doi:10.20944/preprints202008.0369.v2

Extreme capsule is a Bottleneck for Ventral pathway

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September 6, 2020

Abstract

As neuroscience literature suggests, extreme capsule is considered a white matter tract. Nevertheless, it is not clear whether extreme capsule itself is an association fiber pathway or only a bottleneck for other association fibers to pass. Via our review, investigating anatomical position, connectivity and cognitive role of extreme capsule, and by analyzing data from the dissection, it can be argued that extreme capsule is probably a bottleneck for the passage of uncinated fasciculus (UF) and inferior fronto occipital fasciculus (IFOF), and its different role of language processing is due to various tracts that pass it through.

Keywords: Extreme capsule, uncinate fasciculus, IFOF, ventral pathway of language, bottleneck, DTI

Introduction

The extreme capsule (EmC) is a highly thin fiber system that connects the frontal and temporal opercula with the insula. There is a key question, yet unanswered; if the EmC itself is a nerve bundle for the processing of language in the ventral route or is it more a place for nerve fibers such as Inferior fronto-occipital fasciculus (IFOF) and uncinate fasiculus (UF) to pass through. Previous research can only be considered a first step towards a more profound understanding of EmC. As far as we know, no previous research reviews has investigated the role of EmC as a language pathway. Thus we aimed to evaluate the data of the literature on the role of EmC as a language pathway in the current study. This paper is divided into five sections: Section one gives a brief overview of anatomy of the EmC. The next chapter investigates the role of extreme capsule and other communication fibers in human language development and cognitive language functions. The third section reviews various cognitive roles that EmC is involved in. The fourth section introduces and discusses diseases in which the EmC is involved. And in the last section the EmC is described by dissections in monkey.

The Anatomy of the Extreme Capsule

Anatomical location

Extreme capsule and external capsule are two white matter structures, located between insula and putamen. These structures that are separated by claustrum, connect occipital, temporal, and frontal lobe together.[1][2][3]The mid-portion of the superior temporal region connects to the mid-portion of the ventral and lateral parts of the prefrontal cortex through fibers in the EmC. The EmC fibers in the frontal lobe divide into two pathways aiming either the superior ramus or inferior ramus. Superior ramus is placed in the white matter of the inferior frontal lobe, and inferior ramus is located beneath the claustrum on the floor of the orbital cortex, laterally adjacent to the fibers of the Uancinate Fasiculus.[4] It goes to the inferior parietal lobule caudally and is placed next to the other fibers inside the superior temporal gyrus called Middle Longitudinal Fasciculus (MdLF). Although the EmC and MdLF move side by side within the white matter of the caudal superior temporal gyrus and the lower parietal lobule, the two fibers can be distinguished. The EmC fibers are located inside the MdLF fibers in the caudal part. At the posterior area of the insula, EmC fibers enter the frontal lobe along the inner wall of the insula, while the MdLF fibers remain inside the superior temporal gyrus and are located at the top of the temporal pole. Whereas the EmC is located on the lateral side of the claustrum, the external capsule is on the inner side (ventral) of the claustrum. UF is located in the ventral part of the EmC. While arcuate fasciculus (AF) , superior longitudinal fasciculus (SLF) II, and III are in the posterior and lateral parts of the EmC, SLF is in the ventral surface of the EmC.[3](Please see Figure 1)

