# Genetic Determinants of Individual Variation in the Superior Temporal Sulcus of Chimpanzees (Pan troglodytes)

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# Genetic Determinants of Individual Variation in the Superior Temporal Sulcus of Chimpanzees (*Pan troglodytes*)

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Abstract

The superior temporal sulcus (STS) is a conserved fold that divides the middle and superior temporal gyri. In humans, there is considerable variation in the shape, folding pattern, lateralization and depth of the STS that have been reported to be associated with social cognition and linguistic functions. We examined the role that genetic factors play on individual variation in STS morphology in chimpanzees. The surface area and depth of the STS were quantified in sample of 292 captive chimpanzees comprised of two genetically isolated population of individuals. The chimpanzees had been previously genotyped for AVPR1A and KIAA0319, two genes that play a role in social cognition and communication in humans. Single nucleotide polymorphisms in the KIAA0319 and AVPR1A genes were associated with average depth as well as asymmetries in the STS. By contrast, we found no significant effects of these KIA0319 and AVPR1A polymorphism on surface area and depth measures for the central sulcus. The overall findings indicate that genetic factors account for a small to moderate amount of variation in STS morphology in chimpanzees. These findings are discussed in the context of the role of the STS in social cognition and language in humans and their potential evolutionary origins.

The superior temporal sulcus (STS) is a highly conserved fold of the cerebral cortex in primate brains that divides the superior and middle gyri of the temporal lobe (Connolly 1936; Connolly 1950) (see Figure 1). In cercopithecid and platyrrhine monkeys, the STS is largely a smooth fold that begins at the temporal pole and extends posteriorly beyond the most posterior point of the Sylvian fissure and terminates in the parietal lobe. In great apes and humans, there is considerably more variation in the shape and trajectory of the STS, particularly in the posterior region where, posterior and dorsal to the terminal point of the Sylvian fissure, the sulcus can bifurcate into descending and ascending limbs that may or may not be connected to the primary fold (see Figure 2). Further, in humans, and to a lesser extent in chimpanzees, the STS may be split into multiple sections or pieces due to the presence of "pli-de-passages" or buried gyri (Bodin et al. 2021), which has been reported to be more frequently found in the left compared to the right hemisphere in humans (Le Guen et al. 2018). Recently, it has been suggested that asymmetries in the central region of the STS, referred to as the STAP (**S**uperior **T**emporal **A**symmetric **P**it), are a human-specific anatomical landmark that has been hypothesized to be linked to the evolution of language. Specifically, LeRoy et al. (2015) quantified the depth of the STS in regions anterior and posterior to Heschl's gyrus in MRI scans of humans and chimpanzees and reported robust, rightward asymmetries in the STAP region in human subjects, whereas chimpanzees showed a relatively small, and only marginally significant rightward bias. These findings are particularly interesting because previous studies in chimpanzees have reported population-level asymmetries in the perisylvian region, including the posterior STS and planum temporale; results that are quite similar to those in humans

(Hopkins and Nir 2010; Kong et al. 2018; Spocter et al. 2020). Thus, given the role of the posterior STS and superior temporal gyrus (STG) in a variety of linguistic, socio-communicative and cognitive functions (i.e., such as the processing of faces, auditory stimuli and biological motion) (Redcay 2008; Deen et al. 2015; Specht and Wigglesworth 2018) and the purported human uniqueness of asymmetries in the STAP, further studies on the morphology of the STS in other primate species are warranted as a means of characterizing the evolution of this cortical fold, as well as factors that influence individual variation in its expression.

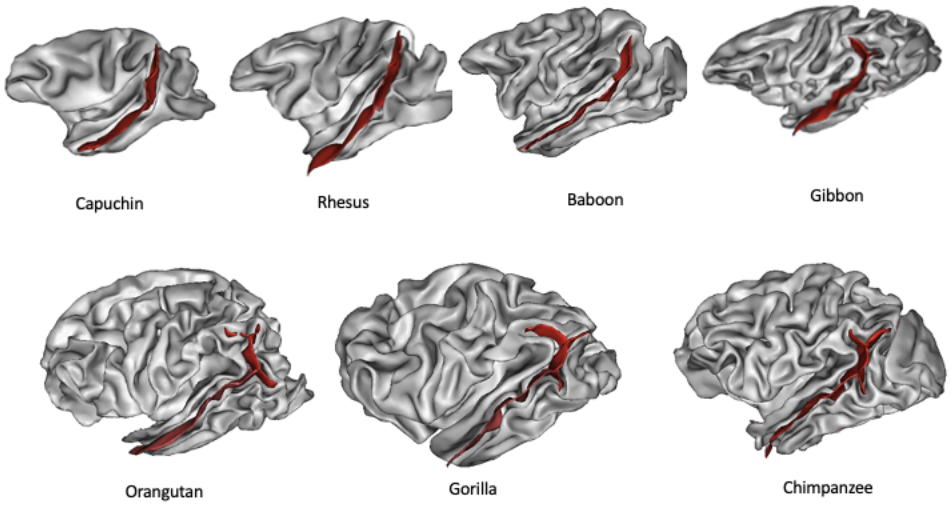


Figure 1: 3D lateral views of the superior temporal sulcus (STS) in different primate species.

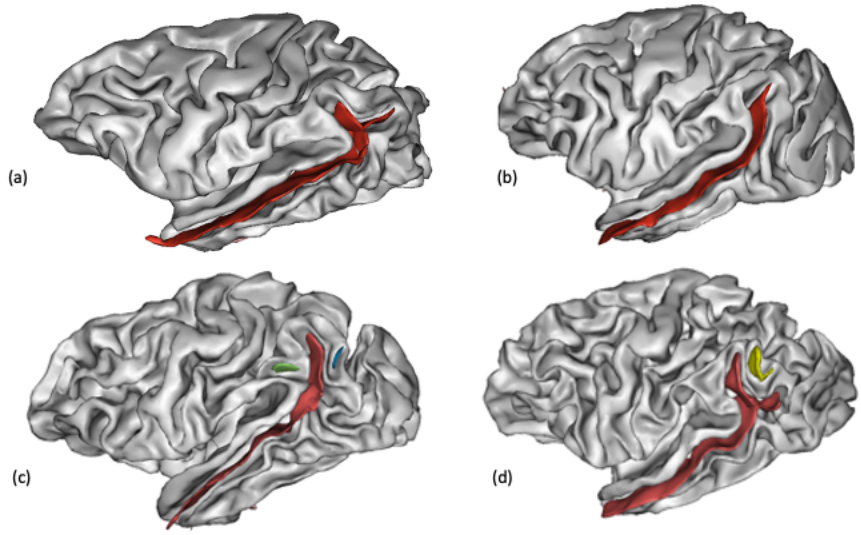


Figure 2: Four different example of variation in the morphology of the STS. (a) typical pattern with a bifurcated anterior and posterior limb (b) less common variants with no bifurcation at the posterior terminal position (c) STS variant with a disconnected anterior (green) and posterior (yellow) limb (d) STS variant with an intermediate fold (yellow).

To this end, we examined the contribution of genetic and non-genetic (environmental) factors to individual variation in the surface area, mean depth and the depth profile along the length of the STS in chimpanzees. In the initial set of analyses, we divided the entire STS into anterior and posterior regions and quantified the overall surface area and mean depth. We next quantified the depth profile of the anterior STS, which included the STAP region, in the left and right hemispheres in the chimpanzee sample. From these data, in one analysis, we tested for population-level asymmetries as a means of evaluating their uniqueness as hypothesized by LeRoy et al. (2015). In a second set of analyses, following methods used in previous studies with human and nonhuman primates (Rogers et al. 2007; Fears et al. 2009; Rogers et al. 2010; McKay et al. 2013; Hopkins, Coulon, Meguerditchian, Autrey, Davidek, Mahovetz, Pope, et al. 2017; Hopkins et al. 2018; Hopkins et al. 2019), we used quantitative genetic analyses

based on the available pedigree information for the chimpanzees to estimate heritability in the STS regions, as well as the contribution of non-genetic factors including their sex, age, rearing history and the magnet strength of the scanner used to obtain the images. One unique aspect of the chimpanzee sample was that it was comprised of two cohorts of apes that were founded by separate wild-born animals and their descendants were raised at two different research facilities with no transfer of individuals between them. Thus, the two cohorts were genetically isolated from each other and this allowed us to evaluate the repeatability of the heritability results.

