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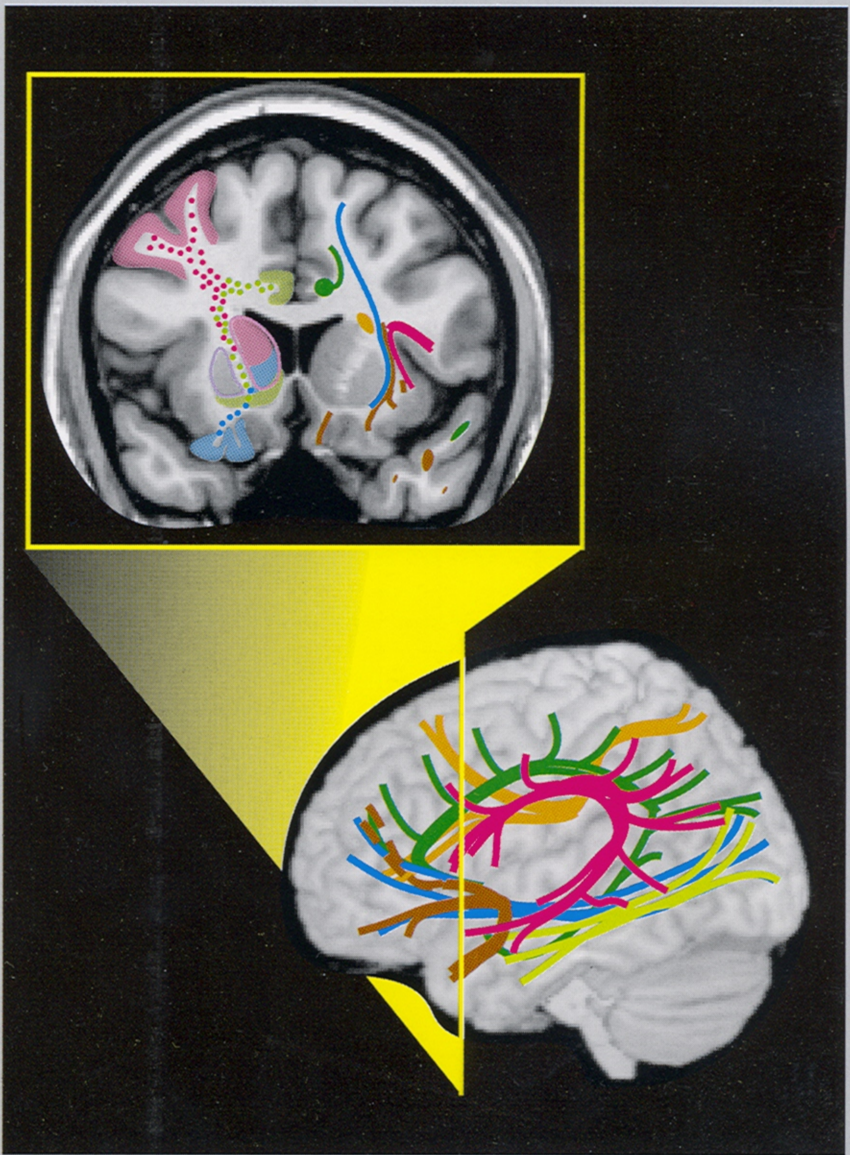

