The Unique Fiber Anatomy of Middle Temporal Gyrus Default Mode Connectivity

BACKGROUND: The middle temporal gyrus (MTG) is understood to play a role in languagerelated tasks such as lexical comprehension and semantic cognition. However, a more specific understanding of its key white matter connections could promote the preservation of these functions during neurosurgery.

OBJECTIVE: To provide a detailed description of the underlying white matter tracts associated with the MTG to improve semantic preservation during neurosurgery.

METHODS: Tractography was performed using diffusion imaging obtained from 10 healthy adults from the Human Connectome Project. All tracts were mapped between cerebral hemispheres with a subsequent laterality index calculated based on resultant tract volumes. Ten postmortem dissections were performed for ex vivo validation of the tractography based on qualitative visual agreement.

RESULTS: We identified 2 major white matter bundles leaving the MTG: the inferior longitudinal fasciculus and superior longitudinal fasciculus. In addition to long association fibers, a unique linear sequence of U-shaped fibers was identified, possibly representing a form of visual semantic transfer down the temporal lobe.

CONCLUSION: We elucidate the underlying fiber-bundle anatomy of the MTG, an area highly involved in the brain's language network. Improved understanding of the unique, underlying white matter connections in and around this area may augment our overall understanding of language processing as well as the involvement of higher order cerebral networks like the default mode network in these functions.

KEY WORDS: Middle temporal gyrus, MTG, DSI, Anatomy, Tractography, White matter

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he middle temporal gyrus (MTG) has been implicated in numerous tasks related to lexical comprehension and semantic cognition.^{1,2} For example, this region is important for understanding visual^{2,3} and auditory messages,^{1,4} and is thought to utilize contextual knowledge to retrieve the relevant semantic information required for these tasks.⁵⁻⁷ In addition, these processes are disrupted in the MTG in several clinical disease states, such as in agraphia⁸ and schizophrenia.⁹⁻¹¹

ABBREVIATIONS: DMN, default mode network; DSI, diffusion spectrum imaging; ILF, inferior longitudinal fasciculus; LI, laterality index; MTG, middle temporal gyrus; SLF, superior longitudinal fasciculus; TPOJ, temporo-parieto-occipital junction

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Current models of language function describe distinct dorsal and ventral pathways; however, there is disagreement regarding the anatomic pathways by which semantic language transfer occurs.¹² Additionally, the role of the MTG in the relationship between the salience and default mode networks (DMN) are contentious, including whether the semantic network is a part of the DMN. There is also uncertainty over how the MTG structurally facilitates these distinct functions.

In this study, we created a cortical model of the MTG utilizing diffusion spectrum imaging (DSI)-based fiber tracking validated by cadaveric brain dissection. By analyzing the subcortical anatomy and key white matter bundle connections of the MTG, we aim to provide a more thorough understanding of the role of the MTG in language processing which can be utilized by the operating neurosurgeon for improved neuro-oncological outcomes following

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cerebral surgery in this area. We discuss our findings in the context of semantic language function and the anatomy of the ventral language stream.

inferior frontal gyrus; MFG, middle frontal gyrus; FP, frontal pole.

METHODS

Defining Regions of Interest

The MTG is 1 of 3 gyri comprising the temporal lobe. It extends from the anterior temporal pole to the junction of the temporal, parietal, and occipital lobes, i.e. the temporo-parieto-occipital junction (TPOJ). In this study, we defined the MTG into 3 regions of interest (ROI): an anterior ROI extending from the temporal pole posteriorly one-third the length of the gyrus, a posterior ROI extending from the posterior point at which the superior temporal sulcus curves dorsally to terminate in the angular gyrus of the inferior parietal lobule, and a middle ROI extending between the boundaries of the anterior and posterior regions (Figure 1). Each ROI occupied approximately one-third the length of the MTG and were bounded by the superior and inferior temporal sulci.

