network properties (Adachi et al., 2012; Vincent et al., 2007). Our results also reveal this aspect of structure-function relationship of functional networks. For example, we found strong functional association between area 3b and area 4 representations, which lack direct anatomical connections. These functional correlations might reflect the indirect anatomical links through somatosensory area 2 and 5 which receive projections from area 3b and send projections to the motor cortex (Darian-Smith et al., 1993; Jones et al., 1978; Vogt and Pandya, 1978).

We found only the face representation in area 3b has significant connectivity with area 4 face representation and not the other somatotopic representations in area 3b (Fig. 8a). Although there is no direct anatomical connectivity between area 3b and area 4, functional connectivity between representations across the central sulcus points to information flow between homologous representations in area 3b and area 4 required for coordinated activity in these brain areas required for sensorimotor tasks. There is also a phylogenetic closeness of the neuronal mass populating the similar body representations that mediate coordinated neural activity in the sensory and

motor regions (Flechsig,1920 as cited in Kuehn et al., 2017). A functional association between motor and somatosensory areas has been observed as spatiotemporal coherence in local field potential (LFP) signals (Arce-McShane et al., 2016; Murthy and Fetz, 1992).

There are other examples illustrating that resting-state functional connectivity also reflects indirect or higher order anatomical connectivity. For example, connectivity of area 3b with insular cortex is likely a reflection of indirect anatomical connectivity via the secondary somatosensory cortex (Burton et al., 1995; Friedman et al., 1986). Functionally, innocuous somatosensory stimulation of face and oral structures is known to elicit neuronal responses in the granular regions of insula (Schneider et al., 1993).

4.4 Resting networks of area 3b are similar in humans and monkeys

Although separated by 25 million years of evolution (Kaas, 2004, 2012), macaque monkeys and humans share similarities in the structural connectivity and functional networks of different brain areas (Goulas et al., 2014; Mantini et al., 2013; Sallet et al., 2013). It has been reported that somatomotor networks have high topological correspondence in humans and monkeys (Mantini et al., 2013). The current study is the first to determine and directly compare resting-state networks of different topographic representations in both humans and macaque monkeys. We used somatotopy specific seed ROIs that were also validated using localizer scans in both macaques and humans, assuring accuracy of the observed networks (Fig. 9).

Our results show that connectivity of different topographic representations in area 3b viz. face3b, hand3b and med3b is similar in monkeys and humans (see Fig. 5, 9). These similarities include (1) face 3b having widespread bilateral

functional connectivity with face4, S2/PV, PMv, insular cortex, and contralateral face3b, and (2) functional connectivity of different area 3b representations with homotopic representations in area 4.

Previous neuroanatomical data from monkeys has shown that connectivity between different areas is strongest between homotopic body part representations (Ashaber et al., 2014; Negyessy et al., 2013; Wang et al., 2013). Our results also show stronger functional connectivity between homotopic body part representations in different areas of the brain thus reinforcing the importance of somatotopic representations in information processing.

The two primate species also had certain differences in the functional connectivity network (see Fig. 9), probably reflecting species specific behavioral differences. The differences are most evident in the functional networks of the hand representation. The hand3b in monkeys showed bilateral connectivity with the hand representation in the motor cortex while in humans it was only with ipsilateral area 4. In addition, the hand3b network included med4 i.e. the motor representations of the hindlimb and foot only in monkeys. These differences might reflect morphological differences in the joint mobility, and locomotor behaviors of the facultative quadrupedal monkeys and fully bipedal humans (Liu et al., 2016; Preuschoft, 2004). Many functional correlations were found only in humans. For example, humans showed correlation of face3b with voxels at M1/SMA border on the medial wall while the monkey brains did not. Bilateral connections between area 3b hand regions were observed only in humans; as well as the significant connectivity between face, hand and the medial regions of area 3b was present only in humans, perhaps reflecting their complex object manipulation abilities that requires fine tactile inputs.

4.5 Limitations of the study and methodological considerations

The difference in functional connectivity between humans and monkeys could reflect evolutionary differences between the two species. However, there are technical considerations that should also be taken into account while interpreting the results.

The inter-species differences in functional connectivity could also be due to the differences in brain organization i.e. the number and sizes of the cortical areas, their specialization, and anatomical connectivity. For example, correlations of area 3b representations with putamen, area 7 and area 5 were found only in macaque monkeys. While anatomical connections in monkeys have been described in detail, information on the anatomical connectivity in humans is sparse and generally indirectly inferred. These, differences in functional connectivity might also be due to the differences in brain sizes of the two species which can give rise to alterations in neuronal wiring and information processing (Kaas, 2000). Larger size of human brain along with its dense white matter fiber connections can give rise to stronger correlation values.

