Neuroanatomical Principles in Neuropsychiatry

CHAPTER 3

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Introduction

Understanding structural and functional neuroanatomy is the key to delineating the relationship between the brain and behaviour. While the connection between neuroanatomical or neuroimaging findings and most primary psychiatric disorders remains nascent, neuropsychiatrists operate at this interface, understanding the behavioural, emotional and cognitive consequences of neurologic disorders, such as TBI, Stroke, Multiple Sclerosis. This type of “lesion-ology” has been a particular line of enquiry in clinical neuroscience[1]. It is therefore critical that neuropsychiatrists have a grasp neuroanatomy.

Neuroanatomy is inherently three-dimensional and relational. It is not well learnt through looking at still, 2D images and verbal descriptions of location and function. Rather, it requires an appreciation of how regions are organised in space, how they are connected, and how they interact within distributed neural networks. This perspective is particularly important in neuropsychiatry, where clinical presentations arise from dysfunction across interconnected circuits rather than from a single discrete brain region.

For the clinician, neuroanatomical knowledge provides a practical model for localising dysfunction and interpreting clinical symptoms**.** Particular patterns or syndromes in personality, executive function, language, memory, motivation, affect or social behaviour can provide clues to the brain regions and networks involved. The cerebral and cerebellar cortex provides much of the brain's capacity for perception, cognition, language, and complex behaviour; subcortical structures contribute to the motivation (emotion), regulation and integration of these processes; and white matter pathways connect these regions into distributed networks. These systems do not operate independently, with human behaviour emerging from their dynamic interaction.

This chapter provides a practical introduction to the neuroanatomy most relevant to neuropsychiatry. It is not intended to replace a comprehensive study of anatomy, but rather to establish a working three-dimensional model of the brain that can be applied to clinical practice, with a focus on neuroimaging.

The Axes of the Brain

Neuroimaging is generally presented as cross-sectional images along a single plane (Axial, Coronal or Sagittal (see Figure 1)). Multiple planes can be presented simultaneously to help localise lesions. As well as being presented as images on these three axes, the brain has an elegant functional organisation along three similar axes; Front-back, Left-right and Top-bottom. Before moving into the more specific localised brain functional areas, we will describe these functional axes describing the specialisation and integration along these axes.

Front–Back: Action and Perception

Along the anterior–posterior axis of the brain there is a transition from executive planning/motor organisation to sensation/perception[2]. This anterior-posterior division is delineated by the central sulcus, either side of which is the precentral gyrus (motor homunculus) and the postcentral gyrus

