doi:10.1093/brain/aws222 Brain 2012: 135; 3529–3550 | 3529

BRAIN
A JOURNAL OF NEUROLOGY

REVIEW ARTICLE

Beyond the arcuate fasciculus: consensus and controversy in the connectional anatomy of language

Anthony Steven Dick[1] **and Pascale Tremblay**[2]

1 Department of Psychology, Florida International University, Miami, FL, 33199, USA
2 Department of Rehabilitation, Université Laval and Centre de Recherche de l'Institut universitaire en santé mentale de Québec, Québec, Qc, G1J 2G3 Canada

Correspondence to: Anthony Steven Dick, Ph.D.
Department of Psychology,
Florida International University,
Modesto A. Maidique Campus,
Deuxieme Maison 296B,
11200 S. W. 8th Street,
Miami, FL 33199, USA
E-mail: adick@fiu.edu

The growing consensus that language is distributed into large-scale cortical and subcortical networks has brought with it an increasing focus on the connectional anatomy of language, or how particular fibre pathways connect regions within the language network. Understanding connectivity of the language network could provide critical insights into function, but recent investigations using a variety of methodologies in both humans and non-human primates have provided conflicting accounts of pathways central to language. Some of the pathways classically considered language pathways, such as the arcuate fasciculus, are now argued to be domain-general rather than specialized, which represents a radical shift in perspective. Other pathways described in the non-human primate remain to be verified in humans. In this review, we examine the consensus and controversy in the study of fibre pathway connectivity for language. We focus on seven fibre pathways—the superior longitudinal fasciculus and arcuate fasciculus, the uncinate fasciculus, extreme capsule, middle longitudinal fasciculus, inferior longitudinal fasciculus and inferior fronto-occipital fasciculus—that have been proposed to support language in the human. We examine the methods in humans and non-human primate used to investigate the connectivity of these pathways, the historical context leading to the most current understanding of their anatomy, and the functional and clinical correlates of each pathway with reference to language. We conclude with a challenge for researchers and clinicians to establish a coherent framework within which fibre pathway connectivity can be systematically incorporated to the study of language.

Keywords: language; arcuate fasciculus; white matter; dorsal stream; ventral stream

Abbreviations: DTI = diffusion tensor imaging; SLF/AF = superior longitudinal fasciculus/arcuate fasciculus

Introduction

Language is one of the most celebrated hallmarks of human cognition. The growing consensus is that the language faculty is supported by distributed, large-scale cortical and subcortical networks, and such a notion has brought with it an increasing focus on how particular fibre pathways connect regions within these networks. Fibre pathways themselves are bundles of axons that

Received December 7, 2011. Revised May 30, 2012. Accepted June 22, 2012. Advance Access publication October 29, 2012

originate from neurons in the cortical and subcortical grey matter. Three types of fibres are usually recognized: (i) commissural fibres, which connect the hemispheres; (ii) projection fibres, which either connect the cortex to the internal capsule, basal ganglia, brainstem and spinal cord (corticofugal fibres) or connect the thalamus to the cortex (corticopedal fibres); and (iii) association fibres, which connect adjacent and non-adjacent cortical regions within the same hemisphere and are referred to as short and long association fibres, respectively. The increased interest in fibre pathway connectivity in the study of brain and language relationships has forced the community to reconsider some of its founding principles. It is these considerations that we review here.

Faced with the rapid growth of this field of research, a central challenge for language researchers is to establish a coherent framework within which the study of fibre pathways can be systematically incorporated to the study of language as well as the study of lesions. While understanding connectivity of the language network can provide critical insights into function, particularly when considered in parallel with clinical correlates (e.g. abnormal, absent or damaged fibre pathways may be associated with particular functional deficits), recent investigations have provided conflicting accounts of pathways central to language. One prevailing notion should be dismissed at the outset. That is, fibre bundles are in fact not as distinct as the individualized names imply—while they can be identified and named, their spatial extent, origin and termination are often difficult to establish.

The objective of this review is to provide the reader with up-to-date about the anatomy, physiology and clinical correlates of the main fibre pathways involved in language. To this aim, we first critically review the most prominent methods that have been used to study connectivity. We then examine seven putative pathways for language: the superior longitudinal fasciculus and arcuate fasciculus, the uncinate fasciculus, extreme capsule, middle longitudinal fasciculus, inferior longitudinal fasciculus and inferior fronto-occipital fasciculus. For conciseness, we restrict our discussion to intrahemispheric cortico-cortical association pathways, and therefore do not discuss the cortico-striatal, cortico-thalamic or cortico-ponto-cerebellar pathways (the reader is referred to other sources for information on these pathways; Duffau *et al*., 2002; Duffau, 2008; Schmahmann and Pandya, 2008; Turken and Dronkers, 2011).

Methods in the study of fibre pathways for language

Post-mortem blunt fibre dissection

Despite significant contributions from recent *in vivo* imaging methods, post-mortem blunt fibre dissection remains the most influential method through which we understand the organization of fibre pathways for language (Fig. 1A). Briefly, post-mortem blunt fibre dissection begins with post-mortem removal and fixation of the brain, and proceeds to the careful peeling away, using a blunt dissection tool, of the grey matter and white matter to display the organized bundles of axons. Post-mortem blunt fibre dissection began with novel brain-fixation techniques in the early 19th century (Reil, 1809*a*, *b*, *c*, *d*, 1812*a*, *b*; Gall and Spurzheim, 1810; Burdach, 1819), continued throughout the century with developments in both gross dissection and brain sections aided by staining (Leuret and Mayo, 1827; Arnold, 1838; Gratiolet, 1839; Foville, 1844; Meynert, 1885), and culminated in the seminal works by Déjèrine (1895, 1901). Investigations using post-mortem blunt fibre dissection have continued to the present day (Trolard, 1906; Johnston, 1908; Curran, 1909; Hoeve, 1909; Jamieson, 1909; Davis, 1921; Klingler, 1935; Ludwig and Klingler, 1956; Ebeling and Reulen, 1988; Ebeling and von Cramon, 1992; Türe *et al*., 1997, 2000; Kier *et al*., 2004; Peuskens *et al*., 2004; Bürgel *et al*., 2006; Peltier *et al*., 2006; N'Dri Oka *et al*., 2007).

Post-mortem blunt fibre dissection has been of tremendous help for the study of human neuroanatomy, but investigators disagree about its utility to trace the origins and terminations of fibre pathways. Curran (1909; p. 651) remarks 'All the fibers . . . can be traced in gross dissection to their origin with perfect distinctness, and there can be no false continuity of fibers . . .'. However, his contemporary, Edinger (1896; p. 239) cautions 'The demonstration of connections between regions lying farther apart from one another is . . . difficult and leads very easily to artefacts [sic] . . .'. Yaşargil (2004; p. 729) further stated 'it is not possible, even when applying careful meticulous microtechniques, to separate a certain fiber system . . . and to guarantee an accurate and reliable anatomical differentiation'. This limitation of post-mortem blunt fibre dissection reveals the necessity to combine various techniques to map the connectional anatomy of language.

Histochemical tract-tracing procedures

Histochemical staining methods identify the stained fibres of passage when the post-mortem brain is cut into sections, a practice that dates back to techniques developed toward the end of the 19th century (Golgi, 1878, 1879; Weigert, 1882; Ehrlich, 1885, 1886; Marchi and Algeri, 1886; Marchi, 1886; Nissl, 1894; Ramón y Cajal, 1903*a*, *b*; Bielschowsky, 1904). These methods can be combined with the observation of Wallerian degeneration (Waller, 1850; Türck, 1851), with the staining of degenerating myelin (e.g. by using the Marchi method or other methods such as silver impregnation; Marchi and Algeri, 1886; Fink and Heimer, 1967; de Olmos *et al*., 1981), or investigation of differences in the degree of myelination across developing fibre tracts (Flechsig, 1901).

Additional histochemical procedures are most effective when the living experimental subject is sacrificed following a period of uptake of particular tracers; it follows that such procedures are precluded in humans (Heimer and Robards, 1981; Heimer and Záborsky, 1989; Lanciego *et al*., 1998, 2000; Swanson, 2000; Heimer *et al*., 2006). Of these, both retrograde (e.g. horseradish peroxidase, lectins, bacterial toxins, fluorescent dyes and viruses; Skirboll *et al*., 1989; Zaborszky and Heimer, 1989; Conte-Perales *et al*., 2010) and anterograde (e.g. tritium-labelled amino acids, *Phaseolus vulgaris* leucoagglutinin and dextran amines; Edwards and Hendrickson, 1981; Gerfen *et al*., 1989; Reiner and Honig, 2006) tracing methods, which rely on axoplasmic transport of a chosen tracer, have been used to investigate long-range fibre

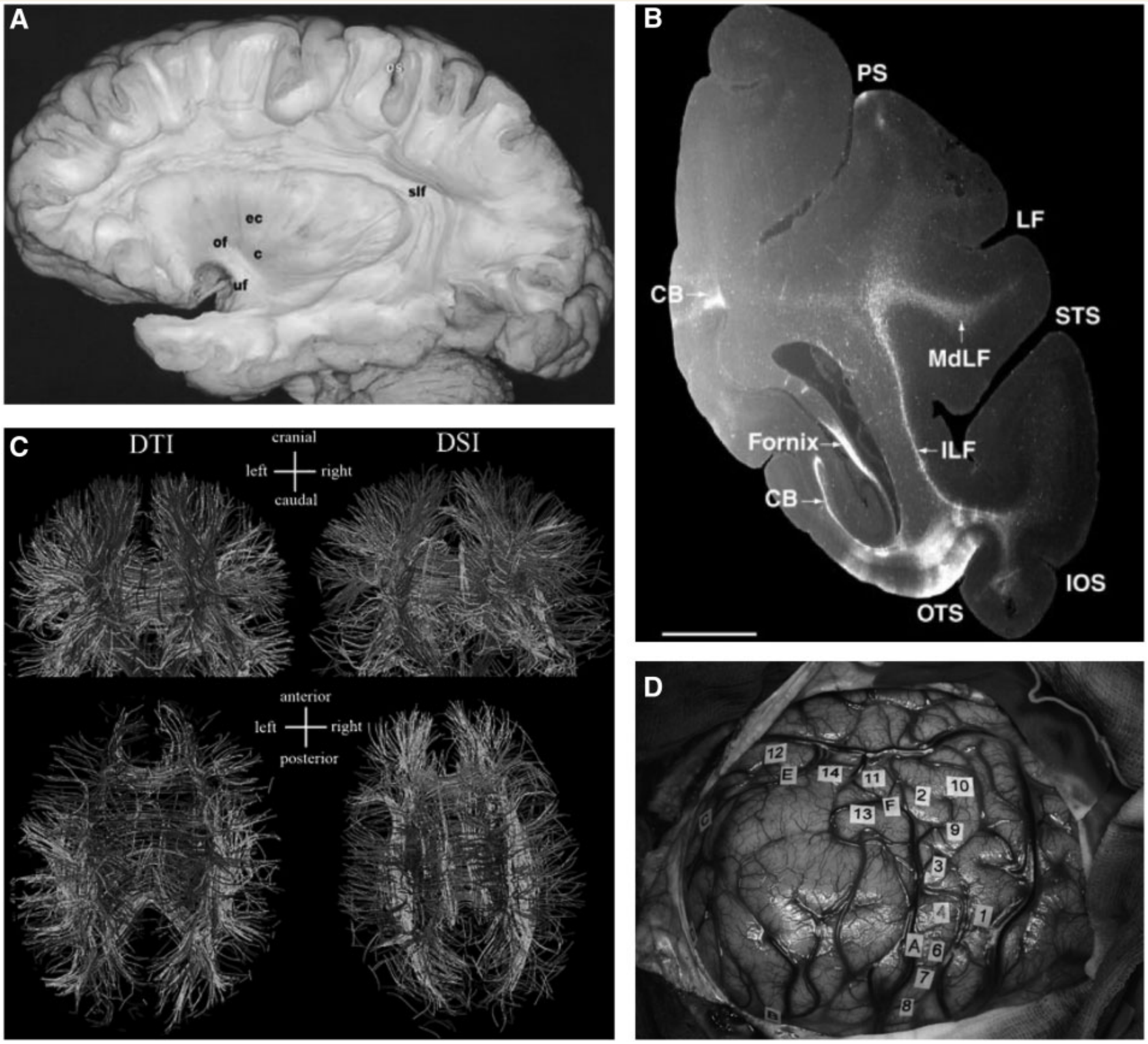


Figure 1 Methods in the study of white matter connectivity. (**A**) Example of post-mortem blunt fibre dissection. Modified with permission from Türe *et al*. (2000). (**B**) Example of a dark field photomicrograph following autoradiography in the macaque, modified with permission from Schmahmann *et al*. (2007). (**C**) Comparison of diffusion tensor imaging (DTI) and diffusion spectrum imaging (DSI) tractography. Modified with permission from Hagmann *et al.* (2006). (**D**) Intraoperative view of the brain before electrostimulation. Modified with permission from Maldonado *et al*. (2011). c = claustrum; CB = cingulum bundle; cs = central sulcus; ec = external capsule; of = occipitofrontal fasciculus; ILF = inferior longitudinal fasciculus; IOS = inferior occipital sulcus; LF = lateral fissure; MdLF = middle longitudinal fasciculus; OTS = occipitotemporal sulcus; PS = principal sulcus; slf = superior longitudinal fasciculus; STS = superior temporal sulcus; uf = uncinate fasciculus.

connectivity in the brain. These have the advantage over other histological methods to significantly reduce of the amount of misidentified crossing 'fibres of passage' (Zaborszky and Heimer, 1989; Lanciego *et al*., 1998, 2000).

The most prominent animal work investigating long association fibre pathways has used an anterograde autoradiographic tracing of radiolabelled amino acids (Yeterian *et al*., 2012 for review; Fig. 1B). Although these tracing methods can reliably identify origin and termination sites for fibre pathways, they are restricted to use in animals. For some this is prohibitive: 'The absence of language in non-human primates raises doubts on the possibility of translating connectional anatomy of putative language pathways from animals to humans' (Catani, 2009; p. 404). However, combined with methods that can be applied to humans, we believe histological methods can contribute to the understanding of white matter connectivity in the human brain.

Imaging procedures

Recent methods allow examination of the living human brain, and considerable effort has been expended to map the fibre pathways *in vivo*. The most popular method is diffusion tensor imaging (DTI, Fig. 1C; Conturo *et al*., 1999; Ciccarelli *et al*., 2003; Mori and Zhang, 2006; Johansen-Berg and Rushworth, 2009; Lazar, 2010; Oishi *et al*., 2011). DTI takes advantage of the anisotropic (i.e. directional) nature of diffusion of water molecules in axons, which can be measured with a MRI scanner. Because axons have a directional structure along which water flows, fractional anisotropy (a measure of diffusion direction and indicator of fibre integrity) is higher in white matter. Furthermore, the diffusion direction of fractional anisotropy can be traced across voxels to map fibre pathways, a procedure known as tractography (Basser *et al*., 2000).

Despite the major advances in understanding fibre pathways in the human brain, DTI tractography suffers from several serious shortcomings that are often minimized (Tournier *et al*., 2002; Assaf and Pasternak, 2008). First, DTI cannot differentiate efferent from afferent projections, and cannot identify axonal collateral pathways. Second, DTI relies more heavily than other experimental methods on *a priori* hypotheses about fibre pathways, which are based on potentially erroneous conclusions of early histological and dissection preparations. This can lead to the perpetuation of such errors into the DTI literature (Schmahmann and Pandya, 2006). Thirdly, DTI assumes that a single diffusion tensor defines each pixel in the image, but this assumption is invalid where white matter voxels overlap with grey matter or CSF (a situation referred to as partial volume averaging), or in cases where there are crossing fibre tracts. Pixels with partial volumes or crossing fibres will appear less intense, falsely indicating a weaker diffusion direction (Tench *et al*., 2002; Lazar and Alexander, 2003). DTI is not very robust under these conditions of uncertainty, which can lead to the premature termination of a fibre, the identification of non-existent fibre tracts, or the misidentification of two or more fibre tracts as one tract (Assaf and Pasternak, 2008).

Methods are being developed to deal with some of these issues. For example, probabilistic methods allow better tracking under uncertainty (Parker *et al*., 2005; Alexander, 2005; Behrens *et al*., 2007) or with minimal prior assumptions (Reisert *et al*., 2011). High angular resolution diffusion imaging and diffusion spectrum imaging both attempt to deal with the misidentification of pathways due to crossing fibres (Tuch *et al*., 2002; Tuch, 2004; Wedeen *et al*., 2005, 2008; Schmahmann *et al*., 2007; Lazar, 2010).

Imaging methods are becoming increasingly common for the study of fibre pathways. Some investigators have great confidence, claiming for example 'the exact location and extent of human white matter fibre pathways can be identified noninvasively *in vivo* by means of DTI' (Brauer *et al*., 2011, p. 459). Others are more reticent to make such claims (Yamada, 2009), and suggest that delineating the entire trajectory of a fibre tract using DTI 'is not feasible for long fibre tracts in the human' (Makris *et al*., 2005, p. 864) and that 'neither DTI images nor post-mortem dissections can trace the trajectory of specific axons.' (Oishi *et al*., 2011, p. 5). These discrepancies obviate the need to validate and compare the findings from *in vivo* diffusion weighted methods with complementary tract-tracing methodologies in experimental animals (Croxson *et al*., 2005; Dyrby *et al*., 2007; Schmahmann *et al*., 2007; Cohen-Adad *et al*., 2011) or with histological and other post-mortem methods in humans (Simonyan *et al*., 2008; Hansen *et al*., 2011; Holl *et al*., 2011; Miller *et al*., 2011).