Tractography

Fiber tracking analysis was completed utilizing diffusion imaging with corresponding T1-weighted images from 10 healthy, unrelated subjects obtained from the Human Connectome Project (Subjects IDs: 100307, 103414, 105115, 110411, 111312, 113619, 115320, 117112, 118730, and 118932).¹³ After brain registration in Montreal Neurologic Institute coordinate space,¹⁴ tractography was performed in DSI

Studio (http://dsi-studio.labsolver.org) using a 2 ROI approach to initiate fiber tracking from a user-defined seed region.^{15,16} The tractography strategy utilized to analyze these data has been previously described elsewhere.¹⁷⁻²⁰

Tractography was completed along the length of the gyrus from the anterior temporal pole to the bend of the superior temporal sulcus into the parietal lobe. Small U-shaped fibers identified during fiber tracking analysis were isolated sequentially along the length of the MTG using the same 2 ROI approach, which was used to isolate larger fiber bundles.¹⁶ All tractography was completed prior to cadaveric study. Laterality indices (LI) were calculated based on resultant tract volumes from major identified tracts, and the unpaired *t*-test was used to assess for significant differences between cerebral hemispheres ($P \leq .05$).

Literature Review

A simulated brain image was created and marked with coordinates for the left temporal pole on multi-image analysis MANGO (Version 4.1; Research Imaging Center, UTHSCSA; http://ric.uthscsa.edu/mango/). This image was then imported into Sleuth software (Version 3.0.4) to conduct a reverse search of functional neuroimaging studies in the BrainMAP Functional database. A search strategy was created focusing only on experiments that included functional magnetic resonance imaging (fMRI) studies of the temporal pole (N = 300). Studies identified were then qualitatively analyzed by one reviewer (N.B.D.) and categorized into 1 of the 6 diagnostic and statistical manual of mental disorders, 5th edition cognitive domains: learning and memory, perceptual-motor function, language, executive function, complex attention, and social cognition. Repeated studies or studies that did not fit into one of the above domains were excluded. Results of this review are presented in Table, **Supplemental Digital Content**.

Postmortem Dissections

To validate the tractography results, we sought to demonstrate the location of white matter tracts connecting to the MTG with gross anatomic dissections for qualitative visual agreement.¹⁷⁻²¹ Ten specimens were used for this study from previously otherwise healthy individuals, obtained from our institution's Willed Body Program with approval from the Oklahoma State Anatomic Board. The methods utilized for postmortem dissection of the cadaveric brains and preservation of relevant white matter tracts of interest have been previously described.^{17-20,22}

All white matter tracts were dissected in both hemispheres.

RESULTS

Long-Range White Matter Tracts of the MTG

Two large fiber bundles were identified during fiber tracking analysis of the MTG: the superior longitudinal fasciculus (SLF) and the inferior longitudinal fasciculus (ILF). The SLF was found to arise predominantly within the middle and posterior thirds of the MTG, with some fibers arising within the anterior temporal pole (Figure 2). The fibers course craniocaudally within the temporal lobe before curving 180° at the level of the angular gyrus to pass anteriorly toward the frontal lobes. Coursing deep to the sensorimotor cortex, fibers from the SLF diverge at the posterior extent of the frontal lobe with terminations in the posterior aspect of the superior, middle, and inferior frontal gyri. Connections





FIGURE 3. Inferior longitudinal fasciculus (ILF). The ILF, cyan and magenta tracts on tractography A-D and depicted with and without blue lines on dissection E-F, arises from the anterolateral aspect of the middle temporal gyrus, and courses posteriorly deep to the SLF, passing deep to the gray matter of the temporo-parieto- occipital junction and lateral to the ventricle. It terminates within the parts of the occipital lobe, including the posterior part of the lingual gyrus and the postero-superior aspect of the cuneus. MTG, middle temporal gyrus; ITG, inferior temporal gyrus; TP, temporal pole; FP, frontal pole.

from the MTG to the inferior frontal gyrus demonstrated some variability across subjects, with fibers terminating in some combination of the pars opercularis, pars triangularis, and pars orbitalis in different brains. The SLF also projects from the posterior part of the MTG to the supramarginal and angular gyri of the inferior parietal lobule. These connections were identified bilaterally without any significant variation across subjects between right and left SLF.