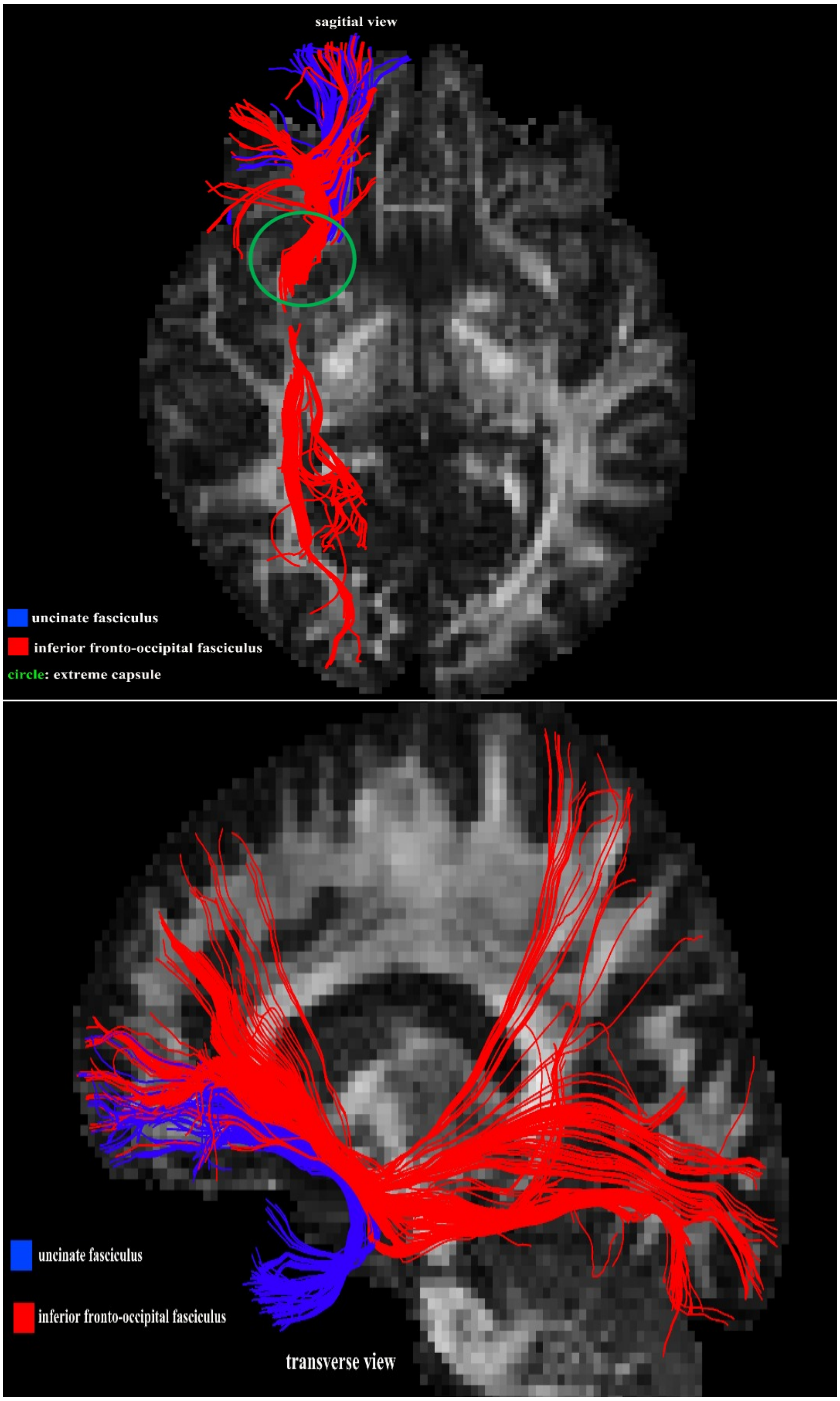

Figure 1: Sagittal and transverse views of IFOF, UF and EmC

Dissection

On the lateral surface of the brain, the insula is identified by removal of the frontal, parietal, and temporal lobes. After removing half of the cortex above the insula, the EmC appears, consisting of association fibers connecting the insula and the operculum.[5] After gentle removal of the insular cortex, from internal to external, external capsule, claustrum and EmC could be seen respectively, as well as putamen.[6]

The EmC is the anchor of the association fibers in the insular cortex itself and the connecting fibers between the insular and the opercular cortex. In angular gyrus, the short association fibers of the EmC become the convergent, and forms the white matter of short and long insular gyrus. Removal of short-circuit fibers re- veals claustrum, claustro-cortical fibers, IFOF, and UF, which move deepest in the EmC. At this point of dissection, the association fibers of the EmC converge toward the insula limen and move toward the temporal pole. In limen insulae, convergent association fibers of the EmC revolve UF. While UF fibers clearly connect the frontal lobe to the temporal pole on the vertical surface, the association fibers of the EmC cross the UF at the oblique surface and move to the mesial temporal lobe, including periamygdaloid cortex. The transverse incision of the temporal pole at the amygdala surface shows the inner surface and the extreme capsule association fibers leading to the temporal pole, mesial temporal lobe, and the amygdaloid complex.[7]

The UF is made up of long association fibers that connect the frontal and temporal lobes. It is located deeply in the Insula border and is therefore seen uncinated. In the lower part of the sulcus the anterior limiter and in the anterior part of the sulcus the inferior limiter is seen. The IFOF connects the middle and anterior frontal gyrus to the temporal, parietal, and occipital lobes and is located above the UF. It is the concave part, which includes the underside of the Putamen nucleus.[8]

The EmC contains white matter, uniting with the white matter which originates from the operculum. The insular cortex and EmC cover the claustrum, the external capsule, putamen, and the globus pallidus. The arcuate fasciculus can be linked to a series of leaves stacked on top of each other separated by a claustrum. The outer part of the leaf forms part of the extreme capsule, while the inner leaf is involved in the formation of the external capsule. The occipito-frontal fasciculus passes through the inferior insular cortex (inside the extreme and external capsules) and connects the frontal, insular, temporal, and occipital regions. The very close anatomical connections between arcuate fasciculus and the occipito-frontal fasciculus prevents accurate and complete dissection of this area.[9]

The insula consists of the cerebral cortex that forms the base of the sylvian fissure.