Intraoperative electrostimulation

The seminal work by Hodgkin and Huxley (1939) showed that direct electrical stimulation of an axon elicits an action potential. Later this principle was applied to the study of white matter function by implantation of electrodes in patients preparing for surgery (Bickford *et al*., 1958; Ojemann and Fedio, 1968) and was shown to act directly on axonal transmission of information (Bignall, 1969; Nowak and Bullier, 1998). Intraoperative electrostimulation (Fig. 1D) implements a similar principle during surgery of awake patients by administering low-frequency stimulation (25–60 Hz), with a hand-held electrode, of certain areas of exposed white matter during performance of a task (see Szelényi *et al*., 2010, for review). When stimulation results in a disruption of a particular task (e.g. picture naming and counting), the pathway is determined to be involved in that task. The method is growing in popularity for the study of fibre pathways for language (Duffau *et al*., 2002, 2003*a*, *b*, 2005, 2008, 2009; Henry *et al*., 2004; Mandonnet *et al*., 2007; Bello *et al*., 2008; Ellmore *et al*., 2009; Leclercq *et al*., 2010; De Witt Hamer *et al*., 2011; Maldonado *et al*., 2011*a*, *b*).

There are some limitations of intraoperative electrostimulation. The procedure must be done on surgery patients, often with the presence of a tumour or lesion near the pathway of interest, which limits generalizability. A more subtle limitation is that identification of the pathway of interest is determined by current labelling convention (often relying on dissection or DTI data). Although there is often general agreement between tractography reconstruction and electrostimulation, there are also reported inconsistencies (Bello *et al*., 2008; Leclercq *et al*., 2010). As is the case for all the tracing methods, results from intraoperative electrostimulation studies must be interpreted within the context of the methodological limitations.

Summary of methods

Despite the methodological advances reviewed in the preceding sections, which have enabled a rich understanding of the fibre connectivity supporting language, important controversies about the utility of each methodology remain, and confidence in the definition of particular fibre pathways must be weighed against the strengths and weaknesses of each methodology. In addition to methodological issues, individual differences in anatomy also contribute to the sometimes cloudy picture of fibre pathway connectivity. The morphology of even well-established pathways, such as the corpus callosum, is influenced by sulcal and regional asymmetries across hemispheres within the same individual (Aboitiz *et al*., 1992; Zaidel *et al*., 1995). Across individuals, such anatomical differences are useful to establish functional correlates with specific pathways (e.g. Loui *et al*., 2011; Yeatman *et al*., 2011), but individual differences also contribute to the difficulty of determining precise trajectories of the pathways (Catani, 2008). These methodological and individual-difference issues should be addressed when integrating fibre pathway connectivity into existing theories of the neurobiology of language.

Language pathways: anatomy, physiology and clinical correlates

The most prominent contemporary model of language neurobiology is a dual-stream architecture analogous to that of the visual system (Ungerleider and Haxby, 1994). This model proposes a dorsal stream for mapping auditory speech sounds to articulatory (motor) representations, and a ventral stream for mapping auditory speech sounds to meaning (Hickok and Poeppel, 2000, 2004, 2007; Rauschecker and Tian, 2000; Hickok, 2009; Rauschecker and Scott, 2009; Rauschecker, 2011; Rogalsky and Hickok, 2011). While most investigators agree with the essence of this model, differences of opinion have arisen about the origins, terminations and extent of the fibre pathways forming the proposed streams, as well as the specific roles played by these pathways. An emphasis has been placed on superior longitudinal fasciculus/arcuate fasciculus (SLF/AF) connectivity for the dorsal stream, although this is not without disagreement. The anatomy of the ventral stream is even more controversial, which may be due to the larger number of putative fibre pathways forming the ventral stream, including the uncinate fasciculus, the extreme capsule, the middle longitudinal fasciculus, the inferior longitudinal fasciculus, and the inferior fronto-occipital fasciculus (Catani and Mesulam, 2008; Duffau, 2008; Frey *et al*., 2008; Saur *et al*., 2008, 2010; Papagno, 2011; Weiller *et al*., 2011; Wong *et al*., 2011). In the following sections, we review the history and functional correlates of the pathways forming the dorsal and ventral language streams.

Fibre pathways of the dorsal stream: the superior longitudinal fasciculus/arcuate fasciculus

Superior longitudinal fasciculus/arcuate fasciculus

The SLF/AF pathway has dominated the study of the white matter connectivity of language for >150 years. Historically, the superior longitudinal fasciculus and arcuate fasciculus have been viewed as synonymous, non-dissociable fibre pathways connecting the inferior frontal gyrus with the inferior parietal lobule and temporal lobe. It is only recently that there have been some attempts to dissociate parts of the SLF/AF, and generally these promote the notion that the arcuate fasciculus represents a partition of a broader superior longitudinal fasciculus. However, this attempt at redefinition is fairly recent; the course of the SLF/AF pathway has remained relatively unchallenged since Geschwind reasserted its prominence for language in his 1970 *Science* publication. There he produced the iconic figure showing the arcuate fasciculus connecting Broca's area (i.e. the posterior part of the inferior frontal gyrus, including two areas with distinct cytoarchitecture: Brodmann areas 44 and 45) with Wernicke's area (in the posterior superior temporal cortex, including the gyrus and sulcus). Despite the simplicity of this model, the history preceding Geschwind's treatment, and study of the pathway since Geschwind, suggests a far greater anatomical and functional complexity.

Establishment of the superior longitudinal fasciculus/arcuate fasciculus as a 'language pathway'

The early understanding of the SLF/AF originates from Burdach (1819), and appears prominently in the major anatomical works of the 19th century (Mayo, 1827; Meynert, 1885; Obersteiner, 1896; Wernicke, 1897; Barker, 1899), especially the two volumes by Déjèrine (1895, 1901). Like those before him, Déjèrine (1895; p. 756) does not dissociate the superior longitudinal fasciculus and arcuate fasciculus fibres, calling the 'faisceau longitudinal supérieur ou faisceau arqué (Arc) ("fasciculus arcuatus de Burdach")' a single fibre pathway named after Burdach. Similarly, Meynert (1885) makes mention of the arcuate fasciculus, but no mention of the superior longitudinal fasciculus, and Wernicke (1897) treats the superior longitudinal fasciculus and arcuate fasciculus as the same pathway (the 'superior longitudinal bundle, or arcuate bundle', p. 20).

Even early on, the course, origins and terminations of the SLF/AF were disputed. Campbell (1905; p. 142) called it 'a difficult bundle to follow'. Regarding its anterior course, Meynert (as cited in Déjèrine, 1895) located the rostral termination within the Rolandic operculum and inferior frontal gyrus, an opinion not shared by Déjèrine. In his 1895 'Anatomie des centres nerveux', Déjèrine (1895; p. 757) states 'the mode of termination of the arcuate fascicle rostrally is greatly disputed' and that 'when [the SLF/AF] is within an old cortical lesion, we cannot really follow degenerated fibres any further than the immediate neighbourhood of the primary focus of the lesion' (p. 758).

Despite his own earlier cautions, 6 years later, in the publication of the second volume of *Anatomie des centres nerveux*, Déjèrine locates SLF/AF terminations in the inferior frontal gyrus (or F_3 for the third frontal convolution; his Fig. 249; Fig. 2 in this review). The temporal stem is also shortened. Déjèrine (1895; p. 757) writes 'the most superficial fibres travel rostrally and cover the lateral aspect of the uncinate fasciculus, radiating in the crest forming the anterior part of the first temporal convolution' (e.g. see p. 755; Fig. 2). But in 1901, the pathway no longer extends to the temporal pole. Instead, the inferior frontal gyrus connects with the angular gyrus and the posterior superior temporal gyrus (labelled T_1 for the first temporal convolution). Specifically, the caption on page 250 shows 'The connections of the area of language, in particular the angular gyrus with Wernicke (T_1) and Broca (F_3) centers…*Arc*, *arcuate fasciculus*, connecting the AG and the first temporal gyrus with the center of Broca'.

The change between the 1895 and 1901 volumes of Déjèrine's classic work is attributable in part to the influence of von Monakow's writings, particularly *Gehirnpathologie* in 1897. Figure 2 shows Déjèrine's account in 1895, in which there is no emphasis on Broca's and Wernicke's centres. In contrast, von Monakow (1897) proposes the direct connection between the inferior frontal gyrus associated with 'motor aphasia', and those posterior temporal 'T_1' regions associated with 'sensory aphasia' (Fig. 2). The figure's influence is very apparent in the contemporary writings of the time. For example, in 1899, Barker translates and reprints von Monakow's figure (Fig. 2), the figure appears in Wernicke's last publication on aphasia (Wernicke, 1908, p. 316),

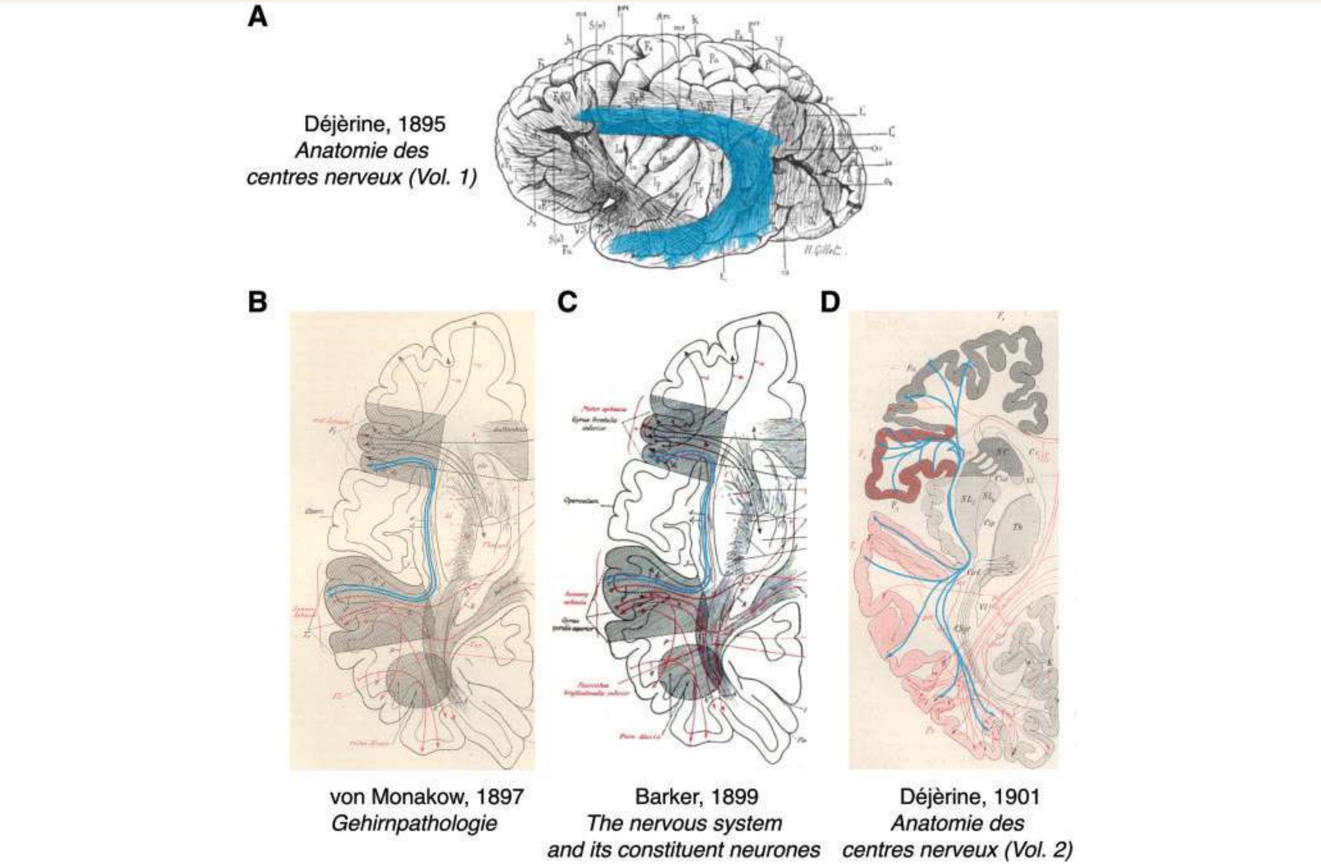


Figure 2 Turn of the 19th century notions of the SLF/AF (marked in blue). (**A**) Déjèrine's (1895) examination of the SLF/AF projects from the *pars triangularis* of the inferior frontal gyrus to the temporal pole. (**B**) In his 1897 *Gehirnpathologie*, von Monakow proposes connectivity via the arcuate fasciculus from the inferior frontal gyrus (F_3), in which damage is associated with 'motor aphasia', to the posterior superior temporal gyrus (T_1), in which damage is associated with 'sensory aphasia'. Modified from von Monakow (1897). (**C**) Barker (1899) and others reprint this figure. (**D**) By 1901, in the second edition of *Anatomie des centres nerveux*, Déjèrine's understanding of the SLF/AF has been modified to be more in line with von Monakow's proposal. The caption to this figure reads 'The connections of the area of language, in particular the angular gyrus with Wernicke (T_1) and Broca (F_3) centers . . . *Arc*, *arcuate fasciculus*, connecting the angular gyrus and the first temporal gyrus with the center of Broca'. Modified from Déjèrine (1901).

and it appears modified in the second edition of Déjèrine's Anatomie des centres nervoux in 1901 (Fig. 2).

In this way, the idea of a central role for the SLF/AF pathway to language became prominent in the latter part of the 19th century. Wernicke (1908) emphasizes the SLF/AF as one of two primary association fibre bundles important for language (the other being the uncinate fasciculus). Later, the emphasis on the SLF/AF was solidified by Konorski *et al.* (1961) and Geschwind (1965, 1970). Geschwind also attached prominence to the arcuate fasciculus terminology with less emphasis on the superior longitudinal fasciculus terminology, and further emphasized the 'shortening' of the pathway to the caudal temporal lobe rather than the rostral temporal lobe termination suggested, for example, by Meynert, Obersteiner and the early Déjèrine (Fig. 3A).

The superior longitudinal fasciculus/arcuate fasciculus since Geschwind

Since Geschwind, a number of divergent and sometimes conflicting descriptions of the SLF/AF fibre pathway have emerged. For example, Catani and colleagues (2005) and Thiebaut de Schotten *et al.* (2011*b*) used DTI to delineate the SLF/AF into three segments. Within this model there is a long 'direct temporo-frontal segment' that is essentially the classical SLF/AF pathway, and two lateral segments that comprise an indirect temporal–parietal–frontal pathway (Fig. 3B). This modifies, to some degree, the classical understanding by suggesting additional connectivity through the parietal lobe—a proposition made by Déjèrine as early as 1901. Other researchers provide an alternative characterization. For example, also using DTI, Glasser and Rilling (2008) propose a division of the SLF/AF into (i) a middle temporal-inferior frontal 'lexico-semantic' segment; and (ii) a superior temporal-inferior frontal 'phonological stream' segment (Fig. 3C).

More recently, data from non-human primates have provided new insights into temporal–parietal–frontal connectivity and challenged the classical notion of the SLF/AF by suggesting separation into four subcomponents—the superior longitudinal fasciculus I, superior longitudinal fasciculus II, superior longitudinal fasciculus III and the arcuate fasciculus (Fig. 3D; Petrides and Pandya, 1984,

