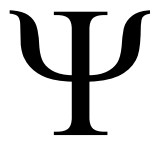




**DET PSYKOLOGISKE FAKULTET**



*Inter-hemispheric asymmetries in STS and AF and the structural relationship between the two*

HOVUDOPPGAVE

*Profesjonsstudiet i psykologi*

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## Forord

Denne hovudoppgåva er basert på data som vart innhenta i forbindelse med ei tidlegare hovudoppgåve (Wigglesworth, 2013). Det vart innhenta fMRI data, vanlege strukturelle MR bilete samt diffusjonsvekta MR bilete meint for DTI-analyse. Sistnemnte har ikkje vorte handsama og analysert før no. Dette arbeidet har eg gjort under god rettleiing av professor Karsten Specht. Eg ynsker å takke for bruk av datamaterialet, hjelp med datahandsaming, statistiske analyser og sjølve skrivearbeidet. Og takk til Trine for gjennomlesing og tilbakemelding.

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### Abstract

Superior temporal sulcus (STS), a grey matter structure, and arcuate fasciculus (AF), a white matter tract, have several characteristics in common. They are structurally asymmetric across brain hemispheres, they seem to hold overlapping cognitive functions, and they are located in close proximity to each other. The purpose of the current study is to explore the structural relationship between STS and AF. Two hypotheses are stated. First, it is hypothesised that the depth asymmetry in STS will correlate negatively with AF volume tract asymmetry, as they are assumed to compete for the same limited space in the brain. The second hypothesis is based on evidence suggesting that STS and AF are involved in language processing. It is hypothesised that a positive correlation between STS asymmetry and AF asymmetry will be found for variables assumed relevant for language processing. To address this, T1-weighted anatomical MR images and diffusion-weighted MR images were acquired from twenty participants. The current findings do not support the hypotheses. Negative correlations were found between left AF volume and left STS depth and between left AF volume and left STS length. In the right hemisphere, positive correlations were found between right AF volume and right STS and between right AF volume and right STS length. In light of this, two new hypotheses are suggested. In the right hemisphere, STS and AF may share social cognitive functionality. In the left hemisphere, a language related compensation mechanism may underlie the correlations.

### Samandrag

Superior temporal sulcus (STS), ein gråsubstans-struktur, og arcuate fasciculus (AF), ein kvitsubstans-fiberbunt, har fleire eigenskapar til felles. Dei er strukturelt asymmetriske på tvers av hjernehemisfærane, dei synest å ha overlappende kognitive funksjonar, og dei ligg i nærleiken av kvarandre. Føremålet med denne studien er å utforske det strukturelle forholdet mellom STS og AF. To hypotesar er føreslått. Først, ein antar at den djupneasymmetrien i STS korrelerer negativt med volumasymmetrien i AF fordi desse tenkast å konkurrere om overlappende områder i hjernen. Den andre hypotesen er basert på forskning som indikerer at både STS og AF er involvert i språkprosessering. Ein antar å finne ein positiv korrelasjon mellom STS-asymmetri og AF-asymmetri for variablar antas å vere relevante for språkprosessering. For å adressere dette vart det innhenta T1-vekta anatomiske MR-bilete og diffusjonsvekta MR-bilete frå tjue deltakarar. Resultatet av studien gir ikkje støtte til hypotesane. Ein finn negative korrelasjonar mellom venstre AF volum og venstre STS djupn og venstre AF volum og STS lengde. I høgre hemisfære finner ein at høgre AF volum korrelerer positive med STS djupn og høgre AF volum korrelerer positivt med høgre STS lengde. I lys av dette, foreslås to nye hypotesar. I høgre hemisfære antas STS og AF å dele sosialkognitiv funksjonalitet. I venstre hemisfære antas ein språkrelatert kompensasjonsmekanisme å ligge til grunn for korrelasjonen.

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Introduction

The brain produces all of the mental phenomena that we experience and the behaviours we execute. This amazing feat is made possible by the 80 billion nerve cells that forms a vast interconnected network in the brain. Examining the brain, we may notice that the tissue on the surface has a pinkish-grey colour (grey matter) while deeper in the brain we find a whitish colour (white matter). Grey matter consists mainly of neuron cell bodies, dendrites and unmyelinated axons, while white matter consist mainly of bundled axons that have myelin sheaths (Brodal, 2016). White matter form highly organised fibre tracts that propagate signals from one area of grey matter to another.

This paper will explore two structures of the brain. The superior temporal sulcus (STS), a furrow in the temporal lobe made of grey matter, and a white matter tract called the arcuate fasciculus (AF) which connects the temporal cortex, including STS, with the frontal cortex.

First, I will review what research has to say about the STS and AF anatomy and function. Then, the rationale for the paper and hypothesis is stated.

**The superior temporal sulcus**

**Anatomy.** STS is one of the longest sulci in the brain extending along the length of the temporal lobe and terminating in the inferior parietal lobe. Looking at the brain from the side, STS lies between the convolutions of superior temporal gyrus (STG) and middle temporal gyrus (as illustrated in Figure 1).



One may also notice that STS is interrupted by several gyri (called pli de passage) along its length. This splits up the structure in several disconnected parts instead of one continuous furrow. These sulcal interruptions are more frequent in the left hemisphere STS of adults (Ochiai et al., 2004).

Leroy et al. (2015) found that, uniquely for humans, STS is on average deeper in the right hemisphere than the left. A particular segment of STS (named the superior temporal asymmetrical pit) which lies at the base of Heschl's gyrus proved to be consistently deeper in the right hemisphere. The asymmetry was detected in almost all humans regardless of age, sex, handedness, functional language lateralisation, situs inversus, autism, Turner syndrome and corpus callosum agenesis. The asymmetry has also been shown in infants (Glasel et al., 2011) and in fetuses (Kasprian et al., 2011). In contrast, this right-deeper-than-left asymmetry is barely detected in chimpanzees or macaques (Leroy et al., 2015).

In addition, STS seem to be asymmetric with regard to length. In a study examining the trajectory of STS in children, adolescents and adults, it was shown that the left STS was consistently longer in the left hemisphere compared to the right, in all age groups (Bonte et al., 2013). The fact that STS is deeper in the right hemisphere but at the same time longer the left hemisphere may explain why STS seems to not be asymmetric with regard to surface area or volume size (Glasel et al., 2011). It may be that the statistical impact of depth and length asymmetry on surface and volume differences cancel each other out.

Using in vivo imaging techniques, Kasprian et al. (2011), managed to pinpoint when this inter-hemispheric asymmetry become visible. They found that in most fetuses the right STS becomes visible earlier than the left STS (23th-gestational week vs the 25th). The right STS was also deeper than the left in 94.2% of the fetus cases. The fact that the asymmetry occurs early suggests that it is genetically driven. In addition, the responsible genes have probably entered the human genome at a relatively recent evolutionary stage because the STS

asymmetry is absent in our primate cousins (Leroy et al., 2015). It is however unclear how this asymmetry relates to cognitive functions and functional lateralisation.

**Function.** STS is a fascinating brain structure as it is implicated in a whole range of cognitive functions. Here, I will briefly summarise the three main domains: speech processing, multisensory integration and social perception and cognition.

**Speech processing.** The role of STS has probably been most explored in relation to language and speech processing. This review on STS functionality will therefore spend more time on this domain.

In several functional imaging studies, STS is bilaterally more activated when subjects listen to speech compared to noise (Jancke, Wustenberg, Scheich, & Heinze, 2002; Rimol, Specht, Weis, Savoy, & Hugdahl, 2005; Zatorre, Jones-Gotman, Evans, & Meyer, 1992) and various non-speech sounds (Belin, 2006; Belin, Zatorre, Lafaille, Ahad, & Pike, 2000; Uppenkamp, Johnsrude, Norris, Marslen-Wilson, & Patterson, 2006).

Before reviewing the evidence further, it is useful to briefly outline the different areas of linguistic research. Firstly, there is research on regions in the brain that are involved in auditory processing in general. These regions become activated when subjects listen to a whole range of different sounds: noise, music, different complex non-speech sounds and speech. Looking at the activation pattern, the regions do not discriminate strongly between different classes of stimuli. Parts of STG, including primary auditory cortex, seem to be sensitive to a range of auditory stimuli, probably acting as a general analyser of spectral and temporal aspects of the auditory stimulus (Hickok & Poeppel, 2007). Secondly, researchers are interested in identifying regions of the brain involved in speech perception. This involves processing of sub-lexical components like perception of phonemes, vowels, consonants and consonant-vowels syllables (CV). These are the building blocks of words, hence sub-lexical. Accurate perception of these components is necessary, but not sufficient, for speech



recognition/comprehension to be successful. Speech recognition may be called a third research area. In order for speech to be understood, the brain regions involved in speech perception must project to brain areas downstream that transform these acoustic signals to representations that connect with the mental lexicon. In other words the brain must map speech sound to representations of meaning (Hickok & Poeppel, 2007). All the areas of research mentioned above: general spectral and temporal, speech perception and speech comprehension, can be conceptualised as the ventral stream of speech processing (Hickok & Poeppel, 2007). The ventral stream is thus a stepwise bottom-up process starting with sound-to-phoneme-to-word-to-sentence-to-meaning (Specht, 2013, 2014) . A fourth research area can be said to concern speech production processes (dorsal stream). This involves brain regions that translate speech code to the motor system allowing speech to be articulated effortlessly.

Having outlined the computational tasks that the brain must implement in order for speech to function as we know it, what is then the role of STS? Hickok and Poeppel (2007) suggested that the middle to posterior regions of STS are bilaterally involved in early stages of speech processing, by representing and processing phonological aspects of speech (e.g. vowels and consonants). Various imaging studies support this claim. Binder et al. (2000) found that STS was bilaterally more active when subjects listen to words, pseudowords and reversed speech compared to white noise and frequency-modulated (FM) tones. The fact that STS was more active for all the speech conditions, not just when listening to real words, suggests that STS is sensitive to acoustic/phonological aspects of speech, not higher order linguistic factors. The same conclusion can be drawn from a study by Belin et al. (2000) who found that STS gets more activated in both hemispheres when subjects listen to speech or non-speech sounds like laughter, sighs and coughs compared to non-vocal sounds from various environmental sources. The result led the authors to suggest that STS contain face-

selective areas analogous to the fusiform face area in the visual system (Kanwisher, McDermott, & Chun, 1997).

