

Virtual dissection and comparative connectivity of the superior longitudinal fasciculus in chimpanzees and humans



Erin E. Hecht ^{a,*}, David A. Gutman ^b, Bruce A. Bradley ^c, Todd M. Preuss ^d, Dietrich Stout ^a

^a Department of Anthropology, Emory University, 1557 Dickey Drive, Rm 114, Atlanta, GA 30322, USA

^b Department of Biomedical Informatics, Emory University School of Medicine, 36 Eagle Row, PAIS Building, 5th Floor South, Atlanta, GA 30322, USA

^c Department of Archaeology, University of Exeter, Laver Building, North Park Road, Exeter EX4 4QE, UK

^d Yerkes National Primate Research Center, Div. Neuropharmacology & Neurologic Diseases & Center for Translational Social Neuroscience, Emory University, 954 Gatewood Rd, Atlanta, GA 30329, USA

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ABSTRACT

Many of the behavioral capacities that distinguish humans from other primates rely on fronto-parietal circuits. The superior longitudinal fasciculus (SLF) is the primary white matter tract connecting lateral frontal with lateral parietal regions; it is distinct from the arcuate fasciculus, which interconnects the frontal and temporal lobes. Here we report a direct, quantitative comparison of SLF connectivity using virtual *in vivo* dissection of the SLF in chimpanzees and humans. SLF I, the superior-most branch of the SLF, showed similar patterns of connectivity between humans and chimpanzees, and was proportionally volumetrically larger in chimpanzees. SLF II, the middle branch, and SLF III, the inferior-most branch, showed species differences in frontal connectivity. In humans, SLF II showed greater connectivity with dorsolateral prefrontal cortex, whereas in chimps SLF II showed greater connectivity with the inferior frontal gyrus. SLF III was right-lateralized and proportionally volumetrically larger in humans, and human SLF III showed relatively reduced connectivity with dorsal premotor cortex and greater extension into the anterior inferior frontal gyrus, especially in the right hemisphere. These results have implications for the evolution of fronto-parietal functions including spatial attention to observed actions, social learning, and tool use, and are in line with previous research suggesting a unique role for the right anterior inferior frontal gyrus in the evolution of human fronto-parietal network architecture.

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Introduction

Many of the behaviors that distinguish humans from other primates – including social learning and tool use – rely on activation of, and communication between, frontal and parietal cortical regions (Johnson-Frey, 2004; Fabbri-Destro and Rizzolatti, 2008; Peeters et al., 2009; Caspers et al., 2010). Evidence for human specializations in these circuits is accumulating from a growing number of comparative studies. For example, action observation involves inferior frontal and inferior parietal regions in macaques, chimpanzees, and humans (Fabbri-Destro and Rizzolatti, 2008; Caspers et al., 2010; Rilling and Stout, 2014), but the type of detailed, methods-oriented social learning that is uniquely developed in humans may be related to increased activation and connectivity in inferior fronto-parietal cortex (Hecht et al., 2013a,b). Similarly, tool use involves homologous inferior frontal and inferior parietal regions in monkeys and humans (Johnson-Frey,

2004; Ferrari et al., 2005; Hihara et al., 2006; Obayashi et al., 2007; Quallo et al., 2009; Orban and Rizzolatti, 2012), but a region of human anterior inferior parietal cortex has unique response properties that may support uniquely human capacities for causal understanding (Peeters et al., 2009; Orban and Rizzolatti, 2012). More generally, there is evidence for organizational changes and expansion of gray and white matter in the frontal lobes (Smaers et al., 2010; Preuss, 2011; Passingham and Smaers, 2014), changes in frontal and parietal white and gray matter asymmetry (Schenker et al., 2010; Gilissen and Hopkins, 2013; Hopkins and Avants, 2013; Van Essen and Glasser, 2014) and emergence of new functional response properties in inferior frontal (Neubert et al., 2014) and parietal cortex (Peeters et al., 2009). Together, these studies suggest that fronto-parietal circuits were a likely locus of structural-functional adaptation in human brain evolution. Here we report a direct, quantitative comparison between humans and chimpanzees in the superior longitudinal fasciculus (SLF), the primary white matter tract connecting lateral frontal with lateral parietal regions.

The SLF is an antero-posteriorly oriented tract located in the lateral aspect of the cerebral white matter. The label “superior longitudinal fasciculus” is sometimes used interchangeably with “arcuate fasciculus,” but distinct bundles of fronto-parietal and fronto-temporal fibers can be

* Corresponding author at: Department of Psychology, Center for Behavioral Neuroscience, Georgia State University, P.O. Box 5010, Atlanta, GA 30302, USA.

E-mail addresses: ehecht@emory.edu, ehecht@gsu.edu (E.E. Hecht), dgutman@emory.edu (D.A. Gutman), B.A.Bradley@exeter.ac.uk (B.A. Bradley), tpreuss@emory.edu (T.M. Preuss), dwstout@emory.edu (D. Stout).

recognized in both macaques and humans (Makris et al., 2005; Fernandez-Miranda et al., 2008; Gharabaghi et al., 2009; Petrides and Pandya, 2009; Thiebaut de Schotten et al., 2011a; Martino and Marco de Lucas, 2014). Here we use the term “SLF” to refer specifically to direct fronto-parietal connections and consider the arcuate to consist of fronto-temporal connections (see the [Comparison to previous studies](#) section for a more extensive discussion of terminology). Studies in humans (Makris et al., 2005; Thiebaut de Schotten et al., 2011a) and macaques (Petrides and Pandya, 1984, 2002; Schmahmann et al., 2007; Thiebaut de Schotten et al., 2012) have identified 3 sub-tracts within the SLF. The superior-most branch is SLF I, which links the superior parietal lobule with the supplementary motor area, posterior dorsolateral prefrontal cortex, dorsal premotor cortex, and the rostral part of primary motor cortex. SLF II is located inferior and lateral to SLF I and links posterior inferior parietal cortex with dorsal premotor cortex and dorsolateral prefrontal cortex. SLF III is the inferior- and lateral-most of these tracts, traveling in the opercular white matter. It connects the posterior inferior prefrontal and ventral premotor cortex with anterior inferior parietal cortex. Functionally, SLF has been linked with motor planning and visuospatial processing in humans and monkeys (Petrides and Pandya, 2002; Thiebaut de Schotten et al., 2011a) and is thus one likely locus of evolutionary changes supporting uniquely human capacities for tool-use and social learning of observed actions.

Although macaques and chimpanzees are capable of simple tool-use, humans are distinguished by the complexity of their tool-use and tool-making, including the use of tools to make other tools, the construction of multi-component tools, and the accumulation of complexity in tool design through social learning (Johnson-Frey, 2003; Frey, 2007). In humans, tool use involves a distributed network of interconnected frontal, parietal, and occipitotemporal regions (Johnson-Frey, 2004; Ramayya et al., 2010; Rilling and Stout, 2014). This network overlaps with an evolutionarily ancient fronto-parietal network for object-directed grasping (Rizzolatti and Fadiga, 1998) but human tool-use networks are undoubtedly more complex than macaque object-grasping networks. It has been proposed that use of “complex” tools (those that alter the functional properties of the hand) requires additional causal understanding resulting from an integration of dorsal (“how”) and ventral (“what”) processing streams in a left-lateralized network of temporal, frontal and parietal areas (Frey, 2007). This capacity may be supported by the evolution of new functional response properties in left anterior inferior parietal cortex (Peeters et al., 2009) and by the expansion of gray matter and extension of white matter in lateral temporal cortex, particularly the middle temporal gyrus, which plays an important role in semantic representation (Orban et al., 2004; Rilling et al., 2008; Hecht et al., 2013a).

Beyond tool-use, actual tool-making involves longer action chains with more complex, abstract goals. There has been relatively little study of such multi-step technological actions, but lesion (Hartmann et al., 2005) and neuroimaging (Frey and Gerry, 2006; Hamilton and Grafton, 2008) evidence implicate right frontoparietal cortex in the representation of action sequences and goals. Experimental studies of stone tool-making, a behavior practiced by human ancestors for more than 2.5 million years, have reported left anterior inferior parietal–ventral premotor activation during simple tool-making and increased right inferior parietal–inferior frontal (ventral premotor, *pars triangularis* of the inferior frontal gyrus) during more complex tool-making. A longitudinal study of stone tool-making skill acquisition identified training-related changes (increased fractional anisotropy) in white matter underlying these fronto-parietal cortical regions, including right *pars triangularis* (Hecht et al., 2014). A “mirror-system” or “simulation” account of action understanding suggests that similar neural systems would be involved in the social learning of tool-making methods, and this has been supported by an fMRI study of stone tool-making action observation (Stout et al., 2011).