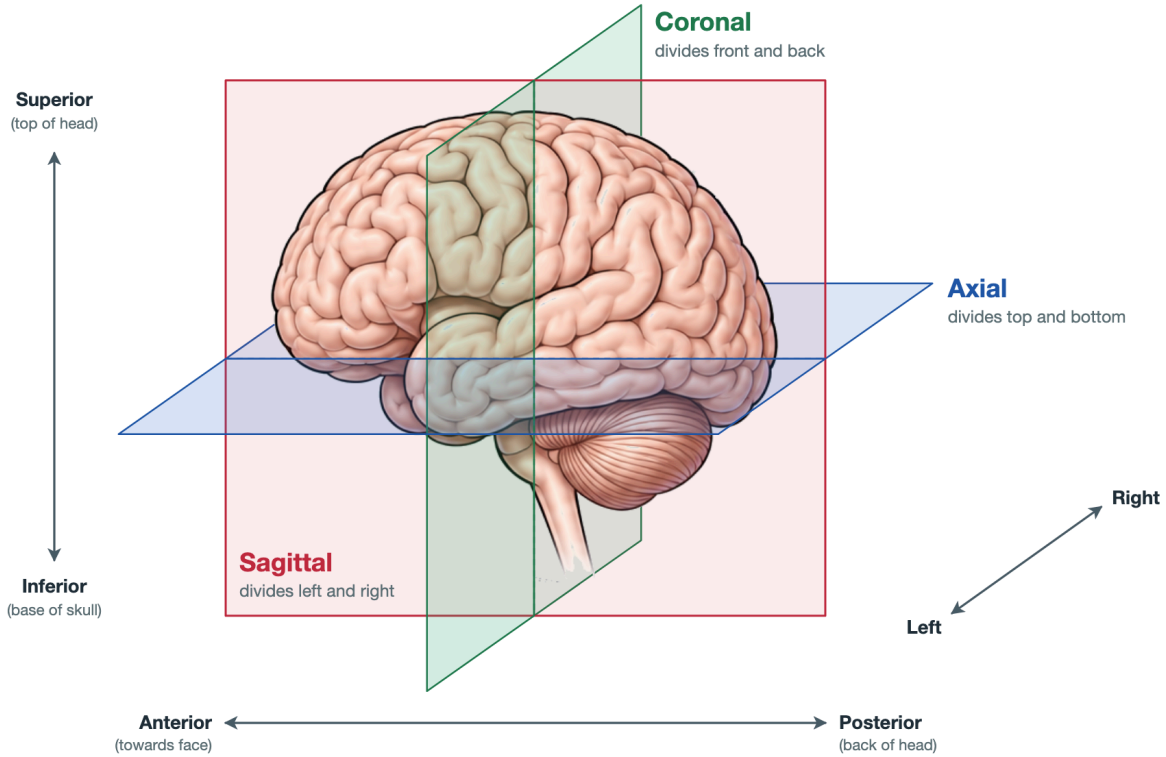


Figure 1 – Imaging planes (Axial, Coronal and Saggital) of the brain showing superior-inferior, anterior-posterior and Left-Right axes.

(sensory homunculus). In the posterior region the occipital, temporal and parietal cortices are heavily involved in processing and integrating visual, auditory and somatosensory information respectively. The frontal and pre-frontal regions are involved in selecting actions, planning behaviour, decision-making, executive control and motor movements. Data about the external world and the body are processed posteriorly and progressively integrated with goals, intentions and plans in the anterior regions. Important while matter tracts connecting the anterior and posterior regions include the superior longitudinal fasciculus, inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, cingulum, and uncinate fasciculus.

Right–Left: Hemispheric Specialisation

The left and right cerebral hemispheres demonstrate minor structural asymmetry called “brain torque” or Yakovlevian torque in which the right frontal pole is shifted slightly further anteriorly, protruding towards the left of the midline, while the left occipital pole is shifted posteriorly, protruding to the right[3]. These structural asymmetries are associated with important differences in their functional organisation[4]. The left hemisphere is typically dominant for language (i.e, fluency, comprehension, repetition, naming) and is more strongly involved in some forms of sequential and analytical processing. This left hemisphere language “dominance” is present in more than 95% of right-handed individuals and approximately 70% of left-handed individuals[5]. The left-hemisphere is also dominant for praxis (i.e. the ability to perform skilled purposeful movements). Consequently, many instances of apraxia will occur in those with left-sided brain damage and will co-occur with aphasias[6].

The right hemisphere has important roles in visuospatial processing, aspects of attention, prosody and assessment of the whole or "gestalt" of things. Because the right hemisphere tends to assess holistically, those with left hemisphere damage (i.e. a functioning right side) will have no hemi-spatial neglect, whereas those with right hemisphere damage (i.e. only functioning left hemisphere) will experience the "gnosis" syndromes ("gnosis" in Greek translates to knowledge), including left-sided hemi-spatial neglect. The hemispheric differences in specialisations are particularly evident in higher-order association cortices, whereas the basic sensory and motor functions show considerably greater bilateral representation. Table 1 lists functions primarily mediated by either right or left hemispheres as well as their corresponding deficits[7]. It is important that "left brain versus right brain" concepts do not leave readers with the impression of a strict dichotomisation. Most complex behaviours require the coordinated activity of both hemispheres, with information transferred through commissural (between the sides) pathways, the largest of which is the thick front to back fibre bundle known as the corpus callosum. Even functions that show strong hemispheric dominance, such as language, involve distributed networks extending beyond a single hemisphere. The brain therefore is not made up of strictly segregated modules but specialised AND integrated regions, with some limited ability of other parts to perform those functions in the case of the primary region failing.

Table 1 - Abilities mediated primarily by the right or left hemisphere and corresponding clinical deficits resulting from lateralized lesions. Adapted from Arciniegas et al (2018)[7]

Hemispheric function	Correlated clinical deficit
Left hemisphere	**Left Hemisphere**
Language • Execution • Comprehension • Reading • Writing	Aphasia • Nonfluent aphasia • Comprehension defect • Alexia • Agraphia
Verbal fluency (word list generation)	Reduced verbal fluency
Mathematical abilities	Anarithmetia
Praxis	Apraxia
Contralateral spatial attention	Right-sided neglect
Contralateral motor function	Right hemiparesis
Contralateral sensory function	Right hemisensory loss
Contralateral visual field perception	Right homonymous hemianopia
Right hemisphere	**Right hemisphere**
Speech prosody	Aprosodia
Nonverbal memory	Nonverbal amnesia
Design fluency (novel figure generation)	Reduced design fluency
Visuospatial skills • Familiar face recognition • Familiar place recognition • Unfamiliar face discrimination	Visuospatial deficits • Impaired facial discrimination • Prosopagnosia • Environmental agnosia
Visuomotor abilities • Constructional ability • Dressing (garment orientation)	Visuomotor deficits • Constructional disturbance • Dressing disturbance
Contralateral spatial attention	Left-sided neglect
Contralateral motor function	Left hemiparesis
Contralateral sensory function	Left hemisensory loss
Contralateral visual field perception	Left homonymous hemianopia