Using a different paradigm than Binder et al. (2000) and Belin et al. (2000), Specht, Osnes, and Hugdahl (2009) reported similar results. They used a sound-morphing paradigm (Specht, Rimol, Reul, & Hugdahl, 2005) where subjects are exposed to a white noise sound that gradually transforms into either speech sound (CV syllables) or sounds from musical instrument. In this way, subjects are progressively exposed to the experimental or control condition. The researchers found that the left middle STS became increasingly active as white noise turned into speech sounds, but not for music. This result is in line with previous findings. The same activation pattern was not observed in the right STS (Specht et al., 2009). It seems that some studies implicate both left and right STS in phonological processing while others find that only the left STS is sensitive to these aspects. For instance, Liebenthal, Binder, Spitzer, Possing, and Medler (2005) found that left middle and anterior STS is more activated during an auditory discrimination task involving CV syllables compared to non-phonetic sound patterns of similar complexity (Liebenthal et al., 2005). Such findings led Hickok and Poeppel (2007) to suggest in their dual process model of speech processing that STS, while believed to be bilaterally involved, might have a mild leftward bias with regard to phonological processing. In trying to account for observed inter-hemispheric differences in functional imaging studies, it has been suggested that the hemispheres differ in their computational operations. Zatorre, Belin, and Penhune (2002) proposed that the left hemisphere is selective to temporal variations apt for analysing aspects of acoustic signals that change rapidly and the right hemisphere is sensitive to spectral variations, i.e. analysing the distribution of frequencies that make up the sound. Others have suggested that the hemispheres differ in the number of samples taken from the acoustic signal per second (i.e. sampling rate). Specifically, the left hemisphere samples the signal more rapidly (25-50Hz)

whereas the right hemisphere favours slower-rate sampling (4-8 Hz) (Poeppel, 2003). At this point, it is unclear what the true computational differences are.

As discussed above, a part of STS seems to be involved in phonological processing of speech. It is worth noting that this places that specific region, according to the dual stream model (Hickok & Poeppel, 2007), upstream to subsequent ventral and dorsal processing. Phonological elements are analysed, and then the processing bifurcates into the ventral stream responsible for speech comprehension, which is located bilaterally in the temporal lobes, and into the dorsal stream for speech production, located mainly in the left hemisphere, specifically in the parietal-temporal junction and frontal lobe.

As a matter of fact, other parts of STS have been implicated in such upstream ventral stream processes. For instance, in one study subjects listened to sentences with different degree of semantic ambiguity-clarity, and it was reported that high-ambiguity sentences produced greater activity in posterior STS (as well as other regions) compared to low-ambiguity sentences (Rodd, Davis, & Johnsrude, 2005). Presumably the high-ambiguity sentences activate brain regions associated with language comprehension to a greater degree than sentences with low ambiguity. This fits well with a study which examined 101 patients with lesions to the left hemisphere (Bates et al., 2003). They found an association between language comprehension deficits and left posterior lobe damage, including STS, although the damage was most notably in middle temporal gyrus. Other studies have also implicated the left anterior STS in semantic processing of spoken words (Spitsyna, Warren, Scott, Turkheimer, & Wise, 2006). In a recent review of neuroimaging studies on ventral stream processes, Specht (2013) concluded that there seems to exist a structural-functional relationship within the superior temporal lobe along the posterior-anterior axis, where increasingly anterior locations are associated with increasingly complex ventral stream processes.

Consistent with this, it has been shown that when examining patterns of coactivation across studies, the anterior STS tend to coactivate more with other ventral stream structures while the posterior STS more often activate together with dorsal stream structures (Erickson, Rauschecker, & Turkeltaub, 2016). Taken together, the evidence suggests that other parts of STS may be involved in linguistic processes beyond phonological processing.

In fact, some research even indicates that the left and right STS differ with regard to the linguistic level of processing. For instance, left STS may be more involved in phonological processing, while right STS may be more involved in speaker identity (Belin & Zatorre, 2003) and emotional prosody (Beaucousin et al., 2007).

Despite indications of functional language lateralisation of STS, it is unclear how this relates to STS structural asymmetry. Leroy et al. (2015), for instance, found no association between STS depth asymmetry and functional language lateralisation. On the other hand, STS anatomical abnormalities, like reduced grey matter concentration, have been observed in people with autism (Saitovitch et al., 2012) – a population characterised by language and communication dysfunction.

***Multisensory integration.*** STS has also been implicated in integration of visual and auditory information. At the level of neurons, the phenomena of multisensory integration may arise when individual neurons respond more greatly to the combined presentation of auditory and visual stimuli than to stimuli presented separately (Gazzaniga, Ivry, & Mangun, 2009). Anatomically, STS seems to be suited for this purpose as it has been shown that STS in macaques receives input from auditory cortex and extrastriate visual cortex (Seltzer et al., 1996; Seltzer & Pandya, 1978). In a study by Hikosaka, Iwai, Saito, and Tanaka (1988), electrodes were placed on macaque monkey's brains in areas corresponding to STS and found that 50% of neurons were unimodal and 20% bimodal. Using functional imaging, it has been shown that STS is involved in multisensory integration for a range of stimuli (Beauchamp,

2005) although the integration of auditory and visual information is the most researched. For instance, one fMRI study compared brain activation under three conditions: presentation of speech segments (extracts from Orwell's 1984) together with a video recording of the speaker, presentation of speech segments together with a mismatching video recording (different story mouthed) and a baseline condition (Calvert, Campbell, & Brammer, 2000). The sum activation of each stimuli was presented separately. They found that activation in the left posterior STS was greater during matching stimuli compared to baseline (supra-additive) and lower during mismatched stimuli compared to baseline (sub-additive). This suggests that a portion of STS is involved in the binding of auditory and visual information.

Nath and Beauchamp (2011) used a different paradigm where they manipulated the reliability or quality of the speech sounds and video recording. In one condition subjects listen to less reliable (noisy) speech along with reliable video, and in one condition subjects listen to reliable speech with unreliable (noisy) video. Ideally, reliable sensory information should be given more weight than unreliable information. They found increased functional connectivity between STS and auditory cortex when the auditory stimulus was more reliable (less noisy) and increased connectivity between STS and visual cortex when the visual stimulus was more reliable. The authors conclude that these functional connectivity patterns may be a neural substrate for noisy speech perception.

STS has also been implicated in the McGurk effect, an illusion which occurs when speech sound does not match the lips producing it, e.g. one may perceive /da/ when the speech sound /ba/ is presented together with lip movements of /ga/. Nath and Beauchamp (2012) found that greater activity in the left STS predicted higher likelihood to experience the McGurk illusion. Conversely, lower activity was associated with less likelihood to perceive the illusion. Consistent with this, the McGurk effect can be temporarily disrupted by inducing "virtual lesions" in STS with transcranial magnetic stimulation methodology (Beauchamp,

Nath, & Pasalar, 2010). Taken together, STS seem to be an important neural correlate of the McGurk effect.

Lastly, there are a few studies that have examined other sensory modalities besides visual and auditory perception. Beauchamp, Yasar, Frye, and Ro (2008) reported that posterior STS responded to somatosensory/tactile stimuli, as well as auditory and visual stimuli, when presented separately. Interestingly, they also found that STS showed a supra-additive response to simultaneous auditory-tactile stimulation compared to summed separate presentations. This indicate that parts of STS may be involved in multisensory processes more generally.

***Social perception and cognition.*** Yet another area STS has been implicated in is mental processes related to the social domain. STS has been shown to be involved in social perception, i.e. the process whereby we evaluate the intensions and psychological dispositions of others, using biological motion cues such as movement of eyes, mouth, hands and body (Allison, Puce, & McCarthy, 2000). One fMRI study found that STS activation was greater when subjects observed biological motion (walking human, walking robot) compared to complex meaningful motion (grandfather clock) and complex nonmeaningful motion (mechanical figure) (Pelphrey, Mitchell, et al., 2003). Interestingly, a region in the extrastriate cortex known to be involved in motion perception (V5/MT), did not differentiate between biological and nonbiological motion as STS does. Furthermore, there is evidence that STS is not simply involved in tracking biological motion, but rather coding the intention of the other person based on biological motion cues and other contextual information. In an fMRI study by Pelphrey, Singerman, Allison, and McCarthy (2003) subjects observed an animated character shift eye gaze either toward (congruent) or away from (incongruent) a checkerboard. This is based on an idea that one can infer mentalistic information from observing whether someone looks toward an environmental cue or away from it. They found

that posterior STS responded more strongly to the incongruent condition. Similarly, there has been shown greater activation in STS when an animated character shifts eye gaze away from the subject compared to eye contact (Pelphrey, Viola, & McCarthy, 2004). It may be noted that in all the studies by Pelphrey and his colleagues mentioned above, the effect is most evident in STS in the right hemisphere.

As mentioned STS also seems to be involved in the perception of faces (Allison et al., 2000). According to one model by Haxby, Hoffman, and Gobbini (2000), brain regions responsible for face perception are distributed in the brain. Posterior STS forms the core system together with fusiform face area and inferior occipital gyrus, each with different computational tasks. It is proposed that STS analyses dynamic aspects of faces like eye gaze and lip movements (Haxby et al., 2000).

STS is also implicated in imitation processes. Imitation of other's behaviour involves the mirror neuron system of which posterior STS is part of (Iacoboni & Dapretto, 2006). In this network, posterior STS provide a higher-order visual representation of the other person's behaviour. Then information from STS feed forwards to other brain regions involved in motoric processing and the goal of the imitated action. According to the model, STS also receives feedback signals from the other brain regions which allows for a comparison between the observed behaviour and motor plan. In one fMRI study, participants were in the following conditions: passive observation of pantomimed hand movements (e.g. stroking a cat), imitation of observed behaviour, execution of behaviour on word cue instruction and execution of self-selected behaviour (Molenberghs, Brander, Mattingley, & Cunnington, 2010). Consistent with the mirror neuron system described by Iacoboni and Dapretto (2006), STS, as well as other regions, were more active in all conditions. STS was also the only region displaying greater activation during imitation of behaviour condition. It is suggested

that STS is involved in representing the degree of agreement between the observed behaviour and imitated behaviour (Iacoboni & Dapretto, 2006)

Furthermore, posterior STS has been implicated in theory of mind processes. Theory of mind is the cognitive ability to attribute mental states to self and others (Premack & Woodruff, 1978). In order to stimulate theory of mind processing in the brain, a false belief task might be used. In one study, for example, the subjects listened to a story of a boy ripping newspaper into strips as preparation for a papier-mâché project. The boy then leaves the house, and as the mother comes home and sees the paper strips, she throws them away (Saxe & Kanwisher, 2003). To make sense of the story, the subjects must infer that the mother's behaviour emanates from a false belief (Premack & Woodruff, 1978).

In a review of functional imaging studies on theory of mind tasks, STS was, along with a few other brain regions, consistently activated across several studies on theory of mind (Gallagher & Frith, 2003).

In a recent meta-analysis, Yang, Rosenblau, Keifer, and Pelphrey (2015) examined the role of STS in three domains mentioned briefly above: social perception, action observation and theory of mind. First, they identified multiple neuroimaging studies on each domain and then did a conjunction analysis (statistical method for estimating whether two tasks activate the same region of the brain) and found that only right side posterior STS was active across all domains. Thus, right posterior STS seems to be fundamentally important across these domains, possibly functioning as a network hub, with reciprocal connections to brain networks involved in different social domains.

