A new human-specific brain landmark: The depth asymmetry of superior temporal sulcus

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Identifying potentially unique features of the human cerebral cortex is a first step to understanding how evolution has shaped the brain in our species. By analyzing MRI images obtained for 177 humans and 73 chimpanzees, we observed a human-specific asymmetry in the superior temporal sulcus at the heart of the communication regions and which we have named as the Superior Temporal Asymmetrical Pit (STAP). This 45 mm-long segment ventral to Heschl's gyrus is deeper in the right hemisphere than in the left in 95% of typical human subjects, from infanthood till adulthood, and is present irrespective of handedness, language lateralization and gender despite being greater in males than in females. The STAP is also seen in several atypical groups of subjects including situs inversus, Turner syndrome and patients with corpus callosum agenesis. It is partly explained by the larger number of sulcal interruptions in the left than in the right hemisphere. Its early presence in the infants of this study as well as in fetuses and prematures suggests strong genetic influence. Since this asymmetry is barely visible in chimpanzees, we recommend the STAP region during mid-gestation as an important phenotype to investigate asymmetrical variations of gene expression among the primate lineage. This genetic target may provide with important insights regarding evolution of the crucial cognitive abilities sustained by this sulcus in our species, namely communication and social cognition.

Brain | Anatomy | Asymmetry | Human-specific | STS

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Since Geschwind et Levitsky's (1) first attempt to identify a specifically human cortical landmark, the identification of unique features of the human brain that might explain the cognitive success of the human species has remained elusive so that anatomical targets still do not exist to inform the search for genetic mutations contributing to the human cognitive phenotype. Hemispheric asymmetry and language processing being fundamental human traits, the perisylvian language areas have been especially scrutinized for such markers but up until now none has been forthcoming. In particular, the reported asymmetries in the *planum temporale* (1) and the inferior frontal region (2) are not as robust as initially thought either anatomically (3) or functionnally (4), and are also observed, albeit often less marked, in other primates (5). However, we show here that asymmetry of the superior temporal sulcus (STS), at the core of the human communication system, represents a species-specific perisylvian anatomical marker. This finding is consistent with functional brain imaging studies that have emphasized the importance of STS not only for language processing in the left hemisphere but also for social communication in the right hemisphere (6, 7). Notably, in the left hemisphere a hierarchy of areas sensitive to increased levels of acoustical complexity is observed along superior temporal regions, which become specifically linguistic along the STS (8, 9), whereas in the right hemisphere the presence of areas involved in voice and face recognition, gaze perception and theory of mind confirms the importance of right superior temporal cortex in social cognition (7, 10).

As is the case for many cortical sulci, the STS appears one or two weeks earlier in the right hemisphere than in the left during gestation (11-13) but contrary to other sulci for which the left hemisphere catches up, a depth asymmetry in the STS is also reported later in life (14-16), with a reproducible location in the posterior STS, at least in young adults and adolescents (10, 14 and 24 years) (17). The principal objectives of the present study were to firstly accurately define the location and extent of STS asymmetry, secondly to examine whether the STS asymmetry has the same characteristics right through from infanthood, when sulcation is on-going, to adulthood and finally to compare to the same measurements obtained in chimpanzees.

Further to the above, by investigating several factors known to impact on brain asymmetry an assessment was made of how widespread STS asymmetry is across the human species. First, because of the critical role of the STS in verbal and non-verbal human communication, analyses were extended to cohorts with atypical communication profiles, namely adults with right hemispheric dominance for language and autistic children, who have previously been reported to show anatomical and functional ab-

Significance

In the human brain from early in development through to adulthood, the superior temporal sulcus is deeper in the right than the left cerebral hemisphere in the area ventral of Heschl's gyrus. Being irrespective of gender, handedness and language lateralization, as well as present in several pathologies, this asymmetry is widely shared among the human population. Its early appearance in life suggests strong genetic control over this part of the brain. In contrast, it is barely visible in chimpanzees. Thus this asymmetry is probably a key locus to look for variations of gene expression among the primate lineage, which have favored the evolution of crucial cognitive abilities sustained by this sulcus in our species, namely communication and social cognition.