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WINDOWS TO THE BRAIN

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Section Editors

Traumatic Axonal Injury: Atlas of Major Pathways

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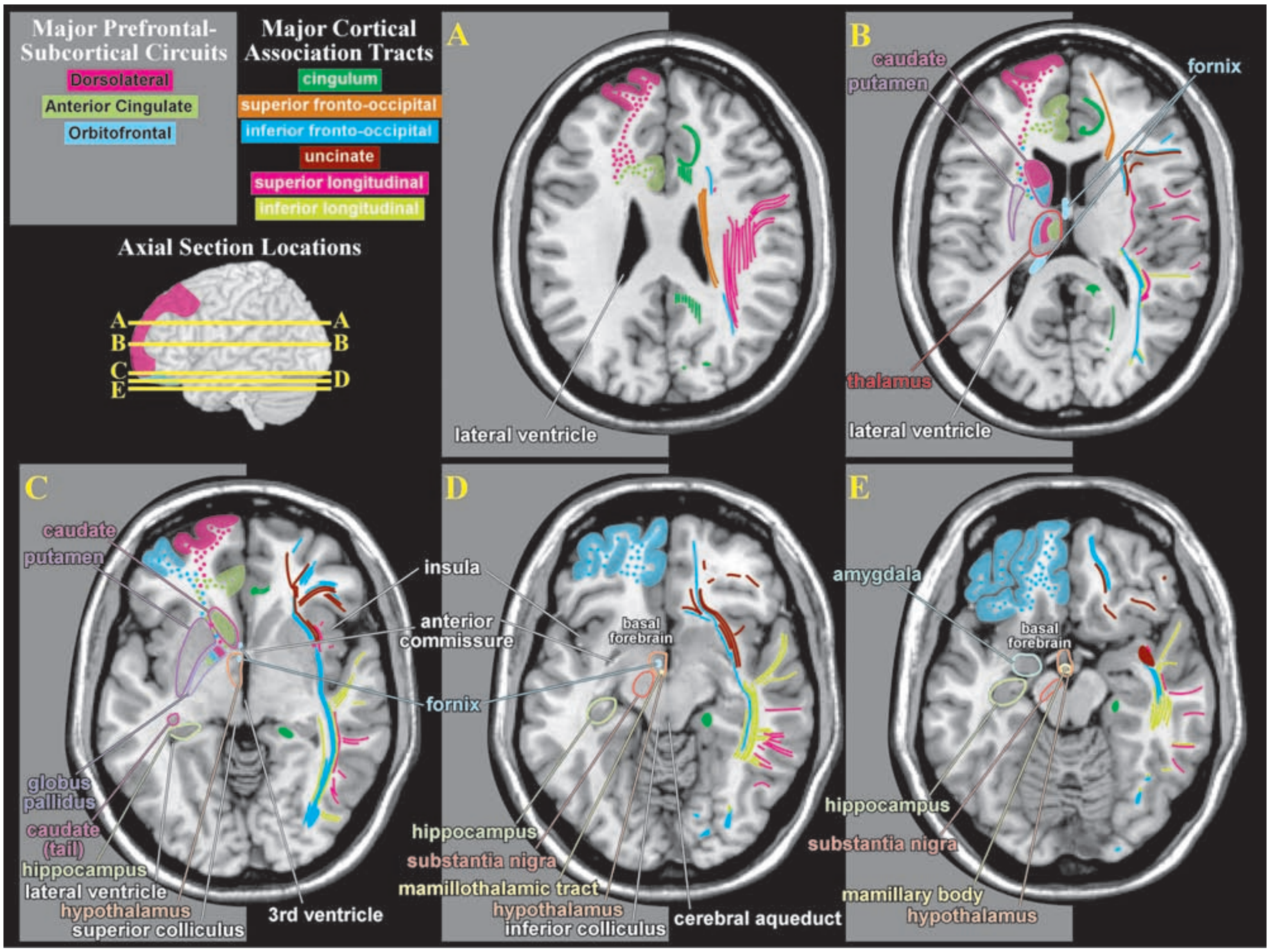

Cover and Figure 1. The structures involved in the dorsolateral (pink), anterior cingulate (green), and orbitofrontal (blue) prefrontal-subcortical circuits are color-coded onto the left side of axial magnetic resonance images (A–E). The approximate extent and locations of the classic major long cortical association tracts are color-coded onto the right side of axial magnetic resonance images (A–E) and summarized in cartoon form on a lateral view of the brain (Cover).[1,2]