Comparative evidence relevant to understanding the anatomy and evolution of these left and right fronto-parietal circuits is limited. In a

previous comparative DTI study, we used probabilistic tractography to compare frontal–parietal–temporal connectivity in macaques, chimpanzees, and humans and found a gradient in the pattern of network organization (Hecht et al., 2013a). In macaques, frontal–temporal connections via the extreme and/or external capsules dominated this network, while in humans, frontal–parietal–temporal connections via the superior and middle longitudinal fasciculi were more prominent; chimpanzees were intermediate. Thiebaut de Schotten et al. (2012) employed a “virtual dissection” approach to obtain more detailed anatomical reconstructions. They concluded that SLF is “highly conserved” between humans and macaques. However, they also reported apparent differences, including more anterior frontal terminations of SLF III in humans. The chimpanzee condition is unknown. Human SLF III is right lateralized (Thiebaut de Schotten et al., 2011a,b), but the symmetry/asymmetry of SLF branches in both macaques and chimpanzees is again unknown. Ramayya et al. (2010) used deterministic tractography to examine asymmetries of a putative human tool-use network, confirming the presence of leftwardly-asymmetric connections between the middle temporal gyrus, anterior inferior parietal lobe and inferior frontal cortex but also finding a strongly rightwardly asymmetric pathway between the posterior inferior parietal and frontal cortex. It is tempting to conclude that these patterns of asymmetry and enhanced fronto-parietal connectivity reflect uniquely human adaptations for the execution and social transmission of tool-use and tool-making, but more detailed information on comparative anatomy is needed, particularly from our closest living relative, the chimpanzee. We thus conducted a virtual dissection study of humans and chimpanzees to assess the presence/absence of differences in the relative size, lateralization, and connections of SLF I, II, and III.

Materials and methods

Subjects and data acquisition

Chimpanzees

The current study analyzed archived chimpanzee datasets from previous studies. Chimpanzee subjects were 2 males and 47 females housed at the Yerkes National Primate Research Center. The scans analyzed in the current study were acquired at the Yerkes National Primate Research Center under propofol anesthesia (10 mg/kg/h) using previously described procedures (Chen et al., 2013; Hecht et al., 2013b). All procedures were carried out in accordance with protocols approved by YNPRC and the Emory University Institutional Animal Care and Use Committee (approval no. YER-2001206). 60-direction DTI images with isotropic 1.8 mm³ voxels were acquired on a Siemens Trio 3.0 T scanner (TR: 5900 ms; TE: 86 ms; 41 slices). 5 B0 volumes were acquired with no diffusion weighting. T1-weighted images were acquired on the same scanner with isotropic 0.8 mm³ voxels (TR: 2600 ms; TE: 3.06 ms; slice thickness: 0.8 mm).

Humans

One group of human subjects consisted of 5 males and 1 female recruited from the undergraduate and graduate programs at the University of Exeter, all right-handed by self-report, with no neurological or psychiatric illness. Scans were acquired at the Wellcome Department of Imaging Neuroscience at University College London. All subjects provided written consent. The National Hospital for Neurology and Neurosurgery and Institute of Neurology Joint Research Ethics Committee approved the study. 61-direction DTI images with isotropic 1.7 mm³ voxels were acquired on a Siemens Trio 3.0 T scanner (TR: 1820 ms; TE: 102 ms; 80 slices). 6 B0 volumes were acquired with no diffusion weighting. T1-weighted images were acquired on the same scanner with isotropic 1 mm³ voxels (TR: 1820 ms; TE: 102 ms; 80 slices).

A second group of human subjects consisted of 58 females, 2 left-handed and the rest right-handed by self-report, with no known neurological or psychiatric illness. Scans were acquired at the Yerkes National

Primate Research Center at Emory University. All subjects provided written consent. The Emory Institutional Review Board approved the study. 60-direction DTI images with isotropic 2.0 mm³ voxels were acquired on a Siemens Trio 3.0 T scanner. 4 B0 volumes were acquired with no diffusion weighting (TR: 8500 ms; TE: 95 ms; 64 slices). T1-weighted images were acquired on the same scanner with isotropic 1 mm³ voxels (TR: 2600 ms; TE: 3.02 ms; slice thickness: 1 mm).

Image processing and registration

Image processing and analysis were carried out using the FSL software package (Smith et al., 2004; Woolrich et al., 2009; Jenkinson et al., 2012). T1 images underwent noise reduction using SUSAN (Smith and Brady, 1997) and bias correction using FAST (Zhang et al., 2001). DTI data underwent correction for distortion caused by eddy currents using EDDY (the new tool which replaces EDDY_CORRECT). Both T1 images and the averaged B0 images underwent brain extraction using BET (Smith, 2002). BEDPOSTX, part of the FDT software package (Behrens et al., 2003, 2007), was used to build up a Bayesian distribution of diffusion information in 3D space for each voxel, modeling 3 fibers at each voxel. BEDPOSTX automatically estimates the number of crossing fibers at each voxel. Linear transformations with 6 degrees of freedom were computed from each subject's DTI dataset to their T1-weighted structural image using FLIRT, a linear registration algorithm (Jenkinson and Smith, 2001; Jenkinson et al., 2002). Nonlinear transformations were computed from each subject's T1 image to a template brain for that species – i.e., a chimpanzee template (Li et al., 2010) or the human 1 mm nonlinearily-registered T1 MNI template – using FNIRT, a nonlinear registration algorithm (Andersson et al., 2007). Registration of images from native diffusion space to template space was achieved by combining these linear diffusion-to-structural plus nonlinear structural-to-template transformations and applying them in a single step in order to avoid repeated reslicing. Registration of images from template space to native diffusion space was achieved by inverting each of these transformations, combining them, and applying the combined transformation in a single step. Tractography analyses used PROBTRACKX, a probabilistic algorithm that samples from Bayesian distributions of multiple diffusion directions in order to facilitate tracking through crossing fibers and into gray matter (Behrens et al., 2003, 2007).

Control tractography

The comparative tractography methods used here have previously been shown to identify species differences in tracts generally acknowledged to have undergone anatomical change in the human lineage while producing a lack of species differences in tracts thought not to have undergone major changes in the human lineage (Hecht et al., 2013a). In order to additionally ensure that any measured between-species laterality differences in the SLF were not due to between-species differences in imaging parameters or image quality, we performed tractography in the left and right retinogeniculostriate tracts. Seeds were placed at the optic chiasm and in coronal cross-sections of the occipital lobe (Supplementary Fig. 1a). These ROIs were drawn on individual subjects' B0 images in native diffusion space. We ran symmetric waypoints-mode tractography with the following parameters: 25,000 samples/voxel, loopchecks enabled, curvature threshold at 0.2 ($\pm 78.45^\circ$), steplength at 0.5, fiber threshold at 0.1, and tractography not explicitly constrained by fractional anisotropy. We mapped streamlines that passed through both masks in each subject. Tractography results were thresholded to 0.1% of the waytotal (a measure of the total number of streamlines in a particular tractography analysis) and registered to template space as described above in the **Image processing and registration** section.

Proportional tract volume was quantified in the native-space thresholded tractography images as the number of above-threshold voxels in the tract divided by the number of total voxels in the brain. Template-space tracts were binarized and combined to produce group-composite images where the intensity at a given voxel corresponds to the number of subjects with above-threshold connectivity at that location (Hecht et al., 2013a). This produced no qualitative differences in tract anatomy (Supplementary Fig. 1b) or quantitative differences in proportional tract volume (Supplementary Fig. 1c).

Segmentation of SLF based on frontal connectivity

In a previous study, Thiebaut de Schotten et al. performed virtual dissection of the human SLF using differential frontal connectivity (Thiebaut de Schotten et al., 2011a). The same method was later also used in a macaque–human comparative study (Thiebaut de Schotten et al., 2012). We used a similar method here. Seeds were placed in the inferior, middle, and superior frontal gyri of each hemisphere, and in superior parietal cortex, anterior inferior parietal cortex, and posterior inferior parietal cortex. SLF I was defined as the tract connecting superior frontal cortex with superior parietal cortex; SLF II was defined as the tract connecting the middle frontal gyrus with posterior inferior parietal cortex; and SLF III was defined as the tract connecting the inferior frontal gyrus with anterior inferior parietal cortex. Also, because we have previously observed tractography results that track across known synapses (i.e., from the optic chiasm through the LGN to the visual cortex (Hecht et al., 2013a)), we took some additional steps to reduce the number of streamlines representing multi-synaptic connections. Specifically, a large, general inclusion mask was placed in the white matter between the frontal and parietal lobes at the level of the central sulcus in order to retain only streamlines that passed through this route. The entire mid-sagittal plane of each scan was used as an exclusion mask in order to exclude interhemispheric connections between the seeds so that we could analyze connectivity within each hemisphere separately. We also placed exclusion masks in the temporal cortex and in a coronal slice in the white matter in the vicinity of the extreme/external capsules in order to exclude connections passing through these tracts. Supplementary Figs. 2 and 3 show the tractography seeds and inclusion and exclusion masks in chimpanzees and humans. These ROIs were drawn on the chimpanzee and human (MNI) templates and registered to individuals' native diffusion space as described above in the **Image processing and registration** section. We ran symmetric waypoints-mode tractography with the following parameters: 25,000 samples/voxel, loopchecks enabled, curvature threshold at 0.2, steplength at 0.5, fiber threshold at 0.1, and tractography not explicitly constrained by fractional anisotropy (but later steps that measured white matter tract volume did so after white matter/gray matter segmentation). Tractography results were thresholded to 0.1% of the waytotal and registered to template space as described above in the **Image processing and registration** section. Template-space tracts were binarized and combined to produce group-composite images. Quantification of proportional tract volume and cortical connectivity occurred in the thresholded native-space tractography images. Proportional tract volume was measured as the number of above-threshold voxels within the white matter of each thresholded tract, expressed as a percentage of that subject's total SLF volume. Cortical connectivity was measured as the number of voxels in each target region that received above-threshold connectivity from each tract. Target regions included dorsolateral prefrontal cortex, inferior frontal gyrus, dorsal precentral gyrus (dorsal premotor cortex), and ventral precentral gyrus (ventral premotor cortex). Homologous chimpanzee and human ROIs for each of these regions were produced as part of a previous study (Hecht et al., 2013b). These ROIs are illustrated in Fig. 4a and described anatomically in Table 1.