Reserved for Publication Footnotes

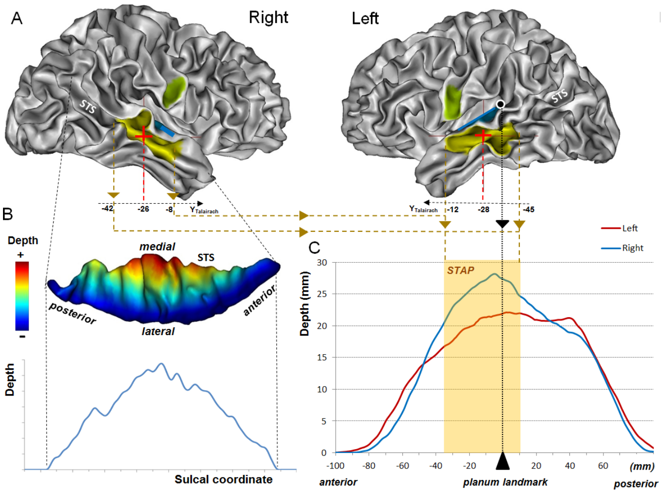

Fig. 1. A. Location of the STAP (*in yellow*) relative to Heschl's gyrus (*in blue*) and the ventral tip of the central sulcus (in *green*) on both left and right inner cortical surfaces of an individual adult brain. The STAP center is shown with a cross. The *black* dot with *white* contour line shows the *planum temporale* landmark. B. top: Sulcal depth as a colour coding of the sulcal mesh (seen from above); bottom: Sulcal depth profile in the right hemisphere of an individual subject. C. Adult sulcal depth profile; STAP anterior and posterior ends as well as the *planum* landmark are drawn in *dotted* lines. The *light orange* overlay illustrates the STAP (deeper on the right), defined as the common asymmetrical segment in the three typical groups (infant, right-handed children and adults).

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normalities in the STS (18). Second, the effects of handedness and gender, which have been shown to modulate asymmetries of both the *planum temporale* and Heschl's gyrus in nearby temporal regions (19, 20) were investigated by including also patients with Turner syndrome (X0). Third, two general mechanisms have been proposed to explain brain asymmetries, namely a left-right reversed pattern of body axis orientation and a competition between homotopic regions across hemispheres through the *corpus callosum* (21), and these were investigated by studying cohorts of subjects with *situs inversus* and patients with *corpus callosum* agenesis (AgCC). In *situs inversus*, the main organs of the body are flipped relative to their usual position (i.e. the heart is on the right side) and the brain is reported to exhibit reversed petalia (22).

Finally, a detailed characterization of STS asymmetry was attempted via the measurement of the shape of individual sulcal profiles and the assessment of how anatomical interruptions of the sulcus might influence overall STS asymmetry. Sulcal interruption, also referred to as a "*pli de passage*", might signal enhanced connectivity between adjacent gyri, and have been used by anatomists to characterize primate brains (23). Since human STS has been reported to contain more *pli de passage* in the left hemisphere than in the right (24), an investigation was made of whether this is the underlying cause of STS asymmetry.

Results

For each subject the brain and sulci were segmented on individual T1 weighted 3D MR images using the Brainvisa Morphologist pipeline (25), normalized to Talairach space and a mesh representing the STS in each cerebral hemisphere constructed. When the sulcus was disconnected, sulcal parts were concatenated, and with regard to potential extension of STS into parietal lobe only the caudal rami within the angular gyrus were considered. Subsequently, a new coordinate system was defined along and across the STS (26) and with an origin referenced to where the *planum temporale* has greatest depth (14). Subsequently, depth profiles were computed along the long axis of the sulcus and aligned across hemispheres and subjects (Fig. 1). A depth asymmetry index ($AI= 2*(R-L)/(R+L)$) was computed e.g, AI=+20% for right (R) depth = +26mm and left (L) depth = +21mm.

Location and Extent of Sulcal Asymmetry in Typical Groups

STS asymmetry was measured in 14 infants, 28 right-handed children and 47 right-handed adults. The right STS was on average deeper than the left in each age group ($ps \leq 0.004$; Table 1). By using permutation tests for 5mm-long intervals along the length of the STS, an asymmetrical sulcal segment was detected in each group. A large region of overlap of these asymmetrical sulcal segments across the three age groups was termed the Superior Temporal Asymmetrical Pit (STAP; Fig. 1 and 2). The STAP is a 45mm-long sulcal segment located at the base of Heschl's gyrus (mid-STS) with its center slightly forward of the *planum* landmark. Specifically, the STAP has the following position within Talairach space: left anterior border: (x=-59, y=-12, z=-9), right anterior border: (54, -8, -14), left center: (-55, -28, -3), right center: (50, -26, -4), left posterior border: (-52, -45, 5), right posterior border: (51, -42, 7). Based on criterion previously developed for studies of the *planum temporale* (27), 96% of subjects had an AI>0 and 74% had an AI>10%. The left-right magnitude difference was around 29%, 19% and 28% in infants, children and adults, respectively, but these potential differences across the lifespan were not significant (One-way ANOVA, $F_{2,86}=1.5$, p=0.2).