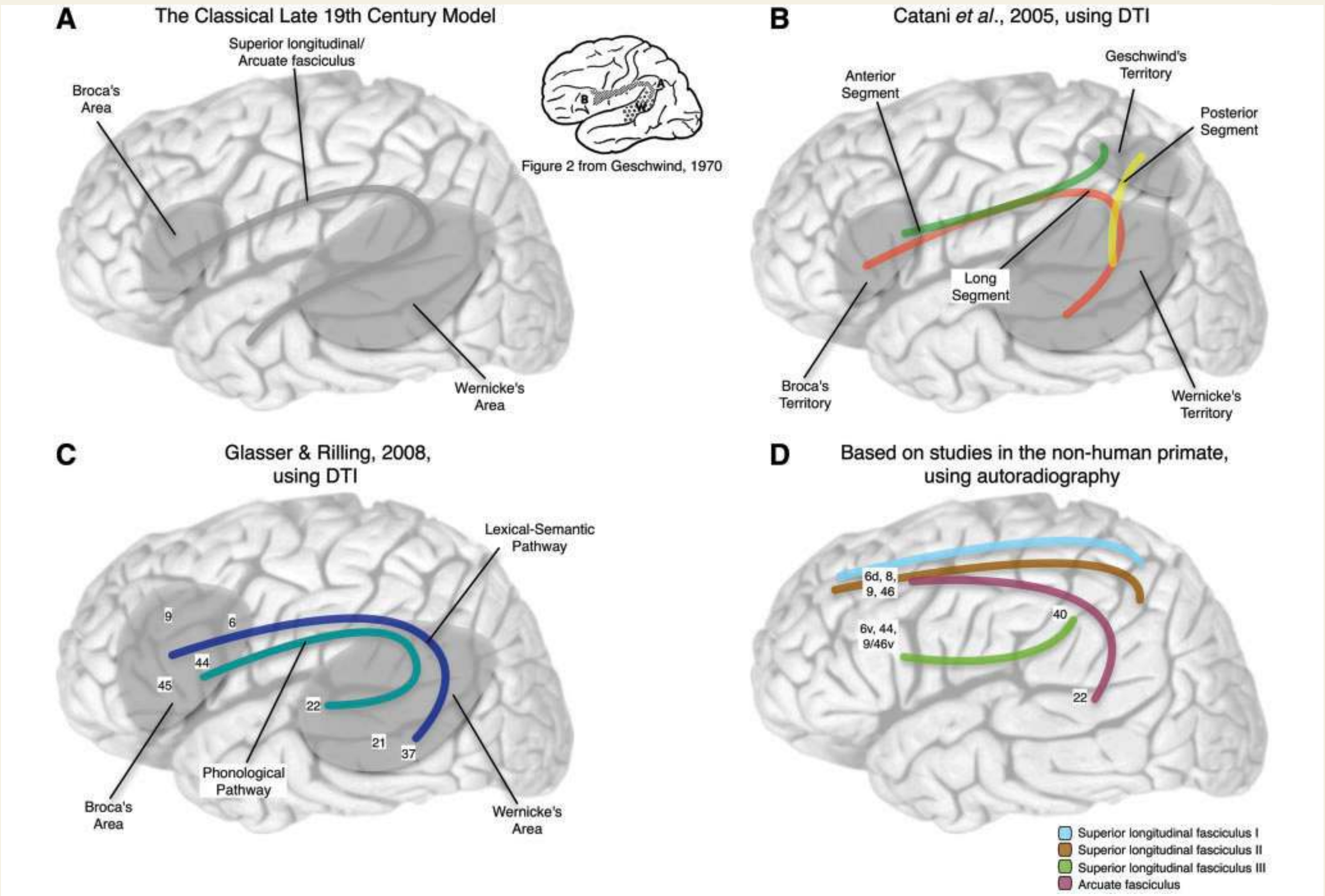


Figure 3 Contemporary and sometimes conflicting notions of SLF/AF connectivity. (**A**) The classical notion, weighted heavily toward the connectivity profile presented in Déjèrine's 1895 *Anatomie des centres nerveux.* The inset shows Geschwind's second figure from Geschwind (1970) (with permission). The caption for Fig. 2 of Geschwind's 'The organization of language and the brain' reads: 'Fig. 2. Lateral surface of the left hemisphere of the human brain. B, Broca's area, which lies anterior to the lower end of the motor cortex; W (open circles), Wernicke's area; A (closed circles), arcuate fasciculus, which connects Wernicke's to Broca's area. (See text.)'. (**B**) The 'three segment' model presented by Catani *et al*. (2005) (with permission). This model of SLF/AF better reflects von Monakow's and Geschwind's notions. (C) The 'two segment' model presented by Glasser and Rilling (2008) (with permission). Note that the frontal and temporal terminations are expanded in this model. Corresponding Brodmann's area for the origins and terminations were reported in the original paper. (**D**) A putative human connectivity profile adapted from tract-tracing studies in the macaque monkey. This model splits the superior longitudinal fasciculus into three segments in addition to the arcuate fasciculus. There is no direct posterior inferior frontal/posterior superior temporal connectivity in this model. Numbers refer to the corresponding Brodmann's areas for putative origins and terminations for the third superior longitudinal fasciculus segment and the arcuate fasciculus.

1988, 2006, 2009; Schmahmann and Pandya, 2006; Schmahmann *et al*., 2007; Yeterian *et al*., 2012). The superior longitudinal fasciculus III and arcuate fasciculus have received the most attention for language. The superior longitudinal fasciculus III connects the anterior inferior parietal lobule with the ventral premotor and posterior inferior frontal gyrus (Petrides and Pandya, 1984, 1988; Schmahmann and Pandya, 2006). Furthermore, using autoradiography, Petrides and Pandya (2009) verified that fibres originating from the inferior parietal lobule terminate in areas of the macaque brain that match the cytocarchitectonic profile of Brodmann areas 44 and 45 in the human brain (i.e. the classic Broca's area). This connectivity profile suggests the superior longitudinal fasciculus III is a candidate language pathway (Schmahmann and Pandya, 2006; Schmahmann *et al*., 2007).

The connectivity of the arcuate fasciculus component is more controversial. A prominent notion is that the human arcuate fasciculus connects the posterior superior temporal gyrus with the posterior inferior frontal gyrus. However, modern autoradiography studies suggest no such connection exists in the non-human primate (also see earlier work by Krieg, 1963, lesion 112). Tracer injections in the posterior superior temporal gyrus of the macaque do not terminate in the inferior frontal gyrus (an exception reported by Petrides and Pandya, 2009, is discussed later). Rather, several studies show that tracer injections in the posterior superior temporal gyrus (specifically area Tpt, proposed to be homologous to a small part of human Wernicke's area; Tranel *et al*., 1988) terminate in the more dorsal premotor and lateral prefrontal cortex distal to the classic language homologues (i.e. areas 9/46d, 8Ad and 6d) (Petrides and Pandya, 1984, 1988, 2006; Schmahmann and Pandya, 2006). See for example, Cases 6–8 of Petrides and Pandya (1984), Cases 7 and 8 of Petrides and Pandya (1988); and Cases 7 and 8 of Schmahmann and Pandya (2006). These tracer injection findings have been verified by studies using alternative histochemical tracing methods (Hackett *et al*., 1999, Cases 1 and 3; Romanski *et al*., 1999, Case CA), and histochemical techniques combined with electrode recording of the auditory cortex (Romanski *et al*., 1999). In addition, the course of the pathway is verified when tracer injections are placed in the frontal lobe regions (particularly area 8Ad; Petrides and Pandya, 2006, e.g. Case 1). Only one study in the macaque proposes a direct pathway connecting the posterior superior temporal gyrus and superior temporal sulcus with the inferior frontal gyrus through the arcuate fasciculus component of the superior longitudinal fasciculus (Petrides and Pandya, 2009). However, this appears to rest on data from one animal (Case 5) in which injection in parietal area ventral PG extended into the superior temporal sulcus and thus requires replication. The findings of Petrides and Pandya (2009) notwithstanding, work in the non-human primate challenges the notion that arcuate fasciculus connects the posterior superior temporal gyrus with posterior inferior frontal gyrus. Some human DTI work also corroborates the primate data (Makris *et al*., 2005; Rushworth *et al*., 2006; Frey *et al*., 2008; Saur *et al*., 2008; 2010; Thiebaut de Schotten *et al*., 2011*a*), in particular the finding that the rostral arcuate fasciculus terminates in the more dorsal premotor cortex (Frey *et al*., 2008; Bernal and Altman, 2010). However, it must be noted that there are DTI reports of inferior frontal gyrus-superior temporal gyrus connectivity through the arcuate fasciculus (Catani *et al*., 2002; Parker *et al*., 2005; Powell *et al*., 2006; Anwander *et al*., 2007; Wakana *et al*., 2007; Glasser and Rilling, 2008; Kaplan *et al*., 2010; Thiebaut de Schotten *et al*., 2011*a*).

Superior longitudinal fasciculus/arcuate fasciculus: functional and clinical notions relevant to language

The link between SLF/AF and language dates back to the proposal by Wernicke (1874), who suggested that lesion to association fibres connecting the sensory and motor speech areas would lead to a disconnection syndrome termed conduction aphasia (‘Leitungsaphasie’), a notion that was re-established in the 20th century by Geschwind (1965) and Konorski (1961). Conduction aphasia is a complex syndrome characterized by fluent, meaningful spontaneous speech with normal prosody and intact comprehension, but frequent phonemic paraphasic errors (substitution of sounds), and difficulty repeating heard speech (Bernal and Ardila, 2009; Ardila, 2010). The description of the syndrome and its relationship with SLF/AF was instrumental in crystalizing the ‘Broca–Wernicke–Geschwind’ language model, which emphasizes the inferior frontal gyrus as a motor speech centre, the posterior temporal cortex as the receptive language centre, and the SFL/AF as the connection between receptive and expressive language areas. Consistent with these early notions, contemporary models of language neurobiology propose that the SLF/AF connects brain regions involved in sensorimotor processes supporting speech production and speech perception (Warren *et al*., 2005; Hickok and Poeppel, 2007; Rauschecker and Scott, 2009; Rauschecker, 2011).

The emerging picture regarding the origins, terminations and general course of the SLF/AF pathway may lead to substantial revision of this model. As discussed in the previous section, one notion is that posterior superior temporal neurons project to the premotor cortex and not to the posterior inferior frontal gyrus, which calls into question the classical posterior inferior frontal gyrus–posterior temporal connection. However, although traditionally the posterior inferior frontal gyrus was seen as the primary motor speech centre, evidence suggests that the premotor cortex is involved in producing and also in perceiving speech (Duffau *et al*., 2003; Wilson *et al*., 2004; Bohland and Guenther, 2006; Callan *et al*., 2010; Peeva *et al*., 2010; Tremblay and Small, 2011). Hence, even if the temporal projection terminates in the premotor cortex rather than in the posterior inferior frontal gyrus, it may still be important for phonological processing and speech production. Furthermore, the superior longitudinal fasciculus III pathway, which has been proposed to connect the supramarginal gyrus with the posterior inferior frontal gyrus (Makris *et al*., 2005), may be important for both speech production and perception. Consistent with the idea of a role for both the superior longitudinal fasciculus III and arcuate fasciculus segments in phonological processing, it has been shown that electrical stimulation of the white matter underneath the inferior frontal, inferior parietal and posterior superior temporal cortex results in phonemic paraphasias (Duffau *et al*., 2002) and also speech arrest/articulation disturbance (Duffau *et al*., 2002, 2003; Maldonado *et al*., 2011*a*). Marchina *et al*. (2011) found in a group of 30 left hemisphere stroke patients that measures of fluency are scaled to SLF/AF lesion load, but not to uncinate fasciculus or extreme capsule lesion load (also see Tanabe *et al*., 1987). Similarly, Breier *et al*. (2008) measured DTI fractional anisotropy in a group of 20 patients with left hemisphere stroke and showed a relationship between damage to superior longitudinal fasciculus and arcuate fasciculus (separately) and verbal repetition, independent of damage to surrounding cortical areas.

In spite of such evidence, the importance of connectivity via the SLF/AF for speech, and particularly for conduction aphasia, has been regularly challenged (Bernal and Ardila, 2009). Lesions resulting in conduction aphasia are rarely focal and occur concomitant with damage to surrounding grey matter in the insula, superior temporal cortex, and/or inferior parietal lobule (Goldstein and Marmor, 1938; Benson *et al*., 1973; Green and Howes, 1977; Damasio and Damasio, 1980; Kempler *et al*., 1988). Furthermore, damage to white matter does not appear to be necessary for repetition deficits (Mendez and Benson, 1985; Shuren *et al*., 1995; Selnes *et al*., 2002). Electrical stimulation of the posterior superior temporal cortex can lead to a repetition deficit (Anderson *et al*., 1999), and even complete agenesis of the left SLF/AF is not associated with conduction aphasic symptoms (Bernal *et al*., 2010). Thus, it is difficult to ascertain whether the observed deficits are due to white matter rather than cortical defects.

Some more comprehensive studies focusing on these issues have been conducted. For example, in a detailed examination of the role of the SLF/AF for conduction aphasia, Axer and colleagues

(2001) identified three subtypes of conduction aphasia based on the lesion site. Only the third subtype, mixed conduction aphasia, was associated with lesion to SLF/AF, and these patients were also most impaired in the repetition tasks. This apparent diversity of findings across subtypes of conduction aphasia may be related to the complex symptomatology of the disorder, which includes a repetition disorder, but also impaired word-finding and phonemic paraphasias.

Another way of looking at role of the SLF/AF in speech is to examine the effect of damage on individual symptoms such as repetition difficulty, rather than collection of symptoms such as conduction aphasia, since different clinical manifestations may be related to different lesion sites. This was the approach taken by Fridriksson and colleagues (2010), who showed that repetition difficulty in a group of 45 patients with left hemisphere stroke is predicted by both a lesion to the SLF/AF, and hypoperfusion in the supramarginal gyrus. This is consistent with findings of a role for the posterior temporal cortex/supramarginal gyrus in repetition tasks (Dhanjal *et al*., 2008; Peschke *et al*., 2009, 2012; Tremblay *et al*., 2011) and speech production (Hickok *et al*., 2000), and potentially with the proposed connectivity of the superior longitudinal fasciculus III component. Thus, there is some evidence for a double dissociation, with reported cases of repetition deficits not associated with lesions to the SLF/AF (Mendez and Benson, 1985; Shuren *et al*., 1995; Selnes *et al*., 2002), and cases of lesions to the SLF/AF not leading to repetition deficits (Mendez and Benson, 1985; Shuren *et al*., 1995; Selnes *et al*., 2002; Bernal *et al*., 2010).

In addition to a much discussed role in speech processing and production, some researchers have proposed other functions for the SLF/AF. For example, some have suggested that part of this pathway supports semantic processing (Glasser and Rilling, 2008) or reading (Yeatman *et al*., 2011). Others (Friederici, 2009; Brauer *et al*., 2011; Papoutsi *et al*., 2011) have proposed that the dorsal stream is also involved in processing syntactic complexity during language comprehension. Still others have suggested that the arcuate fasciculus part of the superior longitudinal fasciculus is involved in non-linguistic sound localization and auditory-spatial awareness, and do not consider it to be a language pathway (Petrides and Pandya, 2002; Makris *et al*., 2005; Schmahmann and Pandya, 2006). In summary, the role of the SLF/AF in phonological processing during speech perception and production is supported, but there is no consensus about its importance in (i) the aetiology of conduction aphasia; (ii) semantic or syntactic processing during language production and comprehension or in (iii) auditory-spatial processing.

Summary of the dorsal stream

The current status of the anatomical connectivity of the dorsal stream is represented by a tension between those maintaining the classical understanding, suggesting that 'there is the well-established direct pathway connecting Wernicke's territory in the left temporal lobe with Broca's territory in the left frontal lobe through the arcuate fasciculus' (Catani *et al*., 2007, p. 17163), and those suggesting a significant revision—e.g. those claiming that 'the arcuate fasciculus does not link the mid-superior temporal region with the cortex homologous to Broca's area' (Schmahmann *et al*., 2007, p. 648). Currently, the field has no clear model of SLF/AF connectivity. A number of studies still support an extensive fronto-temporal connectivity identified in the classical literature (Fig. 3A). Recent work by Catani and colleagues (2005) and by Glasser and Rilling (2008) suggests a revision to the classical model based on DTI (Fig. 3B and C). Finally, work in the non-human primate using tract-tracing methodologies suggests that the SLF/AF can be further divided into constituent components (Fig. 3D). To reconcile these models of SLF/AF connectivity, more work is needed. Most promising are the investigations comparing directly the findings from diffusion-weighted imaging and autoradiography in the non-human primate (Schmahmann *et al*, 2007; Thiebaut de Schotten *et al*, 2011*a*), as this will help establish more accurate *in vivo* tract tracing methods in humans. A clearer model of connectivity will help to establish the function(s) of the dorsal language stream, and constrain models of the neurobiology of language (e.g. Hickok and Poeppel, 2007, Fig. 1, p. 395, and Vigneau *et al*., 2006, Fig. 5, p. 1422).

Fibre pathways of the ventral stream

Uncinate fasciculus

The uncinate fasciculus is a relatively short pathway connecting anterior temporal to inferior frontal areas. The earliest descriptions date from Reil (1809*c*,*d*) and Burdach (1819) who located its rostral termination in the orbital and lateral frontal cortex. The posterior termination was ascribed to the anterior superior temporal gyrus and superior temporal sulcus, and temporal pole. This description was largely unmodified in the latter part of the 19th century (Meynert, 1885; Sachs, 1893; Déjèrine, 1895; Obersteiner, 1896; Wernicke, 1897; Barker, 1899).

These early notions have been confirmed in later studies using post-mortem blunt fibre dissection (Ludwig and Klingler, 1956; Klingler and Gloor, 1960; Ebeling and von Cramon, 1992; Peuskens *et al*., 2004), post-mortem blunt fibre dissection combined with MRI (Kier *et al*., 2004), and stained preparations (Highley *et al*., 2002). In humans, there is also evidence for temporo-frontal connectivity through the amygdala (Klingler and Gloor, 1960; Ebeling and von Cramon, 1992). Work with non-human primates confirms the general course described in humans (Mettler, 1935*b*, *c*; Levin, 1936; Pribram *et al*., 1950; Pribram and MacLean, 1953; Kawamura and Naito, 1984; Petrides and Pandya, 1988, 2002, 2007; Schmahmann *et al*., 2007; Streitfeld, 1980 for review of earlier work), including the connectivity with the amygdala (Ghashghaei and Barbas, 2002; Schmahmann and Pandya, 2006). Work on non-human primates also suggests more widespread connectivity with the frontal cortex (Mettler, 1935*b*; Bailey *et al*., 1943*a*, *b*; Bignall, 1969; Barbas and Pandya, 1989; Ungerleider *et al*., 1989; Carmichael and Price, 1995; Kondo *et al*., 2005; Saleem *et al*., 2008; Muñoz *et al*., 2009), which extend to the medial and rostral frontal cortex (even areas 10 and 11; Muñoz *et al*., 2009; Petrides and Pandya, 1988, especially Cases 1 and 3; Petrides and Pandya, 2007, Cases 1 and 7) and are likely to be bidirectional (Nauta, 1964). DTI studies in humans also corroborate the general course of the uncinate fasciculus (Bürgel *et al*., 2006; Wakana *et al*., 2007; Catani and Thiebaut de Schotten, 2008; Hua *et al*., 2009; Oishi *et al*., 2011; Thiebaut de Schotten *et al*., 2011*b*; Turken and Dronkers, 2011). Hence, at a general level, the existence and course of the uncinate fasciculus is relatively uncontroversial; what remains to be clarified is its specific function.