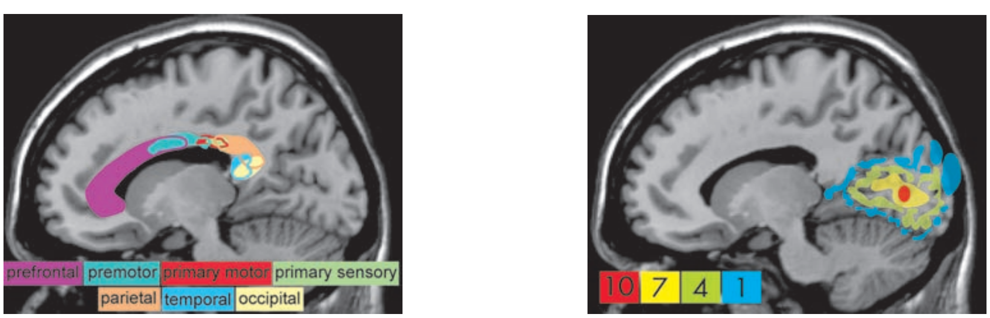

Figure 2. Variability (or probability) maps created by transforming the functional anatomy of individual brains into a common anatomic space indicate considerable normal variation.[3–8] On the right is a variability map for primary visual cortex (Brodmann's area 17), with the number of individuals (out of 10) which overlapped. On the left is a probability map (30% threshold) of the corpus callosum, color-coded by cortical area of fiber origin. Note the large areas of overlap, indicating differences in functional anatomy across individuals.

There is increasing evidence that combat-related traumatic brain injuries are a frequent occurrence. Recent studies detailing the most common injuries have found that approximately one-half involved the head or neck.[9,10] The great majority of injuries were due to explosions. Several studies from the Defense and Veterans Brain Injury Center (DVBIC) of soldiers returning from Afghanistan and Iraq document the occurrence of traumatic brain injury (TBI) in many soldiers.[11–14] Between January 2003 and February 2005, 59% of returning soldiers treated at Walter Reed Army Medical Center who had been near an explosion while deployed had suffered a traumatic brain injury (44% mild, 56% moderate-severe).[11] Common postconcussive symptoms included headache (47%), irritability/aggression (45%), and difficulty with memory (46%) and attention/concentration (41%).[12] A study of 596 active duty soldiers (all serving full-time at regular duty stations in the United States) found that 96 (16.1%) reported an injury while deployed, for which the symptoms (e.g., alternation in or loss of consciousness) were consistent with TBI.[13] This is similar to an earlier study of active duty soldiers, which found that 13.5% of nonparatroopers reported sustaining a TBI while in the Army.[15] The vast majority of these were mild TBIs, as indicated by either no or only brief loss of consciousness. In most cases, these less severe injuries would not have required medical evacuation.[14] It is well known that civilian mild TBI is underrecognized by both medical personnel and patients, resulting in significant underreporting.[16] There is evidence for a similar situation in the military and concern that combat-related mild TBI may often be unrecognized by both medical personnel and soldiers.[13,15,17]

Identification of TBI, particularly mild TBI, is often quite challenging. The most common type of injury, and the most likely injury to occur in mild TBI, is traumatic axonal injury (also called diffuse axonal injury).[18] While magnetic resonance imaging (MRI) is more sensitive than computed tomography (CT) in detecting this type of brain injury, even MRI is often negative.[18–23] In addition, some areas of injury may become less visible with time.[21] In such cases, MRI in the subacute and chronic stages is less likely to be positive than if acquired immediately following injury. There is increasing evidence that functional imaging (e.g., cerebral blood flow, cerebral metabolic rate) may be considerably more sensitive to the effects of TBI than structural imaging.[23–27]

Even small areas of injury within the white matter may have devastating consequences. Knowledge of the locations of major tracts and the brain areas they interconnect is thus critical for understanding clinical symptoms in the context of TBI. White matter tracts of particular importance in neuropsychiatry include those interconnecting areas of cortex (e.g., corpus callosum, association fiber tracts), those connecting areas of cortex to subcortical structures critical for cognitive/emotional functions (e.g., thalamic radiations) and those interconnecting these subcortical areas (e.g., fornix).[2,28] Tables 1 to 3 summarize the classic functional anatomy of the major white matter pathways important for cognitive and emotional functioning (Figure 1). They are based on recent studies delineating the anatomy of white matter in humans, primarily using diffusion tensor imaging.[1,2,6–8,29–33]