Effects of Handedness and Gender

The effect of handedness and gender on STS asymmetry was investigated in 95 adults (Table 1; Fig. 3). The sulcus was found to be asymmetrical, both in male and female left-handers ($ps \leq 0.001$; Table 1). Using permutation statistics, an asymmetrical segment was found in each group, which largely overlapped with the STAP region (≥89%). The STAP was present in 96% of left-handers (AI > 0) with a mean amplitude of 19%. When comparing the asymmetry magnitude between group-specific asymmetrical segments with gender and handedness as between-subject factors, a trend for a gender effect, but no significant handedness effect was observed (Two-way ANOVA, gender: $F_{1,92}=3.3$, p=0.07; handedness: $F_{1,92}<1$; handedness X gender: $F_{1,92}<1$). When the analysis was restricted to the STAP region, the handedness factor remained not significant but the gender effect was strengthened with males having a larger AI than females (Fig. 3B; Two-way ANOVA, gender: $F_{1,92}=8.3$, p=0.001; handedness: $F_{1,92}=1$, p=0.3).

Because of this sexual dimorphism, we analyzed 14 females with Turner syndrome i.e. who have only one X chromosome (Table 1). The STAP was present in every subject and unexpectedly, its magnitude was as large as in typical male adults (Turner AI=+33% ±9%, males: AI=35% ±7%; Welch t-test p=0.9).

Species-specific Asymmetry

In comparison to the complex, twisted shape of human STS, chimpanzee STS is close to linear. No significant STS asymmetry was observed in chimpanzees when either the whole sulcus or the STAP was considered (STS AI=+1% ±9%, p=0.3; STAP AI=+1% ±8%, p=0.2; Table 1). A small asymmetrical segment within the STAP was barely deeper on the right side than the left in 56% of chimpanzees (AI>0, Fig. 2). It was 10mm long in normalized space i.e., 6mm in the native space. However, this right-left difference was smaller than in every human typical group (AI=+4% ±10%, Tukey's test: ps<0.002). Notably, the asymmetrical segment was present in males but not in females (47 females: AI=+1% ±7% p=0.1, 26 males: AI=+7% ±11%, p=0.001); The asymmetry magnitude was not correlated with brain volume (Pearson's p=0.9) despite males' larger brains than females (females: 280cc ±30, males: 304cc ±36, males > females: Welch t-test p<0.01).

Atypical Communication Systems: Right Lateralization for Language and Autism

Table 1. Sulcal depth asymmetry and sulcal interruptions. Sulcal depth asymmetry index (AI) has been assessed in each group using Student's paired t-test. Average values and standard deviations (*in parenthesis*) are expressed as percentages. Group-specific segment relates to the most asymmetrical sulcal part within each group as defined using permutation tests. All human groups with suitable size (≥14) had only one asymmetrical segment except left-handed female adults with left-lateralization for language (only the largest segment is given for this group; see text for details). Range is given in sulcal coordinates. The STAP region is the asymmetrical segment overlap across typical groups (three first rows). The center of the STAP region is given in Talairach space; Percent of subjects having right deeper than left STAP is shown. Finally, the occurrence of sulcal interruptions, also called "*plis de passage*", has been computed across the STAP; left greater than right number of plis de passage tested using Fisher's exact test. Right-Lgg: right lateralization for language; ASD: children with autism spectrum disorders; AgCC: children with agenesis of corpus callosum; SI: Situs inversus adults; *p*<0.05 is shown with "*"; *ns* means "not significant"; *na* means "not applicable" (STAP statistics are not given for the first three groups, which were used to define the STAP, in order to avoid circularity).