Uncinate fasciculus: functional and clinical correlates relevant to language

Wernicke (1908) noted that uncinate fasciculus was one of 'two important association bundles which must be considered in the anatomy of the speech regions . . . some portions of it certainly extend to the third frontal convolution, including Broca's convolution and the speech region of the first temporal convolution' (pp. 314–15). Despite this early call to its functional importance, the uncinate fasciculus has only recently garnered attention as a ventral language pathway (Parker *et al*., 2005; Papagno, 2011; Weiller *et al*., 2011).

One of the potential language-related functions of the uncinate fasciculus concerns semantic processing, a function also ascribed to the anterior temporal cortex (especially the temporal pole), which forms the caudal termination of the uncinate fasciculus. Indeed, the temporal pole has been described as a potential 'hub' of a distributed semantic memory network (Lu *et al*., 2002; Patterson *et al*., 2007; Holland and Lambon Ralph, 2010; Tsapkini *et al*., 2011). In support of a semantic function, reduction in fractional anisotropy (indicative of white matter damage) in the uncinate fasciculus is related to the semantic variant subtype of primary progressive aphasia (Gorno-Tempini *et al*., 2004; Agosta *et al*., 2011; Galantucci *et al*., 2011). Moreover, results of a recent study examining 44 patients undergoing surgical resection of the anterior temporal cortex show that semantic impairments in these patients are selectively associated with damage to the uncinate fasciculus (Papagno *et al*., 2011)—patients with accompanying uncinate fasciculus resection were impaired on picture naming of objects and famous faces. Moreover, uncinate fasciculus electrostimulation induced phonemic paraphasias, but this finding is not replicated by Duffau and colleagues (2009). Papagno (2011*a*) discusses this discrepancy.

In addition to semantic processing, the uncinate fasciculus has been associated with auditory working memory (Frey *et al*., 2004; Fritz *et al*., 2005; Diehl *et al*., 2008; McDonald *et al*., 2008; Muñoz *et al*., 2009). In human, reduced white matter integrity in the uncinate fasciculus is associated with reduced auditory memory (Diehl *et al*., 2008; McDonald *et al*., 2008). Based on the brain regions it connects, it has also been suggested that the uncinate fasciculus may contribute to sound recognition (Clarke *et al*., 2002), and to the attachment of emotional significance to auditory stimuli (Schmahmann and Pandya, 2006). This interpretation is consistent with prior findings linking the anterior superior temporal gyrus/superior temporal sulcus to speech and voice processing in both human (Belin and Zatorre, 2003; Rauschecker and Scott, 2009) and non-human primates (Petkov *et al*., 2008, 2009). In summary, there is suggestive evidence for involvement of the uncinate fasciculus in at least two language-related functions: semantic processing and auditory working memory/sound recognition.

Extreme capsule

The extreme capsule is located between the claustrum and insula, running parallel to the external capsule with which it is sometimes confused (Fig. 4). Although described by Obertsteiner (1896), explicit description of the extreme capsule is conspicuously absent in major anatomical writings of the time (Meynert, 1885; Sachs, 1893; Flechsig, 1896; Barker, 1899; Gordinier, 1899). Déjèrine (1895; pp. 808–9), who distinguished the extreme capsule from both the uncinate fasciculus and the inferior longitudinal fasciculus, believed that the extreme capsule contained both association fibres and fibres of the external capsule, stating that 'the fibers of the external capsule are therefore part of the fibers of the EmC (extreme capsule), which also contain a very large number of short association fibers connecting two convolutions adjacent to, or more or less distant from, the insula'.

Anatomical work focusing on the human extreme capsule is scarce (Rae, 1954). For example, in his description of the inferior fronto-occipital fasciculus, Curran (1909) described the course of the inferior fronto-occipital fasciculus as passing through the extreme capsule territory, but did not explicitly name the extreme capsule as a dissociable association pathway *per se*, consistent with Ludwig and Klingler (1956) and more recently with Kier and colleagues (2004). In contrast, studies focusing on extreme capsule fibres in non-human primates are more common. For example, earlier studies with experimental lesions in the macaque (Mettler, 1935*b*, *c*; Lockard, 1948; Berke, 1960) identified cortical association fibres passing through the extreme capsule and connecting frontal, insular and temporal cortices. More recent autoradiographic studies in non-human primates have suggested that the extreme capsule is a long association fibre pathway connecting the anterior, middle and possibly posterior superior and middle temporal cortex with the caudal and ventrolateral prefrontal cortex [Petrides and Pandya, 1988 (Cases 4 and 5);

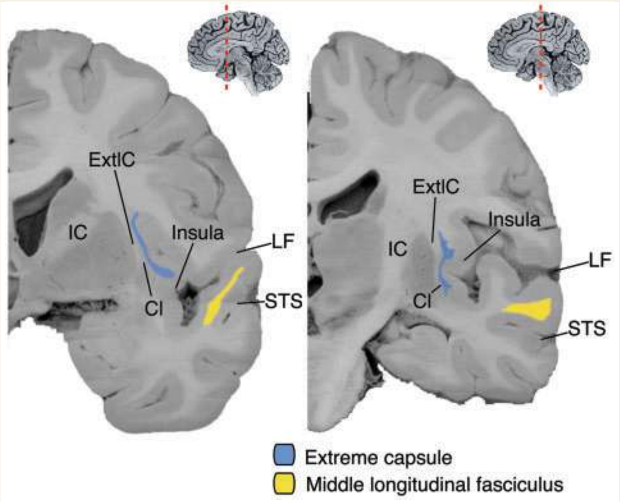


Figure 4 Proposed course of the extreme capsule (blue) and middle longitudinal fasciculus (yellow) in human coronal section. CI = claustrum; ExtIC = external capsule; IC = internal capsule; LF = lateral fissure; STS = superior temporal sulcus.

Schmahmann and Pandya, 2006; Schmahmann *et al*., 2007]. This connectivity appears to be bidirectional (Petrides and Pandya, 2007).

DTI results provide some support for this description of the extreme capsule (Frey *et al*., 2008; Saur *et al*., 2008; Makris and Pandya, 2009; Brauer *et al*., 2011; Wong *et al*., 2011). For example, Makris and Pandya (2009) suggested that the extreme capsule could be dissociated from the uncinate fasciculus and inferior longitudinal fasciculus in the anterior temporal lobe. However, the pathway they identified extends more posteriorly, into the angular gyrus, than is typically indicated by autoradiography (Petrides and Pandya, 1988, 2007; Schmahmann and Pandya, 2006; Schmahmann *et al*., 2007) and lesion (Berke, 1960) studies in the non-human primate. Notably, though, the extreme capsule is absent in several other DTI studies (Bürgel *et al*., 2006; Wakana *et al*., 2007; Catani and Thiebaut de Schotten, 2008; Hua *et al*., 2009; Thiebaut de Schotten *et al*., 2011*b*; Turken and Dronkers, 2011). For example, Oishi and colleagues (2011) do not list the extreme capsule in their comprehensive DTI atlas of human white matter because, at the scanning resolution at which their data were acquired (2.5 mm), they could not dissociate it from the claustrum and external capsule (also see Anwander *et al*., 2007). These discrepancies suggest some caution is warranted in interpreting DTI data of this pathway.

Extreme capsule: functional and clinical notions relevant to language

The extreme capsule links the anterior part of the inferior frontal gyrus—associated with, among other processes, the controlled retrieval and selection among competing semantic representations (Thompson-Schill *et al*., 1997; Wagner *et al*., 2001; Gough *et al*., 2005; Moss *et al*., 2005)—with the middle-to-posterior portion of the superior and middle temporal cortex, associated with the long-term storage of semantic information (Martin and Chao, 2001; Hickok and Poeppel, 2007; Binney *et al*., 2010; Price, 2010). It has therefore been suggested that the extreme capsule functions as part of the ventral language system for processing sound-to-meaning (Saur *et al*., 2008). Empirical evidence for this possibility comes from recent studies using DTI, functional imaging and electrostimulation. Using DTI and functional MRI, Saur and colleagues (2008, 2010) showed that this tract, along with the inferior longitudinal fasciculus and middle longitudinal fasciculus, connected regions that were active during auditory comprehension of meaningful compared to non-meaningful sentences. Wong and colleagues (2011) showed that DTI fractional anisotropy of the posterior part of this pathway was associated with participants' ability to link meaning with changes in pitch pattern within syllables embedded in an unfamiliar language. Using electrostimulation, Duffau and colleagues (2005) found that stimulating extreme capsule white matter resulted in semantic paraphasias (i.e. substitution of a target word by a semantically related word, such as cat → dog), although these authors also labelled this the inferior fronto-occipital fasciculus (see Kier *et al*., 2004 for a discussion of the confusion among these pathways and the uncinate fasciculus). Overall, these data are consistent with the idea that the extreme capsule is part of a ventral language stream for semantic processing. However, there is also some evidence for the involvement of the extreme capsule in phonological working memory, which is consistent with the proposal that the extreme capsule is part of a network supporting expressive language (Makris and Pandya, 2009). Specifically, DTI fractional anisotropy of the extreme capsule is related to individual differences in learning a simplified artificial language under conditions of linguistic interference that tax phonological working memory (Lopez-Barroso *et al*., 2011), and there is association of conduction aphasia with lesion of the extreme capsule (Damasio and Damasio, 1980). In summary, at least two functions have been ascribed to the extreme capsule: semantic processing during language comprehension and phonological working memory.

Middle longitudinal fasciculus

The middle longitudinal fasciculus is a white matter tract that connects inferior parietal lobule with temporal cortices. It was first described by Seltzer and Pandya (1984), who found that injections in the middle and caudal thirds of the macaque inferior parietal lobule, corresponding to human angular gyrus and lower bank of the intraparietal sulcus, resulted in radiolabelled isotope indicating substantial projections to the temporal lobe (e.g. Cases 16–19). In contrast, injections in the rostral inferior parietal lobule (area PF and rostral PFG), corresponding to the human supramarginal gyrus, did not result in substantial terminal labelling in the temporal lobe (e.g. Cases 12 and 13; but see Case 14). From these data, Seltzer and Pandya (1984) defined the middle longitudinal fasciculus as a unique fibre bundle coursing through the superior temporal gyrus and terminating in the superior temporal sulcus intermittently as the bundle runs rostrally in the temporal lobe (Fig. 4). They also dissociated this fibre pathway from the inferior longitudinal fasciculus, superior longitudinal fasciculus and arcuate fasciculus pathways.

Historically, evidence for an extensive long association pathway connecting the parietal cortex to the superior temporal cortex in the non-human primate is equivocal. For example, using a combination of surgical lesion with Marchi staining (Mettler, 1932), Mettler (1935*a*) found little evidence for such a connection after a focal lesion to the posterior end of the superior temporal sulcus (caudal area PG and Opt; Case 2). However, more recent non-human tract-tracing studies replicate Seltzer and Pandya (2006). For example, in Case 4 of Schmahmann and Pandya (2006), fibres leaving an injection site in the same area defined by Mettler (caudal area PG and Opt) did descend rostrally into the white matter of the superior temporal gyrus, forming a fibre bundle that they defined as the middle longitudinal fasciculus. Further replications using a number of different histochemical methods have strengthened the claim of the existence of the middle longitudinal fasciculus in the non-human primate (Ban, 1986; Neal *et al*., 1988; Cavada and Goldman-Rakic, 1989; Seltzer and Pandya, 1989; Barnes and Pandya, 1992; Schmahmann and Pandya, 2006).

In contrast, the middle longitudinal fasciculus is less well-established in humans. It is absent in both historic (Burdach, 1819; Foville, 1844; Meynert, 1885; Déjèrine, 1895, 1901) and contemporary atlases of white matter connectivity (e.g. Oishi *et al*., 2011*b*). Most recent DTI studies in humans fail to define it (Bürgel *et al*., 2006; Wakana *et al*., 2007; Catani and Thiebaut de Schotten, 2008; Hua *et al*., 2009; Thiebaut de Schotten *et al*., 2011*b*), even when the focus is on association pathways of the temporal lobe (Catani *et al*., 2005; Holl *et al*., 2011), or when multiple methods are used (e.g. DTI, post-mortem blunt fibre dissection and histology; Holl *et al*., 2011). However, a few investigators have identified the pathway in humans. For example, studies using histology (Makris, 1999) and DTI (Frey *et al*., 2008; Saur *et al*., 2008; Makris *et al*., 2009; Turken and Dronkers, 2011; Wong *et al*., 2011) have identified a middle longitudinal fasciculus pathway in the white matter of the superior temporal gyrus, extending from the angular gyrus to the anterior superior temporal cortex, and running dorsal and medial to the SLF/AF. The discrepancies may be explained by historical misidentification of the middle longitudinal fasciculus as the temporal stem of the SLF/AF, or as the inferior longitudinal fasciculus.

Middle longitudinal fasciculus: functional and clinical notions relevant to language

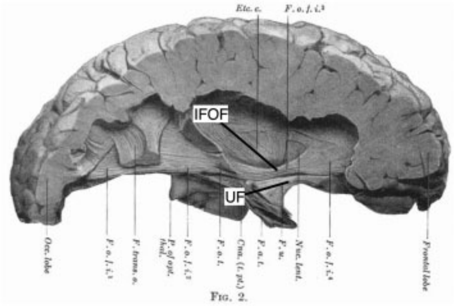
Like the extreme capsule and uncinate fasciculus, the middle longitudinal fasciculus has historically received very little attention in relation to language, but this is beginning to change. For example, Saur and colleagues (2008, 2010) and Wong and colleagues (2011) recently identified the middle longitudinal fasciculus as part of the ventral sound-to-meaning pathway. Wong *et al*. (2011) also suggested that the middle longitudinal fasciculus carries information downstream from primary and secondary auditory association areas to posterior and anterior superior temporal gyrus/superior temporal sulcus. Makris and colleagues (2009) noted the functional importance for language of connections between the angular gyrus and superior temporal gyrus, particularly on the left hemisphere. Such connectivity would potentially have implications for both phonological and semantic processing, as both functions are associated with the superior temporal gyrus/superior temporal sulcus, and angular gyrus (Hickok and Poeppel, 2007; Binder *et al*., 2009; Brownsett and Wise, 2010). However, De Witt Hamer and colleagues (2011) did not find evidence for any language disturbance following incomplete resection of and electrostimulation of the anterior part of the left middle longitudinal fasciculus in eight patients, even though they were able to elicit semantic paraphasias during electrostimulation of the more medial inferior fronto-occipital fasciculus in these same patients. Notably, though, resection in all patients consisted of the anterior part of the middle longitudinal fasciculus (anterior to the Heschl's gyrus), and therefore it is unclear if lesion to the posterior stem of the middle longitudinal fasciculus would elicit language disturbance. Overall, the available evidence suggests that this pathway may be important for sound processing and possibly auditory language processing/comprehension. However, given the small number of studies that have been conducted examining the middle longitudinal fasciculus, it is best to treat ascribed functions of this pathway as speculative.

The inferior longitudinal fasciculus and inferior fronto-occipital fasciculus

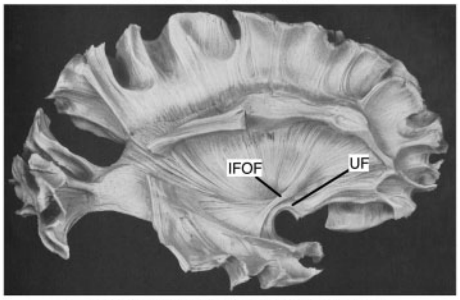
The inferior longitudinal fasciculus and inferior fronto-occipital fasciculus fibre pathways are proposed to connect occipital cortices to the anterior temporal and inferior frontal cortices (note the inferior fronto-occipital fasciculus pathway is synonymous with the inferior occipito-frontal fasciculus). There is also a fronto-occipital fasciculus that is distinct from, but often confused with, the inferior fronto-occipital fasciculus. The literature on the inferior longitudinal fasciculus and inferior fronto-occipital fasciculus is marked by two important controversies. The first one concerns the nature of these fibres, whether they really form a long association fibre system, or whether these fibres are actually misidentified projection fibres to the occipital lobe. The second controversy concerns the status of these fibres as either one or two association fibre pathways.

Investigation of the inferior longitudinal fasciculus begins more or less with Burdach (1819) who identified a bundle of fibres originating in the occipital pole, coursing laterally through the temporal lobe, and terminating in the lateral frontal pole. He termed this (p. 152) the 'untre Längenbündel (fasciculus longitudinalis inferior)' and distinguished its anterior course from the uncinate fasciculus. Dèjèrine (1895) updated this account and identified the inferior longitudinal fasciculus as one of five cortico-cortical long association fibre pathways, although he, like Sachs (1897), located the rostral termination of inferior longitudinal fasciculus in the temporal pole: 'The inferior longitudinal fasciculus of Burdach is an anteroposterior bundle . . . extending from the occipital pole to the temporal pole' (p. 765). Furthermore, although he acknowledged the superior part might contain thalamo-cortical projection fibres, Déjèrine emphasized that the inferior longitudinal fasciculus 'is exclusively an association bundle in its lower part' to be distinguished from thalamo-cortical projection fibres to the occipital lobe identified by the 19th century investigators Gratiolet, Meynert, Wernicke, Charcot, Ballet and Brisaud (p. 773). Here, he hits upon one point of contention, whereby some investigators argued that the inferior longitudinal fasciculus was a visual projection system (Flechsig, 1895; Probst, 1901; Niessl-Mayendorf, 1903; Redlich, 1905)—Flechsig (1896) called it 'nothing more than a part of the optic radiation of Gratiolet' (p. 2). Others took the position that it was an association system as promoted by Burdach, Sachs, Déjèrine and others (e.g. Edinger, 1896; von Monakow, 1905; a more extensive historical account of these conflicting interpretations is offered in Davis, 1921; Schmahmann and Pandya, 2006). While some recent work has challenged the notion of a separate long association fibre system in the temporal lobe (Tusa and Ungerleider, 1985), other investigations in the non-human primate (Mettler, 1935*b*; Seltzer and Pandya, 1984; Schmahmann and Pandya, 2006), and DTI and electrostimulation in humans (Catani *et al*., 2002, 2003; Mandonnet *et al*., 2007; Wakana *et al*., 2007; Hua *et al*., 2009; Oishi *et al*., 2011; Thiebaut de Schotten *et al*., 2011*b*) do support the existence of an association inferior longitudinal fasciculus separate from a projection system.