Another line of evidence comes from research on autism spectrum disorders and STS. Autistic individuals have difficulties that overlap with many of the social functions implicated in studies on STS, for instance eye gaze, joint attention, theory of mind processes (Baron-Cohen, 1997). As it turns out, several studies find anatomical and functional abnormalities in



STS in persons with autism spectrum disorders (ASD) (Saitovitch et al., 2012; Zilbovicius et al., 2006). With regard to anatomical abnormalities, studies comparing autistic children with controls have found decreased grey matter concentration and volume bilaterally in STS (Boddaert et al., 2004; McAlonan et al., 2005). There is also evidence for reduced regional cerebral blood flow (hypoperfusion) to STS at rest in children with autism (Saitovitch et al., 2012). Thus, the same regions which display anatomical abnormalities also seem to demonstrate hypoperfusion (Boddaert et al., 2004).

In addition, there are also studies that specifically implicates right STS abnormalities in autism. In a study comparing high-functioning autistic adults with controls, a correlation was found between cortical thinning of right STS and severity of autism symptoms (Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2006). Similar results have been found in a population without an ASD diagnosis. Wallace et al. (2012) assessed degree of autistic traits in typically developing children and adolescents, and found that higher autistic traits were associated with thinner cortex in right STS. One study using a similar approach, found that increasing autistic traits were positively correlated with decreased white matter volume in right posterior STS.

STS abnormalities is also observed during social cognitive tasks. Using the same eye gaze paradigm as described above, Pelphrey, Morris, and McCarthy (2005) found that whereas the control group expectedly demonstrated greater right STS activity during incongruent trials, the STS of autistic individuals did not differentiate between the congruent and incongruent trials. That is, STS activity was not modulated by the interaction of eye gaze shift and contextual cues. Such evidence has led some researchers to propose that STS is a crucial brain region for understanding the biological underpinnings of autism spectrum disorders (Saitovitch et al., 2012).

As discussed above, STS is involved in multiple functions: speech processing, multisensory integration and social cognitive processes. There has been disagreements however, regarding how to conceptualise this multifunctionality. Some have argued that STS functionality is predominantly domain-general (Hein & Knight, 2008) others that it is more domain-specific (Deen, Koldewyn, Kanwisher, & Saxe, 2015).

***Domain-general vs domain-specificity.*** A domain general view of STS holds that while STS is involved in several functions, these are uniformly distributed across STS and cannot be localised as independent units of function or modules. Hein and Knight (2008) have argued for this view. They went through previous fMRI-studies on STS, assessing the location of peak activity during different tasks: motion processing, speech processing, theory of mind, audiovisual integration and face processing. They found that STS seems to be functionally differentiated in an anterior part, primarily active during speech processing, and a posterior part, which activates during the remaining functions mentioned above. They conclude that on the whole, STS is not functionally subdivided into different brain modules. Instead, they argue that the different functions seen in STS depend on which other brain regions that are activated simultaneously. As described above, STS is indeed part of different brain networks depending on which cognitive task is performed. For instance, STS seem to coactivate with a mirror neuron system during imitation tasks (Iacoboni & Dapretto, 2006), while during face perception tasks it seem to coactive with the core system described by Haxby et al. (2000). STS may in other words seem functionally specialised for narrow cognitive tasks when examined through individual studies. However, when examining several imagery studies that implicate STS, Hein and Knight (2008) find little evidence for functional subdivision within STS.

A domain specific view, on the other hand, holds that STS is actually comprised of different modules operating on certain kinds of inputs which STS processes in a certain kind

of way. The modules are assumed to be organised spatially across STS. In an fMRI study by Deen et al. (2015), the STS response of 20 participants were measured during processing of language, faces, voices, biological motion and theory of mind-tasks. They found that each task resulted in different peak locations in the STS along the anterior-posterior-direction. Deen et al. (2015) found that the most anterior part of STS peaked during the language task, consistent with Hein and Knight (2008). Then during the voice task, face task and biological motion, STS had a progressively more posterior peak activation with finally theory of mind-tasks with peak activation at the most posterior location. This applied to STS in both hemispheres. They also measured the extent of activation for each task and found some overlap in activation between different tasks. They found that theory of mind and language both activated most of STS, especially in the left hemisphere. Thus, their respective activation pattern overlapped greatly in STS. Other tasks also produced activation overlap, for instance between faces and voices. The authors conclude that STS both contains areas that are sensitive to different tasks in line with the domain specific view, as well as areas that are responsive to multiple tasks in keeping with the domain general view. The different conclusions drawn in these studies might be due to different methodology. Hein and Knight (2008) approach the question of functional subdivision with an examination of imaging studies which report average group data. Thus, when individual differences are aggregated and attenuated it may overestimate the degree of overlap (Beauchamp, 2015). Deen et al. (2015) on the other hand used a within-subjects methodology that preserves individual variability to a greater degree and is therefore more suitable for revealing functional subdivision (Beauchamp, 2015; Specht, 2013).

### **The arcuate fasciculus**

**Anatomy.** Arcuate fasciculus is a white matter tract which connects the temporal lobe with the frontal lobe through a dorsal projection that arches around the lateral sulcus.

Traditionally, AF is thought to connect Wernicke's area with Broca's area (Catani & Thiebaut de Schotten, 2012), although more recent examinations have shown that its fibres are often more diffuse in its projections, connecting parts of the frontal, parietal and temporal lobes (Dick & Tremblay, 2012). In addition, there is also a considerable amount of variation between individuals (Catani et al., 2007). To stress this inexactness, some researchers prefer the term of "territory" over "area" when describing AF projections (Catani & Thiebaut de Schotten, 2012).

Much of the recent research on AF has been done using diffusion tensor imaging (DTI) methodology. This method allows researchers to noninvasively reconstruct and identify white matter structures and assess their macrostructural properties such as tract volume and microstructural properties such as fractional anisotropy (FA). FA is often interpreted as an indirect measure of white matter integrity and may be influenced by aspects such as axon count and density, degree of myelination and relative membrane permeability (Curran, Emsell, & Leemans, 2016).

Catani, Jones, and ffytche (2005) examined AF using diffusion tensor imaging (DTI) and identified three segments of AF (as illustrated in Figure 2).

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INSERT FIGURE 2 HERE  
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A long segment, roughly corresponding to the traditional notion of AF, connects Wernicke's territory with Broca's territory. An anterior segment connects Broca's territory with Geschwind's territory and a posterior segment connects Wernicke's with Geschwind's territory. It can be noted that there is no absolute consensus on how to conceptualise AF and

its segments, as there exist other models of AF (Dick & Tremblay, 2012; Glasser & Rilling, 2008).

It is well documented that AF is asymmetric across the hemispheres (Catani et al., 2007; Powell et al., 2006; Propper et al., 2010; Thiebaut de Schotten et al., 2011; Vernooij et al., 2007). Catani et al. (2007) examined this asymmetry in 50 right-handed adult subjects and reported individual differences as well as gender differences. 62.5% of subjects showed an extreme leftward asymmetry, meaning that AF in the right hemisphere is barely detectable. 20% showed moderate leftward asymmetry and 17.5 % demonstrated a bilateral/symmetrical pattern. Vernooij et al. (2007) reported similar results in a sample of left-handed subjects. Handedness may nevertheless moderate the leftward volume asymmetry typically reported in studies. In a study by Propper et al. (2010), it was found that consistently-handed individuals, either left or right, have relatively larger AF volumes in the left hemisphere, whereas individuals with inconsistent handedness seem to have more symmetrical AF volumes.

Catani et al. (2007) have also reported gender differences where men are more likely to show a strong left lateralisation compared to women. 85% of men displayed extreme left lateralisation compared to 40% of women. Only 5% men displayed a symmetrical pattern while 30% of women did.

There is also evidence suggesting that there are systematic inter-hemispheric differences in AF with regard to the average length of streamlines. One study found that the average length was relatively greater in the left AF tract (Propper et al., 2010).

Furthermore, it seems that the asymmetric tendency of AF is not uniform across its respective segments (Thiebaut de Schotten et al., 2011). Specially, the anterior segment has a significantly greater volume in the right hemisphere while the long segments has a significantly greater volume in the left hemisphere. This means that in some individuals, it may not be possible to reconstruct the long segment in the right hemisphere (Catani et al.,

2007). The posterior segment however seems to be symmetrical (Thiebaut de Schotten et al., 2011).

In addition to differences in volume and average streamline length, tract measures such as fractional anisotropy, streamline count, and fibre density indicate that there are systematic asymmetries in the microstructure of AF (Catani & Thiebaut de Schotten, 2012). In adults, several studies have reported greater FA in the left hemisphere (Catani et al., 2007; James et al., 2015; Lebel & Beaulieu, 2009; Ocklenburg, Hugdahl, & Westerhausen, 2013; Powell et al., 2006). Thiebaut de Schotten et al. (2011) reported greater FA in the right anterior segment of AF compared to the left anterior, and also a non-significant leftward FA asymmetry in the long segment. FA is commonly interpreted as an indirect measure of tract integrity (Curran et al., 2016). For instance, it may indicate the tract is densely packed with axons and has fewer crossing fibres (Dubois et al., 2016).

There has also been reported greater relative fibre density in the left AF compared to the right AF (Nucifora, Verma, Melhem, Gur, & Gur, 2005; Vernooij et al., 2007), as well as greater tract length in the left AF (Propper et al., 2010).

As described above, several studies report inter-hemispheric anatomical differences in AF in adults. There is also evidence that these observed differences emerge relatively early in development. One study successfully reconstructed AF in both hemispheres in the 30th-gestational week though it was small, sparse and with few branches (Song et al., 2015). With a sample of 12 children ranging from ages 30th-gestational week to 3 years old, the study was not able to report statically significant inter-hemispheric asymmetry in AF with regard to tract volume, FA and the apparent diffusion coefficient. The non-significant result might be due to small sample size and other methodological issues (Dubois et al., 2016). In samples with infants in their first post-natal months, several studies have reported structural asymmetries in AF with regard to volume and FA (Dubois et al., 2009; Dubois et al., 2016; Liu et al., 2010).

The same asymmetric tendency is also observed in children, adolescents and young adults (Catani & Thiebaut de Schotten, 2012; Lebel & Beaulieu, 2009). In short, the asymmetry observed seem to arise early and persist throughout adulthood. Next, arcuate functionality will be considered.

**Function.** Most of the research on the functional significance of AF has focused on its involvement in language processes (Dick & Tremblay, 2012). This is not surprising considering that it is surrounded by regions known to be involved in language processing. In fact, neuroscientists have had an interest in AF for over a hundred years for this reason (Dick & Tremblay, 2012).

There are several studies demonstrating correlations between language lateralisation and AF asymmetry. Powell et al. (2006) examined the relationship between AF asymmetry and lateralised brain activation patterns in a right-handed sample. Subjects underwent three fMRI tasks: a verbal fluency task, verb generation task, and language comprehension task, as well as a DTI tractography procedure. They reported statistically significant correlations between mean FA and lateralised activation pattern during verb generation as well as reading comprehension. In other words, as FA increased relatively in the left AF, language areas like the inferior frontal cortex and superior temporal cortex became relatively more active in the left hemisphere compared to the right during language tasks. Other studies have reported similar results (James et al., 2015; Ocklenburg et al., 2013). Converging results have also been obtained in a study which used a dichotic listening task to assess language dominance instead of functional imaging data (Ocklenburg, Schlaffke, Hugdahl, & Westerhausen, 2014).