We also examined whether polymorphisms in two different genes were implicated in individual variation in STS morphology. In one set of analyses, we tested whether single nucleotide polymorphisms (SNPs) in the *KIAA0319* gene potentially explain individual variation in the STS and, specifically in the STAP region. *KIAA0319* is a gene strongly implicated in language functions and polymorphisms in this gene have been repeatedly implicated in developmental dyslexia (DD) in humans, a reading disorder that is primarily manifest in difficulties learning associations between sounds with letters and/or words (Cope et al. 2005; Dennis et al. 2009; Scerrl et al. 2011). Meta-analyses have shown that individuals with DD show atypical patterns of gray matter volume, cortical thickness and white matter connectivity in brain regions implicated in language (Eckert et al. 2016; Eicher et al. 2016). Studies in humans have also shown that SNPs in the *KIAA0319* gene are associated with the prevalence of DD and are linked to differences in grey and white matter cortical organization, particularly within the posterior superior-temporal lobe and parietal junction within the left hemisphere (Robichon et al. 2000; Darki et al. 2012; Pinel et al. 2012). Similarly, in

chimpanzees, a recent study identified two SNPs in the *KIAA0319* gene that were associated with individual variation in gray matter covariation in the posterior superior temporal gyrus (Hopkins et al. in press). For this reason, we hypothesized that these same polymorphisms might also be associated with variation in the surface area and depth of the chimpanzee STS.

We also tested for associations between polymorphisms in the gene coding for arginine vasopressin receptor 1A, *AVPR1A*, and variation in STS morphology. *AVPR1A* has been shown to play a role in social behavior and cognition in mammals (Goodson and Bass 2001; Donaldson and Young 2008; French et al. 2016; Hopkins and Latzman 2021) and has been hypothesized to be a candidate gene for psychological disorders in which deficits in social behavior are prominent, such as autism spectrum disorder (ASD) (Hammock and Young 2006; Yirmiya et al. 2006; Carter 2007; Donaldson and Young 2008; Melke 2008; Francis et al. 2016; Parker et al. 2018). Consistent with this view, neuroimaging studies have shown that gray matter volume and white matter connectivity in the STS differ between individuals with and without a diagnosis of ASD (Zilbovicius et al. 2006) and other neuropsychiatric disorders (Plaze et al. 2011). Previous studies have shown that chimpanzees possess an indel deletion in the *AVPR1A* microsatellite, resulting in a bimodal distribution of subjects with (DupB+/-) or without (DupB-/-) the RS3 duplication (Hammock 2005; Donaldson et al. 2008). Behaviorally, DupB+/- (which can include a small cohort of DupB+/+ individuals) and DupB-/- chimpanzees have been found to differ significantly in dimensions of personality and social behavior (Hopkins et al. 2012; Anestis et al. 2014; Latzman et al. 2014; Staes et al. 2014; Wilson et al. 2017) . For example, Mahovetz et al. (2016)

recorded the social behavior of chimpanzees when presented with a mirror and found that DupB+/- males showed higher rates of scratching (reflecting anxiety) and agonistic behaviors compared to DupB-/- males and both DupB+/- and DupB-/- females. Polymorphisms in AVPR1A are also associated with a composite score reflecting ASD phenotypes (Weiss et al. 2021) as well as social cognition measures linked to ASD, notably receptive joint attention (RJA) (Hopkins, Keebaugh, et al. 2014). Previous studies have also found that both humans and chimpanzees with poor joint attention skills differ in gray matter volume of the posterior, but not anterior, portion of the superior temporal gyrus (Hopkins, Misiura, et al. 2014; Mundy 2018). Finally, Mulholland et al. (2020) using source-based morphometry, found that DupB-/- chimpanzees had significantly higher covariation in gray matter within the superior temporal gyrus compared to DupB+/- apes. In light of the significant differences found between DupB+/- and DupB-/- apes in behavior and gray matter covariation within the superior temporal gyrus, we hypothesized that chimpanzees with these two genotypes would also differ on measures of STS surface area and depth.

Finally, we tested whether the influence of polymorphisms in the KIAA0319 and AVPR1A were specific to the STS. To test this hypothesis, we examined the influence of polymorphisms in KIAA0319 and AVPR1A on depth and surface area measures of the central sulcus (CS). The surface area and depth of the CS in chimpanzees has been previously reported to be significantly heritable and associated with manual and oro-facial motor skills in this same chimpanzee sample (Hopkins, Coulon, Meguerditchian, Autrey, Davidek, Mahovetz, S., et al. 2017). If the influence of polymorphisms in the KIAA0319 and AVPR1A genes were specific to the STS, then we

hypothesized that no significant effects would be found for the surface area and depth of the CS.

## Methods

### *Subjects*

For the quantitative genetic analyses on STS heritability, magnetic resonance images (MRI) were obtained from 292 captive chimpanzees housed at either the Yerkes National Primate Research Center (YNPRC, n = 133) or the National Center for Chimpanzee Care (NCCC, n = 157) of The University of Texas MD Anderson Cancer Center. There were 170 females and 122 males ranging from 6 to 54 years of age (Mean = 27.99 years, *SD* = 11.11). Within this sample, there were 136 mother-reared, 92 nursery-reared and 64 wild-born individuals. A breakdown in the composition of relatedness of the two chimpanzee samples has been previously reported in Hopkins, Reamer, et al. (2015). With the exception of two individuals, nursery-reared (NR) chimpanzees were separated from their mothers within the first 30 days of life, due to unresponsive care, sickness, or injury, and leaving them in their circumstance at the time would have increased the risk of death (Bard et al. 1992; Bard 1994). The NR chimpanzees were placed in incubators, fed standard human infant formula, and cared for by humans until they could sufficiently care for themselves, at which time they were placed with other infants of the same age until they were 3 years of age (Bard *et al.* 1992; Bard 1994). At 3 years of age, NR chimpanzees were integrated into larger social groups of adult and sub-adult chimpanzees. Mother-reared (MR) chimpanzees were not separated from their mother for at least the first 2.5 years of life and were raised in nuclear family groups ranging from 4 to 20 individuals. The two exceptions of NR

individuals were Lana and Panzee, chimpanzees that were born at the YNPRC but raised in a rich social-linguistic environment by humans at the Language Research Center (LRC) as part of an initiative to investigate the linguistic skills of chimpanzees (Rumbaugh 1977; Brakke and Savage-Rumbaugh 1995, 1996). Wild-born (WB) chimpanzees were individuals who had been captured in the wild and subsequently brought to research facilities within the United States prior to 1974, when the importation of chimpanzees was banned. All scanning procedures performed with the chimpanzees were approved by the local Institutional Animal Care and Use Committees and followed all recommendations by the Institute of Medicine for the ethical treatment of chimpanzees in research.

*KIAA0319 and AVPR1A Genotypes*

All genotyping was performed on DNA extracted from banked blood samples obtained from the chimpanzees during their annual physical examination within each facility prior to 2015. DNA samples were not available on the entire sample of 292 chimpanzees; thus, all analyses examining the influence of genotype on the STS involved fewer individuals. The details for DNA extraction, primer sequences and analyses have been provided in detail in previous publications (Hopkins *et al.* 2012; Hopkins et al. 2021). For *KIAA0319*, one SNP, RS_P1, had allele frequencies of 99 (AA), 104 (AT) and 46 (TT). For the second SNP, RS_63, the allele frequencies within our population were 78 (AA), 116 (AC) and 54 (CC). For *AVPR1A*, there were 85 DupB+/- and 153 DupB-/- within the sample.

*MRI Image Collection*

Both *in vivo* (n = 228*)* and *ex vivo* (n = 64) post-mortem MRI scan data were used in this study. *In vivo* scans were obtained at the time the chimpanzees were being surveyed for their annual physical examinations beginning in 1998 and continuing until 2014. Subjects were first immobilized by ketamine (10 mg/kg) or telazol (3-5mg/kg) and subsequently anaesthetized with propofol (40–60 mg/(kg/h)) following standard procedures at the YNPRC and NCCC facilities. YNPRC subjects were then transported to the MRI facility, while NCCC subjects were wheeled to a mobile imaging unit. The subjects remained anaesthetized for the duration of the scans, as well as the time needed to transport them between their home cage and the imaging facility (between 5 and 10 minutes) or mobile imaging unit (total time ~ 5 minutes). Subjects were placed in the scanner chamber in a supine position with their head fitted inside the human-head coil. Scan duration ranged between 40 and 60 minutes as a function of brain size.

Seventy-seven chimpanzees were scanned using a 3.0 Tesla scanner (Siemens Trio, Siemens Medical Solutions USA, Inc., Malvern, Pennsylvania, USA) at YNPRC. T1-weighted images were collected using a three-dimensional gradient echo sequence (pulse repetition= 2300 ms, echo time= 4.4 ms, number of signals averaged= 3, matrix size = 320 X 320). Additionally, 139 NCCC and 13 YNPRC chimpanzees were scanned using a 1.5 Tesla Phillips or GE machine. T1-weighted images were collected in the transverse plane using a gradient echo protocol (pulse repetition= 19.0 ms, echo time= 8.5 ms, number of signals averaged= 8, and a 256 x 256 matrix). After completing MRI procedures, the subjects were temporarily housed in a single enclosure for 6–12 h to allow the effects of the anesthesia to wear off, after which they were returned to their social group. Post-mortem T2-scans were obtained from 64 chimpanzees that had died

from natural causes. For the post-mortem scanning, either 4.7 or 7T magnets were used and T2-weighted images were collected in the transverse plane using a gradient echo protocol (pulse repetition = 22.0 s, echo time = 78.0 ms, number of signals averaged = 8-12, and a 256 × 192 matrix reconstructed to 256 × 256).