Table 1
Anatomical definitions of homologous human and chimpanzee regions of interest for quantifying frontal SLF terminations. Chimpanzee ROIs were drawn by hand based on previous anatomical research (Brodmann, 1909; Economo and Parker, 1929; Bailey, 1948; Von Bonin, 1950; Bailey and Von Bonin, 1950; Schenker et al., 2010). Human ROIs were created using the Jülich probabilistic cytoarchitectonic atlas (Eickhoff et al., 2007) and the Harvard/Oxford probabilistic structural atlas (Desikan et al., 2006). Reproduced with permission and modified from Hecht et al. [J. Neurosci 2013;33(35):14117–34].

| Region of interest | Chimpanzees | | Humans | | Cyto-architectonic region(s) |
|---|--|---|--|---|------------------------------|
| | Anatomical description | Anatomical description | Cyto-architectonic region(s) | Anatomical description | |
| Dorsal premotor cortex (PMd) | At its dorsal aspect, it extends anteriorly to an imaginary line drawn from the tip of the inferior pre-central sulcus at a 90° angle with the lateral sulcus. The inferior part of the ROI is bordered anteriorly at the inferior frontal sulcus, curving down and back to meet the PMv ROI. The border between PMd and PMv is an imaginary line drawn parallel to the lateral sulcus at the dorsal tip of the fronto-occipital sulcus so that the superior borders of PMv and Broca's area are continuous. | Bordered posteriorly by the M1/S1 ROI, superiorly as described above, and anteriorly by the inferior precentral sulcus. | FB (BA 6), FC (BA 8) | Its posterior border is a vertical line from the lateral sulcus to the superior tip of the superior pre-central sulcus. Its anterior border is a 45° line from the antero-superior edge of the PMv ROI. The border between PMd and PMv is the gyrus that splits the superior and inferior precentral sulci. | BA 6, BA 8 |
| Ventral premotor cortex (PMv) | Bordered dorsally by the interhemispheric fissure, posteriorly by the PMd ROI, inferiorly by the Broca's area ROI, and anteriorly by an imaginary line which is an extension of the orbital sulcus drawn past the tip of the middle frontal sulcus. | FBA (BA 6) | Its anterior border is the inferior precentral sulcus. Its posterior border is a vertical line from the lateral sulcus to the superior tip of superior pre-central sulcus (M1). Its superior border is the gyrus that splits the inferior and superior pre-central gyri. | Its inferior border is the inferior frontal sulcus. Its anterior border is a 45° line drawn from tip of anterior horizontal ramus (the sulcus that borders the anterior edge of Broca's area). | BA 6 |
| Dorso-lateral prefrontal cortex (DLPFC) | Includes the pars opercularis and pars triangularis of the inferior frontal gyrus. Bordered posteriorly by the inferior precentral sulcus, anteriorly by the small sulcus that extends anteriorly from the fronto-orbital sulcus, and superiorly by the inferior frontal sulcus. | FCbm (BA 44), Fdpa (BA 45) | Same. | BA 44, BA 45 | |
| Inferior frontal gyrus (IFG) | | | | | |

Validation of connectivity-based segmentation using direct seeding in each subject's color map

The branches of the SLF are visible as discrete bundles of anterior-posterior fibers in the frontal and parietal lobes (see Fig. 1). An alternative method for tracking the components of SLF is to use the color map to place seeds directly in the white matter of each branch of the SLF in each subject. Several previous studies have used this type of approach for tractography in the SLF and other tracts (e.g., Makris et al., 2005; Catani et al., 2005; Rilling et al., 2008; Thiebaut de Schotten et al., 2012). Therefore, in addition to the cortical-connectivity-based segmentation method described above in the Segmentation of SLF based on frontal connectivity section, we also re-segmented SLF using this method in 8 chimpanzees and 6 humans. Seeds were placed in single coronal slices in SLF I, II, and III and tractography was acquired as in the Segmentation of SLF based on frontal connectivity section.

Results

Examination of SLF I, II, and III in the color map

In many subjects, portions of the branches of the SLF can be discerned without tractography in the DTI color map (e.g., (Makris et al., 2005)). In DTI, water diffusion is modeled as a tensor (ellipsoid). The orientation and length of each of the ellipsoid's 3 axes correspond to the direction and amount of diffusion of water in 3D space within that voxel. The color map represents this information using hue to indicate diffusion direction and brightness to indicate diffusion magnitude. Fig. 1 shows portions of SLF I, II, and III that were apparent in representative subjects' color maps for the primary direction of water diffusion (the longest axis of the ellipsoid modeled in each voxel). Note that green anterior-posterior tracts were in some places interrupted by tracts traveling in other directions. This was particularly apparent in the inferior frontal region of SLF II and especially SLF III in humans (white arrow in Fig. 1b). The red medial-lateral fibers here correspond to callosal connections between the corresponding region of the other hemisphere and might speculatively be related to putative enhancements of human capacities for bimanual coordination (Byrne, 2005).

Segmentation of the SLF

Segmentation of the SLF on the basis of frontal and parietal connectivity produced 3 semi-discrete but partially overlapping tracts. Fig. 2 shows these tracts in individual subjects; Fig. 3 shows 2D slices and 3D renderings of group composite images combining individual subjects' data in a common template space. A superior tract, traveling in the superior frontal white matter, connected superior parietal cortex with the superior frontal gyrus (the frontal seed used in previous studies (Thiebaut de Schotten et al., 2011a, 2012) to segment SLF I). A middle tract, traveling in the white matter surrounding and beneath the inferior frontal sulcus, connected posterior inferior parietal cortex with the middle frontal gyrus (the frontal seed used in previous studies (Thiebaut de Schotten et al., 2011a, 2012) to segment SLF II). An inferior tract, traveling in the frontal operculum and deeper underlying white matter, connected anterior inferior parietal cortex with the inferior frontal gyrus (the frontal seed used in previous studies (Thiebaut de Schotten et al., 2011a, 2012) to segment SLF III).

In order to validate the connectivity-based segmentation method, we also carried out segmentation in the same subjects using direct seeding in 6 subjects' color maps (Supplementary Fig. 4). This produced 3 tracts that were very similar to the results produced using the first method (Figs. 2 & 3), although less extensive cortical connectivity was achieved. This is likely because the seeds contained a smaller number of voxels, resulting in a smaller number of initiated streamlines, and because the placement of waypoint masks in white matter rather than gray matter meant that streamlines were not required to travel into

cortex. Given this, we derived our quantitative measurements using the cortical connectivity-based tractography method.

Quantification of gray matter connectivity

Homologous chimpanzee and human regions of interest used to quantify the frontal connectivity of each branch of the SLF are shown in Fig. 4a. The anatomical borders and component cytoarchitectonic areas of these ROIs are listed in Table 1. We first quantified the volume of each branch's total frontal gray matter connectivity relative to the total gray matter connectivity of the entire SLF. In other words, we measured the total volume of frontal cortex that received SLF connectivity, and then measured what proportion of this volume was reached by SLF I, II, and III in each subject. This measurement took place in individuals' native diffusion space and used each subject's own segmentation results. These results are depicted by the red, green, and blue bands surrounding the pie charts in Fig. 4b. A repeated measures ANOVA revealed a significant effect of tract ($F(2,109) = 4.759, p = .010$) and a tract X species interaction ($F(2,109) = 14.272, p < .001$). SLF I supplied a greater proportion of frontal connectivity in chimpanzees ($t(110) = 3.740, p < .001$). Measurements for SLF II were not significantly different between chimpanzees and humans ($t(110) = .923, p = .358$). SLF III supplied a greater proportion of frontal connectivity in humans ($t(110) = -5.652, p < .001$).

Next, in order to examine potential changes to individual branches' cortical connectivity with specific frontal regions, we quantified the gray matter terminations of each individual SLF tract relative to all gray matter terminations of the SLF. In other words, we measured the total volume of frontal cortex that received SLF connectivity, and then expressed the connectivity of each ROI as a fraction of that total volume. Again, this measurement took place in individuals' native diffusion space and used each subject's own segmentation results. These results are represented in Fig. 4b. Fig. 4c represents the distribution of frontal connectivity of each individual tract.

In SLF I, chimpanzees showed strong connectivity with PMd, a moderate level of connectivity with DLPFC, and weak connectivity with IFG and PMv. Humans showed a very similar pattern. A repeated-measures ANOVA with a within-subjects factor of region (4) and a between-subjects factor of species (2) showed a main effect of region ($F(3,108) = 127.985, p < .001$) and a region X species interaction ($F(3,108) = 4.492, p = .005$). Chimpanzees had a greater proportional volume of SLF II connectivity with the gray matter of IFG ($t(110) = 4.342, p < .001$), DLPFC ($t(110) = 2.641, p = .009$), and PMv ($t(110) = 3.013, p = .003$). There was a nonsignificant trend toward greater chimpanzee SLF I connectivity with PMd ($t = 1.780, p = .078$). This reflects the fact that SLF I supplied a significantly greater proportion of overall frontal connectivity in humans, as noted above; the pattern of SLF I connectivity across frontal regions was quite similar between chimpanzees and humans.

