Connectivity profiles reveal the relationship between brain areas for social cognition in human and monkey temporoparietal cortex

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The human ability to infer the thoughts and beliefs of others, often referred to as "theory of mind," as well as the predisposition to even consider others, are associated with activity in the temporoparietal junction (TPJ) area. Unlike the case of most human brain areas, we have little sense of whether or how TPJ is related to brain areas in other nonhuman primates. It is not possible to address this question by looking for similar task-related activations in nonhuman primates because there is no evidence that nonhuman primates engage in theory-of-mind tasks in the same manner as humans. Here, instead, we explore the relationship by searching for areas in the macaque brain that interact with other macaque brain regions in the same manner as human TPJ interacts with other human brain regions. In other words, we look for brain regions with similar positions within a distributed neural circuit in the two species. We exploited the fact that human TPJ has a unique functional connectivity profile with cortical areas with known homologs in the macaque. For each voxel in the macaque temporal and parietal cortex we evaluated the similarity of its functional connectivity profile to that of human TPJ. We found that areas in the middle part of the superior temporal cortex, often associated with the processing of faces and other social stimuli, have the most similar connectivity profile. These results suggest that macaque face processing areas and human mentalizing areas might have a similar precursor.

comparative anatomy | cooperation | comparative cognition

For a social species like our own, evolutionary success necessitates the ability to navigate a world full of conspecifics. Consequently, humans are extremely sensitive to information about others' emotional states or intentions as provided by cues such as facial expression or body movement. Supporting these abilities, the human temporal cortex contains a number of areas involved in the processing of such social information (1–5). An area that has received particular emphasis in the study of human social abilities is located at the posterior end of the superior temporal sulcus (STS), at the junction with the parietal cortex. This temporoparietal junction (TPJ) area has been implicated in the human ability to attribute belief states to others, so-called "mentalizing" or "theory of mind" (ToM). It has been argued that this ability is uniquely human (6) and forms the basis of our distinctive ability to cooperate, leading to culture and ultimately language (7). TPJ is also associated with "social preferences" and the predisposition to take into account the benefit that might accrue to others as well as to oneself when making a decision (8, 9). Such predispositions are present in monkeys but their neural basis is only beginning to be elucidated (10, 11).

In trying to establish the evolutionary origin of human social abilities, research into the processing of social information in the macaque temporal cortex has demonstrated the existence of a number of areas responsive to faces (12). Functional imaging studies in humans and monkeys have generally suggested similarities between the macaque face-sensitive regions in the inferior temporal cortex and middle STS on the one hand and the human fusiform face area (FFA), lateral occipital face area, and posterior STS on the other hand. However, although the human FFA is generally accepted to be sensitive to facial identity, the human posterior STS face area seems more sensitive to the social information provided by faces, such as eye gaze (13). Similarly, the macaque STS areas contain neurons that are sensitive to social information conveyed by faces, rather than facial identity (14), and even to other social cues such as others' body postures and actions (15). This has led a number of researchers to speculate whether the macaque mid-STS might bear a functional similarity to some of the human social STS regions, even beyond those sensitive to facial information and involved in complex behaviors such as ToM (16–18).

Functional imaging studies aimed at comparing activity profiles of areas in the human and macaque brain have, however, been limited by the complexity of the tasks that macaques can perform in the scanner. Although responses to faces have been demonstrated repeatedly in both species (16, 19), more complicated social tasks have yet to be reported in the macaque. Moreover, there is still an ongoing debate as to whether the two species are capable of similar social tasks—the ability of macaques to engage in ToM has been questioned, as has even the possibility of resolving this debate using behavioral experiments (20). Therefore, rather than looking for brain activity elicited by different types of social tasks, we here test whether there are areas like the human TPJ in monkeys by focusing on different criteria, namely by looking at functional connectivity profiles of brain areas at rest. A connectivity profile is a description of how an area is connected to a network of other brain areas. It constitutes a unique fingerprint for each cortical area, illustrating the type of information an area receives and the areas it can influence (21). Note, however, that a finding of areas with a similar connectivity profile in different species, although suggestive of their shared evolutionary origins, will not indicate equivalence of function.