Top–Bottom: Cognition and Emotion

The brain also has a top-bottom organisation in which the lower parts of the brain perform basic physiological functions (e.g. pons, medulla in respiration and cardiac function), the subcortical circuits and nuclei are the key contributors to basic emotions (e.g. amygdala, peri-aqueductal grey in fear/anger) and the cortical regions are primarily responsible for higher order cognition. As with the previous axes, these patterns describe overlapping functions, and the cortical and subcortical regions are clearly both involved in various elements of cognition and emotion. Despite the overlap, it is primarily subcortical structures such as the amygdala, hippocampus, thalamus, basal ganglia, hypothalamus and pituitary that contribute to emotional salience, motivation, arousal and autonomic regulation. It has been shown in repeated experiments[8,9] that there is reciprocal inhibition between the amygdala and parts of the prefrontal cortex, demonstrating both top-down and bottom-up control of the system. This mechanism is key to understanding and implementing psychotherapy, which largely seeks to activate cognitive processes (i.e. prefrontal activity) as a way on inhibiting intense, negative emotions (i.e. lower subcortical circuits). These cortical-subcortical regions co-regulate one another and thus are closely connected by white matter tracts including the internal capsule, corona radiata and corticospinal tract.

In healthy functioning, however, this top-bottom cognition-emotion axes is best understood as an integrated processes[10,11]. Cortical regions continuously receive information about internal bodily states, reward, threat and emotional significance from subcortical systems, while cortical appraisal and executive control can modify subcortical responses. For example, the amygdala may rapidly signal potential threat, while prefrontal and hippocampal systems determine whether that threat is relevant in the current context and how it should influence behaviour. Similarly, the basal ganglia integrate motivational and reward information with cortical plans to influence the selection and initiation of behaviour. Neuropsychiatric symptoms can therefore arise when the balance or connectivity between cortical and subcortical systems is disrupted, producing abnormalities in emotion regulation, cognition and motivation.

Brain regions on Structural Imaging

A critical skill for the neuropsychiatrist is the interpretation of neuroimaging. Specialist radiologist assistance in interpreting images will always be important. However, there is no substitute to being able to examine and understand normal and abnormal neuroanatomy on structural brain scans, so that practitioners can make the clinico-radiological correlations themselves. Figure 2 shows labelled axial, coronal and sagittal sections of the brain on T2 FLAIR-weighted MRI imaging identifying the different cerebral lobes, subcortical structures, brainstem and cerebellum.

The important structures and regions in Figure 2 are defined by their relationship with sulci, gyri, fissures and ventricles. These landmarks should be understood with the caveat that variation is the rule of biology and the sulci/gyri in each individual may be configured somewhat differently. The frontal lobe extends anteriorly from the central sulcus to the frontal pole; the central sulcus separates it from the parietal lobe, while the precentral gyrus, immediately anterior to the central sulcus, contains the primary motor cortex. The parietal lobe lies posterior to the central sulcus and anterior to the parieto-occipital sulcus on the medial surface. Its postcentral gyrus, immediately posterior to the central sulcus, contains the primary somatosensory cortex, while the intraparietal sulcus

separates the superior and inferior parietal lobules. The temporal lobe lies inferior to the lateral (Sylvian) fissure and contains the superior, middle and inferior temporal gyri; its posterior boundary with the occipital lobe is less sharply defined on the lateral surface. The occipital lobe forms the posterior pole of the cerebral hemisphere and is best delineated medially by the parieto-occipital sulcus; the calcarine sulcus is a particularly important landmark because the cortex immediately surrounding it contains the primary visual cortex (V1).

The insula is a buried cortical region located deep within the lateral sulcus and is surrounded by the frontal, parietal and temporal opercula. The precuneus occupies the medial parietal cortex between the marginal branch of the cingulate sulcus anteriorly and the parieto-occipital sulcus posteriorly and is particularly well visualised on sagittal MRI. Among the deep grey-matter structures, the caudate nucleus has a characteristic C-shaped configuration that follows the lateral ventricle, with its head adjacent to the frontal horn, body alongside the ventricular body and tail extending into the temporal lobe towards the amygdala. The putamen lies lateral to the globus pallidus and medial to the insular cortex, with the external capsule separating it from the insula and the internal capsule separating it from medial structures. The globus pallidus lies immediately medial to the putamen; together, the putamen and globus pallidus form the lentiform nucleus, with the internal segment of the globus pallidus situated closest to the internal capsule.