The outer layer of the EmC contains the arcuate fibers that connect the insulato the operculum in the area of the preinsular sulcus. Removal of the EmC shows claustrum in the apx area, and the external capsule is seen around the claustrum. The deeper part of the extreme and external capsules contains the occipito-frontal fibers and the uncinate fasciculus. These bundles are located beneath the basal cortex of the insula.[9]

Structural Connectivity

EmC is not a white matter structure (unlike UF and arcuate fasciculus); rather, a place for several fibers and bundles to course through. Some of them could be found under the insula on their way. Regarding language processing, the main pathways ap- pear to include IFOF and a branch of the Middle longitudinal fasciculus (MdLF) that passes through the EmC.[10]

All nodes in the frontal and temporal lobes pass through the ventral pathway , i.e. the EmC, and internally to the insula and orbitofrontal cortex. Starting from the anterior temporal lobe, the fibers are first internally connected to the MdLF in the posterior direction before entering the EmC.[11]
It seems that EmC contains association fibers connecting the cortex of the frontal lobe with cortex of insula and temporal lobe. Some fibers enter the white matter of superior temporal gyrus, continue as part of Mdlf and terminate in the superior temporal gyrus and superior temporal sulcus; Whereas the other fibers enterthe UF and project to temporal pole and amygdala.[12]

There are three ventral pathways between the frontal and temporal regions that pass below the insula, including: 1) UF, which connects the temporopolar regions to the orbital and the medial prefrontal cortices. The UF connects the anterior temporal lobe with the orbitofrontal cortex by forming a curve deep to the limen insula and courses the ventral extreme and external capsules. It projects to rostral part of the insula, the superior temporal gyrus, and the multimodal area of superior temporal sulus.[13] 2) The "extreme capsule fiber system" behind the UF which connects the superior and middle temporal to the inferior frontal regions (particularly the pars triangularis and the frontal operculum). Its long association fibers, connect the insula and the frontal / temporal operculum 3) The IFOF, which is located above the UF and connects the orbitofrontal and occipital cortices. It moves in the inner part of the "extreme capsule fiber system", internally and caudally, along the middle temporal gyrus.[14]
As indicated earlier, both IFOF and UF pathways pass through the EmC. While it is difficult to separate them anatomically, they are functionally separable.

From the posterior temporal nodes, the fibers join the MdLF in the anterior direction and then continue into the EmC, from fusiform gyrus, the fibers first move posteriorly in the inferior longitudinal fasciculus and then rotate in the caudal temporal lobe and join the MdLF in the anterior direction to reach the EmC. The EmC fibers are divided into two branches after entering the frontal lobe; the inferior branch which passes through the white matter on the floor of the orbital cortex and is connected to the orbitofrontal cortex, and the superior branch which passes through the white matter of the inferior frontal gyrus and terminates in the pars triangularis. Therefore, the EmC is the ventral communication pathway that connects the anterior temporal lobe to the lateral ventricle prefrontal cortex. The fibers coursing the EmC include two communication pathways originating from the temporal region: MdLF and ILF, which pass through the white matter of the superior and inferior temporal lobes and are connected by fibers from adjacent cortices. Therefore, composite fibers from EmC, MdLF, and ILF provide a structural connection for language processing through an ventral pathway.[11]

Signing Anatomy

The nerve network involved in Singing is located in the center of the superior longitudinal fasciculus, which includes the arcuate fasciculus, which extends to the "extreme capsule fiber system" and the U fibers that connect the branches of matter to adjacent pathways. The "extreme capsule fiber system" is the pathway of white matter association fibers that connects the temporal lobe to the frontal lobe through the EmC (connecting the 45th pars triangularis region to the superior temporal gyrus).[15]

To the process of learning a verbal stimulus with an image, it is found that the clusters of parietal temporal regions are related. In fact, these two areas are among the ones most of whose connections are via the extreme capsule fibers system. And the sound to meaning mapping function of the extreme capsule fibers system appears to be the most meaningful. This ventral pathway includes 1) a branch of the MdLF running along the superior temporal gyrus, a short piece of SLFI, and the EmC, and 2) longitudinal fibers that connect the temporal-parietal regions to the inferior frontal region.[16]

The ventral pathway includes the UF, which connects the anterior temporal to the lateral ventral cortex and the frontal orbital, and the fibers that pass more posteriorly through the EmC.[17]

Human Language Development and Cognitive Language Functions

Anatomically, human language development is not only due to an increase in the volume of the Broca area in our species, but also due to further brain growth, particularly the presence of long white matter pathways that have spread throughout the brain. Along with the arcuate fasciculus, it is necessary to examine the anatomy of the structures associated with the language.[18]

Examining the neural pathways that lead to language processing function of the ventral pathway, it is found that the structure connects the frontal and temporal regions, passes through the IFOF via the extreme and external capsules, and is, in some cases, known as the extreme capsule fiber system (ECFS). The ventral pathway of language includes at least two bundles, the IFOF and UF.[19]