			Mean sulcal depth asymmetry			**Group-specific asymmetrical segment**		**STAP region Range (mm): [-35;+10]; Center L:[-55, -28, -3] R: [50, -26, -4]**				***Plis de passage* (frequency)**		
Group	Sub-type	n	AI (%)	*p(R>L)*		Range (mm)	AI (%)	AI (%)	*p(R>L)*		#subj R > L	L (%)	R (%)	*p L>R*
Infants		*14*	+20 (±17)	< 0.001	*	[-35,+10]	+29 (±21)	+29 (±21)	*na*		100%	29	7	*ns*
Right-handed children		*28*	+8 (±15)	0.004	*	[-45,+15]	+18 (±21)	+19 (±25)	*na*		96%	50	7	*
Right-handed adults	All	*47*	+13 (±17)	< 0.001	*	[-45, +10]	+23 (±21)	+28 (±28)	*na*		94%	53	6	*
	Males	*24*	+11 (±18)	0.004	*	[-35, +5]	+25 (±32)	+35 (±33)	*na*		96%	67	13	*
	Females	*23*	+15 (±15)	< 0.001	*	[-45, +20]	+20 (±17)	+20 (±19)	*na*		91%	39	0	*
Left-handed adults	All	*48*	+12 (±13)	< 0.001	*	[-45, +10]	+18 (±16)	+19 (±19)	< 0.001	*	96%	54	17	*
	Males	*14*	+20 (±12)	< 0.001	*	[-35, +30]	+26 (±13)	+29 (±16)	< 0.001	*	100%	79	14	*
	Females	*34*	+8 (±13)	< 0.001	*	[-45, 5]	+16 (±17)	+15 (±18)	< 0.001	*	94%	44	18	*
	Left-Lgg	*17*	+10 (±12)	0.002	*	[-15, +30]	+15 (±18)	+17 (±21)	0.002	*	94%	35	12	*ns*
	Right-Lgg	*17*	+6 (±13)	0.03	*	[-30, 0]	+18 (±18)	+14 (±16)	0.001	*	94%	53	24	*ns*
Other humans	ASD	*15*	+7 (±16)	0.05	*	[-35, 0]	+16 (±10)	+17 (±15)	< 0.001	*	93%	60	27	*ns*
	Turner	*14*	+14 (±13)	0.001	*	[-35;+15]	+32 (±20)	+33 (±21)	< 0.001	*	100%	64	7	*
	AgCC	*5*	+2 (±15)	0.4	*ns*	*na. (small sample size)*		+4 (±8)	0.2	*ns*	80%	20	20	*ns*
	SI	*6*	+16 (±19)	0.05	*	*na. (small sample size)*		+30 (±21)	0.008	*	100%	50	0	*ns*
Chimpanzees	All	*73*	+1 (±9)	0.3	*ns*	[-5, +5]	+4 (±10)	+1 (±8)	0.2	*ns*	56%	10	7	*ns*
	Males	*26*	+2 (±10)	0.2	*ns*	[-5, +5]	+7 (±11)	+1 (±7)	0.2	*ns*	62%	8	4	*ns*
	Females	*47*	0 (±8)	0.4	*ns*	*none*		0 (±9)	0.4	*ns*	53%	11	9	*ns*

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Since the STS is at the heart of the human communication system, an investigation was first made of whether the STAP was affected by language dominance. In particular, two groups of 17 young adults with either left or right cerebral hemisphere dominance for language, matched in age and handedness (28) were studied. Permutation tests revealed asymmetrical segments along the sulcus in each group, which overlapped with the STAP region. In particular, in subjects with right-lateralization for language one 30 mm-long segment fully included in the STAP was recognised, whereas in left-lateralized subjects two segments (one 15mm-long anterior segment with 66% overlap and one 45mm-long posterior segment with 56% overlap) were recognised. When restricted to the STAP, asymmetry was present (AI >0) in 94% of subjects with right-lateralization for language, and was not significantly different between groups (left language dominance: AI=+17% ±21%, right language dominance=+14% ±16; left lat. vs right lat., Welch t test: p=0.6; Fig. 2C and Table 1).

Next 15 autistic boys, matched for age, handedness and developmental quotients with the typical group of right-handed boys, were studied. Rightward asymmetry of the STAP region was similar in autistic children and their matched controls (AI=+17% ±15%, controls AI=+16% ±26%; autistic boys vs controls, Welch t test p=0.9).