In SLF II, chimpanzees showed the strongest connectivity with PMd and moderate connectivity with PMv, DLPFC, and IFG. Humans showed a slightly different pattern, with the strongest connectivity with DLPFC, PMd, and PMv, and weaker connectivity with IFG. A repeated measures ANOVA revealed a main effect of region ($F(3,108) = 31.338, p < .001$) and a region X species interaction ($F(3,108) = 6.316, p = .001$). Step-down two-tailed t-tests showed that human SLF II had significantly less connectivity with IFG ($t(110) = 2.955, p = .004$) and more connectivity with DLPFC ($t(110) = -2.149, p = .034$). There were no significant differences in PMd ($t(110) = 1.874, p = .064$) or PMv ($t(110) = -.527, p = .600$).

SLF III showed disparity in connectivity between chimpanzees and humans. Chimpanzees showed strong connectivity with PMv, more moderate connectivity with IFG, and weak connectivity with PMd and DLPFC. In contrast, humans showed strongest connectivity with IFG, strong connectivity with PMv, and weak connectivity with DLPFC and PMd. A repeated measures ANOVA revealed a main effect of region

($F(3,108) = 110.497, p < .001$) and a region X species interaction ($F(3,108) = 46.478, p < .001$). Step-down two-tailed t-tests showed that human SLF III had significantly more connectivity with IFG ($t(110) = -8.916, p < .001$) and less connectivity with PMd ($t(110) = 6.142, p < .001$). There were no significant differences in DLPFC ($t(110) = -1.578, p = .117$) or PMv ($t(110) = -.186, p = .853$).

Quantification of proportional white matter volume and lateralization

The proportional volumes of the left and right SLF I, SLF II, and SLF III were compared using a repeated measures ANOVA with within-subjects factors of tract (3) and hemisphere (2) and a between-subjects factor of species (2) (Fig. 5). This revealed a significant main effect of tract ($F(2,109) = 7.761, p = .001$), a main effect of hemisphere ($F(1,110) = 10.773, p = .001$), a tract X species interaction ($F(2,109) = 13.533, p < .001$), and a tract X hemisphere X species interaction ($F(2,109) = 10.003, p < .001$). The SLF was right-lateralized as a whole across species ($t(111) = -3.410, p = .001$). The white matter of SLF I was significantly larger in chimpanzees ($t(110) = 5.220, p < .001$). The proportional volume of SLF II did not differ between species ($t(110) = .002, p = .998$). SLF III was significantly proportionally larger in humans ($t(110) = -4.347, p < .001$). In chimpanzees, SLF I was right-lateralized ($t(48) = -2.718, p = .009$), but there was no significant lateralization of SLF II ($t(48) = -1.068, p = .291$) or SLF III ($t(48) = -.441, p = .661$). In humans, there was no significant lateralization of SLF I ($t(62) = .776, p = .441$). There was a nearly-significant right-lateralization of SLF II ($t(62) = -1.981, p = .052$) and a significant right-lateralization of SLF III ($t(62) = -3.785, p < .001$).

We also observed an interesting species difference in the frontal terminations of SLF III. In chimpanzees, there were no apparent hemispheric differences in the frontal connectivity of SLF III; the tract terminates mainly in the ventral precentral gyrus of both hemispheres (Fig. 6a). In humans, however, a projection of SLF III into the gray matter of the *pars opercularis* and *pars triangularis* of the inferior frontal gyrus was prominent in the right but not the left hemisphere (Fig. 6b). Assessing this quantitatively, we found that in chimpanzees, a greater proportional volume of SLF III connectivity reached PMv than IFG in both hemispheres (left hemisphere: $t(48) = 8.176, p < .001$; right hemisphere: $t(48) = 4.579, p < .001$; Fig. 6c). By contrast, in humans, both hemispheres showed a larger proportional volume of above-threshold connectivity in IFG than in PMv (left: $t(63) = -2.157$, right: $t(63) = -4.522, p < .001$; Fig. 6d).

Discussion

Comparison to previous studies

SLF anatomy has been addressed by a number of previous studies which have used varying naming conventions, so the correspondence in terminology between this study and previous studies bears examination. Early anatomists used the terms "superior longitudinal fasciculus" and "arcuate fasciculus" interchangeably. Some modern researchers do not recognize a superior longitudinal fasciculus at all and instead refer to all perisylvian fronto-parietal tracts as the arcuate fasciculus (e.g., Catani et al., 2005; Lawes et al., 2008), or consider the arcuate to be a subcomponent of the SLF (e.g., Fernandez-Miranda et al., 2008; Gharabaghi et al., 2009; Petrides and Pandya, 2009). Others treat the SLF and arcuate as separate entities: the SLF is a fronto-parietal tract with terminations in both frontal and parietal gray matter, while the arcuate is a fronto-temporal tract that travels through the parietal white matter beneath the SLF without making terminations in parietal cortex (e.g., Makris et al., 2005; Thiebaut de Schotten et al., 2012; Martino and Marco de Lucas, 2014). Here we follow this latter conceptualization. The current data do not include any tracts that correspond to this definition of the arcuate fasciculus, since our exclusion

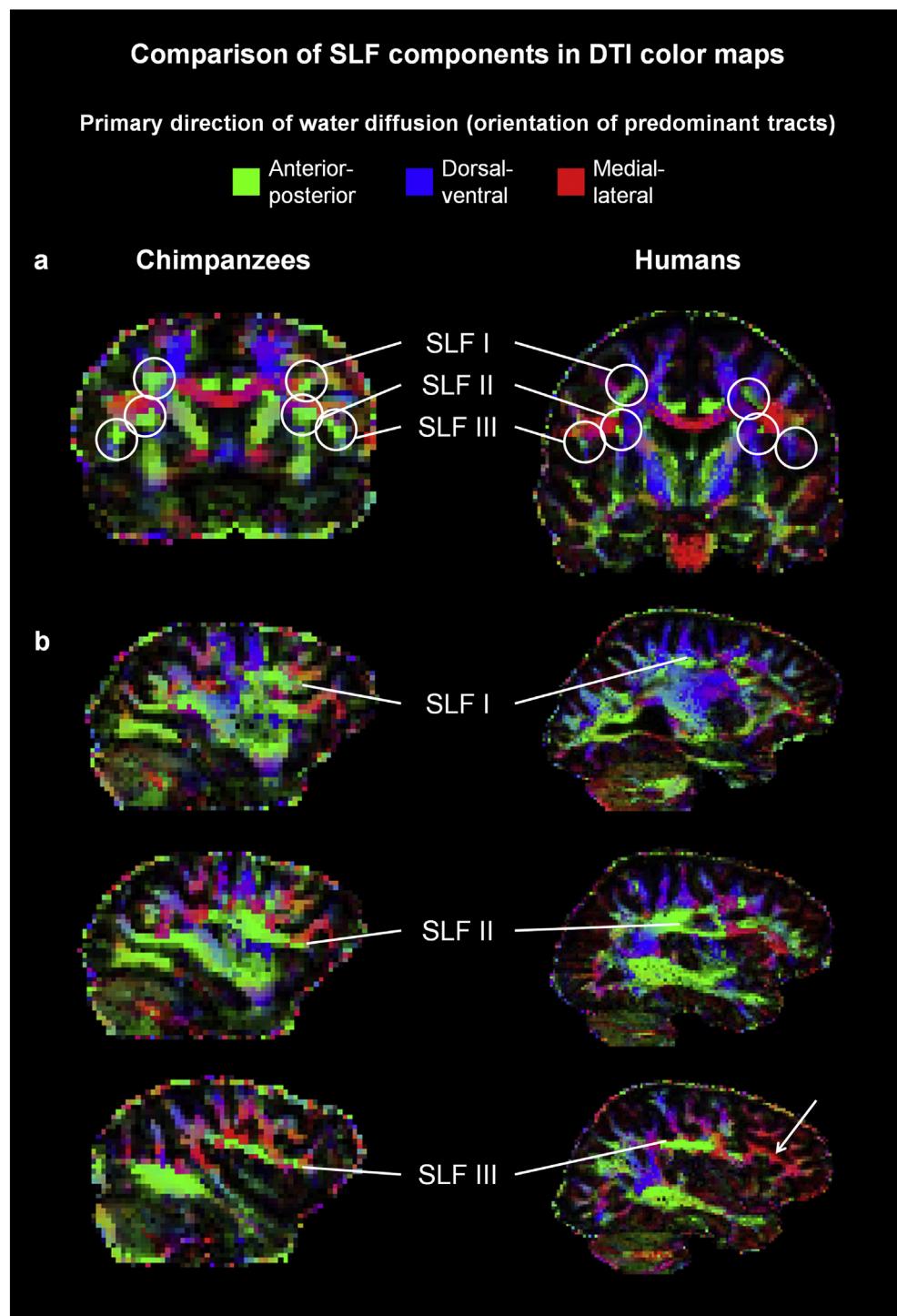


Fig. 1. Portions of SLF I, II, and III visible in the DTI color map before tractography. (a) Coronal slice in representative chimpanzee and human subjects showing all 3 tracts. (b) Parasagittal slices showing each tract. Note the medial-lateral crossing fibers in the inferior frontal sections of SLF II and especially SLF III in humans (white arrow).

masks precluded the tracking of any temporal cortex connections. Moreover, as discussed below, the arcuate exhibits a different pattern of asymmetry than the SLF.