The IFOF connects the occipital, internal parietal, and posterior temporal regions to the frontal lobe via the EmC / EC. The IFOF dissection shows that this bundle has two parts. One is a superficial tract involved in the lingual network, which terminates in pars triangularis (45 Brodmann) and pars orbitalis; and the second one, is a deep tract ending in three parts of the frontal region: 1) the anterior part of the frontal pole and the orbitofrontal cortex (OFC), 2) the middle part in the medial frontal gyrus and 3) the posterior part in the medial frontal gyrus and the lateral posterior prefrontal cortex. The deep tract moves through the EmC and the superficial tract moves through both the extreme and external capsules. The UF moves through EmC, laterally and ventrally to the IFOF.[19]
The pathway of these fibers is similar to that of the "extreme capsule fibers system" in monkeys, which consists of frontal and temporal connective fibers. It has also been shown that some of these connections, along with the MdLF in the monkey, connect the frontal lobe and the parietal lobe via the EmC. As a result, they make very similar connections to the IFOF front-parietal branches.[20]

Concerning the development of these pathways in childhood, it appears that the superficial ventral tract, moving through the extreme capsule, is not only formed earlier than the other pathways but matures earlier than the dorsal pathway.[19]

Examining and comparing the three language pathways in infants with adults, it was found that in newborns, the ventral pathway connects the ventral inferior frontal gyrus to the auditory cortex via ECFS. Moreover, the dorsal pathway that connects the temporal and prefrontal cortex is clearly seen in infants at birth. However, in contrast to adults, the dorsal pathway that connects the temporal cortex and the Broca area is not visible in newborns, standing for the inability of the newborn to speak.[21]

The EmC is a bundle that connects the temporal lobe to the inferior frontal gyrus and the inferior prefrontal regions. A study on determining its exact location on the sagittal plate, placed the DTI (diffusion tensor imaging) seeds both on the white matter below the pars orbitalis and pars triangularis in the inferior frontal gyrus, and in the middle part of the white matter below the superior temporal gyrus. The study found that damage to the UF and external capsule, which make up the ventral language pathway, was neither a good predictor of the level of damage to speech speed and fluency, nor of the person's ability to name.[22]

The EmC fibers play a role in semantic processing and language development, proved by the following observations: Immaturity of these pathways (EmC and UF) in premature newborns and maturity or increased functional connections following music therapy.[23]

Increased testosterone levels is associated with increased functional connections and the integrity of the fibers coursing the white matter structure of the EmC. The fibers appear to be the thicker (shown by higher fractional anisotropy), in boys with higher testosterone levels, and respectively thinner, in those less skilled in language than girls.[24]

In order to speech comprehension, the acoustic input must be transformed into semantic conceptual representations. On the other hand, the brain must connect the information from speech acoustics to the speech motor system to produce vocals, via the sound pathway. Since there are various actions involved in converting sound mapping to meaning in words, and since sounds are varied in the manner of their acoustic properties, each of these steps has different computational tasks and consequently, particular neural pathways. The dual pathway model shows that ventral pathway which includes structures in the superior and middle parts of the temporal lobe, is involved in the processing of perceptual signals, while the dorsal pathway, which includes structures in the posterior region of the planum temporale, plays a role in converting acoustic signals into productive representations, which is essential for speech production.[25]

Ventral and Dorsal pathway of Language

There are three main bundles that create the ventral linguistic network: the IFOF, the ILF and the UF.(Fig.2) Ventral pathway is projected on the ventral-lateral side and includes cortices in the superior temporal sulcus (STS) and in the posterior inferior temporal lobe (parts of the middle temporal gyrus (MTG)) and the inferior temporal gyrus.[25]

The dorsal tracts go posteriorly to the parietal lobe and finally to the frontal lobe.

The main parts of this route are located inside the posterior part of the Sylvian fissure, on the border between the parietal and temporal lobes (Sylvian parietal temporal (Spt)).[25] Sensory representations in this pathway are encoded by the superior temporal sulcus, whereas movement-based representations are encoded by motor areas. Finally, the Spt region, as a sensory-motor integration system, transfers between sensory and motor representations.[26]
Pars opercularis and pars tringularis play a much more important functional role in form-to-articulation, as a part of the dorsal pathway. In fact, pars opercularis,which is the posterior part of the Broca in the contemporary literature, premotor cortex and medial frontal gyrus, plays the key role in this process. Also, the Spt region, located at the border of both dorsal and ventral pathways, plays an important role in converting information to articulation. In fact, the ventral pathway includes the structures of the posterior temporal lobe that extend to the inferior parietal lobe. And the inferior frontal lobe, which is connected by the UF, is involved in the processing of the shape to meaning. And the dorsal pathway, which extends from the anterior speech areas, including the pars opercularis and the premotor areas to the posterior areas in the supramarginal gyrus and on the Spt pole, is involved in the conversion of shape information into production.[27]