The mean correlation strengths of connections in monkeys were always lower than in humans (e.g. Figs 6, 7 & 8). This could be due to differences in the sizes of the monkey and human brain scanned in the same magnet. Although we used a knee coil for monkeys to improve the filling factor, the signal to noise ratio was better for the human brain.

The difference between the human and monkey data could also be due to the brain state differences. We scanned monkeys in anesthetized state while human participants were awake. The monkeys were anesthetized due to ease of handling. Due to the anesthetized state of monkeys, there could be a reduction in the BOLD signal strength and consequently reduction in the calculated correlation strengths (Bettinardi et al., 2015; Grandjean et al., 2014; Logothetis

et al., 1999). Isoflurane, used in the current study, is known to depress the brain activity and cause general nonselective suppressive effects on local functional connectivity of fine-scale cortical circuits in a dose dependent manner (Hutchison et al., 2014; Wu et al., 2016). Thus, the dynamic nature of connectivity during awake state might be reflected as widespread interareal connectivity across different topographic representations within area 3b only in humans, but was more restricted in anaesthetized monkeys.

Different anaesthetic agents affect the connectivity patterns differently (Paasonen et al., 2018). Ketamine, an NMDA antagonist, has been shown to reduce the intrinsic brain connectivity in primary somatosensory and auditory cortices (Niesters et al., 2012). However, comparative studies using different anesthetic agents show that isoflurane is an ideal candidate for resting state connectivity studies using animal models (Grandjean et al., 2014; Jonckers et al., 2014; Lv et al., 2016). Moreover, the isoflurane levels in the current study (0.8% maximum) were lower than the most resting-state studies which use up to 1.25%-1.5% isoflurane (Hutchison et al., 2014; Vincent et al., 2007; Wu et al., 2016). Although the amplitude of functional correlations might reduce under anesthesia, the conservation of functional networks across different brain states such as arousal and sleep has been described (Fukunaga et al., 2006; Hutchison et al., 2013). This suggests that despite the differences in the brain state while scanning, the differences observed between the two species could be actual species-specific differences.

We used averaged connectivity measures from each ROI for the analysis, although there are reports that the functional connectivity is not static but dynamically variable across different time scales (Chang and Glover, 2010; Hutchison et al., 2013). Certainly, different analysis methods considering non-stationary transient state changes in connectivity can give more complete information regarding the baseline spontaneous activity in the brain. However,

the topographic variation of resting functional networks across different body part representations was visible even while using zero-lag, time averaged correlation measures. Despite these limitations we found remarkable similarities between humans and monkeys.

5.0 CONCLUSIONS

Our results show that the network architecture described as 'somatomotor network' is a composite structure and is comprised of multiple independent and different networks of different topographic representations. Care needs to be taken while assigning the network characteristics uniformly to the participating nodes. A similar recent study has described the non-uniformity of the task negative default mode network (DMN) in humans and has found that subnetworks exist within the DMN (Braga and Buckner, 2017). Previous reports on the intrinsic functional connectivity of human brain discuss the intra network heterogeneity within somatomotor network and suggest the importance of topographic areas in delineating network boundaries (Kuehn et al., 2017; Long et al., 2014; Power et al., 2011; Yeo et al., 2011). The current study extends the understanding of the normal structure of spontaneous connectivity and describes how it varies across different body part representations in somatosensory area 3b in macaque monkeys and humans. In all the acquired fMRI sessions in both the species, the somatosensory ROIs consistently described distinct functional subnetworks which largely reflected the underlying anatomical connectivity patterns. The results suggest that rather than considering the entire 'somatomotor' area as a whole network, connectivity network analysis should take body area representations into consideration. This knowledge of the somatotopy dependent connectivity is crucial in understanding the changes in the information processing within these networks in disease and injury

conditions such as spinal cord injury that cause large-scale somatotopic reorganization.

COMPETING FINANCIAL INTERESTS

The authors declare no competing financial interests.

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Table 1. *p*-values for ROI-ROI correlations for monkeys. LH, left hemisphere; RH, right hemisphere. Only significant pair-wise correlations i.e. where *p-value* < 0.01 (one sample t-test) are shown. Grey boxes are auto-correlations.