In a study with both right- and left-handed subjects (7 and 13 respectively), no correlation was found between language lateralisation and asymmetric relative fibre density in AF (Vernooij et al., 2007). Interestingly, a correlation was found when data from right-handed subjects was considered exclusively, suggesting that handedness might moderate the

relationship between language lateralisation and AF asymmetry. It is well documented that handedness correlates with language lateralisation, with only 4% of strong right-handed individuals showing right-hemisphere language dominance compared to 27% of strong left-handed individuals (Knecht et al., 2000). Nevertheless, Propper et al. (2010) found in a left-handed sample a positive correlation between language lateralisation (measured during an antonym generation task) and AF volume and length asymmetries. This conflicts somewhat with the study by Vernooij et al. (2007), and further research will be needed to clarify the effect of handedness.

Correlations between structural AF asymmetries and language lateralisation have also been shown in preadolescent children (Sreedharan, Menon, James, Kesavadas, & Thomas, 2015) and in patient samples (Matsumoto et al., 2008).

Another line of evidence that may shed evidence on the functional underpinnings of AF comes from studies which examine the relationship between AF asymmetry and behavioural data. In a study with a sample of right-handed individuals, Catani et al. (2007) reported a significant correlation between degree of AF asymmetry (strong left lateralisation of the long segment versus symmetrical pattern) and performance on the total number of words recalled on the California Verbal Learning Test (CVLT) which presumably measures verbal memory. Specifically, extreme left lateralisation was associated with worse performance on CVLT while bilateral symmetry was associated with better performance. This tendency was true for both men and women. Another study used a similar methodology, but with children (Lebel & Beaulieu, 2009). Just as Catani et al. (2007), the researchers divided the children into three groups: a left-only group, where the right arcuate was not detectable, a left lateralisation group and a right lateralisation group. They found that children in the left-only groups performed significantly better than the right lateralisation group on the Peabody Picture Vocabulary Test. Furthermore, children in the left lateralised group scored



significantly better than the right lateralised group on NEPSY Phonological Processing task. These results are somewhat conflicting as the result from Catani et al. (2007) seem to suggest that bilateral symmetry is preferable for verbal memory while the data from Lebel and Beaulieu (2009) seem to favour left lateralisation for receptive vocabulary. Still, these studies indicate that AF asymmetry is related to language performance, although the specific mechanisms underlying the correlation are far from clear. There is also evidence that radial diffusivity in the left long segment of AF correlates negatively with word learning performance (Lopez-Barroso et al., 2013). The authors suggest that AF mediates word learning ability, and that higher microstructural integrity, suggested by lower radial diffusivity, may facilitate word learning performance.

Furthermore, there is evidence of a relationship between acquisition of literacy, reading ability and AF plasticity (Thiebaut de Schotten, Cohen, Amemiya, Braga, & Dehaene, 2014). In one study, researchers compared three groups: literate adults, ex-literate adults (who have acquired literacy in adulthood) and illiterate adults, with regard to structural properties of AF. They found that the illiterate group displayed lower FA value in the left posterior segment of AF compared to literate and ex-literate subjects. Similarly, there was a correlation between reading performance and FA in the left posterior segment. The authors suggest that the posterior segment connects the brain regions involved in reading, specifically visual word form area in the temporal lobe with parietal lobe regions involved in phonological processing. It is worth noting that no difference was found between literates and ex-literates with regard to AF structure, suggesting that AF plasticity is not confined to childhood.

Plasticity in AF has also been observed in musical training (Wan & Schlaug, 2010). In a study by Halwani, Loui, Ruber, and Schlaug (2011), singers, instrumentalists and non-musicians were compared in order to examine the relationship between musical training and structural properties of AF. They found that singers and instrumentalists had larger tract

volume and FA in both right and left AF compared to non-musicians. Though the evidence is correlational, the authors suspect that musical training leads to plastic changes in AF. Looking at different segments of AF, they found differences between singers and instrumentalists in a branch of left side AF, which specifically connects STG with inferior frontal gyrus (superior branch). They found that singers had larger tract volume and lower FA in this left superior branch compared to instrumentalist. Moreover, FA in the left superior branch was negatively correlated with years of vocal training. Thus, vocal-motor training may lead to changes in the superior branch of AF. The authors speculate that lower FA may indicate that the superior branch is more complex, containing more fibre crossings, and may in fact facilitate singing competency (Halwani et al., 2011).

Researchers have also shed light on the functional significance of AF by studying autistic individuals – a population with impaired language development. Fletcher et al. (2010) compared white matter integrity in AF in a group of high functioning adolescent autistic males to that of a control group, and found a significant increase in mean diffusivity (MD) and radial diffusivity (RD) in the group with autism. Assessing AF asymmetry, they found that both MD and FA were less lateralised compared to the healthy subjects. Based on this, Fletcher et al. (2010) suggest that white matter microstructure in AF is affected in autism and that there is less language specialisation in the left arcuate compared with controls. This may in some way be related to a lower level of language functioning.

The subjects in the study mentioned above were high functioning autistic individuals, and while their language was impaired, they did still have functional language. Wan, Marchina, Norton, and Schlaug (2012) studied hemispheric asymmetry in AF in young completely nonverbal children with autism using DTI, and found that the nonverbal children did not show the common left-right asymmetry in AF, compared to the control group, but rather the opposite. They suggest that this pattern reversal may be the underlying brain basis

in the language impairments typically found in autism.

Moseley et al. (2016) studied eighteen high functioning adult males with ASD (seventeen of which had Asperger's Syndrome), and found that even though the subjects presented no clinically manifest language deficits, AF was still affected. AF volume was significantly reduced bilaterally when compared with controls. The degree of volumetric reduction of right AF was negatively correlated with the severity of autistic symptoms. Moseley et al. (2016) suggest that structural changes in right AF may be involved in more subtle impairments of a pragmatic and semantic are, as seen in high functioning individuals with ASD.

There seems to be less research on the specific role of AF in the right hemisphere. There are some indications that it may be involved in the processes prosodic elements of language (Glasser & Rilling, 2008). The previously mentioned study by Moseley et al. (2016) also point to this. This would fit well with the general trend in language dominance studies, showing that the right hemisphere is important for prosodic and paralinguistic aspects of language processing (Lindell, 2006).

There is also evidence that it may be associated with visuospatial processing, with one study reporting that parietal-frontal white matter lesions, including AF, may be associated with neglect syndromes (Doricchi, Thiebaut de Schotten, Tomaiuolo, & Bartolomeo, 2008).

In addition, both left and right AF may be involved in imitation and model learning processes through its supposed involvement in the mirror neuron system (Iacoboni & Dapretto, 2006). As discussed above, the mirror neuron system of imitation consists of three brain regions, STS, ventral premotor cortex and inferior frontal gyrus. These regions tend to be bilaterally activated during imitation task (Iacoboni & Dapretto, 2006), with exception of STS, which demonstrate a rightward activation (Yang et al., 2015). Iacoboni and Dapretto (2006) observed that the "three segment" model presented by Catani et al. (2005) seem to fit

quite well with the structures involved in the mirror neurons system. Based on this, one might speculate that AF is also involved in imitation processes.

### **The purpose of the paper**

As described above STS, a grey matter structure, and AF, a white matter tract, is located in close proximity to each other, and they seem to be involved in many of the same cognitive processes, most notably auditory/language processing. In addition, both structures demonstrate reliable inter-hemispheric asymmetries. However, whether these asymmetries are related to each other has never been explored. The purpose of this paper is to do just that; to shed light on the relationship between the two. Two hypothesis are stated – one relating to a gross anatomical relationship and one based on their assumed shared functionality. The first hypothesis predicts a negative correlation between STS depth and AF volume. As STS becomes deeper, thus occupying more space medially in the temporal lobe, less space is available to AF (Dubois et al., 2010). The second hypothesis predicts a positive correlation between STS leftward asymmetry and AF leftward asymmetry. This is based on the assumption that STS and AF are involved in similar processes underlying functional language lateralisation. In other words, if STS asymmetry (e.g. greater surface area, grey matter thickness) and AF asymmetry (e.g. volume, FA) is associated with functional language lateralisation, one can expect these to correlate.

### **Diffusion tensor imaging**

The current study utilises DTI methodology, and it is therefore appropriate to present an overview of the underlying principles of the methodology.

DTI is a variant of diffusion-weighted MR imaging which allows the researcher to noninvasively estimate anatomical properties of white matter structures. In short, DTI is based on the principle that water molecules are in constant motion (diffusion). If a water molecule is allowed to move relatively freely, for instance in the ventricles of the brain, which are filled

with cerebrospinal fluid (CSF), then diffusion occurs randomly in all directions. In contrast, diffusion may be more restricted in tissue where cellular, subcellular and extracellular structures impede motion. Various types of tissue (e.g. white matter, grey matter) differ in their diffusion properties which can be utilised for imaging purposes by making the MR image sensitive to diffusion. This is basically done by exposing the brain to strong gradient magnetic fields causing MR signal loss as a function of diffusion. For example, because water diffuses more freely in CSF, more signal will be lost relative to brain tissue. Thus, CSF can easily be identified on a diffusion-weighted MR image.

With DTI, one is not only able to characterise the magnitude of diffusion at each voxel in the brain, but also the direction of diffusion. This is described in each voxel by a three-dimensional ellipsoid called the diffusion tensor. The tensor itself is represented by three eigenvectors as can be seen in Figure 3. Depending on the configuration of the vector, the shape of the tensor may be a sphere, an ellipsoid or even a line.

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INSERT FIGURE 3 HERE  
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A voxel in CSF would have tensor approximating a sphere because diffusion is likely to occur in any direction (i.e. isotropic diffusion). In contrast, a voxel in a white matter structure like AF will not diffuse freely, but diffuse along the direction of the tract (i.e. anisotropy). Its tensor would therefore resemble a cigar shape, where the length of the cigar indicates the preferred direction of diffusion (i.e. the principle eigenvector). The magnitude of diffusion along this direction is called axial diffusivity (AD).

Radial diffusivity is based on the magnitude of the two remaining eigenvectors, reflecting the diffusivity perpendicular to direction of the principal eigenvector. Visually, this

may be represented as the girth of the cigar. Thus, it indicates the homogeneity of the diffusion direction. If the diffusion is perfectly focused in a single direction, the tensor would simply become a line. These aspects are often computed in the measure called fractional anisotropy (FA) ranging from 0 (isotropy, spherical tensor) to 1 (anisotropy, line tensor). Moreover, the mean diffusivity (MD) can be calculated based on the mean of the axial and radial diffusivities, reflecting the overall diffusivity in a given voxel.