We have recently demonstrated the cortical network in which mentalizing areas in the human superior temporal cortex, including the TPJ but also a more anterior superior temporal cortex region (STSa), participate (22, 23). We showed that these areas are especially distinguished from adjacent brain areas, including parts of the nearby inferior parietal lobule and TPJ involved in attentional processes, by their connectivity with a selective set of brain regions characterized by strong interactions with the posterior cingulate

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cortex (PCC) and anterior cingulate cortex (ACC) and by the absence of interactions with the cingulate motor areas (CMA) and anterior insula (AI). This connectivity profile of human mentalizing areas can be demonstrated noninvasively using resting state functional connectivity, a functional MRI technique that looks at spontaneous coupling of activity in distant brain areas in the absence of explicit task performance. One can visualize the strength of the functional connectivity of the TPJ with each of the four target areas in a "connectivity fingerprint" (24). The connectivity fingerprint of TPJ with PCC, ACC, CMA, and AI in 36 healthy volunteers is shown in Fig. 1. We will treat this as TPJ's "template" connectivity profile. In this study, we aim to identify regions in the macaque temporoparietal cortex with a similar connectivity profile to this human template.

Results

We first sought to test the applicability of the approach by testing whether searching for voxels with the TPJ connectivity fingerprint allowed us to identify the TPJ in a second group of human subjects. We achieved this by first creating for each of 12 human participants a map of the resting state fMRI functional connectivity with each of the four target areas described above (Fig. 2) and then at the group level testing for a contrast that gave each of the functional connectivity maps the weighting equal to their functional connectivity strength with TPJ in the template (Fig. 1). In the human temporoparietal cortex, the voxels most likely to have the template connectivity profile were located at the posterior end of the superior temporal sulcus, at the location previously attributed to the part of the TPJ area associated with ToM and social preference (8, 9, 22) (Fig. 2, *Upper Right*). In addition, it identified voxels in the STSa, which, as discussed above, is known to participate in similar neural networks as the TPJ (23). Thus, although this connectivity profile does not exclusively identify TPJ, it importantly identifies areas in the human temporoparietal cortex that (*i*) participate in the same cortical network and (*ii*) are implicated in ToM. Below we demonstrate some differences between the connectivity of TPJ and STSa that become apparent on finer-grained analysis.

Having established that the technique of searching for the TPJ template connectivity profile allowed us to identify TPJ in another group of human subjects, we then performed the analogous analyses on resting state fMRI data from 12 macaque monkeys to test which areas have a connectivity profile most similar to the template.

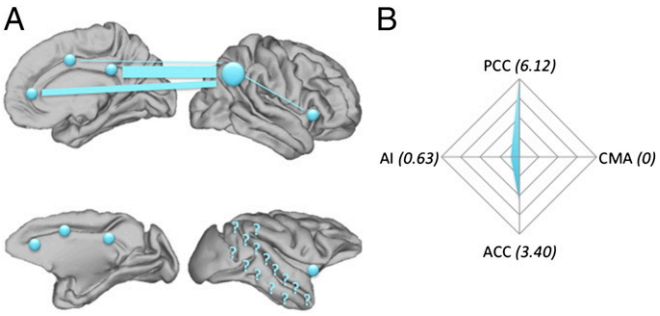

Fig. 1. Logic of the study and template functional connectivity fingerprint of human right TPJ. We know that the part of human TPJ associated with social cognition is distinguished from adjacent nonsocial TPJ regions by the possession of a connectivity profile with the four target regions represented here schematically on a human standard brain (*A*, *Upper*). The width of the lines indicate the strength of functional connectivity between TPJ and each target region in a dataset of 36 participants, as also illustrated in the connectivity fingerprint on the *Right* and the numbers in parentheses (*B*). In this study, we look for areas in the macaque temporal and parietal cortex with a similar connectivity fingerprint with the homologous macaque target areas illustrated schematically in the *Lower* row of *A*.