The midbrain is the superior portion of the brainstem, situated between the diencephalon and pons, and is characterised by the cerebral peduncles anteriorly and the tectum posteriorly, with the cerebral aqueduct passing through its centre. The pons lies between the midbrain and medulla and is readily recognised by its prominent anterior bulge; the middle cerebellar peduncles extend laterally from it to the cerebellum. The medulla forms the inferior portion of the brainstem, extending from the pons to the cervicomedullary junction, where it transitions into the spinal cord. The cerebellum is divided into anterior and posterior lobes by the primary fissure. The anterior lobe lies anterior to this fissure and occupies the superior-anterior portion of the cerebellum, whereas the much larger posterior lobe lies posterior to the primary fissure and comprises most of the cerebellar hemispheres and vermis. The posterolateral fissure separates the posterior lobe from the smaller flocculonodular lobe.

There is no substitute to scrolling through many scans and identifying the various elements of normal and abnormal anatomy, developing a 3D conception of how each of the components fits together, with the clinical scenario in mind. Chapter 4 provides detailed neuroimages and descriptions of the how a range of neuropsychiatric conditions present with abnormal neuroradiological findings. Table 2 outlines broad functions of brain regions and the general effects of lesions to those areas.

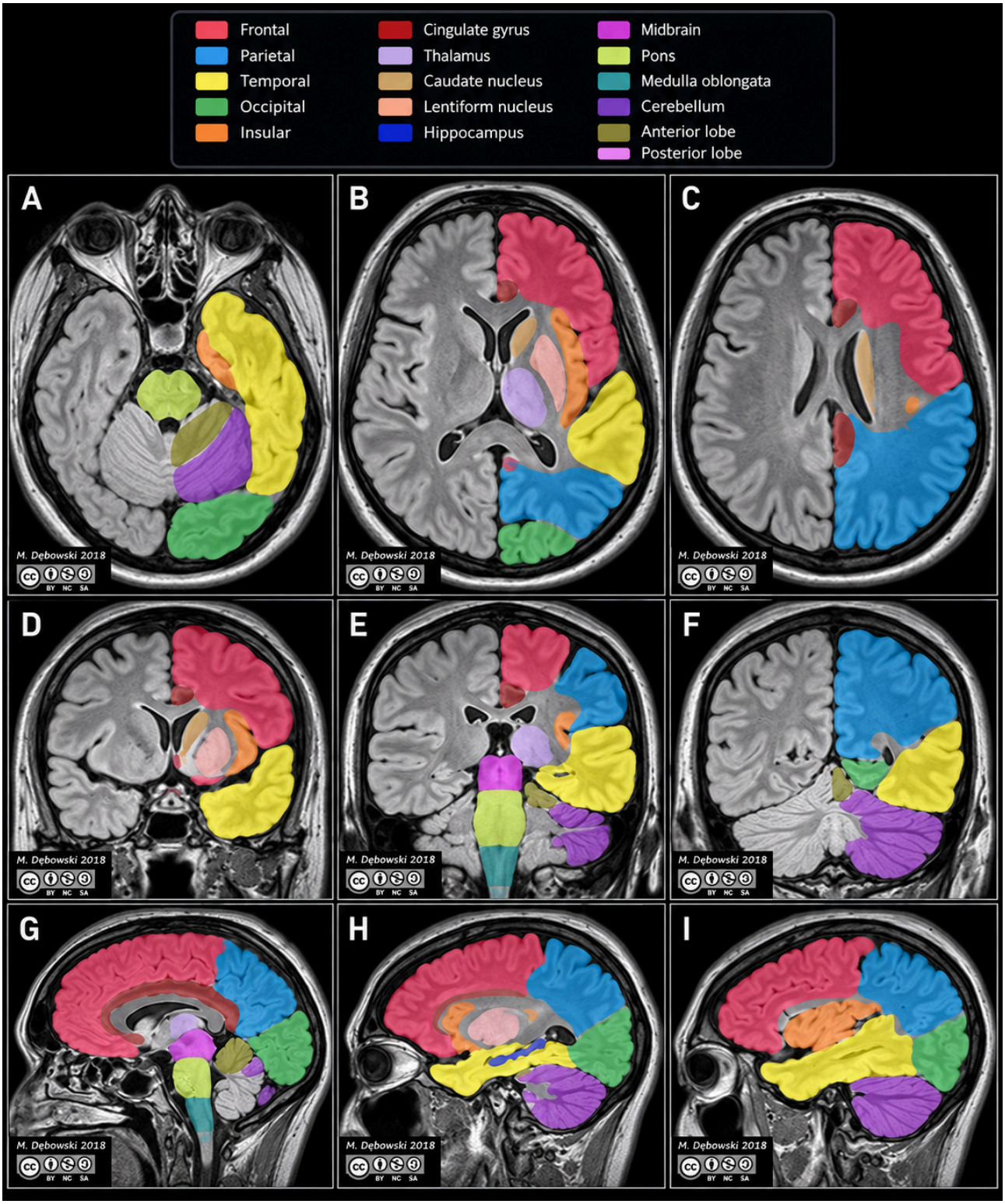


Figure 2 – Labelled T2-weighted FLAIR MRI brain images showing the cerebral lobes, subcortical structures, brainstem, and cerebellum. Panels A-C show axial sections in inferior to superior order. Panels D-F show coronal sections in anterior to posterior order. Panels G-I show sagittal sections in medial to lateral order. Case contributed by Maciej Debowski and reused under CC-NC-BY-SA licence – Full scan available at https://radiopaedia.org/cases/brain-lobes-annotated-mri-1)