Finally, some form of tractography procedure is often used in DTI studies. One may start with a relevant voxel and then examine whether the principal eigenvectors of surrounding voxels align with the principal vector of the seed voxel. If so, a continuous tract like AF may be reconstructed. It may be noted that the alignment checking process is performed by an algorithm constrained by certain pre-defined criteria. For instance, to avoid unlikely angles, curvature thresholds limit the maximally allowed angle between two neighbouring voxels and FA thresholds limits the problem of partial volume contamination. Voxels containing grey matter have lower FA values than white matter. By excluding voxels with FA values lower than 0.2, the reconstructed tract is less likely to contain grey matter. Such criteria are necessary in order avoid implausible tract reconstructions.

In summary, DTI allows researchers to identify white matter structures and assess their macrostructural (e.g. tract volume) and microstructural properties (e.g. FA).

## **Method**

### **Participants**

Twenty healthy subjects (all male; mean age 25.6 years, standard deviation (SD) 2.4 years) participated in this study. They were recruited from the student population in Bergen and from the staff at Haukeland university hospital. The study was approved by the regional ethic committee of western Norway (REK-VEST) and participants gave informed consent in

accordance with the declaration of Helsinki. Each participant was screened by trained radiographers to avoid any possible harm during the scanning procedure.

The participants were mostly right handed (mean 0.9; SD 0.3) as measured by the Edinburgh handedness inventory (Annett, 1970).

### **Data acquisition**

All images were obtained using a 3.0 T GE Signa Excite scanner (General Electric Medical Systems, Milwaukee, WI, USA). The imaging protocols were the same for every subject, and comprised both structural as well as functional scans. However, for the present thesis, only the structural scans were used, while the functional scans were utilised in another thesis (Wigglesworth, 2013). The structural images include standard anatomical MR images and diffusion weighted MR images for DTI analysis.

MR images (10min:43s) were obtained using a T1-weighted gradient echo pulse sequence (MPRAGE). The data was analysed using the BrainVISA software (<http://brainvisa.info>). This software semi-automatically transforms the individual MR images into a standard reference space and performs segmentation and labelling of anatomical structures, including sulci, and then measures volume, length, depth, and surface of these structures. Here, only the parameters from the superior temporal sulcus were used.

Diffusion weighted images (8min:38s) were acquired using the following parameters: 30 diffusion directions with  $b=1000 \text{ s/m}^2$  and six  $b=0 \text{ s/m}^2$ , TR=9 ms, TE=91 ms, field-of-view  $220 \times 220 \text{ mm}^2$ , voxel size  $1.72 \times 1.72 \times 2.4 \text{ mm}^3$  and 56 slices with no inter-slice gap.

Imaging data was not successfully acquired in all the twenty participants. Standard MR images were obtained from nineteen subjects and diffusion weighted images were obtained from seventeen of the twenty participants. In sixteen subjects, both forms of structural images were acquired. This entails, necessarily, that in the subsequent analysis of the data, depending on what is being examined, the sample sizes differ.

**DTI preprocessing and analysis**

All the preprocessing and analyses were performed using the ExploreDTI software developed at University Medical Center, Utrecht, The Netherlands (Leemans, Jeurissen, Sijbers, & Jones, 2009). The diffusion data was first subjected to multiple preprocessing steps meant to correct for subject motion, eddy-current-induced geometrical distortions and susceptibility distortions typically seen with echo planar imaging sequences. The latter steps were done by re-sampling the diffusion weighted images to a T1-weighted image which has fewer of these distortions.

Following data preprocessing steps, a diffusion tensor was calculated for each voxel in the brain with the purpose of describing various diffusion properties.

**Tractography procedure**

The tract of arcuate fasciculus was dissected using a deterministic tractography approach. First, in order to increase the robustness of the procedure, an algorithm automatically seeds all voxels in the brain which satisfies certain predefined criteria (whole-brain tractography). The criteria are designed to avoid false positive tracts such as tracts contained streamlines with unlikely angles and tracts containing grey matter (partial volume contamination). The criteria used for whole-brain tractography was as follows: fractional anisotropy set to  $>0.2$ , angular threshold  $30^\circ$  and minimum streamline length of 50 mm.

Secondly, two regions of interest (ROI) were manually drawn to carve out streamlines belonging to the AF tract (Figure 4 illustrates the ROI locations in each hemisphere for one subject). ROI locations were based on knowledge about AF anatomy and well-researched protocols that have been developed to identify AF (Stieltjes, Brunner, Fritzsche, & Laun, 2013; Wakana et al., 2007).



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INSERT FIGURE 4 HERE  
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It is worth noting that different studies adopt slightly different anatomical descriptions of AF, and even label it differently (Catani & Thiebaut de Schotten, 2012). What the current study labels as arcuate fasciculus roughly corresponds to the classical notion of AF (Dick & Tremblay, 2012), or what Catani et al. (2005) labels as the long segment of AF and Wakana et al. (2007) calls the temporal component of the superior longitudinal fasciculus. In any case, this is the tract which connects the temporal lobe with the frontal lobe via a long dorsal projection that arches around the lateral sulcus. The reason for focusing on this segment of AF is that it seems to be the most asymmetric part of AF, and seems to be related to language dominance (Catani et al., 2007).

A series of “pilot drawings” were done as to ensure the accuracy and reliability of the drawing process. The first ROI was drawn in the coronal plane which is perpendicular to the anterior segment of AF (follows the anterior-posterior direction). On a colour-coded directional map, AF can easily be seen as a green triangle in the coronal plane. This is because streamlines that are aligned in the anterior-posterior direction are encoded green in this map. Where AF was seen to be largest, the first ROI was placed. As can be seen in Figure 4, the circumference of the first ROI is large and so exceeds the area occupied by AF by a large margin. This is preferable because a large ROI better ensures that as many streamlines as possible belonging to AF is captured (Caan, 2016). The second ROI was drawn in the axial plane where AF makes a U-turn in the superior-inferior direction towards the temporal lobe. In a few cases, NOT-ROIs were used to exclude streamlines which clearly appeared as outliers (e.g. streamlines belonging to uncinate fasciculus). It may be noted that in fibre

tractography it is generally advisable to use NOT-ROIs conservatively (Caan, 2016). The described procedure was repeated for every subject and for both the left and right hemisphere

Lastly, for each tract the following measures were calculated: tract volume, length, FA, MD, AD, RD. For each tract, FA, MD, AD, RD, were averaged across all voxels in the tract.

Tract volume ( $\text{mm}^3$ ) is the total space that a tract occupies. It is identical to the number of voxels occupied by the traced when these are sized 1 x 1 x 1 mm. Tract length is the average length of streamlines in one tract.

Axial diffusivity ( $\lambda_1$ ) is the eigenvalue of the principal eigenvector in a voxel. That is, the magnitude of diffusion along what appears to be the dominant direction of diffusion in a voxel. Radial diffusivity ( $\lambda_{\perp}$ ) is the mean diffusion magnitude of the two smaller eigenvectors ( $\lambda_1$  &  $\lambda_3$ ), i.e. the amount of diffusion perpendicular to the dominant direction. As described above, RD can be visually represented as the girth of the diffusion tensor. FA is derived from  $\lambda_1$ ,  $\lambda_2$  and  $\lambda_3$ , and represents the homogeneity of the diffusion direction. That is, the degree to which diffusion occurs along a single direction. It ranges from 1 (perfect anisotropy) to 0 (perfect isotropy). Mean diffusivity is simply the average of the three eigenvalues reflecting the amount of diffusion regardless of direction.

### **Statistical analysis**

Statistical analysis performed by SPSS software (version 23; SPSS Inc., Chicago, IL, USA).

First, the descriptive statistics for both superior temporal sulcus and arcuate fasciculus were calculated. Then, asymmetry indices (AI) were calculated to assess whether there were reliable structural differences between the hemispheres (i.e. inter-hemispheric asymmetry). The equation is as follows:  $AI = ((X_{\text{left}} - X_{\text{right}}) / (X_{\text{left}} + X_{\text{right}})) \times 100$ . A parameter, such as STS

depth or AF volume, is inserted for X. The fraction is multiplied with 100 for no other reason than to simply to make the data more presentable.

If some structural parameter (e.g. STS depth) is identical in both hemispheres, it follows from the equation that AI will equal zero. However, if the structural parameter is greater on the left side, then AI will equal a positive number. The magnitude of AF will also increase as the relative inter-hemispheric difference increases. On the other hand, if the right side structure is larger, then AI results in a negative value.

Each AI was subjected to one sample t-tests with the test value of zero. It follows from the null hypothesis, i.e. no inter-hemispheric difference, that various asymmetry indices are expected to approximate zero. The one sample-test are able to statistically determine whether the observed asymmetry indices are likely or unlikely to occur under the null hypothesis. If the data are deemed unlikely, defined as exceeding the p-value = .05 in any direction (i.e. two tailed), then the null hypothesis is rejected, and one may reasonably assume that the structure is asymmetrical.

Finally, STS and AF asymmetries were examined in combination to reveal any statistical relationships that might exist between the asymmetry observed in STS and AF. This was examined in two ways. One where Pearson product-moment correlation coefficients (Pearson's  $r$ ) were computed to test the linear relationship between asymmetry indices of STS and AF. Another way where multiple Pearson's  $r$  were calculated between measures of STS and AF on a unihemispheric level. This includes correlations between STS and AF that are ipsilateral (e.g. left STS depth  $\times$  left AF volume) and contralateral (e.g. left STS depth  $\times$  right AF volume).

A p-value of .05 was used for the all correlations coefficients. Bonferroni correction for multiple comparisons were not carried out (see discussion).

## Results

### Inter-hemispheric asymmetry of superior temporal sulcus

Descriptive statistics and asymmetry indices obtained from STS are summarized in Table 1, including STS surface, mean depth, maximum depth, length and grey matter thickness.

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 INSERT TABLE 1 HERE  
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One sample t-tests were conducted to determine if statistically significant differences exist between STS in left and right hemisphere. It may be noted that these statistical analyses are based on data from a sample size of nineteen subjects.

The average depth of STS was greater in the right hemisphere ( $M = 19.25$ ,  $SD = 1.41$ ) compared to the left hemisphere ( $M = 16.95$ ,  $SD = 1.26$ ),  $t(18) = -6.036$ ,  $p = .000$ . In addition, the maximum depth of the right STS ( $M = 31.42$ ,  $SD = 1.48$ ) was significantly larger than left STS ( $M = 28.39$ ,  $SD = 2.13$ ),  $t(18) = -5.778$ ,  $p = .000$ . This is consistent with previous findings (Bonte et al., 2013; Leroy et al., 2015)

The difference in length was also statistically significant,  $t(18) = 2.954$ ,  $p = .009$ , with the left STS ( $M = 161.30$ ,  $SD = 23.50$ ) being reliably longer than STS in the right hemisphere ( $M = 139.89$ ,  $SD = 25.99$ ). This replicates previous studies (Bonte et al., 2013).

There was no difference between the surface area of right STS and left STS surface,  $t(18) = .708$ ,  $p = .488$ . Likewise, no difference was found between average grey matter thickness on left STS and STS in the right hemisphere,  $t(18) = .780$ ,  $p = .446$ .