*Sulci Extraction and Measurement*

The sequence of post-image processing steps performed on the images are shown in Figures 3a to 3h and have been described in detail elsewhere (Hopkins et al. 2010; Bogart et al. 2014; Hopkins, Coulon, Meguerditchian, Autrey, Davidek, Mahovetz, S.*, et al.* 2017). The processing used to extract the sulci from the raw T1-weighted image derives from a pipeline initially dedicated to the human brain and freely distributed as a BrainVISA toolbox (http://brainvisa.info) (Mangin et al. 2004). To account for the differences in chimpanzee anatomy compared to humans, a number of adjustments were performed before the scans were processed using the pipeline procedure within BrainVISA (BV). Specifically, chimpanzee MRI volumes were skull-stripped, cropped, denoised (Coupe et al. 2008), and reformatted at 0.625 mm isotropic resolution using ANALYZE 11.0 software and subsequently imported into BV. The pipeline process of extracting the sulci from the cortex involved a number of steps (Mangin *et al.* 2004) (see Figure 3a to 3h). To align the template brain, the anterior and posterior commissures were manually specified on the MRI at the point where they intersect with the mid-sagittal slice. The first step was to correct for spatial inhomogeneities in the signal intensity, providing a spatially smooth bias field with a stable distribution of tissue intensities (Figure 3b). Next, the analysis of the signal histogram and mathematical morphology were performed using an automatic analysis

of the voxel intensities for the entire brain to obtain a binary mask of the brain (Figure 3c). Adjustments were sometimes needed in the histogram process to determine gray and white matter means for chimpanzee brain scans. The mask was then split into the left and right hemispheres and the cerebellum (Figure 3d). A negative cast of the white matter was computed from the split-brain mask. The outside boundary of this cast results from a 5 mm morphological closing of the masked hemisphere, filling up the folds. The gray/white interface is the inside boundary and is computed using deformations that assure the spherical topology of the cast (Figure 3e). Finally the cast was skeletonised to detect cortical folding, while topological constraints guaranteed the resulting surfaces would have no holes (Mangin 2000; Mangin *et al.* 2004) (Figure 3f & 3g). The STS and the CS in each hemisphere was selected manually (Figure 3h) by the user, using a 3D visualization interface (Bailey et al. 1950; Hopkins, Meguerditchian, et al. 2014).

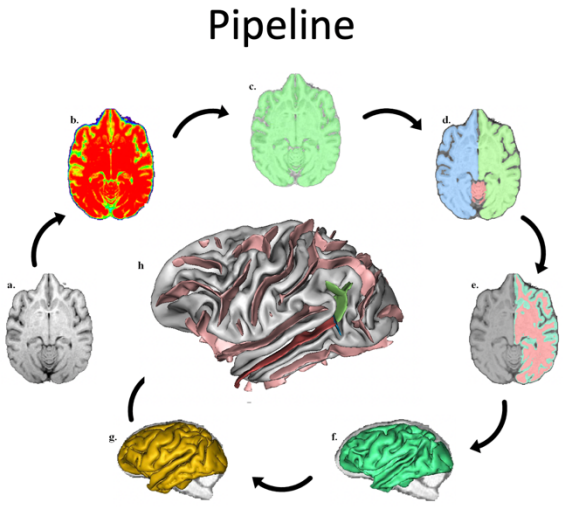


Figure 3: Pipeline process in BrainVisa for sulci extraction.

To divide the STS into its anterior and posterior sections, we used a sulcus that was present in the majority of brains (lablled as A3 in Connolly 1936) and could be used to divide the STS into anterior and posterior regions (see Figure 4). In more than 75% of the hemispheres, the BV pipeline produced a natural break in the STS at the A3 sulcus. In the absence of a natural break, we used the scissors tool in BV to manually bisect the fold along the medial-lateral axis of A3. Using this landmark, the STS was divided into the anterior (STS_Ant) and posterior (STS_Post) regions. For the STS_Post, we included all the folds that were dorsal to the STS_ventral, including those that were disconnected from the main STS fold. The STS_Post excluded any sulci that were part of the lunate, posterior central and intraparietal sulci. The STS_Ant and STS_Post were manually labelled for the left and right hemisphere and we calculated the surface area and mean depth for each region.

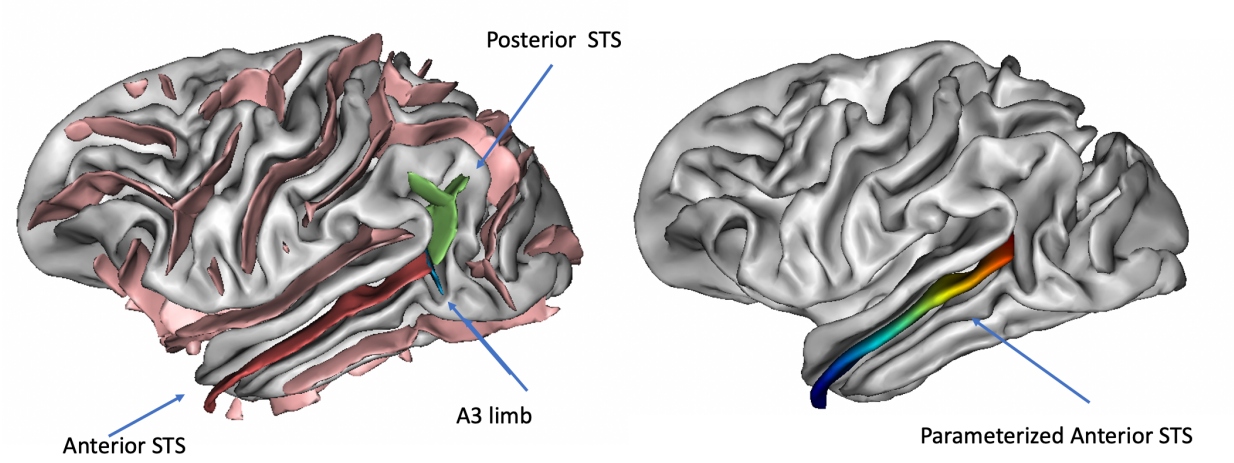


Figure 4: Left panel: 3D rendering of chimpanzee brains with the STS extracted and the landmarks identified to distinguish between the anterior and posterior sections. Right panel: 3D rendering of chimpanzee brain showing the STS_Ant section that the parameterization analyses were performed for each subject.

*Parameterization of the STS_Ant*

The selected STS_Ant was meshed using a triangular mesh, and the resulting surface was parameterized in order to create a longitudinal coordinate system (Coulon et al. 2015) (Figure 5a to 5d). The parameterization process was constrained by the anterior and posterior sulcus extremities, automatically detected using the extrema of the first non-zero eigenfunction of the mesh Laplacian ($e_1$ and $e_2$, Fig. 5b). From these points, a smooth and quasi-isometric (i.e. with minimal metric distortions) coordinate field is extrapolated, that localizes all mesh surface points according to their relative position along the sulcus between the two extremities (Fig. 5c). The coordinate field extends along the length of the STS_Ant from the anterior (y = 1) to the posterior (y = 100) ends of the sulcus. Depth was measured at 100 sulcal length positions in an anterior-to-posterior progression along the parameterized sulcal mesh surface. Position 1 was located at the most anterior point of STS_Ant, while position 100 was located at the most posterior point of the STS_Ant where the A3 sulcus was located (see Fig 5c). At each position, y, along the length, the depth is computed by measuring a geodesic distance (in millimeters) from the brain envelope to the fundus of the sulcus (Fig. 5d). To simplify the analyses, within the left and right hemispheres, we averaged every 5 depth measures from point 0 to 100 to create 20 STS_Ant regions along the anterior-posterior plane.

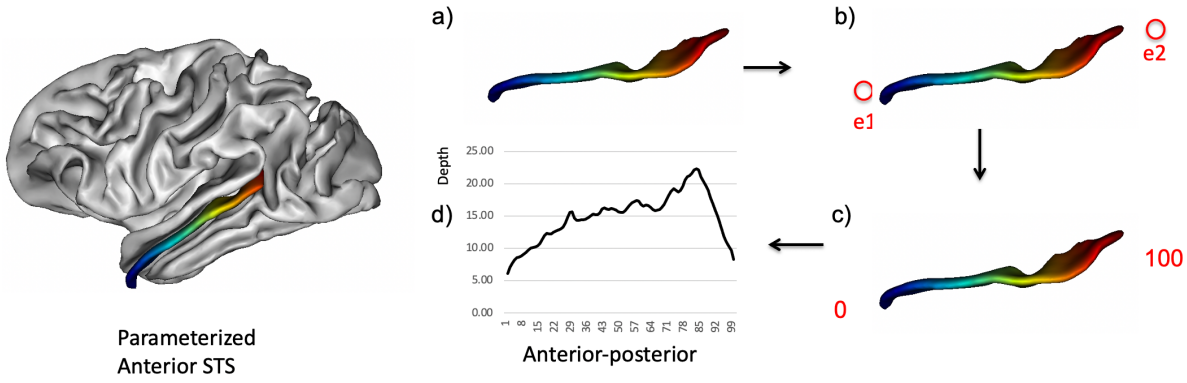


Figure 5: Parameterization steps of the STS_Ant of the chimpanzee brain (see text for description).