General Structural Factors: Hemispheric Asymmetry, Body Axis Orientation and Interhemispheric Interaction

Because sulcal asymmetry may potentially be explained by a more general brain asymmetry, the volume asymmetry of the hemispheres was computed. Right-handed children and adults had on average a slightly bigger right than left hemisphere (ps≤0.01) but not left-handed adults (ps ≥0.7). However, no correlation was found between brain asymmetry and any asymmetrical STS segment in these groups (ps≥0.15). In chimpanzees, the left hemisphere was slightly larger than the right in females (p=0.02) but an asymmetrical STS segment was only found in males.

Six subjects with *situs inversus* (5 men), and for whom a reverse pattern of brain petalia has been shown, were also studied. Despite the small sample size, the right STS was again deeper than the left in the STAP (AI=+30% ±21%, p=0.008), with a similar magnitude as in the right-handed adult male group used as controls (controls: AI=+28% ±28%; *situs inversus* vs. controls, Welch t test: p=0.7).

Finally, five girls with complete or partial agenesis of the *corpus callosum* (AgCC) were studied. The STAP was present (AI >0) in 4 out of the 5 patients, although was smaller than in the right-handed girls used as controls (AgCC: AI=+4% ±8%, p=0.2, controls: AI=+24% ±23%; AgCC vs. controls, Welch t test: p=0.03).

Sulcal Interruptions

Because it has previously been shown in adults that a greater occurrence of sulcal interruptions (*plis de passage)* occurs on the left than on the right STS (24), a *post hoc* analysis was run over all

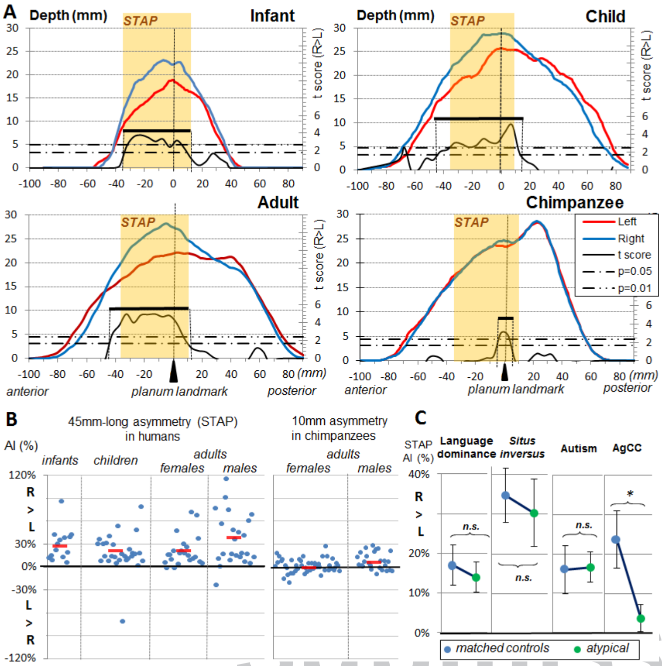

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Fig. 2. A. Left (*red line*) and right (*blue line*) STS depth profiles from the temporal pole to its parietal caudal end. Depth profiles are shown for infants, right-handed children and adults, as well as chimpanzees. The asymmetrical part of the STS is computed for each group by permutation tests over 5mm-long intervals along the sulcus. Two statistical thresholds are given with horizontal dotted lines (p_{corr}=0.05, p_{corr} =0.01). The extent of the asymmetrical segment is given by the range of the Student t variable (in black line) above the lower threshold and is identified by a black bar (see also Table 1). The extent of the common region across the three typical human groups (STAP) is shown in light orange overlay. B. STAP (%) in individuals (typical humans and chimpanzees). Mean group values are shown with a short *red* line. C. STAP in atypical human groups ie, adults with right-lateralization for language, *situs inversus* adults (reversed *petalia*), children with autism spectrum of disorders and children with agenesis of *corpus callosum* (AgCC). “n.s.”: not significant, “*”:p<0.05.

human subjects to assess the effect of these interruptions on depth asymmetry. An interruption can either be full when the sulcus is made of several disconnected parts or partial when a transverse gyrus is buried in the depth of the sulcus (Fig. S1). We computed the occurrence and size of *plis de passage* in each hemisphere in each group over the STAP. By using Fisher’s exact test, more sulcal interruptions were identified in the left than the right hemisphere in typical children and adult groups irrespective of gender or handedness (last column of Table 1). Notably, patients with *corpus callosum* agenesis had few sulcal interruptions on the left (20%). In chimpanzees, there were few sulcal interruptions and the number was not significantly different in the left and right STS.