Subcomponents of the SLF have also been distinguished from each other according to several different categorization schemas. Several reports use the SLF I/II/III nomenclature to refer to tracts that link frontal and parietal cortex at various dorsal–ventral levels, with SLF I always being the most superior and SLF III being the most inferior (e.g. Makris et al., 2005; Thiebaut de Schotten et al., 2011a, 2012); the SLF I, II, and III in the present study are directly comparable to, and were segmented

using parallel methods as, the SLF I, II, and III in these studies. Others subdivide the SLF into an anterior or horizontal segment linking inferior frontal and inferior parietal regions, and a posterior or vertical segment linking inferior parietal and posterior temporal regions; these tracts should not be confused with the arcuate fasciculus, which is located less superficially and does not make parietal terminations (Fernandez-Miranda et al., 2008; Martino and Marco de Lucas, 2014). It should also be noted that this anterior/horizontal-posterior/vertical segmentation scheme does not recognize any dorsal frontal–parietal connections as belonging to SLF. Our SLF III can be considered comparable to these studies'

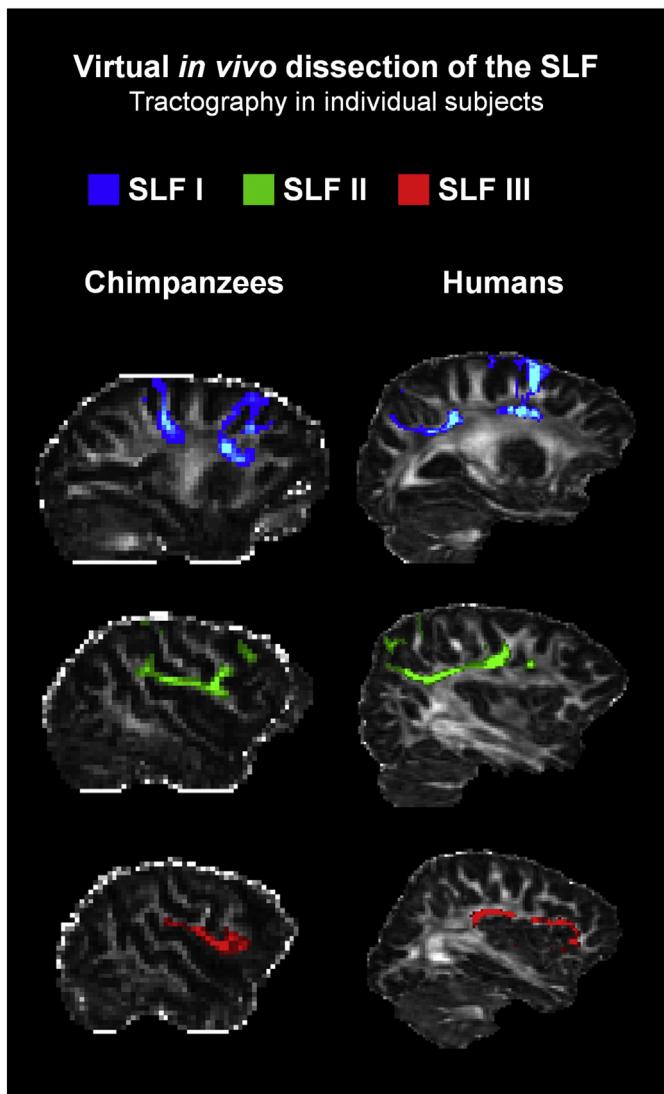


Fig. 2. SLF tracts in individual subjects. Parasagittal slices in representative chimpanzee and human subjects showing SLF I (top, blue), SLF II (middle, green), and SLF III (bottom, red).

anterior/horizontal segment, while our SLF I and II have no correlates in this classification scheme. Some researchers refer to the posterior, superficial, vertically-oriented parietal–temporal tract as the middle longitudinal fasciculus (Makris et al., 2009; Petrides and Pandya, 2009) or as a posterior segment of the arcuate fasciculus (Catani et al., 2005; Lawes et al., 2008). This tract does not correspond to any in the current study, since our exclusion masks specifically precluded the possibility of measuring any tracts with cortical terminations in temporal cortex.

Limitations of the present study

Several limitations to the present study should be noted. First, while the homological relationships between human and chimpanzee cortical regions discussed here are well supported by existing architectonic data, these data are not as extensive as those bearing on human–macaque homologies. There were several extensive cytoarchitectonic studies of the chimpanzee brain several decades ago (Brodmann, 1909; Economo and Parker, 1929; Bailey, 1948; Von Bonin, 1948; Bailey and Von Bonin, 1950; Schenker et al., 2010). Bonin and Bailey, who produced a map of chimpanzee cortex, did so in the context of a broader, explicitly comparative project which was intended to identify homologous areas across primate species (Bailey and Von Bonin, 1947,

1951). More recent, focused studies have also been performed, including in inferior frontal cortex (Schenker et al., 2008, 2010). Glasser et al. produced myeloarchitectonic maps using MRI imaging, and the distribution of myelin density is consistent with the homologies used here (Glasser et al., 2014). For many chimpanzee cortical regions it is possible to identify a relatively straightforward correspondence with human and macaque cytoarchitectonic regions. However, a more complete account of homological correspondence would also take functional activation and connectivity into account, and these types of studies have been rare in chimpanzees.

A second limitation of the present study is that the voxel size:brain size ratio is lower in the human scans than the chimpanzee scans in the present study, meaning that the human scans have relatively higher spatial resolution. Thus, our chimpanzee tractography results may be anatomically coarser than our human results. Also, both our chimpanzee and human datasets had a relatively low representation of males, so potential sex differences could not be investigated. Finally, it must be remembered that DTI does not track individual axons, and that the relationship between quantitative DTI measures and actual anatomical connectivity is still unclear (see Jones et al., 2013). DTI does not approach the sensitivity or specificity of gold-standard techniques like injection tract tracing and it should be considered a reflection of fascicle-level rather than cellular-level connectivity. Terms like “difference in connectivity” in the current paper should be taken to refer to differences in the morphology and trajectory of white matter tracts; DTI cannot shed light on finer-grained levels of connectivity like the number of axons or synapses in an area. However, it is the only whole-brain *in vivo* anatomical connectivity method available for species like chimpanzees and humans.

Species comparisons in SLF anatomy

The present study found both similarities and differences in the connectivity, size, and laterality of the superior longitudinal fasciculus in chimpanzees and humans. These findings are summarized in Fig. 7. We will discuss these separately for SLF I, II, and III.

SLF I

SLF I provided a significantly larger proportional volume of frontal cortical connectivity in chimpanzees than in humans, and it was right-lateralized in chimpanzees. However, the pattern of SLF I's frontal connectivity was quite similar between chimpanzees and humans. This tract is thought to facilitate information transfer related to the higher-order regulation of motor behavior (Petrides and Pandya, 2002). Our results suggest that this tract may be related to some aspect of motor regulation that is or more developed in chimpanzees than in humans and/or may be more prominent in chimpanzees due to the relative human expansion of SLFIII.

SLF II

SLF II did not show evidence of asymmetry or species differences in the proportional volume of the main stem of white matter. However, we did observe species differences in the cortical terminations of this tract: in humans, SLF II had relatively weaker connectivity with the inferior frontal gyrus and relatively stronger connectivity with dorsolateral prefrontal cortex.

SLF III

This tract comprised a significantly greater fraction of the proportional volume of the main body of SLF white matter in humans. It was also right-lateralized in humans, in agreement with previous research (Thiebaut de Schotten et al., 2011a,b). Note that this is in contrast to the arcuate fasciculus, which is left-lateralized both in humans (Nucifora et al., 2005; Vernooy et al., 2007; Glasser and Rilling, 2008) and chimpanzees (Rilling et al., 2011). Humans showed stronger SLF