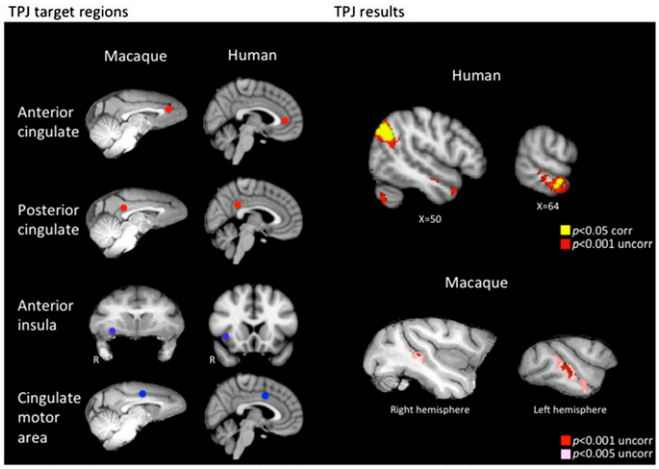

Fig. 2. Voxels showing a similar connectivity profile as human TPJ. (*Left*) Schematically shows the target areas in the macaque and human. (*Right*) This profile best fits the connectivity of TPJ and anterior STS voxels in the human and mid-STS in the macaque.

The target areas for the macaques were in the known homologs of the human target areas (Fig. 2). In the macaque temporal and parietal cortex, the voxels most likely to have a connectivity profile similar to that of human TPJ were located in the middle part of the STS (mid-STS; Fig. 2, *Lower Right*). This pattern was more extended in the left hemisphere with voxels also identified along the STS. Importantly, even at the lenient threshold of $P < 0.005$ uncorrected voxels identified were predominantly confined to the mid-STS. The mid-STS area with the connectivity profile most similar to human TPJ is close to the area whose gray matter density has previously been shown to be positively modulated by macaques' social group size (25). Macaque mid-STS is involved in the processing of social stimuli, particularly faces but also body parts (19, 26). This demonstrates that one of the macaque brain areas specialized for facial and body part processing and human TPJ participate in similar distributed neural systems in both species and suggests they share a common precursor.

This result may seem surprising if it is assumed that the macaque face processing areas in the STS simply correspond with human face areas such as the FFA (19). However, the human FFA is implicated in processing facial identity, whereas face-responsive areas in the human STS are more associated with processing social clues from faces, such as eye gaze (13). The macaque mid-STS region identified in our analysis contains face cells that are generally more responsive to social cues, rather than identity (14). Therefore, to explore the relationship between human areas involved in processing faces and in ToM, we performed two activation likelihood estimation (ALE) metaanalyses of human neuroimaging data using the BrainMap database (27). We independently created ALE maps for activity elicited by ToM paradigms and by face discrimination or processing. ToM was associated with activity in the same posterior TPJ and STSa we identified in our first analysis (Fig. 3*A*, green). Outside the temporoparietal cortex, ToM activated the posterior cingulate and medial frontal cortex. In contrast, activity associated with face processing was present in the FFA, the posterior STS (STSp), and extended amygdala (Fig. 3*A*, blue). Outside the temporal cortex, face processing recruited large parts of lateral frontal cortex, smaller parts of which were observed in ToM as well. The conjunction between the two maps was determined using the minimum statistic (28). Overlap in activity elicited during ToM and face processing was most prominent in the STSp and amygdala (Fig. 3*A*, red). A small focus of overlap was also present in the TPJ, although this seems to be the intersection between two