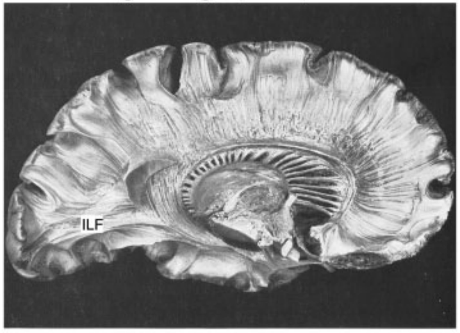
A second pathway coursing through the inferior temporal lobe, which is proposed to establish a continuous connection between the occipital lobe and the frontal lobe, is termed the inferior fronto-occipital fasciculus. As mentioned above, there is debate about whether the inferior longitudinal fasciculus and inferior fronto-occipital fasciculus are really two distinct pathways. Instead, it has been suggested (i) that there is only one pathway, the inferior fronto-occipital fasciculus (Davis, 1921) and (ii) that



Curran, 1909; Figure 2



Ludwig & Klingler, 1956; Tabula 8



Ludwig & Klingler, 1956; Tabula 34

Figure 5 Blunt fibre dissection of the inferior fronto-occipital fasciculus (IFOF), uncinate fasciculus (UF), and inferior longitudinal fasciculus (ILF). *Top*: Modified from Curren (1909) showing one of the first identifications of the inferior fronto-occipital fasciculus. *Middle* and *Bottom*: Modified with permission from the comprehensive atlas of Ludwig and Klingler (1956). Middle: The uncinate fasciculus and anterior part of the inferior fronto-occipital fasciculus. *Bottom*: The posterior part of the inferior longitudinal fasciculus.

the inferior fronto-occipital fasciculus is actually the inferior longitudinal fasciculus continuing into the already-discussed middle longitudinal fasciculus, extreme capsule and uncinate fasciculus fibre pathways (Schmahmann and Pandya, 2006).

Although Burdach (1822) claimed that inferior longitudinal fasciculus fibres extended to the frontal pole, explicit definition of the inferior fronto-occipital fasciculus would wait until the early 20th century (Trolard, 1906; Curran, 1909). Curran believed he had defined a new, continuous pathway from the occipital to frontal lobes (Fig. 5), although Barker (1899, p. 1065) noted that 'the anterior part of its course is extremely difficult to differentiate fibres which belong to it from other fibres which are adjacent to it or even mixed up with it', a sentiment that is echoed by contemporary researchers (Martino *et al*., 2010; Peltier *et al*., 2010).

More recent fibre dissection studies (Kier *et al*., 2004; Peuskens *et al*., 2004; Martino *et al*., 2010; Holl *et al*., 2011) have failed to clarify whether there are one or two inferior long association pathways in the temporal lobe, and whether there is a direct connection between the occipital and frontal lobes. DTI studies consistently suggest that two pathways exist (Catani *et al*., 2002, 2003; Wakana *et al*., 2007; Hua *et al*., 2009; Holl *et al*., 2011; Oishi *et al*., 2011; Thiebaut de Schotten *et al*., 2011*b*; Turken and Dronkers, 2011). In contrast, in the non-human primate, autoradiography studies consistently argue the opposite—that while there is an inferior longitudinal fasciculus in the inferior temporal lobe, there is no inferior fronto-occipital fasciculus that courses uninterrupted from the occipital to the frontal lobe (Mettler, 1935*d*; Schmahmann and Pandya, 2006; Yeterian *et al*., 2011).

In summary, notwithstanding earlier controversy, evidence for an association system in the inferior temporal lobe is substantial across post-mortem blunt fibre dissection, DTI and autoradiography methods. However, it remains unclear whether there are one or two such pathways, and/or whether there is uninterrupted occipito-frontal connectivity.

Inferior longitudinal fasciculus and inferior fronto-occipital fasciculus: functional and clinical notions relevant to language

Several authors have focused on the visual functions of the inferior longitudinal fasciculus/inferior fronto-occipital fasciculus, as the occipito-temporal connectivity of this pathway has been proposed to support object recognition, face processing and visual semantic memory as part of the ventral visual pathway (Ross, 1980; Milner and Goodale, 2008; Schmahmann *et al*., 2008). Such functions are also relevant to language, as the ventral pathway may be involved in linking speech to higher-level semantic representations (Vigneau *et al*., 2006; Hickok and Poeppel, 2007). Indeed, Duffau and colleagues (2005) and Mandonnet *et al.* (2007) have shown that intraoperative electrostimulation of the white matter under the superior temporal sulcus leads to semantic paraphasias. They identified this as the white matter of the inferior fronto-occipital fasciculus (Duffau *et al*., 2005; Mandonnet *et al*., 2007), and Mandonnet and colleagues (2007) further suggested that no naming disturbance was associated with stimulation of the inferior longitudinal fasciculus. In contrast, Saur and colleagues (2008, 2010) and Wong and colleagues (2011) suggest that the inferior longitudinal fasciculus is also part of a temporal lobe fibre network supporting language comprehension, together with the middle longitudinal fasciculus and extreme capsule as part of the ventral semantic stream. Turken and Dronkers (2011) proposed a similar function, but, based on the suggested connectivity of the temporal cortex to the inferior frontal gyrus, emphasized the contribution of the inferior fronto-occipital fasciculus to semantic working memory. However, they too noted the difficulty of dissociating anatomically and functionally the contribution of inferior fronto-occipital fasciculus/inferior longitudinal fasciculus pathways and the adjacent uncinate fasciculus and extreme capsule fibre pathways. To this point, investigation of the functional significance of these inferior temporal pathways is sparse; resolution of the controversies surrounding their anatomy will proceed concurrently with investigation of their function.

Summary of the ventral stream

Clarifying the connectivity of the ventral pathway is crucial for many prominent theoretical models of the neurobiology of language. While classical language models propose one dorsal route, there are likely to be multiple such routes. For example, understanding extreme capsule connectivity in humans is very important, as this pathway potentially establishes an alternative ventral route from the anterior superior temporal lobe to the anterior inferior frontal gyrus, a region that may be important for processing semantic information during language comprehension (Hagoort *et al*., 2004; Hagoort, 2005). Moreover, the importance of the anterior (as opposed to posterior) superior temporal gyrus and sulcus has been emphasized for speech comprehension and syntactic processing (Binder *et al*., 2000; Scott *et al*., 2000; Humphries *et al*., 2001, Humphries *et al*., 2006; Scott and Johnsrude, 2003; Cohen *et al*., 2004; Obleser *et al*., 2011; Dewitt and Rauschecker, 2012). In a recent meta-analysis, DeWitt and Rauschecker (2012) argued that the extant functional MRI evidence suggests speech comprehension proceeds from primary auditory cortex along an anterior-directed ventral stream pathway (*cf*. Saur *et al*., 2008). Vigneau and colleagues (2006) also suggested revising the classic Broca–Wernicke–Geschwind model to account for additional semantic processing along this ventral pathway, specifically via the inferior longitudinal fasciculus and uncinate fasciculus.

Summary and concluding remarks

> ‘In all domains, physiology has its firmest foundations in anatomy’ (Brodmann, 1908).

Language is an extremely complex faculty that allows us to express and comprehend ideas and emotions in the service of communication. Probably, the only universal consensus is that such a complex behaviour emerges from the interaction of a number of functionally and anatomically specified cortical and subcortical regions connected by a complex system of fibre pathways. Modern neuroscience methods have brought with them a sea change in the theoretical approach to the neurobiology of language, suggesting that the language network is widely distributed, and that its connections are numerous. This is a major shift in focus—the number of pathways that have garnered attention for language connectivity has expanded considerably since recent major reviews of this topic (Catani and Mesulam, 2008; Bernal and Ardila, 2009), which focused on SLF/AF connectivity. This largely reflects the growing dissatisfaction with the ability of those classical language models to explain the diversity of neuroimaging and clinical findings (Bernal and Ardila, 2009). Indeed, even the connectivity profile of the SLF/AF pathway has come under reconsideration since the establishment of the classical model. Figure 6 summarizes emerging and competing models of perisylvian connectivity. While most of these models propose a dual (dorsal, ventral) architecture for language, the function and connectivity of both pathways remains controversial.

As Fig. 6 suggests, there is no consensus model of either dorsal or ventral stream connectivity. The following are the major controversies that we expect will drive research in this area. With respect to the dorsal stream, controversy surrounds (i) the possible division of the human SLF/AF pathway into several components; (ii) the existence of direct posterior temporal-inferior frontal (i.e. Wernicke–Broca) connectivity; (iii) whether the caudal (temporal) component of the SLF/AF extends to the temporal pole; (iv) the specific location of the rostral terminations of the SLF/AF; and (iv) the nature of fronto-parietal and temporo-parietal connectivity via the SLF/AF. With respect to the ventral stream, outstanding questions focus on: (i) the parietal-temporal connectivity via the middle longitudinal fasciculus; (ii) the existence of direct occipital-frontal connectivity via the inferior fronto-occipital fasciculus; and (iii) the existence of direct connectivity via the extreme capsule between the anterior superior temporal cortex and the anterior inferior frontal gyrus.

There are at least two promising means to answering these questions. One is to improve the reliability and validity of tract-tracing methods in humans by comparing the results of these methods with autoradiography in the non-human primate. Some of these investigations are already underway (Schmahmann *et al*, 2007; Thiebaut De Schotten *et al*, 2011*a*). An alternative is to investigate anatomy simultaneous with function or with the investigation of other anatomical markers of cortical organization. For example, connectivity of the language system can be constrained not only by the sulcal and gyral patterns of the cortex, but also by the physiology that maps to that cortex (Saur *et al*., 2008*b*), or by other morphological measures (e.g. regional cortical thickness or myelin content; Fischl and Dale, 2000; Glasser and Van Essen, 2011). Finally, it is important to consider how emerging models of connectivity relate to clinical correlates, as these contribute significantly to understanding the putative functional roles of these pathways for language.

These methods will help to clarify the anatomy and function of the dorsal and ventral streams, and further to dissociate the different components of each. Identifying the nature of these different pathways will help to ground theoretical frameworks of the functional neurobiology of language (Hickok and Poeppel, 2004, 2007; Hagoort, 2005; Vigneau *et al*., 2006; Price, 2010; Dewitt and Rauschecker, 2012), and to institute a more coherent framework within which fibre pathway connectivity can be systematically incorporated to the study of language.

In this article, we have reviewed current knowledge about seven putative language pathways. We hope to have drawn attention to the fact that language pathways extend beyond the arcuate fasciculus, but also that the anatomy and functional correlates of additional pathways remain to be determined. We have attempted to provide some tools for the non-expert reader to be able to appraise and evaluate the connectional anatomy of language, including knowledge of the key methods and a detailed historical perspective (the reader is also referred to more extensive histories by Jamieson, 1909; Polyak and Kluver, 1968; Clarke and O’Malley, 1996; Finger, 2001; ffyche and Catani, 2005; Schmahmann and Pandya, 2006; 2007; York, 2009; Weiller *et al*., 2011). We also reviewed the clinical correlates of each pathway, for the function of each can only be revealed by the

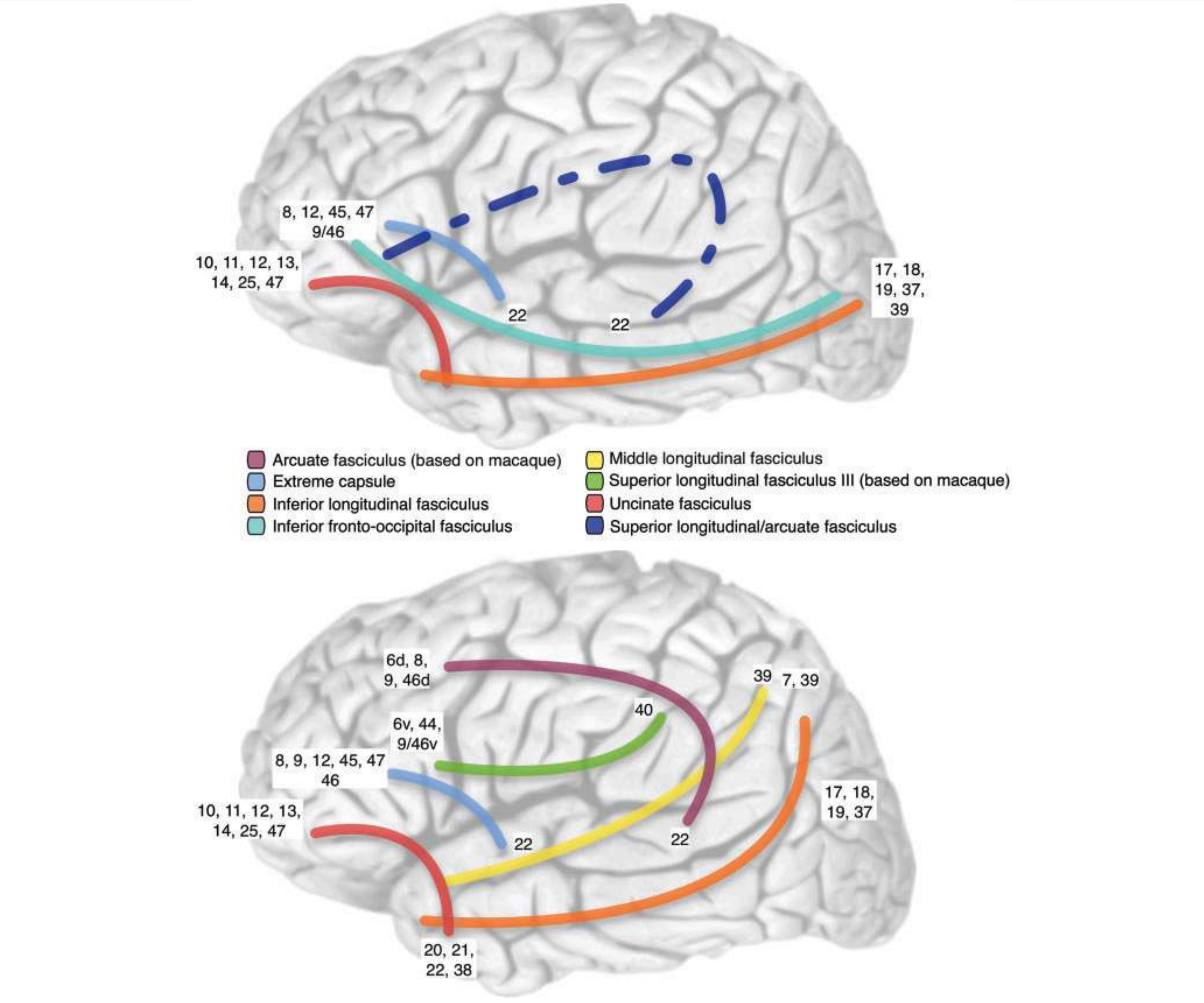


Figure 6 Competing models of perisylvian connectivity. *Top*: Heavily influenced by DTI and post-mortem blunt fibre dissection methods in humans, the top figure suggests as many as five dissociable fibre pathways relevant for language. The middle longitudinal fasciculus is notably absent in this conceptualization, and the connectivity profile of the SLF/AF remains a focus of debate (represented by dashed line). *Bottom*: Heavily influenced by autioradiographic tract-tracing studies in the macaque monkey, the bottom figure suggests different connectivity for the third subcomponent of the superior longitudinal fasciculus and arcuate fasciculus. Additional connectivity to the parietal lobe is suggested for the inferior longitudinal fasciculus. The autoradiography data also suggest the existence of a middle longitudinal fasciculus, but dispute the existence of an inferior fronto-occipital fasciculus. Numbers refer to the corresponding Brodmann's areas for putative terminations and connections.

careful examination of both connectivity and clinical correlates. We suggest that the available data, while still far from conclusive, point to a richer language model than those that have dominated the study of the neurobiology of language since the 19th century.

Acknowledgements

P.T. translated works only available in French. We thank Phillip Agres, who provided translations for works only available in German. Thanks also to Michael Andric, Isabelle Deschamps, and Uri Hasson for review of earlier drafts.

References

Aboitiz F, Scheibel AB, Fisher RS, Zaidel E. Individual differences in brain asymmetries and fiber composition in the human corpus callosum. Brain Res 1992; 598: 154–61.

Agosta F, Scola E, Canu E, Marcone A, Magnani G, Sarro L, et al. White matter damage in frontotemporal lobar degeneration spectrum. Cereb Cortex 2011. Advance Access published on 10 October 2011, doi:10.1093/cercor/bhr288.

Anderson JM, Gilmore R, Roper S, Crosson B, Bauer RM, Nadeau S, et al. Conduction aphasia and the arcuate fasciculus: a re-examination of the Wernicke-Geschwind model. Brain Lang 1999; 70: 1–12.

Anwander A, Tittgemeyer M, von Cramon DY, Friederici AD, Knösche TR. Connectivity-based parcellation of broca's area. Cereb Cortex 2007; 17: 816–25.

Ardila A. A review of conduction aphasia. Curr Neurol Neurosci Rep 2010; 10: 499–503.

Arnold F. Tabulae anatomicae (4 vols). Turici: Impensis Orelii, Fuesslini et sociorum 1838.