Based on the dual-pathway language processing model, the cortical areas of the language are connected by several white matter pathways. The dorsal pathway contains superior longitudinal fasciculus (SLF) and its branches, while the ventral pathways include the extreme capsule fiber system (ECFS), the UF, the inferior longitudinal fasciculus (ILF), and the middle longitudinal fasciculus (MdLF).[28]
Also in the comprehension processing of sentences, children, unlike adults, use areas 45 that are connected to the superior temporal gyrus and superior temporal sulcus by the EmC. This use may be due to immaturity of the dorsal pathway of the language.[29]

Comparison of bilingual and monolingual children also showed that in bilingual children, the FA (fractional anisotropy) values in the ventral pathway of language processing are higher than in monolingual children.[30]
Comparison of FA values in adults showed that FA values were associated with the ability to learn syntactic rules and spell words. Also, in the case of trauma, damage to the dorsal pathway or immaturity of it during infancy, the language network changes from the dorsal pathway to the ventral route.[19]

In adults, the dorsal pathway consists of two parts, one that connects the inferior frontal gyrus (Broca) to the temporal cortex via SLF/AF, and one part of the ALF/AF that connects the precentral gyrus (pre-motor cortex) to the temporal cortex. In newborns, only part of the ALF / AF that binds the precentral gyrus to the temporal cortex is recognizable, but the ventral pathway that connects the ventral inferior frontal gyrus through the EmC to the temporal cortex, can be seen in both infants and adults.[31]

Semantic and Comprehension Process

In dual pathway models of language processing, superior temporal and premo- tor regions are connected to each other via a dorsal pathway consisting of AF/SLF and are activated with repetition of acts or words and speech production.[11][10] In contrast, middle and inferior temporal regions and the ventrolateral prefrontal cortex, interact via a ventral pathway that runs through the EmC and has a role in semantic processing and comprehension.[11][10][32][33]

In fact, the ventral pathway includes the primary auditory cortex, the middle superior temporal gyrus, the anterior superior temporal gyrus, the opercularis triangularis, the insula, and the motor cortex connected by the MdLF, and the EmC and possibly the arcuate fasciculus which are related to lexical-semantic features in word repetition and it plays a role in extracting meaning from the acoustic-phonetic derivations.[34][35]
In the semantic network of the left hemisphere, the nodes in the middle temporal gyrus are directly connected to the orbital prefrontal nodes. Middle temporal gyrus (and adjacent areas in the inferior temporal gyrus), connected to the prefrontal region via the EmC, is involved in storing and accessing lexical-semantic representations. Thus, this anatomical relationship between temporal and prefrontal areas, mediated by the EmC, appears to play a role in the choice of lexical information, as well as adjusting linguistic meanings to the stored knowledge about the world.[36]

Stephanie et al. used different ROIs to separate ventral language pathways. One ROI was placed on the occipital lobe on the coronal plate just behind the parieto-occipital sulcus, the second on the extreme and external capsules' white matter, and the third on the anterior white matter of the anterior temporal lobe. The pathway between the occipital and the ROI of EmC was considered the IFOF, the occipital-anterior temporal pathway was considered the ILF, and the pathway between the anterior temporal and the extreme/ external capsules was considered the UF.[37]

The process of language comprehension is supported by the ventral pathway. The IFOF, or called the ECFS, mediates the interaction between temporal and prefrontal areas and participates in the process of auditory perception. IFOF is the longest association bundle in the brain that connects the distributed areas of brain. The IFOF connects the frontal lobe, temporobasal areas, and superior parietal lobe to the frontal lobe and passes through the temporal lobe and insula. The superior part of the IFOF is near the Broca's area and includes the pars triangularis and opercularis, and part of it, is located in the middle temporal lobe on the roof of the temporal

horn. Its proximity to the two classical regions of language reflects its importance in today's linguistic models and appears to play a role in the comprehension process, naming and reading. Reduction of FA in IFOF is associated with impairment in many language modalities.[38]
The EmC connects BA 45 to the middle part of the superior temporal gyrus. This nerve fiber is located in the posterior part of the UF and appears to play a role in auditory comprehension of speech. The IFOF is a group of nerve fibers located at the caudal part of the external capsule and the lateral part of the UF.[39]
[39]

The placement of the EmC in the lingual area indicates the central role of this path- way in language processing, particularly the connection of the Broca area in the frontal lobe with the Wernicke's area in the temporal and parietal lobes. Electrical stimulation of the anterior floor of the EmC, which corresponds to parts of the IFOF, can cause semantic paraphrasing. Meynert also considered the areas of Claustrum and Insula, along with the ascending acoustic fibers of EmC, as the central linguistic complex. EmC has a strategic position in the language comprehension network. Within the "Distributed comprehension Network", all cortical areas in the temporal lobe (middle and anterior gyrus, fussiform gyrus) are connected to areas in the inferior gyrus (areas 45 and 47 Brodmann) through relatively short pathways in the EmC. Therefore, the EmC is considered a bottleneck, by whose damage, the entire comprehension network could be involved.[40]