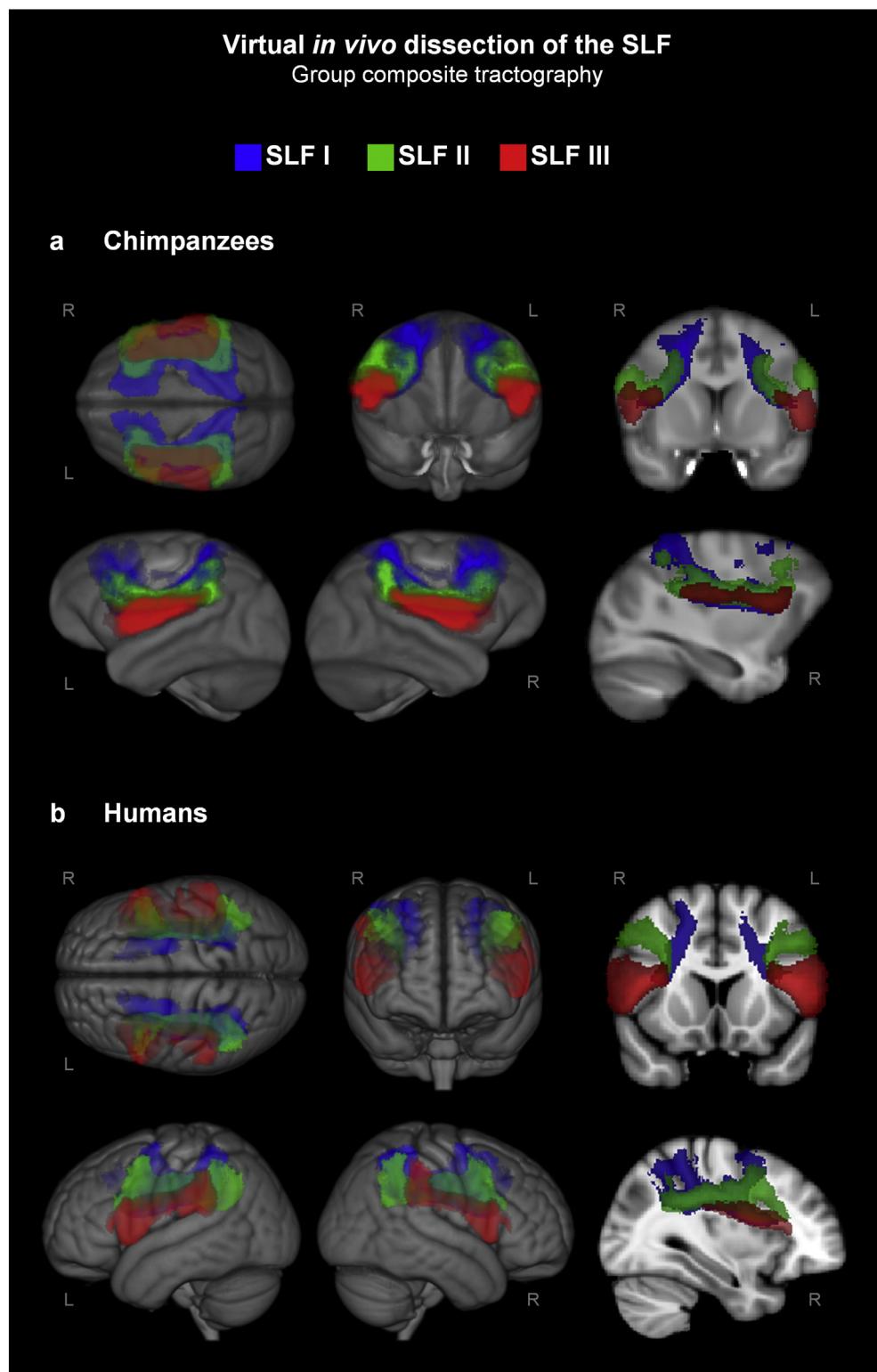


Fig. 3. Group composite images of SLF tracts. Results in individual subjects were thresholded at .1% of the waytotal, binarized, registered to template space, and summed, so that in these composite images, intensity corresponds to the number of subjects with above-threshold connectivity at that voxel. Group composite tracts were thresholded to show only above-threshold connectivity common to at least 50% of subjects. (a) Chimpanzees. (b) Humans. The right-most images in each row are 2D slices; the rest are 3D renderings of white matter tracts onto the brain surface.

III connectivity with the inferior frontal gyrus and weaker SLF III connectivity with the dorsal premotor cortex.

Additionally, humans showed an asymmetry in the frontal terminations of this tract which was not present in chimpanzees. In chimpanzees, SLF III frontal terminations occurred mainly in ventral premotor cortex in both hemispheres. In humans, both the left and right SLF III made

significantly more terminations in the inferior frontal gyrus, with this effect being strongest in the right hemisphere. Thus it appears that SLF III has generally more prefrontal connectivity in humans than in chimpanzees, and this effect is especially pronounced in the right hemisphere, with extension of human right SLF III into the more anterior regions of the inferior frontal gyrus.

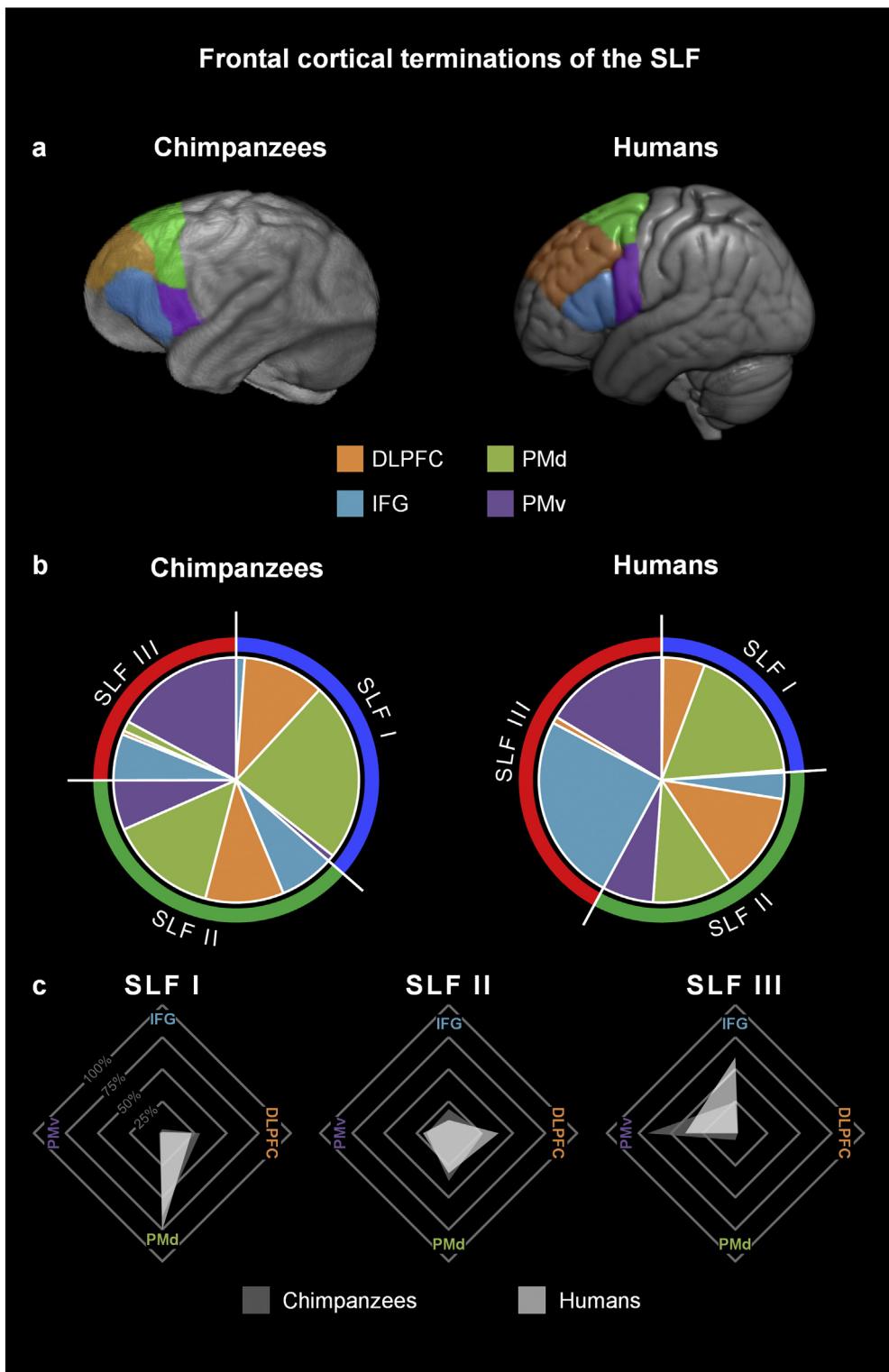


Fig. 4. Quantification of SLF tracts. (a) Regions of interest used to quantify frontal cortical connectivity. (b) Blue, green, and red bands represent proportion of total SLF frontal connectivity from SLF I, II, and III, respectively. Pie charts show connectivity of each frontal region relative to the entire SLF (percent of the entire SLF's total frontal gray matter terminations). (c) Radar plots show connectivity of each frontal region relative to a particular branch of the SLF (percent of that particular tract's total frontal gray matter terminations). IFG, inferior frontal gyrus. DLPFC, dorsolateral prefrontal cortex. PMd, dorsal premotor cortex. PMv, ventral premotor cortex. Anatomical boundaries for each ROI are listed in Table 1. Panel a is modified with permission from Hecht et al., J Neurosci 2013 33(35):14117-34.