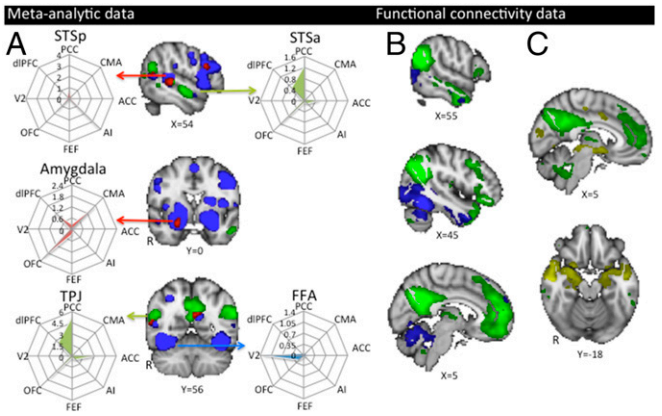

Fig. 3. Metaanalyses and functional connectivity of theory-of-mind and face processing areas. (*A*) Metaanalyses show areas activated during ToM tasks (green) and face processing (blue) and their overlap (red). The functional connectivity fingerprint of regions of interest within these areas (see main text for precise locations) are shown, scaled to the minimum and maximum value of each area's connectivity strength. (*B*) Functional connectivity of TPJ (green) and the fusiform face area (blue). (*C*) Direct contrast of the functional connectivity of TPJ and STSa, showing regions with higher functional connectivity with TPJ in green and regions with higher functional connectivity with STSa in yellow. All functional connectivity maps thresholded at $z > 3.5$.

largely separated areas of activation, one related to ToM and a separate one related to face processing.

We explored the similarity in connectivity between the areas resulting from these metaanalyses with that of the macaque mid-STS. We calculated the resting state functional connectivity of each of the temporal areas identified in the ToM and face processing metaanalyses in the original group of 36 participants and determined their functional connectivity fingerprint in the right hemisphere. In addition to the four target areas PCC, ACC, CMA, and AI, we also looked at their functional connectivity with areas that were shown in the metaanalyses to have some differential interactions with ToM and face processing areas, namely the lateral orbitofrontal cortex (lOFC), the frontal eye field (FEF), the dorsolateral prefrontal cortex (specifically area 9/46D, dlPFC) and the early visual cortex area V2. This showed that the TPJ has additional interactions with dlPFC and lOFC, but not with V2 (Fig. 3*A*).

The anterior part of the STS has the most similar connectivity profile to TPJ, as also suggested earlier in the whole-brain connectivity matching. Therefore, we decided to directly test the whole-brain functional connectivity of TPJ and STSa. This showed that the functional connectivity of TPJ with PCC and ACC target areas was much stronger than that of STSa (Fig. 3 *A* and *C*), whereas STSa had stronger functional connectivity with the hypothalamus and temporal pole (Fig. 3*C*). Hypothalamic connectivity with the mid-STS is known to occur in the macaque (29). Thus, although the two human areas, TPJ and STSa, have a very similar connectivity profile, they each retain slightly different aspects of macaque mid-STS connectivity. In contrast, FFA's functional connectivity profile showed interactions mostly confined to extrastriate cortex and lOFC (Fig. 3 *A* and *B*). Areas that are activated in both ToM and face processing tasks have a connectivity profile that is different from either the ToM or face processing profile.

Finally, we aimed to further characterize the results of the above whole-brain connectivity matching and subsequent metaanalyses. Specifically, we aimed to illustrate the specificity of the macaque mid-STS connectivity profile and the functional connectivity of this area with the larger range of target areas used when describing the metaanalyses results. We created the analogous connectivity fingerprints for a series of 32 areas along the ventral and dorsal banks of macaque STS (Fig. 4*A*). The target regions were the macaque homologs of the human target areas in a larger dataset based on 20 macaques. We then calculated the distance between each STS seed connectivity fingerprint and the human TPJ fingerprint (Fig. 4*D*). The seed with the smallest distance to human TPJ, in other words the region most similar to human TPJ, was in the fundus of the STS [seed 27, at location 18.75 −10.00 −2.25, according to the Montreal Neurological Institute (MNI) macaque atlas] (30). As can be seen in Fig. 4*B*, its connectivity profile is quite similar to that of human TPJ (Fig. 4*C*), although it has a slightly higher relative connectivity to the FEF and AI. In addition, the relative connectivity between human TPJ and ACC is stronger than the connectivity between macaque STS and ACC. It therefore seems that, whereas macaque mid-STS may be the area that most closely corresponds to human TPJ, its functional connectivity pattern is not identical. Moreover some features of the macaque mid-STS coupling pattern, such as the coupling with the anterior insula are reminiscent of the region of the human brain anterior to TPJ here termed the pSTS. One possibility, therefore, is that whereas human TPJ and pSTS have distinct functions concerned with, for example, ToM and social preference on the one hand and the processing of dynamic and social aspects of faces on the other hand, they both share a common precursor with macaque mid-STS.