An assessment was made regarding whether an asymmetry of sulcal interruptions might explain STS depth asymmetry. Accordingly, all human subjects were divided into two groups: one group of 100 subjects having an interruption in one or other hemisphere within the STAP and one group with continuous sulci in both hemispheres (77 subjects). As expected in the former group, the left-right difference in interruption size was correlated with the STAP (R^2=0.45, p<0.001; Fig. S2A). The larger the *plis de passage* in the left hemisphere, the larger the STAP. However, the STAP remained significant in 97% of subjects without *plis de passage* (Fig. S2B). Thus, the STAP is only partly explained by a greater occurrence of interruptions in the left than right cerebral hemispheres.

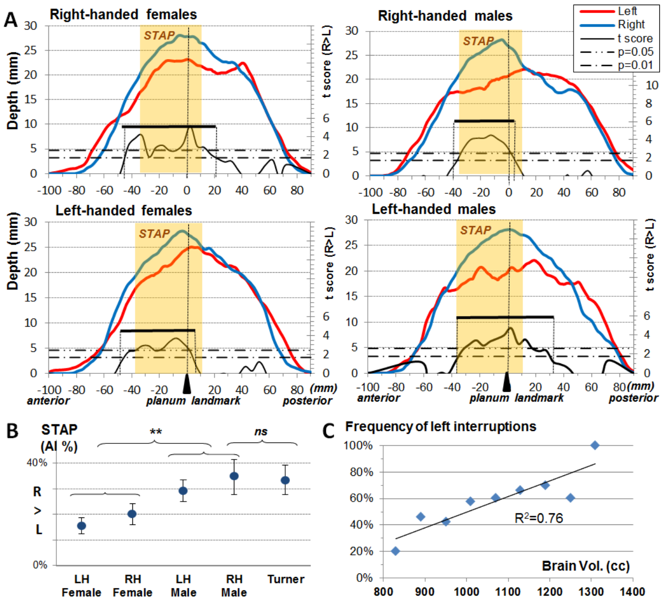

Fig. 3. The STAP in relation to gender and handedness in adults. A. Left (*red line*) and right (*blue line*) STS depth profiles. The extent of the asymmetrical segment is given by the range of the Student t variable (in *black line*) above the lower threshold and is identified by a *black* bar (see also Table 1). The extent of the STAP region is shown in *light orange* overlay. B. STAP statistics (mean and standard error) in healthy right-handers and left-handers and in patients with Turner syndrome. C. Frequency of left sulcal interruptions in relation to brain volume. LH: left-handed; RH: right-handed; “n.s.”: not significant; “**”: p<0.01; “***”: p<0.001.

Finally, since a larger STAP had been observed in males than females, sulcal interruptions were compared across gender in the adult groups. There were more interruptions in males than in females in the left hemisphere (females: 42%; males: 71%; Fisher exact test: p=0.004), whereas no gender effect on AI was found in adults without any interruption (30 females and 9 males; females: AI=+12% ±10%, males: AI=+12% ±5%; Welch t-test p=1). Since this sexual dimorphism might be explained by differences in brain size (brain volume in females: 978cc ±94cc, in males: 1094cc ± 106cc, males > females: Welch t-test p<0.001), we computed the frequency of interruptions as a function of brain size intervals. We found a linear relationship between the number of interruptions and brain size (Fig 3C; R^2=0.76, p=0.001, using 60cc-wide intervals in the range [800cc, 1340cc]).

Discussion

A significant depth asymmetry in STS ventral to the Heschl’s gyrus is identified as a feature widely shared among the human population but scarcely visible in chimpanzees. This so-called STAP region overlaps to a large extent with other asymmetrical areas previously reported in the STS (Fig. 5 in (11), Fig. 6 in (29), Fig. 2 in (16), Fig. 13 in (15), both middle and posterior segments in (17)). The STAP is in many respects as important as the widely studied asymmetry of the *planum temporale.* First, results obtained in infants, children and adults, together with studies at other age periods, e.g. in fetuses (12), toddlers (16) and adolescents (17), suggest that the STAP has its origin during mid-gestation and is present throughout the human life-span. Second, the STAP, like *planum temporale* asymmetry is found to be present irrespective of gender (30), handedness (19) and language lateralization (31). Third, the STAP is present in adults with a similar prevalence (72% with the criterion defined in (27)) as *planum temporale* asymmetry (32). Finally since both *planum temporale* asymmetry and the STAP are preserved in *situs inversus* subjects (22, 33), these temporal asymmetries may have a distinctly different origin than visceral and petalia asymmetries. Despite these common features however, notable differences suggest that the STAP might be a more species-distinctive feature than the *planum.* Atypical asymmetry (i.e. to the other side) is larger for the *planum temporale* (AI>10% in 15% of subjects (32)) than for the STS (AI<-10% in 2% of typical subjects in our study). Most importantly, the small spatial extent and weak magnitude of asymmetry in chimpanzees might constitute a major difference with the *planum temporale,* which asymmetry has been reported to be also present in chimpanzees (5, 34).