### Inter-hemispheric asymmetry of arcuate fasciculus

Descriptive tractography statistics as well as asymmetry indices for tract volume, length, FA, MD, AD and RD are summarized in Table 2.

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INSERT TABLE 2 HERE  
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First, it is on occasion reported in studies that AF, for some subjects, cannot be reconstructed in the right hemisphere (Catani et al., 2007; Propper et al., 2010). In the current study however, AF was successfully tracked in both hemispheres in all subjects.

To assess the presence of any reliable asymmetries in AF across the hemispheres, one sample t-tests were performed. The data used in these analyses are based on a sample of seventeen subjects.

The tract volume ( $\text{mm}^3$ ) was significantly larger in the left AF ( $M = 6943.53$ ,  $SD = 2130.07$ ) compared to AF in the right hemisphere ( $M = 3932.66$ ,  $SD = 2398.51$ ),  $t(16) = 4.513$ ,  $p = .000$ . Other studies have found similar results (Catani et al., 2007; Propper et al., 2010).

No difference was found between the average length of streamlines (mm) in the left hemisphere AF and the right AF,  $t(16) = -.064$ ,  $p = .950$ . One previous study has reported significant differences with regard to length (Propper et al., 2010)

Examining the microstructural properties of AF, FA was found to be significantly greater in the left AF ( $M = .50$ ,  $SD = .02$ ) compared to AF in the right hemisphere ( $M = .48$ ,  $SD = .29$ ),  $t(16) = 2.835$ ,  $p = .012$ . Consequently, the current study replicates previous studies which have found greater FA values in the left AF compared to the right (Catani et al., 2007; Powell et al., 2006). FA is often considered as a biomarker of white matter integrity possibly influenced by aspects such as axon count and density, degree of myelination and relative membrane permeability (Curran et al., 2016).

No difference was observed between the average MD on the left AF and AF in the right hemisphere.  $t(16) = -1.330$ ,  $p = .202$ . Likewise, no statically significant difference was

found between the left AF and right AF with regard no either AD,  $t(16) = 1.263, p = .255$  or RD,  $t(16) = -1.805, p = .090$ .

### **Correlations between STS and AF**

Lastly, STS and AF were examined in combination to assess whether the asymmetry seen separately in STS and AF correlates. Notice that the data for these statistical analyses, are based on a sample size of sixteen subjects.

First, multiple Pearson's  $r$  were computed between asymmetry indices of STS and AF. A positive correlation would mean that as the AI of some STS parameter increases (the left side becoming relatively larger), the AI of a AF parameter increases (relatively larger left side). A negative correlation on the other hand, means that as a STS parameter gets relatively larger in the left hemisphere, the AF parameter in the right hemisphere relativity becomes larger.

No statistically significant correlation could be obtained. The three largest non-significant correlations were all between the AI of STS mean depth and various AI parameters of AF. First RD,  $r(14) = -.485, p = .057$ , then AD,  $r(14) = .413, p = .122$  and finally FA,  $r(14) = .385, p = .141$ . According Cohen (1988), these correlation coefficients may be considered as "moderate" in strength. They seem to point in a direction of a statistical relationship between STS and AF. In a cases where STS is relatively deeper in the right hemisphere, AF in the right hemisphere tend to have relatively larger FA and AD as well as lower RD. Keep in mind that this is all relative. For instance, FA is still, in most cases, greatest in the left AF. But in instances where STS is relatively deeper on the right side, FA may be more symmetrical between the hemispheres, or even greater in the right hemisphere. However, this must be interpreted with caution as the correlations are deemed non-significant.

The second set of statistical analyses also consisted of multiple Pearson's  $r$ , but this time examined the linear dependence between unihemispherical measures of STS and AF.

Starting with the left hemisphere. Two statistically significant negative correlations was found between left AF tract volume and left STS surface area,  $r(14) = -.525, p = .037$ , and between left AF volume and left STS length,  $r(14) = -.550, p = .027$ . That is, in cases as the volume of left AF increases, the surface area and length of STS tend to decrease, in a strictly correlational sense.

Examining the right hemisphere, two statistically significant positive correlations were found. One of these was between right AF volume and right STS surface area,  $r(14) = .502, p = .048$ . The second positive correlation was found between right AF AD and right STS mean depth and,  $r(14) = .541, p = .031$ . Some studies have decreases in AD to be associated with axonal damage and fragmentation (Curran et al., 2016).

In addition, it was also observed a positive non-significant correlation between right AF volume and right STS length,  $r(14) = .496, p = .051$ . Thus, contrary to what was observed in the left hemisphere, increasing right AF volume is associated with increasing STS surface area and length.

A couple of observations can be made. The reported unihemispherical correlations may be judged to be large (Cohen, 1988). In addition, all significant correlations are ipsilateral (occurring in the same hemisphere).

It seems that the statistical relationship between STS and AF is not straightforward. Left STS parameters correlates negatively with left AF volume while right STS parameters correlates positively with right AF. This may explain why there were no significant correlation between AI of STS and AI of AF.

## Discussion

The first hypothesis stated in this paper was that there would be a negative correlation between STS depth asymmetry and AF volume as these would, to some degree, compete for the same limited space in the temporal lobe. The second hypothesis was that there would be a

positive correlation between leftward STS asymmetry for parameters like surface area and grey matter thickness and AF parameters like volume and FA. This was based on an assumption that STS and AF may partially constitute the neural substrate for functional language lateralisation, and consequently one could expect relevant STS and AF parameters to correlate positively.

The current study found no evidence to support any of these claims. With regard to the first hypothesis, no statistical relationship was found between STS depth and AF volume. When it comes to second hypothesis, no correlations between the asymmetry indices of STS and AF were found. It is worth to emphasise that the asymmetry index of some structure property (e.g. STS depth, AF tract volume) is a compound measure based on the relative difference between the left and right hemisphere. In other words, the relative inter-hemispheric difference of STS and AF, does not correlate significantly.

However, looking beyond the asymmetry indices, and instead focusing on structure properties separately in each hemisphere (e.g. left AF tract volume), several significant correlations were found between STS and AF. Specifically, negative correlations between left AF volume and left STS surface area and between left AF volume and left STS length. In addition, positive correlations between right AF volume and right STS surface area and between right AF AD and right STS mean depth. In addition, a positive correlation close to significance level between right AF volume and left STS length.

These correlation coefficients have a magnitude of around .5, which may be considered large according to the rule of thumb interpretation of Pearson correlation effect sizes (Cohen, 1988).

Before further discussion of the significance of these results for the STS x AF relationship however, it is appropriate to consider the STS and AF asymmetries separately.



**Replications of previously observed inter-hemispheric asymmetries**

Starting with STS, this study found statically significant rightward asymmetries in STS with regard to mean depth across STS as well as maximum depth. In addition, a significant leftward asymmetry with respect to STS length was also found. The remaining asymmetry indices of STS were not close to statistical significance.

These results are consistent with previous studies which find that STS is systematically deeper in the right hemisphere and longer in the left hemisphere (Bonte et al., 2013; Glasel et al., 2011; Leroy et al., 2015). It may be noted that for current study, the STS measures used in statistical analysis are based on the entire STS. Recently, it has been reported that one segment of STS located at the base of Heschl's gyrus, named the superior temporal asymmetrical pit, seem to be the most consistently asymmetric region of STS (Leroy et al., 2015).

With regard to reported leftward length asymmetry in STS, it is worth specifying that this refers to the trajectory of STS, or the summed vertex-by-vertex distance. When length is defined as the distance between the most anterior and most posterior part of STS (Euclidean distance), previous studies have found no significant differences between left and right STS (Bonte et al., 2013).

This study also found inter-hemispheric asymmetries in AF. Specifically, statistically significant leftward asymmetries with regard to tract volume and FA. These findings are in line with previous studies on AF. Several studies have reported greater tract volume and FA in the left AF compared to AF in the right hemisphere (Catani et al., 2007; James et al., 2015; Ocklenburg et al., 2013; Powell et al., 2006). FA may be indicative of the microstructural integrity of AF. Some studies have found an association between FA and fibre density, fibre coherence, myelination and axonal diameter (Curran et al., 2016). The current study did not find significant differences in average streamline length between the left and right hemisphere

AF. This is contrary to a study by Propper et al. (2010), who found that left AF contains longer streamlines compared to AF in the right hemisphere. The different result may be due to different sample sizes. Seventeen in the current study versus twenty-six in the study by Propper et al. (2010). Moreover, the current study included a sample of mostly right-handed males whereas Propper et al. (2010) used a mixed sample of men and women, as well as individuals that were left-handed, right-handed and individuals with inconsistent handedness. Further research is needed to clarify the nature of the length asymmetry, and to identify moderators that might influence it.

### **The relationship between STS and AF**

As described in the results, correlational analyses between AI of STS and AF did not produce statistically significant results. There are, however, some indications of a statistical trend where increasing mean depth asymmetry in STS is associated with increasingly efficient AF microstructure. If true, this could indicate that the structures are involved in similar functional domains such as language processing. FA asymmetry has indeed been associated with language dominance in multiple studies (Catani et al., 2007; Powell et al., 2006; Propper et al., 2010). However, while it has been repeatedly reported that STS is involved in speech and language processing, there is little evidence at this point to suggest that the specific depth asymmetry is a neural correlate of functional language lateralisation (Leroy et al., 2015). Thus, even if the AI correlations between STS and AF were to hold up, it is unclear what the correct interpretation is.

Focusing on the unihemispherical correlations between STS and AF, the results indicate that there are negative correlations between left AF volume and right STS surface area and between left AF volume and STS length. In the right hemisphere, an opposite relationship is reported. Specifically, there seems to be positive correlations between right AF

volume and right STS surface, between right AF volume and length, and between right AF AD and right STS mean depth.

One approach that may be helpful in the interpretation of the results is to identify structural-functional relationships indicated in STS and AF from previous studies, and look for regularities across the structures. For instance, if a certain cognitive function is associated with the structural properties of both right STS and right AF, one may reasonably argue that the right STS and right AF are positively correlated because they are involved in the same underlying processes.

However, this interpretational process is not as straightforward as it seems. There are several reasons for this. First, it seems that most studies that have examined the functional significance of AF have utilised asymmetry indices in their analyses. For instance, AI of AF may be correlated with neuroimaging data reflecting language dominance or with behavioural measures like language performance tests. If the AI of AF correlates with language dominance, one may assume that degree of AF asymmetry is a neural correlate of functional language lateralisation.

Unfortunately for the interpretation of the current study, the AI is a compound measure contrasting the relative contribution of the left and right hemisphere with regard to some structural parameter. In the current study however, the variables of interest are not compound measures, but unihemispherical variables. For instance, an individual may display a relatively large volume in the left AF compared to other individuals, but in asymmetry terms, the individual's AF may be bilaterally symmetrical or extreme leftward asymmetric depending on the volume in the right AF. Thus, the conclusions drawn in previous studies may not be easily transferable to the interpretation of the current study.