The coding of auditory information related to objects, which includes short phrases, is done by the lateral ventral cortex in the monkey and the inferior ventral frontal cortex in humans. These connections are made by the UF and the "extreme capsule fiber system" with the anterior part of the superior temporal gyrus and are considered as the auditory ventral pathway in both types.[41]

The fact that myelination of the EmC of the right hemisphere is greater than the left, might be associated with greater comprehension and expression skills in children.[42][42]

Verbal Retrieval

The communication of the lateral ventral frontal cortex (Broca's area) takes place through different routes. In fact, the posterior part (area 44 Brodmann) is connected to the inferior parietal cortex through the third branch of the superior longitudinal fasciculus (SLFIII); and the anterior part (area 45 Brodmann) is connected to the middle part of the superior temporal gyrus - right in front of Heschl's gyrus - through the "extreme capsule fiber system" (ECFS). Area 45 of Brodmann has direct communications with Region 44 and is related to the belt region of the superior temporal auditory cortex via the EmC; hence it may play a role in the top-down language processing involved in verbal retrieval.[18]

Syntax processing

Many regions of the frontal and temporal cortex appear to play a role in both syntactic processing and syntactic expression. Following that, both the arcuate fasciculus and the EmC appear to be involved in the syntactic process. Studies have shown that the Brodmann's area 44, 45, 47 are active in the process of comprehension syntax.[43]

Steven et al. show semantic role of EmC in recovery of long-term storage and sentence comprehension.[44] In adolescents who were born premature, dorsal pathway trauma does not stand for language function insufficiency. It is however the corpus callosum, anterior commissure, and language ventral pathway (the fibers of the EmC and UF) that appear to be a better predictor of language outcomes. Bilateral reduction in FA is seen in the ventral pathway in adolescents with syntactic and semantic problems.[45][45]

In fact, with respect to the key role of EmC in semantic processing, it seems that damage to the extreme capsule could disrupt all components of language processing. In cases of damage to dorsal pathway in infancy, all functions of language and its components could be affected.[46] Therefore, the extreme capsule is the main route of language processing.

Other cognitive Functions of Extreme Capsule

Attention

In the attentional system, a ventral pathway that connects the parietal and temporal lobes to the anterior insula and lateral ventricle of the prefrontal cortex, is involved in integrating the perception of space for the intended action and for accurate estimation of the associated stimulus. In the locomotor system, the posterior parietal and prefrontal regions are involved in imaging the movement and pantomime use of objects. We hypothesize that a more general function of the ventral system could be to extract, link, and execute a set of fixed properties of perceived elements (in a limited number of specific features, e.g. "predecessor" categories) which is related to semantic memory and meaning. Thus, processing along the ventral pathway does not depend on the chronological or spatial sequence of the elements, but is optimized to test possible compounds for the extraction of meaning.[40]

Moreover, the activity of the right hemisphere temporo-parietal regions, includ- ing the supramarginal gyrus, the caudal superior temporal gyrus, the anterior insula, and the caudal part of the inferior frontal gyrus, the pars opercularis, and the pars triangularis, is associated with the "attention" network. The triangularis inferior frontal gyrus, which is responsible for processing information related to purpose, and filtering and removing the disturbing signal and selecting the appro- priate target, and insula, responsible for integrating self-awareness and conscious representation, as well as the middle temporal gyrus, are directly connected to each other by the EmC and is related to the ventral pathway of spatial visual attention.[47]

Active Visual Exploration

In active visual exploration, the superior temporal gyrus/ superior temporal sulcus, temporoparietal junction, and the inferior frontal gyrus are very active. Since the EmC and MdLF are the parts of the white matter that connects these areas, these two pathways appear to play a role in visual exploration and target search (spatial orientation and attention).[48]

Truth Recovery

Processing related to truth recovery is accomplished by both posterior and ventral routes. By recall of mathematical facts, these connections between the parietal and frontal cortices are made by the extreme and external capsule. External/Extreme capsule system is the ventral pathway that moves between the insula and the putamen and connects the angular gyrus to the inferior frontal gyrus, pars triangularis (45 Brodmann and Broca). The EC/EmC system corresponds to the anterior sections of the rostral IFOF bundle (IFOF).[49]

Social Behaviors

The neural circuitry associated with social behavior, passes through frontal and temporal connections, in which various neural pathways are involved. The EmC appears to be a part of the brain circuit associated with social behavior, along with the ILF, cingulum, and arcuate fasciculus.[50]