*Heritability Analyses*

Consistent with previous studies, we used the software package SOLAR to estimate heritability in the STS (Almasy and Blangero 1998) (http://solar-eclipse-genetics.org). SOLAR uses a variance component approach to estimate the polygenic component of variance when considering the entire pedigree (see Rogers *et al.* 2007; Fears *et al.* 2009; Fears et al. 2011; Hopkins, Keebaugh*, et al.* 2014). Total additive genetic variance ($h^2$) is the amount of total phenotypic variance that is attributable to all genetic sources. Total phenotypic variance attributable to genetic and non-genetic variables is constrained to a value of 1; therefore, all non-genetic contributions to the phenotype are equal to 1 - $h^2$. We used SOLAR to determine heritability in the average surface area and average depth of the overall STS_Ant and STS_Post regions by adding the left and right hemisphere values and dividing by two. We also computed an asymmetry quotient (AQ) for the surface area and mean depth measures for both the STS_Ant and STS_Post region following the formulas [AQ = (R – L) / ((R + L ) *.5)]

where R and L represent the right and left hemisphere values. Positive AQ values indicated rightward and negative values indicated leftward biases. We also used SOLAR to estimate heritability in the STS_Ant depth values based on the parameterization data by calculating the average for the right and left hemisphere and AQ values for each of the 20 regions. For all heritability analyses, scanner strength (1.5T, 3T, and 7T), sex, age, and rearing history served as covariates in the analyses. Heritability estimates and genetic correlations at $p \leq .05$ were considered significant.

## Results

### Quantitative Genetic Analyses

*Global Results*

For descriptive purposes, shown in Table 1 are the average mean surface areas and mean depth for the STS_Ant and STS_Post regions in males and females, and between each rearing group. Heritability results on the combined sample showed the average surface area and mean depth of the STS_Ant and STS_Post regions were significantly heritable, while AQ values for both measures were not (see Table 2). With respect to average surface area and mean depth, scanner magnet was found to be a significant covariate, an expected finding, given the known differences in gray and white matter resolution as a function of field strength. Sex was also found to be a significant covariate, which was also expected, because we did not adjust for brain/body size between males and females (see Table 1). Neither age nor rearing history accounted for a significant proportion of variance in average surface area or mean depth. Also shown in Table 2 are the heritability results within the YNPRC and NCCC cohorts. Heritability in the surface areas were largely consistent between the two cohorts, but

this was not the case for the average depth measures for the STS_Ant and STS_Post measures.

Table 1: Average Mean Surface Area and Mean Depth (+/- s.e.) for the STS_Ant and STS_Post as a Function of Sex and Rearing History

| | Sex | | Rearing | | |
|---|---|---|---|---|---|
| | Female | Male | MR | NR | WB |
| *Surface Area ($mm^2$)* | | | | | |
| STS_Ant | 1339.28 (19.54) | 1483.65 (22.84) | 1462.47 (22.09) | 1419.75 (27.37) | 1397.19 (42.63) |
| STS_Post | 584.46 (13.35) | 666.36 (15.60) | 641.57 (15.09) | 628.90 (18.69) | 605.74 (29.11) |
| *Mean Depth (mm)* | | | | | |
| STS_Ant | 11.57 (.094) | 12.13 (.110) | 12.02 (.106) | 11.78 (.132) | 11.76 (.205) |
| STS_Post | 7.98 (.106) | 7.94 (.124) | 8.37 (.120) | 8.08 (.148) | 7.43 (.231) |

Values in parentheses represent standard errors. MR = mother-reared, NR – nursery-reared, WB = wild-born. Surface area and mean deoth are

Table 2: Heritability in STS_Ant and STS_Post Surface Area and Mean Depth for the Combined, YNPRC and NCCC Samples

| | $h^2$ | se | p | Covariates | Variance |
|---|---|---|---|---|---|
| Combined Sample | | | | | |
| Anterior Surface Area | .455 | .123 | .00003 | Sc, Sex | .116 |
| Posterior Surface Area | .316 | .150 | .0145 | Sc, Sex | .135 |

| | | | | | |
|---|---|---|---|---|---|
| Anterior Mean Depth | .345 | .122 | .0004 | Sc, Sex | .083 |
| Posterior Mean Depth | .183 | .105 | .0211 | Sc, Rear | .027 |
| YNPRC | | | | | |
| Anterior Surface Area | .501 | .189 | .003 | Sc, Sex, Rear | .117 |
| Posterior Surface Area | .356 | .162 | .005 | Sc, Sex, Rear | .135 |
| Anterior Mean Depth | .640 | .205 | .0004 | Sc, Sex, Rear | .119 |
| Posterior Mean Depth | .000 | ------ | .500 | Sc | .016 |
| NCCC | | | | | |
| Anterior Surface Area | .537 | .154 | .0003 | Sc, Sex | .165 |
| Posterior Surface Area | .660 | .209 | .0009 | Sc, Sex | .091 |
| Anterior Mean Depth | .000 | ------ | .500 | Sc, Sex | .181 |
| Posterior Mean Depth | .254 | .143 | .017 | Sc, Sex | .068 |

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se = standard error

We note here that surface area for the entire brain was significantly heritable ($h^2$ = .298, se = .148, $p$ = .011). To determine whether the surface area heritability values for the STS were region specific or could be accounted for by overall surface area, we calculated the percentage of STS_Ant and STS_Post by dividing the mean surface areas for each area by the total surface area of the brain and multiplying by 100. We then re-ran the heritability analyses using the percentage STS_Ant and STS_Post measures with sex, age rearing and scanner as covariates. For both the STS_Ant ($h^2$ = .325, se = .116, $p$ = .0008) and STS_Post ($h^2$ = .223, se = .129, $p$ = .033) regions, the adjusted surface as measures remained significantly heritable. Thus, the heritability in

the STS surface area appears to be independent of genetic influences on total surface area.

*Parameterized STS_Ant Depth*

We next considered heritability in the STS_Ant depth measures at the 20 points along the anterior-posterior plane. Results for the average STS_Ant depth for the entire sample, as well as for the separate results for the NCCC and YNPRC cohorts, are shown in Figure 6a. For the combined sample, significant heritability was found for 13 of the 20 regions (regions 6 to 18); thus, the majority of regions along the anterior-posterior axis of the sulcus were significantly heritable with values ranging from .294 to .616. As with the global results and as expected, sex and scanner were significant covariates for 17 and 15 regions, respectively (see Table 3). Rearing was a significant covariate for regions 18 and 19 (see Table 3). The mean depth at the 20 STS regions for males and females and between the three rearing groups are shown in Table 4. As can be seen, when sex was a significant covariate, males had higher values than females. Further, for STS 18 and 19, MR apes had higher values than NR individuals who, in turn, had higher values than WB apes. Between the NCCC and YNPRC chimpanzee cohorts, the results were largely consistent, with significant heritability found in both the NCCC and YNPRC cohorts for STS regions 7 through 18 (see Figure 6b and 6c). For the AQ measures for each STS_Ant region, we found no evidence of significant heritability for any of the 20 STS regions, after adjustment for multiple comparisons, in either the combined sample or in each separate cohort.