The ILF arises from the anterolateral aspect of the MTG and courses posteriorly through the subcortical white matter of the temporal lobe deep to the SLF (Figure 3). It passes deep to the gray matter of the TPOJ junction lateral to the ventricle to terminate within different parts of the occipital lobe, including the postero-superior aspect of the cuneus and the posterior part of the lingual gyrus at the occipital pole. Although there was no noted variation bilaterally between the hemispheres, terminations
 TABLE.
 Lateralization Indices for the Middle Temporal White Matter

 Tracts
 Tracts

Tract	Volume/tract (left)	Volume/tract (right)	LI	P value
SLF	54.7	35.1	0.215	.039
ILF	47.0	36.0	0.103	.260

of the ILF demonstrated some variability across subjects. Specifically, the ILF would either terminate in both the cuneus and lingual gyrus or it would terminate in either the cuneus or lingual gyrus. Single termination tracts of the ILF were more common in the lingual gyrus at the occipital pole.

LIs based on the tract volumes calculated for the SLF and ILF are shown in the Table. The LI for the ILF was not statistically different bilaterally (*P*-value = .260). In contrast, the



FIGURE 4. Short association fibers of the middle temporal gyrus. An abundance of local U-fibers was identified on dissection **A** and tractography **B**. These fibers connect the middle temporal gyrus to the superior (green lines) and inferior (orange lines) temporal gyri.

SLF was noted to be lateralized to the left cerebral hemisphere (P-value = .039).

Short-Range White Matter Tracts of the MTG

An abundance of local association fibers was identified while performing the fiber tractography and gross anatomic dissections of the MTG. These local white matter pathways have a characteristic morphology consisting of U-shaped fibers that connect adjacent areas of cortex across a sulcal structure. U-shaped fibers were identified within the MTG and between the MTG and the superior and inferior temporal gyri. Examples of the different types of U-fibers identified during fiber tractography and gross anatomic dissection are shown in Figure 4.

During fiber tracking analysis, we also noted a unique sequential arrangement of U-fibers coursing from the posterior MTG to the temporal pole (Figure 5). Superficial dissection of the MTG confirmed the existence of this linear sequence of short fiber bundles in both the left and right cerebral hemispheres. The fibers run in sequence along the lateral aspect of the gyrus, superficial to the SLF and ILF which run within the deep subcortex of the temporal lobe. At times, these U-shaped fibers branch to connect the MTG to parts of the superior and inferior temporal gyri.

DISCUSSION

The role of the MTG in semantic language has been well established¹; however, its simultaneous involvement in the DMN has raised questions over a possible role of the DMN in language. In this study, we used diffusion tractography validated by gross anatomic dissection to describe the connections of the MTG in relation to gross anatomic structures. Although dissection allowed for qualitative understanding of tract orientation, tractography further allowed us to quantify tract volumes to understand laterality. As mentioned, the discovery of a unique U-fiber sequence helps to explain a fundamental pattern of connectivity within the MTG and the significance of the DMN in language processing.

The MTG and the Dual Stream Model of Language Function

Contemporary understanding of the human language network rests on its segmentation into 2 distinct, but interacting, language streams.²³ A model by Catani²⁴ proposes ventral semantic language transfer occurs from the posterior temporal lobe at the TPOJ down the length of the temporal lobe to the anterior temporal pole, with the uncinate then relaying the semantic information to the frontal lobe.^{24,25} The identification and description of a linear sequence of "U"-shaped fibers traversing the length of the MTG between the TPOJ and the anterior temporal pole in this study suggest that semantic transfer may occur according to this model. This helps to explain a fundamental pattern of resting state functional activity, namely that parcellations of the MTG are functionally linked sequentially to their anterior neighbors down the length of the gyrus. Although we did not identify the uncinate fasciculus during fiber tracking analysis of the MTG, the anterior temporal pole has been shown to connect to the frontal lobe in several other studies.²⁵⁻²⁷