There are however some indications of how the functional significance of AI can be related to its constituent unihemispherical variables. One study of preadolescent children

found that AF volume asymmetry correlates with language dominance (Sreedharan et al., 2015) which is in line with previously mentioned research. Interestingly, they also reported that leftward functional language lateralisation correlated positively with left AF volume, and negatively with right AF volume. Thus, both right and left AF volume may impact language dominance, but in opposite directions.

Secondly, there seems to be few studies that provide evidence on the functional significance of the structural asymmetry seen in STS. One study that examined the depth asymmetry in STS, found that it was not related to functional language lateralisation (Leroy et al., 2015). To my knowledge, no studies have examined the relationship between language dominance, or any other cognitive function, and STS variability in surface area and length.

In the absence of solid data connecting structural and functional asymmetry, one may infer, based on functional neuroimaging data mapping function to structure, that structural variability is related to functional variability.

It turns out that this assumption may be wrong in many instances. As mentioned, despite multiple functional neuroimaging studies implicating STS in language processes, Leroy et al. (2015) was not able to show that STS depth asymmetry is related to functional differences. One study reported a similar tendency examining grey matter volume asymmetries in subjects with either leftward- or rightward language dominance (Greve et al., 2013). Specifically, they examined asymmetries in Heschl's gyrus, planum temporale, pars opercularis, pars triangularis and insula. Although most of these structures display leftward volume asymmetries, and are known to be involved in language processing, only structural asymmetry in insula correlated significantly with language dominance. The authors conclude that the result "casts doubts on the hypothesis that the anatomical asymmetry of the human brain is the direct cause of the functional asymmetries observed" (p. 10).

Expressing similar dissatisfaction between generally weak correlations between structural asymmetries and functional lateralisation, Ocklenburg, Friedrich, Gunturkun, and GenC (2016) proposed a so called triadic model of functional lateralisation. They suggested that researchers ought to take into account asymmetries in grey matter structures, asymmetries in intrahemispheric white matter structures and asymmetries in corpus callosum in order to explain functional lateralisation phenomena. Researchers typically consider structures in isolation, potentially missing connections between structures that may be illuminate the structural-functional-relationship. As the authors exemplify, one might imagine that in an individual with an inefficient corpus callosum, asymmetry in AF may be strongly related to language dominance, having been forced to rely on intrahemispheric processing. In an individual with an efficient corpus callosum however, asymmetry in AF might have less impact on language dominance (Ocklenburg et al., 2016). Thus, utilising the triadic model may shed light the structural relationship between STS and AF by incorporating more relevant variables.

### **Two new hypotheses regarding the nature of the relationship between STS and AF**

As described, there are several challenges concerning the interpretation of the data presented in the current paper. This is not to say that it is impossible to generate hypotheses based on the results and previous research. Here, two hypotheses are suggested that may guide future research.

The first hypothesis is that the observed positive correlations between right AF volume and right STS depth, between right AF volume and right STS length, is due to a shared functionality with regard to social processing.

This is based on the following evidence. Several functional neuroimaging studies associates the right STS, in some cases specifically the right posterior STS, with various social processes (Yang et al., 2015). These include social perception, biological motion,

action observation, imitation and theory of mind tasks (Allison et al., 2000; Gallagher & Frith, 2003; Pelphrey, Singerman, et al., 2003; Yang et al., 2015). Even though there are some studies finding structural abnormalities in both left and right STS in autistic individuals (Boddaert et al., 2004), there is also mounting evidence that associates autistic traits with abnormalities in the right STS specifically (Hadjikhani et al., 2006; von dem Hagen et al., 2011; Wallace et al., 2012).

When it comes to AF, there are some indications that the right AF is involved in social processing as well. As it is well known that AF is involved in language processing, researchers have explored a possible connection between AF abnormalities and autism. As expected, an absence of the common left-right asymmetry in AF has been shown in nonverbal children with autism (Wan et al., 2012). However, in a study mostly consisting of adult males diagnosed with Asperger's syndrome, abnormalities in AF was still observed, even though the subjects presented no clinically manifest language deficits (Moseley et al., 2016).

Furthermore, the researchers found that decreasing volume in right AF was correlated with the severity of autism symptoms as measured by the Autism-Spectrum Quotient (AQ) questionnaire. This finding is somewhat surprising, assuming that language deficits underlies the connection between AF abnormalities and autism. The authors try to resolve the issue by suggesting that more subtle aspects of language processing may be impaired, which would explain the correlation. Another possibility, is that impairments in social interaction, characteristic for ASD and measured by AQ, underlie the correlation between AF and autism. This would seem to fit with the proposed mirror neuron system of which posterior STS plays a vital part (Iacoboni & Dapretto, 2006). In short, the mirror neuron system is thought to underlie imitation processes which undoubtedly is important for social interaction. Moreover, AF is thought to connect the three structures constituting the system: posterior STS, ventral premotor cortex and inferior frontal gyrus (Iacoboni & Dapretto, 2006). As the right posterior

STS seems to be particularly involved in social processes, it may be that the right AF is also somehow involved in social processes through its supposed involvement in the mirror neuron system, connecting posterior STS with relevant brain structures.

If both right STS and right AF is involved in social processes, it might explain the positive correlations between them. At this point however, there is not sufficient evidence to support this. Further research is needed to resolve the issue.

The second hypothesis proposed regards the structural STS-AF-relationship in the left hemisphere. Specifically, the observed negative correlations between left AF volume and left STS surface area and between left AF volume and left STS length may be due to a language compensation mechanism. Assuming that structural variability in left AF and left STS, is associated with functional language variability, it may be that smaller surface area and length in left STS is compensated by increasing AF tract volume or vice versa.

To my knowledge no studies have examined the relationship between language variability and left STS surface area or length variability. This part of the hypothesis is thus highly speculative. For AF, there are some evidence to suggest that left AF volume is correlated with leftward language lateralisation (Sreedharan et al., 2015).

Regarding the direction of the compensation mechanism, it seems more likely that AF would change structurally as a result of STS. First, STS asymmetry is observed early in development, while AF becomes asymmetric somewhat later (Catani & Thiebaut de Schotten, 2012; Kasprian et al., 2011). In addition, multiple studies have indicated plastic changes in AF, both in children and adults, which leads to the question whether the AF asymmetry is a state or trait effect (Halwani et al., 2011; Thiebaut de Schotten et al., 2014; Wan & Schlaug, 2010).

As with the first hypothesis, it must be emphasised this hypothesis is also speculative, and further research is needed to validate its claims. A promising approach might be to utilise

the triadic model outlined by Ocklenburg et al. (2016). This would involve incorporating structural data on STS and AF with data on corpus callosum asymmetry and functional neuroimaging data. Presumably, the structural relationship between STS and AF might become more apparent if examined in combination with other data.

### **Limitations**

One limitation of the current study was that the correlations were not corrected for multiple comparisons. In short, the problem of multiple comparisons appears when correlating several variables with each other. For instance, if one were to compute a hundred correlation coefficients, and assuming that the null hypothesis is true for all comparisons, five correlations would be deemed statistically significant under p-value of .05. In other words, unlikely findings nevertheless become probable given sufficient number of comparisons. Consequently, one would falsely reject the null hypothesis in five instances (called type 1 error).

One way to correct for multiple comparisons is the Bonferroni correction. It involves dividing the statistical threshold by the number of number of correlations performed. For instance, if a study consists of twenty correlations the corrected p-value would be .0025 (.05/20).

In the current study, the statistical significance of the reported correlations, does not survive Bonferroni correction. It may be noted that Bonferroni is generally considered a conservative correction which consequently may even produce false negative results. In fact, it is not unusual for DTI studies that findings are deemed non-significant under Bonferroni correction (Van Hecke, Leemans, & Emsell, 2016). As the current study may be regarded as an exploratory study on the structural relationship between STS and AF, the correlation coefficients are reported without correction. Future work is needed to confirm the statistical relationships reported here.



A further limitation is that the sample included only male participants. This may be advantageous in an exploratory study as males are more consistently asymmetric with regard to AF (Catani et al., 2007). On the other hand, results may not be representative of women as previous research have indicated that there are gender differences in AF asymmetry (Catani et al., 2007). For this reason, both genders will participate in a planned study in the future.

As described above, there are some indications that the structure of AF may be dependent on behavioural tendencies like musical training and literacy (Halwani et al., 2011; Thiebaut de Schotten et al., 2014). These variables have not been accounted for in the present study. Musical training might be confounding variable that correlates with the variables of interest. In the same planned study mentioned above, these aspects will be registered and accounted for.

## **Conclusion**

The present study has explored the structural relationship between STS and AF. It was hypothesised that asymmetry indices of STS and AF would correlate because they might compete for the same limited space and because they both might underlie functional language lateralisation. The results did not meet these expectations. Instead the relationship between STS and AF seem to be more complex in nature. It is hypothesised that the observed positive correlations between right AF volume and right STS surface area, and between right AF volume and right STS length, is due to a shared functionality relating to social processing. Furthermore, it is hypothesised that the observed negative correlations between left AF volume and left STS surface area, and between left AF volume and left STS length, reflects a language compensation mechanism. These hypotheses are meant to help guide further thinking and research on the structural relationship between STS and AF.

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Table 1

*Descriptive statistics and asymmetry indices for morphological features of STS*

Measure	<u>Left hemisphere</u>		<u>Right hemisphere</u>		<u>Asymmetry index</u>	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Surface area	5600.86	913.49	5415.14	901.73	1.67	10.30
Mean depth	16.95	1.26	19.25	1.41	-6.32	4.56
Maximum depth	28.39	2.13	31.42	1.48	-5.14	3.88
Length	161.30	23.50	139.89	25.99	7.32	10.81
Grey matter thickness	4.33	0.27	4.31	0.29	0.30	1.70