Table 3: Heritability in STS_Ant Parameterized Regions and Variance Accounted for By Covariates

| | $h^2$ | s.e. | p | Covariates | Variance |
|---|---|---|---|---|---|
| STS1 | .024 | .106 | .407 | Sex | .015 |
| STS2 | .130 | .107 | .091 | Sex, Scanner | ,047 |
| STS3 | .175 | .102 | .025 | Sex, Scanner | .078 |
| STS4 | .129 | .106 | .089 | Sex, Scanner | .120 |
| STS5 | .129 | .110 | .098 | Sex, scanner | .163 |
| STS6 | .294 | .121 | .002 | Sex, Scanner | .124 |
| STS7 | .453 | .127 | .00002 | Sex, Scanner | .163 |
| STS8 | .478 | .132 | .00001 | Sex, Scanner | .158 |
| STS9 | .467 | .131 | .00002 | Sec, Scanner | .152 |
| STS10 | .514 | .129 | .000007 | Sex, Scanner | .157 |
| STS11 | .616 | .118 | .00000001 | Sex, Scanner | .162 |
| STS12 | .482 | .119 | .00003 | Sex, Scanner | .160 |
| STS13 | .499 | .117 | .000001 | Sex, Scanner | .164 |
| STS14 | .604 | .114 | .0000001 | Sex, Scanner | .154 |
| STS15 | .655 | .119 | .0000001 | Sex, Scanner | .118 |
| STS16 | .501 | .131 | .00002 | Sex, Scanner | .058 |
| STS17 | .482 | .125 | .0001 | Sex | .032 |
| STS18 | .385 | .137 | .0009 | Rear | .018 |
| STS19 | .105 | .118 | .159 | Rear | .017 |
| STS20 | .000 | .000 | .500 | None | |

Table 4: Mean (+/- s.e.) STS Depth at the 20 STS locations as a Function of Sex and Rearing Group

| | Sex | | Rearing History | | |
|---|---|---|---|---|---|
| | Male | Female | MR | NR | WB |
| STS1 | 4.93 | 4.71 | 4.74 | 4.95 | 4.87 |
| | (.089) | (.075) | (.085) | (.097) | (.156) |
| STS2 | 7.43 | 7.06 | 7.26 | 7.37 | 7.11 |
| | (.113) | (.095) | (.108) | (.123) | (.197) |
| STS3 | 8.90 | 8.37 | 8.75 | 8.60 | 8.55 |
| | (.119) | (.101) | (.114) | (.130) | (.208) |
| STS4 | 9.80 | (9.28) | 9.60 | 9.46 | 9.56 |
| | (.130) | (.110) | (.124) | (.142) | (.226) |
| STS5 | 10.46 | 9.96 | 10.19 | 10.11 | 10.34 |
| | (.135) | (.114) | (.129) | (.148) | (.236) |

| | | | | | |
|---|---|---|---|---|---|
| STS6 | 11.12 | 10.63 | 10.84 | 10.76 | 11.03 |
| | (.136) | (.115) | (.130) | (.149) | (.238) |
| STS7 | 11.89 | 11.29 | 11.59 | 11.49 | 11.71 |
| | (.131) | (.111) | (.125) | (.144) | (.229) |
| STS8 | 12.69 | 12.01 | 12.31 | 12.19 | 12.54 |
| | (.132) | (.111) | (.125) | (.144) | (.230) |
| STS9 | 13.40 | 12.71 | 13.01 | 12.85 | 13.30 |
| | (.131) | (.111) | (.125) | (.143) | (.229) |
| STS10 | 14.05 | 13.31 | 13.68 | 13.48 | 13.87 |
| | (.130) | (.110) | (.124) | (.142) | (.233) |
| STS11 | 14.62 | 13.86 | 14.34 | 14.03 | 14.34 |
| | (.131) | (.111) | (.125) | (.143) | (.228) |
| STS12 | 15.12 | 14.31 | 14.74 | 14.48 | 14.88 |
| | (.134) | (.113) | (.127) | (.146) | (.233) |
| STS13 | 15.48 | 14.58 | 15.08 | 14.77 | 15.24 |
| | (.139) | (.118) | (.133) | (.152) | (.243) |
| STS14 | 15.73 | 14.82 | 15.26 | 15.03 | 15.53 |
| | (.147) | (.124) | (.140) | (.160) | (.256) |
| STS15 | 16.05 | 15.22 | 15.58 | 15.31 | 16.03 |
| | (.161) | (.136) | (.154) | (.176) | (.282) |
| STS16 | 16.60 | 15.95 | 16.25 | 15.91 | 16.67 |
| | (.183) | (.155) | (.175) | (.200) | (.320) |
| STS17 | 16.91 | 16.30 | 16.75 | 16.42 | 16.64 |
| | (.200) | (.169) | (.191) | (.219) | (.350) |
| STS18 | 15.32 | 14.76 | 15.63 | 15.09 | 14.40 |
| | (.242) | (.204) | (.230) | (.264) | (.421) |
| STS19 | 11.31 | 11.25 | 11.81 | 11.41 | 10.63 |
| | (.223) | (.189) | (.213) | (.244) | (.390) |
| STS20 | 6.64 | 6.75 | 6.90 | 6.76 | 6.42 |
| | (.150) | (.127) | (.143) | (.164) | (.262) |

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Values in parentheses represent standard errors. MR = mother-reared, NR = nursery-reared, WB = wild-born.

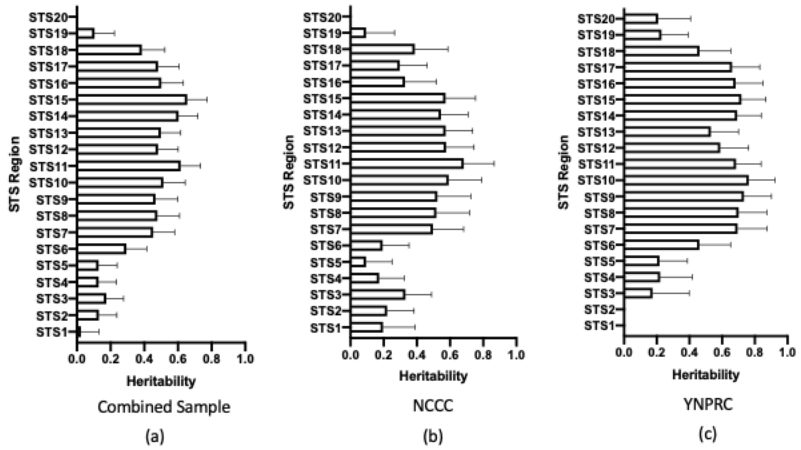


Figure 6: Heritability (+/- s.e.) for each of the 20 regions within the parameterized STS in the chimpanzees for the combined sample (a), NCCC (b) and YNPRC (c) samples.

**Population-Level Asymmetry**

Because LeRoy *et al.* (2015) emphasized the significance of asymmetries in the STAP as a uniquely human feature, we initially tested for population-level asymmetries in the global measures of the STS_Ant as well as its 20 antero-posterior depth measures in our sample. After adjustment to alpha using Bonferroni's correction procedure (adjusted $p = .002$), significant rightward asymmetries were found for STS regions 12 $t(290) = 3.555$, $p < .001$, 13 $t(290) = 4.065$, $p < .001$, 14 $t(290) = 4.183$, $p < .001$, 15 $t(290) = 3.863$, $p < .001$ and 16 $t(290) = 3.310$, $p < .001$ (see Figure 7). Separate one-sample *t*-tests within the NCCC and YNPRC cohorts revealed a consistent pattern of results (see Figure 8). For the NCCC sample, significant rightward asymmetries were found for STS 13 $t(157) = 2.201$, $p < .029$, 14 $t(157) = 2.598$, $p < .010$, 15 $t(157) = 2.873$, $p < .005$ and 16 $t(157) = 2.740$, $p < .007$. For the YNPRC sample, significant rightward asymmetries were found for STS regions 12 $t(128) =$

2.702, $p < .008$, 13 $t(128) = 3.21$, $p < .002$, 14 $t(128) = 3.068$, $p < .003$, and 15 $t(128) = 2.305$, $p < .023$. To test for rearing and sex effects, a MANCOVA was performed with the 20 STS regions serving as the dependent measures. No significant main effects or interactions were found.

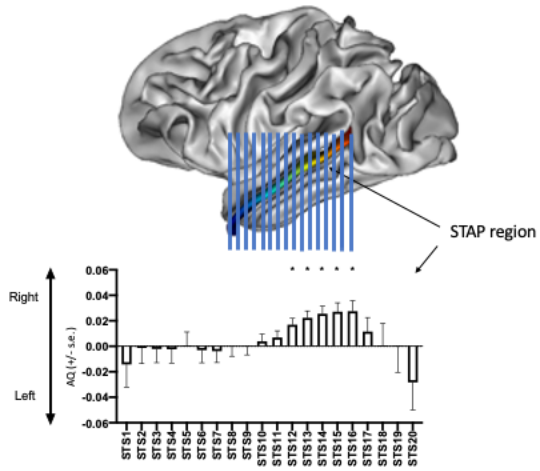


Figure 7: Upper panel: 3D rendering of chimpanzee brain with the STS_Ant region identified and that portion on which significant rightward asymmetries are evident. Lower panel: Mean AQ (+/- s.e.) scores for each of the 20 STS regions for the combined sample.