Assaf Y, Pasternak O. Diffusion tensor imaging (DTI)-based white matter mapping in brain research: a review. J Mol Neurosci 2008; 34: 51–61.

Axer H, von Keyserlingk AG, Berks G, von Keyserlingk DG. Supra- and infrasylvian conduction aphasia. Brain Lang 2001; 76: 317–31.

Bailey P, Bonin G, McCulloch WS. Long association fibers in cerebral hemispheres of monkey and chimpanzee. J Neurophysiol 1943a; 6: 129–34.

Bailey P, Bonin GV, Garol HW, McCulloch WS. Functional organization of temporal lobe of monkey (macaca mulatta) and chimpanzee (*pan satyrus*). J Neurophysiol 1943b; 6: 121.

Ban T. Cortical neurons projecting to the posterior part of the superior temporal sulcus with particular reference to the posterior association area. An HRP study in the monkey. Arch Ital Biol 1986; 124: 95–109.

Barbas H, Pandya DN. Architecture and intrinsic connections of the prefrontal cortex in the rhesus monkey. J Comp Neurol 1989; 286: 353–75.

Barker LF. The nervous system and its constituent neurones. New York: D. Appleton & Co. 1899.

Barnes CL, Pandya DN. Efferent cortical connections of multimodal cortex of the superior temporal sulcus in the rhesus monkey. J Comp Neurol 1992; 318: 222–44.

Basser PJ, Pajevic S, Pierpaoli C, Duda J, Aldroubi A. *In vivo* fiber tractography using DT-MRI Data. Magn Reson Med 2000; 44: 625–32.

Behrens TEJ, Berg HJ, Jbabdi S, Rushworth MFS, Woolrich MW. Probabilistic diffusion tractography with multiple fibre orientations: what can we gain? Neuroimage 2007; 34: 144–55.

Belin P, Zatorre RJ. Adaptation to speaker's voice in right anterior temporal lobe. Neuroreport 2003; 14: 2105–9.

Bello L, Gambini A, Castellano A, Carrabba G, Acerbi F, Fava E, et al. Motor and language DTI fiber tracking combined with intraoperative subcortical mapping for surgical removal of gliomas. Neuroimage 2008; 39: 369–82.

Benson DF, Sheremata WA, Bouchard R, Segarra JM, Price D, Geschwind N. Conduction aphasia. A clinicopathological study. Arch Neurol 1973; 28: 339–46.

Berke JJ. The claustrum, the external capsule and the extreme capsule of macaca mulatto. J Comp Neurol 1960; 115: 297–331.

Bernal B, Altman N. The connectivity of the superior longitudinal fasciculus: a tractography DTI study. Magn Reson Imaging 2010; 28: 217–25.

Bernal B, Ardila A. The role of the arcuate fasciculus in conduction aphasia. Brain 2009; 132: 2309–16.

Bernal B, Rey G, Dunoyer C, Shanbhag H, Altman N. Agenesis of the arcuate fasciculi in congenital bilateral perisylvian syndrome: a diffusion tensor imaging and tractography study. Arch Neurol 2010; 67: 501–5.

Bickford RG, Mulder DW, Dodge HW, Svien HJ, Rome HP. Changes in memory function produced by electrical stimulation of the temporal lobe in man. Res Publ Assoc Res Nerv Ment Dis 1958; 36: 227–40; discussion 241–3.

Bielschowsky M. Die silberimpragnation der neurofibrillen. J Psychol Neurol 1904; 3: 169–89.

Bignall KE. Bilateral temporofrontal projections in the squirrel monkey: origin, distribution and pathways. Brain Res 1969; 13: 319–27.

Binder JR, Desai RH, Graves WW, Conant LL. Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. Cereb Cortex 2009; 19: 2767–96.

Binder JR, Frost JA, Hammeke TA, Bellgowan PSF, Springer JA, Kaufman JN, et al. Human temporal lobe activation by speech and nonspeech sounds. Cereb Cortex 2000; 10: 512–28.

Binney RJ, Embleton KV, Jefferies E, Parker GJ, Ralph MA. The ventral and inferolateral aspects of the anterior temporal lobe are crucial in semantic memory: Evidence from a novel direct comparison of distortion-corrected fmri, rtms, and semantic dementia. Cereb Cortex 2010; 20: 2728–38.

Bohland JW, Guenther FH. An fmri investigation of syllable sequence production. Neuroimage 2006; 32: 821–41.

Brauer J, Anwander A, Friederici AD. Neuroanatomical prerequisites for language functions in the maturing brain. Cereb Cortex 2011; 21: 459–66.

Breier JI, Hasan KM, Zhang W, Men D, Papanicolaou AC. Language dysfunction after stroke and damage to white matter tracts evaluated using diffusion tensor imaging. AJNR Am J Neuroradiol 2008; 29: 483–7.

Brownsett SL, Wise RJ. The contribution of the parietal lobes to speaking and writing. Cereb Cortex 2010; 20: 517–23.

Burdach KF. Vom bau und leben des gehirns und rückenmarks. Vol. 3. Leipzig: In der dyk'schen buchandlung; 1819.

Bürgel U, Amunts K, Hoemke L, Mohlberg H, Gilsbach JM, Zilles K. White matter fiber tracts of the human brain: three-dimensional mapping at microscopic resolution, topography and intersubject variability. Neuroimage 2006; 29: 1092–105.

Callan D, Callan A, Gamez M, Sato MA, Kawato M. Premotor cortex mediates perceptual performance. Neuroimage 2010; 51: 844–58.

Campbell AW. Histological studies on the localisation of cerebral function. Cambridge, UK: University Press; 1905.

Carmichael ST, Price JL. Limbic connections of the orbital and medial prefrontal cortex in macaque monkeys. J Comp Neurol 1995; 363: 615–41.

Catani M. Diffusion MRI: from quantitative measurement to *in-vivo* neuroanatomy. In: Johansen-Berg H, Behrens TEJ, editors. The connectional anatomy of language: recent contributions from diffusion tensortractography. London: Academic Press; 2009. p. 403–15.

Catani M, Allin MP, Husain M, Pugliese L, Mesulam MM, Murray RM, et al. Symmetries in human brain language pathways correlate with verbal recall. Proc Natl Acad Sci USA 2007; 104: 17163–8.

Catani M, Howard RJ, Pajevic S, Jones DK. Virtual *in vivo* interactive dissection of white matter fasciculi in the human brain. Neuroimage 2002; 17: 77–94.

Catani M, Jones DK, Donato R. Occipito-temporal connections in the human brain. Brain 2003; 126: 2093–107.

Catani M, Jones DK, ffytche DH. Perisylvian language networks of the human brain. Ann Neurol 2005; 57: 8–16.

Catani M, Mesulam M. The arcuate fasciculus and the disconnection theme in language and aphasia: history and current state. Cortex 2008; 44: 953–61.

Catani M, Thiebaut de Schotten M. A diffusion tensor imaging tractography atlas for virtual *in vivo* dissections. Cortex 2008; 44: 1105–32.

Cavada C, Goldman-Rakic PS. Posterior parietal cortex in rhesus monkey: I. Parcellation of areas based on distinctive limbic and sensory corticocortical connections. J Comp Neurol 1989; 287: 393–421.

Ciccarelli O, Toosy AT, Parker GJM, Wheeler-Kingshott CAM, Barker GJ, Miller DH, et al. Diffusion tractography based group mapping of major white-matter pathways in the human brain. Neuroimage 2003; 19: 1545–55.

Clarke E, O'Malley CD. The human brain and spinal cord: a historical study illustrated by writings from antiquity to the twentieth century. San Francisco: Norman; 1996.

Clarke S, Bellmann Thiran A, Maeder P, Adriani M, Vernet O, Regli L, et al. What and where in human audition: selective deficits following focal hemispheric lesions. Exp Brain Res 2002; 147: 8–15.

Cohen-Adad J, Leblond H, Delivet-Mongrain H, Martinez M, Benali H, Rossignol S. Wallerian degeneration after spinal lesions in cats detected with diffusion tensor imaging. Neuroimage 2011; 57: 1068–76.

Cohen L, Jobert A, Le Bihan D, Dehaene S. Distinct unimodal and multimodal regions for word processing in the left temporal cortex. Neuroimage 2004; 23: 1256–70.

Conte-Perales L, Barroso-Chinea P, Rico AJ, Gómez-Bautista V, López IP, Roda E, et al. Neuroanatomical tracing combined with in situ hybridization: analysis of gene expression patterns within brain circuits of interest. J Neurosci Methods 2010; 194: 28–33.

Conturo TE, Lori NF, Cull TS, Akbudak E, Snyder AZ, Shimony JS, et al. Tracking neuronal fiber pathways in the living human brain. Proc Natl Acad Sci USA 1999; 96: 10422–7.

Croxson PL, Johansen-Berg H, Behrens TE, Robson MD, Pinsk MA, Gross CG, et al. Quantitative investigation of connections of the prefrontal cortex in the human and macaque using probabilistic diffusion tractography. J Neurosci 2005; 25: 8854–66.

Curran EJ. A new association fiber tract in the cerebrum with remarks on the fiber tract dissection method of studying the brain. J Compar Neurol Psychol 1909; 19: 645–56.

Damasio H, Damasio AR. The anatomical basis of conduction aphasia. Brain 1980; 103: 337–50.

Davis LE. An anatomic study of the inferior longitudinal fasciculus. Arch Neurol Psychiatry 1921; 5: 370–81.

Déjèrine JJ. Anatomie des centres nerveux. Vol. 1. Paris: Rueff et Cie; 1895.

Déjèrine JJ. Anatomie des centres nerveux. Vol. 2. Paris: Rueff et Cie; 1901.

Dewitt I, Rauschecker JP. Phoneme and word recognition in the auditory ventral stream. Proc Natl Acad Sci USA 2012; 109: E505–14.

De Witt Hamer PC, Moritz-Gasser S, Gatignol P, Duffau H. Is the human left middle longitudinal fascicle essential for language? A brain electrostimulation study. Hum Brain Mapp 2011; 32: 962–73.

Dhanjal NS, Handunnetthi L, Patel MC, Wise RJ. Perceptual systems controlling speech production. J Neurosci 2008; 28: 9969–75.

Diehl B, Busch RM, Duncan JS, Piao Z, Tkach J, Lüders HO. Abnormalities in diffusion tensor imaging of the uncinate fasciculus relate to reduced memory in temporal lobe epilepsy. Epilepsia 2008; 49: 1409–18.

Duffau H. The anatomo-functional connectivity of language revisited: new insights provided by electrostimulation and tractography. Neuropsychologia 2008; 46: 927–34.

Duffau H, Capelle L, Denvil D, Gatignol P, Sichez N, Lopes M, et al. The role of dominant premotor cortex in language: a study using intraoperative functional mapping in awake patients. Neuroimage 2003a; 20: 1903–14.

Duffau H, Capelle L, Sichez N, Denvil D, Lopes M, Sichez J-P, et al. Intraoperative mapping of the subcortical language pathways using direct stimulations: an anatomo-functional study. Brain 2002; 125: 199–214.

Duffau H, Gatignol P, Denvil D, Lopes M, Capelle L. The articulatory loop: study of the subcortical connectivity by electrostimulation. Neuroreport 2003b; 14: 2005–8.

Duffau H, Gatignol P, Mandonnet E, Peruzzi P, Tzourio-Mazoyer N, Capelle L. New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. Brain 2005; 128: 797–810.

Duffau H, Gatignol P, Moritz-Gasser S, Mandonnet E. Is the left uncinate fasciculus essential for language? J Neurol 2009; 256: 382–9.

Dyrby TB, Søgaard LV, Parker GJ, Alexander DC, Lind NM, Baaré WF, et al. Validation of *in vitro* probabilistic tractography. Neuroimage 2007; 37: 1267–77.

Ebeling U, Reulen HJ. Neurosurgical topography of the optic radiation in the temporal lobe. Acta Neurochir (Wien) 1988; 92: 29–36.

Ebeling U, von Cramon D. Topography of the uncinate fascicle and adjacent temporal fiber tracts. Acta Neurochir (Wien) 1992; 115: 143–8.

Edinger L. Vorlesungen über den bau der nervösen zentralorgane des menschen und der tiere. Hall WS, Holland PL, Carlton EP, translator. Philadelphia, New York, Chicago: The F.A. Davis company; 1896.

Edwards SB, Hendrickson A. The autoradiographic tracing of axonal connections in the central nervous system. In: Heimer L, Robards J, editors. Neuroanatomical tract-tracing methods. New York and London: Plenum Press; 1981. p. 171–205.

Ehrlich P. Zur biologischen verwertung des methylenblau. Centralblatt für die medicinischen Wissenschaften 1885; 23: 113–7.

Ehrlich P. Ueber die methylenblaureaktion der lebenden nervensubstanz. Dtsch. med. Wochenschr., Bd; 1886. p. 12–49.

Ellmore TM, Beauchamp MS, O'Neill TJ, Dreyer S, Tandon N. Relationships between essential cortical language sites and subcortical pathways. J Neurosurg 2009; 111: 755–66.

ffyche DH, Catani M. Beyond localization: from hodology to function. Philos Trans R Soc London B Biol Sci 2005; 360: 767–79.

Finger S. Origins of neuroscience: a history of explorations into brain function. New York: Oxford University Press; 2001.

Fink RP, Heimer L. Two methods for selective silver impregnation of degenerating axons and their synaptic endings in the central nervous system. Brain Res 1967; 4: 369–74.

Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proc Natl Acad Sci USA 2000; 97: 11050.

Flechsig P. Weitere mitteilungen über den stabkranz des menschlichen grosshirns. Neurologishes Centralblatt. Vol. 15. 1896. p. 2–4.

Flechsig P. Developmental (myelogenetic) localization of the cerebral cortex in the human subject. The Lancet. Vol. 2. 1901. p. 1027–30.

Flechsig PE. Weitere mittheilungen über die sinnes- und associationscentren des menschlichen gehirns. Neurologisches Centralblatt. Vol. 14. 1895. p. 1118–24.

Flechsig PE. Gehirn und seele. Leipzig: Verlag von Veit & Comp; 1896.

Foville M. Traité complet de l'anatomie, de la physiologie et de la pathologie systéme nerveux cérébro-spinal. Premiere partie. Anatomie. Paris: Fortin, Masson et cie; 1844.

Frey S, Campbell JSW, Pike GB, Petrides M. Dissociating the human language pathways with high angular resolution diffusion fiber tractography. J Neurosci 2008; 28: 11435–44.

Frey S, Kostopoulos P, Petrides M. Orbitofrontal contribution to auditory encoding. Neuroimage 2004; 22: 1384–9.

Fridriksson J, Kjartansson O, Morgan PS, Hjaltason H, Magnusdottir S, Bonilha L, Rorden C. Impaired speech repetition and left parietal lobe damage. J Neurosci 2010; 30: 11057–61.

Friederici AD. Pathways to language: fiber tracts in the human brain. Trends Cogn Sci 2009; 13: 175–81.

Fritz J, Mishkin M, Saunders RC. In search of an auditory engram. Proc Natl Acad Sci USA: 2005. Vol. 102. p. 9359–64.

Galantucci S, Tartaglia MC, Wilson SM, Henry ML, Filippi M, Agosta F, et al. White matter damage in primary progressive aphasias: a diffusion tensor tractography study. Brain 2011; 134: 3011–29.

Gall FJ, Spurzheim G. Anatomie et physiologie du systeme nerveux général, et du cerveau en particulier. Atlas. Paris: Chez F. Schoell; 1810.

Gerfen CR, Sawchenko PE, Carlsen J. The PHA-L anterograde axonal tracing method. In: Heimer L, Záborsky L, editors. Neuroanatomical tract-tracing methods 2. New York: Plenum Press; 1989. p. 19–47.

Geschwind N. Disconnexion syndromes in animals and man: Part II. Brain 1965; 88: 585–644.

Geschwind N. The organization of language and the brain. Science 1970; 170: 940–4.

Ghashghaei HT, Barbas H. Pathways for emotion: interactions of prefrontal and anterior temporal pathways in the amygdala of the rhesus monkey. Neuroscience 2002; 115: 1261–79.

Glasser MF, Rilling JK. DTI tractography of the human brain's language pathways. Cereb Cortex 2008; 18: 2471–82.

Glasser MF, Van Essen DC. Mapping human cortical areas in vivo based on myelin content as revealed by T1- and T2-weighted MRI. J Neurosci 2011; 31: 11597–616.

Goldstein K, Marmor J. A case of aphasia, with special reference to the problems of repetition and word-finding. J Neurol Psychiatry 1938; 1: 329–41.

Golgi C. Di una nuova reazione apparentemente nera delle cellule nervosa cerebrali ottenuta col bicloruro di mercurio. Arch Sci Med 1878; 3: 1–7.

Golgi C. Un nuovo processo di tecnica microscopica. Rend d r Ist Lomb di sc e let 1879; 12: 206–10.

Gordinier HC. The gross and minute anatomy of the central nervous system. Philadelphia: P. Blakiston's Son & Co. 1899.

Gorno-Tempini ML, Dronkers NF, Rankin KP, Ogar JM, Phengrasamy L, Rosen HJ, et al. Cognition and anatomy in three variants of primary progressive aphasia. Ann Neurol 2004; 55: 335–46.

Gough PM, Nobre AC, Devlin JT. Dissociating linguistic processes in the left inferior frontal cortex with transcranial magnetic stimulation. J Neurosci 2005; 25: 8010–6.

Green E, Howes DH. The nature of conduction aphasia: a study of anatomic and clinical features and of underlying mechanisms. Stud Neurolinguistics 1977; 3: 123–56.