Discussion

We set out to examine whether the macaque monkey brain contains an area similar to the TPJ area in the human brain that is involved in mentalizing or ToM, the ability to represent the thoughts, intentions, and beliefs of others. Rather than looking at functional activation of brain areas during task performance we focused on anatomical criteria. We exploited the fact that TPJ is characterized by a profile of functional connectivity with a number of areas that are clearly identifiable in both the human and macaque brain. We searched throughout the macaque temporal and parietal cortex for areas with the same connectivity profile as the human TPJ and found that areas in the mid-STS have the most similar connectivity profile.

The most tempting conclusion to draw is that macaque mid-STS is the homolog of human mentalizing areas and that these areas perform similar functions in the two species. That is, however, a difficult conclusion to draw, given that the human and

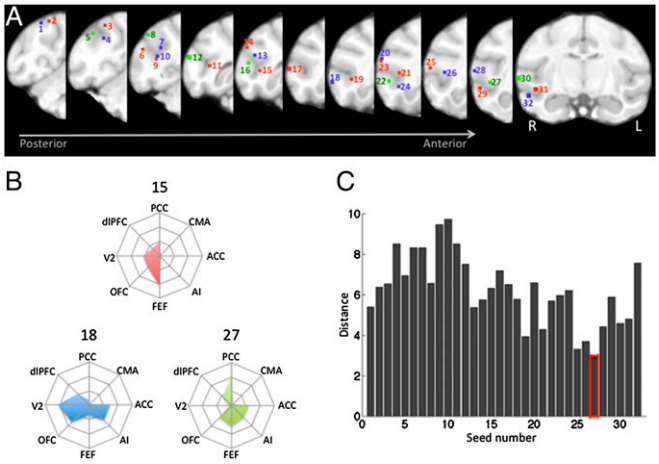

Fig. 4. Matching functional connectivity of human TPJ and 32 macaque STS seeds. (*A*) Location of seed areas along the macaque STS. (*B*) Functional connectivity fingerprint of three representative seeds, each plotted on the same scale, for comparison with the TPJ connectivity profile in Fig. 3*A*. (*C*) Distance between human TPJ and all macaque STS seed areas, showing that seed 27 has the smallest distance.

macaque lineages diverged ~29 million years ago. Indeed, the temporal cortex is an area that has been suggested to have undergone substantial reorganization since the last common ancestor of humans and macaques. Both the middle part of the temporal cortex and the parietal cortex adjacent to the temporal cortex have preferentially expanded in the human brain compared with the macaque brain (31) and it is conceivable that this has resulted in subregions with different functional specializations in the human brain. However, the present results do suggest that areas in the macaque STS might share a common precursor with areas in the human brain involved in more advanced social processes such as mentalizing. Interestingly, it has been suggested that the areas that are most expanded in the human brain are also the ones that are last to mature during ontogeny (32). The network of regions that TPJ is part of and its connections seems to mature only between childhood (>9 y of age) and adulthood (33). Although outside the scope of the current investigation, tracking the development of TPJ connectivity during ontogeny is a potentially fruitful avenue for future studies, especially in light of impaired functioning of this network in certain disorders (34).

As indicated above, the superior temporal area is one of the areas that seem to have expanded most in the human brain, compared with the macaque brain, and it can be expected that such expansions are associated with changes in the organization of the brain and hence its connectivity. The reorganization of the superior temporal area proposed here should therefore be seen in light of other changes that have been identified recently. For instance, the middle part of the inferior parietal lobule (IPL), an area that also appears to have expanded in the human, is coupled with the anterior lateral prefrontal cortex that, in turn, is also expanded (24, 35). Importantly, the target areas used to identify similarities between human TPJ and macaque mid-STS in the present study are all known to be homologous.