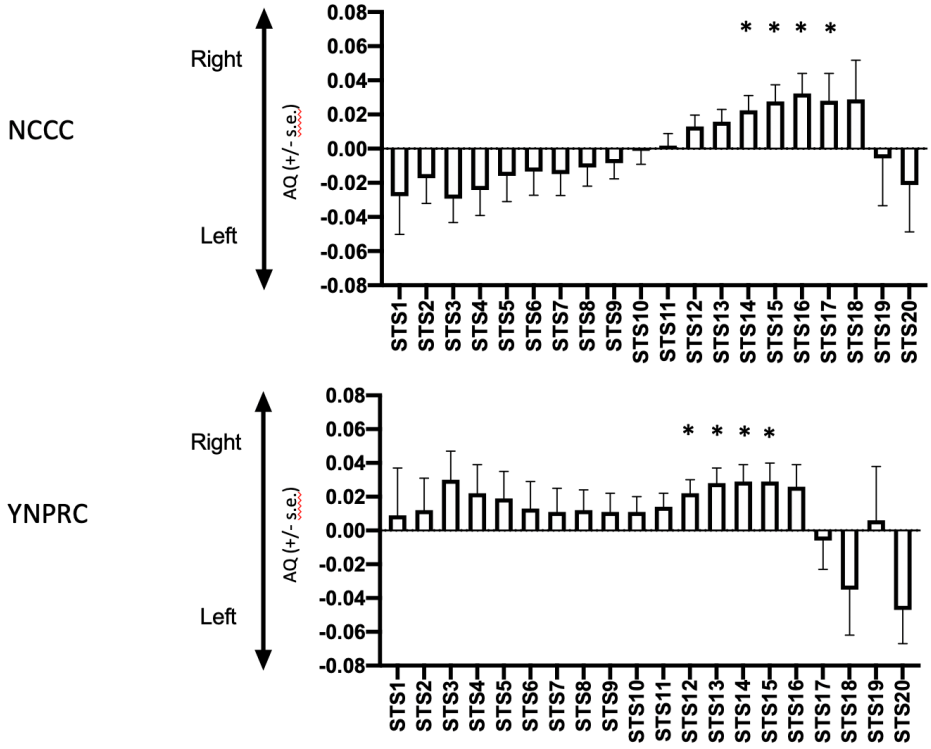


Figure 8: Mean AQ (+/- s.e.) scores for each of the 20 STS regions for the NCCC (upper panel) and YNPRC (lower panel) samples.

### ***KIAA0319*** **SNPs and STS Morphology**

*Global*

RS_P1: To test for the effect of the RS_P1 and RS_63 SNPs on STS_Ant and STS_Post, separate mixed model analyses of co-variance were performed with STS region as the repeated measure and genotype as between-group factors. Sex, rearing and scanner magnet were covariates. Further, because the STS measures were heritable, we also included the genetic relatedness score of each chimpanzee as an additional covariate. The genetic relatedness scores were based on the entire pedigree and reflected how related each chimpanzee subject was to all other individuals in the population. We found a significant main effect for RS_P1 genotype on average mean

depth $F(2, 242)=4.508$, $p = .012$, as well as a two-way interaction between STS region and genotype $F(2, 242)=7.179$, $p < .001$. Post-hoc analysis indicated that, for STS_Ant, average mean depth was significantly greater in chimpanzees with the AA compared to TT, but not the AT genotypes (see Table 5). In contrast, for the STS_Post, average mean depth was significantly higher in chimpanzees with the TT compared to AA, but not the AT genotypes (see Table 5). For the average surface area, as well as the AQ scores for the surface area and mean depth measure, we found no significant main effects or interactions for the RS_P1 genotypes.

Table 5: Descriptive Data for STS_Ant and STS_Post Average and Asymmetry Data for Chimpanzees with Different KIAA0319 Genotypes

| | Genotype | | |
|---|---|---|---|
| RS_P1 | AA | AT | TT |
| *Surface Area* | | | |
| Mean STS_Ant | 1441.56 (22.64) | 1409.56 (21.74) | 1389.87 (32.97) |
| Mean STS_Post | 623.60 (15.34) | 601.06 (14.73) | 635.78 (22.34) |
| AQ STS_Ant | -0.011 (.014) | +0.040 (.014) | +0.013 (.021) |
| AQ STS_Post | -0.024 (.035) | -0.029 (.034) | -0.020 (.052) |
| *Mean Depth* | | | |
| **Mean STS_Ant** | **12.05 (.108)** | **11.65 (.104)** | **11.69 (.158)** |
| **Mean STS_Post** | **7.95 (.122)** | **7.95 (.117)** | **8.72 (.177)** |
| AQ STS_Ant | -0.006 (.009) | +0.010 (.009) | +0.013 (.014) |
| AQ STS_Post | -0.015 (.022) | -0.036 (.021) | -0.045 (.032) |
| RS_63 | AA | AC | CC |
| *Surface Area* | | | |

| | | | |
|---|---|---|---|
| Mean STS_Ant | 1454.34 (25.38) | 1408.65 (21.05) | 1382.29 (30.23) |
| Mean STS_Post | 623.26 (17.52) | 605.38 (14.53) | 602.86 (20.87) |
| AQ STS_Ant | -0.006 (.016) | +0.018 (.013) | +0.027 (.019) |
| AQ STS_Post | +0.001 (.040) | -0.025 (.033) | -0.033 (.047) |

*Mean Depth*

| | | | |
|---|---|---|---|
| Mean STS_Ant | 12.01 (.122) | 11.69 (.101) | 11.70 (.145) |
| Mean STS_Post | 8.12 (.142) | 8.03 (.118) | 8.07 (.169) |
| AQ STS_Ant | +0.024 (.010) | -0.002 (.009) | -0.012 (.012) |
| AQ STS_Post | -0.035 (.025) | -0.020 (.021) | -0.029 (.030) |

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**Bolded** values indicated significant effect of KIAA0319 genotype. Values in parentheses represent standard errors.

RS_63: No significant main effects or interactions were found for this SNP.

*STS_Ant Parameterization*

To test for the effect of the RS_P1 and RS_63 SNPs on STS depth, separate mixed model analyses of co-variance were performed with STS region as the repeated measure and genotype as between-group factors. As above, genetic relatedness, sex, rearing and scanner magnet were covariates. For RS_P1, we found a significant main effect for genotype on average mean depth $F(2, 242)= 7.553$, $p = .021$ (see Figure 9a). Post hoc analysis indicated that chimpanzees with the AA allele had deeper folds than TT, but not AT individuals. No significant difference was found between chimpanzees with the AT and TT alleles. For the AQ values, we similarly found a main effect for genotype $F(2, 239) = 3.234$, $p = .041$ (see Figure 9b). Chimpanzees with the TT and AT genotypes showed significantly greater rightward asymmetries compared to the AA individuals. No significant difference was found in AQ scores for the chimpanzees with the AT and TT alleles. For RS_63 SNP, there were no significant main effects or interactions for either the average or AQ depth scores on the different alleles.

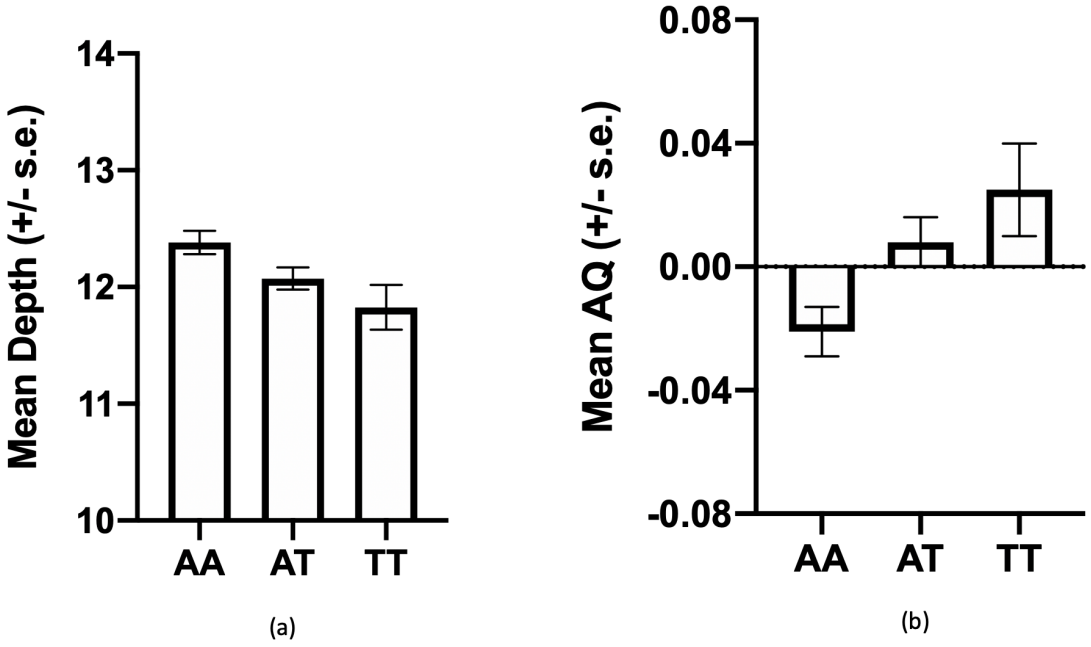


Figure 9: (a) Mean depth (+/- s.e.) and (b) Mean AQ (+/-s.e.) for chimpanzees with different polymorphism in RS_P1 in the KIAA0319 gene.