Diseases in which Extreme capsules are involved

Huntington's disease

In Huntington's disease, fractional anisotropy (FA) of commissural fibers such as Corpus callosum, fornix, association fibers of EmC, external capsule, the IFOF, and the inferior longitudinal fasciculus is decreased in both hemispheres. Damage to the corpus callosum and the extreme and external capsules, may indicate severe damage to the white matter due to the degeneration of valerian in the end stages of the disease. Therefore, investigation of these tracts can help better diagnose the degenerative process of this disease.[51]

Alzheimer's disease

Analyzing changes in the white matter in healthy elderly, people with mild cognitive impairment and patients with Alzheimer's disease, a significant difference between FA and MD values, in the corpus callosum, from the genu to the splenium, the anterior interface, the external capsule /EmC/ temporal stem, cingulum and SLF could be observed. The results show that in addition to examining the association fibers between the hemispheres, examining the ventral pathways can be a helpful marker in diagnosing cognitive impairment.[52]

Stroke

Temporofrontal interactions during language perception are performed by the EmC, which connects the middle temporal lobe to the lateral ventricle prefrontal cor- tex. Injuries associated with perceptual impairments include involvement of the middle and superior temporal gyrus, the inferior frontal gyrus, the insular cortex, and large sections of subcortical tissue including the subinsular and preventricular white matter and the basal ganglia. The lesions associated with impaired perception in the depth of the white matter between the insular cortex and the putamen are in the projections of the EmC. Executive semantic processing (choice between several words) involves the contention of the lateral ventricle prefrontal cortex, which requires a strong frontotemporal connection. Because the lateral ventricle prefrontal cortex and the anterior temporal lobe are involved in the prefrontal cortex comprehension process, and since their connections are made by the EmC, damage to the EmC appears to damage the perception. In fact, in the statistical analysis of people with acute stroke, it was found that inability to repeat a word was due to damage to the arcuate fasciculus, whereas perception incapability was most associated with damage to the ventral pathway of the EmC.[32]

Analyzing the location of injury in the left hemisphere of people with a history of stroke, who were also able to tell stories, it was found that damage to the EmC was associated with inability to tell memory-based stories and stories with emotional load. In fact, the damage to the extreme capsule/ external capsule pathway was associated with damage to speech speed in response to questions related to what happened to the person at the time of the stroke (what happened to you during the stroke?). The ventral pathway connects the middle part of the tem- poral to

the frontal region through the inferior part of the EmC (Temporo-Frontal Extreme Capsule). A more detailed analysis revealed that insufficiency of speech speed was not related to damages to putamen, and since the EmC fibers are followed by putamen as the main target, this insufficiency is probably the consequence of damage to the EmC.[53]
The use of visual and auditory feedbacks in speech increases activity in the anterior insula regions and 47 Brodmann and 37 Brodmann bilaterally. The communication between hemispheres in these areas are made by the corpus callosum and the communications within a hemisphere are made by the EmC. Therefore, it appears that language can play an important role in the treatment process by using visual and auditory clues.[54]

Conduction Aphasia

In Conduction aphasia, where the dorsal pathway (Arcuate fasciculus) is damaged, activation of the ventral pathway (the EmC, the UF) and interaction with the dorsal pathway help to repeat the word correctly. Under normal circumstances, the repetition process takes place through the phonetic system. However, in conditions of damage to this system and the arcuate fasciculus, the ventral system participates in the process of repetition, particularly the repetition of real words, by using the semantic system.[55]

Semantic network connections between regions in both hemispheres, including temporal areas (the anterior and posterior middle temporal gyrus) and prefrontal (orbitalis, triangularis, deep frontal operculum, and inferior frontal gyrus), is made by logitudinal fibers of EmC. In fact, the deep frontal operculum is connected to the superior temporal gyrus through the EmC, and to the premotor region through the short fibers. Superior temporal gyrus appears to indirectly control the sensorimotor loop during speech perception.[36]
Examination of aphasic patients revealed that damage to the EmC may cause difficulty in speech comprehension.[56]
Also, the electrical stimulation of white matter below the 45th Brodmann area, which includes the EmC, causes errors in naming the living objects.[57]

Developmental Language Disorders

Children with developmental language disorders, SLF, ILF, mdlf, and external capsule hyperactivity were most commonly seen in the right hemisphere. In addition to the dorsal pathways, the ventricular pathways also play a role in the compensatory mechanisms of the language that are formed by the right hemisphere.[28]

Autism

In autistic children, not only is there the involvement of white matter structures AF, SLF, MLF, and ILF, but ventral pathways including UN, IFOF, and the EmC, are abnormal.[58] Moreover, FA changes in the EmC seem to be associated with IQ.[59]
Improvement in word production in these children is apparently associated with the arcuate fasciculus of the left hemisphere and EmC of the right. Thus it can be concluded that EmC has a compensatory role in language development.[60]