Table 2 – Functions, lesion effects and neuropsychiatric symptoms in regions of the brain[7, 10]

Area	Location	Principal functions	Typical effects of a lesion
Frontal/Prefrontal	**Orbitofrontal cortex**	Inhibition, reward evaluation, social behaviour	Personality change, disinhibition, impulsivity, emotional lability, impaired social judgement (e.g. Phineas Gage)
	Dorsolateral prefrontal cortex	Working memory, planning, cognitive flexibility, problem solving	Executive dysfunction, poor planning, reduced cognitive flexibility and problem solving
	Medial prefrontal cortex / anterior cingulate	Motivation, initiation, attention, monitoring	Apathy, abulia, reduced spontaneous behaviour; severe lesions may cause akinetic mutism
	Primary motor cortex/Brocas area	Voluntary movement	Contralateral weakness or paralysis, non-fluent aphasia of in dominant hemisphere
Parietal	**Dominant parietal lobe**	Language-related processing, calculation, reading, writing, body schema	Gerstmann Syndrome (AALF) - Acalculia, agraphia, finger agnosia, left–right disorientation. Fluent/receptive aphasia. Dyspraxia. Contralateral hemisensory loss, poor proprioception and paraesthesia.
	Non-dominant parietal lobe	Spatial attention and awareness	Contralateral neglect. Anosognosia, constructional difficulties. Contralateral hemisensory loss, poor proprioception and paraesthesia.
Temporal	**Lateral temporal lobe/Auditory cortex**	Auditory processing and receptive language	Central hearing loss, receptive aphasias, semantic processing deficits. In some case auditory hallucinations, emotional and behavioural changes.
	Hippocampus/Medial temporal lobe	Learning and episodic memory	Impaired formation of new memories. Anterograde amnesia and in some cases retrograde amnesia. Reduced spatial orientation and direction.
	Amygdala / Medial temporal structures	Emotional salience, fear, threat processing	Abnormal fear processing, emotional dysregulation and social behaviour; Kluver-Bucy syndrome if bilateral (hyperorality, overeating, hyposexuality, docility, visual agnosia)
Occipital	**Occipital lobe/Visual Cortex**	Primary and higher-order visual processing	Contralateral visual field loss, visual agnosia or cortical blindness. Homonymous hemianopia. In some cases, visual hallucinations.
Insula	**Insula**	Interoception, salience, taste, autonomic and emotional processing	Altered visceral sensation, taste disturbance and autonomic responses. Disordered salience and awareness of emotional states.

Area	Location	Principal functions	Typical effects of a lesion
Subcortical	**Thalamus**	Central relay station of brain including sensory relay, arousal, attention and cortico-subcortical integration	Contralateral sensory loss: Central pain syndrome, altered arousal, cognition or behaviour. Memory and attention difficulties.
	Basal ganglia	Movement selection, habit learning, motivation and behavioural regulation	Bradykinesia, rigidity, involuntary movements, resting tremors; Apathy, impulsivity and abnormalities of motivation; Obsessive compulsive traits in some cases.
	Hypothalamus	Homeostasis, endocrine regulation, appetite, autonomic function	Increased or reduced appetite, sleep disturbances, temperature dysregulation. Diabetes insipidus, Secondary hypothyroidism, and adrenal insufficiency. Memory and concentration loss. Mood swings and aggression.
Other	**Corpus callosum**	Interhemispheric communication	Disconnection syndromes; Slowed thinking, memory and reduced ability to complete complex tasks. Ataxia and incoordination. Visual/tactile agnosias depending on side of presentation.
	Cerebellum	Coordination, balance, timing and motor learning; contributes to cognitive and affective regulation	Ataxia, dysmetria, dysarthria, nystagmus; cognitive/affective changes can occur
	Brainstem	Arousal, cranial nerve function, autonomic regulation and major ascending/descending pathways	Cranial nerve deficits, altered consciousness, motor/sensory abnormalities, autonomic dysfunction (respiration, cardiac function); severe lesions can be life-threatening

Brain Networks and Functional Imaging

As our understanding of functional neuroanatomy has developed clinicians have increasingly moved away from the idea of cognitive functions being subserved by isolated regions or areas. Rather the various functions of the brain are performed by networks of regions that are distributed widely across the brain. Some of these networks that have already been touched in this chapter include the limbic system (emotions, motivations, basic drives), the somatomotor/sensory system (voluntary movement and sensation), visual system (images, movement, colour), the language system (speech comprehension and expression), and the reticular activating system (awareness, basic physiological function). The following section will briefly outline the neuroanatomical elements and function of four other networks that are critical in neuropsychiatry and behavioural neurology: the Default Mode Network (DMN), Central Executive Network (CEN), Salience Network (SN), and the Dorsal/Ventral Attention Networks (DAN and VAN).