Hackett TA, Stepniewska I, Kaas JH. Prefrontal connections of the parabelt auditory cortex in macaque monkeys. Brain Res 1999; 817: 45–58.

Hagoort P. On broca, brain, and binding: a new framework. Trends Cogn Sci 2005; 9: 416–23.

Hagoort P, Hald L, Bastiaansen M, Petersson KM. Integration of word meaning and world knowledge in language comprehension. Science 2004; 304: 438–41.

Hansen B, Flint JJ, Heon-Lee C, Fey M, Vincent F, King MA, et al. Diffusion tensor microscopy in human nervous tissue with quantitative correlation based on direct histological comparison. Neuroimage 2011; 57: 1458–65.

Heimer L, Robards MJ. Neuroanatomical tract tracing methods. New York and London: Plenum Press; 1981.

Heimer L, Záborsky L. Neuroanatomical tract tracing methods 2. New York and London: Plenum Press; 1989.

Heimer L, Záborszky L, Wouterlood FG, Lanciego JL. Neuroanatomical tract-tracing 3: molecules, neurons, and systems. New York: Springer Verlag; 2006.

Henry RG, Berman JI, Nagarajan SS, Mukherjee P, Berger MS. Subcortical pathways serving cortical language sites: initial experience with diffusion tensor imaging fiber tracking combined with intraoperative language mapping. Neuroimage 2004; 21: 616–22.

Hickok G. The functional neuroanatomy of language. Phys Life Rev 2009; 6: 121–43.

Hickok G, Erhard P, Kassubek J, Helms-Tillery AK, Naeve-Velguth S, Strupp JP, et al. A functional magnetic resonance imaging study of the role of left posterior superior temporal gyrus in speech production: implications for the explanation of conduction aphasia. Neurosci Lett 2000; 287: 156–60.

Hickok G, Poeppel D. Towards a functional neuroanatomy of speech perception. Trends Cogn Sci 2000; 4: 131–8.

Hickok G, Poeppel D. Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. Cognition 2004; 92: 67–99.

Hickok G, Poeppel D. The cortical organization of speech processing. Nat Rev Neurosci 2007; 8: 393–402.

Highley JR, Walker MA, Esiri MM, Crow TJ, Harrison PJ. Asymmetry of the uncinate fasciculus: a post-mortem study of normal subjects and patients with schizophrenia. Cereb Cortex 2002; 12: 1218.

Hodgkin AL, Huxley AF. Action potentials recorded from inside a nerve fiber. Nature 1939; 144: 710–1.

Hoeve HJJ. A modern method of teaching anatomy of the brain. Ana Record 1909; 3: 247–57.

Holland R, Lambon Ralph MA. The anterior temporal lobe semantic hub is a part of the language neural network: selective disruption of irregular past tense verbs by rTMS. Cereb Cortex 2010; 20: 2771–5.

Holl N, Noblet V, Rodrigo S, Dietemann JL, Mekhbi MB, Kehrli P, et al. Temporal lobe association fiber tractography as compared to histology and dissection. Surg Radiol Anat 2011; 33: 713–22.

Hua K, Oishi K, Zhang J, Wakana S, Yoshioka T, Zhang W, et al. Mapping of functional areas in the human cortex based on connectivity through association fibers. Cereb Cortex 2009; 19: 1889.

Humphries C, Binder JR, Medler DA, Liebenthal E. Syntactic and semantic modulation of neural activity during auditory sentence comprehension. J Cogn Neurosci 2006; 18: 665–79.

Humphries C, Willard K, Buchsbaum B, Hickok G. Role of anterior temporal cortex in auditory sentence comprehension: an fmri study. Neuroreport 2001; 12: 1749–52.

Jamieson EB. The means of displaying, by ordinary dissection, the larger tracts of white matter of the brain in their continuity. J Anat Physiol 1909; 43: 225–34.

Johansen-Berg H, Rushworth MFS. Using diffusion imaging to study human connectional anatomy. Annu Rev Neurosci 2009; 32: 75–94.

Johnston JB. A new method of brain dissection. Anat Record 1908; 2: 345–58.

Kaplan E, Naeser MA, Partin PI, Ho M, Wang Y, Baker E, Pascual-Leone A. Horizontal portion of arcuate fasciculus fibers track to pars opercularis, not pars triangularis, in right and left hemispheres: a DTI study. Neuroimage 2010; 52.

Kawamura K, Naito J. Corticocortical projections to the prefrontal cortex in the rhesus monkey investigated with horseradish peroxidase techniques. Neurosci Res 1984; 1: 89–103.

Kempler D, Metter EJ, Jackson CA, Hanson WR, Riege WH, Mazziotta JC, et al. Disconnection and cerebral metabolism. The case of conduction aphasia. Arch Neurol 1988; 45: 275–9.

Kier EL, Staib LH, Davis LM, Bronen RA. MR imaging of the temporal stem: anatomic dissection tractography of the uncinate fasciculus, inferior occipitofrontal fasciculus, and Meyer's loop of the optic radiation. Am J Neuroradiol 2004; 25: 677–91.

Klingler J. Erleichterung der makroskipischen präparation des gehirns durch den gefrierprozeß. Schweizer Archiv für Neurologie und Psychiatrie 1935; 36: 247–56.

Klingler J, Gloor P. The connections of the amygdala and of the anterior temporal cortex in the human brain. J Comp Neurol 1960; 115: 333–69.

Kondo H, Saleem KS, Price JL. Differential connections of the perirhinal and parahippocampal cortex with the orbital and medial prefrontal networks in macaque monkeys. J Comp Neurol 2005; 493: 479–509.

Konorski J, Kozniewska H, Stephen L. Analysis of symptoms and cerebral localization of audio-verbal aphasia. Proc VII Int Congr Neurol 1961; 2: 234–6.

Krieg W. Connections of the cerebral cortex. Evanston, IL: Brain Books; 1963.

Lanciego JL, Luquin MR, Guillen J, Gimenez-Amaya JM. Multiple neuroanatomical tracing in primates. Brain Res Protoc 1998; 2: 323–332.

Lanciego JL, Wouterlood FG, Erro E, Arribas J, Gonzalo N, Urra X, et al. Complex brain circuits studied via simultaneous and permanent detection of three transported neuroanatomical tracers in the same histological section. J Neurosci Methods 2000; 103: 127–35.

Lazar M. Mapping brain anatomical connectivity using white matter tractography. NMR Biomed 2010; 23: 821–35.

Lazar M, Alexander AL. An error analysis of white matter tractography methods: synthetic diffusion tensor field simulations. Neuroimage 2003; 20: 1140–53.

Leclercq D, Duffau H, Delmaire C, Capelle L, Gatignol P, Ducros M, et al. Comparison of diffusion tensor imaging tractography of language tracts and intraoperative subcortical stimulations. J Neurosurg 2010; 112: 503–11.

Leuret F, Gratiolet P. Considéré dans ses rapports avec l'intelligence. Atlas des 32 planches dess inées d'après nature et gravées. Anatomir comparée du système nerveux. Paris: J-B Bailliére et fils; 1839.

Levin PM. The efferent fibers of the frontal lobe of the monkey, macaca mulatta. J Comp Neurol 1936; 63: 369–419.

Lockard I. Certain developmental relations and fiber connections of the triangular gyrus in primates. J Comp Neurol 1948; 89: 349–86.

Lopez-Barroso D, de Diego-Balaguer R, Cunillera T, Camara E, Münte TF, Rodriguez-Fornells. Language learning under working memory constraints correlates with microstructural differences in the ventral language pathway. Cereb Cortex 2011; 12: 2742–50.

Loui P, Li HC, Schlaug G. White matter integrity in right hemisphere predicts pitch-related grammar learning. Neuroimage 2011; 55: 500–7.

Ludwig E, Klingler J. Atlas cerebri humani. Boston, Toronto: Little, Brown; 1956.

Lu LH, Crosson B, Nadeau SE, Heilman KM, Gonzalez-Rothi LJ, Raymer A, et al. Category-specific naming deficits for objects and actions: semantic attribute and grammatical role hypotheses. Neuropsychologia 2002; 40: 1608–21.

Makris N. PhD Thesis. Delineation of human association fiber pathways using histologic and magnetic resonance methodologies. Boston University; 1999.

Makris N, Kennedy D, McInerney S, Sorensen AG, Wang R, Caviness V, Pandya DN. Segmentation of subcomponents within the superior longitudinal fascicle in humans: a quantiative, *in vivo*, DT-MRI study. Cereb Cortex 2005; 15: 854–69.

Makris N, Pandya DN. The extreme capsule in humans and rethinking of the language circuitry. Brain Struct Funct 2009; 213: 343–58.

Makris N, Papadimitriou GM, Kaiser JR, Sorg S, Kennedy DN, Pandya DN. Delineation of the middle longitudinal fascicle in humans: a quantitative, *in vivo*, DT-MRI study. Cereb Cortex 2009; 19: 777.

Maldonado IL, Moritz-Gasser S, de Champfleur NM, Bertram L, Moulinié G, Duffau H. Surgery for gliomas involving the left inferior parietal lobule: new insights into the functional anatomy provided by stimulation mapping in awake patients. J Neurosurg 2011a; 115: 770–9.

Maldonado IL, Moritz-Gasser S, Duffau H. Does the left superior longitudinal fascicle subserve language semantics? A brain electrostimulation study. Brain Struct Funct 2011b; 216: 263–74.

Mandonnet E, Nouet A, Gatignol P, Capelle L, Duffau H. Does the left inferior longitudinal fasciculus play a role in language? A brain stimulation study. Brain 2007; 130: 623.

Marchina S, Zhu LL, Norton A, Zipse L, Wan CY, Schlaug G. Impairment of speech production predicted by lesion load of the left arcuate fasciculus. Stroke 2011; 42: 2251–6.

Marchi V. Sulle degenerazioni consecutive allestirpazione totale e parziale del cervelletto. Rivista sperimentale di freniatria e di medicina legale in relazione con lanthropologia e le scienze giuridiche e sociale 1886; 12: 50–6.

Marchi V, Algeri EG. Sulle degenerazioni discendenti consecutive a lesioni in diverse zone della corteccia cerebrale. Riv Sper Freniatr Med Leg Alien Ment 1886; 14: 1–49.

Martin A, Chao LL. Semantic memory and the brain: structure and processes. Curr Opin Neurobiol 2001; 11: 194–201.

Martino J, Brogna C, Robles SG, Vergani F, Duffau H. Anatomic dissection of the inferior fronto-occipital fasciculus revisited in the lights of brain stimulation data. Cortex 2010; 46: 691–9.

Mayo H. A series of engravings intended to illustrate the structure of the brain and spinal cord in man. London: Burgess and Hill; 1827.

McDonald CR, Ahmadi ME, Hagler DJ, Tecoma ES, Iragui VJ, Gharapetian L, et al. Diffusion tensor imaging correlates of memory and language impairments in temporal lobe epilepsy. Neurology 2008; 71: 1869–76.

Mendez MF, Benson DF. Atypical conduction aphasia. A disconnection syndrome. Arch Neurol 1985; 42: 88691.

Mettler FA. The marchi method for demonstrating degenerated fiber connections within the central nervous system. Stain Technol 1932; 7: 95–106.

Mettler FA. Corticifugal fiber connections of the cortex of macaca mulatta. The parietal region. J Comp Neurol 1935a; 62: 263–91.

Mettler FA. Corticifugal fiber connections of the cortex of macaca mulatta. The temporal region. J Comp Neurol 1935b; 63: 25–47.

Mettler FA. Corticifugal fiber connections of the cortex of macaca mullatta. The frontal region. J Comp Neurol 1935c; 61: 509–42.

Mettler FA. Corticifugal fiber connections of the cortex of macaca mullatta. The occipital region. J Comp Neurol 1935d; 61: 221–56.

Meynert T. Psychiatry. A clinical treatise on diseases of the forebrain based upon a study of its structure, functions and nutrition. Part I. The anatomy, physiology, and chemistry of the brain. Sachs B, translator. New York and London: G. P. Putnam's Sons; 1885.

Miller KL, Stagg CJ, Douaud G, Jbabdi S, Smith SM, Behrens TE, et al. Diffusion imaging of whole, post-mortem human brains on a clinical MRI scanner. Neuroimage 2011; 57: 167–81.

Milner AD, Goodale MA. Two visual systems re-viewed. Neuropsychologia 2008; 46: 774–85.

Mori S, Zhang J. Principles of diffusion tensor imaging and its applications to basic neuroscience research. Neuron 2006; 51: 527–39.

Moss HE, Abdallah S, Fletcher P, Bright P, Pilgrim L, Acres K, et al. Selecting among competing alternatives: selection and retrieval in the left inferior frontal gyrus. Cereb Cortex 2005; 15: 1723–35.

Muñoz M, Mishkin M, Saunders RC. Resection of the medial temporal lobe disconnects the rostral superior temporal gyrus from some of its projection targets in the frontal lobe and thalamus. Cereb Cortex 2009; 19: 2114–30.

Nauta WJH. Some efferent connections of the prefrontal cortex in the monkey. The frontal granular cortex and behaviour. New York: McGraw-Hill; 1964, p. 397–409.

N'Dri Oka D, Haidara A, Broalet E, Velut S, Bazeze V. Etude micro anatomique du faisceau longitudinal superieur et ses implications cliniques. Afr J Neurol Sci 2007; 26: 110–9.

Neal JW, Pearson RC, Powell TP. The cortico-cortical connections within the parieto-temporal lobe of area PG,7a, in the monkey. Brain Res 1988; 438: 343–50.

Niessl-Mayendorf V. Vom fasciculus longitudinalis inferior. Eur Arch Psychiatry Clin Neurosci 1903; 37: 537–63.

Nissl F. Ueber eine neue untersuchungsmethode des centralorgans zur feststellung der localisation der nervenzellen. Neurol Centralbl 1894; 13: 507–8.

Nowak LG, Bullier J. Axons, but not cell bodies, are activated by electrical stimulation in cortical gray matter I. Evidence from chronaxie measurements. Exp Brain Res 1998; 118: 477–88.

Obersteiner H. Anleitung beim studium des baues der nervösen centralorgane im gesunden und kranken zustande. Leipzig und Wien. Franz Deuticke, 1896.

Obleser J, Meyer L, Friederici AD. Dynamic assignment of neural resources in auditory comprehension of complex sentences. Neuroimage 2011; 56: 2310–20.

Oishi K, Faria AV, Zijl PCM, Mori S. MRI atlas of human white matter. New York: Academic Press; 2011.

Ojemann G, Fedio P. Effect of stimulation of the human thalamus and parietal and temporal white matter on short-term memory. J Neurosurg 1968; 29: 51–9.

de Olmos JS, Ebbesson SOE, Heimer L. Silver methods for the impregnation of degenerating axoplasm. In: Heimer L, Robards MJ, editors. Neuroanatomical tract-tracing methods. New York and London: Plenum Press; 1981. p. 117–70.

Papagno C. Naming and the role of the uncinate fasciculus in language function. Curr Neurol Neurosci Rep 2011; 11: 553–9.

Papagno C, Miracapillo C, Casarotti A, Romero Lauro LJ, Castellano A, Falini A, et al. What is the role of the uncinate fasciculus? Surgical removal and proper name retrieval. Brain 2011; 134: 405–14.

Papoutsi M, Stamatakis EA, Griffiths J, Marslen-Wilson WD, Tyler LK. Is left fronto-temporal connectivity essential for syntax? Effective connectivity, tractography and performance in left-hemisphere damaged patients. Neuroimage 2011; 58: 656–64.

Parker GJ, Alexander DC. Probabilistic anatomical connectivity derived from the microscopic persistent angular structure of cerebral tissue. Philos Trans R Soc Lond B Biol Sci 2005; 360: 893–902.

Parker GJ, Luzzi S, Alexander DC, Wheeler-Kingshott CA, Ciccarelli O, Lambon Ralph MA. Lateralization of ventral and dorsal auditory-language pathways in the human brain. Neuroimage 2005; 24: 656–66.

Patterson K, Nestor PJ, Rogers TT. Where do you know what you know? The representation of semantic knowledge in the human brain. Nat Rev Neurosci 2007; 8: 976–87.

Peeva MG, Guenther FH, Tourville JA, Nieto-Castanon A, Anton JL, Nazarian B, et al. Distinct representations of phonemes, syllables, and supra-syllabic sequences in the speech production network. Neuroimage 2010; 50: 626–38.

Peltier J, Travers N, Destrieux C, Velut S. Optic radiations: a microsurgical anatomical study. J Neurosurg 2006; 105: 294–300.

Peltier J, Verclytte S, Delmaire C, Pruvo JP, Godefroy O, Le Gars D. Microsurgical anatomy of the temporal stem: clinical relevance and correlations with diffusion tensor imaging fiber tracking. J Neurosurg 2010; 112: 1033–8.

Peschke C, Ziegler W, Eisenberger J, Baumgaertner A. Phonological manipulation between speech perception and production activates a parieto-frontal circuit. Neuroimage 2012; 59: 788–99.

Peschke C, Ziegler W, Kappes J, Baumgaertner A. Auditory-motor integration during fast repetition: the neuronal correlates of shadowing. Neuroimage 2009; 47: 392–402.

Petkov CI, Kayser C, Steudel T, Whittingstall K, Augath M, Logothetis NK. A voice region in the monkey brain. Nat Neurosci 2008; 11: 367–74.

Petkov CI, Logothetis NK, Obleser J. Where are the human speech and voice regions, and do other animals have anything like them? Neuroscientist 2009; 15: 419–29.

Petrides M, Pandya DN. Projections to the frontal cortex from the posterior parietal region in the rhesus monkey. J Comp Neurol 1984; 228: 105–16.