Moreover, investigating the relationship between IQ and maturation of extreme capsule can be effective in determining the role of this pathway in cognitive processes. In children with autism, an increase in the size of the arcuate fasciculus in the left hemisphere and in the EmC of both hemispheres was observed.[61]
Due to the damage of the pathways connecting the frontal and temporal lobes of autistic children, the use of music-based therapies and other therapies that target the EmC pathways, the arcuate fasciculus and the UF in the right hemisphere can enhance their communication skills.[62]

Chromosome 22q11.2 deletion Syndrome

The chromosome 22q11.2 deletion syndrome is represented with learning difficulties, poor social skills and intelligence, poor performance and emotional problems. It is found in these patients that ILF, MLF, and EmC grow significantly less than normal children.[63]

Schizophrenia

It has been observed that in people with schizophrenia, the right EmC and the left occipital thalamus are significantly distinguishable from the normal group due a lower level of integrity. This reduces the processing speed in these people.[64]

Investigating Extreme Capsule Anatomy and Language Pathway in Monkey

There are long communication pathways in monkeys, that connect the various parts of the lateral surface of the superior temporal gyrus and the supratemporal plane to the frontal cortex. They consist of three distinct fibers:1) AF that connects the top part of the superior temporal gyrus to the medial and orbitofrontal cortex, 2) The EmC that connects the middle parts of the superior temporal gyrus to the lateral surface of the frontal lobe, and 3)UF that connects the most posterior part of superior tem- poral gyrus to the dorsal part of the posterior lateral frontal cortex.[65]

The anterior to middle sections of the superior lateral temporal region send their axons through the EmC to the lateral ventral frontal cortex. Most of these fibers appear to reach region 45 and some region 44. These Fronto-Temporal axons, which form the EmC, are not only from the anterior temporal gyrus but also originate from the following: multisensory cortex in the superior bank, the depth of the temporal sulcus, the visual communication cortex in the superior temporal sulcus ventral bank and the posterior inferior temporal region. The axons that move through the EmC, and go to the lateral ventral area 12/47, originate from the ventricle bank of the superior temporal sulcus and the adjacent inferotemporal region, while the axons moving through the UF terminate in the orbital section of the frontal lobe, including the orbital section 12/47.[66]

In monkeys, Region 45 (equivalent to pars triangularis in humans) is connected bilaterally through the EmC with the middle part of the superior temporal gyrus and the superior temporal cortex sulcus. Superior temporal gyrus is involved in the processing of auditory information specific to one modality, and superior temporal sulcus is involved in multi-modality processing.

In monkeys, the superior temporal gyrus and superior temporal sulcus are connected to the PG-Opt region in the parietal lobe (equivalent to the angular gyrus in humans) via MdLF. Thus, in monkeys, a fronto-parietotemporal pathway consists of three cortical centers: 1)the prefrontal region 45, 2) the middle temporal region, 3) the caudal inferior parietal lobule. Through the two longitu-dinal association fibers, the EmC (Fronto-Temporal) and MdLF (Parieto-Temporal) are connected. Cortical regions related to language connections, involved in comprehension and expression, are organized as follows: The caudal inferior frontal gyrus (Broca) connects to the superior temporal region (Wernicke's area) through the EmC, and the angular gyrus through the MdLF.[3]

In monkeys, the posterior inferotemporal dorsal and frontal eye fields are connected to each other by the inferior longitudinal fasciculus and the EmC.[67]

In monkeys, the EmC is the principal association pathway, linking the middle superior temporal region with the caudal parts of the orbital cortex and the ven- trolateral prefrontal cortex, including BA 45. These areas are homologous to the Wernicke and Broca language areas in human, and thus the EmC (rather than the AF) may have an important role in language.[68]

The medial boundary of the insula is a band of white matter called the EmC. The anterior and posterior boundaries of the insula were viewed best from the sagittal plane. The coronal plane was utilized to define the superior, inferior and medial boundaries of the superior sulcus, inferior sulcus, and EmC respectively.[69]This pathway, normally involved in retrieval of memories stored in posterior association cortex, was adapted during human evolution for controlled retrieval of verbal information in the human left hemisphere.[70]

In monkeys, the EmC is associated with auditory processing and memory recovery. In humans it is related to verbal recovery. Ventral route is related to goal-directed observations –observation of an act which reaches a point-, while the posterior pathway is involved in extracting detailed information from observed actions. The pattern of connections in these two directions varies in chimpanzees, monkeys and humans. While monkeys and chimpanzees have more connections in the ventral route, the connections in humans are more posteriorly.[71]

conclusion:

Through our review, it seems like the EmC itself is not a nerve bundle, rather a place for nerve fibers to pass through. It mostly contains fibers of white matter. It appears that IFOF is the major fiber that crosses it through, in humans, and the "extreme capsule fiber system" in monkeys.

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