Default Mode Network

The DMN is primarily comprised by the **Ang**ular **gy**ri, the medial **P**refrontal **C**ortex, **P**osterior **C**ingulate cortex and **P**re**C**uneus[12] (Mnemonic: "**Ang**ry **G**u**y**s think **PC, PC, PC**"). It is particularly active during periods of relatively unconstrained, internally directed cognition, such as autobiographical memory, imagining the future, daydreaming, self-reflection and mentalising (i.e. considering the mental states of others). DMN activity tends to decrease when attention is directed towards an externally demanding task, although this distinction is not absolute. The network contributes to integrating information with personal experience and context, allowing an individual to construct a coherent sense of self and relate current experiences to memories and anticipated future events.

Dysfunction or altered connectivity within the DMN has been implicated across a range of neuropsychiatric disorders, including post-traumatic stress disorder, major depressive disorder, schizophrenia, and anxiety disorders.

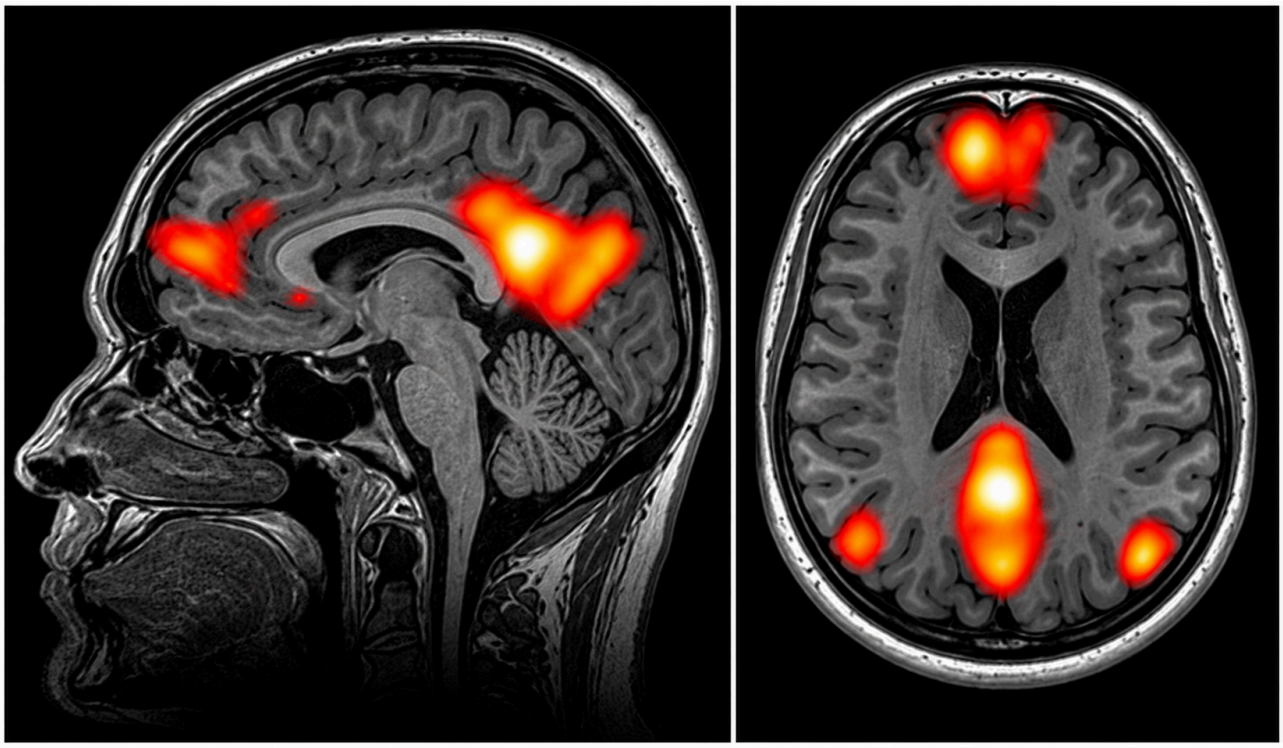


Figure 3 - Magnetic resonance imaging of areas of the brain in the default mode network including the medial pre-frontal cortex, posterior cingulate cortex, precuneus, and angular gyrus. Credit to John Graner, Neuroimaging Department, National Intrepid Center of Excellence, Walter Reed National Military Medical Center, 8901 Wisconsin Avenue, Bethesda, MD 20889, USA. Public domain, via Wikimedia Commons

Central Executive Network

The CEN is located primarily on the dorsolateral prefrontal cortex (DLPFC) and posterior parietal cortex (PPC)[13]. It is engaged when cognitive resources need to be deliberately allocated towards a particular goal or task. The CEN underlies cognitive functions of working memory, sustained attention, planning, decision-making, and problem solving. The CEN is a major system for deliberate cognitive control. It allows information to be held and manipulated in working memory, competing responses to be evaluated and behaviour to be adjusted according to goals and changing

circumstances. Dysfunction of CEN areas or their connections may manifest clinically as impaired executive functioning, reduced attentional control, poor planning and difficulties adapting behaviour to changing demands.