Petrides M, Pandya DN. Association fiber pathways to the frontal cortex from the superior temporal region in the rhesus monkey. J Comp Neurol 1988; 273: 52–66.

Petrides M, Pandya DN. Comparative cytoarchitectonic analysis of the human and the macaque ventrolateral prefrontal cortex and corticocortical connection patterns in the monkey. Eur J Neurosci 2002; 16: 291–310.

Petrides M, Pandya DN. Efferent association pathways originating in the caudal prefrontal cortex in the macaque monkey. J Comp Neurol 2006; 498: 227–51.

Petrides M, Pandya DN. Efferent association pathways from the rostral prefrontal cortex in the macaque monkey. J Neurosci 2007; 27: 11573–86.

Petrides M, Pandya DN. Distinct parietal and temporal pathways to the homologues of broca's area in the monkey. PLoS Biol 2009; 7:e1000170.

Peuskens D, van Loon J, Van Calenbergh F, van den Bergh R, Goffin J, Plets C. Anatomy of the anterior temporal lobe and the frontotemporal region demonstrated by fiber dissection. Neurosurgery 2004; 55: 1174–84.

Polyak S, Kluver H. The vertebrate visual system. Chicago: The University of Chicago Press; 1968.

Powell HW, Parker GJ, Alexander DC, Symms MR, Boulby PA, Wheeler-Kingshott CA, et al. Hemispheric asymmetries in language-related pathways: a combined functional MRI and tractography study. Neuroimage 2006; 32: 388–99.

Pribram KH, Lennox MA, Dunsmore RH. Some connections of the orbito-fronto-temporal, limbic and hippocampal areas of macaca mulatta. J Neurophysiol 1950; 13: 127–35.

Pribram KH, MacLean PD. Neuronographic analysis of medial and basal cerebral cortex. II. Monkey. J Neurophysiol 1953; 16: 324–40.

Price CJ. The anatomy of language: a review of 100 fmri studies published in 2009. Ann N Y Acad Sci 2010; 1191: 62–88.

Probst M. Ueber den verlauf der centralen sehfasern (rindensehhügelfasern) und deren endigung im zwischen-und mittelhirne und über die associations-und commissurenfasern der sehsphäre. Eur Arch Psychiatry Clin Neurosci 1901; 35: 22–43.

Rae ASL. The form and structure of the human claustrum. J Comp Neurol 1954; 100: 15–39.

Ramón y Cajal S. Sobre un sencillo proceder de impregnación de las fibrillas interiores del protoplasma nervioso. Arch Latinos de Med y Biol 1903a; 1: 3–8.

Ramón y Cajal S. Un sencillo método de coloración selectiva del retículo protoplásmico y sus efectos en los diversos órganos nerviosos. Trab Lab Investig Biol Univ Madr 1903 b; 2: 129–221.

Rauschecker JP. An expanded role for the dorsal auditory pathway in sensorimotor control and integration. Hear Res 2011; 271: 16–25.

Rauschecker JP, Scott SK. Maps and streams in the auditory cortex: nonhuman primates illuminate human speech processing. Nat Neurosci 2009; 12: 718–24.

Rauschecker JP, Tian B. Mechanisms and streams for processing of "what" and "where" in auditory cortex. Vol. 97. USA: Proc Natl Acad Sci; 2000. p. 11800.

Redlich K. Zur vergleichenden anatomie der assoziationssysteme des gehirns der säugetiere. II. Der fasciculus longitudinalis inferior (stratum sagittale oecipitale laterale s. Externum). Von. Arbeiten aus dem Neurologischen Institute (Institut für Anatomic und Physiologie des Centralnervensystems) an der Wiener Universität 1905; 12: 109.

Reil JC. Das balken-system oder die balken-organisation im großen gehirn. Archiv für die Physiologie 1809a; 9: 172–95.

Reil JC. Das hirnschenkel-system oder die hirnschenkel-organisation im großen gehirn. Archiv für die Physiologie 1809b; 9: 147–71.

Reil JC. Die sylvische grube oder das thal, das gestreifte große hirnganglium, dessen kapsel und die seitentheile des großen gehirns. Archiv für die Physiologie 1809c; 9: 195–208.

Reil JC. Die vördere commissur im großen gehirn. Archiv für die Physiologie 1812a; 12: 89–100.

Reil JC. Mangel des mittleren und freyen theils des balkens im menschengehirn. Archiv für die Physiologie 1812b; 11: 341–4.

Reiner A, Honig MG. Dextran amines: versatile tools for anterograde and retrograde studies of nervous system connectivity. In: Záborsky L, Wouterlood FG, Lanciego JL, editors. Neuroanatomical tract-tracing 3. New York: Springer; 2006. p. 304–35.

Reisert M, Mader I, Anastasopoulos C, Weigel M, Schnell S, Kiselev V. Global fiber reconstruction becomes practical. Neuroimage 2011; 54: 955–62.

Rogalsky C, Hickok G. The role of broca's area in sentence comprehension. J Cogn Neurosci 2011; 23: 1664–80.

Romanski LM, Bates JF, Goldman-Rakic PS. Auditory belt and parabelt projections to the prefrontal cortex in the rhesus monkey. J Comp Neurol 1999; 403: 141–57.

Romanski LM, Tian B, Fritz J, Mishkin M, Goldman-Rakic PS, Rauschecker JP. Dual streams of auditory afferents target multiple domains in the primate prefrontal cortex. Nat Neurosci 1999; 2: 1131–6.

Ross ED. Sensory-specific and fractional disorders of recent memory in man: I. Isolated loss of visual recent memory. Arch Neurol, 1980; 37–193.

Rushworth MFS, Behrens TEJ, Johansen-Berg H. Connection patterns distinguish 3 regions of human parietal cortex. Cereb Cortex 2006; 16: 1418–30.

Sachs H. Vorträge über bau und thätigkeit des grosshirns und die lehre von der aphasie und seelenblindheit: Für aerzte und studirende. Breslau: Preuss & Jünger 1893.

Sachs H. Eur Neurol. Ueber flechsig's verstandescentren. Vol. 1. 1897. p. 199–210.

Saleem KS, Kondo H, Price JL. Complementary circuits connecting the orbital and medial prefrontal networks with the temporal, insular, and opercular cortex in the macaque monkey. J Comp Neurol 2008; 506: 659–93.

Saur D, Kreher BW, Schnell S, Kümmerer D, Kellmeyer P, Vry M-S, et al. Ventral and dorsal pathways for language. Proc Natl Acad Sci USA 2008; 105: 18035–40.

Saur D, Schelter B, Schnell S, Kratochvil D, Küpper H, Kellmeyer P, et al. Combining functional and anatomical connectivity reveals brain networks for auditory language comprehension. Neuroimage 2010; 49: 3187–97.

Schmahmann JD, Pandya DN. Fiber pathways of the brain. Oxford, England: Oxford University Press; 2006.

Schmahmann JD, Pandya DN. Cerebral white matter–historical evolution of facts and notions concerning the organization of the fiber pathways of the brain. J Hist Neurosci 2007; 16: 237–67.

Schmahmann JD, Pandya DN. Disconnection syndromes of basal ganglia, thalamus, and cerebrocerebellar systems. Cortex 2008; 44: 1037–66.

Schmahmann JD, Pandya DN, Wang RP, Dai G, D'Arceuil H, de Crespigny AJ, Wedeen VJ. Association fibre pathways of the brain: parallel observations from diffusion spectrum imaging and autoradiography. Brain 2007; 130: 630–53.

Schmahmann JD, Smith EE, Eichler FS, Filley CM. Cerebral white matter: neuroanatomy, clinical neurology, and neurobehavioral correlates. Ann N Y Acad Sci 2008; 1142: 266–309.

Scott SK, Blank CC, Rosen S, Wise RJS. Identification of a pathway for intelligible speech in the left temporal lobe. Brain 2000; 123: 2400–6.

Scott SK, Johnsrude IS. The neuroanatomical and functional organization of speech perception. Trends Neurosci 2003; 26: 100–7.

Selnes OA, van Zijl PCM, Barker PB, Hillis AE, Mori S. MR diffusion tensor imaging documented arcuate fasciculus lesion in a patient with normal repetition performance. Aphasiology 2002; 16: 897–902.

Seltzer B, Pandya DN. Further observations on parieto-temporal connections in the rhesus monkey. Exp Brain Res 1984; 55: 301–12.

Seltzer B, Pandya DN. Intrinsic connections and architectonics of the superior temporal sulcus in the rhesus monkey. J Comp Neurol 1989; 290: 451–71.

Shuren JE, Schefft BK, Yeh HS, Privitera MD, Cahill WT, Houston W. Repetition and the arcuate fasciculus. J Neurol 1995; 242: 596–8.

Simonyan K, Tovar-Moll F, Ostuni J, Hallett M, Kalasinsky VF, Lewin-Smith MR, et al. Focal white matter changes in spasmodic dysphonia: a combined diffusion tensor imaging and neuropathological study. Brain 2008; 131: 447–59.

Skirboll LR, Thor K, Helke C, Hökfelt T, Robertson B, Long R. Use of retrograde fluorescent tracers in combination with immunohistochemical methods. In: Heimer L, Záborsky L, editors. Neuroanatomical tract-tracing methods. New York and London: Plenum Press; 1989. p. 5–18.

Streitfeld BD. The fiber connections of the temporal lobe with emphasis on the rhesus monkey. Int J Neurosci 1980; 11: 51–71.

Swanson LW. Brain mapping: the applications. In: Toga AW, Mazziotta JC, editors. A history of neuroanatomical mapping. San Diego: Academic Press; 2000. p. 77–109.

Szelényi A, Bello L, Duffau H, Fava E, Feigl GC, Galanda M, et al. Intraoperative electrical stimulation in awake craniotomy: methodological aspects of current practice. Neurosurg Focus 2010; 28: E7.

Tanabe H, Sawada T, Inoue N, Ogawa M, Kuriyama Y, Shiraishi J. Conduction aphasia and arcuate fasciculus. Acta Neurol Scand 1987; 76: 422–7.

Tench CR, Morgan PS, Wilson M, Blumhardt LD. White matter mapping using diffusion tensor MRI. Magn Reson Med 2002; 47: 967–72.

Thiebaut de Schotten M, Dell'acqua F, Valabregue R, Catani M. Monkey to human comparative anatomy of the frontal lobe association tracts. Cortex 2011a; 48: 82–96.

Thiebaut de Schotten M, Ffytche DH, Bizzi A, Dell'Acqua F, Allin M, Walshe M, et al. Atlasing location, asymmetry and inter-subject variability of white matter tracts in the human brain with MR diffusion tractography. Neuroimage 2011b; 54: 49–59.

Thompson-Schill SL, D'Esposito M, Aguirre GK, Farah MJ. Role of left inferior prefrontal cortex in retrieval of semantic knowledge: s reevaluation. Proc Natl Acad Sci USA 1997; 94: 14792–7.

Tournier J, Calamante F, King MD, Gadian DG, Connelly A. Limitations and requirements of diffusion tensor fiber tracking: an assessment using simulations. Magn Reson Med 2002; 47: 701–8.

Tranel D, Brady DR, Van Hoesen GW, Damasio AR. Parahippocampal projections to posterior auditory association cortex (area Tpt) in old-world monkeys. Exp Brain Res 1988; 70: 406–16.

Tremblay P, Deschamps I, Gracco VL. Regional heterogeneity in the processing and the production of speech in the human planum temporale. Cortex 2011 [Epub ahead of print] doi: 10.1016/j.cortex.2011.09.004.

Tremblay P, Small SL. On the context-dependent nature of the contribution of the ventral premotor cortex to speech perception. Neuroimage 2011; 57: 1561–71.

Trolard P. Le faisceau longitudinal inférieur du cerveau. Rev Neurol 1906; 14: 440–6.

Tsapkini K, Frangakis CE, Hillis AE. The function of the left anterior temporal pole: evidence from acute stroke and infarct volume. Brain 2011; 134: 3094–105.

Tuch DS. Q-ball imaging. Magn Reson Med 2004; 52: 1358–72.

Tuch DS, Reese TG, Wiegell MR, Makris N, Belliveau JW, Wedeen VJ. High angular resolution diffusion imaging reveals intravoxel white matter fiber heterogeneity. Magn Reson Med 2002; 48: 577–82.

Turken AU, Dronkers NF. The neural architecture of the language comprehension network: converging evidence from lesion and connectivity analyses. Front Syst Neurosci 2011; 5: 1.

Tusa RJ, Ungerleider LG. The inferior longitudinal fasciculus: a reexamination in humans and monkeys. Ann Neurol 1985; 18: 583–91.

Türck L. Über sekundäre erkrankung einzelner rückenmarksstränge und ihrer fortsetzungen zum gehirne. Sitzungsberichte der mathematisch-naturwissenschafilichen Classe der kaiserlichen Akademie der Wissenschafien 1851; 6: 288–312.

Türe U, Yaşargil MG, Friedmanm AA, Al-Mefty O. Fiber dissection technique: lateral aspect of the brain. Neurosurgery 2000; 47: 417–26.

Türe U, Yaşargil MG, Pait TG. Is there a superior occipitofrontal fasciculus? A microsurgical anatomic study. Neurosurgery 1997; 40: 1226–32.

Ungerleider LG, Gaffan D, Pelak VS. Projections from inferior temporal cortex to prefrontal cortex via the uncinate fascicle in rhesus monkeys. Exp Brain Res 1989; 76: 473–84.

Ungerleider LG, Haxby JV. 'What' and 'where' in the human brain. Curr Opin Neurobiol 1994; 4: 157–65.

Vigneau M, Beaucousin V, Hervé PY, Duffau H, Crivello F, Houdé O, et al. Meta-analyzing left hemisphere language areas: phonology, semantics, and sentence processing. Neuroimage 2006; 30: 1414–32.

von Monakow C. Gehirnpathologie. Allgemeine einleitung. I. Localisation. II. Gehirnblutungen. III. In: Nothnagel H, editor. Spezielle pathologie und therapie. Wien: Alfred Hölder; 1905.

Wagner AD, Paré-Blagoev EJ, Clark J, Poldrack RA. Recovering meaning: left prefrontal cortex guides controlled semantic retrieval. Neuron 2001; 31: 329–38.

Wakana S, Caprihan A, Panzenboeck MM, Fallon JH, Perry M, Gollub RL, et al. Reproducibility of quantitative tractography methods applied to cerebral white matter. Neuroimage 2007; 36: 630–44.

Waller A. Experiments on the section of the glossopharyngeal and hypoglossal nerves of the frog, and observations of the alterations produced thereby in the structure of their primitive fibres. Philos Trans R Soc Lond 1850; 140: 423–9.

Warren JE, Wise RJ, Warren JD. Sounds do-able: auditory-motor transformations and the posterior temporal plane. Trends Neurosci 2005; 28: 636–43.

Wedeen VJ, Hagmann P, Tseng WYI, Reese TG, Weisskoff RM. Mapping complex tissue architecture with diffusion spectrum magnetic resonance imaging. Magn Reson Med 2005; 54: 1377–86.

Wedeen VJ, Wang RP, Schmahmann JD, Benner T, Tseng WYI, Dai G, et al. Diffusion spectrum magnetic resonance imaging (DSI) tractography of crossing fibers. Neuroimage 2008; 41: 1267–77.

Weigert C. Uber eine neue untersuchungsmethode des centralnervensystems. Z Med Wiss 1882; 20: 753–7.

Weiller C, Bormann T, Saur D, Musso M, Rijntjes M. How the ventral pathway got lost—and what its recovery might mean. Brain Lang 2011; 118: 29–39.

Wernicke C. Der aphasiche symptomen complex. Breslau: Taschen; 1874.

Wernicke C. Photographischer atlas de gehirns. Schniktte durch das menschliche gehirn in photographischen originalen. Abteilung I — 32 frontalschnitte durch eine grosshirn- hemisphaüre. Breslau: Schletter'schen Buchhandlung (Franck & Weigert); 1897.

Wernicke C. The symptom-complex of aphasia. Diseases of the nervous system. New York: Appleton; 1908. p. 265–324.

Wilson SM, Saygin AP, Sereno MI, Iacoboni M. Listening to speech activates motor areas involved in speech production. Nat Neurosci 2004; 7: 701–2.

Wong FC, Chandrasekaran B, Garibaldi K, Wong PC. White matter anisotropy in the ventral language pathway predicts sound-to-word learning success. J Neurosci 2011; 31: 8780–5.

Yamada K. Diffusion tensor tractography should be used with caution. Proc Natl Acad Sci USA 2009; 106: E14.

Yaşargil MG. Impact of temporal lobe surgery. J Neurosurg 2004; 101: 725–38.

Yeatman JD, Dougherty RF, Rykhlevskaia E, Sherbondy AJ, Deutsch GK, Wandell BA, et al. Anatomical properties of the arcuate fasciculus predict phonological and reading skills in children. J Cogn Neurosci 2011; 23: 3304–17.

Yeterian EH, Pandya DN, Tomaiuolo F, Petrides M. The cortical connectivity of the prefrontal cortex in the monkey brain. Cortex 2012; 48: 58–81.

York GK. Localization of language function in the twentieth century. J Hist Neurosci 2009; 18: 283–90.

Zaborszky L, Heimer L. Combinations of tracer techniques, especially HRP and PHA-L, with transmitter identification for correlated light and electron microscopic studies. In: Heimer L, Záborsky L, editors. Neuroanatomical tract-tracing methods 2. New York: Plenum Press; 1989. p. 49–96.

Zaidel E, Aboitiz F, Clarke J. Sexual dimorphism in interhemispheric relations: anatomical-behavioral convergence. Biol Res 1995; 28: 27–43.