Potential evolutionary significance

A previous human DTI study also reported that SLF III reaches Brodmann Areas 45 and 47 (inferior frontal gyrus—*pars triangularis*

and *pars orbitalis*) (Thiebaut de Schotten et al., 2012). Interestingly, one macaque tract-tracing study found that macaque SLF III terminates in Brodmann Area 44/Area 6VA (Petrides and Pandya, 2009), which is thought to be homologous to the cortex of the human inferior frontal

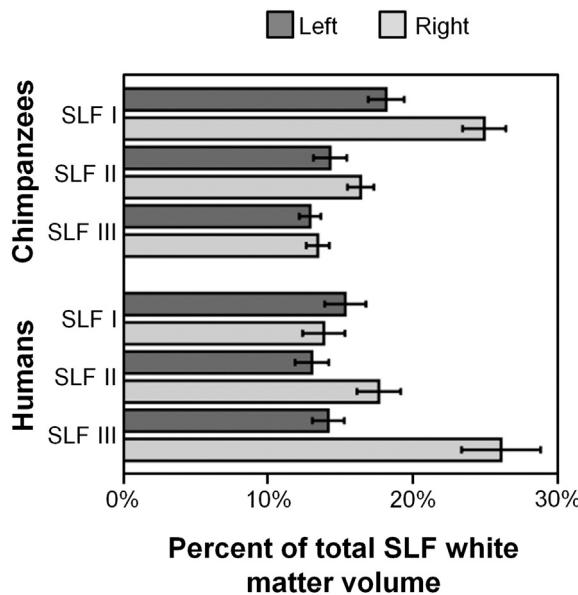


Fig. 5. Quantification of each branch of the SLF in chimpanzees and humans. Proportional volume measurements for each tract are expressed relative to the entire SLF summed across both hemispheres.

gyrus—*pars opercularis*. Another macaque tract-tracing study found SLF III terminations in 44 and 9/46v (Petrides and Pandya, 2002), areas thought to be homologous to the human inferior frontal gyrus—*pars opercularis* and to the adjacent prefrontal cortex of the middle frontal gyrus, respectively. These results, in combination with the results of the present study, suggest an evolutionary trajectory for the frontal extension of SLF III. In this scenario, the macaque–chimpanzee–human last common ancestor (~25–32 million years ago (Goodman et al., 1998; Chatterjee et al., 2009; Perelman et al., 2011)) did not have SLF

III connections with ventrolateral prefrontal cortex, a condition retained in modern macaques. Sometime after this point, the chimpanzee–human lineage began to develop an extension of SLF III into ventrolateral prefrontal cortex, but in modern chimpanzees the premotor terminations still predominate over the ventrolateral prefrontal terminations. Sometime after the divergence of the human lineage from our last common ancestor with chimpanzees (~6–7 million years ago (Goodman et al., 1998; Perelman et al., 2011)), human ancestors developed additional SLF III connectivity with the inferior frontal gyrus, especially in the right hemisphere, where SLF III connectivity with the inferior frontal gyrus now overshadows connectivity with the precentral gyrus.

The functional roles of the regions connected by these tracts may provide some clues about the relevance of these white matter adaptations. The inferior frontal gyrus is generally implicated in cognitive control and action selection (Petrides, 2005a,b; Koechlin and Jubault, 2006); right IFG is especially associated with inhibition and task-set shifting (Aron et al., 2004, 2014; Levy and Wagner, 2011). Right IFG also appears to play a specific role in fine motor control, as evidenced by a recent neuroimaging meta-analysis (Liakakis et al., 2011). Learning a complex sequence of finger movements causes initial increases in right IFG activation, followed by decreased right IFG activation and increased basal ganglia activation, suggesting that right IFG may support the acquisition and automation of new manual sequences (Seitz et al., 1990; Seitz and Roland, 1992). Parietal cortex is generally implicated in the representation of action and object metrics, including spatial location, movement trajectory, temporal ordering, and quantity (Assmus et al., 2003; Fias et al., 2003; Bueti and Walsh, 2009). Thus, interactions between parietal cortex and inferior frontal gyrus (especially in the more anterior, prefrontal part of the right inferior frontal gyrus) would seem to be relevant to behaviors that require cognitive control of fine manual actions through space and time. The evolution of primate fronto-parietal networks, on a general level, has been hypothesized to be related to selection pressure for cognition about abstract relationships between potential action outcomes, perhaps initially driven by selection pressure for more effective foraging early in the primate

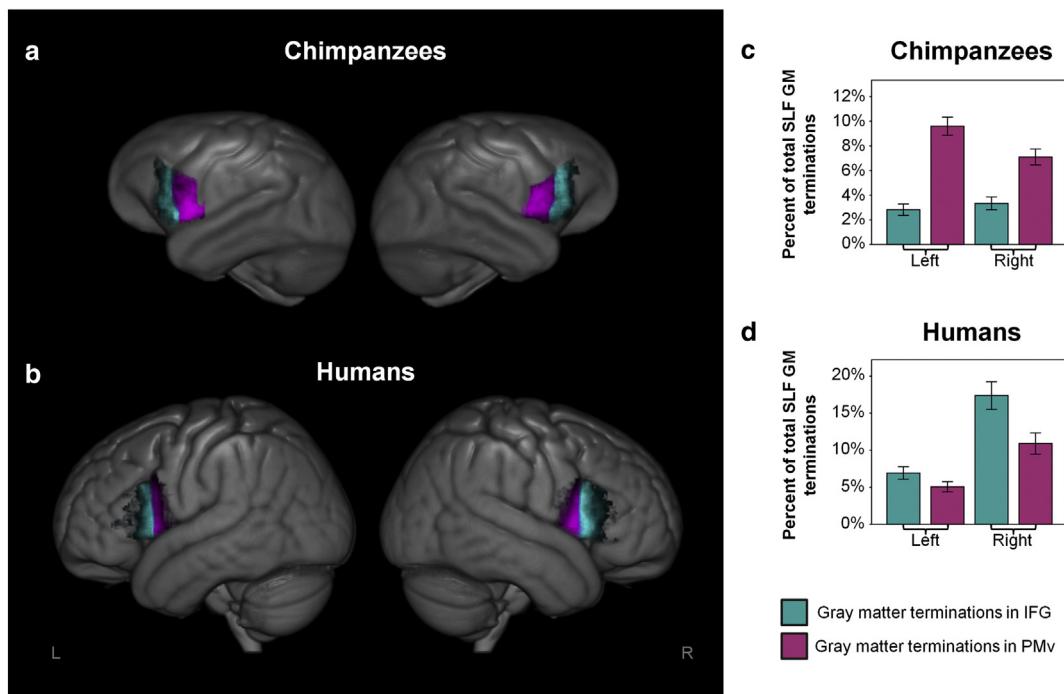


Fig. 6. Lateralization of the frontal terminations of SLF III. (a) In chimpanzees, the gray matter terminations of SLF III occur mainly in the ventral precentral gyrus in both hemispheres. (b) In humans, the anterior termination of the left SLF III occurs largely in the *pars opercularis* of the inferior frontal gyrus, while the right SLF III terminates more anteriorly, in the *pars triangularis* and *pars orbitalis*. (c) In chimpanzees, PMv connections outweigh IFG connections in both hemispheres. (d) In humans, IFG connections are significantly greater than PMv connections in both hemispheres.

lineage (Genovesio et al., 2014). We suggest that the particular fronto-parietal anatomical changes reported here may have been driven by pressures that became substantial forces more recently in primate evolution: tool use and social learning. We discuss potential implications for each of these domains below.

Social learning

Spatial attention to observed actions. Chimpanzee/human differences in the frontal connectivity of SLF II may be related to differences in spatial attention to observed action. Human SLF II has been implicated in the production of both overt and imagined movements (Vry et al., 2012), as well as in spatial orienting and spatial attention (Suchan et al., 2014). In a study of subjects with damage in various frontal and parietal locations, damage to SLF II was the best single predictor of spatial neglect (Thiebaut de Schotten et al., 2014). Furthermore, a previous human DTI study found that while this tract was not lateralized at the group level, subjects with a larger right SLF II deviated to the left on a line bisection task and were faster to detect targets in the left visual hemifield (Thiebaut de Schotten et al., 2011a). In monkeys, section of the white matter between the fundus of the intraparietal sulcus and the lateral ventricle produces spatial neglect (Gaffan and Hornak, 1997), suggesting a similar role for SLF in spatial attention across macaques, humans and presumably chimpanzees. However, the relative contribution of different SLF branches across species is not known.

We suggest that chimpanzee/human organizational differences in SLF II could be related to species differences in attention to the means vs. goals of observed actions. Several studies have indicated that attention to observed action differs between chimpanzees and humans: chimpanzees attend more to the higher-order goals of actions, whereas humans devote more attention to fine-grained, immediate details like specific movements or methods ((Tomasello et al., 1993; Call et al., 2005; Horner and Whiten, 2005; Myowa-Yamakoshi et al., 2012); for a review, see Whiten et al., 2009). Across monkeys and humans, lateral prefrontal cortex is generally implicated in executive function, working memory, and attentional control (Petrides, 2005a,b; Koechlin and Jubault, 2006; Badre and D'Esposito, 2009) and displays an apparent functional segregation between preferential processing of spatial information in DLPFC vs. non-spatial (feature-based) information in ventrolateral PFC (Wilson et al., 1993; Meyer et al., 2011). This is consistent with the fact that ventrolateral prefrontal cortex is also a major target for ventral stream visual input from inferotemporal cortex (Webster et al., 1994) via the extreme/external capsules (Hecht et al., 2013a). Thus, the human pattern of greater SLF II connectivity to DLPFC may help to support attention to the spatial and kinematic details necessary to understand and reproduce action means, whereas the

chimpanzee pattern of greater IFG connectivity is consistent with attention to objects as the goal of actions. This anatomical distinction may be related to our previous functional finding that during the observation of a simple object-directed grasping action, chimpanzees show comparatively more activation in the inferior frontal gyrus and humans show comparatively more activation in ventral premotor cortex (Hecht et al., 2013b).