The sexual dimorphism of the STS asymmetry found in both chimpanzees and humans encourages the search for a relationship with the sex chromosomes, which have also rapidly diverged between both species (35). Furthermore, XY aneuploidies are often associated with verbal or social cognition deficits and anomalies of the temporal regions (36). As a first approach, we examined females with Turner syndrome (X0). The STAP was similar in this group to typical males. Studies of other types of XY aneuploidies are required to better understand the role of these chromosomes on the STAP but we would like to emphasize that most of the sexual dimorphism observed in humans might be simply related to differences in brain size in the human species. Indeed, we found a close relationship between the STAP, the number of sulcal interruptions and the brain size, consistent with a previous report of an increase of gyrification patterns in larger cortices (37). Males' larger brain size than females increases the number of sulcal interruptions in the left hemisphere and subsequently the STAP magnitude. Thus, a human universal STAP, present in adults with no *pli de passage* or in small brains (infants), might be enhanced in bigger brains (usually males) by a left *pli de passage* (17, 24).

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The relationship between the STAP and sulcal interruptions may shed light on the biological mechanisms responsible for this asymmetry. A recent study has shown that the number of pits, and subsequently interruptions, increases in the left STS between birth and two years of age (38). This increase of sulcal interruptions might correspond to the growth of a transverse gyrus in the depth of the left sulcus. According to models of cortical folding, gyral growth can be explained by variations of cortical thickness and/or constraints of the underlying white matter (39, 40). Several findings suggest a large connectivity in this brain region: a dense local connectivity between the many areas useful for the correct encoding of phonemes (41) intermingles with many long range tracts (42): the arcuate fasciculus, the middle longitudinal fasciculus, the inferior occipito-frontal fasciculus and transcallosal fibers. The latter fibers might be an important factor as both reduced STAP magnitude and fewer *plis de passage* were observed in our agenesis patients. The arcuate fasciculus might also participate since it shares several features with the STAP: it is much larger in humans than in chimps; it expands near the STAP region to a larger extent on the left hemisphere than on the right (43); it is asymmetric since early in life (44) and irrespective of language lateralization (45). These observations suggest that the STAP might be related to a dense and asymmetrical development of the underlying white matter in the superior temporal region.

To understand the functional significance of the STAP, a human distinctive anatomical marker, two groups of subjects with atypical communication systems were investigated, namely autistic children and right language dominant adults. Dysfunction of the STS region has been reported in autism, including decreased gray matter density, hypoperfusion at rest and decreased activations in tasks involving voice and face recognition, gaze perception and social cognition in general (18). However, in the present study no alteration in STS asymmetry was observed in this group. Similarly, the present study has revealed that STS asymmetry is not related to language lateralization. Yet, the STAP region is at a key location along the linguistic ventral pathway mapping sounds to meaning (8, 46, 47). The classical criteria of hemispheric language dominance based on functional lateralization in Broca's area during a word production task (48) may not reflect the functional role of the STAP region closer to the language receptive areas. Indeed independent analysis by Greve et al. (31) of the same database as was investigated in the present study, found no difference in the asymmetry of the *planum temporale* between groups of subjects with opposite hemispheric dominance for language. Apart from communication systems, the STS is involved in several non-communication processing including audio-visual integration and biological motion related to social cognition (7, 10), which should also be investigated. Besides, the search for the STAP function would be greatly facilitated with a more detailed description of the cytoarchitectonic organization in this brain region.