*Note.* Statistics based on sample size = 19



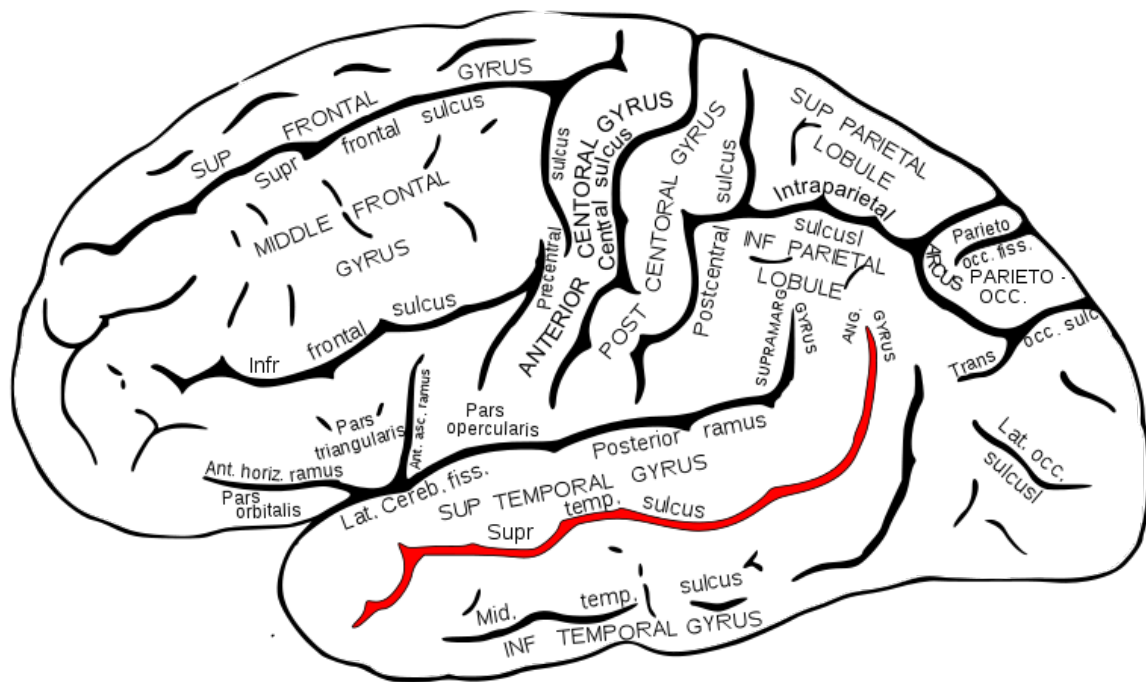
Table 2

*Descriptive statistics and asymmetry indices for structural properties of AF*

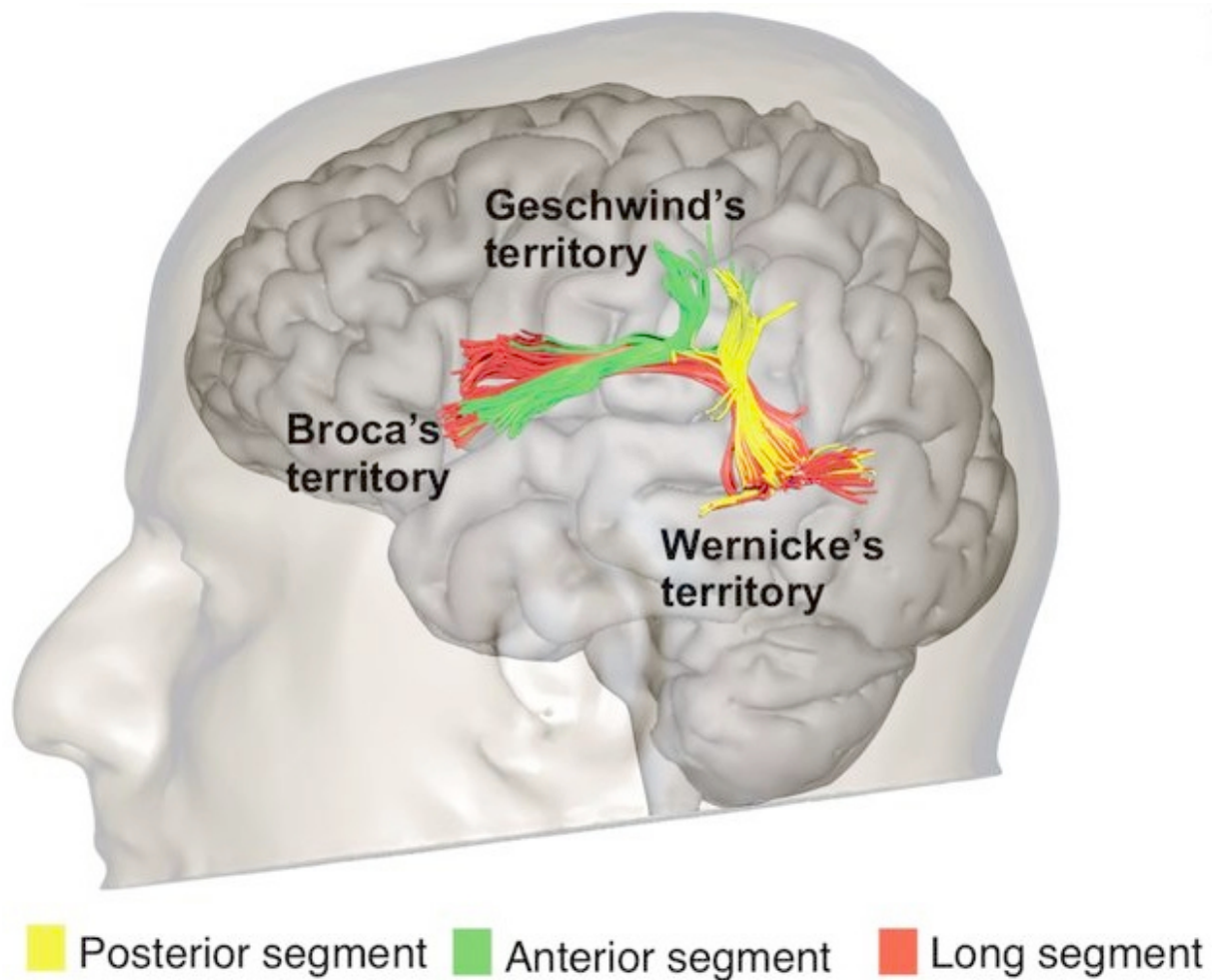
Measure	<u>Left hemisphere</u>		<u>Right hemisphere</u>		<u>Asymmetry index</u>	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Fibre volume (mm <sup>3</sup> )	6943.53	2130.07	3932.66	2398.51	32.36	29.57
Fibre length (mm)	109.11	13.68	109.07	10.14	-0.11	7.13
FA	0.50	0.02	0.48	0.03	2.08	3.02
MD (mm <sup>2</sup> /s)	7.62×10 <sup>-4</sup>	2.40×10 <sup>-5</sup>	7.67×10 <sup>-4</sup>	1.80×10 <sup>-5</sup>	-0.37	1.13
AD (mm <sup>2</sup> /s)	1.23×10 <sup>-3</sup>	3.00×10 <sup>-5</sup>	1.22×10 <sup>-3</sup>	2.90×10 <sup>-5</sup>	0.00	0.01
RD (mm <sup>2</sup> /s)	5.30×10 <sup>-4</sup>	2.70 ×10 <sup>-5</sup>	5.43×10 <sup>-4</sup>	2.90×10 <sup>-5</sup>	-0.01	0.03

*Note.* *FA* fractional anisotropy, *MD* mean diffusivity, *AD* axial diffusivity, *RD* radial

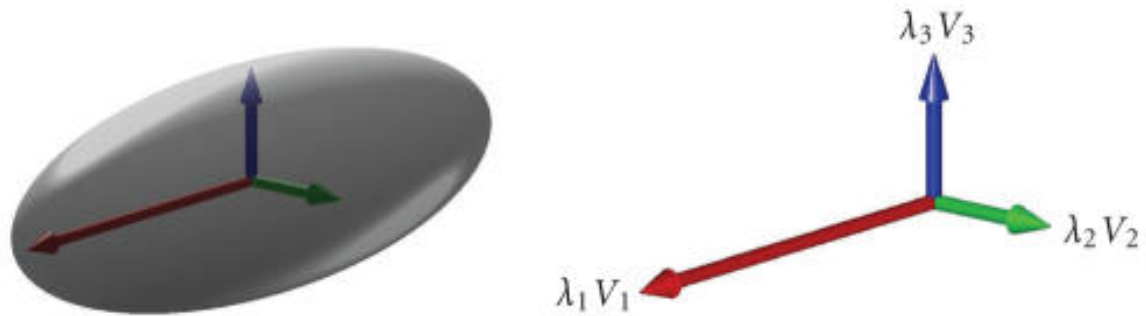
diffusivity, *AF* arcuate fasciculus. Statistics based on sample size = 17



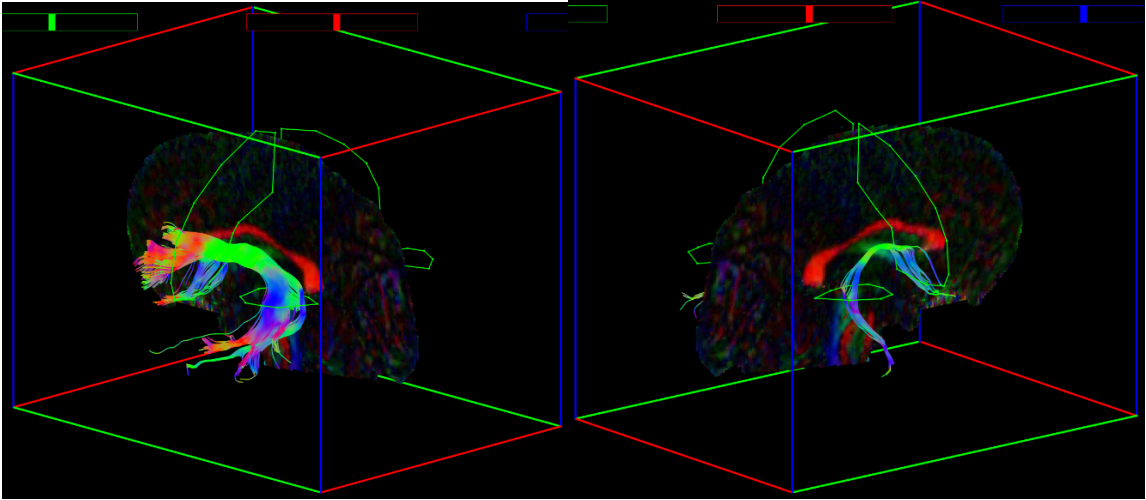
*Figure 1.* The superior temporal sulcus is the sulcus separating the superior temporal gyrus from the inferior temporal gyrus. Adapted from *Anatomy of the Human Body* (p. 819), by H. Gray and W. H. Lewis, 1918, Philadelphia and New York: Lea and Febiger. This work is in the public domain.



*Figure 2.* Tractography dissections of the three segments of the arcuate fasciculus. Reprinted from “Frontal networks in adults with autism spectrum disorder,” by M. Catani, F. Dell'Acqua, S. Budisavljevic, H. Howells, M. Thiebaut de Schotten, S. Froudist-Walsh,... D. G. Murphy, 2016, *Brain*, 139(2), 616-630, doi:10.1093/brain/awv351. This is an open access article distributed under the terms of the Creative Commons Attribution License.



*Figure 3.* The diffusion tensor. The diffusion is anisotropic because the magnitude or eigenvalue of the principal eigenvector ( $V_1$ ) is clearly greater than eigenvalue of the two remaining vectors. Reprinted from “Total variation regularization of matrix-valued images” by O. Christiansen, T. M. Lee, J. Lie, U. Sinha & T. F. Chan, 2007, *International Journal of Biomedical Imaging*, Article ID: 27432, doi:10.1155/2007/27432. This is an open access article distributed under the terms of the Creative Commons Attribution License.



*Figure 4.* Arcuate fasciculus as the result of a tractography procedure using two regions of interests (ROI) in each hemisphere. The ROI are coloured green.