Target \ Seed		area3b		face3b		hand3b		med3b	
		RH	LH	RH	LH	RH	LH	RH	LH
face3b	RH	3.27×10^{-18}	3.64×10^{-04}		1.02×10^{-03}	-	-	-	-
	LH	-	5.31×10^{-12}			-	-	-	-
hand3b	RH	1.85×10^{-22}	-				-	-	
	LH	-	1.27×10^{-18}					-	-
med3b	RH	5.99×10^{-16}	-						1.90×10^{-03}
	LH	4.82×10^{-03}	3.27×10^{-17}						
face4	RH	3.80×10^{-03}	4.26×10^{-04}	1.12×10^{-04}	6.76×10^{-04}	-	-	-	-
	LH	3.61×10^{-04}	2.48×10^{-05}	8.98×10^{-06}	4.52×10^{-05}	-	-	-	-
hand4	RH	-	8.75×10^{-03}	-	-	2.68×10^{-03}	2.04×10^{-03}	-	
	LH	7.44×10^{-03}	1.43×10^{-06}	-	-	2.28×10^{-04}	1.45×10^{-09}	-	
med4	RH	-	-	8.39×10^{-03}	7.39×10^{-04}	3.81×10^{-03}	-	2.70×10^{-03}	-
	LH	-	-	-	-	-	5.28×10^{-03}	-	9.64×10^{-03}
S2	RH	9.28×10^{-06}	4.17×10^{-06}	1.11×10^{-06}	1.47×10^{-05}	-	-	-	-
	LH	2.11×10^{-03}	2.08×10^{-05}	3.64×10^{-04}	9.52×10^{-05}	-	-	-	-
PMv	RH	5.37×10^{-04}	2.43×10^{-06}	4.98×10^{-06}	6.52×10^{-08}	-	-	-	-
	LH	2.45×10^{-03}	9.16×10^{-06}	4.37×10^{-05}	2.97×10^{-07}	-	-	-	-

Table 2. P-values for ROI-ROI correlations for humans. LH, left hemisphere; RH, right hemisphere. Only significant pair-wise correlations i.e. where *p-value* < 0.00001 (one sample t-test) are shown. Grey boxes are auto-correlations.

Target \ Seed		area3b		face3b		hand3b		med3b	
		RH	LH	RH	LH	RH	LH	RH	LH
face3b	RH	3.70×10^{-12}	3.13×10^{-09}		6.66×10^{-10}	5.80×10^{-08}	3.80×10^{-06}	5.86×10^{-09}	6.21×10^{-06}
	LH	3.19×10^{-08}	5.85×10^{-12}			4.82×10^{-06}	1.91×10^{-08}	6.70×10^{-06}	1.71×10^{-07}
hand3b	RH	6.94×10^{-14}	1.91×10^{-08}				4.03×10^{-07}	8.03×10^{-10}	3.51×10^{-07}
	LH	8.38×10^{-09}	1.92×10^{-12}					5.15×10^{-06}	8.35×10^{-09}
med3b	RH	5.40×10^{-14}	1.66×10^{-09}						2.34×10^{-09}
	LH	1.00×10^{-08}	1.68×10^{-15}						
face4	RH	-	-	1.18×10^{-08}	2.53×10^{-06}	-	-	-	-
	LH	5.90×10^{-08}	1.92×10^{-08}	9.59×10^{-09}	1.29×10^{-08}	-	9.64×10^{-06}	-	-
hand4	RH	2.84×10^{-07}	1.40×10^{-06}	-	-	1.07×10^{-07}	-	-	-
	LH	8.16×10^{-06}	1.68×10^{-08}	2.44×10^{-06}	2.72×10^{-07}	-	2.77×10^{-08}	-	1.35×10^{-07}
med4	RH	3.39×10^{-07}	-	-	-	9.68×10^{-07}	-	2.52×10^{-06}	-
	LH	-	1.79×10^{-07}	-	-	-	-	-	3.56×10^{-07}
S2	RH	2.54×10^{-07}	-	1.00×10^{-08}	4.87×10^{-06}	-	-	4.48×10^{-06}	-
	LH	5.04×10^{-07}	4.36×10^{-06}	5.86×10^{-07}	3.08×10^{-06}	-	-	8.91×10^{-06}	-
PMv	RH	9.49×10^{-07}	-	8.76×10^{-09}	1.73×10^{-06}	-	-	-	-
	LH	1.21×10^{-07}	2.52×10^{-09}	1.46×10^{-08}	4.71×10^{-09}	-	8.40×10^{-06}	8.94×10^{-06}	-

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