The mid-STS region identified in the macaque contains neurons responsive to face stimuli. Importantly these cells are mostly selective for the angle at which the face or head is viewed rather than for its identity per se (14). Apart from head direction, cells in this area are often sensitive to eye gaze, leading some authors to suggest that this area is important in determining where another individual is looking (14). Some evidence for this view was provided by experimental lesions of macaque STS, which impaired eye gaze discrimination (36) but not face discrimination (37). Moreover, parts of macaque STS contain cells sensitive to other sources of social information, such as body parts and actions performed by others (15). Thus, the macaque areas identified as most similar to human mentalizing areas seems to be involved in processing socially relevant information conveyed by faces and bodies rather than just facial identity. This dissociation is reminiscent of the separation of areas activated in ToM paradigms and face recognition paradigms in our metaanalysis of human imaging data. The functional connectivity profile of ToM areas, but not face processing areas, was most similar to the macaque mid-STS connectivity profile. It should be noted that our results are based on group-based statistics, and the relative location of social- and face-related regions can best be quantified in individual participants. Studies on macaque face processing have developed localizers powerful enough to identify face patches in individuals (16), and similar localizers have been developed for human ToM (38) (http://saxelab.mit.edu/superloc.php).

One part of the macaque mid-STS's functional connectivity profile, its coupling with the anterior insula, was absent from human TPJ. By contrast, the human brain region immediately anterior to TPJ, the pSTS, exhibits coupling with the anterior insula. The human pSTS area may not be concerned with the same social cognitive processes as the TPJ but it is sensitive to eye gaze (13). It is possible that human TPJ and pSTS share a common precursor with macaque mid-STS even though these two human brain regions now have differentiated functions, albeit both concerned with aspects of social cognition.

Although there is debate on whether monkeys attribute beliefs to conspecifics, it is known that they at least predict some aspects of others' behavior and, possibly, knowledge (39), and the STS has been suggested to be involved in this process (15). Whereas macaques might use areas in the STS to predict behavior of others, the human TPJ may also allow us to predict the intentions of others (40). One potential evolutionary route for the human TPJ region to have appeared is by an expansion and subsequent division and specialization of mid-STS regions sensitive to facial cues in the common ancestor of humans and macaques. This type of evolutionary trajectory has been proposed as a part of a framework for understanding variations of the common mammalian brain organization (41). This suggestion, derived purely from comparative connectivity, provides important unique hypotheses to test in comparative psychological and neuroscientific research. Finally, these results suggest that for researchers interested in investigating social cognition in macaques, the mid-STS might bear further scrutiny.

Methods

Analysis 1: Determining Human TPJ Connectivity. Resting state functional magnetic resonance imaging (fMRI) and structural MRI data were collected from 36 human participants (15 females, mean age 28.5 y) on a Siemens 3T Trio scanner. All participants gave informed written consent in accordance with ethical approval from the local ethics committee (Oxford Research Ethics Committee A, ref. 10/H0606/34). Participants were lying in the scanner in dimmed light with their eyes open. They were instructed to think of nothing in particular and to not fall asleep. Whole-brain functional imaging was performed using a gradient echo planar imaging sequence [repetition time (TR) = 2,000 ms, echo time (TE) = 28 ms, flip angle = 89°, field of view = 224 mm, voxel dimension = 3 × 3 × 3.5 mm, acquisition time 6 min 4 s). High-resolution 3D T1-weighted MRI scans were also acquired using a magnetization prepared rapid gradient echo sequence (TR = 2,040 ms, TE = 4.7 ms, voxel dimension = 1 mm isotropic).

Data from all experiments were analyzed using tools from FSL (www.fmrib.ox.ac.uk/fsl) and custom tools written in Matlab (MathWorks). The first six volumes of each functional dataset were discarded, after which the following preprocessing was performed: motion correction, nonbrain removal, spatial smoothing [using a Gaussian 5-mm full width at half maximum (FWHM) kernel], grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor, high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50.0 s). Functional images were registered to the skull-stripped structural and MNI template.

Analysis of the connectivity of TPJ was performed using methods described previously (24). A 3 × 3 × 3 voxel region of interest at the MNI coordinates of the part TPJ concerned with ToM as established previously (22) [54 −55 26] was transferred to each individual's functional space and the first major Eigen time course of activity of the TPJ was calculated. The correlation of this time series with each voxel in the brain was then calculated, while taking into account confounding effects of movement and the time course of the white matter and cerebral-spinal fluid. Each participant's correlation map was then used as input in a second level group general linear model (GLM) analysis showing the resting state functional connectivity of TPJ in the population.