### *AVPR1A* and STS Morphology

*Global*

A mixed model analysis of variance was performed on the *AVPR1A* gene with STS region as the repeated measure while genotype (DupB+/-, DupB-/) and sex served as between-group factors. Genetic relatedness, rearing history and scanner magnet were covariates. Separate analyses were performed for the average and AQ measures because they reflected different dimensions of STS morphology. There was a significant main effect for *AVP1A* genotype on average surface area $F(1, 232) = 4.407$, $p = .004$, but not average mean depth. DupB-/- chimpanzees had larger values than DupB+/-

apes (see Table 6). Regarding the AQ data, we found a significant main effect for *AVPR1A* genotype on surface area $F(1, 232) = 9.644$, $p < .001$ and mean depth $F(1, 232) = 7.127$, $p = .008$. For both measures, DupB-/- chimpanzees had greater rightward asymmetries than DupB+/- apes (see Figure 10a and 10b).

Table 6: Descriptive Data for STS_Ant and STS_Post Average and Asymmetry Data for Chimpanzees with Different AVPR1A Genotypes

| | Genotype | |
|---|---|---|
| AVPR1A | DupB -/- | DupB +/- |
| *Surface Area* | | |
| **Mean STS_Ant** | **1440.81 (17.99)** | **1377.85 (23.91)** |
| Mean STS_Post | 606.90 (12.97) | 604.45 (17.25) |
| **AQ STS_Ant** | **+0.030 (.012)** | **+0.014 (.015)** |
| **AQ STS_Post** | **-0.007 (.030)** | **-0.102 (.039)** |
| *Mean Depth* | | |
| Mean STS_Ant | 11.90 (.085) | 11.65 (.112) |
| Mean STS_Post | 7.88 (.100) | 8.25 (.133) |
| *AQ STS_Ant* | *+0.009 (.007)* | *+.006 (.010)* |
| *AQ STS_Post* | *-0.011 (.019)* | *-0.085 (.025)* |

**Bolded** values indicated significant effect of AVPR1A genotype. *Italicized* values indicate significant interaction between STS region and AVPR1A genotype. Values in parentheses represent standard errors.

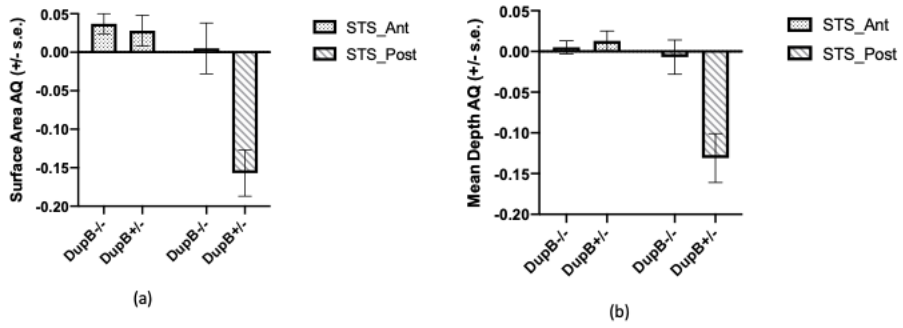


Figure 10: Mean surface area AQ (+/- s.e.) (a) and Mean depth AQ (+/- s.e.) (b) for the STS_Ant and STS_Post measures in chimpanzees with different alleles for the AVPR1A gene.

*STS Parameterization*

A mixed model analysis of variance was performed on the *AVPR1A* gene with STS region as the repeated measure while genotype (DupB+/-, DupB-/) and sex served as between-group factors. Genetic relatedness, rearing history and scanner magnet were covariates. For the average depth measures, a significant main effect for *AVPR1A* genotype was found $F(1, 234)= 7.602$, $p = .006$, as well as a two-way interaction between *AVPR1A* and STS region $F(19, 4446)= 1.747$, $p = .023$. For the *AVPR1A* genotype by STS region interaction, post-hoc analysis indicated that DupB-/- apes had greater mean depth values than DupB+/- individuals for regions 7 through 19 (see Figure 11, left panel). Regarding STS asymmetry, the analysis revealed a significant two-way interaction between *AVPR1A* genotype and STS region $F(19, 4446)= 2.378$, $p < .001$ (Figure 11, right panel). For regions 12, 13, 14 and 18, post-hoc analysis indicated that DupB-/- apes had greater rightward asymmetries than Dup+/-

apes. By contrast, DupB-/- apes had greater leftward asymmetries than Dup+/- apes for region 3.

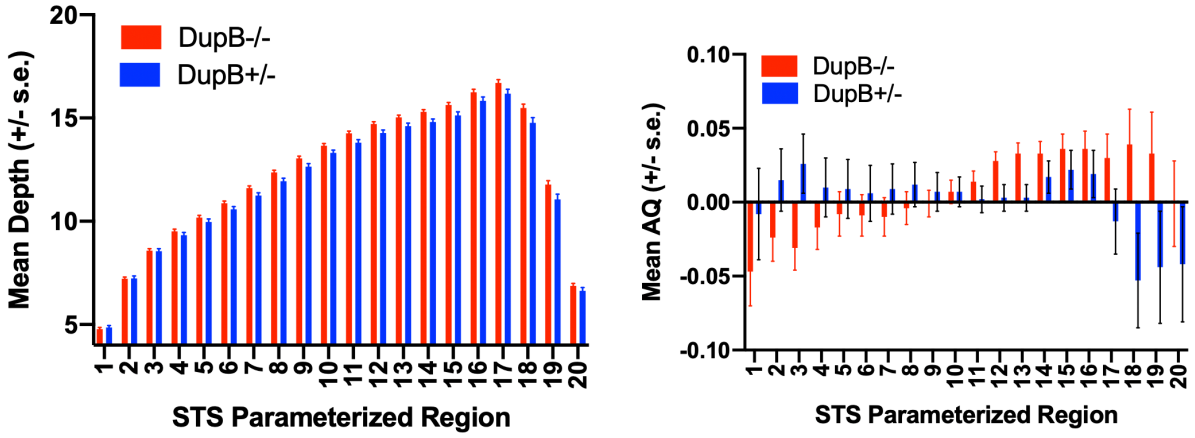


Figure 11: Mean depth (+/- s.e.) (left panel) and Mean AQ (+/-s.e.) (right panel) for chimpanzees with different AVPR1A alleles within the parameterized STS_Ant region.

### *Effect of KIAA0319 & AVPR1A* on Central Sulcus (CS) Surface Area and Depth

In this final analysis, we tested for the influence of the KIAA0319 and AVPR1A SNPs on the surface are and depth of the CS. The details for extraction, labeling and parameterization of the CS were identical to those used for the STS and have been described in detail elsewhere (REFS). The only major difference was in the parameterization direction which was performed along the superior-inferior plane for the CS as opposed to the anterior-posterior plane for the STS. As with the STS, depth of the CS was measured at 100 sulcal length positions in an superior-to-inferior progression along the parameterized sulcal mesh surface. Position 1 was located at the most superior point of CS while position 100 was located at the most inferior point of the CS. As with the STS, to simplify the analyses, within the left and right hemispheres, we averaged every 5 depth measures from point 0 to 100 to create 20 CS regions along the

anterior-posterior plane. We also computed AQ values at each of the 20 CS regions following the formula described above for the STS.

*Global Measures*

In the initial analysis, we tested whether the influence of polymorphisms in the KIAA0319 and AVPR1A genes influenced the average surface area (CS_ASA), average mean depth (CS_AMD), overall surface area AQ (CSSA_AQ) and overall mean depth AQ (CSMD_AQ) values of the CS. To test for the effect of the RS_P1 and RS_63 SNPs on these 4 CS measures, multiple analyses of covariance (MANCOVA) was performed with CS_ASA, CS_AMD, CSSA_AQ and CSMD_AQ as dependent measures while sex and genotype were between-group factors. Rearing, scanner magnet and relatedness coefficients were covariates. No significant main effect or interactions were found for either of the KIAA0319 SNP polymorphisms. With respect to AVPR1A, the MANCOVA revealed a significant main effect for AVPR1A $F(4, 228) = 2.575$, $p = .03$. Subsequent univariate *F*-test revealed a significant effect for the CSMD_AQ values. DupB-/- individuals had greater rightward asymmetry values compared to DupB+/- apes (see Table 7).