These areas are affected in various disorders ranging from frontotemporal dementia to depression and the DLFPC is the main target for neurostimulation (TMS, TDCS) in those with depression.

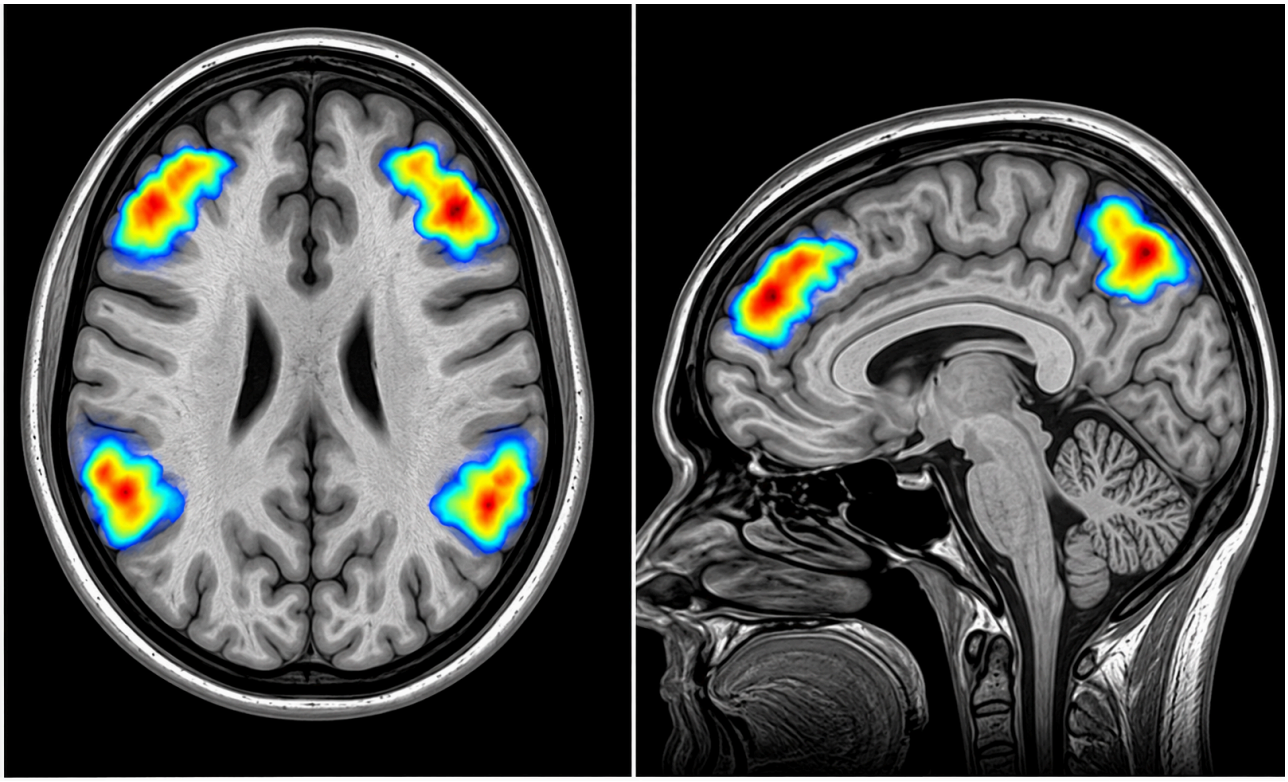


Figure 4 – Example functional magnetic resonance imaging of areas of the brain in the central executive network including the dorsolateral prefrontal cortex and the posterior parietal cortex.

Salience Network

The SN is primarily comprised of the anterior insula and dorsal anterior cingulate cortex, with important connections to the amygdala, thalamus, hypothalamus and other subcortical and brainstem structures[14]. It integrates information about both the internal state of the body and events occurring in the external environment to identify stimuli that are behaviourally or emotionally significant. The SN helps crucially determine what is important and requires a response, supporting interoception and motivation.
Research indicates that the SN is the switching network, facilitating shifts between the internally focused DMN and the externally focused, goal-directed CEN[14].