We have previously shown that the human TPJ area concerned with social cognition is distinguished from adjacent parts of TPJ by its strong functional connectivity with PCC and ACC, but not with CMA and AI (22). Therefore, we determined the connectivity fingerprint of TPJ with these areas. We determined the functional connectivity of TPJ by calculating the average *z* value of the group *z*-statistical map (thresholded to include only values ≥0) in a 3 × 3 × 3 voxel region in each of the four target regions. The target voxels' coordinates in MNI standard 2-mm space were based on previously published studies from other groups: ACC, 4 42 6 (42), PCC, 4 −42 30 (43), CMA, in particular the rostral cingulate zone, posterior division, 4 6 42 (44), and AI, 38 18 −2 (45). These four target regions were also chosen because their homologs in the macaque brain are known and they are capable of reliably distinguishing TPJ from its immediate neighboring regions (22). The resulting connectivity profile (Fig. 1*C*) is taken to be the template TPJ connectivity profile for *Analysis 2*.

Analysis 2: Voxel-by-Voxel Matching of TPJ Connectivity in Human and Macaque. In *Analysis 2*, we search for voxels with a connectivity profile with PCC, ACC,

CMA, and AI similar to that of the template TPJ connectivity profile in the macaque temporal and parietal cortex. However, to validate our method, first we tested whether we are able to identify TPJ in a separate group of human participants. For this test we used a different human dataset than used above, consisting of 12 participants (right handed, 5 female, mean age 31.1 y, 128 volumes of resting state fMRI scan each using the following parameters: TR = 2,410 ms, TE = 30 ms, voxel size = 3 × 3 × 3 mm, 3T Siemens Magnetom Verio scanner). All participants gave informed written consent in accordance with ethical approval from Oxford Research Ethics Committee B, ref. 10/H0605/48. The data were preprocessed as in *Analysis 1*, above, with the addition of a fieldmap correction using FSL's FUGUE tool, to ensure maximum signal in the temporal cortex. We calculated the connectivity map of PCC, ACC, CMA, and AI for each participant. At the group level, we then tested these correlation maps in a model where each map was given the weight corresponding to the functional correlation of that region with TPJ in the template dataset of analysis 1, using the permutation testing as implemented in FSL's Randomise tool. Significance testing was done across the whole brain. Given the focus of this study on the temporal and parietal cortex, we will limit our discussion of the results to these regions but not surprisingly the analysis also identified PCC and ACC because each of these areas has activity that is functionally correlated both with itself and the other area.

We then sought to perform the same test in an equally large number of macaque monkeys. Macaque fMRI and anatomical scans were collected for 12 healthy macaque monkeys under light anesthesia using isoflurane (*Macaca mulatta*, five females, average age 4.56 y; average weight 6.55 kg) on a 3T whole body MRI scanner. Protocols for animal care, magnetic resonance imaging, and anesthesia were carried out under authority of personal and project licenses in accordance with the UK Animals (Scientific Procedures) Act (1986) issued by the Home Office and approved by the University of Oxford Animal Care and Ethical Review Committee. It has previously been shown that light anaethesia using this agent, although it might affect activity levels, does not influence the distributed patterns of functional connectivity (46), which still reflects known anatomical connections (24) and is similar during rest and task performance (47).

A four-channel phased-array radio-frequency coil in conjunction with a local transmission coil was used for data acquisition (H. Kolster, Windmiller Kolster Scientific, Fresno, CA). Resting state fMRI data were collected for 53 min and 26 s from each animal, using the following parameters: 36 axial slices, in-plane resolution 2 × 2 × 2 mm, no slice gap, TR = 2,000 ms, TE = 19 ms, 1,600 volumes, 3T scanner. Structural scans were acquired for each macaque in the same session, using a T1-weighted MP-RAGE sequence (voxel size 0.5 mm isotropic, TR = 2,500 ms, TE = 4.01 ms, 128 slices). The first six volumes of each functional dataset were discarded, and the following preprocessing was performed: nonbrain removal, 0.1 Hz low-pass filtering to remove respiratory artifacts, motion correction, spatial smoothing (using Gaussian 3-mm FWHM kernel), grand-mean intensity normalization of the entire 4D dataset by a single multiplicative factor, high-pass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50.0 s), and denoising using independent component analysis (ICA). Analyses procedures were then performed in an analogous manner to the human data, including the use of nuisance regressors to capture effects of movement and the time course of any signal change in the white matter and cerebral-spinal fluid, using four target areas identified as homologs between humans and macaques.