Intriguing results from sophisticated radioisotope tract-tracing studies in nonhuman primates suggests that there may be significant errors in the classic view of cerebral white matter.[34,35] For example, this work has delineated three different components (in both location and areas connected) of the superior longitudinal fasciculus. A fourth pathway, which this research group considered to be the arcuate fasciculus, was also identified. A recent diffusion tensor imaging study[36] supports the existence of all four of these pathways in humans. Methods for delineating connections within the intact brain are undergoing rapid development and refinement. It is extremely likely that over the next decade, our understanding of the pathways within the brain that are important for cognitive and emotional functioning will change dramatically.

CONCLUSIONS

Care must be taken in applying this summary of functional anatomy to individual patients, as studies comparing pathway topography between subjects have shown considerable normal variability (Figure 2).[6–8]

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TABLE 1. Commissures Connecting Cortical Areas in Left and Right Hemispheres

Pathway (Areas Connected)	Functional Deficits[2]
Corpus Callosum[2,7,29,30]	Callosal disconnection syndromes
Rostrum, genu and anterior body (prefrontal cortex)	Cognitive dysfunctions; alien hand syndromes; apraxias
Mid-body (pre and supplementary motor cortices)	Compulsive/impulsive grasping/reaching due to loss of voluntary inhibition
Posterior Body (primary motor, primary sensory, parietal cortex)	Ideomotor and constructional apraxias; alien hand syndromes; dysomia; agnosias; agraphia; motor neglect; akinesias; tactile-verbal disconnection
Splenium (temporal and occipital cortices)	Visuomotor impairments; optic aphasia; optic ataxia; visual agnosia; memory impairments
Anterior Commissure[2,29,30]	Minimal information for discrete lesions—left hand apraxia and hearing deficits if injured along with the genu of the corpus callosum
Anterior division (olfactory bulbs and nuclei, anterior perforated substance)	
Posterior division (parahippocampal region, amygdala, inferior temporal and occipital cortex)	

TABLE 2. Long Tracts Connecting Cortical Areas Within Each Hemisphere

Pathway (Areas Connected)	Functional Deficits[2]
Superior Longitudinal Fasciculus[2,29,30]	Left: conduction aphasia; ideational apraxia; depression; anomia
aka **Arcuate Fasciculus**	Right: left hemispatial neglect
Medial long fibers (lateral frontal [Broca's area] to dorsolateral parietal, temporal [Wernicke's area] & occipital cortex)	
Lateral short fibers (frontal to parietal, parietal to occipital, parietal to temporal cortex)	
Inferior Longitudinal Fasciculus[2,29,30]	Disruption of information transfer between visual and limbic/memory areas
aka **Inferior Occipitotemporal Fasciculus**	
Long fibers (superior, middle and inferior temporal to lingula, cuneus, lateral occipital and posterior occipital cortex)	Left: alexia (if splenium also injured); bilateral tactoverbal dysfunction
Short fibers (temporal to temporal, occipital to occipital, occipital to parietal cortex)	Left or Right: impaired visual recent memory
	Bilateral: prosopagnosia
	Bilateral or Unilateral: visual object agnosia; contralateral visual field hemiachromatopsia
	Bilateral or Right: visual hypoemotionality
Superior Fronto-Occipital Fasciculus[2,29,30]	Left: akinetic mutism; disordered initiation and preparation of speech movements; transcortical motor aphasia; anomia and reduction in spontaneous speech with normal articulation
aka **Subcallosal Fasciculus, Superior Occipitofrontal Fasciculus**	
(Dorsolateral prefrontal to superior parietal cortex; classic occipital and temporal connections now in question)	
Inferior Fronto-Occipital Fasciculus[2,29–31]	Seldom injured alone—based on anatomy, injury might cause visuospatial abnormalities; visual recognition abnormalities; topognosia
aka **Inferior Occipitofrontal Fasciculus**	
(Dorsolateral & ventrolateral prefrontal to posterior temporal and occipital cortex; classic occipital connections now in question)	Bilateral: oculomotor apraxia; akinsia
	Bilateral more than Unilateral: optic ataxia; visual agnosia; impaired visual memory
	Bilateral or Right: impaired simultaneous perception; impaired spatial relations
	Right more than Left: impaired orienting of attention—
Uncinate Fasciculus[2,29–31]	important for retrieval of past information
(Orbital and inferior frontal to temporal pole, uncus, hippocampal gyrus and amygdala)	Right: impaired retrieval of episodic (autobiographical) memory
	Left: impaired retrieval of general knowledge of facts
Cingulum[2,29,30]	Lesion-deficit literature provides no way to distinguish between injury to the cingulum and injury to the cingulate cortex
Longest fibers (sub-genu frontal and paraolfactory area to uncus and parahippocampal gyrus)	Anterior cingulate cortex (agranular cortex) is motor-related (connections to amygdala; nucleus accumbens; medial dorsal thalamus; dorsolateral prefrontal & parietal cortex); injury may cause lack of emotional affective response to pain, depression, anxiety, akinetic mutism, impaired saccades
Short fibers (interconnects portions of frontal, parietal and temporal cortex)	Posterior cingulate cortex (granular cortex) is sensory-related (connections to temporal, parietal and orbitofrontal cortex); injury may cause
	Left or Right: Retro-splenial amnesia
	Right: loss of memory for spatial relationships; topographical disorientation
	Left: loss of verbal memory; blurring of right sides of objects