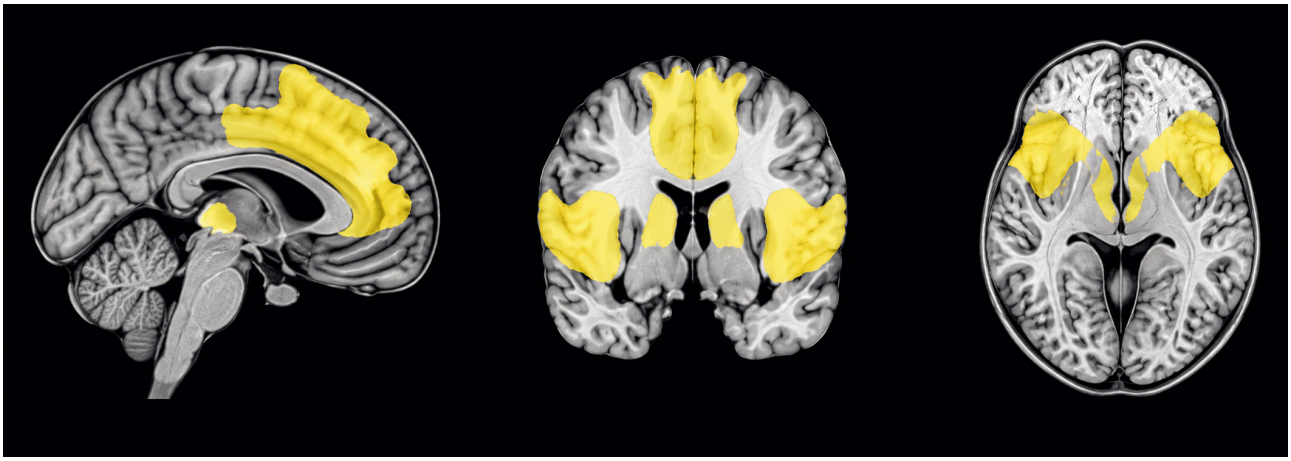


Figure 5 – Example imaging of areas of the brain in the salience network including the anterior insula and dorsal anterior cingulate cortex. Credit to Oudeisplus, CC BY-SA 3.0, via Wikimedia Commons.

Dorsal and Ventral Attention Networks

The DAN is a bilateral frontoparietal network involved in the voluntary, goal-directed allocation of attention[15]. Its primary constituents are the frontal eye fields in the dorsomedial frontal cortex and the superior parietal lobule in the parietal cortex. The DAN supports the deliberate selection of relevant information, directing attention towards specified locations, objects or sensory features and maintaining attention on task-relevant stimuli. It is particularly critical for spatial attention, visual search, orienting of eye movements and sustained goal-directed attention.

The Ventral Attention Network (VAN) is predominantly right lateralised and is involved in the detection of behaviourally relevant or unexpected stimuli and the reorienting of attention[15]. Its principal regions include the temporoparietal junction and the ventral frontal cortex, particularly the inferior frontal gyrus. Unlike the DAN, which maintains attention according to current goals, the VAN acts as a stimulus-driven interrupt system, detecting salient or unexpected events and redirecting attention towards them when appropriate. It is important for attention switching, responding to novel or salient stimuli, and reorienting attention when environmental information conflicts with current expectations or goals.

Chapter Summary

- **The Axes of the Brain:** Neuroanatomy can be understood through three complementary axes: back-front (Perception and sensory processing to action/executive control); right–left (hemispheric specialisation); and top–bottom (higher-order cognition and subcortical emotion/motivation).
- **Front–Back: Action and Perception:** The anterior brain is primarily involved in planning, decision-making, executive control and the selection of behaviour, while posterior regions process and integrate sensory information.
- **Right–Left: Hemispheric Specialisation:** The left hemisphere is typically dominant for language, praxis and sequential or analytical processing, whereas the right hemisphere has important roles in visuospatial processing, attention and gestalt. Complex behaviours depend on communication between both hemispheres.
- **Top–Bottom: Cognition and Emotion:** Higher-order cognitive cortical processes interact continuously with subcortical systems involved in emotion, motivation, reward, arousal and autonomic regulation. Some cortical and subcortical regions have reciprocal inhibitory effects on one another, indicating both top-down and bottom-up control.
- **Brain Regions and Clinical Syndromes:** Different regions make characteristic contributions to cognition, emotion, language, memory, movement, attention and behaviour, and lesions can produce recognisable neuropsychiatric syndromes.
- **Brain Networks and Functional Imaging:** Modern neuroanatomy increasingly conceptualises brain function in terms of distributed networks. The Default Mode Network supports internally directed cognition and "daydreaming", the Central Executive Network supports deliberate cognitive control and external action, and the Salience Network identifies behaviourally relevant information and facilitates switching between internally and externally directed states. The Dorsal Attention Network supports voluntary, goal-directed allocation of attention, while the predominantly right-lateralised Ventral Attention Network detects unexpected or salient stimuli and reorients attention towards them.

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