Analysis 3: Metaanalysis of Human Functional Imaging Data and Related Connectivity Profiles. ALE was performed using the modified algorithm of Turkeltaub and colleagues (48). ALE aims to identify areas showing a convergence of findings across experiments, which is higher than expected under a random spatial association. In brief, ALE assumes all reported foci to be the center of 3D Guassian probability distributions and aims to create a modeled activation map based on all experiments, which can be tested against a null-distribution reflecting random spatial association between experiments. Reported activation maps are thresholded at $P < 0.05$ (corrected for multiple comparisons using the false discovery rate) and a minimum cluster size of 200 mm^3.

The BrainMap database was queried on December 19, 2012. To identify activations related to face processing, we selected studies using the following criteria: subjects: diagnosis is normals + experiments: paradigm class is face monitor/discrimination + conditions: stimulus is visual (all types) + experiments: activation is activations only. This yielded 141 papers, with 585 of 768 experiments matching criteria. To identify activations related to ToM, we selected studies using the following criteria: Subjects: diagnosis is normals + experiments: paradigm class is theory-of-mind task + conditions: stimulus is visual (all types) + experiments: activation is activations only. This yielded 25 papers, with 99 of 127 experiments matching criteria.

Subsequently, we investigated the functional connectivity fingerprint of these ToM and face processing areas. ROIs of 3 × 3 x 3 voxels were created in the TPJ [54 −55 26] (22) and STSa [58 −10 −12] ToM areas, the FFA [40 −52 −12] (49), and the STSp [50 −38 6] (50) and amygdala [24 −2 −20] conjunction areas. Using the same fMRI data as in *Analysis 1*, we calculated the connectivity fingerprints (Fig. 3*A*) of these areas with the same PCC, ACC, CMA, and AI target areas as well as the lateral OFC [32 48 −14] (51), FEF [30 8 54] (52), dlPFC [26 40 32] (area 9/6D), and V2/area 18 [16 −84 −8] (53).

Analysis 4: Matching Human TPJ Connectivity Profile to That of 32 Macaque Seeds. Finally, we aimed to illustrate further the functional connectivity profiles of the macaque STS. Analysis 2 suggests that the mid-STS is the macaque region most similar to human TPJ and that this effect is specific. For this follow-up analysis, we expanded the number of target areas used to characterize the functional connectivity profiles of the regions resulting from the metaanalyses and show how their connectivity profile compares to that of macaque STS. Therefore, we calculated the connectivity profile of 32 seed areas along the macaque STS (Fig. 4*A*) in an expanded dataset of 20 healthy macaque monkeys (*M. mulatta*, six females, average age 4.38 y; average weight 6.53 kg; includes the 12 participants of analysis 2) collected under identical circumstances. Following preprocessing as described for *Analysis 2*, separate analyses were carried out for each of 32 seed regions in the superior temporal sulcus. These analyses were performed in an analogous way to those conducted for the human TPJ area in analyses 1 and 3. Connectivity fingerprints were established from the group *z*-statistical maps (thresholded ≥0) using four target locations that were the homologs of the four human areas used in analyses 1 and 2 (Fig. 2) as well as lOFC, FEF, dlPFC, and V2.

To formally compare the connectivity profiles between species, the sum of the absolute differences of each seed's normalized connectivity profile and the normalized human TPJ connectivity fingerprint (the so-called "Manhattan distance") was then calculated, providing a distance measure between the connectivity profiles of each macaque seed and the human TPJ (Fig. 1*C*). The seed with the smaller distance score has the connectivity profile most similar to that of human TPJ. This analysis illustrates features of the brain areas identified in *Analysis 2* and *Analysis 3* but it is not meant to provide new inferences at the population level.

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