In conclusion, a robust asymmetry in the depth of the STS is present at the base of Heschl's gyrus in the vast majority of human subjects. Because STS asymmetry is barely visible in chimpanzees, and likely absent in macaques (49), the presence of the STAP is interpreted as a recent evolutionary change. Furthermore, the fact that this asymmetry is present in infants, and even fetuses (12) suggests an early genetically driven mechanism and stimulates the search for genes of recent evolution expressed differently in the superior temporal region during mid-gestation (50). Although observed in all human groups, the magnitude of the STAP asymmetry is modulated by gender, may be because of males' larger brains than females. Since children with *corpus callosum* dysgenesis were the less asymmetric human group, further studies should examine how the dense underlying fiber pathways (42) act upon this region. Understanding how evolution differently shaped this cortical area in each hemisphere would most likely highlight a critical feature of one of the several cognitive networks involved in this region (10, 42, 51).

Material & Methods

See SOM for further details on subjects, scanning parameters, brain segmentation as well as sulcal identification, measurement of interruptions and landmarks.

Subjects

Three typical subject groups were defined, namely infants, right-handed children and right-handed adults: 14 healthy full-term infants (mean age = 11.1 ± 3.9 weeks; 9 males, 5 females), whose data have already been published (14); 18 right-handed boys (mean age = 10.6 ± 1.3 years) from the Kennedy Krieger Institute, as part of the Autism Brain Imaging Data Exchange (ABIDE) project (52); 10 right-handed girls (mean age = 9.6 ± 0.4 years) imaged at the Neurospin center (CEA, Gif sur Yvette, France); and 47 young right-handed adults (mean age=21 ± 1.2 years; 23 females, 24 males) imaged at the Neurospin center (CEA, Gif sur Yvette, France).

The following atypical human groups were also studied: 48 young left-handed adults from a study by Van der Haegen et al. (28), consisting of 14 males (mean age = 22 ± 4 years), 17 females with left hemisphere lateralization for language (mean age = 20 ± 1.6 years) and 17 females with right hemisphere lateralization for language (mean age= 20.2 ± 1.5 years); 15 autistic right-handed boys (mean age = 10.0 ± 1.5 years) from the Kennedy Krieger Institute recruited as part of the ABIDE project matched with the typical child group defined above; 5 right-handed girls with prenatal diagnosis of isolated *corpus callosum* agenesis (mean age = 11.4 ± 1.5 years) imaged at the Neurospin center (CEA, Gif sur Yvette, France) (53); 6 *situs inversus* adults from the *Situs Inversus* Project managed by N. Roberts; and 14 patients with Turner syndrome (mean age 24.5 ± 6 years) from a study by Molko et al. (54)

Finally 73 adult chimpanzees (47 females, 26 males; mean age = 23 years ± 12 years) from the Division of Developmental and

Cognitive Neuroscience at the Yerkes National Primate Research Center, Atlanta, Georgia, USA (49) were studied.

Computing and Aligning Sulcal Depth Profiles

A model-driven parameterization (26) was used to define a coordinate system along the length and depth of the sulcus. Once parameterized, local sulcal depth may be computed as the geodesic distance between the most and least superficial sulcal locations at each length coordinate. A depth profile is the curve made of all these local depth measurements along the sulcus. A common landmark was applied to define the origin of the depth profile in all subjects. As in Glasel et al. (14), the landmark was provided by the deepest location of the *planum temporale*, which is located in the posterior part of the insula posterior to the medial tip of Heschl's gyrus. This location has been shown to be relatively stable across subjects (14). In cases where there is a duplication of Heschl's gyrus, the anterior border of the *planum temporale* was set posterior to the most anterior transverse gyrus (27). Finally, the *planum* landmark was projected onto the STS along the dorso-ventral axis in order to set the profile origin. Depth profiles both within and across groups of subjects were aligned according to this common origin.

Location and Extent of Asymmetry using Permutation Tests

As in Glasel et al (14), the asymmetrical part of the STS was identified by applying permutation tests to groups of suitable size (≥14), i.e., infants, normally developing and autistic children, all adult groups but *situs inversus* subjects as well as chimpanzees. Paired t-tests were applied between right and left depth profiles at each sulcal location using a sliding window and the most asymmetrical segment which provided the maximum t_{max} score was determined. Next, 5000 random inversions of right and left profiles across subjects were performed to estimate the random distribution of t-score maximal values. Finally, the measured t_{max} was compared to this distribution to obtain the corrected p-value. This procedure was performed in Talairach space with a 5 mm-wide sliding window and enabled 5mm-long segments with significant asymmetry to be identified along the sulcus. Adjacent segments were concatenated in order to define the extent of asymmetry in each group (Table 1).

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