Relevance of the DMN to the MTG and Semantic Retrieval

The potential relationship between the DMN and semantic function was proposed because of the role of several nodes of the network in language. Additionally, fMRI studies have



FIGURE 5. The unique "U"-shaped fiber sequence of the middle temporal gyrus. A sequential arrangement of U-shaped fibers from the posterior aspect of the middle temporal gyrus to the temporal pole is highlighted on tractography A and dissection B-F. These fibers are present bilaterally and run along the lateral aspect of the gyrus, superficial to the SLF and ILF. All images A-F are similarly oriented caudal-rostral.

shown a lack of deactivation of the DMN in semantic tasks,^{28,29} though this has not been consistently observed and may be dependent on task difficulty.³⁰ The involvement of the DMN in semantic function is however consistent with the growing understanding of its important role in cognition. Recently, a distinct semantic network was proposed to underlie multimodal semantic cognition, which overlaps with areas of the extended DMN.³¹ Whether the semantic network is truly distinct from this system is therefore still under discussion.

The MTG is one region common to both networks; however, only the posterior MTG is primarily involved in semantic cognition,⁶ though fMRI studies involving language function often show activation of the entire MTG.³⁰ The unique Ufiber sequence identified here may explain activation patterns down the length of the MTG and is also concordant with the Catani model.^{24,25} The internal organization of the MTG may therefore explain the integration of the DMN with the semantic network or underlie the role of the DMN in language function, as it facilitates a link between the posterior MTG and the temporal pole where different aspects of cognition may be integrated. Furthermore, when conducting a search of the literature for fMRI studies highlighting the temporal pole, the majority of research focused on the cognitive domain of learning and memory, and more specifically verbal memory, supporting this hypothesis (Supplemental Digital Content). Conversely, it may link the DMN and semantic network and form the basis of their difficult segregation. The exact role of each network in semantic function is yet to be determined, though future studies should target the MTG as a ROI when evaluating these networks.

CONCLUSION

The MTG is an important part of the cortex involved in language comprehension and contextually guided semantic retrieval. The identification and description of a linear sequence of local "U"-shaped fiber bundles down the length of the MTG may explain how semantic transfer occurs in the ventral language stream and may also underlie the DMN connectivity of the MTG. Additional studies are needed to better understand the role of the MTG in language function, and the DMN within this domain.

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Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article. Dr Sughrue is the Chief Medical Officer of Omniscient Neurotechnologies.

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Supplemental Digital Content. Table. Literature review. A, A reverse search of the literature was conducted using coordinates of the left temporal gyrus for fMRI studies with Sleuth software. B, Results of this search were qualitatively categorized based on their relation to the 6 key domains of cognitive function according to the diagnostic and statistical manual of mental disorders, 5th edition. Abbreviations: L_TGv, left temporal gyrus; MNI, Montreal Neurological Institute; fMRI, functional magnetic resonance imaging; ROI, region of interest.

COMMENT

• he authors have presented an interesting anatomical study of the MTG and its connections using a combination of MR tractography and postmortem dissections. Through this investigation, authors identified a linear sequence of "U-shaped' fibers traversing the length of the MTG which sheds light on its internal organization, corroborating the model proposed by Catani et al¹ of ventral semantic language transfer down the temporal lobe. It also speaks to its potential role in connecting the default mode network (DMN) with language processing. It would be interesting to know whether these short fiber bundles had a hemispheric predominance since authors note that these fibers traveled bilaterally. Additionally, authors note that at times these fibers branched to parts of the superior and inferior temporal gyri. Future studies focusing on these other U-fiber connections, including laterality and whether there were any patterns to branching points along the MTG, may further enlighten our understanding of the middle temporal gyrus and its relationships and roles in language processing. Papers like this defining the different fiber tracts in the brain will result in better understanding of the neuroanatomy, safer operations, and better outcomes in neurosurgery.

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