Table 7: Mean CS_ASA, CS_AMD, CSSA_AQ and CSMD_AQ Values (+/- s.e.) for Chimpanzee with Different KIAA0319 and AVPR1A Genotypes

| | CS_ASA | CS_AMD | CSSA_AQ | CSDM_AQ |
|---|---|---|---|---|
| *KIAA0319* | | | | |
| RS_P1 | | | | |
| AA | 1544.58 | 9.32 | +0.002 | +0.001 |
| | (19.87) | (.073) | (.014) | (.010) |
| AT | 1493.76 | 9.24 | +0.019 | -0.003 |
| | (19.57) | (.071) | (.013) | (.010) |
| TT | 1544.00 | 9.56 | +0.002 | -0.007 |

| | | | | |
|---|---|---|---|---|
| | (29.09) | (.106) | (.020) | (.014) |
| RS_63 | | | | |
| AA | 1551.75 | 9.35 | +0.014 | -0.015 |
| | (23.29) | (.085) | (.016) | (.011) |
| AC | 1512.40 | 9.23 | +0.019 | +0.003 |
| | (18.47) | (.067) | (.012) | (.009) |
| CC | 1491.11 | 9.26 | -0.008 | +0.004 |
| | (28.59) | (.10) | (.019) | (.014) |
| *AVPR1A* | | | | |
| DupB-/- | 1542.87 | 9.38 | +0.016 | **+0.008** |
| | (17.09) | (.063) | (.014) | **(.008)** |
| DupB+/- | 1498.25 | 9.19 | -0.012 | **-0.018** |
| | (22.41) | (.082) | (.014) | **(.010)** |

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**Bolded** values indicated significant effect of AVPR1A genotype. Values in parentheses represent standard errors.

*CS Parameterization*

For these analyses, the mean depth and AQ values at the 20 CS locations were the repeated measures while sex and genotype were the between group factors. Rearing, scanner and genetic relatedness were the covariates. Regarding KIAA0319, we found no significant main effects or interactions for RS_P1 nor RS-63 on either average depth or the depth AQ values. By contrast, for the AVPR1A genotypes, we found a significant main effects for genotype on the AQ score $F(1, 237) = 4.002$, $p = .047$. DupB-/- apes had significantly greater rightward asymmetry values (*Mean AQ* = .128, s.e. = .075) compared to DupB+/- (*Mean AQ* = -.123, s.e. = .100) chimpanzees.

## Discussion

The results of this study are straightforward. First, the surface area and depth of the STS, particularly in the central portions, were found to be significantly heritable and

these findings were consistent between the NCCC and YNPRC cohorts of chimpanzees. Second, and consistent with the previous report by LeRoy et al. (2015), chimpanzees show a small, but nonetheless significant, population-level rightward asymmetry in the STAP region within the STS. Lastly, one SNP within the *KIAA0319* gene was found to have a significant impact on the depth and asymmetry in the STAP regions within the STS. Similarly, an indel deletion with the arginine vasopressin receptor 1A gene, *AVPR1A*, was found to be associated with both the mean depth and asymmetry within the STS.

Regarding the results on lateralization, the significant rightward asymmetries in the STAP region are of interest for two reasons. First, as we have reported for measures of the planum temporale in chimpanzees (Spocter *et al.* 2020), the findings were largely consistent between the NCCC and YNPRC cohorts of captive chimpanzees suggesting that this bias is repeatable in at least two genetically isolated populations of apes. Second, the STS was quantified slightly differently than the method used by LeRoy et al. (2015). Therefore, it also appears that the small but significant rightward asymmetries in the STAP region are evident independent of the methods used to quantify it. More generally, the overall significant rightward asymmetries in the STAP region clearly challenge the claim that these asymmetries are uniquely human, though admittedly, the magnitude of the bias is decidedly smaller in chimpanzees compared to humans. We also note that significant rightward asymmetries have been reported in the overall surface area of the STS in macaques (Bogart et al. 2012; Suwada 2020), though it is unclear if these effects are attributable to lateralization within the STAP region because these previous studies did not delineate

the STS in the manner that was utilized in this report. Future studies in other species should seek to clarify the nature of STS asymmetry in the context of the location of STAP region.

We also found that the overall surface area, overall mean depth and the mean depth for the majority of STS depth regions were significantly heritable. Further, heritability results were similar between the NCCC and YNPRC samples, suggesting that the contributions of genetic factors to individual variation in STS morphology are consistent and repeatable. The evidence of consistent and repeatable heritability in the STS is not surprising, in some ways, because the STS is a conserved fold that evolved early in primate brain evolution (Zilles et al. 1989; Gilissen 1992; Sawada et al. 2010) and, ontogenetically, emerges during embryonic development in human and nonhuman primates (White et al. 2010; Habas et al. 2012; Meng et al. 2018). More evolutionary conserved sulci have been found to be more strongly heritable in humans and chimpanzees (Gomez-Robles et al. 2015) and our findings on the STS appear to be consistent with these previous results. It is of further note that the heritability in the overall surface area and depth of the STS in our chimpanzee sample are within the range of values reported in humans in a recent paper by Pizzagalli et al. (2020) who similarly used BrainVisa to quantify the STS (and many other sulci).

We failed to find any evidence whatsoever that asymmetries in the STS were significantly heritable, a finding consistent with previous results for sulci within the inferior frontal gyrus (Hopkins, Misiura, et al. 2015) and central sulcus (Hopkins, Coulon, Meguerditchian, Autrey, Davidek, Mahovetz, S.*, et al.* 2017) of chimpanzees. This implies that there are no genes that specifically code for left-right difference in surface

area and depth within the STS and other sulci of the chimpanzee cerebral cortex. Some have hypothesized that one evolutionary shift that occurred in brain organization after the split between chimpanzees and humans from their common ancestor was a genetic basis for the expression of population-level lateralization in structure and function (Warren 1980; Annett 2002; Crow 2009; Corballis et al. 2012). The results reported here are consistent with this view, at least as it pertains to a lack of evidence for a genetic basis for asymmetries in the STS of chimpanzees. However, there are at least two caveats to this conclusion. First, recall that we found that polymorphisms in the RS_P1 SNP of the *KIAA0319* gene and the indel deletion of the *AVPR1A* gene were associated with asymmetries in the overall anterior portion of the STS. Thus, though AQ values were not heritable, at least one SNP in the *KIAA0319* and a deletion in the *AVPR1A* gene were associated with variation in the AQ values which would suggest a genetic basis for STS asymmetry. Second, it is worth noting that the evidence for a genetic basis in determining directional asymmetries in humans is not terribly robust (Armour et al. 2014; Pletikos et al. 2014; Carrion-Castillo et al. 2019; de Kovel and Francks 2019; Schmitz et al. 2019; Carrion-Castillo et al. 2020; Sha et al. 2021) and certainly does not support single or dual allele models of asymmetry that have been postulated in previous genetic models of behavioral and brain asymmetry. In short, the role of genetic factors on the determination of population-level structural and functional asymmetries remains unclear but merits further investigation (Ocklenburg and Gunturkun 2018; Schmitz *et al.* 2019).

In our view, the overall findings of this study support the view of Redcay (2008) with respect to the diverse roles and function that are subserved by the STS, particularly

in the context of the role of the *KIAA0319* and *AVPR1A* genes on behavior. Specifically, Redcay (2008) has suggested that the STS plays a fundamental role in the processing of visual and auditory sequential information and interpreting the meaning or communicative function of these stimuli. This general neural processing principle would apply to a broad range of stimuli and arguably across species but particularly among other closely-related primate species such as chimpanzees. For instance, chimpanzee communication is multimodal and involves the processing and integration of facial, vocal and gestural signals. Within this framework, the computational need to interpret these sequential, multimodal signals might explain why polymorphisms in purported language genes, such as *KIAA0319*, would have anatomical consequences on STS morphology in species that lack full-blown language.

The potential specificity of the role of KIAA0319 and AVPR1A on STS morphology is further supported by the findings (or lack thereof) of the effect of the polymorphisms for each these genes on variation in the CS. Notably, neither of SNPs for the KIAA0319 gene had a significant effect on CS surface area, mean depth or asymmetries in these measures. A significant main effect for AVPR1A was found for the overall CS depth asymmetry values with DupB-/- individuals showing greater rightward asymmetries. This pattern in directional asymmetry is similar to the findings reported for the STS_ant parameterization results; however, the influence of the AVPR1A polymorphisms were specific to the posterior regions and not the entire fold as was the case for the CS. Therefore, interpreting the collective effect of AVPR1A on asymmetries in sulci surface area and depth is not straight forward. Conservatively, when comparing the overall influence of these genes on sulci surface area and depth,

our findings suggest a more region-specific impact of KIAA0319 on STS morphology and asymmetry compared to AVPR1A.

In summary, we found that chimpanzees show a small but significant rightward asymmetry in the STAP region within the STS. Additionally, the surface area and depth of the STS was found to be significantly heritable and these results were repeatable in two genetically isolated populations of chimpanzees. Asymmetries in the surface area and depth of the STS were not found to be significantly heritable. Single nucleotide polymorphisms in two genes, *KIAA0319* and *AVPR1A*, were also found to be associated with individual variation in the depth of the STS. Collectively, the data provide new insights into factors that influence individual variation and evolution of STS morphology in hominids.

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