This is parallel to the normal variation in size, shape, and location of Brodmann's areas (Figure 2).[3–5] This known phenomenon adds a distinct level of uncertainty in predicting individual functional deficits following a brain injury. It should also be kept in mind that in many places multiple pathways travel close together, making it likely that a TBI will affect more than one and produce complex symptom clusters. These symptoms may not become evident for extended periods of time. Atlases and other visual external memory aids can assist clinicians in rapid memory recall of functional circuits and areas for review on patient imaging examinations.

TABLE 3. Pathways Connecting Cortical With Subcortical Areas Within Each Hemisphere

Pathway (Areas Connected)	Functional Deficits[2]
Internal Capsule[2,29,30,34]	**Anterior limb**
Anterior limb (anterior thalamic connections and frontopontine motor connections)	Bilateral: confusion, impaired initiative; impaired affect; impaired verbal memory
Genu (anterior and inferior thalamic connections and corticonuclear motor connections)	Unilateral: impaired reflexive eye saccades; eye deviation to lesion site
Posterior limb (superior, posterior, inferolateral thalamic connections and corticospinal, corticopontine and corticotegmental motor connections)	**Genu** Bilateral: somnolence; apathy; amnesia; abulia Unilateral: faciolingual weakness; dysarthria; dysphagia; cognitive impairment; executive dysfunction; contralesional asterixis
Note: Recent studies suggest that connections with frontal cortex extend further posterior in the internal capsule than previously thought, encompassing both the anterior limb and the genu.[1,37]	**Genu-Posterior limb** Unilateral: contralesional motor paresis; dizziness or vertigo Left: verbal memory deficits Posterior limb: Bilateral: pseudobulbar mutism; visual deficits; cortical deafness Unilateral: apathy; impaired consciousness; contralesional hemiparesis/hemiplegia; contralesional anesthesia/ataxia Left: verbal memory deficits
Fornix[2,29,38]	Recent memory deficits, with recall more affected than recognition; learning dysfunction
Precommissural (hypothalamus, septal nuclei, ventral striatum; orbital and anterior cingulate cortex)	Right: nonverbal memory deficits; visual retention disturbances, including deficits in anterograde visual memory, revisualization, visuospatial organization, construction ability, and topographical memory
Postcommissural (anterior nucleus of thalamus, hypothalamus—primarily mamillary body)	Left: verbal memory deficits; cognitive deficits

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