Integration of right inferior frontal gyrus with the ventral premotor-inferior parietal circuit. The extension of SLF III into more anterior inferior prefrontal regions may also be relevant for social learning. In a previous study, we used DTI to compare frontal-parietal-temporal connectivity in macaques, chimpanzees, and humans and found a gradient in the pattern of network organization (Hecht et al., 2013a). In macaques, frontal-temporal connections via the extreme/external capsules dominated this network, while in humans, frontal-parietal-temporal connections via the superior and middle longitudinal fasciculi were more prominent; chimpanzees were intermediate. We hypothesized that these species differences in network organization could be the underlying neural basis for species differences in social learning behavior: macaques emulate, or copy the goal of observed actions (Visalberghi and Fragazy, 2002); chimpanzees typically emulate but are also capable in certain situations of imitation, or copying both the goal and the specific methods (Whiten et al., 2009); humans have a strong bias toward imitation (Whiten et al., 2009). Emulation requires recognition of objects (temporal cortex) and higher-order action goals (frontal cortex), while imitation also requires processing the spatial and temporal dynamics of observed movements (parietal cortex). Thus, we suggested that the increasing connectivity of parietal cortex within this network could underlie the increasing bias toward imitation over emulation in the primate lineage leading to humans. This hypothesis was supported by our later finding that humans activate inferior parietal cortex more than chimpanzees during action observation (Hecht et al., 2013b).

The extension of human SLF III into right anterior inferior prefrontal cortex means that in humans, this region is part of both the dorsal network which links frontal and parietal regions via the SLF, and the ventral network which links frontal and temporal regions via the extreme/internal capsules and arcuate fasciculus. Thus in humans and to a lesser extent chimpanzees, this region may have access not only to information about object identities and affordances from temporal cortex, as it does in macaques, but also to information about movement kinematics and temporal dynamics from inferior parietal cortex. Action goals are represented with decreasing specificity from posterior to anterior inferior frontal cortex, with anterior inferior prefrontal regions participating in action planning, response selection, hierarchical

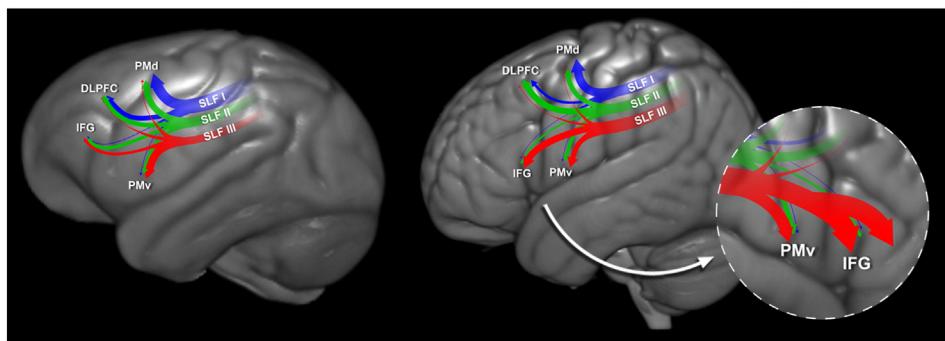


Fig. 7. Diagram of the frontal connectivity of the superior longitudinal fasciculus in chimpanzees and humans (a) Chimpanzees. (b) Humans. The width of the main body of each tract is proportional to the volume of that tract's white matter relative to the total white matter of the SLF. The widths of the cortical terminations of each tract are proportional to the volume of gray matter connectivity of that tract within that region relative to the total gray matter connectivity of the SLF. All measurements represent average measurements across both hemispheres, except for the inferior frontal terminations of SLF III, which are depicted separately for the left and right hemisphere. The pattern of SLF I connectivity was similar across species. In SLF II, humans showed more DLPFC connectivity and less IFG connectivity. In SLF III, humans showed more IFG connectivity and less PMd connectivity. Humans also showed a lateralization effect in the inferior frontal terminations of SLF III which was not apparent in chimpanzees, namely, an extension of right SLF III into the more anterior aspects of the inferior frontal gyrus.

sequencing, and cognitive control (Petrides, 2005a,b; Badre and D'Esposito, 2009). Therefore, we hypothesize that the extension of human SLF III into right anterior inferior frontal gyrus could enable increased incorporation of kinematic detail into processing of higher-order action goals. This function would be especially important for behaviors where the achievement of hierarchical action goals is causally dependent on kinematics, as it is in stone toolmaking (Nonaka et al., 2010; Stout, 2013).

Tool use

Chimpanzee/human differences in the relative size and anterior terminations of SLF III may be related to differences in tool-use ability. Chimpanzee tool-use is impressive, and includes the dexterous use, making, and sequential combination of multiple tools to achieve a goal (Sanz and Morgan, 2010). It is widely assumed that the common ancestor of chimpanzees and humans had similar tool-using capacities (e.g. Panger et al., 2002). The earliest known uniquely hominin tools are 2.6 million years old, consist of sharp stone flakes struck from river cobbles using another stone, and were likely used to butcher animal carcasses (Semaw et al., 2003). There is some debate whether these simple "Oldowan" tools represent a departure from shared, "ape-grade" cognitive capacities (Wynn et al., 2011), but their manufacture does require bimanual coordination of accurate, forceful blows that appears difficult or impossible for apes (Byrne, 2005). In keeping with this, studies of actual Oldowan tool-making by modern human subjects using FDG-PET methodology, which enables imaging of behavior that occurs outside the scanner (Stout and Chaminade, 2007; Stout et al., 2008), document task-related activations in a distributed frontal-parietal-occipitotemporal network for visually-guided object manipulation similar to that identified in other studies of complex tool-use (e.g. Frey, 2007), but no activations in more anterior portions of prefrontal cortex typically associated with cognitive control functions. Intriguingly, the current study did find evidence of increased medial-lateral fibers in human inferior prefrontal cortex (Fig. 1b), which if they do indeed correspond to interhemispheric callosal connections, may play a role supporting enhanced human capacities for bimanual coordination.

After approximately 1.7 million years ago (Lepre et al., 2011; Beyene et al., 2013), Oldowan technology began to be replaced by "Acheulean" tool-making methods based the intentional shaping of stones to produce large cutting tools known as 'picks', 'handaxes' and 'cleavers'. Such shaping requires more extended sequences of contingent actions organized with respect to a distal goal (Stout, 2011) and is commonly thought to represent a major increase in cognitive complexity. By 500,000 years ago, some Acheulean tools exhibited a high level of refinement requiring even more complex production sequences including, for example, the careful preparation of edges and surfaces prior to flake removal (Stout et al., 2014). FDG-PET data show that, unlike Oldowan tool-making, such refined Acheulean tool-making is associated with increased activation of right fronto-parietal cortex generally and right IFG—*pars triangularis* specifically (Stout et al., 2008). A similar preferential response of right *pars triangularis* to Acheulean tool-making was observed in an fMRI study of action observation. This study also reported an effect of technology (Acheulean > Oldowan) in left inferior frontal sulcus bordering IFG—*pars triangularis* (Stout et al., 2011). Finally, a recent longitudinal DTI study of stone tool-making (especially Acheulean) skill acquisition over a two-year period found training-related changes (increased fractional anisotropy) in SLF III underlying inferior parietal and frontal cortex, again including right IFG—*pars triangularis* (Hecht et al., 2014).

Experimental evidence thus links increased IFG functional response and white matter connectivity to archeologically documented variation in tool-making complexity over the course of human evolution. We propose that the enhanced human SLF III connectivity with IFG reported here, and especially that of right SLF III, comprises part of the anatomical basis for the unique technological capacities of *Homo sapiens*. The IFG bilaterally is associated with the hierarchical control of behavior

(Koechlin and Jubault, 2006) and right IFG in particular is associated with inhibitory and set-shifting functions (Aron et al., 2004, 2014; Levy and Wagner, 2011) that are important to execution of multi-step action plans (e.g. Hartmann et al., 2005). Right parietal cortex is involved in representing the sequential order of behavior (Frey and Gerry, 2006; Jubault et al., 2007), and the right hemisphere in general appears to be specialized for integration of perception and action across larger spatio-temporal frames (Deacon, 1997; Serrien et al., 2006; Stout and Chaminade, 2012). Increased human connectivity between the right inferior frontal gyrus and parietal cortex via SLF III may provide an anatomical basis for enhanced cognitive control over the complex goals and multi-step action sequences characteristic of human technology (Stout, 2013).

Conclusions

Our results indicate that during human evolution, SLF II underwent selection for increased connectivity with dorsolateral prefrontal cortex, whereas SLF III underwent selection for increased relative size and increased connectivity with the inferior frontal gyrus, in particular the more anterior aspects of the right inferior frontal gyrus. Thus the neural substrate for integrating right inferior frontal cortex with the lateral frontal-parietal-occipitotemporal network likely emerged relatively recently in primate evolution, after humans' divergence from chimpanzees. We suggest that the driving force behind these changes may have been the intertwined selective pressures for spatial attention to observed actions, toolmaking, and social learning, all of which likely depend on integration of spatial, kinematic and sequential information for action perception and control.

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.neuroimage.2014.12.039>.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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